

carboxamide (Example Compound 12)

(13) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 13)

(14) (R,E)-4-amino-N-(benzo[d]oxazol-2-yl)-1-(1-(but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 14)

(15) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 15)

[0085]

(16) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(ethyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 16)

(17) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(diethylamino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 17)

(18) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 18)

(19) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-

(34) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-diethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 34)

(35) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 35)

(36) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 36)

(37) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 37)

(38) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-methoxybenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 38)

(39) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-cyanobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 39)

(40) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-(2-methoxyethyl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 40)

47)

(48) (R)-7-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 48)

(49) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 49)

(50) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 50)

(51) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 51)

(52) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 52)

(53) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 53)

(54) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-

(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 54)

(55) (R)-7-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 55)

(56) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 56)

(57) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 57)

(58) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 58)

(59) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 59)

(60) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound

60)

[0088]

(61) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 61)

(64) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(7-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 64)

(65) (S)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 65)

(66) 1-((1-Acryloylpyrrolidin-3-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 66)

(67) 1-((1-Acryloylpiperidin-3-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 67)

(68) 1-((1-Acryloylpiperidin-4-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 68)

(69) 1-(1-Acryloylpiperidin-4-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 69)

(70) 1-((1-Acryloylazetidin-3-yl)methyl)-4-amino-N-

to 5 mg of (R)-tert-butyl-3-(4-amino-3-((5-chlorobenzo[d]oxazol-2-yl)carbamoyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carboxylate obtained in Step 1 of Example 1, and the mixture was stirred for 10 minutes. Thereafter, the solvent was removed using an evaporator, and the system was azeotropically distilled with toluene. The residue was dissolved in 1 ml of DMF, and 8.5 μ l of diisopropylethylamine, 2.4 mg of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride, and 5.5 mg of HATU were added thereto. The mixture was stirred for 1 hour at room temperature, and then the solution was concentrated under reduced pressure. The residue was purified by reverse phase preparative HPLC purification (water/acetonitrile (0.1% formic acid)), and thus 3.96 mg of the title compound was obtained as a white solid.

[0191]

Example 16 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(ethyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 16)

The title compound was obtained as a white solid according to the procedure described in Example 15, using (E)-4-(ethyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0192]

Example 17 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(diethylamino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 17)

The title compound was obtained as a white solid according to the procedure described in Example 15, using (E)-4-(diethylamino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0193]

Example 18 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 18)

The title compound was obtained as a white solid according to the procedure described in Example 15, using (E)-4-(isopropyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0194]

Example 19 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 19)

Example 3 (Step 2).

[0197]

Example 22 Synthesis of (R)-4-amino-N-(benzo[d]oxazol-2-yl)-1-(1-(but-2-ynoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 22)

The title compound was obtained as a pale yellow solid according to the procedure described in Example 15, using (R)-tert-butyl-3-(4-amino-3-((benzo[d]oxazol-2-yl)carbamoyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carboxylate obtained in Example 13 (Step 1), and but-2-ynoic acid instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0198]

Example 23 Synthesis of (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5,6-dimethylbenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 23)

(Step 1) Synthesis of (R)-1-(1-acyloxypiperidin-3-yl)-4-amino-1H-pyrazolo[3,4-d]pyrimidine-3-carboxylic acid

To 1 g of (R)-4-amino-1-(1-(tert-butyloxycarbonyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxylic acid of Synthetic Example 3, 15 ml of 4 N hydrochloric acid/1,4-dioxane was added, and the mixture was stirred for 1 hour at room temperature.

with toluene. The residue was dissolved in 1 ml of DMF, and 13 μ l of diisopropylethylamine, 3.7 mg of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride, and 8.4 mg of HATU were added thereto. After the mixture was stirred for 1 hour at room temperature, the solution was concentrated under reduced pressure. The residue was purified by reverse phase preparative HPLC purification (water/acetonitrile (0.1% formic acid)), and thus 4.2 mg of the title compound was obtained as a white solid.

[0211]

Example 33 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 33)

The title compound was obtained as a white solid according to the procedure described in Example 32, using (E)-4-(ethyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0212]

Example 34 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 34)

The title compound was obtained as a white solid

according to the procedure described in Example 32, using (E)-4-(diethylamino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0213]

Example 35 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 35)

The title compound was obtained as a white solid according to the procedure described in Example 32, using (E)-4-(isopropyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0214]

Example 36 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide (Example Compound 36)

The title compound was obtained as a white solid according to the procedure described in Example 32, using (E)-4-(pyrrolidin-1-yl)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0215]

the title compound was obtained as a white solid.

[0242]

Example 49 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 49)

To 13 mg of (R)-tert-butyl 3-(4-amino-5-((5-chlorobenzo[d]oxazol-2-yl)carbamoyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)pyrrolidine-1-carboxylate obtained in Step 3 of Example 48, 1 ml of 4 N hydrochloric acid/1,4-dioxane was added, and the mixture was stirred for 1 hour. Thereafter, the solvent was removed, and the residue was azeotropically distilled with 1 ml of toluene. The residue was dissolved in 1 ml of DMF, and 14.4 µl of diisopropylethylamine, 4.1 mg of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride and 9.6 mg of HATU were added thereto. The mixture was stirred for 1 hour at room temperature, and then the solution was concentrated under reduced pressure. The residue was purified by reverse phase preparative HPLC purification (water/acetonitrile (0.1% formic acid)), and thus 6.66 mg of the title compound was obtained.

[0243]

Example 50 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(ethyl(methyl)amino)but-

2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 50)

The title compound was obtained as a white solid according to the procedure described in Example 49, using (E)-4-(ethyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0244]

Example 51 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 51)

The title compound was obtained as a white solid according to the procedure described in Example 49, using (E)-4-(diethylamino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0245]

Example 52 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 52)

The title compound was obtained as a white solid according to the procedure described in Example 49, using (E)-4-(isopropyl(methyl)amino)but-2-enoic acid

hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0246]

Example 53 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 53)

The title compound was obtained as a white solid according to the procedure described in Example 49, using (E)-4-(pyrrolidin-1-yl)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0247]

Example 54 Synthesis of (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 54)

The title compound was obtained as a white solid according to the procedure described in Example 49, using (E)-4-(piperidin-1-yl)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0248]

Example 55 Synthesis of (R)-7-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7H-

pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 55)

(Step 1) Synthesis of (R)-tert-butyl 3-(4-amino-5-((5-phenylbenzo[d]oxazol-2-yl)carbamoyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)pyrrolidine-1-carboxylate

The title compound was obtained as a brown solid according to the procedure described in Step 3 of Example 48, using 5-phenylbenzo[d]oxazol-2-amine instead of 5-chlorobenzo[d]oxazol-2-amine. Physical property value: m/z [M+H]⁺ 540.3
[0249]

(Step 2) Synthesis of Example Compound 55

The title compound was obtained as a white solid according to the procedure described in Step 4 of Example 48, using (R)-tert-butyl 3-(4-amino-5-((5-phenylbenzo[d]oxazol-2-yl)carbamoyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)pyrrolidine-1-carboxylate obtained in the above Step 1.
[0250]

Example 56 Synthesis of (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 56)

To 13 mg of (R)-tert-butyl 3-(4-amino-5-((5-phenylbenzo[d]oxazol-2-yl)carbamoyl)-7H-pyrrolo[2,3-

d]pyrimidin-7-yl)pyrrolidine-1-carboxylate obtained in Step 1 of Example 55, 1 ml of 4 N hydrochloric acid/1,4-dioxane was added, and the mixture was stirred for 1 hour.

Thereafter, the solvent was removed, and the residue was azeotropically distilled with 1 ml of toluene. The residue was dissolved in 1 ml of DMF, and 14.4 µl of diisopropylethylamine, 4.1 mg of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride, and 9.6 mg of HATU were added thereto. After the mixture was stirred for 1 hour at room temperature, the solution was concentrated under reduced pressure. The residue was purified by reverse phase preparative HPLC purification (water/acetonitrile (0.1% formic acid)), and thus 6.66 mg of the title compound was obtained.

[0251]

Example 57 Synthesis of (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 57)

The title compound was obtained as a white solid according to the procedure described in Example 56, using (E)-4-(ethyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0252]

Example 58 Synthesis of (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 58)

The title compound was obtained as a white solid according to the procedure described in Example 56, using (E)-4-(diethylamino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0253]

Example 59 Synthesis of (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 59)

The title compound was obtained as a white solid according to the procedure described in Example 56, using (E)-4-(isopropyl(methyl)amino)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0254]

Example 60 Synthesis of (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 60)

The title compound was obtained as a white solid

according to the procedure described in Example 56, using (E)-4-(pyrrolidin-1-yl)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0255]

Example 61 Synthesis of (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide (Example Compound 61)

The title compound was obtained as a white solid according to the procedure described in Example 56, using (E)-4-(piperidin-1-yl)but-2-enoic acid hydrochloride instead of (E)-4-(dimethylamino)but-2-enoic acid hydrochloride.

[0256]

Example 62 Synthesis of (R,E)-7-(3-((2-(4-(4-(3-(4-amino-3-(benzo[d]oxazol-2-yl)carbamoyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-oxobut-2-en-1-yl)piperazin-1-yl)ethyl)amino)-3-oxopropyl) 5,5-difluoro-1,3-dimethyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-4-ium-5-uide (Example Compound P-1)

(Step 1) Synthesis of (E)-4-(4-(2((tert-butoxycarbonyl)amino)ethyl)piperazin-1-yl)but-2-enoic acid

2 g of tert-butyl-(2-(piperazin)-1-yl)ethyl)carbamate was dissolved in 20 ml of DMSO, and 1.35 ml of

obtained in Step 2, 5 mL of chloroform and 1.7 mL of trifluoroacetic acid were added. After the mixture was stirred for 1 hour, the solvent was removed using an evaporator. 12 mL of chloroform and 810 μ L of triethylamine were added to the residue, and after the mixture was ice-cooled, 89 μ L of acryloyl chloride was added thereto. After the mixture was stirred for 30 minutes, the reaction was terminated with a saturated aqueous solution of sodium bicarbonate, and extracted with chloroform. The organic layer was dried over sodium sulfate, and then a residue obtained after removal of the solvent was purified using silica gel column (eluant: ethyl acetate:methanol). Thus, 350 mg of the title compound was obtained as a white solid.

[0266]

(Step 4) Synthesis of (S)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

20 mg of (S)-1-(3-(4-amino-3-iodo-1H-pyrazolo[3,4-d]pyrimidin-1-yl) pyrrolidin-1-yl)prop-2-en-1-one obtained in Step 3 was dissolved in 5.20 mL of DMF, and 13 mg of benzo[d]oxazol-2-amine, 3.65 mg of $\text{PdCl}_2(\text{PPh}_3)_2$ and 23 μ L of DBU were added thereto. The mixture was stirred for 2 hours at 120 degrees in a carbon monoxide atmosphere, and then the solvent was removed using an evaporator. DMSO was

invention have an excellent effect that the level of side effects is low despite that the amount of exposure is far larger than that of the Reference compound 1.

[0386]

As described above, it was made clear that the compounds of the present invention are compounds having superior profiles with reduced toxicity compared with the Reference compound 1.

[0387]

Test Example 6 Detection by BTK labeling using fluorescent labeling compound (in vitro)

The human B-cell lymphoma-derived cell line, Ramos cells were suspended in RPMI1640 medium containing 10% bovine serum, and then the cells were inoculated in a culture plate at a concentration of 2.0×10^6 (cells/well). The cells were cultured in a CO₂ incubator (Sanyo Electric Biomedical Co., Ltd.) at 37°C for 24 hours. Example Compound P-1 and fluorescent labeled compounds which is a derivative of Reference compound 1 (PCI-33380, Non-Patent Document 2) (10 mM stock) were respectively diluted with DMSO. Each of the dilutions was added to the plate inoculated cells, and the cells were cultured in a CO₂ incubator for 1 hour. Thereafter, the cells were harvested, and 50 µl of (a cell extract (NP-40; Invitrogen, Inc.) containing 1× protease inhibitor (Hoffmann-La Roche AG) and

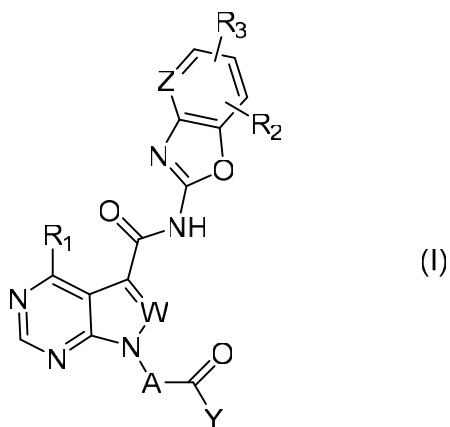
1× phosphatase cocktail (Sigma-Aldrich Co.)) was added to the cell pellets. The cell pellets were left to stand for 10 minutes on ice. The amount of protein in the collected cell extract was quantitatively analyzed by a DC protein assay (Bio-Rad Laboratories, Inc.), and 20 µg of proteins per lane was applied to a SDS-concentration gradient gel (4% to 20%) (Wako Pure Chemical Industries, Ltd.). After electrophoresis was performed, images of electrophoretic gels were taken using a Molecular Dynamics Typhoon Scanner (GE Healthcare, Inc.). Thereafter, Western blotting was performed using an i-Blot (Invitrogen, Inc.), and BTK protein was detected with a LAS4000 (GE Healthcare, Inc.) using a BTK antibody (Abcam) (Fig. 1).

[0388]

As shown in Fig. 1, it was made clear that the probe according to the present invention is a useful tool for detecting BTK in an in vitro test.

CLAIMS

1. A compound represented by the following general formula (I), or a salt thereof:



wherein A represents $-(CH_2)_n-X-$, $-(CH_2)_m-NH-$, or $-(C3-C7 \text{ cycloalkylene})-NH-$;

n represents an integer from 0 to 2;

m represents an integer from 1 to 4;

X represents a nitrogen-containing C3-C10 heterocycloalkylene which may have one or more substituents;

Y represents $-C(R_4)=C(R_5)(R_6)$ or $-C\equiv C-R_7$;

W and Z each independently represent N or CH;

R₁ represents an amino group which may have one or more substituents;

R₂ and R₃, which may be identical or different, each represent a hydrogen atom, a halogen atom, a C1-C6 alkyl group which may have one or more substituents, a C1-C6 alkoxy group which may have one or more substituents, a C3-C7 cycloalkyl group which may have one or more substituents, a C6-C14 aromatic hydrocarbon group which may have one or more substituents, a 4-membered to 10-membered monocyclic or polycyclic unsaturated heterocyclic group containing 1 to 3 heteroatoms of the same kind or different kinds selected from a nitrogen atom, an oxygen atom and a sulfur atom, which may have one or more substituents, or a cyano group; and

R₄, R₅, R₆ and R₇, which may be identical or different, each represent a hydrogen atom, or a C1-C6 alkyl group which may have

one or more substituents.

2. The compound according to claim 1, or a salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

X represents a nitrogen-containing C3-C10 heterocycloalkylene; and

R₁ represents an amino group.

3. The compound according to claim 1 or 2, or a salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

X represents azetidinylene, pyrrolidinylene, or piperidinylene; and

R₁ represents an amino group.

4. The compound according to any one of claims 1 to 3, or a salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

X represents azetidinylene, pyrrolidinylene, or piperidinylene;

Y represents $-C(R_4)=C(R_5)(R_6)$ or $-C\equiv C-R_7$;

R₁ represents an amino group;

any one of R₂ and R₃ represents a hydrogen atom or a C1-C6 alkyl group, while the other represents a hydrogen atom, a halogen atom, a C1-C6 alkyl group, a halogeno-C1-C6 alkyl group, a C1-C4 alkoxy-substituted C1-C6 alkyl group, a C1-C6 alkoxy group, a phenyl group which may have one or more substituents with a halogen atom, a 4-membered to 6-membered monocyclic unsaturated heterocyclic group containing one sulfur atom, or a cyano group;

when Y represents $-C(R_4)=C(R_5)(R_6)$,

R₄, R₅ and R₆, which may be identical or different, each

represent a hydrogen atom, a C1-C6 alkyl group, a C1-C6 alkyl group that is substituted with an amino group substituted with two C1-C6 alkyl groups (the C1-C6 alkyl groups may form a 4-membered to 8-membered heterocycloalkyl group together with the nitrogen atom to which these alkyl groups are bonded); and

when Y represents $-C\equiv C-R_7$,

R_7 represents a hydrogen atom or a C1-C6 alkyl group.

5. The compound according to any one of claims 1 to 4, or a salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

X represents 1,3-azetidinylene, 1,3-pyrrolidinylene, or 1,3-piperidinylene;

Y represents $-C(R_4)=C(R_5)(R_6)$ or $-C\equiv C-R_7$;

when Z represents N, W represents N, while when Z represents CH, W represents N or CH;

R_1 represents an amino group;

any one of R_2 and R_3 represents a hydrogen atom or a C1-C4 alkyl group, while the other represents a hydrogen atom, a halogen atom, a C1-C4 alkyl group, a halogeno-C1-C4 alkyl group, a C1-C4 alkoxy-substituted C1-C4 alkyl group, a C1-C4 alkoxy group, a phenyl group which may have one or more substituents with a halogen atom, a 4-membered to 6-membered monocyclic unsaturated heterocyclic group containing one sulfur atom, or a cyano group;

when Y represents $-C(R_4)=C(R_5)(R_6)$,

R_4 , R_5 and R_6 , which may be identical or different, each represent a hydrogen atom, a C1-C6 alkyl group, a C1-C6 alkyl group that is substituted with an amino group substituted with two C1-C6 alkyl groups (the C1-C6 alkyl groups may form a 4-membered to 8-membered heterocycloalkyl group together with the nitrogen atom to which these alkyl groups are bonded); and

when Y represents $-C\equiv C-R_7$,

R_7 represents a hydrogen atom or a C1-C4 alkyl group.

6. The compound according to any one of claims 1 to 5, or a salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

X represents 1,3-azetidinylene, 1,3-pyrrolidinylene, or 1,3-piperidinylene;

Y represents $-C(R_4)=C(R_5)(R_6)$ or $-C\equiv C-R_7$;

when Z represents N, W represents N, while when Z represents CH, W represents N or CH;

R₁ represents an amino group;

any one of R₂ and R₃ represents a hydrogen atom or a methyl group, while the other represents a hydrogen atom, a halogen atom, a methyl group, a trifluoromethyl group, a methoxyethyl group, a methoxy group, a phenyl group, a 4-chlorophenyl group, a 2-thienyl group, or a cyano group;

when Y represents $-C(R_4)=C(R_5)(R_6)$,

R₄, R₅ and R₆, which may be identical or different, each represent a hydrogen atom, a methyl group, a dimethylaminomethyl group, a methylethylaminomethyl group, a diethylaminomethyl group, a methylisopropylaminomethyl group, a 1-piperidinylmethyl group, or a 1-pyrrolidinylmethyl group; and

when Y represents $-C\equiv C-R_7$,

R₇ represents a methyl group.

7. The compound according to any one of claims 1 to 6, or a salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

R₁ represents an amino group;

any one of R₂ and R₃ represents a hydrogen atom or a methyl group, while the other represents a hydrogen atom, a halogen atom, a trifluoromethyl group, a methoxyethyl group, a phenyl group, a 2-thienyl group, or a cyano group;

(1) when Z represents N, and W represents N,

X represents 1,3-piperidinylene,

and Y represents a vinyl group;

(2) when Z represents CH, and W represents N,
X represents 1,3-pyrrolidinylene or 1,3-piperidinylene,
and Y represents $-C(R_4)=C(R_5)(R_6)$ or $-C\equiv C-(R_7)$, and
when Y represents $-C(R_4)=C(R_5)(R_6)$,

R_4 , R_5 and R_6 , which may be identical or different, each
represent a hydrogen atom, a methyl group, a dimethylaminomethyl
group, a methylethylaminomethyl group, a diethylaminomethyl group,
a methylisopropylaminomethyl group, a 1-piperidinylmethyl group,
or a 1-pyrrolidinylmethyl group;

when Y represents $-C\equiv C-(R_7)$,

R_7 represents a methyl group; and

(3) when Z represents CH, and W represents CH,
X represents 1,3-azetidinylene or 1,3-pyrrolidinylene,
and Y represents $-C(R_4)=C(R_5)(R_6)$, and

R_4 , R_5 and R_6 , which may be identical or different, each
represent a hydrogen atom, a dimethylaminomethyl group, a
methylethylaminomethyl group, a diethylaminomethyl group, a
methylisopropylaminomethyl group, a 1-piperidinylmethyl group, or
a 1-pyrrolidinylmethyl group.

8. The compound according to any one of claims 1 to 7, or a
salt thereof, wherein in general formula (I),

A represents $-(CH_2)_n-X-$;

n represents 0;

X represents 1,3-piperidinylene;

Y represents a vinyl group;

Z represents CH;

W represents N;

R_1 represents an amino group; and

any one of R_2 and R_3 represents a hydrogen atom, while the
other represents a hydrogen atom, a halogen atom, or a cyano group.

9. A compound described in any one of the following (1) to (86),
or a salt thereof:

- (1) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (2) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-bromobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (3) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-(thiophen-2-yl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (4) (R)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-methacryloylpiperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (5) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (6) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-cyanobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (7) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-methoxybenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (8) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-(2-methoxyethyl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (9) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(oxazolo[4,5-b]pyridin-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (10) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(4-methylbenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (11) (R)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1-(1-methacryloylpiperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (12) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (13) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

- (14) (R,E)-4-amino-N-(benzo[d]oxazol-2-yl)-1-(1-(but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (15) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (16) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(ethyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (17) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(diethylamino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (18) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (19) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (20) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(piperidin-1-yl)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (21) (R,E)-4-amino-N-(5-(thiophen-2-yl)benzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (22) (R)-4-amino-N-(benzo[d]oxazol-2-yl)-1-(1-(but-2-ynoyl)piperidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (23) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(5,6-dimethylbenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (24) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (25) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,
- (26) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(3-

methylbut-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(27) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(28) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-(thiophen-2-yl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(29) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-methylbenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(30) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(31) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-(4-chlorophenyl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(32) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(33) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(34) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(35) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(36) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(37) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(38) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-

methoxybenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(39) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-cyanobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(40) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-(2-methoxyethyl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(41) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(42) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(43) (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-(trifluoromethyl)benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(44) (R,E)-4-amino-N-(5-(trifluoromethyl)benzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(45) 1-(1-acryloylazetidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide,

(46) 7-(1-acryloylazetidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(47) (E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)azetidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(48) (R)-7-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(49) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(50) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(51) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(52) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(53) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(54) (R,E)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-7-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(55) (R)-7-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(56) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(57) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(ethyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(58) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(diethylamino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(59) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(isopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(60) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(pyrrolidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-d]pyrimidine-5-carboxamide,

(61) (R,E)-4-amino-N-(5-phenylbenzo[d]oxazol-2-yl)-7-(1-(4-(piperidin-1-yl)but-2-enoyl)pyrrolidin-3-yl) 7H-pyrrolo[2,3-

d]pyrimidine-5-carboxamide

(64) (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-N-(7-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(65) (S)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(66) 1-((1-acryloylpyrrolidin-3-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(67) 1-((1-acryloylpiperidin-3-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(68) 1-((1-acryloylpiperidin-4-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(69) 1-(1-acryloylpiperidin-4-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(70) 1-((1-acryloylazetidin-3-yl)methyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(71) 1-((1S,4S)-4-acrylamidocyclohexyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(72) 1-((1R,4R)-4-acrylamidocyclohexyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(73) (S,E)-4-amino-N-(benzo[d]oxazol-2-yl)-1-(1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(74) 1-(1-acryloylazetidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(75) 1-((1-acryloylazetidin-3-yl)methyl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(76) 1-((1-acryloylazetidin-3-yl)methyl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(77) 1-((1-acryloylpiperidin-4-yl)methyl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(78) 1-((1S,4S)-4-acrylamidocyclohexyl)-4-amino-N-(5-

chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(79) 1-(1-acryloylazetid-3-yl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(80) 1-((1-acryloylpiperidin-4-yl)methyl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(81) 1-((1S,4S)-4-acrylamidocyclohexyl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(82) 1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(83) 1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-fluorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(84) 1-(1-acryloylpyrrolidin-3-yl)-4-amino-N-(5-chlorobenzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(85) 1-(3-acrylamidopropyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

(86) 1-(2-acrylamidoethyl)-4-amino-N-(benzo[d]oxazol-2-yl)-1H-pyrazolo[3,4-d]pyrimidine-3-carboxamide

10. A probe comprising the compound according to any one of claims 1 to 9 or a salt thereof, a detectable label or affinity tag, and a linker, wherein the linker links the compound with the label or the affinity tag.

11. A BTK inhibitor comprising the compound according to any one of claims 1 to 9 or a salt thereof as an active ingredient.

12. A pharmaceutical composition comprising the compound according to any one of claims 1 to 9 or a salt thereof.

13. An antitumor agent comprising the compound according to any one of claims 1 to 9 or a salt thereof as an active ingredient.

14. The compound according to any one of claims 1 to 9 or a salt thereof, for use for the treatment of a tumor.

15. The compound according to any one of claims 1 to 9 or a salt thereof, for use for the production of an antitumor agent.