

N-[5-(2,3-dihydrobenzofuryl)sulfonyl]-N'-(3,4-dichlorophenyl)urea, N6-[4-deoxy-4-[N2-[2(E),4(E)-tetradecadienoyl]glycylamino]-L-glycero-B-L-mannoheptopyranosyl]adenine, aplidine, ecteinascidin, troxacitabine, 4-[2-amino-4-oxo-4,6,7,8-tetrahydro-3H-pyrimidino[5,4-b]-1,4-thiazin-6-yl-(S)-ethyl]-2,5-thienoyl-L-glutamic acid, aminopterin, 5-fluorouracil, alanosine, 11-acetyl-8-(carbamoyloxymethyl)-4-formyl-6-methoxy-14-oxa-1,11-diazatetracyclo(7.4.1.0.0)tetradeca-2,4,6-trien-9-ylacetic acid ester, swainsonine, lometrexol, dexrazoxane, methioninase, 2'-cyano-2'-deoxy-N4-palmitoyl-1-B-D-arabinofuranosyl cytosine and 3-aminopyridine-2-carboxaldehyde thiosemicarbazone. "Antiproliferative agents" also include monoclonal antibodies to growth factors other than those listed under "angiogenesis inhibitors", such as trastuzumab, and tumour suppressor genes, such as p53, which can be delivered via recombinant virus-mediated gene transfer (see US Patent No. 6,069,134, for example).

Test for the inhibition of IKK ϵ

IKK ϵ – Kinase Assay (IKKepsilon)

Summary

The kinase assay is performed either as 384-well Flashplate assay (for e.g. Topcount measurement).

1 nM IKK ϵ , 800 nM biotinylated I κ B α (19-42) peptide (Biotin-C6-C6-GLKKERLLDDRHDSGLDSMKDEE) SEQ ID NO.: 1 and 10 μ M ATP (spiked with 0.3 μ Ci ^{33} P-ATP/well) are incubated in a total volume of 50 μ l (10 mM MOPS, 10 mM Mg-acetat, 0.1 mM EGTA, 1 mM Dithiothreitol, 0.02 % Brij35, 0.1 % BSA, 0.1 % BioStab, pH 7.5) with or without test compound for 2 hours at 30°C. The reaction is stopped with 25 μ l 200 mM EDTA. After 30 Min at room temperature the liquid is removed and each well washed thrice with 100 μ l 0.9% sodium chloride solution. Non-specific reaction is determined in presence of 3 μ M MSC2119074 (BX-795). Radioactivity is measured with Topcount (PerkinElmer). Results (e.g. IC₅₀-values) are calculated with program tools provided by the IT-department (e.g. AssayExplorer, Symyx).

Test for the inhibition of TBK1

Enzyme Test

Summary

The kinase assay is performed as 384-well Flashplate assay (for e.g. Topcount measurement).

0.6 nM TANK binding kinase (TBK1), 800 nM biotinylated MELK-derived peptide (Biotin-Ah-Ah-AKPKGNGDYHLQTCCGSLAYRRR) SEQ ID NO.: 2 and 10 μ M ATP (spiked with 0.25 μ Ci ^{33} P-ATP/well) are incubated in a total volume of 50 μ l (10 mM MOPS, 10 mM Mg-acetat, 0.1 mM EGTA, 1 mM DTT, 0.02 % Brij35, 0.1 % BSA, pH 7.5) with or without test compound for 120 Min at 30°C. The reaction is stopped with 25 μ l 200 mM EDTA. After 30 Min at room temperature the liquid is removed and each well washed thrice with 100 μ l 0.9% sodium chloride solution. Nonspecific reaction is determined in presence of 100 nM Staurosporine. Radioactivity is measured in a Topcount (PerkinElmer). Results (e.g. IC₅₀-values) are calculated with program tools provided by the IT-department (e.g. AssayExplorer, Symyx).

Cell Test

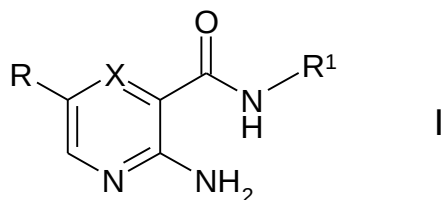
Dose Response Inhibition of Phospho-IRF3 @ Ser 386
cell/MDAMB468/INH/PHOS/IMAG/pIRF3

1. Scope

Although TBK1 and IKK ϵ are best known as key players in the innate immune response, recent findings have pointed towards a role for TBK1 and IKK ϵ in Ras-induced oncogenic transformation. TBK1 was identified as a RalB effector in the Ras-like (Ral)-guanine nucleotide exchange factor (GEF) pathway that is required for Ras-induced transformation. TBK1 directly activates IRF3 which, upon phosphorylation, homodimerizes and translocates to the nucleus where it activates

Patent Claims

1. Compounds of the formula I



in which:

X denotes CH or N,

R denotes Ar or Het,

R¹ denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, pyridyl, pyrimidyl, pyridazinyl, indolyl, isoindolyl, benzimidazolyl, indazolyl, quinolyl, 1,3-benzodioxolyl, benzothiophenyl, benzofuranyl, imidazopyridyl or furo[3,2-b]pyridyl, each of which is unsubstituted or mono- or disubstituted by Hal, A, OR⁵, CN, COOA, COOH, CON(R⁵)₂ and/or NR⁵COA',

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by Hal, A, Het¹, (CH₂)_nOR⁵, (CH₂)_nN(R⁵)₂, NO₂, CN, (CH₂)_nCOOR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NR⁵COA, NHCOOA, NR⁵SO₂A, COR⁵, SO₂Het², SO₂N(R⁵)₂ and/or S(O)_pA,

Het denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, thiadiazole, pyridazinyl, pyrazinyl, indolyl, isoindolyl, benzimidazolyl, indazolyl, quinolyl, 1,3-benzodioxolyl, benzothiophenyl, benzofuranyl or imidazopyridyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, COA, (CH₂)_pHet², OH, OA, Hal, (CH₂)_pN(R⁵)₂, NO₂, CN, (CH₂)_pCOOR⁵, (CH₂)_pCON(R⁵)₂, NR⁵COA, (CH₂)_pCOHet² and/or (CH₂)_pphenyl,

3. Compounds according to Claim 1 ~~or 2~~, in which:

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to Claim 1, in which:

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂.

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

5. ~~Compounds according to one or more of Claims 1-3~~ claim 1, in which:

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or (CH₂)_pphenyl,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to claim 2, in which:

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or (CH₂)_pphenyl.

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to claim 3, in which:

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, $(CH_2)_pHet^2$, $(CH_2)_pCON(R^5)_2$ and/or $(CH_2)_p$ phenyl,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

5-8. Compounds according to ~~one or more of Claims 1-4~~ claim 1, in which:

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to claim 2, in which:

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to claim 3, in which:

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

11. Compounds according to claim 4, in which:

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

6 12. Compounds according to ~~one or more of Claims 1-5~~ claim 1, in which:

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

13. Compounds according to claim 2, in which:

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

14. Compounds according to claim 3, in which:

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

15. Compounds according to claim 4, in which:

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

16. Compounds according to claim 5, in which:

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A, and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

17. ~~Compounds according to one or more of Claims 1-6~~ claim 1, in which:

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

18. Compounds according to claim 2, in which:

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

19. Compounds according to claim 3, in which:

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

20. Compounds according to claim 4, in which:

A denotes unbranched or branched alkyl having 1-6 C atoms, in
which one or two non-adjacent CH and/or CH₂ groups may be
replaced by N and/or O atoms and/or in addition 1-7 H atoms may
be replaced by F,
and pharmaceutically usable salts, tautomers and stereoisomers thereof,
including mixtures thereof in all ratios.

21. Compounds according to claim 5, in which:

A denotes unbranched or branched alkyl having 1-6 C atoms, in
which one or two non-adjacent CH and/or CH₂ groups may be
replaced by N and/or O atoms and/or in addition 1-7 H atoms may
be replaced by F,
and pharmaceutically usable salts, tautomers and stereoisomers thereof,
including mixtures thereof in all ratios.

22. Compounds according to claim 6, in which:

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,
and pharmaceutically usable salts, tautomers and stereoisomers thereof,
including mixtures thereof in all ratios.

§ 23. Compounds according to ~~one or more of Claims 1-7~~ claim 1, in which:

X denotes CH ~~oder N~~,

R denotes Ar or Het,

R¹ denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR⁵, COOA, COOH, CON(R⁵)₂ and/or NR⁵COA',

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂,

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or (CH₂)_pphenyl,

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

A' denotes unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be

replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

R^5 denotes H or unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2, 3 or 4,

p denotes 0, 1 or 2,

q denotes 1, 2, 3 or 4,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

24. Compounds according to claim 2, in which:

X denotes CH,

R denotes Ar or Het,

R^1 denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR^5 , COOA, COOH, $CON(R^5)_2$ and/or NR^5COA' ,

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het^1 , COR^5 , $CON(R^5)_2$, $CONH(CH_2)_qNHCOOA'$, $CON[R^5(CH_2)_nHet^1]$, $NHCOOA$, $(CH_2)_nN(R^5)_2$, $(CH_2)_nOR^5$, $(CH_2)_nCOOR^5$, SO_2Het^2 and/or $SO_2N(R^5)_2$,

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, $(CH_2)_pHet^2$, $(CH_2)_pCON(R^5)_2$ and/or $(CH_2)_pphenyl$,

Het^1 denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

Het^2 denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

A' denotes unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

R⁵ denotes H or unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2, 3 or 4,

p denotes 0, 1 or 2,

q denotes 1, 2, 3 or 4,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

25. Compounds according to claim 3, in which:

X denotes CH,

R denotes Ar or Het,

R¹ denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR⁵, COOA, COOH, CON(R⁵)₂ and/or NR⁵COA',

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂,

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or (CH₂)_pphenyl,

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

A' denotes unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

R⁵ denotes H or unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2, 3 or 4,

p denotes 0, 1 or 2,

q denotes 1, 2, 3 or 4,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

26. Compounds according to claim 4, in which:

X denotes CH,

R denotes Ar or Het,

R¹ denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR⁵, COOA, COOH, CON(R⁵)₂ and/or NR⁵COA',

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂,

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, $(\text{CH}_2)_p\text{Het}^2$, $(\text{CH}_2)_p\text{CON}(\text{R}^5)_2$ and/or $(\text{CH}_2)_p\text{phenyl}$.

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,

A' denotes unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH_2 groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

R⁵ denotes H or unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2, 3 or 4,

p denotes 0, 1 or 2,

q denotes 1, 2, 3 or 4,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

27. Compounds according to claim 5, in which:

X denotes CH_2 ,

R denotes Ar or Het,

R¹ denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR^5 , COOA , COOH , $\text{CON}(\text{R}^5)_2$ and/or NR^5COA ,

Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR^5 , $\text{CON}(\text{R}^5)_2$,

CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA,
(CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or
SO₂N(R⁵)₂.

Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or
 mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or
 (CH₂)_pphenyl.

Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or
 monosubstituted by A.

Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl,
 piperazinyl, each of which is unsubstituted or monosubstituted by
 OH and/or A.

A' denotes unbranched or branched alkyl having 1-6 C atoms, in
 which 1-7 H atoms may be replaced by F.

A denotes unbranched or branched alkyl having 1-6 C atoms, in
 which one or two non-adjacent CH and/or CH₂ groups may be
 replaced by N and/or O atoms and/or in addition 1-7 H atoms may
 be replaced by F.

R⁵ denotes H or unbranched or branched alkyl having 1-6 C atoms, in
 which 1-7 H atoms may be replaced by F.

Hal denotes F, Cl, Br or I.

n denotes 0, 1, 2, 3 or 4.

p denotes 0, 1 or 2.

q denotes 1, 2, 3 or 4.

and pharmaceutically usable salts, tautomers and stereoisomers thereof,
including mixtures thereof in all ratios.

28. Compounds according to claim 6, in which:

X denotes CH.

R denotes Ar or Het.

<u>R¹</u>	<u>denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR⁵, COOA, COOH, CON(R⁵)₂ and/or NR⁵COA',</u>
<u>Ar</u>	<u>denotes phenyl, biphenyl or naphtyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂.</u>
<u>Het</u>	<u>denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or (CH₂)_pphenyl,</u>
<u>Het¹</u>	<u>denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,</u>
<u>Het²</u>	<u>denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,</u>
<u>A'</u>	<u>denotes unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,</u>
<u>A</u>	<u>denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,</u>
<u>R⁵</u>	<u>denotes H or unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,</u>
<u>Hal</u>	<u>denotes F, Cl, Br or I,</u>
<u>n</u>	<u>denotes 0, 1, 2, 3 or 4,</u>
<u>p</u>	<u>denotes 0, 1 or 2,</u>
<u>q</u>	<u>denotes 1, 2, 3 or 4,</u>
	<u>and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.</u>

29. Compounds according to claim 7, in which:X denotes CH,R denotes Ar or Het,R¹ denotes pyridyl, pyrimidyl, pyridazinyl or furo[3,2-b]pyridyl, each of which is unsubstituted or monosubstituted by Hal, A, OR⁵, COOA, COOH, CON(R⁵)₂ and/or NR⁵COA',Ar denotes phenyl, biphenyl or naphthyl, each of which is unsubstituted or mono-, di- or trisubstituted by A, Hal, Het¹, COR⁵, CON(R⁵)₂, CONH(CH₂)_qNHCOOA', CON[R⁵(CH₂)_nHet¹], NHCOOA, (CH₂)_nN(R⁵)₂, (CH₂)_nOR⁵, (CH₂)_nCOOR⁵, SO₂Het² and/or SO₂N(R⁵)₂,Het denotes thienyl, pyrazolyl, pyridyl, each of which is unsubstituted or mono- or disubstituted by A, (CH₂)_pHet², (CH₂)_pCON(R⁵)₂ and/or (CH₂)_pphenyl,Het¹ denotes pyrazolyl or imidazolyl, each of which is unsubstituted or monosubstituted by A,Het² denotes pyrrolidinyl, piperidinyl, morpholinyl, [1,3]dioxolanyl, piperazinyl, each of which is unsubstituted or monosubstituted by OH and/or A,A' denotes unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,A denotes unbranched or branched alkyl having 1-6 C atoms, in which one or two non-adjacent CH and/or CH₂ groups may be

replaced by N and/or O atoms and/or in addition 1-7 H atoms may be replaced by F,

R⁵ denotes H or unbranched or branched alkyl having 1-6 C atoms, in which 1-7 H atoms may be replaced by F,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2, 3 or 4,

p denotes 0, 1 or 2,

q denotes 1, 2, 3 or 4,

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

9 30. Compounds according to Claim 1, selected from the group consisting of:

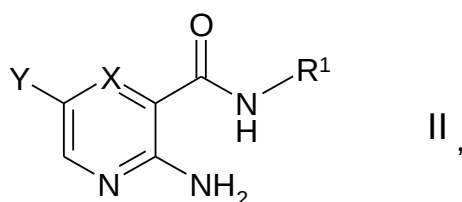
compound nr.	name
"A1"	2-Amino-5-(5-piperidin-1-ylmethyl-thiophen-2-yl)-N-pyridin-4-yl-nicotinamide
"A2"	2-Amino-N-pyridin-4-yl-5-(5-pyrrolidin-1-ylmethyl-thiophen-2-yl)-nicotinamide
"A3"	2-Amino-5-(5-methyl-thiophen-2-yl)-N-pyridin-4-yl-nicotinamide
"A4"	2-Amino-5-(3-pyrazol-1-yl-phenyl)-N-pyridin-4-yl-nicotinamide
"A5"	2-Amino-5-(4-pyrazol-1-yl-phenyl)-N-pyridin-4-yl-nicotinamide
"A6"	2-Amino-5-[1-(2-methoxy-ethyl)-1H-pyrazol-4-yl]-N-pyridin-4-yl-nicotinamide
"A7"	2-Amino-N-pyridin-4-yl-5-(4-sulfamoyl-phenyl)-nicotinamide
"A8"	2-Amino-N-(2-methyl-pyridin-4-yl)-5-(5-morpholin-4-ylmethyl-thiophen-2-yl)-nicotinamide
"A9"	2-Amino-N-(2-ethoxy-pyridin-4-yl)-5-(5-morpholin-4-ylmethyl-thiophen-2-yl)-nicotinamide
"A10"	3-Amino-6-(5-morpholin-4-ylmethyl-thiophen-2-yl)-pyrazine-2-carboxylic acid pyridin-4-ylamide

"A45"	2-Amino-5-furan-3-yl-N-pyridin-4-yl-nicotinamide
"A46"	2-Amino-5-(1-benzyl-1H-pyrazol-4-yl)-N-pyridin-4-yl-nicotinamide
"A47"	2-Amino-5-(1-methyl-1H-pyrazol-3-yl)-N-pyridin-4-yl-nicotinamide
"A48"	2-Amino-5-(3,5-dimethyl-1H-pyrazol-4-yl)-N-pyridin-4-yl-nicotinamide
"A49"	2-Amino-N-pyridin-4-yl-5-thiophen-3-yl-nicotinamide
"A50"	2-Amino-5-(1-methyl-1H-pyrrol-2-yl)-N-pyridin-4-yl-nicotinamide
"A51"	2-Amino-5-[1-(2-morpholin-4-yl-ethyl)-1H-pyrazol-4-yl]-N-pyridin-4-yl-nicotinamide
"A52"	2-Amino-5-benzo[b]thiophen-2-yl-N-pyridin-4-yl-nicotinamide
"A53"	5-(5-Acetyl-thiophen-2-yl)-2-amino-N-pyridin-4-yl-nicotinamide
"A54"	2-Amino-5-(5-morpholin-4-ylmethyl-thiophen-2-yl)-N-pyridin-4-yl-nicotinamide
"A55"	2-Amino-5-(1H-indol-2-yl)-N-pyridin-4-yl-nicotinamide
"A56"	2-Amino-5-(1H-indol-3-yl)-N-pyridin-4-yl-nicotinamide
"A57"	2-Amino-N-pyridin-4-yl-5-(1H-pyrrol-2-yl)-nicotinamide
"A58"	2-Amino-5-(1H-imidazo[1,2-a]pyridin-2-yl)-N-pyridin-4-yl-nicotinamide
"A59"	2-Amino-N-pyridin-4-yl-5-(1H-pyrrol-3-yl)-nicotinamide
"A60"	2-Amino-5-benzofuran-3-yl-N-pyridin-4-yl-nicotinamide
"A61"	2-Amino-5-(1-methyl-1H-pyrazol-4-yl)-N-pyridin-4-yl-nicotinamide

and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

10 31. Process for the preparation of compounds of the formula I according to Claims 1-9 and pharmaceutically usable salts, tautomers and stereoisomers thereof, characterised in that

a) a compound of the formula II



in which Y denotes an Br or I,

X and R¹ have the meanings indicated in Claim 1,

is reacted with a compound of formula III

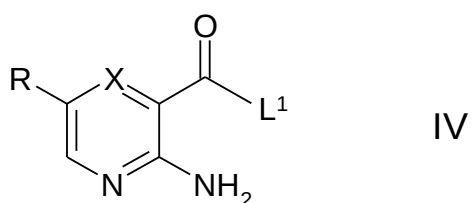


in which R has the meaning indicated in Claim1 and

L denotes a boronic acid or a boronic acid ester group,

or

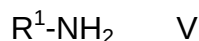
b) a compound of the formula IV



in which R and X have the meanings indicated in Claim 1 and

L^1 denotes Cl, Br, I or a free or reactively functionally modified OH group,

is reacted with a compound of the formula V



in which R^1 has the meaning indicated in Claim 1,

or

c) that it is liberated from one of its functional derivatives by treatment with a solvolysing or hydrolysing agent,

and/or

a base or acid of the formula I is converted into one of its salts.

~~11 32.~~ Medicaments comprising ~~i) at least one~~ compound of the formula I according to Claim 1-9 and/or ~~ii) pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.~~

~~12 33.~~ ~~Compounds~~ A method of treating diseases selected from the group consisting of: according to Claim 1-9 and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, for the use for the treatment of cancer, septic shock, Primary open Angle Glaucoma (POAG), hyperplasia, rheumatoid arthritis, psoriasis, arteriosclerosis, retinopathy, osteoarthritis, endometriosis, chronic inflammation, and/or neurodegenerative diseases comprising administering compounds of the formula I, according to claim 1, to a patient presenting at least one symptom of said diseases.

34. A method for the treatment of tumours comprising administering to a patient having a tumour the compounds of formula I according to claim 1 in combination with a compound from the group consisting of: oestrogen receptor modulator, androgen receptor modulator, retinoid receptor modulator, cytotoxic agent, antiproliferative agent, prenyl-protein transferase inhibitor, HMG-CoA reductase inhibitor, HIV protease inhibitor, reverse transcriptase inhibitor and angiogenesis inhibitors.

~~13~~ 35. Compounds A method for the treatment of tumours comprising administering to a patient having a tumour the compounds of the formula I according to Claim 1-9 and/or physiologically acceptable salts, tautomers and stereoisomers thereof for the use for the treatment of tumours, where a therapeutically effective amount of a compound of the formula I is administered in combination with a compound from the group consisting of: 1)

oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitor, 7) HMG-CoA reductase inhibitor, 8) HIV protease inhibitor, 9) reverse transcriptase inhibitor and 10) further angiogenesis inhibitors.

14 36. ~~Compounds~~ A method for the treatment of tumours comprising administering to the patient having a tumour the compounds of the formula I according to Claim 1-9 and/or physiologically acceptable salts, tautomers and stereoisomers thereof for the use for the treatment of tumours, where a therapeutically effective amount of a compound of the formula I is administered in combination with radiotherapy and a compound from the group consisting of: 1) oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitor, 7) HMG-CoA reductase inhibitor, 8) HIV protease inhibitor, 9) reverse transcriptase inhibitor and 10) further angiogenesis inhibitors.