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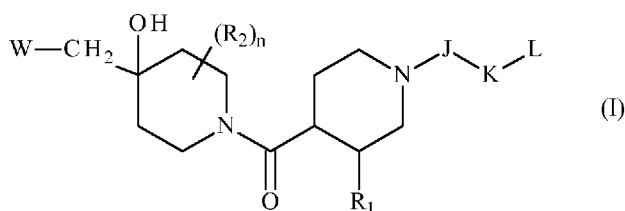
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(54) Title: NEW (HETERO)ARYL-SUBSTITUTED-PIPERIDINYL DERIVATIVES, A PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM



(57) Abstract: Compounds of formula (I) wherein R₁, R₂, J, K, L, n and W are as defined in the description. Medicaments.



The present invention relates to new (hetero)aryl-substituted-piperidinyl derivatives, to a process for their preparation and to pharmaceutical compositions containing them.

The compounds of the present invention are new and have very valuable pharmacological characteristics in the field of apoptosis and oncology.

5 Ubiquitination is a process controlling essential cellular functions such as protein turnover and homeostasis, protein activation and localisation. Ubiquitin is a 76 amino acids polypeptide which is covalently attached to postrationally modified protein substrates via an isopeptide bond. Deubiquinating enzymes (DUBs) are in majority cysteine proteases that cleave the ubiquitin-ubiquitin bond or ubiquitin-protein bond at the Cter glycine of
10 Ubiquitin. Approximately 100 DUBs regulate the thousands ubiquitinated proteins and then some redundancy of deubiquitinase substrates regulation are observed.

Dysregulation of DUBs have been associated with several diseases such as neurodegenerative and infectious diseases (Edelman et al., *Expert Rev. Mol. Med.* 2011, 13, 1-17) and human malignancies (Pal et al., *Cancer Res.* 2014, 74, 4955-4966).
15 Accordingly, overexpression of DUBs or increase of their activity have been associated to numerous types of cancers (Luise et al., *Plos One* 2011, 6, e15891; Rolen et al., *Mol. Carcinog.* 2006, 45, 260-269) and poor prognosis.

Ubiquitin Specific Protease 7 (USP7), also known as Herpes-virus-Associated Ubiquitin-Specific Protease (HAUSP), belongs to the deubiquitinating family. USP7 has been
20 reported to stabilize numerous oncogenes involved in survival and proliferations *via* cell cycle progression, apoptosis, DNA repair, DNA replication and epigenetic factors regulation (Nicholson et al., *Cell Biochem. Biophys.* 2011, 60, 61-68). In addition, USP7 has been shown to regulate immune response via inflammation and Treg modulation (Van Loosdregt et al., *Immunity* 2013, 39, 259-27; Colleran et al., *Proc. Natl. Acad. Sci. USA*
25 2013, 110, 618-623). USP7 has also been implicated in other pathologic states such as neurodevelopmental disorder (Hao et al., *Mol. Cell* 2015, 59, 956-969) and viral infection (Holowaty et al., *Biochem. Soc. Trans.* 2004, 32, 731-732).

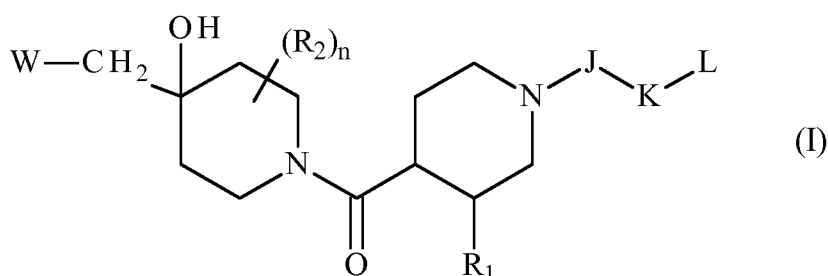
USP7 overexpression has been associated with late stages of cancers and poor prognosis in lung, neuroblastoma, myeloma, prostate, colon and breast cancers. Although some
30 inhibitors have been published in the literature, most of them were not selective and, to

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date, no USP7 inhibitors have entered the clinic (Kemp et al., *Progress in Medicinal Chemistry* 2016, 55, 149-192). There is, therefore, a therapeutic need for compounds that inhibit the activity of the protein USP7.

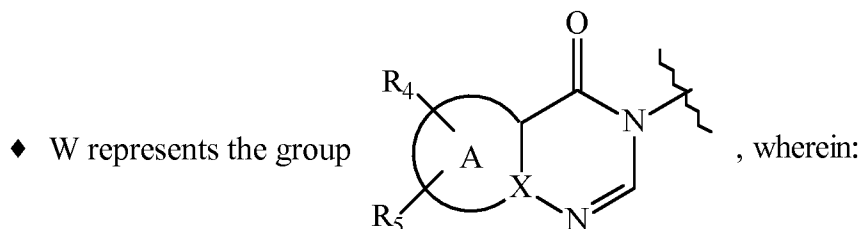
In addition to being new, the compounds of the present invention have pro-apoptotic and/or anti-proliferative properties making it possible to use them in pathologies involving a defect in apoptosis, such as, for example, in the treatment of cancer and of immune and auto-immune diseases.

The present invention relates more especially to compounds of formula (I):



wherein:

- ◆ R_1 represents an aryl group or a heteroaryl group,
- ◆ R_2 represents a hydrogen atom or a halogen atom,
- ◆ n is an integer equal to 0, 1 or 2,
- ◆ J represents a $-C(O)-$ group, a $-CH(R_3)-$ group, or a $-SO_2-$ group,
- ◆ R_3 represents a hydrogen atom or a linear or branched (C_1-C_6) alkyl group,
- ◆ K represents a bond or a $-Cy_1-$ group,
- ◆ L represents a $-Cy_2$ group or a $-CH_2-Cy_2$ group,



- A represents a heteroaryl ring,
- X represents a carbon atom or a nitrogen atom,
- R_4 represents a hydrogen atom, a halogen atom, a linear or branched

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(C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₂-C₆)alkynyl group, a -Y₁-NR₆R₇ group, a -Y₁-OR₆ group, a linear or branched halo(C₁-C₆)alkyl group, an oxo group, a -Y₁-Cy₃ group, a -Cy₃-R₇ group, a -Cy₃-OR₇ group, or a -Y₁-NR₆-C(O)-R₇ group,

- 5 ▪ R₅ represents a hydrogen atom, a halogen atom, or a linear or branched (C₁-C₆)alkyl group,
- R₆ represents a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,
- R₇ represents a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, or a -Y₂-Cy₄ group,
- 10 ▪ Y₁ and Y₂ independently of one another represent a bond or a linear or branched (C₁-C₄)alkylene group,
- ♦ Cy₁ represents a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, which is linked to the group J and to the group L,
- ♦ Cy₂, Cy₃ and Cy₄ independently of one another, represent a cycloalkyl group, a
15 heterocycloalkyl group, an aryl group, or a heteroaryl group,

it being understood that:

- “aryl” means a phenyl, naphthyl, or indanyl group,
- “heteroaryl” means any mono- or fused bi-cyclic group composed of from 5 to 10
20 ring members, having at least one aromatic moiety and containing from 1 to 3
heteroatoms selected from oxygen, sulphur and nitrogen,
- “cycloalkyl” means any mono- or fused bi-cyclic non-aromatic carbocyclic group
containing from 3 to 7 ring members,
- “heterocycloalkyl” means any non-aromatic mono- or fused bi-cyclic group
containing from 3 to 10 ring members, and containing from 1 to 3 heteroatoms
25 selected from oxygen, sulphur and nitrogen,

it being possible for the aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups so defined to be substituted by from 1 to 4 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched (C₂-C₆)alkenyl, linear or branched (C₂-C₆)alkynyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', -Y₁-S(O)_m-R', oxo (or *N*-oxide where
30 appropriate), nitro, cyano, -C(O)-R', -C(O)-OR', -O-C(O)-R', -C(O)-NR'R'',

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-Y₁-NR'-C(O)-R'', -Y₁-NR'-C(O)-OR'', halogen, cyclopropyl, and pyridinyl which can be substituted by a linear or branched (C₁-C₆)alkyl group,

it being understood that R' and R'' independently of one another, represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group,
5 a linear or branched (C₁-C₆)alkoxy group, a linear or branched halo(C₁-C₆)alkyl, a linear or branched hydroxy(C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy(C₁-C₆)alkyl group, a phenyl group, a cyclopropylmethyl group, a tetrahydropyranyl group,
or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition
10 to the nitrogen a second heteroatom selected from oxygen and nitrogen, it being understood that the second nitrogen in question may be substituted by from 1 to 2 groups representing a hydrogen atom, or a linear or branched (C₁-C₆)alkyl group,

and it being understood that m is an integer equal to 0, 1 or 2,

their enantiomers, diastereoisomers and addition salts thereof with a pharmaceutically
15 acceptable acid or base.

Among the pharmaceutically acceptable acids there may be mentioned, without implying any limitation, hydrochloric acid, hydrobromic acid, sulphuric acid, phosphonic acid, acetic acid, trifluoroacetic acid, lactic acid, pyruvic acid, malonic acid, succinic acid, glutaric acid, fumaric acid, tartaric acid, maleic acid, citric acid, ascorbic acid, oxalic acid,
20 methanesulphonic acid, camphoric acid etc.

Among the pharmaceutically acceptable bases there may be mentioned, without implying any limitation, sodium hydroxide, potassium hydroxide, triethylamine, *tert*-butylamine etc.

Among the heteroaryl groups there may be mentioned, without implying any limitation, pyrrolyl, furyl, thienyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl,
25 pyridinyl (also known as pyridyl), pyrazinyl, pyridazinyl, pyrimidinyl, pyridinonyl, indolyl, dihydroindolyl, dihydroisoindolyl, indazolyl, dihydrocyclopentathienyl,

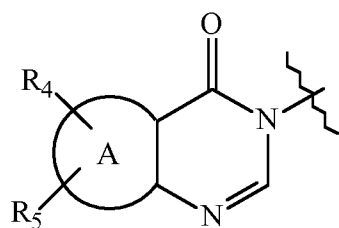
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benzothienyl, tetrahydrobenzothienyl, benzofuranyl, imidazopyridinyl, benzotriazolyl, benzodioxolyl, dihydrobenzodioxinyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, quinoxalinyl, dihydroquinoxalinyl, dihydrothienodioxinyl, quinazolinonyl, pyrrolopyridazinyl, dihydropyrrolizinyl, tetrahydroindolizinyl, etc.

- 5 Among the cycloalkyl groups there may be mentioned, without implying any limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, etc.

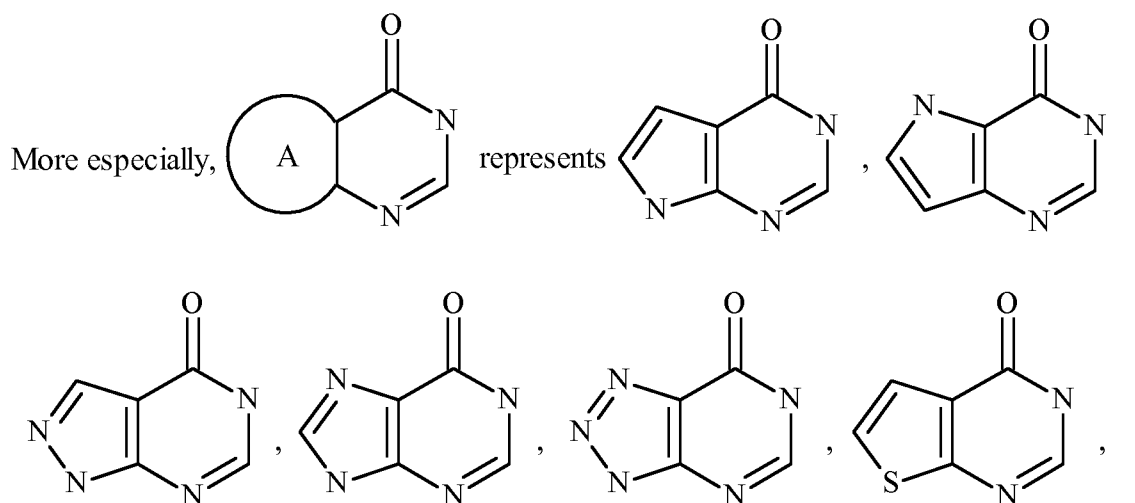
Among the heterocycloalkyl groups there may be mentioned, without implying any limitation, pyrrolidinyl, tetrahydropyranyl, piperidinyl, piperazinyl, morpholinyl, etc.

In another embodiment of the invention, W advantageously represents the group

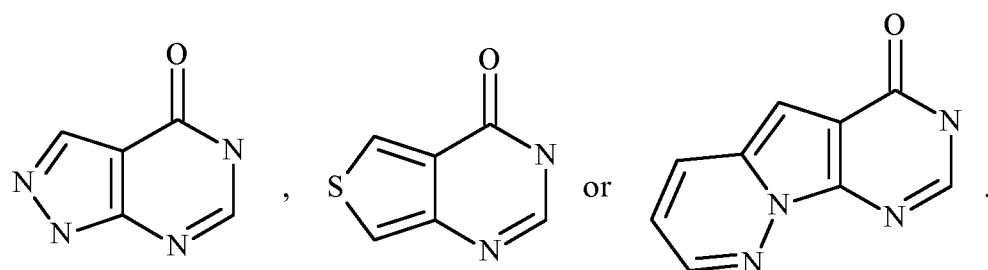
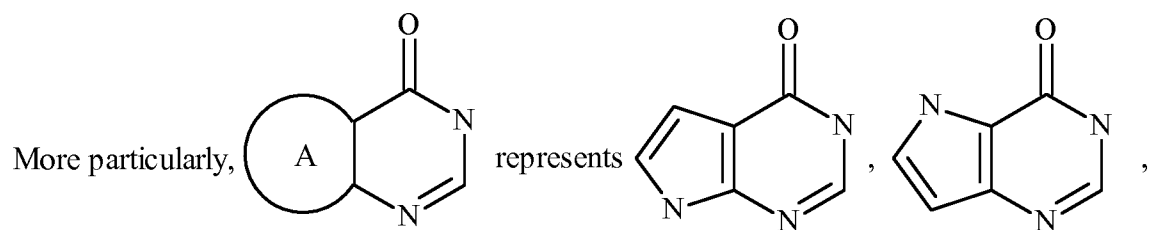
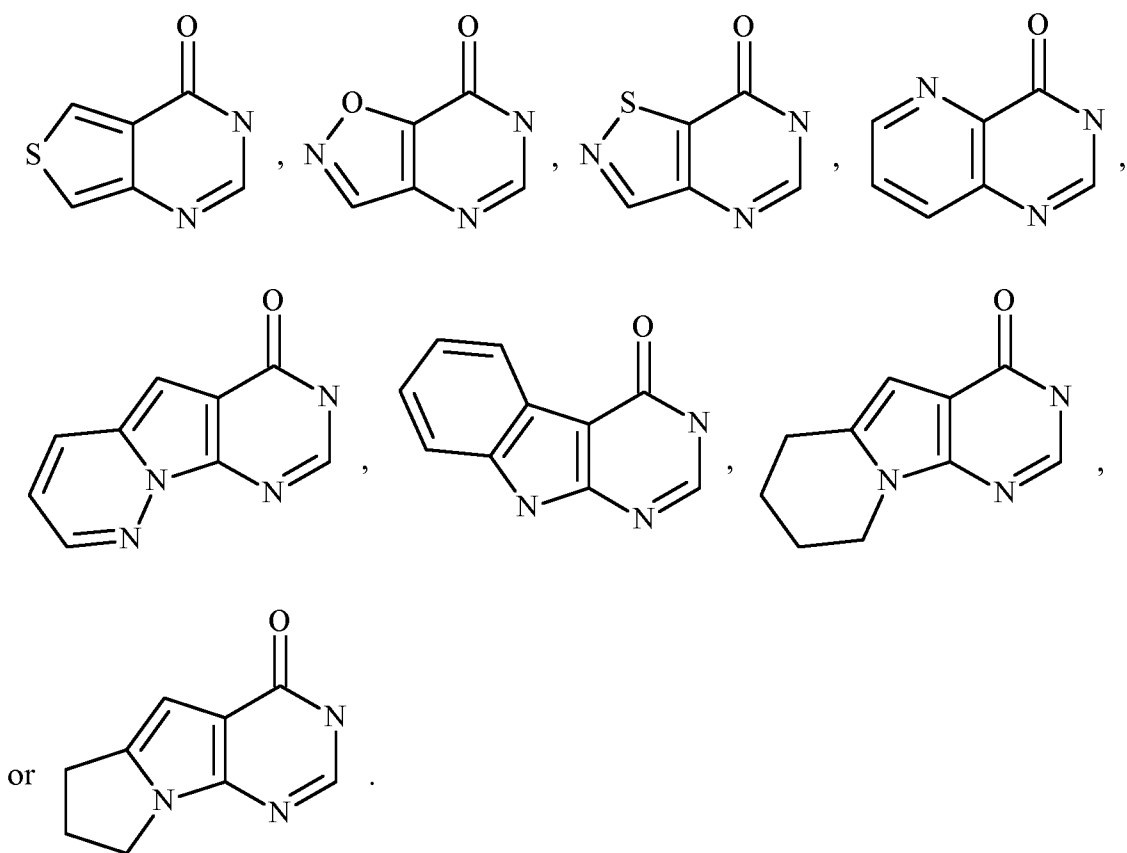


wherein R₄, R₅ and A are as defined for formula (I).

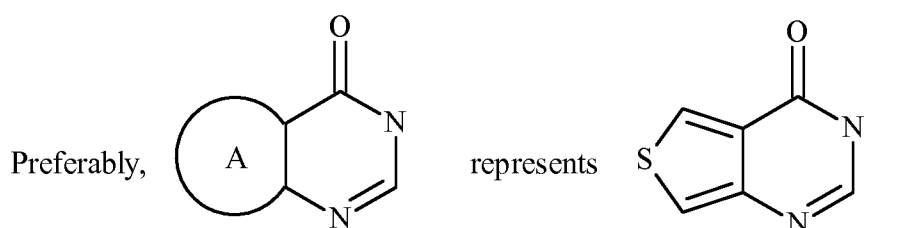
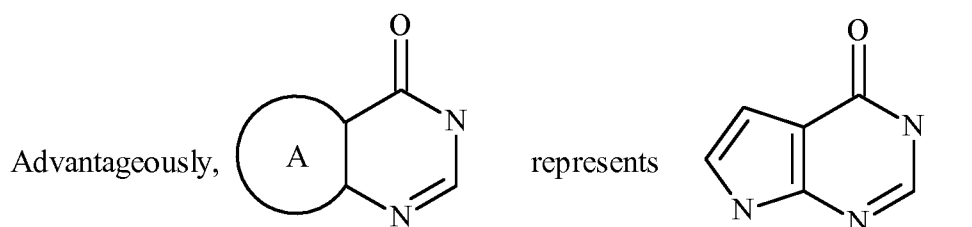
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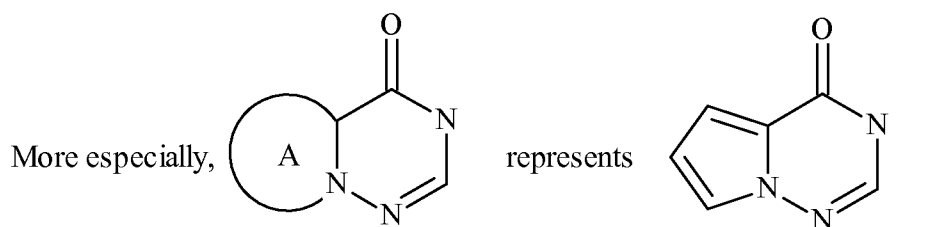
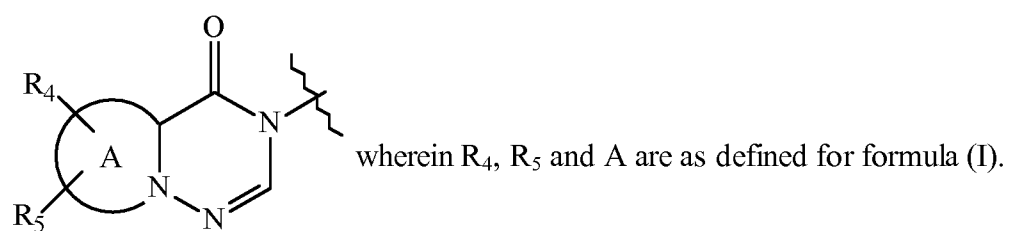
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In another embodiment of the invention, W advantageously represents the group

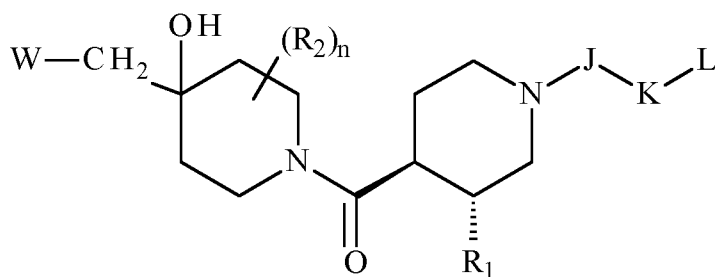


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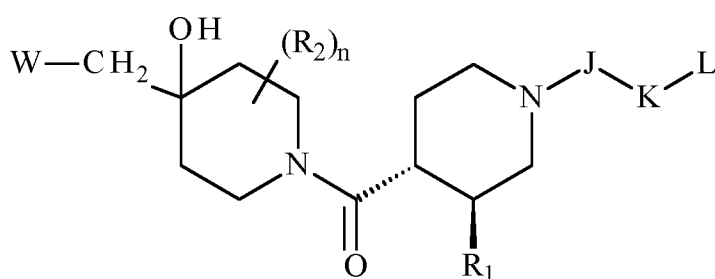
R₁ advantageously represents a phenyl group or a thienyl group. More preferably, R₁ represents a phenyl group.

Advantageously, the compounds of formula (I) display a *trans* configuration as follows:

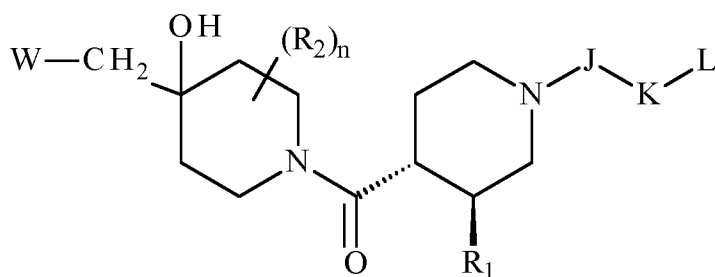
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or



More preferably, the compounds of formula (I) display a *trans* configuration as follows:



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Preferably, R_2 represents a hydrogen atom or a fluorine atom. More preferably, R_2 represents a hydrogen atom. Advantageously, the $-(R_2)_n$ group represents a gem-difluoro group.

10 In some preferred embodiment of the invention, R_3 represents a hydrogen atom or a methyl group. More preferably, R_3 represents a hydrogen atom.

In the preferred compounds of the invention, J represents a $-C(O)-$ group or a $-CH_2-$ group. Preferably, J represents a $-C(O)-$ group. Advantageously, J represents a $-CH_2-$ group.

K preferably represents a bond or a -Cy₁- group selected from a phenyl group, a pyrrolyl group, a thienyl group, a thiazolyl group, a pyridinyl group, a tetrahydrobenzothienyl group, a dihydrothienodioxinyl group, a cyclopropyl group, a cyclobutyl group, or a pyrrolidinyl group. More preferably, K preferably represents a bond or a -Cy₁- group selected from a thienyl group, a thiazolyl group or a pyridinyl group.

Advantageously, L represents a -Cy₂ group. More preferably, Cy₂ represents a phenyl group, an indanyl group, a pyrrolyl group, a furyl group, a thienyl group, a thiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyrazolyl group, a pyridinyl group, a pyrazinyl group, a pyridazinyl group, a pyrimidinyl group, a pyridinonyl group, an indolyl group, a dihydroindolyl group, a dihydroisoindolyl group, an indazolyl group, a dihydrocyclopentathienyl group, a tetrahydrobenzothienyl group, a benzofuranyl group, an imidazopyridinyl group, a benzotriazolyl group, a benzodioxolyl group, a dihydrobenzodioxinyl group, a quinolinyl group, a tetrahydroquinolinyl group, a tetrahydroisoquinolinyl group, a quinoxalinyl group, a dihydroquinoxalinyl group, a quinazolinonyl group, or a pyrrolidinyl group. Even more preferably, Cy₂ represents a phenyl group, a pyrrolyl group, a furyl group, a thienyl group, a thiazolyl group, an oxazolyl group, an isoxazolyl group, a pyrazolyl group, a pyridinyl group, a pyrazinyl group, a pyridazinyl group, a pyrimidinyl group, or an imidazopyridinyl group.

Preferably, Cy₂ represents a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group which are substituted by 1 or 2 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', *N*-oxide, cyano, -C(O)-OR', -C(O)-NR'R'', halogen, in which R' and R'' independently of one another represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy group, a tetrahydropyranyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen, it being understood that the second nitrogen in question may be substituted by a linear or branched (C₁-C₆)alkyl group.

In some preferred embodiment of the invention, K represents a thienyl group, a thiazolyl group or a pyridinyl group and L represents a pyrrolyl group, a furyl group, a thienyl

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group, a pyrazolyl group, a pyridinyl group, a pyrimidinyl group, or an imidazopyridinyl group, each said heteroaryl group may be substituted by 1 or 2 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', N-oxide, cyano, -C(O)-NR'R'', halogen, in which R' and R'' independently of one another
5 represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy group, a linear or branched (C₁-C₆)alkoxy(C₁-C₆)alkyl group, a tetrahydropyranyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen
10 and nitrogen. More preferably, K represents a thiazolyl group and L represents a pyridinyl group.

Other compounds of the invention to which preference is given are those wherein K represents a bond and L represents a phenyl group, a thiazolyl group, an oxazolyl group, an isoxazolyl group, a pyrazolyl group, a pyridinyl group, a pyrazinyl group, a pyridazinyl
15 group or a pyrimidinyl group, each said group may be substituted by 1 or 2 groups selected from linear or branched (C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', cyano, -C(O)-OR', halogen, it being understood that R' and R'' independently of one another represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to
20 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen, it being understood that the second nitrogen in question may be substituted by from 1 to 2 groups representing a hydrogen atom, or a linear or branched (C₁-C₆)alkyl group.

In a preferred embodiment, the -J-K-L group linked to the piperidinyl ring is defined such
25 as J represents a -C(O)- group, K represents a -Cy₁- group and L represents a -Cy₂ group.

In another preferred embodiment, the -J-K-L group is defined such as J represents a -CH₂- group, K represents a bond and L represents a -Cy₂ group.

In another preferred embodiment, the -J-K-L group is defined such as J represents a -C(O)- group, K represents a bond and L represents a -Cy₂ group.

30 In another preferred embodiment, the -J-K-L group is defined such as J represents

a -CH₂- group, K represents a -Cy₁- group and L represents a -Cy₂ group

In the preferred compounds of the invention, R₄ represents a halogen atom, a linear or branched (C₁-C₆)alkyl group, or a -Y₁-Cy₃ group. Preferably, R₄ represents a bromine atom, a methyl group, or a -Cy₃ group.

5 Advantageously, Cy₃ represents a phenyl group, a naphthyl group, a pyrrolyl group, a furyl group, a thienyl group, a thiazolyl group, a pyrazolyl group, an imidazolyl group, a pyridinyl group, a pyrimidinyl group, a pyridinonyl group, an indolyl group, a benzodioxolyl group, a dihydrobenzodioxinyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a pyrrolidinyl group, a tetrahydropyranyl group, or a piperidinyl group.

10 Cy₃ preferably represents a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group which are substituted by from 1 to 3 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', cyano, halogen, in which R' and R'' independently of one another represent a hydrogen atom or a
15 linear or branched (C₁-C₆)alkyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen.

20 Advantageously, R₅ represents a hydrogen atom or a methyl group. More preferably, R₅ represents a hydrogen atom.

In the preferred compounds of the invention, R₆ represents a hydrogen atom or a methyl group.

R₇ preferably represents a hydrogen atom, a methyl group, or a -CH₂-Cy₄ group.

Preferably, Cy₄ represents a phenyl group or a dihydroindolyl group.

25 Preferred compounds of the invention are:

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[3-methyl-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{[(3*R*,4*R*)-1-{[5-(6-aminopyridin-3-yl)-3-fluorothiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-cyclopropyl-3-[(1-{[(3*R*,4*R*)-1-{[3-fluoro-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{[(3*R*,4*R*)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(pyridin-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(naphthalen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(furan-3-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2-fluorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(dimethylamino)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[4-(4-methylpiperazin-1-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-(1*H*-pyrrol-1-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{1-({(3*R*,4*R*)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl}methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-(5-{{(3*R*,4*R*)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl}carbonyl}-4-methyl-1,3-thiazol-2-yl)pyridine-2-carbonitrile;
- 3-[(1-{{(3*R*,4*R*)-1-({2-[6-(dimethylamino)pyridin-3-yl]-4-methyl-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-({4-methyl-2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-fluorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{{(3*R*,4*R*)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(4-fluorophenyl)-3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{(3*R*,4*R*)-1-({2-[6-(morpholin-4-yl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{(3*R*,4*R*)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(1-{(3*R*,4*R*)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-6,8-dimethylpyrimido[5',4':4,5]pyrrolo[1,2-*b*]pyridazin-4(3*H*)-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[4-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methyl-1-oxidopyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-(2-[6-(piperazin-1-yl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-(2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,4-dichlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-(5-{[(3*R*,4*R*)-4-(4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl}-1,3-thiazol-2-yl)pyridine-2-carbonitrile;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(pyridin-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[4-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,4-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,4-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(pyridin-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 4-{3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-4-oxo-3,4-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl} benzonitrile;

- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(1-methyl-1*H*-pyrazol-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(1-methyl-1*H*-pyrazol-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[3-(hydroxymethyl)phenyl]-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(1-methyl-1*H*-pyrazol-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-bromo-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]pyrrolo[2,1-*f*][1,2,4]triazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(hydroxymethyl)phenyl]-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[4-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylpyrrolo[2,1-*f*][1,2,4]triazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylpyrrolo[2,1-*f*][1,2,4]triazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylthieno[3,4-*d*]pyrimidin-4(3*H*)-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylthieno[3,4-*d*]pyrimidin-4(3*H*)-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-{[1-({(3*R*,4*R*)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-[6-(hydroxymethyl)pyridin-3-yl]-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[1-(difluoromethyl)-1*H*-pyrazol-4-yl]-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[1-(difluoromethyl)-1*H*-pyrazol-4-yl]-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(3-methyl-3*H*-imidazo[4,5-*b*]pyridin-6-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-fluorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{{(3*R*,4*R*)-1-{{2-(5-fluoro-6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-(5-{{(3*R*,4*R*)-4-((4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl}-1,3-thiazol-2-yl)pyridine-3-carboxamide;

- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-({2-[5-(hydroxymethyl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-({2-[6-(tetrahydro-2*H*-pyran-4-yloxy)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{{(3*R*,4*R*)-1-{{2-(5-amino-6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{1-({(3*R*,4*R*)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{2-(thiophen-2-yl)-1,3-thiazol-5-yl}methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{2-(pyrimidin-5-yl)-1,3-thiazol-5-yl}methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(1-methyl-1*H*-pyrazol-5-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(1-methyl-1*H*-pyrazol-4-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(1-methyl-1*H*-pyrrol-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{2-(thiophen-3-yl)-1,3-thiazol-5-yl}methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{[1-((3*R*,4*R*)-1-[(2-bromopyridin-4-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{[1-((3*R*,4*R*)-1-[(5-bromopyridin-3-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chlorophenyl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[1-{{(3*R*,4*R*)-1-{{[2-(furan-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[1-{{(3*R*,4*R*)-1-{{[2-(furan-2-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{[2-(thiophen-2-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{[2-(pyrimidin-5-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(1-methyl-1*H*-pyrazol-5-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(1-methyl-1*H*-pyrazol-4-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(1-methyl-1*H*-pyrrol-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-{[2-(thiophen-3-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{[(3*R*,4*R*)-1-{[2-(furan-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-{[(3*R*,4*R*)-1-{[2-(furan-2-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{1-((3*R*,4*R*)-1-[(5-bromopyridin-3-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-(pyridin-3-ylmethyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{4-hydroxy-1-((3*R*,4*R*)-1-[(6'-methyl-3,3'-bipyridin-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-(pyridin-4-ylmethyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-[5-((3*R*,4*R*)-4-[(4-hydroxy-4-{{7-(3-methoxyphenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl}methyl}piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- 5-[5-((3*R*,4*R*)-4-[(4-{{7-(4-chlorophenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl}methyl)-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;

- 5-[5-((3*R*,4*R*)-4-[(4-hydroxy-4-{[7-(4-methoxyphenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl}piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(morpholin-4-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-({2-[6-(2-methoxyethoxy)pyridin-3-yl]-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-({2-(4-methylpiperazin-1-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-({2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-((3*R*,4*R*)-1-[(4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-((3*R*,4*R*)-1-[(2-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[1-((3*R*,4*R*)-1-[(2-chloro-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(1,3-thiazol-5-ylmethyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 5-[5-((3*R*,4*R*)-4-[(4-{[7-(4-fluorophenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- methyl 3-[[[(3*R*,4*R*)-4-((4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl)-3-phenylpiperidin-1-yl]carbonyl]benzoate;
- 5-[(4-hydroxy-1-[[[(3*R*,4*R*)-1-[[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-1-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 5-[(4-hydroxy-1-[[[(3*R*,4*R*)-1-[[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-1-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 5-[(4-hydroxy-1-[[[(3*R*,4*R*)-1-[[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-1-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-((3*R*,4*R*)-1-[(2-{6-[(2-methoxyethyl)amino]pyridin-3-yl}-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-((3*R*,4*R*)-1-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[[[(3*R*,4*R*)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-((3*R*,4*R*)-1-[(5-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[1-((3*R*,4*R*)-1-[(5-bromopyridin-3-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

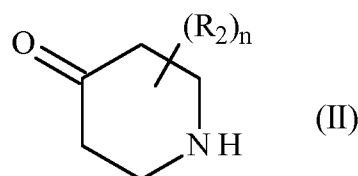
- methyl 5- {[(3*R*,4*R*)-4- ({4-hydroxy-4- [(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl} carbonyl)-3-phenylpiperidin-1-yl] carbonyl} pyridine-3-carboxylate;
- 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5- [(4-hydroxy-1- {[(3*R*,4*R*)-1- {[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl] carbonyl}-3-phenylpiperidin-4-yl] carbonyl} piperidin-4-yl)methyl]-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5- [(4-hydroxy-1- {[(3*R*,4*R*)-1- {[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl] methyl}-3-phenylpiperidin-4-yl] carbonyl} piperidin-4-yl)methyl]-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 3- {[4-hydroxy-1- ({ (3*R*,4*R*)-1- [(5-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3- {[4-hydroxy-1- ({ (3*R*,4*R*)-1- [(3-methyl-1,2-oxazol-5-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3- {[1- ({ (3*R*,4*R*)-1- [(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3- [(4-hydroxy-1- {[(3*R*,4*R*)-1- (1,3-oxazol-4-yl)methyl)-3-phenylpiperidin-4-yl] carbonyl} piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3- {[4-hydroxy-1- ({ (3*R*,4*R*)-1- [(5-methyl-1,3-oxazol-2-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5- {[(3*R*,4*R*)-4- ({4-hydroxy-4- [(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl} carbonyl)-3-phenylpiperidin-1-yl]methyl} pyridine-2-carbonitrile;
- 3- [[4-hydroxy-1- [(3*R*,4*R*)-1- [4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-[4-(hydroxymethyl)phenyl]pyrrolo[2,1-*f*][1,2,4]triazin-4-one;

- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-[4-(hydroxymethyl)phenyl]thieno[3,4-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(3-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[3,3-difluoro-4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[3,3-difluoro-4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;

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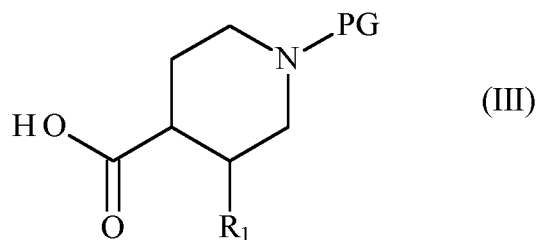
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(6-methoxypyridazin-3-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-*d*]pyrimidin-4-one.

The invention relates also to a process for the preparation of compounds of formula (I), which process is characterized in that there is used as starting material the compound of formula (II):



wherein R_2 and n are as defined for formula (I),

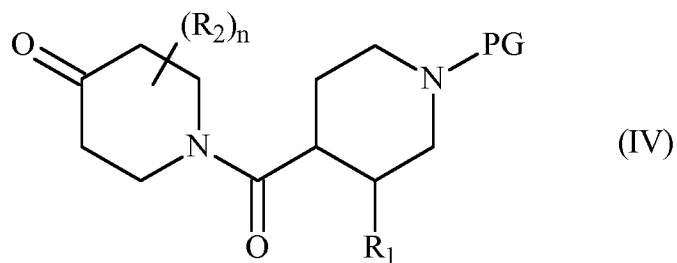
which is subjected to coupling with a compound of formula (III):



wherein R_1 is as defined for formula (I), and PG represents a protecting group of the amine function,

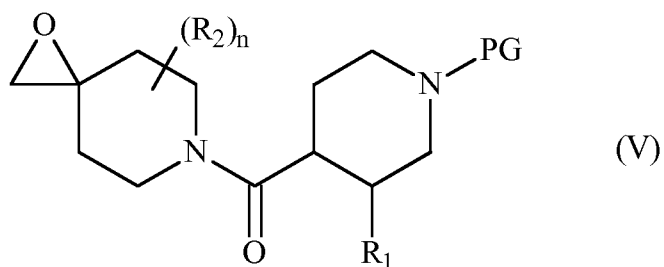
to yield the compound of formula (IV):

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wherein R_1 , R_2 , n and PG are as defined hereinbefore,

compound of formula (IV) which is further converted to an epoxide compound of formula (V):



5

wherein R_1 , R_2 , n and PG are as defined hereinbefore,

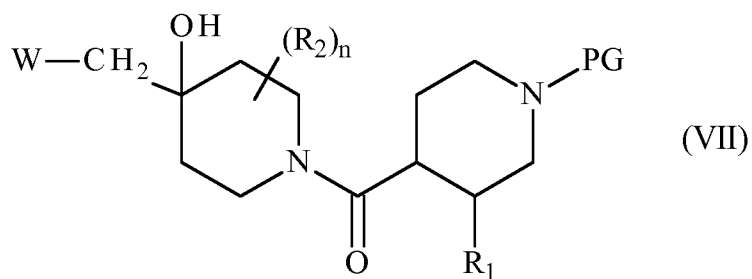
compound of formula (V) which is further subjected to coupling with compound of formula (VI):



10

wherein W is as defined for formula (I),

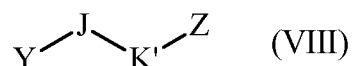
to yield the compound of formula (VII):



wherein R_1 , R_2 , n , W and PG are as defined hereinbefore,

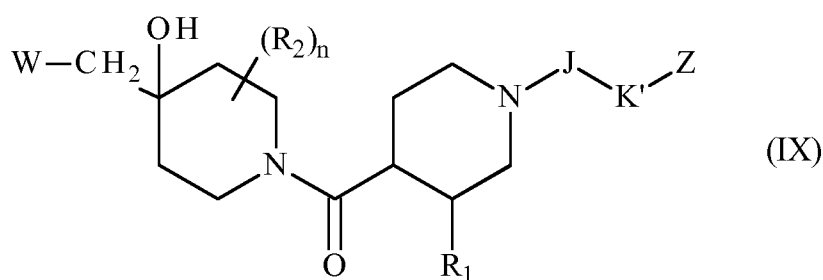
compound of formula (VII) which, after a reaction removing the protecting group PG, is further subjected to:

- **either** coupling with compound of formula (VIII):



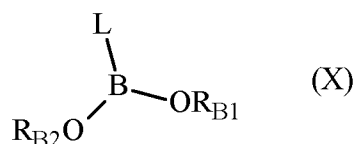
5 wherein J is as defined in formula (I), K' represents a -Cy₁- group, Y represents a hydroxy group or a halogen atom, and Z represents a halogen atom,

to yield the compound of formula (IX):



wherein R₁, R₂, J, K', n, W and Z are as defined hereinbefore,

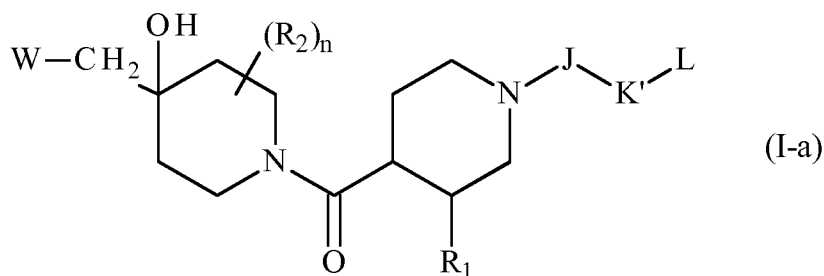
10 compound of formula (IX) which is further subjected to coupling with compound of formula (X):



wherein L is as defined for formula (I), and R_{B1} and R_{B2} represent a hydrogen atom, a linear or branched (C₁-C₆) alkyl group, or R_{B1} and R_{B2} are linked together by a
15 linear or branched (C₂-C₆)alkylene group,

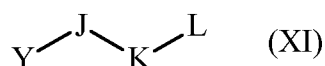
to yield the compound of formula (I-a), a particular case of the compounds of formula (I):

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wherein R_1 , R_2 , J, K' , L, n and W are as defined hereinbefore,

- or coupling with compound of formula (XI):



5 wherein J, K and L are as defined in formula (I), and Y represents a hydroxy group or a halogen atom,

to yield the compound of formula (I),

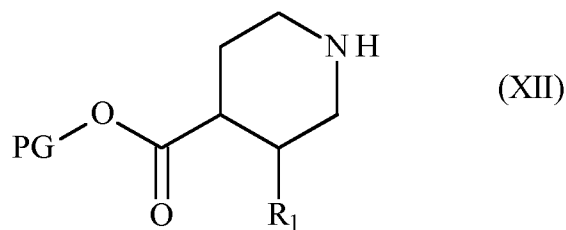
compound of formula (I) or compound of formula (I-a), which is a particular case of compound of formula (I), may then be purified according to a conventional separation technique, which is converted, if desired, into its addition salts with a pharmaceutically acceptable acid or base and which is optionally separated into its isomers according to a conventional separation technique,

10 it being understood that at any moment considered appropriate during the course of the process described above, some groups (hydroxy, amino...) of the starting reagents or of the synthesis intermediates can be protected, subsequently deprotected and functionalized, as

15 required by the synthesis.

In another embodiment of the invention, compounds of formula (I) may be obtained using an alternative process, which process is characterized in that there is used as starting material the compound of formula (XII):

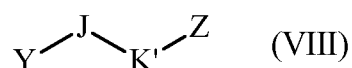
- 36 -



wherein R_1 is as defined for formula (I), and PG represents a protecting group of the carboxylic acid function,

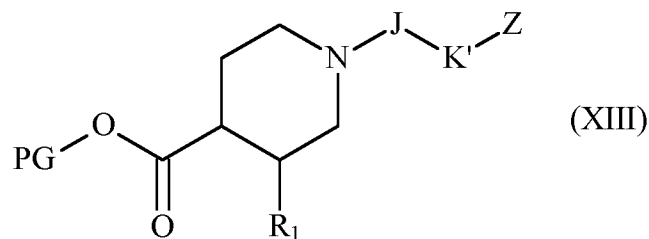
which is subjected to:

- 5 ▪ **either** coupling with compound of formula (VIII):



wherein J is as defined in formula (I), K' represents a $-C_{Y1}-$ group, Y represents a hydroxy group or a halogen atom, and Z represents a halogen atom,

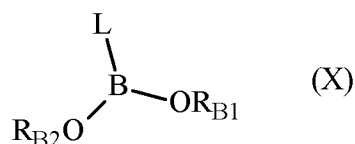
to yield the compound of formula (XIII):



10

wherein R_1 , J, K' , Z and PG are as defined hereinbefore,

compound of formula (XIII) which is further subjected to coupling with compound of formula (X):



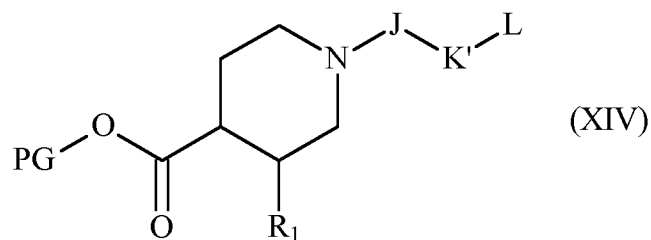
15

wherein L is as defined for formula (I), and R_{B1} and R_{B2} represent a hydrogen atom, a linear or branched (C_1 - C_6) alkyl group, or R_{B1} and R_{B2} are linked together by a

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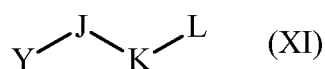
linear or branched (C₂-C₆)alkylene group,

to yield the compound of formula (XIV):



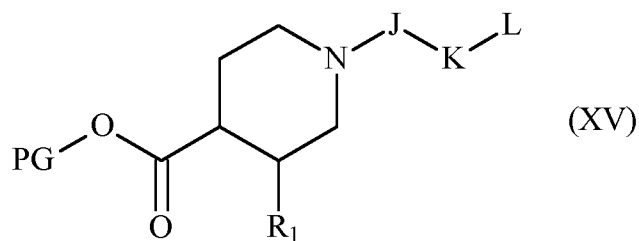
wherein R₁, J, K', L and PG are as defined hereinbefore,

- 5 ▪ or coupling with compound of formula (XI):



wherein J, K and L are as defined in formula (I), and Y represents a hydroxy group or a halogen atom,

to yield the compound of formula (XV),



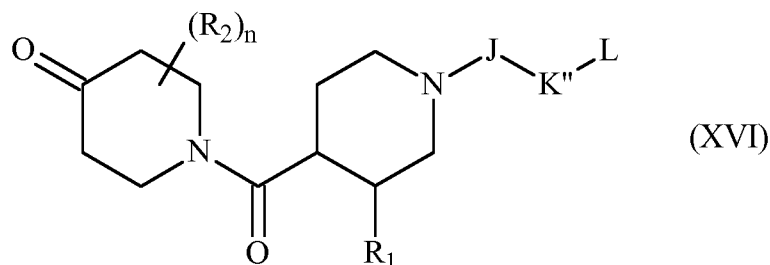
10

wherein R₁, J, K, L and PG are as defined hereinbefore,

compounds of formula (XIV) and (XV) which, after a reaction removing the protecting group PG, are further subjected to coupling with a compound of formula (II),

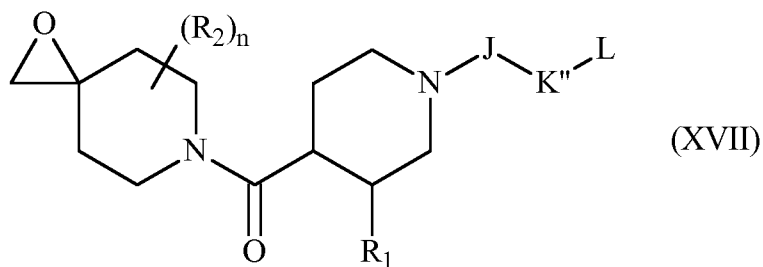
to yield the compound of formula (XVI):

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wherein R_1 , R_2 , J, L and n are as defined hereinbefore, and K'' is either K' or K as defined hereinbefore,

compound of formula (XVI) which is further converted to an epoxide compound of formula (XVII):



wherein R_1 , R_2 , J, K'' , L and n are as defined hereinbefore,

compound of formula (XVII) which is further subjected to coupling with compound of formula (VI):



wherein W is as defined for formula (I),

to yield the compound of formula (I), which may be purified according to a conventional separation technique, which is converted, if desired, into its addition salts with a pharmaceutically acceptable acid or base and which is optionally separated into its isomers according to a conventional separation technique,

it being understood that at any moment considered appropriate during the course of the process described above, some groups (hydroxy, amino...) of the starting reagents or of the synthesis intermediates can be protected, subsequently deprotected and functionalized, as

required by the synthesis.

The compounds of formulae (II), (III), (VI), (VIII), (X), (XI) and (XII) are either commercially available or can be obtained by the person skilled in the art using conventional chemical reactions described in the literature.

Pharmacological studies of the compounds of the invention have shown pro-apoptotic and/or anti-proliferative properties. The ability to reactivate the apoptotic process in cancerous cells is of major therapeutic interest in the treatment of cancers and of immune and auto-immune system diseases.

Accordingly, in another aspect the present invention relates to the use of a pharmaceutical composition comprising a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base in the manufacture of a medicament for use as a pro-apoptotic and/or anti-proliferative agent, wherein the pro-apoptotic or anti-proliferative activity is associated with USP7 inhibition.

In another aspect the present invention relates to the use of a pharmaceutical composition comprising a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base in the manufacture of a medicament for the treatment of cancers or auto-immune and immune system diseases involving USP7 or in which USP7 is implicated.

In another aspect the present invention relates to the use of a pharmaceutical composition comprising a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base in the manufacture of a medicament for the treatment of a disease or condition involving USP7 or in which USP7 is implicated, wherein the disease or condition is selected from cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas, melanomas, malignant haemopathies, myelomas,

ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer.

In another aspect the present invention relates to a method for the treatment of a disease or condition involving USP7 or in which USP7 is implicated, wherein the disease or condition is selected from cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas, melanomas, malignant haemopathies, myelomas, ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer, the method comprising administering to a patient in need thereof an effective amount of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base, or a pharmaceutical composition thereof.

In another aspect the present invention relates to the use of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base, in the manufacture of a medicament for the treatment of a disease or condition involving USP7 or in which USP7 is implicated, wherein the disease or condition is selected from cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas, melanomas, malignant haemopathies, myelomas, ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer.

In another aspect the present invention relates to a combination of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base, with one or more anti-cancer agents selected from genotoxic agents, mitotic poisons, anti-metabolites, proteasome inhibitors, kinase inhibitors, protein-protein interaction inhibitors, immunomodulators, E3 ligase inhibitors, chimeric antigen receptor T-cell therapy and antibodies.

In another aspect the present invention relates to a pharmaceutical composition comprising a combination of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base, with one or more anti-cancer agents as defined herein in combination with one or more pharmaceutically acceptable excipients.

In another aspect the present invention relates to a method for the treatment of cancer involving USP7 or in which USP7 is implicated, the method comprising administering to a patient in need of such treatment an effective amount of a combination of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base, with one or more anti-cancer agents as defined herein or a pharmaceutical composition thereof.

In another aspect the present invention relates to the use of a combination of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base with one or more anti-cancer agents as defined herein in the manufacture of a medicament for the treatment of cancers involving USP7 or in which USP7 is implicated.

In another aspect the present invention relates to a method for the treatment of cancers requiring radiotherapy, wherein the cancer involves USP7 or is one in which USP7 is implicated, the method comprising administering to a patient in need of such treatment an effective amount of a compound of formula (I) or an addition salt thereof with a pharmaceutically acceptable acid or base, or a pharmaceutical composition thereof.

Among the cancer treatments envisaged there may be mentioned, without implying any limitation, treatment of cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas, melanomas, malignant haemopathies, myelomas, ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer. More especially, the compounds according to the invention will be useful in the treatment of chemo-, targeted therapy- or radio-resistant cancers.

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The present invention relates also to pharmaceutical compositions comprising at least one compound of formula (I) in combination with one or more pharmaceutically acceptable excipients.

Among the pharmaceutical compositions according to the invention there may be mentioned more especially those that are suitable for oral, parenteral, nasal, per- or trans-cutaneous, rectal, perlingual, ocular or respiratory administration, especially tablets or dragées, sublingual tablets, sachets, paquets, capsules, glossettes, lozenges, suppositories, creams, ointments, dermal gels, and drinkable or injectable ampoules.

The pharmaceutical compositions according to the invention comprise one or more excipients or carriers selected from diluents, lubricants, binders, disintegration agents, stabilisers, preservatives, absorbents, colorants, sweeteners, flavourings etc.

By way of non-limiting example there may be mentioned:

- ♦ *as diluents*: lactose, dextrose, sucrose, mannitol, sorbitol, cellulose, glycerol,
- ♦ *as lubricants*: silica, talc, stearic acid and its magnesium and calcium salts, polyethylene glycol,
- 5 ♦ *as binders*: magnesium aluminium silicate, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and polyvinylpyrrolidone,
- ♦ *as disintegrants*: agar, alginic acid and its sodium salt, effervescent mixtures.

The dosage varies according to the sex, age and weight of the patient, the administration route, the nature of the therapeutic indication, or of any associated treatments, and ranges
10 from 0.01 mg to 1 g per 24 hours in one or more administrations.

Furthermore, the present invention relates also to the combination of a compound of formula (I) with anti-cancer agents selected from genotoxic agents, mitotic poisons, anti-metabolites, proteasome inhibitors, kinase inhibitors, protein-protein interaction inhibitors, immunomodulators, E3 ligase inhibitors, chimeric antigen receptor T-cell therapy and
15 antibodies, and also to pharmaceutical compositions comprising that type of combination and their use in the manufacture of medicaments for use in the treatment of cancer.

The combination of a compound of formula (I) with an anticancer agent may be administered simultaneously or sequentially. The administration route is preferably the oral route, and the corresponding pharmaceutical compositions may allow the instantaneous or
20 delayed release of the active ingredients. The compounds of the combination may moreover be administered in the form of two separate pharmaceutical compositions, each containing one of the active ingredients, or in the form of a single pharmaceutical composition, in which the active ingredients are in admixture.

The compounds of formula (I) may also be used in combination with radiotherapy in the
25 treatment of cancer.

The following Preparations and Examples illustrate the invention but do not limit it in any way.

General Procedures

All reagents obtained from commercial sources were used without further purification.
5 Anhydrous solvents were obtained from commercial sources and used without further drying.

Flash chromatography was performed on ISCO CombiFlash Rf 200i with pre-packed silica-gel cartridges (RediSep[®] Rf Gold High Performance).

10 Thin layer chromatography was conducted with 5 x 10 cm plates coated with Merck Type 60 F254 silica-gel.

Microwave heating was performed in an Anton Parr MonoWave or CEM Discover[®] instrument.

Preparative HPLC purifications were performed on an HANBON NP7000 Liquid Chromatography system with a Gemini-NX[®] 5 μ M C18, 250 mm $\times$ 50 mm i.d. column
15 running at a flow rate of 99.9 mL min⁻¹ with UV diode array detection (210 – 400 nm) using 5 mM aqueous NH₄HCO₃ solution and MeCN as eluents unless specified otherwise.

Analytical LC-MS: The compounds of the present invention were characterized by high performance liquid chromatography-mass spectroscopy (HPLC-MS) on Agilent HP1200 with Agilent 6140 quadrupole LC/MS, operating in positive or negative ion electrospray
20 ionization mode. Molecular weight scan range is 100 to 1350. Parallel UV detection was done at 210 nm and 254 nm. Samples were supplied as a 1 mM solution in MeCN, or in THF/H₂O (1:1) with 5 μ L loop injection. LCMS analyses were performed on two instruments, one of which was operated with basic, and the other with acidic eluents.

Basic LCMS: Gemini-NX, 3 μm , C18, 50 mm $\times$ 3.00 mm i.d. column at 23 $^{\circ}\text{C}$, at a flow rate of 1 mL min⁻¹ using 5 mM ammonium bicarbonate (Solvent A) and acetonitrile (Solvent B) with a gradient starting from 100 % Solvent A and finishing at 100 % Solvent B over various/certain duration of time.

- 5 Acidic LCMS: ZORBAX Eclipse XDB-C18, 1.8 μm , 50 mm $\times$ 4.6 mm i.d. column at 40 $^{\circ}\text{C}$, at a flow rate of 1 mL min⁻¹ using 0.02 % v/v aqueous formic acid (Solvent A) and 0.02 % v/v formic acid in acetonitrile (Solvent B) with a gradient starting from 100% Solvent A and finishing at 100 % Solvent B over various/certain duration of time.

- 10 ¹H-NMR measurements were performed on Bruker Avance III 500 MHz spectrometer and Bruker Avance III 400 MHz spectrometer, using DMSO-d₆ or CDCl₃ as solvent. ¹H NMR data is in the form of delta values, given in part per million (ppm), using the residual peak of the solvent (2.50 ppm for DMSO-d₆ and 7.26 ppm for CDCl₃) as internal standard. Splitting patterns are designated as: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet), brs (broad singlet), brd (broad doublet), brt (broad triplet), brq (broad quartet), brm (broad multiplet), vbrs (very broad singlet), dd (doublet of doublets), td (triplet of doublets), dt (doublet of triplets), dq (doublet of quartet), ddd (doublet of doublet of doublets), dm (doublet of multiplets), tm (triplet of multiplets), qm (quartet of multiplets).
- 15

- 20 Combination gas chromatography and low resolution mass spectrometry were performed on Agilent 6850 gas chromatograph and Agilent 5975C mass spectrometer using 15 m $\times$ 0.25 mm column with 0.25 μm HP-5MS coating and helium as carrier gas. Ion source: EI⁺, 70 eV, 230 $^{\circ}\text{C}$, quadrupole: 150 $^{\circ}\text{C}$, interface: 300 $^{\circ}\text{C}$.

HRMS were determined on a Shimadzu IT-TOF, ion source temperature 200 $^{\circ}\text{C}$, ESI +/-, ionization voltage: (+-)4.5 kV. Mass resolution min. 10000.

- 25 Elementary analyses were performed on a Thermo Flash EA 1112 Elemental Analyzer.

List of abbreviations

	Abbreviation	Name
	abs.	absolute
	aq.	aqueous
5	Ar	argon
	AtaPhos*PdCl ₂	bis(di- <i>tert</i> -butyl(4-dimethylaminophenyl)phosphine) dichloropalladium(II)
	Boc	<i>tert</i> -butoxycarbonyl
	cc.	concentrated
10	DCM	dichloromethane
	DEE	diethyl ether
	DIPO	diisopropyl oxide
	disp.	dispersion
	DMEDA	<i>N,N'</i> -dimethylethylenediamine
15	DMF	dimethylformamide
	EDC.HCl	<i>N</i> -(3-dimethylaminopropyl)- <i>N'</i> -ethylcarbodiimide hydrochloride
	EEO	ethyl ethanoate
	eq.	equivalent
20	LC	liquid chromatography
	LDA	lithium diisopropylamide
	mCPBA	meta-chloro-perbenzoic acid
	MeCN	acetonitrile
	MSM	methylsulfinylmethane
25	MTBE	<i>tert</i> -butyl methylether
	NMP	N-methylpyrrolidone
	PDO	p-dioxane
	r.t.	room temperature
	sat.	saturated
30	SEM	trimethylsilylethoxymethyl
	TBAF	tetrabutylammonium fluoride

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TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMP.MgCl.LiCl	2,2,6,6-tetramethylpiperidine-magnesium chloride-lithium chloride (1:1) complex

5 General Procedure 1

Step 1:

To a stirred solution of 4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (**Preparation R1a**; 1.84 g, 12 mmol, 1 eq.) in abs. DMF (15 ml) sodium-hydride (720 mg, 60 % disp. in mineral oil, 18 mmol, 1.5 eq.) was added, and stirred for 10 minutes at r.t. under Ar. Alkylating agent (13.18 mmol) was added to the reaction mixture and stirred for 1-6 hours at r.t. The mixture was poured into water (150 ml), then it was extracted with EEO (3 x 150 ml). The combined organic layers were washed with water, brine, dried over MgSO₄, and evaporated.

Step 2:

A part of the compound obtained in Step 1 above (1.36 mmol) and lithium-hydroxide monohydrate (571 mg, 13.62 mmol, 10 eq.) were stirred in PDO-water (40 ml, 1:1 v/v) mixture at 110 °C for 7-36 hours. The reaction mixture was neutralized with 1 N aq. HCl solution and the resulted precipitate was filtered off, washed with water and dried.

General Procedure 2

Step 1:

Preparation R1a (460 mg, 3 mmol, 1 eq.), heteroaryl/aryl-boronic acid (7.5 mmol) and copper(II)-acetate (817 mg, 4.5 mmol) were stirred in pyridine (10 ml) at 50-60 °C for 16-72 hours.

Work-up 1:

The mixture was evaporated to Celite and purified by flash chromatography (heptane-EEO,

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gradient).

Work-up 2:

The mixture was filtered and the resulted filtrate was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

5 *Step 2:*

The resulted compound obtained in Step 1 above (1.36 mmol) and lithium-hydroxide monohydrate (571 mg, 13.62 mmol, 10 eq.) were stirred in PDO-water (40 ml, 1:1 v/v) mixture at 110 °C for 7-24 hours. The reaction mixture was neutralized with 1 N aq. HCl solution, the resulted precipitate was filtered off, washed with water, dried.

10 **General Procedure 3**

Step 1:

Preparation R1b (746 mg, 5 mmol, 1 eq.), heteroaryl/aryl-iodide (10 mmol), CuI (286 mg, 1.5 mmol, 0.3 eq.), *R,R*-diaminocyclohexane (171 mg, 1.5 mmol, 0.3 eq.), anhydrous K₃PO₄ (4.24 g, 20 mmol, 4 eq.) was stirred in diglyme (15 ml) for 6-16 hours at
15 120 °C under N₂ atmosphere.

Work-up 1:

After the reaction completed, the mixture was diluted with water (200 ml) (or. 25% aq. NH₃) and cooled to r.t. The mixture was filtered, washed with water (3 x 30 ml), aq. NH₃ solution (40 ml, 25%), water (3 x 50 ml), heptane (50 then 30 ml) and dried in vacuum.

20 Work-up 2:

The reaction mixture was evaporated to Celite and purified by flash chromatography (heptane:EEO, gradient).

Step 2:

The corresponding 4-methoxy-7-heteroaryl/aryl-pyrrolo[2,3-*d*]pyrimidine obtained in
25 Step 1 above (61.3 mmol, 1 eq.), cc. HCl aqueous solution (10 ml, ~12.2 M, 122.5 mmol,

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2 eq.) and PDO (70 ml) was stirred at 100 °C for 0.5-2 hours. After the reaction completed, the mixture was partially evaporated. The formed suspension was filtered and the solid on the filter was washed with water and dried.

General Procedure 4

Step 1:

Preparation R1a (154 mg, 1 mmol, 1 eq.), di-*tert*-butyl-diazodicarboxylate (690 mg, 3 mmol, 3 eq.), triphenylphosphine (786 mg, 3 mmol, 3 eq.) and corresponding alcohol (3 mmol, 3 eq.) were stirred in abs. toluene (10 ml) under Ar atmosphere at 50 °C for 2 hours. The reaction mixture was evaporated, taken in THF and purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

Step 2:

A part of 4-chloro-7-aryl/alkyl-pyrrolo[2,3-*d*]pyrimidine obtained in Step 1 above (1.36 mmol) and lithium-hydroxide monohydrate (571 mg, 13.62 mmol) were stirred in PDO-water (40 ml, 1:1 v/v) mixture at 110 °C for 7-24 hours. The reaction mixture was neutralized with 1 N aq. HCl solution, the resulted precipitate was filtered off, washed with water and dried.

General Procedure 5

Step 1:

Pyrimidine-4-one derivative (1 mmol), epoxide compound **Preparation R1f** (1 mmol) and K₂CO₃ (276.4 mg, 2 mmol, 2 eq.) were stirred in DMF (5 ml) at 75 °C for 2-8 hours.

Work-up 1:

The mixture was poured into ice-water mixture and the resulted precipitate was filtered off, washed with water and dried.

Work-up 2:

The reaction mixture was filtered and the solid was washed with DMF. The resulted filtrate

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was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

Step 2:

5 A part of the compound obtained in Step 1 above (1 mmol) was stirred in aq. HCl solution (1 N, 10 ml, 10 mmol, 10 eq.) and PDO (5 ml) for 1-3 hours at 75 °C.

Work-up 1:

The mixture was cooled to about 0-5 °C with ice bath and the white precipitate was filtered off and dried in vacuum (resulted HCl salt).

Work-up 2:

10 The mixture was totally evaporated and was used to the further step (resulted HCl salt).

Work-up 3:

The mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient, resulted free base).

General Procedure 6

15 Compound obtained in **General Procedure 5** (1 mmol, 1 eq.), aryl/heteroaryl-CH₂-X (1 mmol, 1 eq.; wherein X represents a halogen atom) and K₂CO₃ (483 mg, 3.5 mmol, 3.5 eq.) were stirred in DMF (10 ml) at r.t. for 4-16 hours.

Work-up 1:

20 The mixture was poured into ice-water mixture and the resulted precipitate was filtered off, washed with water and dried.

Work-up 2:

The mixture was filtered and the filtrate was injected to preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

General Procedure 7

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Compound obtained in **General Procedure 5** (2.7 mmol), EDC.HCl (1.183 g, 6.172 mmol) and corresponding carboxylic acid (2.7 mmol) were stirred in pyridine (25 ml) at r.t. for 16 hours.

Work-up 1:

- 5 The reaction mixture was evaporated, the residue was taken in DMF and injected to preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

Work-up 2:

- 10 The reaction mixture was evaporated. The residue was triturated with water and the resulted solid was filtered off.

General Procedure 8

- 15 Compound obtained in **General Procedure 5** (1 mmol, 1 eq.), corresponding sulfonyl chloride (2 mmol, 2 eq.) and K₂CO₃ (553 mg, 4 mmol, 4 eq.) were stirred in DMF (10 ml) at r.t. for 4-28 hours. The mixture was evaporated to Celite and purified by flash chromatography (eluent: DCM-MeOH).

General Procedure 9

- 20 The corresponding halogenated component (0.15 mmol, 1 eq.), corresponding boronic acid (0.375 mol, 2.5 eq.), ATAphos*PdCl₂ (10.6 mg, 0.015 mmol, 0.1 eq.), Cs₂CO₃ (171 mg, 0.525 mmol, 3.5 eq.) was diluted with THF (2.5 ml) and water (2.5 ml). The mixture was flushed with nitrogen and stirred in microwave reactor at 80 °C for 100-150 minutes. The reaction mixture was injected through syringe filter to preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

General Procedure 10

- 25 To the stirred solution of the corresponding O-benzyl or O-methyl containing compound (0.17 mmol) in DCM (5 ml), boron-tribromide (0.3 ml, 440 mg, 1.7 mmol, 10 eq.) was added dropwise at r.t. After 3 hours of stirring, the reaction mixture was quenched with EtOH and evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX

5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

General Procedure 11

The procedure is the same as described under **General procedure 5** using **Preparation R1m** as epoxide component. The residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

General Procedure 12

The mixture of the nitro compound (1.45 mmol), tin(II)-chloride dihydrate (1.64 g, 7.45 mmol, 5 eq.) in EtOH (30 ml) and HCl (1 N, 5 ml, aq.) was stirred for 20 hours at 80 °C. To the reaction mixture sat. aqueous NaHCO_3 (50 ml) was added, then the mixture was evaporated to Celite and purified by flash chromatography (DCM-MeOH).

General Procedure 13

To a stirred mixture of amino/amide compound (0.105 mmol), K_2CO_3 (22 mg, 0.158 mmol, 1.5 eq.) in DMF (1 ml) iodomethane (10 μ l) was added at r.t. After 18 hours of stirring the reaction mixture was filtered and injected to preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

General Procedure 14

The *N*-Boc compound (0.1 mmol) was stirred in aq. HCl solution (1 N, 3 ml, 3 mmol, 30 eq.) and PDO (2 ml) for 2-5 hours at 75 °C. The mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient, resulted as free amine base).

General Procedure 15

The mixture of the corresponding methoxy compound (0.44 mmol), cc. HCl (aq. 37 %, 1.1 ml, 13 mmol, 30 eq.) and PDO (7 ml) was stirred at 100 °C for 3 hours. To the reaction mixture NaOH solution (aq. 2 M, 6.6 ml) was added. The solid compound was filtered off, then purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

Preparation R1b: 4-methoxy-7H-pyrrolo[2,3-d]pyrimidine

Preparation R1a (100 g, 0.651 mol, 1 eq.), NaOH (31.26 g, 0.781 mol, 1.2 eq.) and MeOH (400 ml) was stirred at 90 °C for 24 hours. The mixture was quenched with water (1200 ml) and cooled to r.t. with ice bath. The mixture is stirred for 30 minutes, and
5 filtered through a glass filter. The precipitate was washed with water (3 x 100 ml) then dried and **Preparation R1b** was obtained as a white solid. HRMS calculated for C₇H₇N₃O: 149.0589; found 150.0667 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d₆): δ = 12.02 (vbrs, 1 H), 8.37 (s, 1 H), 7.35 (d, 1 H), 6.47 (d, 1 H), 4.02 (s, 3 H).

10 ¹³C-NMR (100 MHz, MSM-d₆) δ ppm 162.6, 152.9, 150.8, 124.6, 104.8, 98.3, 53.7.

Preparation R1c: 5-[5-(chloromethyl)-1,3-thiazol-2-yl]-2-methylpyridine*Step 1: [2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methanol*

2-Bromothiazole-5-methanol (20 g, 0.103 mol, 1 eq.), 2-methylpyridine-5-boronic acid (18.3 g, 0.134 mol, 1.3 eq.), ATAphos*PdCl₂ (3.65 g, 5.152 mmol, 0.05 eq.), Cs₂CO₃
15 (67.14 g, 0.206 mol, 2 eq.) were dissolved in THF (800 ml) and water (800 ml). The mixture was flushed with nitrogen and stirred at 80 °C for 3 hours. The mixture was cooled to r.t. and diluted with EEO (300 ml). The layers were separated, the aqueous layer was extracted with EEO (3x100 ml), the combined organic layer was dried over MgSO₄ and, after filtration, evaporated. The residue was crystallized from EEO / DIPO, filtered and
20 dried in vacuum to give a brown solid. HRMS calculated for C₁₀H₁₀N₂OS: 206.0514; found 207.0591 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆): δ = 2.52 (s, 3 H), 4.72 (d, J = 10.4 Hz, 2 H), 5.67 (t, J = 11.0 Hz, 1 H), 7.38 (d, J = 16.3 Hz, 1 H), 7.77 (s, 1 H), 8.14 (dd, J = 16.0, 4.8 Hz, 1 H), 8.96 (d, J = 4.5 Hz, 1 H).

Step 2: Preparation R1c

[2-(6-Methyl-3-pyridyl)thiazol-5-yl]methanol (18.23 g, 88.38 mmol, 1 eq.) was dissolved in abs. DMF (1.37 ml, 1.29 g, 17.68 mmol, 0.2 eq.) and dry DCM (400 ml). SOCl₂ (8.36 ml, 13.67 g, 114.9 mmol, 1.3 eq.) was dropped to the mixture in DCM (50 ml) solution (~15 min) at r.t. The mixture was stirred at 50 °C for 2 hours. The mixture was

cooled to r.t. Water (50 ml) was dropped slowly to the mixture, then it was neutralized with sat. NaHCO₃ solution (250 ml, pH 7-8). The layers were separated. The aqueous layer was extracted with DCM (4 x 50 ml). The combined organic layer was dried over MgSO₄, filtered. The solution was diluted with EEO (300 ml) and filtered through silica bed (~20 g). The mixture was evaporated to give **Preparation R1c** as a yellow solid. HRMS calculated for C₁₀H₉ClN₂S: 224.0175; found 225.0247 [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ = 2.53 (s, 3 H), 5.17 (s, 2 H), 7.41 (d, J = 16.5 Hz, 1 H), 7.98 (s, 1 H), 8.17 (dd, J = 16.0, 5.0 Hz, 1 H), 8.99 (d, J = 5.0 Hz, 1 H).

¹³C-NMR (125 MHz, MSM-d₆): δ (ppm) 24.5, 38.4, 124.1, 134.4, 144.4, 146.7.

10 **Preparation R1d: 4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazole-5-carboxylic acid**

Step 1: ethyl 4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazole-5-carboxylate

Ethyl 2-bromo-4-methylthiazole-5-carboxylate (26.9 g, 107.6 mmol, 1 eq.), 2-methylpyridine-5-boronic acid (19.2 g, 139.8 mmol, 1.3 eq.), ATAphos*PdCl₂ (3.05 g, 4.3 mmol, 0.04 eq.), Na₂CO₃ (34.2 g, 322.65 mmol, 3 eq.) were dissolved in THF (250 ml) and water (250 ml). The mixture was flushed with nitrogen and stirred at 80 °C for 2 hours. After the reaction ended, the mixture was cooled to r.t. and diluted with EEO (250 ml). The layers were separated and the aqueous layer was extracted with EEO (2 x 50 ml). The combined organic layer was dried over MgSO₄ and, after filtration, evaporated. The raw product was dissolved in DCM/EEO/heptane (1:1:1 v/v, 600 ml) and filtered through silica (~30 g) and washed with DCM/EEO/heptane (1:1:1 v/v, 100 ml). The mixture was evaporated. The residue was recrystallized from DIPO (100 ml) and dried in vacuum to give a beige solid. HRMS calculated for C₁₃H₁₄N₂O₂S: 262.0776; found 263.0852 [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ = 1.31 (t, J = 17.5 Hz, 3 H), 2.54 (s, 3 H), 2.70 (s, 3 H), 4.30 (q, J = 17.8 Hz, 2 H), 7.42 (d, J = 20.3 Hz, 1 H), 8.24 (dd, J = 20.4, 6.1 Hz, 1 H), 9.04 (d, J=5.4 Hz, 1 H).

Step 2: Preparation R1d

Ethyl 4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carboxylate (21.07 g, 80.33 mmol, 1 eq.) was dissolved in EtOH (40 ml). NaOH (4.82 g, 120.49 mmol, 1.5 eq.) was dissolved in

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water (80 ml). The aq. NaOH was added to the organic mixture and stirred at 80 °C for 45 minutes. After the reaction ended, the mixture was cooled to r.t. After 1 week, the black precipitate was sedimented. The mixture was filtered through a silica/Celite bed. The mixture was acidified with cc. HCl solution (to pH~1), and the resulting precipitate was filtered off, washed with water (50 ml) and dried in vacuum to give **Preparation R1d** as an off-white solid. HRMS calculated for C₁₁H₁₀N₂O₂S: 234.0463; found 235.0533 [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ = 2.52 (s, 3 H), 2.63 (s, 3 H), 7.36 (d, J = 16.2 Hz, 1 H), 8.14 (dd, J = 16.2, 4.8 Hz, 1 H), 8.95 (d, J = 4.8 Hz, 1 H).

Preparation R1e: tert-butyl 1-oxa-6-azaspiro[2.5]octane-6-carboxylate

Trimethyl-sulfoxonium iodide (20.0 g, 150 mmol) was dissolved in abs. MSM (75 ml) then sodium-hydride dispersion (60 % in mineral oil, 6 g, 150 mmol) was added sequentially and stirred for 20 minutes at r.t. *N*-Boc-piperidin-4-one (20.0 g, 100 mmol) solution in MSM (75 ml, abs.) was added to the mixture and stirred for 15 hours at r.t. The reaction mixture was poured into ice-water mixture (200 ml) and extracted with diethyl-ether (4 x 200 ml). The combined organic layer was washed with water, brine, then dried over MgSO₄ and evaporated to give **Preparation R1e**. HRMS calculated for C₁₁H₁₉NO₃: 213.1365; found 158.0811 [(M+H-tBu)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 3.5/3.37 (brm+brm, 4 H), 2.65 (s, 2 H), 1.64/1.38 (m+m, 4 H), 1.4 (s, 9 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 154.3, 79.3, 57.4, 53.3, 42.7, 33, 28.5.

Preparation R1f: tert-butyl (3R,4R)-4-(1-oxa-6-azaspiro[2.5]oct-6-ylcarbonyl)-3-phenylpiperidine-1-carboxylate

Step 1: tert-butyl (3R,4R)-4-[(4-oxopiperidin-1-yl)carbonyl]-3-phenylpiperidine-1-carboxylate

4-piperidone hydrochloride hydrate (0.969 g, 6.3 mmol), EDC.HCl (3.623 g, 18.9 mmol) and (3R,4R)-1-*tert*-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid (1.928 g, 6.3 mmol) were dissolved in pyridine (10 mL) and stirred at r.t. for 16 hours. The reaction mixture was evaporated to Celite and purified by flash chromatography (DCM:MeOH,

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gradient) to give the product of the title. HRMS calculated for $C_{22}H_{30}N_2O_4$: 386.2206; found 409.2093 $[(M+Na)^+ \text{ form}]$.

1H -NMR (500 MHz, $MSM-d_6$): δ 1.42 (s, 9 H), 4.14-1.50 (m, 16 H), 7.32-7.15 (m, 5 H).

Step 2: Preparation R1f

5 *tert*-butyl (3*R*,4*R*)-4-[(4-oxopiperidin-1-yl)carbonyl]-3-phenylpiperidine-1-carboxylate (60 g, 155 mmol 1 eq.) and trimethylsulfoxonium-iodide (85.41 g, 388 mmol, 2.5 eq.) was charged into a round bottom flask and dissolved/suspended in MeCN (150 ml) and MTBE (150 ml). In parallel, NaOH (15.5 g, 388 mmol, 2.5 eq.) was dissolved in water (21.6 ml) (~40 % solution). The aq. NaOH solution was added to the mixture and stirred at 60 °C for
10 2 hours. After the reaction completed, the mixture was cooled to r.t., filtered through a Celite bed and the filter cake was washed with MTBE (2 x 60 ml). Water (150 ml) was added to the organic layer and, after extraction, the layers were separated. The aq. layer was extracted with further MTBE (2 x 60 ml). The combined organic layers were dried over $MgSO_4$ and after filtration evaporated to give **Preparation R1f** as beige solid foam.
15 HRMS calculated for $C_{23}H_{32}N_2O_4$: 400.2362; found 423.2247 $[(M+Na)^+ \text{ form}]$.
 1H -NMR (500 MHz, $MSM-d_6$): δ = 1.41 (s, 9 H), 1.79-0.86 (m, 6 H), 2.61-2.51 (m, 2 H), 4.16-2.73 (m, 10 H), 7.33-7.18 (m, 5 H).

Preparation R1g: 3-fluoro-5-iodo-thiophene-2-carboxylic acid

Step 1: 3-fluoro-5-iodo-thiophene-2-carboxylate and methyl 3-fluoro-4,5-diiodo-
20 *thiophene-2-carboxylate*

To the solution of methyl 3-fluorothiophene-2-carboxylate (2.42 g, 15.1 mmol) in THF (10 ml) at TMP. $MgCl.LiCl$ (1 N, in THF/toluene, 25 ml, 25 mmol) was added dropwise at -45 °C in 5 minutes. After 30 minutes of stirring iodine (4.04 mg, 15.9 mmol) was added in THF (10 ml) at -45 °C to the mixture. After warming up (1 hour) sat. NH_4Cl solution
25 (50 ml, aq.) was added to the mixture while stirring. The mixture was extracted with EEO (5 x 10 ml). The combined organic layer was evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give 3-fluoro-5-iodo-thiophene-2-carboxylate and methyl 3-fluoro-4,5-diiodo-thiophene-2-carboxylate, separately.

Methyl 3-fluoro-5-iodo-thiophene-2-carboxylate

GC-MS calculated for $C_6H_4FIO_2S$: 285.8961; found 285.9 [(M, EI) form].

1H NMR (500 MHz, MSM- d_6): δ ppm 7.52 (s, 1 H), 3.78 (s, 3 H).

^{13}C NMR (125 MHz, MSM- d_6): δ ppm 159.4, 158.8, 128.5, 117.2, 86.4, 52.8.

5 Methyl 3-fluoro-4,5-diiodo-thiophene-2-carboxylate

GC-MS calculated for $C_6H_4FIO_2S$: 411.7927; found 411.9 [(M, EI) form].

1H NMR (500 MHz, MSM- d_6): δ ppm 3.8 (s, 3 H).

^{13}C NMR (125 MHz, MSM- d_6): δ ppm 159, 158.2, 117.4, 96.1, 90.6, 53.1.

Step 2: Preparation R1g

- 10 Methyl 3-fluoro-5-iodo-thiophene-2-carboxylate (1.188 g, 4.135 mmol), lithium-hydroxide monohydrate (867 mg, 20.7 mmol) were stirred in methanol (10 ml) and water (10 ml) at 70 °C for 1 hour. The mixture was partially evaporated and the aqueous residue was acidified with 1 N HCl (25 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1g**. GC-MS calculated for $C_5H_2FIO_2S$: 271.8804; found 271.9 [(M, EI) form].

15 1H NMR (500 MHz, MSM- d_6): δ ppm 13.48 (brs), 7.74 (s, 1 H).

^{13}C NMR (125 MHz, MSM- d_6): δ ppm 160.4, 158.3, 128.5, 119, 85.1.

Preparation R1h: 3-fluoro-4,5-diiodo-thiophene-2-carboxylic acid

- 20 Methyl 3-fluoro-4,5-diiodo-thiophene-2-carboxylate (614 mg, 1.49 mmol), lithium-hydroxide monohydrate (256 mg, 6 mmol) were stirred in methanol (8 ml) and water (8 ml) at r.t. for 5 hours. The mixture was partially evaporated and the aqueous residue was acidified with 1 N HCl (10 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1h**. HRMS calculated for $C_5HFI_2O_2S$: 397.7771; found 352.7798 [(M-H-CO₂)⁺ form].

- 25 1H NMR (500 MHz, MSM- d_6): δ ppm 13.72 (brs, 1 H).

^{13}C NMR (125 MHz, MSM- d_6): δ ppm 160, 157.7, 119.1, 95.1, 90.5.

Preparation R1i: 3-fluoro-4-iodo-5-methyl-thiophene-2-carboxylic acid

Step 1: methyl 3-fluoro-4-iodo-5-methyl-thiophene-2-carboxylate

To the solution of methyl 3-fluoro-5-iodo-thiophene-2-carboxylate **Preparation R1g** (286 mg, 1 mmol) in THF (3 ml) TMP.MgCl.LiCl (1 N, in THF/toluene, 1.5 ml, 1.5 mmol) was added dropwise at -45 °C in 5 minutes. After 60 minutes of stirring iodomethane (123 ml, 282 mg, 2 mmol) was added in THF (2 ml) at -45 °C to the mixture and stirred for 2 hours at -40 °C. After warming up, sat.NH₄Cl solution (5 ml, aq.) was added to the mixture while stirring. The mixture was extracted with EEO (4 x 10 ml). The combined organic layer was evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give the product of the title. HRMS calculated for C₇H₆FIO₂S: 299.9117; 300.9200 [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 3.8 (s, 3 H), 2.43 (s, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 159.8, 158.5, 145.1, 109.6, 77.2, 52.8, 19.1.

Step 2: Preparation R1i

Methyl 3-fluoro-4-iodo-5-methyl-thiophene-2-carboxylate (40 mg, 0.133 mmol), lithium-hydroxide monohydrate (11 mg, 0.266 mmol) were stirred in methanol (1 ml) and water (1 ml) at r.t. for 3 hours. The mixture was partially evaporated and the aqueous residue was acidified with 1 N HCl (3 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1i**. ¹H NMR (500 MHz, MSM-d₆): δ ppm 13.41 (brs, 1 H), 2.41 (s, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 160.8, 158, 144.2, 76.9, 19.1.

Preparation R1j: 3-chloro-5-iodo-thiophene-2-carboxylic acid*Step 1: 3-chloro-5-iodothiophene-2-carboxylic acid methyl ester*

To the solution of 3-chlorothiophene-2-carboxylic acid methyl ester (353 g, 2 mmol) in THF (5 ml) at TMP.MgCl.LiCl (1 N, in THF/toluene, 3 ml, 3 mmol) was added dropwise at -45 °C. After 20 minutes of stirring iodine (507 mg, 4 mmol) was added in THF (2 ml) at -45 °C to the mixture. After warming up, sat.NH₄Cl solution (5 ml, aq.) and Na₂S₂O₃ solution (5 ml, 10 % aq.) was added to the mixture while stirring. The mixture was extracted with EEO (4 x 10 ml). The combined organic layer was evaporated. The residue

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was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give the product of the title. HRMS calculated for C₆H₄ClIO₂S: 301.8665; found 301.9000 [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 37.55 (s, 1 H), 3.8 (s, 3 H).

5 ¹³C NMR (125 MHz, MSM-d₆): δ ppm 159.5, 139.4, 130.9, 130.6, 86.8, 53.

Step 2: Preparation R1j

3-chloro-5-iodothiophene-2-carboxylic acid methyl ester (477 mg, 1.58 mmol), lithium-hydroxide monohydrate (132 mg, 3.16 mmol) were stirred in methanol (5 ml) and water (5 ml) at 50 °C for 2.5 hours. The mixture was partially evaporated and the aqueous
10 residue was acidified with 1 N HCl solution (4 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1j**. GC-MS calculated for C₅H₂ClIO₂S: 287.8509; found 243.8 [(M-CO₂, EI) form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 13.6 (brs, 1 H), 7.51 (s, 1 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 160.6, 139.3, 132.4, 130.1, 85.8.

15 **Preparation R1k: 5-chloro-3-fluoro-4-iodo-thiophene-2-carboxylic acid**

Step 1: methyl 5-chloro-3-fluoro-4-iodo-thiophene-2-carboxylate

To the solution of methyl 3-fluoro-5-iodo-thiophene-2-carboxylate (286 mg, 1 mmol) in THF (5 ml) at TMP. MgCl.LiCl (1 N, in THF/toluene, 1.5 ml, 1.5 mmol) was added dropwise at -45 °C in 5 minutes. After 30 minutes of stirring hexachloroethane (236 mg,
20 1 mmol) was added in THF (2 ml) at -45 °C to the mixture. After warming up, sat.NH₄Cl solution (5 ml, aq.) was added to the mixture while stirring. The mixture was extracted with EEO (4 x 10 ml) and the combined organic layers were evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give the product of the title. GC-MS calculated for C₆H₃ClFIO₂S:
25 319.8571; found 319.9 [(M, EI) form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 3.82 (s, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 159.1, 157.9, 135.9, 111.7, 81.1, 53.2.

Step 2: Preparation R1k

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Methyl 5-chloro-3-fluoro-4-iodo-thiophene-2-carboxylate (76 mg, 0.237 mmol), lithium-hydroxide monohydrate (20 mg, 0.474 mmol) were stirred in methanol (4 ml) and water (4 ml) at r.t. for 2 hours. The mixture was partially evaporated and the aqueous residue was acidified with 1 N HCl (2 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1k**. ¹H NMR (400 MHz, MSM-d₆): δ ppm 13.88 (brs, 1 H).

¹⁹F NMR (376.5 MHz, MSM-d₆): δ ppm -101.7.

¹³C NMR (100 MHz, MSM-d₆): δ ppm 157.4.

Preparation R1l: 5-chloro-3-fluoro-4-methyl-thiophene-2-carboxylic acid

Step 1: methyl 5-chloro-3-fluoro-thiophene-2-carboxylate

To the solution of methyl 3-fluoro-thiophene-2-carboxylate (1826 mg, 11.4 mmol) in THF (5 ml) TMP.MgCl.LiCl (1 N, in THF/toluene, 21 ml, 21 mmol) was added dropwise at -45 °C in 5 minutes. After 30 minutes of stirring at -45 °C, hexachloroethane (2.7g, 11.4 mmol) was added at -45 °C to the mixture and stirred for 1 hour at -40 °C. After warming up, sat.NH₄Cl solution (10 ml, aq.) was added to the mixture while stirring. The mixture was extracted with EEO (4 x 10 ml) and the combined organic layers were evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give the product of the title. GC-MS calculated for C₆H₄ClFO₂S: 193.9604; found 193.9 [(M, EI) form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 7.46 (s, 1 H), 3.81 (s, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 159.5, 157.5, 135.3, 120.2, 111.5, 53.

Step 2: methyl 5-chloro-3-fluoro-4-methyl-thiophene-2-carboxylate

To the solution of methyl 5-chloro-3-fluoro-thiophene-2-carboxylate (579 mg, 3 mmol) in THF (3 ml) TMP.MgCl.LiCl (1 N, in THF/toluene, 6 ml, 6 mmol) was added dropwise at -45 °C in 5 minutes. After 60 minutes of stirring, iodomethane (1.3 ml, 2964 mg, 20.9 mmol) was added in THF (2 ml) at -45 °C to the mixture and stirred for 2 hours at -40 °C. After warming up, sat.NH₄Cl solution (5 ml, aq.) was added to the mixture while stirring. The mixture was extracted with EEO (4 x 10 ml) and the combined organic layers were evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm

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column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give the product of the title. GC-MS calculated for $\text{C}_7\text{H}_6\text{ClFO}_2\text{S}$: 207.9761; found 207.9 found [(M, EI) form].

^1H NMR (500 MHz, MSM- d_6): δ ppm 3.81 (s, 3 H), 2.09 (s, 3 H).

^{13}C NMR (125 MHz, MSM- d_6): δ ppm 159.7, 156.4, 130.8, 127, 109.6, 53, 10.5.

5 *Step 3: Preparation R11*

Methyl 5-chloro-3-fluoro-4-methyl-thiophene-2-carboxylate (316 mg, 1.62 mmol), lithium-hydroxide monohydrate (271 mg, 6.46 mmol) were stirred in methanol (5 ml) and water (5 ml) at r.t. for 4 hours. The mixture was partially evaporated and the aqueous residue was acidified with 1 N HCl (2 ml, aq.). The resulted precipitate was filtered off,
10 washed with water and dried to give **Preparation R11**. ^1H NMR (500 MHz, MSM- d_6): δ ppm 13.57 (brs, 1 H), 2.07 (s, 3 H)

^{13}C NMR (125 MHz, MSM- d_6): δ ppm 160.7, 155.9, 129.8, 126.9, 111.4, 10.5

Preparation R1m: [4-methyl-2-(6-methyl-3-pyridyl)thiazol-5-yl]-[(3R,4R)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-1-piperidyl]methanone

15 *Step 1: ethyl (3R,4R)-3-phenylpiperidine-4-carboxylate hydrochloride*

1-*tert*-butyl 4-ethyl (3R,4R)-3-phenylpiperidine-1,4-dicarboxylate (10 g, 30 mmol) was stirred in the mixture of MeCN (100 ml) and cc. HCl solution (7.38 ml, 90 mmol, aq.) at 80 °C for 30 minutes. The reaction mixture was evaporated, and dried over vacuum to give the product of the title.

20 *Step 2: ethyl (3R,4R)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidine-4-carboxylate*

Ethyl (3R,4R)-3-phenylpiperidine-4-carboxylate hydrochloride (7.89 g, 29.9 mmol), 2-bromo-4-methyl-thiazole-5-carboxylic acid (6.64 g, 29.9 mmol) and EDC.HCl (17.2 g, 89.7 mmol) was dissolved in pyridine (200 ml) and stirred at r.t. for 23 hours. The reaction
25 mixture was evaporated. To the residue, water (200 ml) was added and extracted with DCM (3 x 50 ml). The combined organic layer was dried over MgSO_4 and evaporated to give the product of the title. HRMS calculated for $\text{C}_{19}\text{H}_{21}\text{BrN}_2\text{O}_3\text{S}$: 436.0456; found 437.0546 [(M+H) $^+$ form].

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¹H NMR (500 MHz, MSM-d₆): δ ppm 7.36-7.19 (m, 5 H), 4.96-2.74 (vbrs, 4 H), 3.82 (q, 2 H), 3.03 (m, 1 H), 2.87 (m, 1 H), 2.34 (s, 3 H), 1.98/1.62 (m+m, 2 H), 0.86 (t, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 160.5, 151.6, 136.3, 129.2, 60.1, 47.3, 45.3, 29.2, 16.4, 14.2.

5 *Step 3: ethyl (3R,4R)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidine-4-carboxylate*

In 8 separated microwave tubes, ethyl (3R,4R)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidine-4-carboxylate (8 x 1.87 g, 34.2 mmol), 2-methylpyridine-5-boronic acid (8 x 1.17 g, 68.4 mmol), ATAphos*PdCl₂ (8 x 303 mg, 3.4 mmol) and
10 Cs₂CO₃ (8 x 4.18 g, 102.6 mmol) were dissolved in THF (8 x 25 ml) and water (8 x 15 ml). The 8 tubes were microwave irradiated at once at 80 °C for 2 hours (Anton-Paar Multiwave Pro). The organic layers of 8 tubes were combined, partially evaporated and purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give the product of the title. HRMS calculated for C₂₅H₂₇N₃O₃S:
15 449.1773; found 450.1860[(M+H)⁺ form].

¹H NMR (400 MHz, MSM-d₆): δ ppm 8.98 (d, 1 H), 8.17 (dd, 1 H), 7.4 (d, 1 H), 7.36-7.16 (m, 5 H), 5-2.75 (vbrs, 4 H), 3.83 (q, 2 H), 3.05 (m, 1 H), 2.87 (m, 1 H), 2.53 (s, 3 H), 2.43 (s, 3 H), 2.01/1.64 (dm+qm, 2 H), 0.87 (t, 3 H).

¹³C NMR (100 MHz, MSM-d₆): δ ppm 146.7, 134.4, 124, 60.1, 47.3, 45.5, 29.2, 24.3, 16.5,
20 14.2.

Step 4: (3R,4R)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidine-4-carboxylic acid

Ethyl (3R,4R)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidine-4-carboxylate (7.48 g, 16.64 mmol) and lithium-hydroxide hydrate (1.75 g, 41.6 mmol) were stirred in the mixture of EtOH (30 ml) and water (10 ml) at 75 °C for
25 3.5 hours. The reaction mixture was partially evaporated, to residue was acidified (to pH = 4.5-5.5) with HCl solution (1 N, aq.) and the resulted suspension was filtered. The solid compound on the filter was washed with water and dried to give the product of the title. HRMS calculated for C₂₃H₂₃N₃O₃S: 421.146; found 422.1544 [(M+H)⁺ form].

30 ¹H NMR (400 MHz, MSM-d₆): δ ppm 11.82 (brs, 1 H), 8.97 (d, 1 H), 8.15 (dd, 1 H), 7.39

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(d, 1 H), 7.35-7.18 (m, 5 H), 4.34-4.05 (brm, 4 H), 3.01-2.84 (m, 2 H), 2.54 (s, 3 H), 2.44 (s, 3 H), 2.06/1.66 (m+m, 2 H).

¹³C NMR (100 MHz, MSM-d₆): δ ppm 146.8, 134.4, 123.8, 29.5, 24.3, 16.5.

Step 5: 1-{[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-one

(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidine-4-carboxylic acid (3786 mg, 8.98 mmol), piperidin-4-one hydrate hydrochloride (1518 mg, 9.88 mmol) and EDC.HCl (5.16 g, 26.94 mmol) were stirred in pyridine (30 ml) at r.t. for 16 hours. The reaction mixture was evaporated, the residue was taken in MeOH (20 ml) and poured into water (120 ml) and extracted with DCM (3 x 60 ml). The combined organic layer was washed with water, brine, dried over MgSO₄ and evaporated to give the product of the title. HRMS calculated for C₂₃H₂₃N₃O₃S: 502.2039; found 503.2088 [(M+H)⁺ form].

¹H NMR (400 MHz, MSM-d₆): δ ppm 8.98 (brs, 1 H), 8.17 (dd, 1 H), 7.4 (d, 1 H), 7.36-7.13 (m, 5 H), 4.92-2.76 (m, 10 H), 2.53 (s, 3 H), 2.45 (s, 3 H), 2.25-1.52 (m, 6 H).

Step 6: Preparation R1m

1-{[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-one (3.89 g, 7.74 mmol) and trimethylsulfoxonium-iodide (2.09 g, 9.3 mmol) was stirred in MeCN (19 ml) at r.t. and solution of NaOH (309 mg, 9.3 mmol) in water (0.4 ml) was added to the mixture. Then the reaction mixture was stirred at 70 °C for 2 hours. The reaction mixture was poured into water (200 ml) and neutralized with aqueous HCl solution (1 N, 9 ml) and extracted with DCM (3 x 80 ml). The combined organic layer was washed with water and brine and evaporated to give **Preparation R1m** as solid foam. HRMS calculated for C₂₉H₃₂N₄O₃S: 516.2195; found 517.2267 [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 8.98 (brs, 1 H), 8.17 (dd, 1 H), 7.4 (d, 1 H), 7.37-7.15 (brs/brs, 5 H), 3.82-0.88 (m, 14 H), 3.53 (m, 1 H), 2.97 (brm, 1 H), 2.56 (m, 2 H), 2.53 (s, 3 H), 2.44 (s, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 164.1, 160.8, 152.4, 146.8, 134.5, 125.6, 124.1, 57.4/57.1, 53.4/53.1, 42.9/42.8, 24.5, 16.7.

Preparation R1n: 3-[[4-Hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]pyrimidin-4-one

Step 1: 2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane

Preparation R1a (2.81 g, 18.3 mmol) was dissolved in THF (25 ml) cooled to 0 °C, and
5 NaH (60 % disp., 1.1 g, 27.4 mmol) was added to the mixture and stirred for 1 hour. Then
SEM-Cl (8.1 ml, 45.76 mmol) was added to the mixture and allowed to warm up to r.t.
After 2.5 hours, water (25 ml) was added to the reaction mixture and extracted with EEO
(2 x 30 ml). The combined organic layer was dried over MgSO₄ and evaporated. The
residue was purified by flash chromatography (220 g Silica Gold column, heptane-EEO
10 gradient) to give the product of the title.

Step 2: 7-(2-Trimethylsilylethoxymethyl)-3H-pyrrolo[2,3-d]pyrimidin-4-one

2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (3.5 g,
12.3 mmol) and lithium-hydroxide hydrate (5.17 g, 123 mmol) were stirred at 100 °C for
116 hours in the mixture of PDO (20 ml) and water (20 ml). The reaction mixture was
15 filtered, the filtrate was acidified with aqueous HCl solution (1 N, 80 ml), and the resulted
solid compound was filtered off, washed with water and dried to give the product of the
title.

*Step 3: tert-Butyl 4-hydroxy-4-[[4-oxo-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]
pyrimidin-3-yl]methyl]piperidine-1-carboxylate*

20 7-(2-Trimethylsilylethoxymethyl)-3H-pyrrolo[2,3-d]pyrimidin-4-one (3.11g, 11.7 mmol),
Preparation R1e (2.75 g, 2.9 mmol) and K₂CO₃ (1.78 g, 12.9 mmol) were stirred in DMF
(70 ml) at 60 °C for 40 hours. To the reaction mixture water was added, the resulted solid
compound was filtered off, washed with water to give the product of the title. HRMS
calculated for C₂₃H₃₈N₄O₅Si: 478.2611; found 479.2694 [(M+H)⁺ form].

25 *Step 4: 3-[(4-Hydroxy-4-piperidyl)methyl]-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]
pyrimidin-4-one*

tert-Butyl 4-hydroxy-4-[[4-oxo-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]pyrimidin-

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3-yl]methyl]piperidine-1-carboxylate (1.84 g, 3.86 mmol) was dissolved in DCM (50 ml) and formic acid (5 ml) and TFA (1317 mg, 0.885 ml, 11.58 mmol) were added then the mixture was stirred for 4 days at r.t. To the reaction mixture aqueous sodium-hydroxide solution (1 N, 100 ml) was added, then extracted with DCM (50 ml). The organic layer was dried over MgSO₄, filtered, evaporated to give the product of the title. HRMS calculated for C₁₈H₃₀N₄O₃Si: 378.2087; found 379.2176 [(M+H)⁺ form].

Step 5: tert-Butyl (3R,4R)-4-[4-hydroxy-4-[[4-oxo-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]pyrimidin-3-yl]methyl]piperidine-1-carbonyl]-3-phenyl-piperidine-1-carboxylate

3-[(4-hydroxy-4-piperidyl)methyl]-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]pyrimidin-4-one (1.527 g, 3.77 mmol), (3R,4R)-1-tert-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid (1.152 g, 3.77 mmol) and EDC.HCl (1.446 g, 7.54 mmol) were stirred in pyridine (15 ml) overnight at r.t. The reaction mixture was evaporated to Celite, and purified by flash chromatography (DCM-MeOH) to give the product of the title. HRMS calculated for C₃₅H₅₁N₅O₆Si: 665.3609; found 666.3696 [(M+H)⁺ form].

Step 6: Preparation R1n

The solution of *tert*-butyl (3R,4R)-4-[4-hydroxy-4-[[4-oxo-7-(2-trimethylsilylethoxymethyl)pyrrolo[2,3-d]pyrimidin-3-yl]methyl]piperidine-1-carbonyl]-3-phenyl-piperidine-1-carboxylate (1.6 g, 2.4 mmol), formic acid (3 ml) and TFA (820 mg, 0.55 ml, 7.2 mmol) in DCM (30 ml) was stirred at r.t. for 4 days. To the reaction mixture potassium-carbonate (15 g) was added as aqueous solution and extracted with DCM. The organic layer was evaporated to give **Preparation R1n**. HRMS calculated for C₃₀H₄₃N₅O₄Si: 565.3084; found 566.3138 [(M+H)⁺ form].

Preparation R1o: 5-bromo-4-(tert-butoxycarbonylamino)thiophene-2-carboxylic acid

4-Amino-5-bromo-thiophene-2-carboxylic acid (500 mg, 2.25 mmol) was dissolved in the mixture of PDO (2 ml) and water (2 ml) and sodium-hydroxide (194 mg, 4.8 mmol) was added to the mixture at 0 °C. Then di-*tert*-butyl dicarbonate (1768 mg, 8.1 mmol) was added to the mixture and stirred at 0 °C for 3 hours, then the reaction mixture was allowed to warm up to r.t. and stirred for 116 hours. The reaction mixture water was added and

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acidified by aqueous HCl solution (1 N, 4 ml). The resulted solid was filtered off washed with water and dried. The residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient, resulted as ammonium salt) to give **Preparation R1o**. ¹H NMR (500 MHz, MSM-d₆): δ ppm 8.71 (s, 1 H), 7.44 (brs, 4 H), 7.24 (s, 1 H), 1.44 (s, 9 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 125.8, 28.5.

¹⁵N NMR (470.6 MHz, MSM-d₆): δ ppm 99.

Preparation R1p: 4-nitro-5-(4-pyridyl)thiophene-2-carboxylic acid

Using **General Procedure 9** starting from methyl 5-chloro-4-nitro-thiophene-2-carboxylate and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reactant, the crude product (200 mg, 0.75 mmol) was stirred with lithium-hydroxide hydrate (60 mg, 1.5 mmol) in mixture of water (2 ml) and methanol (10 ml) at r.t. for 4 hours. The reaction mixture was neutralized with aqueous HCl solution (1 N, 1.5 ml). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1p**. ¹H NMR (500 MHz, MSM-d₆): δ ppm 14.18 (vbrs, 1 H), 8.74 (brs, 2 H), 8.19 (s, 1 H), 7.65 (m, 2 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 161.8, 150.4, 145.9, 143.6, 138.2, 134.4, 129.2, 124.3.

Preparation R1q-(3S,4R): (3S,4R)-1-benzyl-3-(2-thienyl)piperidine-4-carboxylic acid

and

Preparation R1q-(3R,4S): (3R,4S)-1-benzyl-3-(2-thienyl)piperidine-4-carboxylic acid

To a stirred suspension of sodium-hydride (60 % disp., 1.4 g, 35.1 mmol) in abs. DEE (135 ml) ethyl 1-benzyl-3-oxo-piperidine-4-carboxylate hydrochloride (3.54 g, 11.9 mmol) was added at 0 °C. After 30 minutes of stirring trifluoromethanesulfonic anhydride (3.88 g, 2.28 ml, 13.5 mmol) was added dropwise to the reaction mixture and stirred for 3 hours while temperature allowed to warm up to r.t. To the reaction mixture water (100 ml) was added, the layers were separated, the aqueous layer was washed with DEE. The DEE layer was dried over MgSO₄, and evaporated.

From a part of the prepared ethyl 1-benzyl-5-(trifluoromethylsulfonyloxy)-3,6-dihydro-2H-pyridine-4-carboxylate (2.184 g, 5.55 mmol), 2-thienylboronic acid (925 mg, 7.23 mmol),

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ATAphos*PdCl₂ (400 mg, 0.55 mmol), Cs₂CO₃ (3.63 g, 11.1 mol) was dissolved in THF (11 ml) and water (11 ml). The mixture was flushed with nitrogen and microwave irradiated at 82 °C for 140 minutes. The layers were separated, the organic layer was evaporated to Celite and purified by flash chromatography (Heptane-EEO, gradient).

5 The previously prepared ethyl 1-benzyl-5-(trifluoromethylsulfonyloxy)-3,6-dihydro-2H-pyridine-4-carboxylate (2.184 g, 5.55 mmol), 2-thienylboronic acid (925 mg, 7.23 mmol), ATAphos*PdCl₂ (400 mg, 0.55 mmol), and Cs₂CO₃ (3.63 g, 11.1 mol) were dissolved in the mixture of THF (11 ml) and water (11 ml). The mixture was flushed with nitrogen and microwave irradiated at 82 °C for 140 minutes. The layers were separated, the organic
10 layer was evaporated to Celite and purified by flash chromatography (Heptane-EEO, gradient).

The resulted ethyl 1-benzyl-5-(2-thienyl)-3,6-dihydro-2H-pyridine-4-carboxylate (2.85 g, 8.7 mmol), Pd on carbon (3 x 1.5 g, 10 %), HCl solution (1 N in ether, 8.7 ml, 8.7 mmol) and EtOH (65 ml) were added into an autoclave. The autoclave was closed, inertized,
15 vacuumized and filled with hydrogen (8 bar) and the reaction mixture was stirred in autoclave at 90 °C for 420 hours. During the course of reaction, the catalyst was filtered out and replaced twice by fresh one. The reaction mixture was removed from the autoclave and filtered through Celite and the filtrate was evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN,
20 gradient).

The resulted methyl *cis*-1-benzyl-3-(2-thienyl)piperidine-4-carboxylate (664 mg, 2 mmol) was dissolved in NaOEt solution (1 N, in EtOH, freshly prepared, 10 ml, 10 mmol) and stirred at 75 °C for 3 hours. Then water (5 ml) was added to the reaction mixture and continued stirring at 75 °C for 4 hours. The reaction mixture was partially evaporated, then
25 neutralized by aqueous 1 N HCl solution, the solid was filtered off, washed with water and dried. The two enantiomers were separated by chiral LC to give **Preparation R1q-(3S,4R)** and **Preparation R1q-(3R,4S)**. HRMS calculated for C₁₇H₁₉NO₂S: 301.1136; found 302.1217 [(M+H)⁺ form].

¹H NMR (400 MHz, MSM-d₆): δ ppm 12.15 (brs, 1 H), 7.37-7.19 (m, 5 H), 7.32 (dd, 1 H),
30 6.91 (dd, 1 H), 6.88 (dd, 1 H), 3.51 (s, 2 H), 3.24 (tm, 1 H), 2.9-2.05 (m, 4 H), 2.39 (tm, 1 H), 1.91-1.67 (dm/qm, 2 H).

Preparation R1s: (4-methyl-2-phenyl-thiazol-5-yl)-[(3R,4R)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-1-piperidyl]methanone

Step 1: 1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-one hydrochloride

tert-butyl (3R,4R)-4-(4-oxopiperidine-1-carbonyl)-3-phenylpiperidine-1-carboxylate
5 (obtained in Step 1 of the **Preparation R1f**, 4.77 g, 12.34 mmol) was stirred in PDO (20 ml) and aqueous HCl solution (20 ml, 1 N) at 70 °C for 1 hour. The reaction mixture was evaporated and dried to give the product of the title. HRMS calculated for C₁₇H₂₂N₂O₂: 286.1681; found 287.1755 [(M+H)⁺ form].

¹H NMR (400 MHz, MSM-d₆): δ ppm 9.68 (brd, 1 H), 9.14 (brq, 1 H), 7.40-7.18 (m, 5H),
10 3.73/3.31 (m/m, 2 H), 3.73/3.31 (m/m, 2 H), 3.56 (m, 1 H), 3.33/3.10 (m/m, 2 H), 3.31-3.13 (m, 2 H), 3.26 (m, 1 H), 2.17/1.56 (m/m, 2 H), 2.15/1.81 (m/m, 2 H), 2.03-1.87 (m, 2 H).

Step 2: 1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]piperidin-4-one

15 1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-one hydrochloride (3.42 g, 10.6 mmol), EDC.HCl (6.64 g, 34.6 mmol) and 4-methyl-2-phenyl-thiazole-5-carboxylic acid (2.32 g, 10.6 mmol) were stirred in pyridine (60 ml) at r.t. for 20 hours. The reaction mixture was evaporated to Celite and purified by flash chromatography (DCM-MeOH/DCM, gradient) to give the product of the title. HRMS calculated for C₂₈H₂₉N₃O₃S: 487.1930; found 488.1991 [(M+H)⁺ form].

¹H NMR (400 MHz, MSM-d₆): δ ppm 7.93/7.51 (brs/brs, 5 H), 7.35/7.15 (brs/brs, 5 H), 4.80-2.80 (brm, 4H), 3.74/3.63 (m/brm, 2 H), 3.74/3.32 (m/m, 2 H), 3.56 (td, 1 H), 2.99 (td, 1 H), 2.44 (s, 3 H), 2.19/1.61 (m/m, 2 H), 2.16/1.84 (m/m, 2 H), 1.89/1.66 (brm/brm, 2 H).

25 *Step 3: Preparation R1s*

To the stirred suspension of 1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]piperidin-4-one (4.5 g, 9.23 mmol) and trimethylsulfoxonium-iodide (2.44 g, 11.1 mmol) in MeCN (25 ml) aqueous sodium-hydroxide (40 w %, 443 mg NaOH/0.664 ml water) was added at r.t., stirred for

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160 minutes. The reaction mixture was diluted with water (20 ml) and MeCN was evaporated. The residue was extracted with DCM and the organic layer was evaporated to give **Preparation R1s**. HRMS calculated for $C_{29}H_{31}N_3O_3S$: 501.2086; found 502.2160 [(M+H)⁺ form].

¹H NMR (400 MHz, MSM-d₆): δ ppm 7.93 (m, 2 H), 7.51 (m, 3 H), 7.40-7.10 (brs/brs, 5 H), 4.88-2.88 (brm, 4H), 3.82 - 2.97 (m, 4 H), 3.54 (m, 1 H), 2.97 (m, 1 H), 2.56 (m, 2 H), 2.43 (s, 3 H), 1.83/1.63 (brd/brq, 2 H), 1.45-0.86 (m, 2 H).

Preparation R1t: 1-ethenyl-1H-indole-2-carboxylic acid

The mixture of ethyl indole-2-carboxylate (2 g, 10.57 mmol), palladium(II)-acetate (119 mg, 0.53 mmol), copper(II)-bromide (2.37 g, 10.57 mmol), vinyl-acetate (20 ml, 248.7 mmol) and sodium-acetate (2.6 g, 31.7 mmol) was heated at 80 °C for 28 hours. The reaction mixture was evaporated to Celite and purified by flash chromatography (heptane-EEO, 0-5% gradient).

The mixture of the resulted ester (1.08 g, 5.017 mmol), lithium-hydroxide hydrate (1.05 g, 25.1 mmol) in ethanol and water (10-10 ml) was stirred at 80 °C for 90 minutes. The reaction mixture was acidified with aqueous HCl solution (1 N, 30 ml) at 0-5 °C, the formed precipitate was filtered off, washed with water (5 x 20 ml) and dried to give **Preparation R1t**. ¹H NMR (400 MHz, MSM-d₆): δ ppm 13.22 (s, 1 H), 7.75 (m, 3 H), 7.51 (m, 1 H), 7.22 (t, 1 H), 5.48 (d, 1 H), 5.28 (d, 1 H)

Preparation R1u: 5-bromo-1-vinyl-pyrrole-2-carboxylic acid

The mixture of methyl 5-bromo-1H-pyrrole-2-carboxylate (1.2 g, 5.88 mmol), palladium(II)-acetate (132 mg, 0.588 mmol), copper(II)-bromide (2.63 g, 11.76 mmol), vinyl-acetate (27 ml, 294 mmol) and sodium-acetate (2.9 g, 35.3 mmol) was heated at 80 °C for 28 hours. The reaction mixture was evaporated to Celite and purified by flash chromatography (heptane-EEO, 0-25% gradient).

The mixture of the resulted ester (403 mg, 1.75 mmol), lithium-hydroxide hydrate (368 mg, 8.75 mmol) in ethanol and water (4-4 ml) was stirred at 80 °C for 60 minutes. The reaction mixture was acidified with aqueous HCl solution (1 N, 10 ml) at 0-5 °C. The formed precipitate was filtered off, washed with water (5 x 20 ml) and dried to give

Preparation R1u. ¹H NMR (400 MHz, MSM-d₆): δ ppm 12.63 (s, 1 H), 7.11 (m, 1 H),

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6.94 (d, 1 H), 6.45 (d, 1 H), 5.42 (m, 2 H)

Preparation R1v: 4-bromo-1-vinyl-pyrrole-2-carboxylic acid

The mixture of methyl 4-bromo-1H-pyrrole-2-carboxylate (1.2 g, 5.88 mmol), palladium(II)-acetate (132 mg, 0.588 mmol), copper(II)-bromide (2.63 g, 11.76 mmol), vinyl-acetate (27 ml, 294 mmol) and sodium-acetate (2.9 g, 35.3 mmol) was heated at 80 °C for 21 hours. The reaction mixture was evaporated to Celite and purified by flash chromatography (heptane-EEO, 0-5% gradient).

The mixture of the resulted ester (338 mg, 1.47 mmol), lithium-hydroxide hydrate (908 mg, 7.35 mmol) in ethanol and water (3.5-3.5 ml) was stirred at 80 °C for 105 minutes. The reaction mixture was acidified with aqueous HCl solution (1 N, 9 ml) at 0-5 °C. The formed precipitate was filtered off, washed with water (2 x 5 ml) and dried to give **Preparation R1v**. ¹H NMR (500 MHz, MSM-d6): δ ppm 12.93 (brs, 1 H), 7.85 (d, 1 H), 7.84 (dd, 1 H), 6.94 (d, 1 H), 5.5/4.9 (dd+dd, 2 H).

¹³C NMR (125 MHz, MSM-d6): δ ppm 131.4, 124.1, 123.4, 120.3, 102.8, 97.9

Preparation R1w: 4,5-dichloro-3-fluoro-thiophene-2-carboxylic acid

Step 1: methyl 4,5-dichloro-3-fluoro-thiophene-2-carboxylate

To the solution of methyl 3-fluoro-thiophene-2-carboxylate (1826 mg, 11.4 mmol) in THF (5 ml) TMP.MgCl.LiCl (1 N, in THF/toluene, 21 ml, 21 mmol) was added dropwise at -45 °C in 5 minutes. After 30 minutes of stirring at -45 °C, hexachloroethane (2.7g, 11.4 mmol) was added at -45 °C to the mixture and stirred for 1 hour at -40 °C. After warming up, sat.NH₄Cl solution (10 ml, aq.) was added to the mixture while stirring. The mixture was extracted with EEO (4 x 10 ml). The combined organic layer was evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give the product of the title. GC-MS calculated for C₆H₃Cl₂FO₂S: 227.9215; found 227.9 found [(M, EI) form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 3.85 (s, 3 H).

¹³C NMR (125 MHz, MSM-d₆): δ ppm 159, 152.8, 130.5, 115.5, 110.8, 53.4.

Step 2: Preparation R1w

Methyl 4,5-dichloro-3-fluoro-thiophene-2-carboxylate (130 mg, 0.567 mmol), lithium-hydroxide monohydrate (95 mg, 2.27 mmol) were stirred in methanol (3 ml) and water (3 ml) at r.t. for 3 hours. The mixture was partially evaporated and the aqueous residue was acidified with 1 N HCl (4 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1w**. ^{13}C NMR (125 MHz, MSM-d_6): δ ppm 160, 152.3, 129.5, 115.3, 112.8.

Preparation R1x: 2-(6-methyl-3-pyridyl)thiazole-5-carboxylic acid

Ethyl 2-(6-methyl-3-pyridyl)thiazole-5-carboxylate (745 mg, 3 mmol), lithium-hydroxide monohydrate (630 mg, 15 mmol) were stirred in ethanol (5 ml) and water (5 ml) at r.t. for 8 hours. The mixture was partially evaporated and the aqueous residue was acidified with 1N HCl (15 ml, aq.). The resulted precipitate was filtered off, washed with water and dried to give **Preparation R1x**. HRMS calculated for $\text{C}_{10}\text{H}_8\text{N}_2\text{O}_2\text{S}$: 220.0307; found 221.0379 [(M+H) $^+$ form].

^1H NMR (500 MHz, MSM-d_6): δ ppm 13.69 (brs, 1 H), 9.07 (d, 1 H), 8.45 (s, 1 H), 8.26 (dd, 1 H), 7.44 (d, 1 H), 2.55 (s, 3 H). ^{13}C NMR (125 MHz, MSM-d_6): δ ppm 149.3, 147.1, 134.9, 124.2, 24.5

Preparation R2b: 7-methyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and iodomethane as alkylating agent, **Preparation R2b** was obtained. HRMS calculated for $\text{C}_7\text{H}_7\text{N}_3\text{O}$: 149.0589; found 150.0668 [(M+H) $^+$ form].

^1H -NMR (500 MHz, MSM-d_6): δ (ppm) 11.85 (brs, 1 H), 7.88 (brs, 1 H), 7.09 (d, 1 H), 6.44 (d, 1 H), 3.70 (m, 1 H).

^{13}C -NMR (125 MHz, MSM-d_6): δ (ppm) 158.7, 147.7, 143.8, 125.1, 108.1, 101.7, 31.8.

Preparation R2c: 7-ethyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and iodoethane as reagents, **Preparation R2c** was obtained. HRMS calculated for $\text{C}_8\text{H}_9\text{N}_3\text{O}$: 163.0746; found 164.0823 [(M+H) $^+$ form].

^1H -NMR (500 MHz, MSM-d_6): δ (ppm) 11.38 (brs, 1 H), 7.87 (d, $J=2.0$ Hz, 1 H), 7.16 (d,

J=3.4 Hz, 1 H), 6.45 (d, J=3.4 Hz, 1 H), 4.14 (q, J=7.1 Hz, 2 H), 1.34 (t, J=7.1 Hz, 3 H).

Preparation R2d: 7-(propan-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 2-iodopropane as reagents, **Preparation R2d** was obtained. HRMS calculated for C₉H₁₁N₃O: 177.0902; found 178.0979 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.83 (brs, 1 H), 7.87 (s, 1 H), 7.24 (d, 1 H), 6.47 (d, 1 H), 4.85 (sept., 1 H), 1.42 (d, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 146.8, 143.5, 120.7, 108.2, 102, 46.5, 23.

¹⁵N-NMR (50.6 MHz, MSM-d6): δ (ppm) 168.

Preparation R2g: 7-cyclopropyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and cyclopropylboronic acid as reagents, **Preparation R2g** was obtained. HRMS calculated for C₉H₉N₃O: 175.0746; found 176.0819 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.88 (brs, 1 H), 7.89 (brs, 1 H), 7.05 (d, 1 H), 6.4 (d, 1 H), 3.53 (m, 1 H), 1.06-0.92 (m, 4 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.7, 148.9, 143.8, 123.4, 108.8, 101.6, 27.5, 6.6.

Preparation R2h: 7-cyclobutyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and cyclobutyl bromide as reagents, **Preparation R2h** was obtained. HRMS calculated for C₁₀H₁₁N₃O: 189.0902; found 190.0974 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.85 (brs, 1 H), 7.88 (brs, 1 H), 7.09 (d, 1 H), 6.44 (d, 1 H), 3.70 (m, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.7, 147.7, 143.8, 125.1, 108.1, 101.7, 31.8.

Preparation R2i: 7-cyclopentyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 4** starting from **Preparation R1a** and cyclopentanol as reagents, **Preparation R2i** was obtained. HRMS calculated for C₁₁H₁₃N₃O: 203.1059; found 204.1139 [(M+H)⁺ form].

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¹H-NMR (400 MHz, MSM-d6): δ (ppm) 11.84 (brs, 1 H), 7.87 (d, 1 H), 7.21 (d, 1 H), 6.46 (d, 1 H), 4.97 (m, 1 H), 2.16-1.57 (m, 8 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 143.5, 121.3, 102, 55.6.

Preparation R2j: 7-cyclohexyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

5 Using **General Procedure 4** starting from **Preparation R1a** and cyclohexanol as reagents, **Preparation R2j** was obtained. HRMS calculated for C₁₂H₁₅N₃O: 217.1215; found 218.1293 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 11.83 (brs, 1 H), 7.86 (d, 1 H), 7.23 (d, 1 H), 6.46 (d, 1 H), 4.45 (m, 1 H), 1.97-1.13 (m, 10 H).

10 ¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 143.4, 121.1, 101.8, 53.8.

Preparation R2k: 7-(1-methylpiperidin-4-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 4** starting from **Preparation R1a** and 4-hydroxy-1-methylpiperidine as reagents, **Preparation R2k** was obtained. HRMS calculated for C₁₂H₁₆N₄O: 232.1324; found 233.1405 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.82 (brs, 1 H), 7.86 (d, 1 H), 7.29 (d, 1 H), 6.46 (d, 1 H), 4.44 (m, 1 H), 2.89/2.05 (m, 4 H), 2.22 (s, 3 H), 2.02/1.82 (m, 4 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 143.9, 121.2, 102.1, 55.1, 52.1, 46.1, 32.3.

Preparation R2l: 7-(tetrahydro-2*H*-pyran-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

20 Using **General Procedure 4** starting from **Preparation R1a** and tetrahydro-4-pyranol as reagents, **Preparation R2l** was obtained. HRMS calculated for C₁₁H₁₃N₃O₂: 219.1008; found 220.1082 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 11.88 (brs, 1 H), 7.88 (d, 1 H), 7.29 (d, 1 H), 6.48 (d, 1 H), 4.71 (m, 1 H), 3.98/3.49 (m+m, 4 H), 2.05/1.82 (m+m, 4 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 143.5, 121.2, 102, 66.7, 51.3, 33.3.

Preparation R2m: 7-(prop-2-yn-1-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1b** (instead of

Preparation R1a) and 3-bromoprop-1-yne as reagents (without the hydrolysis step), the crude methoxypyrimidine product (400 mg, 2.3 mmol) was dissolved in PDO (4 ml) and aqueous HCl solution (37 %, 0.18 ml) was added. The mixture was heated for 100 °C for 30 minutes in a Schlenk tube. After cooling DIPO (4 ml) was added to the reaction mixture, the resulted precipitate was filtered off and dried to give **Preparation R2m**. HRMS calculated for C₉H₇N₃O: 173.0589; found 174.0665 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.98 (brs, 1 H), 7.93 (s, 1 H), 7.19 (d, 1 H), 6.5 (d, 1 H), 4.98 (d, 2 H), 3.42 (t, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.6, 147.3, 144.3, 123.6, 102.5, 79.4, 76, 34.1.

Preparation R2n: 7-(2-methylpropyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 1-bromo-2-methylpropane as reagents, **Preparation R2n** was obtained. HRMS calculated for C₁₀H₁₃N₃O: 191.1059; found 192.1132 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.84 (brs, 1 H), 7.86 (s, 1 H), 7.12 (d, 1 H), 6.45 (d, 1 H), 3.92 (d, 2 H), 2.1 (sept., 1 H), 0.82 (d, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.7, 143.7, 124.5, 108, 101.6, 52, 29.6, 20.2.

Preparation R2o: 7-(2,2,2-trifluoroethyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 2,2,2-trifluoroethyl trifluoromethanesulfonate as reagents, **Preparation R2o** was obtained. HRMS calculated for C₈H₆N₃OF₃: 217.0463; found 218.0543 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.08 (brs, 1 H), 7.97 (s, 1 H), 7.19 (d, 1 H), 6.57 (d, 1 H), 5.06 (q, 2 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.5, 148.4, 144.9, 124.7, 124.4, 108.8, 103.2, 45.1.

¹⁹F-NMR (376.5 MHz, MSM-d6): δ (ppm) -70.3.

Preparation R2p: 7-(2,2-difluoroethyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 2-iodo-1,1-difluoroethane as reagents, **Preparation R2p** was obtained. HRMS calculated for

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C₈H₇N₃OF₂: 199.0557; found 200.0634 ((M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d₆) δ ppm 11.99 (brs, 1 H), 7.93 (s, 1 H), 7.16 (d, 1 H), 6.53 (d, 1 H), 6.37 (tt, 1 H), 4.6 (td, 2 H).

¹³C-NMR (400 MHz, MSM-d₆) δ ppm 144.4, 124.8, 114.3, 102.5, 46.2.

5 **Preparation R2q: 7-(cyclopropylmethyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one**

Using **General Procedure 1** starting from **Preparation R1a** and cyclopropylmethyl bromide as reagents, **Preparation R2q** was obtained. HRMS calculated for C₁₀H₁₁N₃O: 189.0902; found 190.0980 [(M+H)⁺ form].

10 ¹H-NMR (500 MHz, MSM-d₆): δ (ppm) 11.84 (s, 1 H), 7.87 (s, 1 H), 7.2 (d, 1 H), 6.45 (d, 1 H), 3.97 (d, 2 H), 1.21 (m, 1 H), 0.52-0.35 (m, 4 H).

¹³C-NMR (125 MHz, MSM-d₆): δ (ppm) 158.7, 147.3, 143.7, 124, 108.1, 101.7, 49, 12.3, 4.07.

Preparation R2r: 7-(cyclobutylmethyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

15 Using **General Procedure 1** starting from **Preparation R1a** and (bromomethyl)cyclobutane as reagents, **Preparation R2r** was obtained. HRMS calculated for C₁₁H₁₃N₃O: 203.1059; found 204.1134 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆): δ (ppm) 11.83 (brs, 1 H), 7.87 (d, 1 H), 7.12 (d, 1 H), 6.43 (d, 1 H), 4.13 (d, 2 H), 2.72 (m, 1 H), 1.92/1.74 (m+m, 4 H), 1.82 (m, 2 H).

¹³C-NMR (125 MHz, MSM-d₆): δ (ppm) 143.7, 124.2, 101.7, 49.6, 36, 25.6, 18.

20 **Preparation R2s: 7-(buta-2,3-dien-1-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one**

Using **General Procedure 1** starting from **Preparation R1b** (instead of **Preparation R1a**) and 4-bromobuta-1,2-diene as reagents (without the hydrolysis step), the crude methoxypyrimidine product (300 mg, 1.65 mmol) was dissolved in PDO (4 ml) and aqueous HCl solution (37 %, 0.18 ml) was added. The mixture was heated for 100 °C
25 for 30 minutes in a Schlenk tube. After cooling, the reaction mixture was evaporated to give **Preparation R2s**. HRMS calculated for C₁₀H₉N₃O: 187.0745; found 188.0821 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆): δ (ppm) 11.91 (brs, 1 H), 7.89 (s, 1 H), 7.12 (d, 1 H), 6.46 (d, 1 H), 5.48 (m, 1 H), 4.87 (m, 2 H), 4.73 (m, 2 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 208.3, 158.7, 147.4, 143.9, 123.9, 108.2, 102.1, 88.3, 78.1, 43.

Preparation R2t: 7-[3-(dimethylamino)propyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

5 Using **General Procedure 1** starting from **Preparation R1a** and 3-dimethylaminopropyl chloride hydrochloride as reagents, **Preparation R2t** was obtained. HRMS calculated for C₁₁H₁₆N₄O: 220.1324; found 221.1401 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.84 (brs, 1 H), 7.88 (s, 1 H), 7.13 (d, 1 H), 6.44 (d, 1 H), 4.12 (t, 2 H), 2.15 (t, 2 H), 2.1 (s, 6 H), 1.85 (quint, 2 H).

10 ¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.4, 143.8, 124.2, 108.2, 101.7, 56.4, 45.6, 43, 28.6.

Preparation R2u: 7-(2-fluoroethyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 1-fluoro-2-iodoethane as reagents, **Preparation R2u** was obtained. HRMS calculated for C₈H₈NOF: 181.0651; found 182.0728 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6) δ ppm 11.91 (brs, 1 H), 7.9 (s, 1 H), 7.17 (d, 1 H), 6.49 (d, 1 H), 4.74 (dt, 2 H), 4.43 (dt, 2 H).

¹³C-NMR (100 MHz, MSM-d6) δ ppm 144, 124.3, 102, 83.1, 45.1.

Preparation R2v: 7-[2-(dimethylamino)ethyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

20 Using **General Procedure 1** starting from **Preparation R1a** and 2-bromo-*N,N*-dimethylethylamine hydrobromide as reagents, **Preparation R2v** was obtained. HRMS calculated for C₁₀H₁₄N₄O: 206.1168; found 207.1242 [(M+H)⁺ form].

25 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.84 (brs, 1 H), 7.88 (brd, 1 H), 7.16 (d, 1 H), 6.44 (d, 1 H), 4.19 (t, 2 H), 2.6 (t, 2 H), 2.16 (s, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.7, 147.5, 143.7, 124.4, 108.1, 101.7, 59.2, 45.5, 42.6.

Preparation R2w: 7-(2-hydroxyethyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 2-chloroethanol as reagents, **Preparation R2w** was obtained. $^1\text{H-NMR}$ (400 MHz, MSM-d6): δ (ppm) 11.83 (brs, 1 H), 7.86 (d, $J=2.4$ Hz, 1 H), 7.12 (d, $J=3.92$ Hz, 1 H), 6.43 (d, $J=3.14$ Hz, 1 H), 4.92 (t, $J=5.49$ Hz, 1 H), 4.15 (t, $J=6.28$ Hz, 2 H), 3.68 (q, $J=5.49$ Hz, 2 H).

5 **Preparation R2x: 7-[(4-chlorophenyl)methyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one**

Using **General Procedure 1** starting from **Preparation R1a** and 4-chlorobenzyl bromide as reagents, **Preparation R2x** was obtained. HRMS calculated for $\text{C}_{13}\text{H}_{10}\text{ClN}_3\text{O}$: 259.0512; found 260.0583 $[(\text{M}+\text{H})^+ \text{ form}]$.

10 $^1\text{H-NMR}$ (400 MHz, MSM-d6): δ (ppm) 11.93 (s, 7.9 (s, 1 H), 7.39 (m, 2 H), 7.23 (m, 2 H), 7.22 (d, 1 H), 6.51 (d, 1 H), 5.34 (s, 2 H).

$^{13}\text{C-NMR}$ (100 MHz, MSM-d6): δ (ppm) 158.7, 147.4, 144.2, 137.5, 132.5, 129.5, 129, 124.2, 108.3, 102.4, 47.5.

15 **Preparation R2y: 7-[(3-chlorophenyl)methyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one**

Using **General Procedure 1** starting from **Preparation R1a** and 3-chlorobenzyl bromide as reagents, **Preparation R2y** was obtained. HRMS calculated for $\text{C}_{13}\text{H}_{10}\text{ClN}_3\text{O}$: 259.0512; found 260.0580 $[(\text{M}+\text{H})^+ \text{ form}]$.

20 $^1\text{H-NMR}$ (500 MHz, MSM-d6): δ (ppm) 11.94 (brs, 1 H), 7.92 (d, 1 H), 7.35 (m, 1 H), 7.35 (m, 1 H), 7.28 (t, 1 H), 7.25 (d, 1 H), 7.16 (dm, 1 H), 6.51 (d, 1 H), 5.35 (s, 2 H).

$^{13}\text{C-NMR}$ (125 MHz, MSM-d6): δ (ppm) 158.7, 147.6, 144.3, 140.9, 133.6, 131.1, 128, 127.5, 126.4, 124.3, 108.4, 102.4, 47.5.

Preparation R2z: 7-benzyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

25 Using **General Procedure 1** starting from **Preparation R1a** and benzyl bromide as reagents, **Preparation R2z** was obtained. HRMS calculated for $\text{C}_{13}\text{H}_{11}\text{N}_3\text{O}$: 225.0902; found 226.0986 $[(\text{M}+\text{H})^+ \text{ form}]$.

$^1\text{H-NMR}$ (400 MHz, MSM-d6): δ (ppm) 11.91 (brs, 1 H), 7.91 (s, 1 H), 7.36-7.17 (m, 5 H), 7.2 (d, 1 H), 6.49 (d, 1 H), 5.34 (s, 2 H).

$^{13}\text{C-NMR}$ (100 MHz, MSM-d6): δ (ppm) 144.1, 124.3, 102.2, 48.1.

Preparation R2aa: 7-[(2-chlorophenyl)methyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 1** starting from **Preparation R1a** and 2-chlorobenzyl bromide as reagents, **Preparation R2aa** was obtained. HRMS calculated for C₁₃H₁₀ClN₃O: 2590512; found 260.0587 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 11.95 (brs, 1 H), 7.89 (d, 1 H), 7.5 (dm, 1 H), 7.32 (m, 1 H), 7.26 (m, 1 H), 7.17 (d, 1 H), 6.72 (dm, 1 H), 6.55 (d, 1 H), 5.44 (s, 2 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 144.3, 129.8, 129.8, 128.8, 128.1, 124.5, 102.5, 46.

Preparation R2ab: 7-(2-oxopyrrolidin-1-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Preparation R1b (1.74 g, 11.67 mmol) was dissolved in DMF (80 ml) and cooled to 0 °C, sodium hydride (60 % disp., 1.87 g, 46.67 mmol) was slowly added and stirred for 30 minutes at 0 °C. Hydroxylamine-O-sulfonic acid (2.11 g, 18.67 mmol) was added to the reaction mixture and allowed to warm up to r.t. and stirred for 20 hours. Water (100 ml) was added to the reaction mixture and extracted with DCM (4 x 50 ml). The combined organic layer was washed with water and dried over MgSO₄ and evaporated. The residue was dissolved in MSM and purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

A part of the resulted *N*-amine compound (500 mg, 3.05 mmol) was dissolved in DCM (20 ml) and TEA (850 μl, 6.09 mmol, 2 eq.) and 4-chlorobutyryl chloride was (409 μl, 515 mg, 3.65 mmol, 1.2 eq.) added dropwise and stirred for 20 hours at r.t. Then the reaction mixture was evaporated, sat. NaHCO₃ solution (5 ml, aq.), MeCN (20 ml) and water (20 ml) were added to the residue and the mixture was stirred for 3 hours at 80 °C.

The reaction mixture was evaporated and water (50 ml) was added. The solution was extracted with DCM (3 x 10 ml) and the combined organic layers were evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

The resulted pyrrolidone (200 mg, 0.862 mmol) was dissolved in HCl solution (4 ml, 1 N, aq.) and PDO (80 ml) and stirred at 60 °C for 6 hours. The reaction mixture was

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evaporated and the residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) gave **Preparation R2ab**. HRMS calculated for C₁₀H₁₀N₄O₂: 218.0804; found 219.0883 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.11 (brs, 1 H), 7.91 (s, 1 H), 7.2 (d, 1 H), 6.53 (d, 1 H), 3.77 (t, 2 H), 2.47 (t, 2 H), 2.17 (quint., 2 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 173.7, 158.4, 146.6, 145.2, 124.2, 107, 101.3, 49.8, 28.4, 16.9.

Preparation R2ac: 7-(3,4,5-trimethoxyphenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 5-iodo-1,2,3-trimethoxybenzene as reagents, **Preparation R2ac** was obtained. HRMS calculated for C₁₅H₁₅N₃O₄: 301.1063; found 302.1138 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.07 (brs, 1 H), 7.95 (d, 1 H), 7.49 (d, 1 H), 6.99 (s, 2 H), 6.66 (d, 1 H), 3.82 (s, 6 H), 3.7 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.5, 124.6, 103.2, 103, 60.6, 56.6.

Preparation R2ad: 7-(3,5-dichlorophenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 3,5-dichlorophenylboronic acid as reagents, **Preparation R2ad** was obtained. HRMS calculated for C₁₂H₇Cl₂N₃O: 278.9966; found 280.0040 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.03 (vbrs, 1 H), 8.03 (s, 1 H), 7.95 (d, 2 H), 7.64 (t, 1 H), 7.63 (d, 1 H), 6.71 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 145.3, 126.7, 123.8, 122.7, 104.4.

Preparation R2ae: 7-(3-chloro-5-methoxyphenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 3-chloro-5-methoxyphenylboronic acid as reagents, **Preparation R2ae** was obtained. HRMS calculated for C₁₃H₁₀ClN₃O₂: 275.0461; found 276.0541 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.18 (s, 1 H), 8 (d, 1 H), 7.6 (d, 1 H), 7.51 (t, 1 H), 7.33 (t, 1 H), 7.08 (t, 1 H), 6.69 (d, 1 H), 3.85 (s, 3 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 161, 158.7, 147.5, 145, 139.7, 134.5, 124, 116.3, 112.7, 110.2, 109.4, 104, 56.4

Preparation R2af: 7-(3,5-dimethoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 2-(3,5-dimethoxy)-phenyl-4,4,5,5-tetramethyl-(1,3,2)-dioxaborolane as reagents, **Preparation R2af** was obtained. HRMS calculated for C₁₄H₁₃N₃O₃: 271.0957; found 272.1030 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.11 (s, 1 H), 7.95 (d, 1 H), 7.52 (d, 1 H), 6.91 (d, 2 H), 6.66 (d, 1 H), 6.54 (t, 1 H), 3.8 (s, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.5, 124.2, 103.5, 103.1, 98.9.

Preparation R2ag: 7-(3,4-dichlorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3,4-dichlorophenylboronic acid as reagents, **Preparation R2ag** was obtained. HRMS calculated for C₁₂H₇Cl₂N₃O: 278.9966; found 280.003 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.21 (brs, 1 H), 8.15 (t, 1 H), 8.02 (brs, 1 H), 7.82 (d, 1 H), 7.82 (d, 1 H), 7.61 (d, 1 H), 6.72 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 145.1, 131.5, 125.9, 124.3, 123.8, 104.2.

Preparation R2ah: 7-(4-chloro-3-fluorophenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-chloro-3-fluoriodobenzene as reagents, **Preparation R2ah** was obtained. HRMS calculated for C₁₂H₇ClF₂N₃O: 263.0262; found 264.0339 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.21 (s, 1 H), 8.02 (d, 1 H), 7.97 (dd, 1 H), 7.77 (dd, 1 H), 7.72 (dd, 1 H), 7.6 (d, 1 H), 6.72 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 145.1, 131.5, 123.7, 121.5, 112.8, 104.2.

Preparation R2ai: 7-(4-chloro-3-methoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 2-chloro-5-iodoanisole as reagents, **Preparation R2ai** was obtained. HRMS calculated for C₁₃H₁₀ClN₃O₂: 275.0461;

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found 276.0537 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.15 (brs, 1 H), 7.98 (brs, 1 H), 7.58 (d, 1 H), 7.57 (d, 1 H), 7.49 (d, 1 H), 7.36 (dd, 1 H), 6.7 (d, 1 H), 3.93 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.7, 155.3, 147.4, 144.8, 137.7, 130.5, 124.2, 119.8, 117.3, 110, 109.4, 103.7, 56.9.

Preparation R2aj: 7-(4-fluoro-3-methoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-fluoro-4-iodo-2-methoxybenzene as reagents, **Preparation R2aj** was obtained. HRMS calculated for C₁₃H₁₀N₃O₂F: 259.0757; found 260.0818 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.1 (s, 1 H), 7.95 (s, 1 H), 7.51 (d, 1 H), 7.48 (dd, 1 H), 7.38 (dd, 1 H), 7.27 (ddd, 1 H), 6.68 (d, 1 H), 3.9 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.7, 124.5, 117, 116.5, 111, 103.4, 56.8.

Preparation R2ak: 7-(3,4-dimethoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3,4-dimethoxyphenylboronic acid pinacol ester as reagents, **Preparation R2ak** was obtained. HRMS calculated for C₁₄H₁₃N₃O₃: 271.0957; found 272.103 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 7.92 (d, 1 H), 7.43 (d, 1 H), 7.25 (d, 1 H), 7.19 (dd, 1 H), 7.08 (d, 1 H), 6.65 (d, 1 H), 3.8 (s, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.5, 124.6, 116.9, 112.2, 109.3, 103.1, 56.3.

Preparation R2am: 7-(4-methylphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-iodotoluene as reagents, **Preparation R2am** was obtained. HRMS calculated for C₁₃H₁₁N₃O: 225.0902; found 226.0987 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.06 (brs, 1 H), 7.93 (s, 1 H), 7.58 (dm, 1 H), 7.44 (d, 1 H), 7.33 (dm, 1 H), 6.66 (d, 1 H), 2.37 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.3, 144.5, 136.8, 135.4, 130.1, 124.5, 124.1, 109.6, 103.4, 21.

Preparation R2an: 4-{4-oxo-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl}benzonitrile

Using **General Procedure 3** starting from **Preparation R1b** and 4-iodobenzonitrile as reagents, **Preparation R2an** was obtained. HRMS calculated for C₁₃H₈N₄O: 236.0698; found 237.0775 [(M+H)⁺ form].

5 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.25 (brs, 1 H), 8.05 (m, 2 H), 8.03 (m, 2 H), 8.02 (brs, 1 H), 7.66 (d, 1 H), 6.75 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 147.6, 145.2, 141.5, 134, 124.6, 123.6, 119, 110.6, 109.4, 104.7.

Preparation R2ao: 7-[4-(trifluoromethyl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

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Using **General Procedure 3** starting from **Preparation R1b** and 4-iodobenzotrifluoride as reagents, **Preparation R2ao** was obtained. HRMS calculated for C₁₃H₈F₃N₃O: 279.0619; found 280.0691 [(M+H) form].

15 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.23 (brs, 1 H), 8.02 (m, 2 H), 8.01 (d, 1 H), 7.92 (m, 2 H), 7.63 (d, 1 H), 6.74 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.7, 147.6, 145.1, 126.9, 124.7, 123.8, 110.4, 104.5 ¹⁵N-NMR (50.6 MHz, MSM-d6): δ (ppm) 170.9.

Preparation R2ap: 7-[4-(difluoromethyl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

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Using **General Procedure 3** starting from **Preparation R1b** and 1-(difluoromethyl)-4-iodobenzene as reagents, **Preparation R2ap** was obtained. HRMS calculated for C₁₃H₉F₂N₃O: 261.0714; found 262.0784 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.17 (brs, 1 H), 7.99 (d, 1 H), 7.91 (m, 2 H), 7.75 (m, 2 H), 7.58 (d, 1 H), 7.12 (t, 1 H), 6.72 (d, 1 H).

25 ¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.9, 127.2, 124.7, 123.9, 115.1, 104.1.

Preparation R2aq: 7-[4-(hydroxymethyl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-iodobenzyl alcohol as

reagents, **Preparation R2aq** was obtained. HRMS calculated for $C_{13}H_{11}N_3O_2$: 241.0851; found 242.0925 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6): δ (ppm) 12.07 (brs, 1 H), 7.94 (s, 1 H), 7.66 (m, 2 H), 7.47 (m, 2 H), 7.45 (d, 1 H), 6.67 (d, 1 H), 5.31 (t, 1 H), 4.56 (d, 2 H).

5 ^{13}C -NMR (125 MHz, MSM-d6): δ (ppm) 158.9, 147.4, 144.6, 142.2, 136.6, 127.6, 124.3, 124.2, 109.9, 103.5, 62.8.

Preparation R2ar: 7-(4-chlorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-chloro-4-iodobenzene as reagents, **Preparation R2ar** was obtained. HRMS calculated for $C_{12}H_8ClN_3O$: 245.0356; found 246.0427 $[(M+H)^+]$ form].

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1H -NMR (500 MHz, MSM-d6): δ (ppm) 12.15 (brs, 1 H), 7.97 (d, 1 H), 7.78 (dm, 1 H), 7.61 (dm, 1 H), 7.53 (d, 1 H), 6.7 (d, 1 H).

^{13}C -NMR (125 MHz, MSM-d6): δ (ppm) 158.7, 147.3, 144.8, 136.7, 131.7, 129.6, 126.1, 123.9, 109.9, 103.9.

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Preparation R2as: 7-(4-fluorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-fluoroiodobenzene as reagents, **Preparation R2as** was obtained. HRMS calculated for $C_{12}H_8FN_3O$: 229.0651; found 230.0714 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6): δ (ppm) 12.12 (brs, 1 H), 7.95 (d, 1 H), 7.74 (m, 2 H), 7.48 (d, 1 H), 7.39 (m, 2 H), 6.68 (d, 1 H).

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^{13}C -NMR (125 MHz, MSM-d6): δ (ppm) 144.7, 126.8, 124.2, 116.4, 103.5.

Preparation R2at: 7-[4-(dimethylamino)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 4-(dimethylamino)phenylboronic acid as reagents, **Preparation R2at** was obtained. HRMS calculated for $C_{14}H_{14}N_4O$: 254.1168; found 255.1243 $[(M+H)^+]$ form].

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1H -NMR (400 MHz, MSM-d6): δ (ppm) 11.98 (brs, 1 H), 7.89 (d, 1 H), 7.43 (m, 2 H), 7.33 (d, 1 H), 6.82 (m, 2 H), 6.61 (d, 1 H), 2.94 (s, 6 H).

^{13}C -NMR (100 MHz, MSM-d6): δ (ppm) 144.1, 125.6, 124.3, 112.7, 102.7, 40.6.

Preparation R2au: 7-[4-(4-methylpiperazin-1-yl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 4-(4-methylpiperazin-1-yl)phenylboronic acid pinacol ester as reagents, **Preparation R2au** was obtained. HRMS calculated for C₁₇H₁₉N₅O: 309.1590; found 310.1674 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.01 (brs, 1 H), 7.9 (d, 1 H), 7.49 (m, 2 H), 7.37 (d, 1 H), 7.06 (m, 2 H), 6.63 (d, 1 H), 3.2 (brm, 4 H), 2.51 (brm, 4 H), 2.27 (s, 3 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 144.3, 125.4, 124.2, 115.9, 102.9, 54.8, 48.3, 45.9.

Preparation R2av: 7-[4-(morpholin-4-yl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 4-morpholinophenylboronic acid as reagents, **Preparation R2av** was obtained. HRMS calculated for C₁₆H₁₆N₄O₂: 296.1273; found 297.1361 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.01 (brs, 1 H), 7.9 (s, 1 H), 7.51 (m, 2 H), 7.38 (d, 1 H), 7.07 (m, 2 H), 6.63 (d, 1 H), 3.76 (m, 4 H), 3.16 (m, 4 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 484.8, 144.3, 125.4, 124.2, 115.7, 103, 66.5.

Preparation R2ax: 7-(4-methoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-iodoanisole as reagents, **Preparation R2ax** was obtained. HRMS calculated for C₁₃H₁₁N₃O₂: 241.0851; found 242.0929 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.04 (brs, 1 H), 7.92 (d, 1 H), 7.58 (dd, 1 H), 7.4 (d, 1 H), 7.08 (d, 1 H), 6.65 (d, 1 H), 3.81 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 158.8, 147.3, 144.4, 130.9, 126.1, 124.4, 114.8, 109.4, 103.1, 55.9.

Preparation R2ay: 7-[4-(trifluoromethoxy)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-iodo-4-

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(trifluoromethoxy)benzene as reagents, **Preparation R2ay** was obtained. HRMS calculated for $C_{13}H_8F_3N_3O_2$: 295.0569; found 296.0648 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6): δ (ppm) 12.15 (s, 1 H), 7.97 (d, 1 H), 7.86 (m, 2 H), 7.56 (m, 2 H), 7.54 (m, 1 H), 6.71 (d, 1 H).

5 ^{13}C -NMR (125 MHz, MSM-d6): δ (ppm) 144.8, 126.4, 124.1, 122.5, 103.9.

Preparation R2az: 7-[4-(benzyloxy)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-benzyloxyiodobenzene as reagents, **Preparation R2az** was obtained. HRMS calculated for $C_{19}H_{15}N_3O_2$: 317.1164; found 318.1243 $[(M+H)^+]$ form].

10 1H -NMR (500 MHz, MSM-d6): δ (ppm) 12.05 (brs, 1 H), 7.92 (d, 1 H), 7.59 (dm, 2 H), 7.48 (dm, 2 H), 7.41 (d, 1 H), 7.41 (tm, 2 H), 7.35 (tm, 1 H), 7.16 (dm, 2 H), 6.65 (d, 1 H), 5.18 (s, 2 H).

^{13}C -NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 157.6, 147.3, 144.4, 137.4, 131, 129, 128.4, 128.2, 126.1, 124.3, 115.7, 109.4, 103.1, 69.9.

15 **Preparation R2ba: 7-(5-methylthiophen-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one**

Using **General Procedure 3** starting from **Preparation R1b** and 2-iodo-5-methylthiophene as reagents, **Preparation R2ba** was obtained. HRMS calculated for $C_{11}H_9N_3OS$: 231.0466; found 232.0541 $[(M+H)^+]$ form].

20 1H -NMR (400 MHz, MSM-d6): δ (ppm) 12.17 (brs, 1 H), 7.99 (d, 1 H), 7.49 (d, 1 H), 7.14 (d, 1 H), 6.76 (dq, 1 H), 6.67 (d, 1 H), 2.46 (d, 3 H).

^{13}C -NMR (100 MHz, MSM-d6): δ (ppm) 145, 124.2, 123.9, 119.4, 103.9, 15.4.

Preparation R2bb: 7-(5-chlorothiophen-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

25 Using **General Procedure 3** starting from **Preparation R1b** and 2-chloro-5-iodothiophene as reagents, **Preparation R2bb** was obtained. HRMS calculated for $C_{10}H_6N_3OSCl$: 250.9920; found 252.0005 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 12.28 (brs, 1 H), 8.07 (d, 1 H), 7.67 (d, 1 H), 7.3 (d, 1 H), 7.13 (d, 1 H), 6.72 (d, 1 H)

¹³C-NMR (125 MHz, MSM-d6) δ ppm 158.4, 146.8, 145.6, 136.4, 125.5, 124.6, 123.3, 117.5, 109.3, 104.6

Preparation R2bc: 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

5 Using **General Procedure 2** starting from **Preparation R1a** and 1,4-benzodioxane-6-boronic acid as reagents, **Preparation R2bc** was obtained. HRMS calculated for C₁₄H₁₁N₃O₃: 269.0800; found 270.0881 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.05 (brs, 1 H), 7.92 (d, 1 H), 7.4 (d, 1 H), 7.22 (d, 1 H), 7.13 (dd, 1 H), 6.99 (d, 1 H), 6.63 (d, 1 H), 4.33-4.25 (m, 4 H).

10 ¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.4, 124.3, 117.7, 117.6, 113.8, 103.2.

Preparation R2bd: 7-(2*H*-1,3-benzodioxol-5-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 3,4-methylenedioxyphenylboronic acid as reagents, **Preparation R2bd** was obtained.
15 HRMS calculated for C₁₃H₉N₃O₃: 255.0644; found 256.0719 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.05 (brs, 1 H), 7.92 (d, 1 H), 7.4 (d, 1 H), 7.29 (d, 1 H), 7.12 (dd, 1 H), 7.05 (d, 1 H), 6.63 (d, 1 H), 6.11 (s, 2 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.5, 124.5, 118.2, 108.7, 106.5, 103.1, 102.2.

Preparation R2be: 7-(naphthalen-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

20 Using **General Procedure 2** starting from **Preparation R1a** and 2-naphthaleneboronic acid as reagents, **Preparation R2be** was obtained. HRMS calculated for C₁₆H₁₁N₃O: 261.0902; found 262.0982 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.14 (s, 1 H), 8.25 (d, 1 H), 8.09 (d, 1 H), 8.01 (m, 1 H), 8.01 (m, 1 H), 8 (s, 1 H), 7.91 (dd, 1 H), 7.63 (d, 1 H), 7.6 (tm, 1 H), 7.57 (tm, 1 H), 6.74 (d, 1 H).
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¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.6, 144.8, 135.4, 133.4, 132, 129.4, 128.4, 128.2, 127.4, 126.9, 124.4, 123.5, 122.3, 109.9, 103.8.

Preparation R2bf: 7-(3-methylphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3-iodotoluene as reagents, **Preparation R2bf** was obtained. HRMS calculated for C₁₃H₁₁N₃O: 225.0902; found 226.098 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.08 (brs, 1 H), 7.95 (d, 1 H), 7.52 (brs, 1 H), 7.49 (dm, 1 H), 7.46 (d, 1 H), 7.41 (t, 1 H), 7.22 (brd, 1 H), 6.67 (d, 1 H), 2.39 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.3, 144.6, 139.2, 137.8, 129.5, 128.1, 125.2, 124.2, 121.8, 109.7, 103.5, 21.4.

Preparation R2bg: 7-[3-(trifluoromethyl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3-iodobenzotrifluoride as reagents, **Preparation R2bg** was obtained. HRMS calculated for C₁₃H₈F₃N₃O: 279.0620; found 280.0699 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.19 (brs, 1 H), 8.18 (brs, 1 H), 8.07 (dm, 1 H), 8.02 (d, 1 H), 7.79 (t, 1 H), 7.77 (dm, 1 H), 7.65 (d, 1 H), 6.73 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 145.1, 131.1, 128.3, 124, 123.9, 121, 104.1.

Preparation R2bh: 7-{3-[(4-methylpiperazin-1-yl)methyl]phenyl}-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3-(4-methyl-1-piperazinylmethyl)benzeneboronic acid pinacol ester as reagents, **Preparation R2bh** was obtained. HRMS calculated for C₁₈H₂₁N₅O: 323.1746; found 324.1828 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.37/12.2/11.95 (brs, 3 H), 8.04 (brs, 1 H), 7.98 (s, 1 H), 7.91 (dm, 1 H), 7.67 (dm, 1 H), 7.63 (d, 1 H), 7.62 (t, 1 H), 6.72 (d, 1 H), 4.49 (brs, 2 H), 3.8-3.3 (brm, 8 H), 2.8 (brs, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.8, 130.3, 130, 127.3, 125.7, 124, 103.9, 58.7, 42.7.

Preparation R2bi: 7-[3-(hydroxymethyl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3-iodobenzyl alcohol as reagents, **Preparation R2bi** was obtained. HRMS calculated for C₁₃H₁₁N₃O₂: 241.0851;

found 242.0935 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.11 (brs, 1 H), 7.95 (d, 1 H), 7.64 (brt, 1 H), 7.55 (dm, 1 H), 7.48 (t, 1 H), 7.46 (d, 1 H), 7.35 (dm, 1 H), 6.68 (d, 1 H), 4.58 (s, 2 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.4, 144.6, 144.4, 137.7, 129.4, 125.4, 124.2, 123, 122.5, 109.7, 103.5, 62.9.

Preparation R2bj: 7-(3-chlorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-chloro-3-iodobenzene as reagents, **Preparation R2bj** was obtained. HRMS calculated for C₁₂H₈ClN₃O: 245.0356; found 246.0437 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.17 (brs, 1 H), 8 (d, 1 H), 7.92 (m, 1 H), 7.74 (dm, 1 H), 7.58 (d, 1 H), 7.57 (t, 1 H), 7.47 (dm, 1 H), 6.7 (d, 1 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 145, 131.3, 127.2, 124.1, 123.9, 122.9, 104.

Preparation R2bk: 7-(3-fluorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-fluoro-3-iodobenzene as reagents, **Preparation R2bk** was obtained. HRMS calculated for C₁₂H₈N₃OF: 229.0651; found 230.0729 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.17 (brs, 1 H), 7.99 (d, 1 H), 7.72 (dm, 1 H), 7.64 (m, 1 H), 7.58 (d, 1 H), 7.58 (m, 1 H), 7.25 (m, 1 H), 6.71 (d, 1 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 144.9, 131.4, 130.9, 123.9, 120.2, 114, 111.6.

¹⁹F-NMR (376.5 MHz, MSM-d6): δ (ppm) -111.7.

Preparation R2bl: 7-[3-(dimethylamino)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 3-(*N,N*-dimethylamino)phenylboronic acid as reagents, **Preparation R2bl** was obtained. HRMS calculated for C₁₄H₁₄N₄O: 254.1168; found 255.1229 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.04 (brs, 1 H), 7.92 (d, 1 H), 7.45 (d, 1 H), 7.3 (t, 1 H), 6.94 (m, 1 H), 6.93 (dm, 1 H), 6.74 (dm, 1 H), 6.65 (d, 1 H), 2.95 (s, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.3, 129.9, 124.4, 112.4, 111.4, 108.6, 103.1, 40.5.

Preparation R2bm: 7-[3-(morpholin-4-yl)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 3-(morpholino)phenylboronic acid as reagents, **Preparation R2bm** was obtained. ¹H-NMR (400 MHz, MSM-d₆): δ (ppm) 12.05 (brs, 1 H), 7.93 (s, 1 H), 7.47 (d, J=3.53 Hz, 1 H), 7.36 (t, J=8.13 Hz, 1 H), 7.19 (t, J=2.20 Hz, 1 H), 7.11 (dd, J=1.27, 7.93 Hz, 1 H), 6.98 (dd, J=1.96, 8.49 Hz, 1 H), 6.65 (d, J=3.5 Hz, 1 H), 3.75 (t, J=4.61 Hz, 4 H), 3.18 (t, J=4.61 Hz, 4 H).

Preparation R2bo: 7-(3-methoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3-iodoanisole as reagents, **Preparation R2bo** was obtained. HRMS calculated for C₁₃H₁₁N₃O₂: 241.0851; found 242.0928 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d₆): δ (ppm) 12.1 (brs, 1 H), 7.95 (d, 1 H), 7.51 (d, 1 H), 7.44 (t, 1 H), 7.31 (m, 1 H), 7.3 (m, 1 H), 6.98 (dm, 1 H), 6.67 (d, 1 H), 3.82 (s, 3 H).

¹³C-NMR (100 MHz, MSM-d₆): δ (ppm) 144.6, 130.4, 124.2, 116.7, 112.9, 110.5, 103.5.

Preparation R2bp: 7-[3-(trifluoromethoxy)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 3-(trifluoromethoxy)iodobenzene as reagents, **Preparation R2bp** was obtained. HRMS calculated for C₁₃H₈F₃N₃O₂: 295.0569; found 296.0651 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆): δ (ppm) 12.91 (s, 1 H), 8 (s, 1 H), 7.87 (t, 1 H), 7.82 (ddd, 1 H), 7.68 (t, 1 H), 7.6 (d, 1 H), 7.41 (ddd, 1 H), 6.71 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d₆): δ (ppm) 145.1, 131.5, 123.9, 123.2, 119.5, 117.1, 104.1.

Preparation R2bq: 7-[3-(benzyloxy)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-benzyloxy-3-iodobenzene as reagents, **Preparation R2bq** was obtained. HRMS calculated for C₁₉H₁₅N₃O₂: 317.1164; found 318.1235 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆): δ (ppm) 12.1 (brs, 1 H), 7.95 (d, 1 H), 7.51 (d, 1 H), 7.51-

7.31 (m, 5 H), 7.44 (t, 1 H), 7.41 (m, 1 H), 7.32 (dm, 1 H), 7.05 (dm, 1 H), 6.68 (d, 1 H), 5.18 (s, 2 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.6, 130.5, 124.1, 116.8, 113.6, 111.4, 103.6, 70.

5 **Preparation R2br: 7-(6-methylpyridin-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one**

Using **General Procedure 3** starting from **Preparation R1b** and 2-iodo-6-methylpyridine as reagents, **Preparation R2br** was obtained. HRMS calculated for C₁₂H₁₀N₄O: 226.0855; found 227.0933 [(M+H)⁺ form].

10 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12 (brs, 1 H), 8.25 (dm, 1 H), 8.05 (s, 1 H), 7.9 (t, 1 H), 7.88 (d, 1 H), 7.25 (dm, 1 H), 6.68 (d, 1 H), 2.52 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.9, 139.5, 122, 121.8, 113.8, 103.7, 24.4.

Preparation R2bs: 7-(6-methoxypyridin-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

15 The mixture of **Preparation R1a** (1.0 g, 6.51 mmol), 2-iodo-6-methoxy-pyridine (2.35 g, 9.77 mmol, 1.5 eq.), copper(I)-iodide (125 mg, 0.65 mmol, 0.1 eq.), potassium-phosphate tribasic (2.76 g, 13 mmol, 2 eq.), (1*R*,2*R*)-(-)-1,2-diaminocyclohexane (74 mg, 0.65 mmol, 0.1 eq.) in PDO (50 ml) was stirred under inert atmosphere for 4 hours at 100 °C. The inorganics were filtered off, the filtrate was evaporated, and the resulted residue was purified by flash chromatography (DCM).

20 The obtained arylated product (920 mg, 3.5 mmol) and lithium-hydroxide monohydrate (1.48 g, 35 mmol) were stirred in the mixture of PDO (15 ml) and water (15 ml) at 110 °C for 24 hours. The residue was acidified by aqueous HCl solution (1 N, 50 ml), the resulted precipitate was filtered off and dried to give **Preparation R2bs**.

HRMS calculated for C₁₂H₁₀N₄O₂: 242.0804; found 243.0884 [(M+H)⁺ form].

25 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.21 (brs, 1 H), 8.08 (dd, 1 H), 8.03 (s, 1 H), 7.94 (d, 1 H), 7.9 (t, 1 H), 6.78 (dd, 1 H), 6.7 (d, 1 H), 3.94 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 163.2, 158.5, 147.6, 147.4, 144.9, 141.9, 121.9, 111.2, 108.4, 108.4, 103.8, 53.9.

Preparation R2bt: 7-(naphthalen-1-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 1-naphthaleneboronic acid as reagents, **Preparation R2bt** was obtained. HRMS calculated for $C_{16}H_{11}N_3O$: 261.0902; found 262.0984 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.04 (s, 1 H), 8.12 (d, 1 H), 8.09 (d, 1 H), 7.78 (d, 1 H), 7.67 (t, 1 H), 7.61 (dm, 1 H), 7.6 (t, 1 H), 7.51 (tm, 1 H), 7.39 (d, 1 H), 7.21 (t, 1 H), 6.77 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.9, 149.2, 144.6, 134.2, 134.1, 130.4, 129.5, 128.7, 127.8, 127.2, 126.4, 126.3, 126, 123, 108.7, 103.1

Preparation R2bu: 7-phenyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and iodobenzene as reagents, **Preparation R2bu** was obtained. HRMS calculated for $C_{12}H_9N_3O$: 211.0746; found 212.083 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.1 (brs, 1 H), 7.95 (d, 1 H), 7.71 (m, 2 H), 7.54 (m, 2 H), 7.5 (d, 1 H), 7.4 (m, 1 H), 6.69 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.8, 147.3, 144.6, 137.8, 129.7, 127.4, 124.6, 124.1, 109.8, 103.6.

Preparation R2bv: 7-(2-methylphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 2-methylphenylboronic acid as reagents, **Preparation R2bv** was obtained. HRMS calculated for $C_{13}H_{11}N_3O$: 225.0902; found 226.098 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12 (brs, 1 H), 7.83 (d, 1 H), 7.41 (m, 1 H), 7.41 (m, 1 H), 7.35 (m, 1 H), 7.3 (d, 1 H), 7.21 (d, 1 H), 6.66 (d, 1 H), 2.01 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.9, 148.2, 144.4, 136.9, 135.6, 131.2, 129.2, 128.5, 127.1, 125.3, 108.6, 102.9, 17.9.

Preparation R2bw: 7-(2-chlorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 2-chlorophenylboronic acid as reagents, **Preparation R2bw** was obtained. HRMS calculated for $C_{12}H_8ClN_3O$: 245.0356; found 246.0437 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.06 (brs, 1 H), 7.86 (d, 1 H), 7.73-7.48 (m, 4

H), 7.27 (d, 1 H), 6.68 (d, 1 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 144.7, 125.4, 102.2.

Preparation R2bx: 7-(2-fluorophenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 2-fluorophenylboronic acid as reagents, **Preparation R2bx** was obtained. HRMS calculated for C₁₂H₈N₃O: 229.0651; found 230.0730 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 12.09 (brs, 1 H), 7.9 (d, 1 H), 7.61 (m, 1 H), 7.54 (m, 1 H), 7.48 (m, 1 H), 7.38 (m, 1 H), 7.34 (dd, 1 H), 6.7 (d, 1 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 144.8, 130.6, 129.6, 125.4, 125.3, 117, 103.5.

Preparation R2by: 7-[2-(dimethylamino)phenyl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and dimethyl[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]amine as reagents, **Preparation R2by** was obtained. HRMS calculated for C₁₄H₁₄N₄O: 254.1168; found 255.1237 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12 (brs, 1 H), 7.85 (d, 1 H), 7.36 (m, 1 H), 7.24 (dm, 1 H), 7.2 (d, 1 H), 7.13 (dm, 1 H), 7.02 (m, 1 H), 6.64 (d, 1 H), 2.36 (s, 6 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 144.4, 130.1, 129.4, 125.5, 121.1, 119, 102.9, 42.4.

Preparation R2bz: 7-(2-methoxyphenyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 2-methoxyphenylboronic acid as reagents, **Preparation R2bz** was obtained. HRMS calculated for C₁₃H₁₁N₃O₂: 241.0851; found 242.092 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6): δ (ppm) 11.96 (brs, 1 H), 7.82 (d, 1 H), 7.46 (m, 1 H), 7.37 (dm, 1 H), 7.24 (dm, 1 H), 7.18 (d, 1 H), 7.08 (m, 1 H), 6.6 (d, 1 H), 3.74 (s, 3 H).

¹³C-NMR (100 MHz, MSM-d6): δ (ppm) 144.2, 130.2, 129.3, 126, 120.8, 113.1, 102.4.

Preparation R2ca: 7-(pyridin-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 2-iodopyridine as reagents, **Preparation R2ca** was obtained. HRMS calculated for C₁₁H₈N₄O: 212.0698;

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found 213.0774 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.29 (s, 1 H), 8.55 (dd, 1 H), 8.47 (dd, 1 H), 8.06 (brs, 1 H), 8.03 (t, 1 H), 7.9 (d, 1 H), 7.4 (t, 1 H), 6.7 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 149.1, 145, 139.4, 122.5, 122, 116.9, 104.

5 ¹⁵N-NMR (50.6 MHz, MSM-d6): δ (ppm) 171.2.

Preparation R2cb: 7-(pyridin-3-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and pyridine-3-boronic acid as reagents, **Preparation R2cb** was obtained. HRMS calculated for C₁₁H₈N₄O: 212.0698; found 213.0774 [(M+H)⁺ form].

10 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.29 (s, 1 H), 8.55 (dd, 1 H), 8.47 (dd, 1 H), 8.06 (brs, 1 H), 8.03 (t, 1 H), 7.9 (d, 1 H), 7.4 (t, 1 H), 6.7 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 149.1, 145, 139.4, 122.5, 122, 116.9, 104.

¹⁵N-NMR (50.6 MHz, MSM-d6): δ (ppm) 171.2.

Preparation R2cc: 7-(thiophen-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

15 Using **General Procedure 3** starting from **Preparation R1b** and 2-iodothiophene as reagents, **Preparation R2cc** was obtained. HRMS calculated for C₁₀H₇N₃OS: 217.0310; found 218.0384 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.2 (brs, 1 H), 8.03 (s, 1 H), 7.58 (d, 1 H), 7.43 (dd, 1 H), 7.39 (dd, 1 H), 7.07 (dd, 1 H), 6.69 (d, 1 H).

20 ¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.5, 147.2, 145.3, 138.7, 126, 124.3, 122.8, 119.2, 109.4, 104.2.

Preparation R2cd: 7-(pyridin-4-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and pyridine-4-boronic acid pinacol ester as reagents, **Preparation R2cd** was obtained. HRMS calculated for C₁₁H₈N₄O: 212.0698; found 213.0773 [(M+H)⁺ form].

25 ¹H-NMR (500 MHz, MSM-d6): δ ppm 12.31 (brs, 1 H), 8.69 (m, 2 H), 8.05 (s, 1 H), 7.99 (m, 2 H), 7.73 (d, 1 H), 6.76 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 151.3, 145.6, 122.8, 117.3, 105.

Preparation R2ce: 7-(furan-3-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 2** starting from **Preparation R1a** and 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furan as reagents, **Preparation R2ce** was obtained. HRMS calculated for C₁₀H₇N₃O₂: 201.0538; found 202.0617 [(M+H)⁺ form].

5 ¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.13 (brs, 1 H), 8.32 (dd, 1 H), 8 (d, 1 H), 7.8 (dd, 1 H), 7.52 (d, 1 H), 7.17 (dd, 1 H), 6.66 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.6, 147.1, 145, 143.9, 133.8, 126, 123, 109.6, 106.5, 103.8.

Preparation R2cf: 7-(thiophen-3-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

10 Using **General Procedure 2** starting from **Preparation R1a** and thiophene-3-boronic acid pinacol ester as reagents, **Preparation R2cf** was obtained. HRMS calculated for C₁₀H₇N₃OS: 217.0310; found 218.0390 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.14 (s, 1 H), 7.99 (d, 1 H), 7.92 (dd, 1 H), 7.71 (dd, 1 H), 7.68 (dd, 1 H), 7.57 (d, 1 H), 6.66 (d, 1 H).

15 ¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.6, 147, 144.8, 136.3, 127, 123.8, 123.3, 115.1, 109.5, 103.5.

Preparation R2cg: 7-(1-methyl-1*H*-imidazol-4-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

20 Using **General Procedure 3** starting from **Preparation R1b** and 4-iodo-1-methyl-1*H*-imidazole as reagents, **Preparation R2cg** was obtained. HRMS calculated for C₁₀H₉N₅O: 215.0807; found 216.0879 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 9.24-7.3 (vbrs, 3 H), 7.51 (d, 1 H), 6.72 (brs, 1 H), 3.77 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 121.7, 103.5, 35.

25 ¹⁵N-NMR (50.6 MHz, MSM-d6): δ (ppm) 153.

Preparation R2ch: 7-(1-methyl-1*H*-pyrazol-4-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 4-iodo-1-methyl-1*H*-pyrazole as reagents, **Preparation R2ch** was obtained. HRMS calculated for C₁₀H₉N₅O:

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215.0807; found 216.0889 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.12 (brs, 1 H), 8.27 (s, 1 H), 7.96 (s, 1 H), 7.91 (d, 1 H), 7.42 (d, 1 H), 6.63 (d, 1 H), 3.89 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 158.6, 146.9, 144.7, 132.1, 124.3, 123.4, 121.4, 109, 103.4, 38.5.

Preparation R2ci: 7-[1-(difluoromethyl)-1*H*-pyrazol-4-yl]-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 1-(difluoromethyl)-4-iodo-1*H*-pyrazole as reagents, **Preparation R2ci** was obtained. HRMS calculated for C₁₀H₇F₂N₅O: 251.0619; found 252.0682 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 11.88 (brs, 1 H), 8.83 (d, 1 H), 8.4 (d, 1 H), 8.03 (s, 1 H), 7.91 (t, 1 H), 7.58 (d, 1 H), 6.69 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 145.2, 136.2, 123.2, 121.3, 111, 104.

Preparation R2cj: 7-(pyrimidin-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Preparation R1b (300 mg, 2.011 mmol, 1 eq.), 2-chloropyrimidine (2.413 mmol, 1.2 eq.) and anhydrous K₂CO₃ (417 mg, 3.017 mmol, 1.5 eq.) was heated in DMF (10 ml) at 150 °C for 2 hours. The reaction mixture was filtered and purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MCN, gradient) to give 4-methoxy-7-pyrimidin-2-yl-pyrrolo[2,3-*d*]pyrimidine.

Then the obtained product (0.633 mmol, 1 eq.), 1M HCl aqueous solution (3 ml) and PDO (60 ml) were stirred at 100 °C for 1 hour. After the reaction completed, the mixture was evaporated and purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MCN, gradient) to give **Preparation R2cj**. HRMS calculated for C₁₀H₇N₅O: 213.0651; found 214,0735 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ (ppm) 12.19 (brs, 1 H), 8.94 (d, 1 H), 8.01 (s, 1 H), 7.78 (d, 1 H), 7.54 (t, 1 H), 6.71 (d, 1 H).

¹³C-NMR (125 MHz, MSM-d6): δ (ppm) 159.7, 158.7, 156, 148.1, 145.2, 123.3, 120.1, 111.4, 104.5.

Preparation R2ck: 7-(1,3-thiazol-2-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and 2-iodothiazole as reagents, **Preparation R2ck** was obtained. HRMS calculated for C₉H₆N₄OS: 218.0262; found 219.0335 [(M+H)⁺ form].

¹H-NMR (500 MHz, MeCN-d₃) δ ppm 8.5 (s, 1 H), 7.62 (d, 1 H), 7.52 (d, 1 H), 7.22 (d, 1 H), 6.51 (d, 1 H).

¹³C-NMR (125 MHz, MeCN-d₃) δ ppm 154.5, 137.9, 116.8, 114.8, 104.2.

Preparation R2cl: 7-(1*H*-indol-1-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Preparation R1b (1.74 g, 11.67 mmol) was dissolved in DMF (80 ml) and cooled to 0 °C. Sodium hydride (60 % disp., 1.87 g, 46.67 mmol) was slowly added and stirred for 30 minutes at 0 °C. Hydroxylamine-O-sulfonic acid (2.11 g, 18.67 mmol) was added to the reaction mixture, allowed to warm up to r.t. and stirred for 20 hours. Water (100 ml) was added to the reaction mixture and extracted with DCM (4 x 50 ml). The combined organic layers were washed with water and dried over MgSO₄ and evaporated. The residue was dissolved in MSM and purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

A part of the resulted *N*-amino compound (500 mg, 3.05 mmol) was dissolved in PDO (5 ml) and 2,5-dimethoxy-tetrahydrofuran (454 ml, 462 mg, 3.5 mmol) was added. The mixture was stirred at 100 °C for 115 hours. The reaction mixture was diluted with aqueous HCl solution (5 N, 2 ml) and purified by preparative LC (on C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **Preparation R2cl**. HRMS calculated for C₁₄H₁₀N₄O: 250.0854; found 250.2000 [(M form)].

¹H-NMR (500 MHz, MSM-d₆): δ (ppm) 12.22 (brs, 1 H), 7.86 (s, 1 H), 7.71 (d, 1 H), 7.68 (m, 1 H), 7.58 (d, 1 H), 7.17 (m, 1 H), 7.17 (m, 1 H), 6.86 (m, 1 H), 6.73 (d, 1 H), 6.68 (dd, 1 H).

¹³C-NMR (125 MHz, MSM-d₆): δ (ppm) 158.5, 147.9, 145.9, 137, 129.7, 126.3, 125.4, 123.5, 121.5, 121.5, 109, 107, 102.3, 101.8.

Preparation R2cm: 7-(1*H*-pyrrol-1-yl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Preparation R1b (1.74 g, 11.67 mmol) was dissolved in DMF (80 ml) and cooled to 0 °C. Sodium hydride (60 % disp., 1.87 g, 46.67 mmol) was slowly added and stirred for 30 minutes at 0 °C. Hydroxylamine-O-sulfonic acid (2.11 g, 18.67 mmol) was added to the

reaction mixture, allowed to warm up to r.t. and stirred for 20 hours. Water (100 ml) was added to the reaction mixture and extracted with DCM (4 x 50 ml). The combined organic layers were washed with water and dried over MgSO_4 , evaporated. The residue was dissolved in MSM and purified by preparative LC (on C-18 Gemini-NX 5 μm column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

A part of the resulted *N*-amino compound (500 mg, 3.05 mmol) was dissolved in PDO (5 ml) and 2,5-dimethoxy-tetrahydrofuran (454 ml, 462 mg, 3.5 mmol) was added. The mixture was stirred at 100 °C for 115 hours. The reaction mixture was diluted with aqueous HCl solution (5 N, 2 ml) and purified by preparative LC (on C-18 Gemini-NX 5 μm column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

To a part of the resulted compound (63 mg, 0.294 mmol) PDO (25 ml) and aqueous HCl solution (1 N, 1.3 ml) was added and stirred at 60 °C for 5 hours. The reaction mixture was evaporated and the residue was purified by preparative LC (on C-18 Gemini-NX 5 μm column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **Preparation R2cm**. HRMS calculated for $\text{C}_{10}\text{H}_8\text{N}_4\text{O}$: 200.0698; found 201.0770 $[(\text{M}+\text{H})^+ \text{ form}]$.

^1H -NMR (500 MHz, MSM-d6): δ (ppm) 12.18 (brs, 1 H), 7.92 (s, 1 H), 7.46 (d, 1 H), 7.12 (m, 2 H), 6.61 (d, 1 H), 6.21 (m, 2 H).

^{13}C -NMR (125 MHz, MSM-d6): δ (ppm) 158.4, 147.4, 145.8, 125.1, 122.8, 108, 106.7, 101.1.

Preparation R2de: 6-methyl-7-phenyl-3*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and iodobenzene as reagents, 4-methoxy-7-phenyl-pyrrolo[2,3-*d*]pyrimidine was obtained (without hydrolysis). This crude product (450 mg, 2 mmol) was dissolved in THF (18 ml) stirred at -78 °C, then LDA solution (1.8 M, 1.7 ml, 3 mmol) was added. After one hour of stirring at -78 °C, iodomethane (190 μl , 3 mmol) solution in THF (5 ml) was added, and continued stirring for 90 minutes. Then the reaction mixture was diluted with brine (10 ml) and evaporated to Celite and purified by flash chromatography (Hexane-EEO=7-1).

The resulted crude product (400 mg, 1.6 mmol) was dissolved in cc. HCl aqueous solution (330 μl , ~12.2 M, 4 mmol) and PDO (5 ml) was stirred at 100 °C for 2 hours. After the reaction completed, the mixture was partially evaporated and the formed suspension was filtered. The solid on the filter was washed with water and dried to give

Preparation R2de. HRMS calculated for $C_{13}H_{11}N_3O$: 225.0902; found 226.0985 $[(M+H)^+ \text{ form}]$.

1H -NMR(500 MHz, MSM-d6): δ ppm 11.94 (s, 1 H), 7.76 (d, 1 H), 7.55 (tm, 2 H), 7.49 (tm, 1 H), 7.4 (dm, 2 H), 6.41 (d, 1 H), 2.17 (d, 3 H).

5 ^{13}C -NMR(125 MHz, MSM-d6): δ ppm 158.4, 143.6, 136.2, 132.6, 129.6, 128.7, 128.5, 100.9, 13.3.

Preparation R2df: 9-methyl-3H-pyrimido[4,5-b]indol-4-one

Preparation R1b (500 mg, 3.06 mmol) and 2,5-dimethoxytetrahydrofuran (810 mg, 6.13 mmol, $d = 1.02$, 795 μ l) in PDO (5 ml) were heated up to 100 °C for 102 hours, then
10 1 N aqueous HCl solution (5 ml) was added. The mixture was dissolved in DMF and purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **Preparation R2df**. HRMS calculated for $C_{11}H_9N_3O$: 199.0746; found 200.0827 $[(M+H)^+ \text{ form}]$.

15 1H -NMR(500 MHz, MSM-d6): δ ppm 12.33 (brs, 1 H), 8.21 (s, 1 H), 7.63 (dm, 1 H), 7.41 (ddd, 1 H), 7.29 (td, 1 H), 3.86 (s, 3 H)

^{13}C -NMR(125 MHz, MSM-d6): δ ppm 158.5, 153.5, 148.1, 137, 124.6, 122, 121.8, 121, 110.7, 100.1, 28.5

Preparation R2dg: 6,8-dimethylpyrimido[5,4-b]indolizin-4(3H)-one

Preparation R1b (1.74 g, 11.67 mmol) was dissolved in DMF (80 ml) and cooled to 0 °C. Sodium hydride (60 % disp., 1.87 g, 46.67 mmol) was slowly added and stirred for
20 30 minutes at 0 °C. Hydroxylamine-O-sulfonic acid (2.11 g, 18.67 mmol) was added to the reaction mixture, allowed to warm up to r.t. and stirred for 20 hours. Water (100 ml) was added to the reaction mixture and extracted with DCM (4 x 50 ml). The combined organic layers were washed with water, dried over $MgSO_4$ and evaporated.

25 A part of the resulted *N*-amino compound (300 mg, 1.83 mmol) and acetylacetone (206 μ l, 201 mg 2.01 mmol,) were dissolved in 5 ml acetic acid and heated up to 120 °C for 2.5 hours, then TFA (5 ml) was added. The mixture was heated at 120 °C for 18 hours. Then water (1 ml) and methanol (10 ml) were added and the solution was evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous
30 NH_4HCO_3 -MeCN, gradient), to give **Preparation R2dg**. HRMS calculated for

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C₁₁H₁₀N₄O: 214.0855; found 215.0935 [(M+H)⁺ form].

¹H-NMR(500 MHz, MSM-d6) δ ppm 12.16 (s, 1 H), 8 (s, 1 H), 6.89 (s, 1 H), 6.68 (d, 1 H), 2.45 (d, 3 H), 2.44 (s, 3 H).

¹³C-NMR(125 MHz, MSM-d6) δ ppm 159.7, 152.5, 143.4, 141.2, 138.9, 127.7, 115.5, 109.8, 91.2, 21.9, 17.4.

Preparation R2dh: 6-chloro-7-phenyl-3H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 3** starting from **Preparation R1b** and iodobenzene as reagents, 4-methoxy-7-phenyl-pyrrolo[2,3-d]pyrimidine was obtained (without hydrolysis). The crude product (394 mg, 1.75 mmol) was dissolved in THF (14 ml) stirred at -78 °C, then LDA solution (1.8 M, 1.2 ml, 2.16 mmol) was added. After one hour of stirring at -78 °C, hexachloroethane (632 mg, 2.63 mmol) solution in THF (5 ml) was added, and continued stirring for 90 minutes. Then the reaction mixture was diluted with brine (10 ml), evaporated to Celite and purified by flash chromatography (Hexane-EEO=9-1).

The resulted crude product (110 mg, 0.42 mmol) was dissolved in cc. HCl aqueous solution (82 µl, ~12.2 M, 1 mmol) and PDO (5 ml) was stirred at 100 °C for 2 hours. After the reaction completed, the mixture was partially evaporated. The formed suspension was filtered and the solid on the filter was washed with water and dried to give **Preparation R2dh**. HRMS calculated for C₁₂H₈N₃OCl: 245.0356; found 246.043 [(M+H)⁺ form].

¹H-NMR(500 MHz, MSM-d6) δ ppm 12.16 (s, 1 H), 7.88 (s, 1 H), 7.6-7.52 (m, 5 H), 6.78 (s, 1 H).

¹³C-NMR(125 MHz, MSM-d6) δ ppm 157.6, 148.2, 145.3, 101.6.

Preparation R2di: 6-iodo-7-methyl-3H-pyrrolo[2,3-d]pyrimidin-4-one

To a stirred solution of **Preparation R1a** (8 g, 52.1 mmol) in abs. DMF (50 ml) was cooled down to 0 °C, then sodium-hydride (3.13 g, 60 % disp. in mineral oil, 78.2 mmol, 1.5 eq.) was added and stirred for 20 minutes at r.t. under Ar. Methyl iodide (8.2 g, 57.2 mmol, d=2.28, 3.6 ml) was added to the reaction mixture and stirred for 1.5 hours at r.t. The mixture was poured into water (50 ml) to give a solid compound which was filtered off.

A part of the resulted solid compound (500 mg, 2.98 mmol) was dissolved in 5 ml abs.

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THF and cooled down to -78 °C. Then 2 M LDA (1.7 ml, 3.4 mmol) was added dropwise. The mixture was stirred at -78°C for 1 hour, then iodide (757 mg, 2.98 mmol) was added. The solution was allowed to warm to r.t. and stirred for 22 hours. Finally, 5 ml water was added and a solid compound was formed, which was filtered off, to give

5 **Preparation R2di.** HRMS calculated for C₇H₆IN₃O: 274.9556; found 275.9634 [(M+H)⁺ form].

¹H-NMR(500 MHz, MSM-d6) δ ppm 11.97 (s, 1 H), 7.85 (s, 1 H), 6.79 (s, 1 H), 3.64 (s, 3 H).

¹³C-NMR(125 MHz, MSM-d6) δ ppm 157.3, 149.1, 144.2, 111.4, 110.3, 80.4, 33.2.

10 **Preparation R2dj: 5-fluoro-7-methyl-3H-pyrrolo[2,3-*d*]pyrimidin-4-one**

Using **General Procedure 1** starting from 4-chloro-5-fluoro-7*H*-pyrrolo[2,3-*d*]pyrimidine (instead of **Preparation R1a**) and iodomethane as alkylating agent, **Preparation R2dj** was obtained. HRMS calculated for C₇H₆FN₃O: 167.0495; found 168.0574 [(M+H)⁺ form].

15 ¹H-NMR (500 MHz, MSM-d6) δ ppm 11.97 (brs, 1 H), 7.88 (s, 1 H), 7.07 (s, 1 H), 3.64 (s, 3 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 156.9, 144.6, 144.4, 143.1, 108.1, 97.0, 31.6.

Preparation R2dk: 3,6,7,8-tetrahydro-4*H*-pyrimido[5,4-*b*]pyrrolizin-4-one

*Step 1: 4-methoxy-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine*

20 To a preheated 100 ml two-necked sphere flask equipped with stirring bar and gas inlet, **Preparation R1b** (2.0 g, 11.4 mmol) was dissolved in abs. THF (45 ml). The solution was cooled to 0 °C, and NaH (0.85 g, 3 eq.) was added. The mixture was stirred for 1 hour, then SEM-Cl (3.55 ml, 1.5 eq.) was added via syringe. Yellow solution and white precipitate formed. The mixture was allowed to warm to r.t., while the color faded away.

25 After losing the color, the reaction was quenched with water (30 ml). The mixture was extracted with EEO (3 x 30 ml) and the collected organic layers were dried on Na₂SO₄. After filtration, solvent was evaporated and the crude product was purified with flash chromatography (hexane:EEO = 20:1-9:1) to give the product of the title as a yellowish liquid.

Step 2: 6-iodo-4-methoxy-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-d]pyrimidine

To a preheated 250 ml three-necked sphere flask equipped with a magnetic stirring bar and gas inlet, was added abs. THF (30 ml) and diisopropyl amine (2.7 ml, 1.5 eq.) under nitrogen atmosphere. The mixture was cooled to -78°C and *n*-BuLi (8.0 ml, 1.5 equiv.) was added and stirred for 30 minutes. Then 4-methoxy-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-d]pyrimidine (3.64 g, 13.05 mmol, 1 eq.) dissolved in abs. THF (100 ml) was added slowly over 30 minutes and stirring was continued for 1 hour. Next, iodine (3.95 g, 1.2 eq.) dissolved in abs. THF (35 ml) was added slowly and stirred for an additional 3 hours. Then the cooling bath was removed and the reaction mixture was left to warm to r.t. Brine (500 ml) was added and the solution was extracted with EEO (150 ml) three times. The organic phases were dried, filtered evaporated and purified by flash chromatography (hexane:EEO - 9:1) to give the product of the title as a yellowish white powder.

Step 3: 6-iodo-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine

In a 100 ml Schlenk bomb, 6-iodo-4-methoxy-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-d]pyrimidine (4.72 g, 11.65 mmol) was dissolved in THF (50 ml). To the solution TBAF.3H₂O (11.34 g, 3 eq.) was added with 4Å molecular sieves. The mixture was heated at 95 °C under nitrogen overnight. After cooling, the mixture was filtered through Celite, and the solvent was evaporated. To the resulting brown oil, water was added and an off-white powder precipitated. The precipitation was filtered, washed with water and MeCN (3 x 10 ml). After drying, the product of the title was obtained as an off-white powder.

Step 4: 7-allyl-6-iodo-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine

In a preheated, two-necked 100 ml sphere-flask, equipped with a magnetic stirring bar and a gas inlet, 6-iodo-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine (900 mg, 3.27 mmol) was dissolved in abs. THF (10 ml) under nitrogen. Then, triphenylphosphine (1.048 g, 1.2 eq.) was added. Then, with continuous stirring, allylic alcohol (232 mg, 1.2 eq.) was measured in via syringe. The mixture was cooled to 0 °C and diisopropyl-aza-dicarboxylate (808 mg,

1.2 eq.) was added dropwise via syringe. The mixture was allowed to warm to r.t., and monitored with TLC. After completion, solvent was evaporated, and the crude product was purified by flash chromatography (hexane:EEO=10:1) to give the product of the title as white crystals.

5 *Step 5: 4-methoxy-7,8-dihydro-6H-pyrimido[5,4-b]pyrrolizine*

In a preheated 100 ml Schlenk bomb, 7-allyl-6-iodo-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine (1.60 g, 5.1 mmol) was measured in and dissolved in abs. THF (50 ml). 9-Borabicyclo[3.3.1]nonane (1.87 g, 3 eq.) was measured out in a double-manifold glovebox, dissolved in abs. THF (30 ml), and added into the Schlenk bomb via syringe at
10 0 °C. The reaction was allowed to warm to r.t. and stirred overnight. Then [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (366 mg, 0.1 eq.) and K₂CO₃ (4.93 g, 7 eq.) were measured in under nitrogen and added to the solution. The mixture was warmed to 85 °C for 4 hours. After completion, the solvent was evaporated and the crude product was purified by flash chromatography (hexane:EEO=3:1) to give the product of
15 the title as a dark red solid.

Step 6: Preparation R2dk

The resulted methoxypyrrolizine obtained in Step 5 above (69.7 mg, 0.37 mmol) and lithium-hydroxide monohydrate (155 mg, 3.7 mmol) diluted in mixture of PDO (2 ml) and water (2 ml) and was stirred at 110 °C for 40 hours. After the reaction completed, the
20 mixture was evaporated, purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **Preparation R2dk**. MS calculated for C₉H₉N₃O: 175.07; found 175.2 [(M+H)⁺ EI form].

Preparation R2dl: 6,7,8,9-tetrahydro-3H-pyrimido[5,4-b]indolizin-4-one

Step 1: 7-(but-3-en-1-yl)-6-iodo-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine

25 In a 100 ml sphere-flask, 6-iodo-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine (obtained in Step 3 of **Preparation R2dk**, 1.99 g, 7.23 mmol) was dissolved in DMSO (70 ml), and KOH (690 mg, 1.7 eq.) was added. The mixture was sonicated for 10 minutes, then homoallyl bromide (2.15 ml, 3 eq.) was added at 0 °C. After warming to r.t., the mixture

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was stirred until completion. After completion, water (50 ml) was added and the mixture as extracted with EEO (3 x 120 ml). The organic phases were collected, dried over sodium sulfate and evaporated. The crude product was purified by flash chromatography (hexane:EEO=20:1-5:1) to give the product of the title as a white solid.

5 *Step 2: 4-methoxy-3,4,6,7,8,9-hexahydropyrimido[5,4-b]indolizine*

7-But-3-enyl-6-iodo-4-methoxy-pyrrolo[2,3-*d*]pyrimidine (164 mg, 0.5 mmol) was dissolved in THF (2 ml) in a Schlenk tube under nitrogen atmosphere. The mixture was cooled to 0 °C, and 9-borabicyclo[3.3.1]nonane (305 mg, 2.5 mmol) was added in THF (5 ml) solution via syringe and stirred overnight at r.t.
10 [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (75 mg, 0.1 mmol) and K₂CO₃ (967 mg, 7 mmol) were added to the reaction mixture and stirred for 3 hours at 80 °C. Then the reaction mixture was evaporated to Celite and purified by flash chromatography (hexane-EEO=3-1).

Step 3: Preparation R2dl

15 The resulted methoxyindolizine obtained in Step 2 above (104 mg, 0.51 mmol) and lithium-hydroxide monohydrate (215 mg, 5.1 mmol) diluted in mixture of PDO (2 ml) and water (2 ml) and was stirred at 110 °C for 40 hours. After the reaction completed, the mixture was evaporated, purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **Preparation R2dl**. MS calculated for
20 C₁₀H₁₁N₃O: 189.09; found 190 [(M+H)⁺ EI form].

Preparation R3a: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 5** starting from 3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one as reagent, **Preparation R3a** was obtained. HRMS calculated for C₂₄H₂₉N₅O₃: 435.2270;
25 found 436.2345 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 11.91/11.9 (brs, 1 H), 9.36/8.86 (brd+brq, 2 H), 8.03/7.97 (s, 1 H), 7.32-7.11 (m, 5 H), 7.06/7.04 (dd, 1 H), 6.47/6.43 (dd, 1 H), 4.09-2.6 (m, 12 H), 1.96-0.62 (m, 6 H).

Preparation R3b: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-methyl-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2b** as reagent, **Preparation R3b** was obtained as HCl salt. HRMS calculated for C₂₅H₃₁N₅O₃: 449.2427; found 450.2517 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.16/8.72 (brd/brq, 2 H), 8.02/8.07 (s, 1 H), 7.34-7.11 (m, 5 H), 7.11/7.13 (d, 1 H), 6.45/6.48 (d, 1 H), 4.01/3.73 (d/s, 1 H), 4.00-0.58 (m, 16 H), 3.89 (d, 2 H), 3.71 (s, 3 H).

Preparation R3c: 7-ethyl-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2c** as reagent, **Preparation R3c** was obtained as HCl salt. HRMS calculated for C₂₆H₃₃N₅O₃: 463.2583; found 464.2654 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.16/8.72 (brd/brq, 2 H), 8.01/8.07 (s, 1 H), 7.33-7.09 (m, 5 H), 7.18/7.19 (d, 1 H), 6.45/6.49 (d, 1 H), 4.13/4.15 (q, 2 H), 4.01/3.73 (d/s, 1 H), 4.00-0.58 (m, 16 H), 3.89 (d, 2 H), 1.34/1.35 (t, 3 H).

Preparation R3d: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(propan-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2d** as reagent, **Preparation R3d** was obtained. HRMS calculated for C₂₇H₃₅N₅O₃: 477.274; found 478.2819 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.4/8.89 (brd+brq, 1+1 H), 8.08/8.03 (s/s, 1 H), 7.32-7.09 (m, 5 H), 7.27/7.25 (d/d, 1 H), 6.51/6.47 (d/d, 1 H), 4.84 (m, 1 H), 4.05-0.6 (m, 16 H), 3.48/3.43 (m/m, 1 H), 3.22 (m, 1 H), 1.43 (d, 6 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 147.4, 121.1/121, 102.3/102.2, 46.4, 42.6/42.4, 41/40.6, 23.1.

Preparation R3e: 6-[3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-4-oxo-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1,2-dihydropyridin-2-one

Using **General Procedure 15** starting from **Preparation R3bs** as reagent, **Preparation R3e** was obtained as free base. HRMS calculated for $C_{29}H_{32}N_6O_4$: 528.2485; found 529.2567 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 8.17/8.13 (s/s, 1 H), 7.87/7.86 (d/d, 1 H), 7.83/7.8 (d/d, 1 H), 7.82 (t, 1 H), 7.26-6.99 (m, 5 H), 6.71/6.68 (d/d, 1 H), 6.6 (d, 1 H), 4.85 (brs, 1 H), 4.12-0.75 (m, 16 H), 3.21/3.15 (t/t, 1 H), 2.86 (m, 1 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 148.4, 142, 122.2, 107.9, 107.1, 103.9/103.8, 46.4/46.3, 43.4/42.9.

Preparation R3g: 7-cyclopropyl-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2g** as reagent, **Preparation R3g** was obtained as HCl salt. HRMS calculated for $C_{27}H_{33}N_5O_3$: 475.2583; found 476.2668 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.26/8.78 (brd+brq, 2 H), 8.12-6.38 (m, 8 H), 4.05-0.62 (m, 23 H).

Preparation R3h: 7-cyclobutyl-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2h** as reagent, **Preparation R3h** was obtained. HRMS calculated for $C_{28}H_{35}N_5O_3$: 489.274; found 490.2796 ((M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 8.92 (vbrs, 2 H), 8.06/8.01 (s/s, 1 H), 7.43/7.4 (d/d, 1 H), 7.34-7.08 (m, 5 H), 6.53/6.49 (d/d, 1 H), 5.09 (m, 1 H), 4.85 (s, 1 H), 4.08-0.55 (m, 16 H), 3.47/3.42 (m/m, 1 H), 3.21 (m, 1 H), 2.5/2.38 (m+m, 4 H), 1.82 (m, 2 H)

¹³C-NMR (500 MHz, MSM-d6) δ ppm 147.6/147.5, 122/121.9, 102.5/102.4, 48.5, 42.6/42.5, 41/40.6, 31, 14.8

Preparation R3k: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(1-methylpiperidin-4-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2k** as reagent, **Preparation R3k** was obtained as HCl salt. HRMS calculated for $C_{30}H_{40}N_6O_3$: 532.3162; found 267.1658 [(M+2H)²⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 10.87/10.67 (brs, 1 H), 9.29/8.8 (brq+brd, 2 H), 8.13/8.08 (s, 1 H), 7.35-7.11 (m, 5 H), 7.14/7.12 (d, 1 H), 6.57/6.53 (d, 1 H), 4.82 (brs, 1 H), 4.76 (m, 1 H), 4.08-2.61 (m, 16 H), 2.78 (d, 3 H), 2.47-1.96 (m, 4 H), 1.95-0.59 (m, 6 H).

Preparation R3m: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]

piperidin-4-yl}methyl)-7-(prop-2-yn-1-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2m** as reagent, **Preparation R3m** was obtained as HCl salt. HRMS calculated for C₂₇H₃₁N₅O₃: 473.2427; found 474.2502 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.32/8.83 (brd+brq, 2 H), 8.12/8.06 (s, 1 H), 7.33-7.12 (m, 12 H), 7.33-7.12 (m, 5 H), 7.22/7.2 (d, 1 H), 6.55/6.51 (d, 1 H), 5/4.98 (d, 2 H), 3.44/3.43 (t, 1 H), 1.92-0.62 (m, 6 H).

Preparation R3n: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(2-methylpropyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2n** as reagent, **Preparation R3n** was obtained as HCl salt. HRMS calculated for C₂₈H₃₇N₅O₃: 491.2896; found 492.2963 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.3/8.81 (brd+brq, 2 H), 8.07/8.01 (s, 1 H), 7.33-7.12 (m, 5 H), 7.15/7.13 (d, 1 H), 6.49/6.46 (d, 1 H), 4.05-2.61 (m, 14 H), 2.12 (m, 1 H), 1.92-0.61 (m, 6 H), 0.84/0.83 (d, 6 H).

Preparation R3o: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(2,2,2-trifluoroethyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2o** as reagent, **Preparation R3o** was obtained as HCl salt. HRMS calculated for C₂₆H₃₀F₃N₅O₃: 517.2301; found 518.2386 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.11/8.67 (brq+brd, 2 H), 8.16-6.55 (m, 8 H), 5.15-0.6 (m, 20 H), 4.87 (brs, 1 H).

Preparation R3p: 7-(2,2-difluoroethyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-

4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2p** as reagent, **Preparation R3p** was obtained as HCl salt. HRMS calculated for $C_{26}H_{31}F_2N_5O_3$: 499.2395; found 500.2485 [(M+H)⁺ form].

5 ¹H-NMR (500 MHz, MSM-d6) δ ppm 9.28/8.8 (brd+brq., 2 H), 8.12/8.07 (s/s, 1 H), 7.36-7.11 (m, 5 H), 7.18/7.17 (d/d, 1 H), 6.57/6.53 (d/d, 1 H), 6.39 (tm, 1 H), 4.6 (m, 2 H), 4.07-0.6 (m, 16 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 148.2/148.1, 125.2, 114.4, 102.9/102.8, 46.1, 42.6/42.4, 41/40.6.

10 **Preparation R3q: 7-(cyclopropylmethyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one**

Using **General Procedure 5** starting from **Preparation R2q** as reagent, **Preparation R3q** was obtained as HCl salt. HRMS calculated for $C_{28}H_{35}N_5O_3$: 489.2740; found 490.2817 [(M+H)⁺ form].

15 ¹H-NMR (500 MHz, MSM-d6) δ ppm 9.11/8.68 (brq+brd, 2 H), 8.06/8 (s, 1 H), 7.34-7.1 (m, 5 H), 7.23/7.21 (d, 1 H), 6.5/6.46 (d, 1 H), 4.07-2.6 (m, 14 H), 1.92-0.63 (m, 7 H), 0.54-0.35 (m, 4 H).

20 **Preparation R3r: 7-(cyclobutylmethyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one**

Using **General Procedure 5** starting from **Preparation R2r** as reagent, **Preparation R3r** was obtained as HCl salt. HRMS calculated for $C_{29}H_{37}N_5O_3$: 503.2896; found 504.2957 [(M+H)⁺ form].

25 ¹H-NMR (400 MHz, MSM-d6) δ ppm 9.45/8.92 (brq+brd), 8.09/8.03 (s, 1 H), 7.34-7.08 (m, 5 H), 7.15/7.13 (d, 1 H), 6.47/6.44 (d, 1 H), 4.19-2.59 (m, 15 H), 2.02-0.56 (m, 12 H).

Preparation R3s: 7-(buta-2,3-dien-1-yl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2s** as reagent, **Preparation R3s**

was obtained as HCl. HRMS calculated for $C_{28}H_{33}N_5O_3$: 487.2583; found 488.2657 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.28/8.8 (brd+brq, 2 H), 8.09/8.03 (s, 1 H), 7.34-7.11 (m, 5 H), 7.15/7.14 (d, 1 H), 6.51/6.47 (d, 1 H), 5.5 (m, 1 H), 4.9 (m, 2 H), 4.88 (s, 1 H), 4.73 (m, 2 H), 4.06-2.63 (m, 12 H), 1.94-0.6 (m, 6 H).

Preparation R3t: 7-[3-(dimethylamino)propyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2t** as reagent, **Preparation R3t** was obtained as HCl salt. HRMS calculated for $C_{29}H_{40}N_6O_3$: 520.3162; found 261.1666 [(M+2H)²⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 10.53 (brs, 1 H), 9.33/8.83 (brs+brm, 2 H), 8.13/8.07 (s/s, 1 H), 7.36-7.14 (m, 5 H), 7.23/7.21 (d/d, 1 H), 6.53/6.5 (d/d, 1 H), 4.2 (m, 2 H), 4.06-0.55 (m, 16 H), 3.48/3.43 (m/m, 1 H), 3.22 (m, 1 H), 3.02 (m, 2 H), 2.72/2.71 (s/s, 6 H), 2.17 (m, 2 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 147.9/147.8, 124.4/124.3, 102.4, 54.4, 42.6/42.4, 42.5, 42, 41/40.6, 25.6.

Preparation R3u: 7-(2-fluoroethyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2u** as reagent, **Preparation R3u** was obtained as HCl salt. HRMS calculated for $C_{25}H_{31}FN_5O_3$: 468.2411; found 482.2555 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.16/8.71 (m+m, 2 H), 8.08/8.03 (s, 1 H), 7.34-7.11 (m, 5 H), 7.2/7.18 (d, 1 H), 6.53/6.49 (d, 1 H), 4.82 (brs, 1 H), 4.76 (dt, 2 H), 4.44 (dt, 2 H), 4.11-2.6 (m, 12 H), 1.95-0.6 (m, 6 H).

Preparation R3v: 7-[2-(dimethylamino)ethyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2v** as reagent, **Preparation R3v**

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was obtained as HCl salt. HRMS calculated for $C_{28}H_{38}N_6O_3$: 506.3005; found 254.1581 [(M+2H)²⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 10.48 (brs, 1 H), 9.27/8.8 (brs+brm, 2 H), 8.16/8.11 (s/s, 1 H), 7.37-7.16 (m, 5 H), 7.25 (d, 1 H), 6.57/6.54 (d/d, 1 H), 4.9 (vbrs, 1 H), 4.53 (m, 2 H), 4.13-0.55 (m, 16 H), 3.51 (m, 2 H), 3.48/3.43 (brm/brm, 1 H), 3.22 (m, 1 H), 2.8/2.79 (d/d, 6 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 148.1, 124.4, 103, 55.9, 42.9, 42.6/42.4, 41/40.6, 39.6.

Preparation R3w: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]

piperidin-4-yl}methyl)-7-(2-hydroxyethyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2w** as reagent, **Preparation R3w** was obtained.

¹H-NMR (400 MHz, MSM-d6) δ ppm 8.05/7.99 (s/s, 1 H), 7.27-7.02 (m, 5 H), 7.16/7.14 (d/d, 1 H), 6.47/6.45 (d/d, 1 H), 4.94/4.93 (t/t, 1 H), 4.83/4.8 (s/s, 1 H), 4.15 (m, 2 H), 4.06-0.72 (m, 16 H), 3.71 (m, 2 H), 3.2/3.15 (m/m, 1 H), 2.86 (m, 1 H).

¹³C-NMR (100 MHz, MSM-d6) δ ppm 147.4, 125.1, 101.8/101.7, 60.6, 47.3, 46.5/46.4, 43.4.

Preparation R3x: 7-[(4-chlorophenyl)methyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2x** as reagent, **Preparation R3x** was obtained as HCl salt. HRMS calculated for $C_{31}H_{34}ClN_5O_3$: 559.2350; found 560.2418 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.04/8.63 (brd+brq, 2 H), 8.07/8.02 (s, 1 H), 7.44-7.07 (m, 9 H), 7.26/7.24 (d, 1 H), 6.54/6.5 (d, 1 H), 5.34/5.33 (s, 2 H), 4.81 (brs, 1 H), 4.04-2.61 (m, 12 H), 1.92-0.61 (m, 6 H).

Preparation R3y: 7-[(3-chlorophenyl)methyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2y** as reagent, **Preparation R3y** was obtained as HCl salt. HRMS calculated for $C_{31}H_{34}ClN_5O_3$: 559.2350; found 560.2432 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.1/8.67 (brd+brq, 2 H), 8.09/8.03 (s, 1 H), 7.4-7.08 (m, 9 H), 7.29/7.27 (d, 1 H), 6.55/6.52 (d, 1 H), 5.35/5.34 (s, 2 H), 4.83 (brs, 1 H), 4.05-2.62 (m, 12 H), 1.91-0.61 (m, 6 H).

Preparation R3z: 7-benzyl-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2z** as reagent, **Preparation R3z** was obtained as HCl salt. HRMS calculated for $C_{31}H_{35}N_5O_3$: 525.2740; found 526.2822 [(M+H) form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.31/8.82 (brd+brq, 2 H), 8.1/8.05 (s, 1 H), 7.36-7.09 (m, 10 H), 7.25/7.22 (d, 1 H), 6.53/6.5 (d, 1 H), 5.34/5.33 (s, 2 H), 4.05-2.63 (m, 12 H), 1.92-0.62 (m, 6 H).

Preparation R3aa: 7-[(2-chlorophenyl)methyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2aa** as reagent, **Preparation R3aa** was obtained as HCl salt. HRMS calculated for $C_{31}H_{34}ClN_5O_3$: 559.2350; found 560.2429 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.12/8.68 (brd+brq, 2 H), 8.07/8.01 (s, 1 H), 7.54-6.76 (m, 9 H), 7.2/7.18 (d, 1 H), 6.56/6.55 (d, 1 H), 5.44/5.43 (s, 2 H), 4.86/4.85 (s, 1 H), 4.06-2.61 (m, 12 H), 1.91-0.62 (m, 6 H).

Preparation R3ac: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(3,4,5-trimethoxyphenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ac** as reagent, **Preparation R3ac** was obtained as HCl salt. HRMS calculated for $C_{33}H_{39}N_5O_6$: 601.2900; found 602.2960 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.55/9.01 (brq+brd, 2 H), 8.16/8.12 (s, 1 H), 7.54/7.51 (d, 1 H), 7.36-7.14 (m, 5 H), 7.01/6.99 (s, 2 H), 6.7/6.67 (d, 1 H), 4.95 (brs, 1 H), 4.1-2.61 (m, 12 H), 3.83 (s, 6 H), 3.7 (s, 3 H), 1.98-0.62 (m, 6 H).

Preparation R3ad: 7-(3,5-dichlorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ad** as reagent, **Preparation R3ad** was obtained as HCl salt. HRMS calculated for C₃₀H₃₁N₅O₃Cl₂: 579.1804; found 580.1891 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.06/8.65 (brd+brq, 2 H), 8.18/8.14 (s, 1 H), 7.98/7.97 (d, 2 H), 7.71/7.68 (d, 1 H), 7.67 (t, 1 H), 7.34-7.14 (m, 5 H), 6.77/6.73 (d, 1 H), 4.88 (brs, 1 H), 4.12-2.62 (m, 12 H), 1.96-0.62 (m, 6 H).

Preparation R3ae: 7-(3-chloro-5-methoxyphenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ae** as reagent, **Preparation R3ae** was obtained as HCl salt. HRMS calculated for C₃₁H₃₄ClN₅O₄: 575.2299; found 576.2382 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 8.83 (brs, 2 H), 8.15/8.1 (s, 1 H), 7.64/7.62 (d, 1 H), 7.51/7.5 (t, 1 H), 7.36/7.34 (t, 1 H), 7.36-7.12 (m, 5 H), 7.09 (t, 1 H), 6.74/6.7 (d, 1 H), 4.87 (s, 1 H), 4.11-2.62 (m, 12 H), 3.85 (s, 3 H), 1.94-0.62 (m, 6 H).

Preparation R3af: 7-(3,5-dimethoxyphenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2af** as reagent, **Preparation R3af** was obtained as HCl salt. HRMS calculated for C₃₂H₃₇N₅O₅: 571.2795; found 572.2881 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.11/8.68 (brq+brd, 2 H), 8.12/8.07 (s, 1 H), 7.57/7.55 (d, 1 H), 7.34-7.13 (m, 5 H), 6.93/6.91 (d, 2 H), 6.71/6.67 (d, 1 H), 6.56/6.55 (t,

1 H), 4.86 (brs, 1 H), 4.09-2.62 (m, 12 H), 3.81 (s, 6 H), 1.94-0.64 (m, 6 H).

Preparation R3ag: 7-(3,4-dichlorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

5 Using **General Procedure 5** starting from **Preparation R2ag** as reagent, **Preparation R3ag** was obtained as HCl salt. HRMS calculated for $C_{30}H_{31}Cl_2N_5O_3$: 579.18042; found 580.1870 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.16/8.71 (brq+brd, 2 H), 8.2-7.79 (m, 3 H), 8.17/8.13 (s, 1 H), 7.65/7.63 (d, 1 H), 7.35-7.12 (m, 5 H), 6.76/6.72 (d, 1 H), 4.85 (brs, 1 H), 4.11-2.61 (m, 12 H), 1.95-0.6 (m, 6 H).

Preparation R3ah: 7-(4-chloro-3-fluorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

15 Using **General Procedure 5** starting from **Preparation R2ah** as reagent, **Preparation R3ah** was obtained as HCl salt. HRMS calculated for $C_{30}H_{31}N_5O_3FCl$: 563.2100; found 564.2181 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.08/8.66 (brm/brm, 2 H), 8.16/8.12 (s, 1 H), 7.98/7.97 (dd, 1 H), 7.82-7.72 (m, 1 H), 7.78 (m, 1 H), 7.65/7.63 (d, 1 H), 7.33-7.26 (m, 2 H), 7.26-7.2 (m, 2 H), 7.17 (brt, 1 H), 6.77/6.73 (d, 1 H), 4.86 (vbrs, 1 H), 4.12-0.58 (, 16 H), 4.05/3.94/3.67 (d/s, 2 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 158.3, 157.7, 148.7/148.6, 146.7/146.6, 131.6, 129/128.9, 128.3/128.1, 127.7, 124.1, 121, 112.7, 109.3/109.2, 104.5, 69.4, 53.6/53.3.

Preparation R3ai: 7-(4-chloro-3-methoxyphenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

25 Using **General Procedure 5** starting from **Preparation R2ai** as reagent, **Preparation R3ai** was obtained as HCl salt. HRMS calculated for $C_{31}H_{34}ClN_5O_4$: 575.2230; found 576.2382 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6) δ ppm 8.89 (brs, 2 H), 8.14/8.06 (s, 1 H), 7.62/7.6 (d, 1 H),

7.6 (d, 1 H), 7.51/7.5 (d, 1 H), 7.38/7.36 (dd, 1 H), 7.35-7.13 (m, 5 H), 6.75/6.71 (d, 1 H), 4.87 (s, 1 H), 4.11-2.6 (m, 12 H), 3.93 (s, 3 H), 1.95-0.6 (m, 6 H).

Preparation R3aj: 7-(4-fluoro-3-methoxyphenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2aj** as reagent, **Preparation R3aj** was obtained as HCl salt. HRMS calculated for $C_{31}H_{34}FN_5O_4$: 559.2595; found 560.2638 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.13/8.7 (brd+brq, 1+1 H), 8.12/8.07 (s/s, 1 H), 7.55/7.53 (d/d, 1 H), 7.49 (m, 2 H), 7.39 (m, 2 H), 7.35-7.14 (m, 5 H), 7.28 (m, 2 H), 6.73/6.69 (d/d, 1 H), 4.65-0.6 (m, 16 H), 3.91 (s, 3 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 148.4/148.3, 124.8/124.7, 116.8, 116.6, 110.8, 103.7, 56.8, 42.6/42.5, 41/40.6.

Preparation R3ak: 7-(3,4-dimethoxyphenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ak** as reagent, **Preparation R3ak** was obtained as HCl salt. HRMS calculated for $C_{32}H_{37}N_5O_5$: 571.2795; found 572.2892 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.11/8.69 (brd+brq, 2 H), 8.09/8.04 (s, 1 H), 7.48/7.46 (d, 1 H), 7.35-7.06 (m, 8 H), 6.69/6.68 (d, 1 H), 4.86 (brs, 1 H), 4.11-2.6 (m, 12 H), 3.81 (s, 6 H), 1.96-0.62 (m, 6 H).

Preparation R3am: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(4-methylphenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2am** as reagent, **Preparation R3am** was obtained as HCl salt. HRMS calculated for $C_{31}H_{35}N_5O_3$: 525.2734; found 526.2816 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.31/8.82 (brd+brq, 2 H), 8.11/8.06 (s, 1 H),

7.6/7.58 (m, 2 H), 7.49/7.46 (d, 1 H), 7.35/7.34 (m, 2 H), 7.32-7.11 (m, 5 H), 6.71/6.67 (d, 1 H), 4.81 (brs, 1 H), 4.11-2.61 (m, 12 H), 2.37 (s, 3 H), 1.94-0.61 (m, 6 H).

Preparation R3an: 4-[3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-4-oxo-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-7-yl]benzonitrile

Using **General Procedure 5** starting from **Preparation R2an** as reagent, **Preparation R3an** was obtained as HCl salt. HRMS calculated for $C_{31}H_{32}N_6O_3$: 536.2536; found 537.2599 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.19/8.73 (brd+brq, 2 H), 8.18/8.14 (s/s, 1 H), 8.12-8 (m, 4 H), 7.71/7.69 (d/d, 1 H), 7.35-7.13 (m, 5 H), 6.8/6.76 (d/d, 1 H), 4.85 (vbrs, 1 H), 4.15-0.6 (m, 16 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

Preparation R3ao: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-[4-(trifluoromethyl)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ao** as reagent, **Preparation R3ao** was obtained as HCl salt. HRMS calculated for $C_{31}H_{32}N_5O_3F_3$: 579.2457; found 580.2529 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.13/8.7 (brs+brs, 2 H), 8.17/8.12 (s/s, 1 H), 8.05/8.04 (d/d, 2 H), 7.94/7.93 (d/d, 2 H), 7.68/7.66 (d/d, 1 H), 7.35-7.12 (m, 5 H), 6.79/6.75 (d/d, 1 H), 4.88 (s, 1 H), 4.2-0.59 (m, 16 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

Preparation R3ap: 7-[4-(difluoromethyl)phenyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ap** as reagent, **Preparation R3ap** was obtained as HCl salt. HRMS calculated for $C_{31}H_{33}F_2N_5O_3$: 561.2551; found 562.2636 [(M+H) form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.11/8.68 (brd+brq, 2 H), 8.14/8.09 (s, 1 H), 7.93/7.91 (m, 2 H), 7.76/7.75 (m, 2 H), 7.62/7.6 (d, 1 H), 7.34-7.12 (m, 5 H), 7.13 (t, 1 H), 6.77/6.73 (d, 1 H), 4.87 (s, 1 H), 4.11-2.61 (m, 12 H), 1.93-0.64 (m, 6 H).

Preparation R3aq: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-[4-(hydroxymethyl)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2aq** as reagent, **Preparation R3aq** was obtained as HCl salt. HRMS calculated for $C_{31}H_{35}N_5O_4$: 541.2689; found 542.2787 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.2/8.74 (brd+brq, 1+1 H), 8.11/8.06 (s/s, 1 H), 7.67/7.65 (dm/dm, 2 H), 7.51/7.48 (d/d, 1 H), 7.47 (m, 2 H), 7.34-7.1 (m, 5 H), 6.72/6.68 (d/d, 1 H), 4.56 (s, 2 H), 4.08-0.61 (m, 16 H), 3.48/3.43 (m/m, 1 H), 3.21 (m, 1 H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 148.3/148.2, 127.8, 124.4, 124.2, 103.8, 62.8, 42.6/42.5, 41/40.6.

Preparation R3ar: 7-(4-chlorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ar** as reagent, **Preparation R3ar** was obtained as HCl salt. HRMS calculated for $C_{30}H_{32}ClN_5O_3$: 545.2194; found 546.2288 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.38/8.87 (brs, 2 H), 8.24-6.62 (m, 12 H), 4.13-0.58 (m, 18 H).

Preparation R3as: 7-(4-fluorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2as** as reagent, **Preparation R3as** was obtained as HCl salt. HRMS calculated for $C_{30}H_{32}N_5O_3F$: 529.2489; found 530.2563 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.05/8.64 (brd+brq, 2 H), 8.11/8.06 (s, 1 H), 7.76/7.75 (m, 2 H), 7.52/7.5 (d, 1 H), 7.41/7.4 (m, 2 H), 7.34-7.13 (m, 5 H), 6.73/6.69 (d, 1 H), 4.84 (brs, 1 H), 4.1-2.65 (m, 12 H), 1.95-0.63 (m, 6 H).

Preparation R3at: 7-[4-(dimethylamino)phenyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]

pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2at** as reagent, **Preparation R3at** was obtained as HCl salt. HRMS calculated for $C_{32}H_{38}N_6O_3$: 554.3005; found 555.3076 $[(M+H)^+ \text{ form}]$.

5 $^1\text{H-NMR}$ (500 MHz, MSM-d6) δ ppm 9.15/8.71 (brd+brq, 2 H), 8.07/8.02 (s, 1 H), 7.52 (brm, 2 H), 7.41/7.38 (d, 1 H), 7.33-7.11 (m, 5 H), 6.99 (brs, 2 H), 6.68/6.64 (d, 1 H), 4.07-2.62 (m, 12 H), 2.99 (s, 6 H), 1.93-0.64 (m, 6 H).

Preparation R3ax: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(4-methoxyphenyl)-3H,4H,7H-pyrrolo[2,3-d]

10 **pyrimidin-4-one**

Using **General Procedure 5** starting from **Preparation R2ax** as reagent, **Preparation R3ax** was obtained as HCl salt. HRMS calculated for $C_{31}H_{35}N_5O_4$: 541.2689; found 542.2782 $[(M+H)^+ \text{ form}]$.

15 $^1\text{H-NMR}$ (500 MHz, MSM-d6) δ ppm 9.2/8.74 (brd+brq, 2 H), 8.09/8.04 (s, 1 H), 7.63-7.55 (m, 2 H), 7.44/7.42 (d, 1 H), 7.33-7.12 (m, 5 H), 7.12-7.06 (m, 2 H), 6.69/6.65 (d, 1 H), 4.85 (brs, 1 H), 4.07-2.63 (m, 12 H), 3.82/3.75 (s, 3 H), 1.95-0.61 (m, 6 H).

Preparation R3ay: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-[4-(trifluoromethoxy)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

20 Using **General Procedure 5** starting from **Preparation R2ay** as reagent, **Preparation R3ay** was obtained as HCl salt. HRMS calculated for $C_{31}H_{32}N_5O_4F_3$: 595.2407; found 596.2494 $[(M+H)^+ \text{ form}]$.

$^1\text{H-NMR}$ (400 MHz, MSM-d6) δ ppm 9.08/8.66 (brs, 2 H), 8.13/8.08 (s, 1 H), 7.93-7.53 (m, 4 H), 7.59/7.57 (d, 1 H), 7.36-7.12 (m, 5 H), 6.75/6.72 (d, 1 H), 4.86 (s, 1 H), 4.14-2.59 (m, 12 H), 1.95-0.63 (m, 6 H).

Preparation R3az: 7-[4-(benzyloxy)phenyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2az** as reagent,

Preparation R3az was obtained as HCl salt. HRMS calculated for $C_{37}H_{39}N_5O_4$: 617.3002; found 618.3083 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.12/8.68 (brs+brs, 2 H), 8.08/8.03 (s, 1 H), 7.6/7.58 (m, 2 H), 7.51-7.11 (m, 10 H), 7.45/7.42 (d, 1 H), 7.17 (m, 2 H), 6.69/6.65 (d, 1 H), 5.18 (s, 2 H), 4.85 (s, 1 H), 4.1-2.6 (m, 12 H), 1.95-0.61 (m, 6 H).

Preparation R3ba: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(5-methylthiophen-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ba** as reagent, **Preparation R3ba** was obtained as HCl salt. HRMS calculated for $C_{29}H_{33}N_5O_3S$: 531.2304; found 532.2361 [(M+H) form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.05/8.68 (brs+brs, 2 H), 8.14/8.1 (s, 1 H), 7.53/7.51 (d, 1 H), 7.33-7.11 (m, 5 H), 7.16/7.15 (d, 1 H), 6.77/6.76 (m, 1 H), 6.71/6.67 (d, 1 H), 4.88/4.87 (s, 1 H), 4.09-2.62 (m, 12 H), 2.46 (d, 3 H), 1.92-0.62 (m, 6 H).

Preparation R3bb: 7-(5-chlorothiophen-2-yl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bb** as reagent, **Preparation R3bb** was obtained as HCl salt. HRMS calculated for $C_{28}H_{30}ClN_5O_3S$: 551.1758; found 552.1844 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.06/8.76 (brs+brs, 2 H), 8.21/8.16 (s/s, 1 H), 7.71/7.68 (d/d, 1 H), 7.32/7.31 (d/d, 1 H), 7.32-7.12 (m, 5 H), 7.15/7.14 (d/d, 1 H), 6.76/6.73 (d/d, 1 H), 4.1-0.58 (m, 16 H), 3.47/3.41 (m/m, 1 H), 3.21 (m, 1 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 149.2/149.1, 125.6, 123.6, 117.6/117.5, 104.9, 42.6/42.5, 41/40.6.

Preparation R3bc: 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bc** as reagent,

Preparation R3bc was obtained as HCl salt. HRMS calculated for $C_{32}H_{35}N_5O_5$: 569.2638; found 570.2709 $[(M+H)^+ \text{ form}]$.

$^1\text{H-NMR}$ (500 MHz, MSM-d6) δ ppm 9.42/8.89 (brd+brq, 2 H), 8.11/8.06 (s, 1 H), 7.44/7.41 (d, 1 H), 7.33-7.11 (m, 5 H), 7.23/7.22 (d, 1 H), 7.15/7.13 (dd, 1 H), 7/6.99 (d, 1 H), 6.67/6.63 (d, 1 H), 4.35-4.26 (m, 4 H), 4.09-2.62 (m, 12 H), 1.94-0.61 (m, 6 H).

Preparation R3bd: 7-(2H-1,3-benzodioxol-5-yl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bd** as reagent, **Preparation R3bd** was obtained as HCl salt. HRMS calculated for $C_{31}H_{33}N_5O_5$: 555.2482; found 570.2709 $[(M+H)^+ \text{ form}]$.

$^1\text{H-NMR}$ (500 MHz, MSM-d6) δ ppm 9.21/8.78 (brs+brs, 2 H), 8.1/8.05 (s, 1 H), 7.44/7.42 (d, 1 H), 7.35-7.11 (m, 5 H), 7.3/7.28 (d, 1 H), 7.14/7.13 (dd, 1 H), 7.07/7.06 (d, 1 H), 6.68/6.64 (d, 1 H), 6.12 (s, 2 H), 4.87 (s, 1 H), 4.09-2.62 (m, 12 H), 1.95-0.62 (m, 6 H).

Preparation R3be: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(naphthalen-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2be** as reagent, **Preparation R3be** was obtained as HCl salt. HRMS calculated for $C_{34}H_{35}N_5O_3$: 561.2740; found 562.2831 $[(M+H)^+ \text{ form}]$.

$^1\text{H-NMR}$ (500 MHz, MSM-d6) δ ppm 9.16/8.72 (brd+brq, 2 H), 8.3-7.54 (m, 7 H), 8.16/8.11 (s, 1 H), 7.67/7.65 (d, 1 H), 7.35-7.13 (m, 5 H), 6.79/6.75 (d, 1 H), 4.89 (brs, 1 H), 4.12-2.65 (m, 12 H), 1.96-0.65 (m, 6 H).

Preparation R3bf: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(3-methylphenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bf** as reagent, **Preparation R3bf** was obtained. HRMS calculated for $C_{31}H_{35}N_5O_3$: 525.2740; found 526.2825 $[(M+H)^+ \text{ form}]$.

$^1\text{H-NMR}$ (500 MHz, MSM-d6) δ ppm 9.13/8.69 (brq+brd, 2 H), 8.11/8.06 (s, 1 H), 7.57-7.11 (m, 10 H), 6.71/6.67 (d, 1 H), 4.2-2.62 (m, 12 H), 1.94-0.59 (m, 6 H).

Preparation R3bg: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-[3-(trifluoromethyl)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bg** as reagent, **Preparation R3bg** was obtained as HCl salt. HRMS calculated for $C_{31}H_{32}F_3N_5O_3$: 579.2457; found 580.2509 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6) δ ppm 9.2/8.74 (brd+brq, 2 H), 8.19/8.17 (m, 1 H), 8.17/8.13 (s, 1 H), 8.09/8.07 (dm, 1 H), 7.86-7.74 (m, 2 H), 7.7/7.67 (d, 1 H), 7.35-7.11 (m, 5 H), 6.78/6.74 (d, 1 H), 4.78 (brs, 1 H), 4.11-2.6 (m, 12 H), 1.94-0.62 (m, 6 H).

Preparation R3bh: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-{3-[(4-methylpiperazin-1-yl)methyl]phenyl}-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bh** as reagent, **Preparation R3bh** was obtained as HCl salt. HRMS calculated for $C_{36}H_{45}N_7O_3$: 623.3584; found 624.3656 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 12.37/11.6 (brs, 2 H), 9.33/8.83 (brd+brq, 2 H), 8.18/8.12 (s, 1 H), 8.04-7.5 (m, 5 H), 7.35-7.13 (m, 5 H), 6.75/6.72 (d, 1 H), 4.6-2.6 (m, 22 H), 2.79 (s, 3 H), 1.98-0.66 (m, 6 H).

Preparation R3bi: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-[3-(hydroxymethyl)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bi** as reagent, **Preparation R3bi** was obtained as HCl salt. HRMS calculated for $C_{31}H_{35}N_5O_4$: 541.2689; found 542.2769 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 8.98/8.72 (brs+brs, 2 H), 8.1/8.05 (s/s, 1 H), 7.69-7.33 (m, 4 H), 7.51/7.48 (d/d, 1 H), 7.33-7.11 (m, 5 H), 6.73/6.69 (d/d, 1 H), 5.36 (t, 1 H), 4.59 (d, 2 H), 4.15-0.61 (m, 16 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

Preparation R3bj: 7-(3-chlorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-

4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bj** as reagent, **Preparation R3bj** was obtained as HCl salt. HRMS calculated for $C_{30}H_{32}N_5O_3Cl$: 545.2194; found 546.2277 [(M+H)⁺ form].

- 5 ¹H-NMR (500 MHz, MSM-d6) δ ppm 9.17/8.72 (brd+brq, 2 H), 8.15/8.11 (s, 1 H), 7.94-7.45 (m, 4 H), 7.63/7.6 (d, 1 H), 7.34-7.12 (m, 5 H), 6.75/6.71 (d, 1 H), 4.88 (brs, 1 H), 4.13-2.62 (m, 12 H), 1.95-0.62 (m, 6 H).

Preparation R3bk: 7-(3-fluorophenyl)-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

- 10 Using **General Procedure 5** starting from **Preparation R2bk** as reagent, **Preparation R3bk** was obtained. HRMS calculated for $C_{30}H_{32}FN_5O_3$: 529.2489; found 530.2571 [(M+H)⁺ form].

- ¹H-NMR (500 MHz, MSM-d6) δ ppm 9/8.61 (brd+brq, 1+1 H), 8.14/8.09 (s/s, 1 H), 7.76-7.23 (m, 4 H), 7.62/7.6 (d/d, 1 H), 7.34-7.13 (m, 5 H), 6.75/6.71 (d/d, 1 H), 4.14-0.6 (m, 16 H), 3.47/3.42 (m/m, 1 H), 3.2 (m, 1 H).

- 15 ¹³C-NMR (125 MHz, MSM-d6) δ ppm 148.6/148.5, 124.2, 104.3/104.2, 42.6/42.5, 41/40.6.

Preparation R3bl: 7-[3-(dimethylamino)phenyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

- 20 Using **General Procedure 5** starting from **Preparation R2bl** as reagent, **Preparation R3bl** was obtained as HCl salt. HRMS calculated for $C_{32}H_{38}N_6O_3$: 554.3005; found 555.3086 [(M+H)⁺ form].

- ¹H-NMR (500 MHz, MSM-d6) δ ppm 9.23/8.76 (brd+brq, 1+1 H), 8.1/8.05 (s/s, 1 H), 7.51/7.49 (d/d, 1 H), 7.37 (brt, 1 H), 7.33-7.13 (m, 5 H), 7.18-6.76 (brd, 3 H), 6.7/6.66 (d/d, 1 H), 4.09-0.61 (m, 16 H), 3.47/3.43 (m/m, 1 H), 3.22 (m, 1 H), 2.98 (s, 6 H).

- ¹³C-NMR (125 MHz, MSM-d6) δ ppm 148.2/148.1, 130.2, 124.7, 103.6/103.5, 42.6/42.5, 41.1, 41/40.6.

Preparation R3bm: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]

piperidin-4-yl)methyl)-7-[3-(morpholin-4-yl)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bm** as reagent, **Preparation R3bm** was obtained as HCl salt. HRMS calculated for $C_{34}H_{40}N_6O_4$: 596.3111; found 597.3187 $[(M+H)^+$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.22/8.75 (brd+brq, 1+1 H), 8.1/8.06 (s/s, 1 H), 7.52/7.49 (d/d, 1 H), 7.38/7.37 (t/t, 1 H), 7.33-7.13 (m, 5 H), 7.23/7.21 (brs/brs, 1 H), 7.14/7.12 (d/d, 1 H), 7 (brd., 1 H), 6.7/6.66 (d/d, 1 H), 4.09-0.62 (m, 16 H), 3.76 (m, 4 H), 3.47/3.42 (m/m, 1 H), 3.22 (m, 1 H), 3.19 (m, 4 H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 148.2/148.1, 130.1, 124.7/124.6, 115.3, 114.2, 111.3/111.2, 103.6/103.5, 66.5, 48.7, 42.6, 41/40.5.

Preparation R3bo: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-7-(3-methoxyphenyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bo** as reagent, **Preparation R3bo** was obtained as HCl salt. HRMS calculated for $C_{31}H_{35}N_5O_4$: 541.2689; found 542.2762 $[(M+H)^+$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.21/8.75 (brd+brq, 2 H), 8.12/8.01 (s, 1 H), 7.56/7.54 (d, 1 H), 7.49-6.96 (m, 9 H), 6.72/6.68 (d, 1 H), 4.84 (brs, 1 H), 4.16-2.62 (m, 12 H), 1.95-0.63 (m, 6 H).

Preparation R3bp: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl)-7-[3-(trifluoromethoxy)phenyl]-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bp** as reagent, **Preparation R3bp** was obtained as HCl salt. HRMS calculated for $C_{31}H_{32}N_5O_4F_3$: 595.2407; found 596.2491 $[(M+H)^+$ form].

1H -NMR (400 MHz, MSM-d6) δ ppm 8.87 (brs, 2 H), 8.16/8.11 (s, 1 H), 7.9/7.88 (brs, 1 H), 7.85/7.84 (dm, 1 H), 7.7/7.69 (t, 1 H), 7.66/7.63 (d, 1 H), 7.43 (dm, 1 H), 7.34-7.11 (m, 5 H), 6.77/6.73 (d, 1 H), 4.87/4.86 (s, 1 H), 4.12-2.62 (m, 12 H), 1.97-0.61 (m, 6 H).

Preparation R3bq: 7-[3-(benzyloxy)phenyl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bq** as reagent, **Preparation R3bq** was obtained as HCl salt. HRMS calculated for $C_{37}H_{39}N_5O_4$: 617.3002; found 618.3051 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.24/8.77 (brd+brq, 2 H), 8.12/8.08 (s, 1 H), 7.56/7.53 (d, 1 H), 7.51-7.03 (m, 14 H), 6.72/6.68 (d, 1 H), 5.18 (s, 2 H), 4.09-2.63 (m, 12 H), 1.94-0.62 (m, 6 H).

Preparation R3br: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(6-methylpyridin-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2br** as reagent, **Preparation R3br** was obtained as HCl salt. HRMS calculated for $C_{30}H_{34}N_6O_3$: 526.2692; found 527.2764 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.43/8.91 (brq+brd, 2 H), 8.26/8.25 (dm, 1 H), 8.25/8.2 (s, 1 H), 7.92/7.9 (d, 1 H), 7.92 (m, 1 H), 7.34-7.11 (m, 5 H), 7.26 (m, 1 H), 6.73/6.69 (d, 1 H), 4.12-2.63 (m, 12 H), 2.53/2.52 (s, 3 H), 1.95-0.64 (m, 6 H).

Preparation R3bs: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(6-methoxypyridin-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bs** as reagent, **Preparation R3bs** was obtained as HCl salt. HRMS calculated for $C_{30}H_{34}N_6O_4$: 542.2642; found 543.2698 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 8.95 (brs, 2 H), 8.8/6.81 (dd, 1 H), 8.23/8.18 (s, 1 H), 8.08/8.07 (dd, 1 H), 8/7.98 (d, 1 H), 7.93/7.92 (t, 1 H), 7.35-7.1 (m, 5 H), 6.75/6.72 (d, 1 H), 4.14-2.62 (m, 12 H), 3.95/3.94 (s, 3 H), 1.96-0.62 (m, 6 H).

Preparation R3bt: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(naphthalen-1-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bt** as reagent, **Preparation R3bt** was obtained as HCl salt. HRMS calculated for $C_{34}H_{35}N_5O_3$: 561.2740; found 562.2827 [(M+H) form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.28/8.8 (brq+brd, 2 H), 8.17-6.74 (m, 15 H), 4.82 (brs, 1 H), 4.26-0.57 (m, 18 H).

Preparation R3bu: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-phenyl-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2bu** as reagent, **Preparation R3bu** was obtained as HCl salt. HRMS calculated for $C_{30}H_{33}N_5O_3$: 511.2583; found 512.2675 [(M+H) form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.1/8.67 (brd+brd, 2 H), 8.11/8.06 (s/s, 1 H), 7.75-7.38 (m, 5 H), 7.54/7.52 (d/d, 1 H), 7.34-7.12 (m, 5 H), 6.73/6.69 (d/d, 1 H), 4.86 (s, 1 H), 4.13-0.62 (m, 16 H), 3.47/3.42 (m/m, 1 H), 3.22 (m, 1 H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 148.3/148.2, 124.5/124.4, 103.9/103.8, 42.6/42.5, 41/40.6.

Preparation R3ca: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(pyridin-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ca** as reagent, **Preparation R3ca** was obtained as HCl salt. HRMS calculated for $C_{29}H_{32}N_6O_3$: 512.2536; found 513.2612 [(M+H) form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.07/8.65 (brd+brq, 2 H), 8.56/8.55 (dm, 1 H), 8.48/8.46 (dm, 1 H), 8.22/8.17 (s, 1 H), 8.05 (m, 1 H), 7.94/7.92 (d, 1 H), 7.41 (m, 1 H), 7.33-7.12 (m, 5 H), 6.75/6.71 (d, 1 H), 4.9 (s, 1 H), 4.15-2.63 (m, 12 H), 1.92-0.65 (m, 6 H).

Preparation R3cb: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(pyridin-3-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2cb** as reagent, **Preparation R3cb** was obtained. HRMS calculated for $C_{29}H_{32}N_6O_3$: 512.2536; found 513.261 [(M+H) form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.35/8.85 (brd+brq, 1+1 H), 9.1/9.09 (d/d, 1 H), 8.68 (dd, 1 H), 8.39 (m, 1 H), 8.2/8.15 (s/s, 1 H), 7.75 (dd, 1 H), 7.69/7.67 (d/d, 1 H), 7.34-7.16 (m, 5 H), 6.81/6.77 (d/d, 1 H), 4.1-0.6 (m, 16 H), 3.49/3.43 (m/m, 1 H), 3.23 (m, 1 H)
¹³C-NMR (500 MHz, MSM-d6) δ ppm 148.9/148.8, 146.5, 143.4, 133.6/133.5, 125.4, 124,
5 104.8/104.7, 42.6/42.4, 41/40.6

Preparation R3cc: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(thiophen-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2cc** as reagent, **Preparation R3cc** was obtained as HCl salt. HRMS calculated for C₂₈H₃₁N₅O₃S: 517.2148; found 518.2231 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.15/8.7 (brd+brq, 1+1 H), 8.18/8.13 (s/s, 1 H), 7.62/7.59 (d/d, 1 H), 7.45/7.44 (dd, 1 H), 7.4/7.39 (d/d, 1 H), 7.32-7.11 (m, 5 H), 7.09/7.08 (dd, 1 H), 6.74/6.7 (d/d, 1 H), 4.89 (brs, 1 H), 4.1-0.6 (m, 16 H), 3.47/3.42 (m/m, 1 H), 3.21 (m, 1 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 148.9/148.8, 126.1, 124.6, 122.9, 119.3/119.2, 104.5/104.4, 42.6/42.5, 41/40.6.

Preparation R3cd: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(pyridin-4-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2cd** as reagent, **Preparation R3cd** was obtained. HRMS calculated for C₂₉H₃₂N₆O₃: 512.2536; found 513.2609 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.46/8.94 (brs+brq, 1+1 H), 9 (dm, 2 H), 8.74 (m, 2 H), 8.4/8.36 (s/s, 1 H), 8.05/8.03 (d/d, 1 H), 7.38-7.17 (m, 5 H), 6.95/6.92 (d/d, 1 H), 4.16-0.56 (m, 16 H), 3.5/3.44 (m/m, 1 H), 3.24 (m, 1 H)

¹³C-NMR (500 MHz, MSM-d6) δ ppm 149.8, 144.4, 123.2/123.1, 117.8, 107.4/107.3, 42.6/42.4, 41.1/40.6

Preparation R3cf: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(thiophen-3-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2cf** as reagent,

Preparation R3cf was obtained as HCl salt. HRMS calculated for $C_{28}H_{31}N_5O_3S$: 517.2148; found 518.2233 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.29/8.8 (brd+brq, 2 H), 8.17/8.12 (s, 1 H), 7.97-7.66 (m, 3 H), 7.62/7.6 (d, 1 H), 7.33-7.11 (m, 5 H), 6.71/6.67 (d, 1 H), 4.91 (brs, 1 H),
5 4.12-2.63 (m, 12 H), 1.94-0.63 (m, 6 H).

Preparation R3cg: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(1-methyl-1H-imidazol-4-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2cg** as reagent,
10 **Preparation R3cg** was obtained as HCl salt. HRMS calculated for $C_{28}H_{33}N_7O_3$: 515.2645; found 516.2728 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.3/8.81 (brq+brd), 8.19/8.14 (s, 1 H), 7.85 (brs, 1 H), 7.68 (brs, 1 H), 7.6/7.57 (d, 1 H), 7.33-7.11 (m, 5 H), 6.68/6.64 (brs, 1 H), 4.14-2.63 (brs, 12 H), 3.77 (s, 3 H), 1.95-0.63 (m, 6 H).

15 **Preparation R3ch: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-(1-methyl-1H-pyrazol-4-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one**

Using **General Procedure 5** starting from **Preparation R2ch** as reagent,
20 **Preparation R3ch** was obtained as HCl salt. HRMS calculated for $C_{28}H_{33}N_7O_3$: 515.2645; found 516.2716 $[(M+H)^+]$ form].

1H -NMR (500 MHz, MSM-d6) δ ppm 9.25/8.78 (brd+brq., 2 H), 8.3/8.29 (s/s, 1 H), 8.15/8.1 (s/s, 1 H), 7.94/7.92 (d/d, 1 H), 7.47/7.44 (d/d, 1 H), 7.33-7.11 (m, 5 H), 6.68/6.64 (d/d, 1 H), 4.15-0.6 (m, 16 H), 3.9 (s, 3 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

25 **Preparation R3ci: 7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one**

Using **General Procedure 5** starting from **Preparation R2ci** as reagent,
Preparation R3ci was obtained. HRMS calculated for $C_{28}H_{31}F_2N_7O_3$: 551.2457; found 552.254 $[(M+H)^+]$ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.2/8.78 (brs+brs, 2 H), 8.87/8.85 (d, 1 H), 8.43/8.41 (d, 1 H), 8.2/8.15 (s, 1 H), 7.92 (t, 1 H), 7.61/7.59 (d, 1 H), 7.34-7.13 (m, 5 H), 6.74/6.7 (d, 1 H), 4.91 (s, 1 H), 4.1-2.63 (m, 12 H), 1.92-0.63 (m, 6 H).

Preparation R3cj: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]

piperidin-4-yl}methyl)-7-(pyrimidin-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2cj** as reagent, **Preparation R3cj** was obtained as HCl salt. HRMS calculated for C₂₈H₃₁N₇O₃: 513.2488; found 257.6326 [(M+2H)²⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.24/8.77 (brd+brq, 2 H), 8.96/8.95 (brd, 1 H), 8.18/8.13 (brs, 1 H), 7.87/7.79 (d, 1 H), 7.55 (t, 1 H), 7.34-7.13 (m, 5 H), 6.76/6.72 (d, 1 H), 4.87 (brs, 1 H), 4.13-2.61 (m, 12 H), 1.93-0.63 (m, 6 H).

Preparation R3ck: 3-({4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]

piperidin-4-yl}methyl)-7-(1,3-thiazol-2-yl)-3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ck** as reagent, **Preparation R3ck** was obtained as HCl salt. HRMS calculated for C₂₇H₃₀N₆O₃S: 518.2100; found 519.2181 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.3/8.81 (brd/brq, 2 H), 8.35/8.31 (s, 1 H), 7.91/7.89 (d, 1 H), 7.7/7.69 (d, 1 H), 7.65/7.64 (d, 1 H), 7.33-7.12 (m, 5 H), 6.81/6.77 (d, 1 H), 4.14-2.61 (m, 12 H), 1.95-0.6 (m, 6 H).

Preparation R3cn: 3-[[4-hydroxy-1-[(3S,4S)-3-phenylpiperidine-4-carbonyl]-4-

piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one

Using **General Procedure 5** starting from 3H-pyrido[3,2-d]pyrimidin-4-one and *tert*-butyl (3S,4S)-4-(1-oxa-6-azaspiro[2.5]oct-6-ylcarbonyl)-3-phenylpiperidine-1-carboxylate (instead of **Preparation R1f**) as reagents, **Preparation R3cn** was obtained as HCl salt.

HRMS calculated for C₂₅H₂₉N₅O₃: 447.227; found 448.2365 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.34/8.83 (brs/brd, 2 H), 8.83 (brm, 1H), 8.34/8.30 (s/s, 1H), 8.14/8.12 (d/d, 1H), 7.40-7.09 (m, 5H), aliphatic protons: 4.13-0.52 (8xCH₂), 3.49/3.42 (m, 1H), 3.21 (m, 1H).

¹³C-NMR (500 MHz, MSM-d6) δ ppm 150.3/150.2, 149.8, 136.1, 129.3, 42.6/42.4,

41.0/40.5.

Preparation R3co: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one

Using **General Procedure 5** starting from 3*H*-pyrido[3,2-*d*]pyrimidin-4-one as reagent,

Preparation R3co was obtained as HCl salt. HRMS calculated for C₂₅H₂₉N₅O₃: 447.227; found 448.2365 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆) δ ppm 9.34, 8.83 (brs+brs, 2 H), 8.83 (brs, 1H), 8.34/8.30 (s/s, 1H), 8.14/8.12 (d/d, 1H), 7.40-7.09 (m, 5H), aliphatic protons: 4.13-0.52 (8xCH₂), 3.49/3.42 (m, 1H), 3.21 (m, 1H).

¹³C-NMR (500 MHz, MSM-d₆) δ ppm 150.3/150.2, 149.8, 136.1, 129.3, 42.6/42.4, 41.0/40.5.

Preparation R3cp: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from 3*H*-thieno[2,3-*d*]pyrimidin-4-one as reagent,

Preparation R3cp was obtained as HCl salt. HRMS calculated for C₂₄H₂₈N₄O₃S: 452.1882; found 453.1933 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆) δ ppm 9.23/8.76 (brs/brm, 2 H), 8.83 (brs, 1H), 8.26/8.21 (s/s, 1H), 7.61/7.59 (d/d, 1H), 7.43/7.39 (d/d, 1H) 7.34-7.15 (m, 5H) 4.93/4.92 (s/s, 1H) 4.04, 3.93/ 3.75 (d+d/s, 2H) 4.00-2.60 (m, 4H) 3.48/3.42 (m/m, 1H) 3.41-2.98 (m, 2H) 3.33-3.00 (m, 2H) 3.21 (m, 1H) 1.94-1.80 (m, 2H) 1.51-0.57 (m, 4H).

¹³C-NMR (500 MHz, MSM-d₆) δ ppm 124.8, 122.5/122.4, 47.7/47.2, 42.7, 42.6/42.5, 41.1/40.4, 26.6/26.4.

Preparation R3cq: 6-chloro-3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one

Using **General Procedure 5** starting from 6-chloro-3*H*-pyrido[3,2-*d*]pyrimidin-4-one as reagent, **Preparation R3cq** was obtained as HCl salt. HRMS calculated for C₂₅H₂₈ClN₅O₃: 481.1881; found 482.1949 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d₆) δ ppm 9.13, 8.69 (brs+brm, 2H), 8.33/8.28 (s/s, 1H), 8.18/8.17 (d/d, 1H), 7.93/7.91 (d/d, 1H), 7.38-7.19 (m, 5H), 4.09 (brm, 1H), 4.05,

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3.97/3.75 (d+d/s, 2H), 4.00-2.61 (m, 4H), 3.40-2.99 (brm, 4H), 3.48/3.40 (m/m, 1H), 3.22 (m, 1H) 1.95-1.80 (m, 2H), 1.52-0.52 (m, 4H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 150.8/150.7, 139.9, 130.4, 42.6/42.5, 41.1/40.5.

Preparation R3cr: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-6-methoxy-pyrido[3,2-d]pyrimidin-4-one
and

Preparation R3cs: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-5H-pyrido[3,2-d]pyrimidine-4,6-dione

Using **General Procedure 5** starting from 6-methoxy-3*H*-pyrido[3,2-*d*]pyrimidin-4-one as reagent, **Preparation R3cr** and **Preparation R3cs** (byproduct) were obtained as HCl salt and separated by chromatography.

Preparation R3cr: HRMS calculated for $\text{C}_{26}\text{H}_{31}\text{N}_5\text{O}_4$: 477.2376; found 478.2458 [(M+H)⁺ form].

^1H -NMR (500 MHz, MSM-d6) δ ppm 9.17, 8.72 (brs+brm, 2H) 8.22/8.17 (s/s, 1H) 8.02/8.00 (d/d, 1H), 7.35-7.15 (m, 5H), 7.31/7.29 (d/d, 1H), 4.06, 3.93/3.77, 3.74 (d+d/d+d, 2H), 4.00-2.60 (m, 4H), 3.99/3.96 (s/s, 3H), 3.48/3.42 (m, 1H), 3.34-2.98 (m, 4H), 3.21 (m, 1H), 1.94-1.80 (m, 2H), 1.52-0.57 (m, 4H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 148.2/148.1, 139.5, 119.1, 54.2, 42.6/42.4, 41.1/40.5.

Preparation R3cs: HRMS calculated for $\text{C}_{25}\text{H}_{29}\text{N}_5\text{O}_4$: 463.222; found 464.2312 [(M+H)⁺ form].

^1H -NMR (500 MHz, MSM-d6) δ ppm 11.67 (vbrs, 1H), 9.11, 8.68 (brs+brs, 2H), 8.08/8.04 (s/s, 1H), 7.75/7.73 (d/d, 1H), 6.83/6.81 (d/d, 1H), 7.36-7.18 (m, 5H), 4.89 (vbrs, 1H), 4.00-2-60 (m, 4H), 3.99, 3.93/3.74, 3.70 (d+d/d+d, 2H), 3.48/3.41 (m, 1H), 3.34-3.01 (m, 4H), 3.20 (m, 1H), 1.92-1.80 (m, 2H), 1.51-0.48 (m, 4H).

^{13}C -NMR (125 MHz, MSM-d6) δ ppm 146.2/146.1, 140.3, 129.4, 42.6/42.5, 41.0/40.6.

Preparation R3ct: 6-(benzylamino)-3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one

Using **General Procedure 5** starting from 6-chloro-3*H*-pyrido[3,2-*d*]pyrimidin-4-one as reagent without the deprotection step, the resulted crude Boc-protected compound

(0.76 mmol) and K_2CO_3 (1.51 mmol) were stirred in benzylamine (5 ml) at 120 °C for 17 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

The resulted crude product (187 mg, 0.283 mmol) was stirred in aqueous HCl solution (1 N, 3 ml, 3 mmol) and PDO (3 ml) at 70 °C for 2 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **Preparation R3ct** as HCl salt. HRMS calculated for $C_{32}H_{36}N_6O_3$: 552.2849; found 277.1497 [(M+2H)²⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.37/8.86 (m/m, 2 H), 8.31-7.12 (m, aromatic protons, 13 H), 4.78-0.49 (m, aliphatic protons, 20 H).

Preparation R3cu: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-6-[(4-methoxyphenyl)methylamino]pyrido[3,2-d]pyrimidin-4-one

Using **General Procedure 5** starting from 6-chloro-3*H*-pyrido[3,2-*d*]pyrimidin-4-one as reagent without the deprotection step, the resulted crude Boc-protected compound (0.76 mmol) and K_2CO_3 (1.51 mmol) were stirred in benzylamine (5 ml) at 120 °C for 17 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

The resulted crude product (187 mg, 0.283 mmol) was stirred in aqueous HCl solution (1 N, 3 ml, 3 mmol) and PDO (3 ml) at 70 °C for 2 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **Preparation R3cu** as HCl salt. HRMS calculated for $C_{33}H_{38}N_6O_4$: 582.2955; found 292.1552 [(M+2H)²⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.33/8.83 (brt/brd, 2 H), 8.23/8.18 (s/s, 1 H), 7.91 (vbrs, 1 H), 7.35-7.15 (m, 5 H), 7.34 (d/d, 2 H), 7.27 (brm, 1 H), 6.92/6.91 (d/d, 2 H), 4.62/4.59 (s/s, 2 H), 4.08-0.54 (m, aliphatic protons, 8 H), 3.73 (s, 3 H), 3.48/3.42 (m/m, 1 H), 3.21 (m, 1 H).

Preparation R3cv: 6-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-triazolo[4,5-*d*]pyrimidin-7-one

Using **General Procedure 5** starting from 3-phenyl-6*H*-triazolo[4,5-*d*]pyrimidin-7-one as reagent, **Preparation R3cv** was obtained as HCl salt. HRMS calculated for $C_{28}H_{31}N_7O_3$:

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513.2488; found 514.2576 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.28/8.79 (brd+brq, 2 H), 8.5/8.47 (s, 1 H), 8.06-7.54 (m, 5 H), 7.4-7.19 (m, 5 H), 4.98/4.96 (brs, 1 H), 4.17-2.6 (m, 12 H), 1.96-0.53 (m, 6 H).

5 **Preparation R3cw: 1-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-9-phenyl-purin-6-one**

Using **General Procedure 5** starting from 9-phenyl-1*H*-purin-6-one as reagent, **Preparation R3cw** was obtained as HCl salt. HRMS calculated for C₂₉H₃₂N₆O₃: 512.2536; found 513.2616 [(M+H)⁺ form].

10 ¹H-NMR (500 MHz, MSM-d6) δ ppm 9.25/8.77 (brd+brq, 2 H), 8.52/8.5 (s, 1 H), 8.28/8.23 (s, 1 H), 7.82-7.46 (m, 5 H), 7.37-7.18 (s, 5 H), 4.91 (brs, 1 H), 4.14-2.63 (m, 12 H), 1.96-0.58 (m, 6 H).

Preparation R3cx: 5-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-1-phenyl-pyrazolo[3,4-*d*]pyrimidin-4-one

15 Using **General Procedure 5** starting from 1-phenyl-5*H*-pyrazolo[3,4-*d*]pyrimidin-4-one as reagent, **Preparation R3cx** was obtained as HCl salt. HRMS calculated for C₂₉H₃₂N₆O₃: 512.2536; found 513.2627 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.22/8.76 (brs+brs, 2 H), 8.39/8.36 (s, 1 H), 8.34/8.3 (s, 1 H), 8.09-7.38 (m, 5 H), 7.36-7.16 (m, 5 H), 4.94/4.93 (s, 1 H), 4.12-2.59 (m, 12 H),
20 1.95-0.58 (m, 6 H).

Preparation R3cy: 7-bromo-3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-*f*][1,2,4]triazin-4-one

Using **General Procedure 5** starting from 7-bromo-3*H*-pyrrolo[2,1-*f*][1,2,4]triazin-4-one as reagent, **Preparation R3cy** was obtained as HCl salt. HRMS calculated for
25 C₂₄H₂₈BrN₅O₃: 513.1376; found 514.1462 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.25/8.77 (brs+brs, 2 H), 8.03/8 (s, 1 H), 7.33-7.1 (m, 5 H), 7.03/6.99/6.77/6.75 (d, 2 H), 4.93/4.91 (s, 1 H), 4.02-2.61 (m, 12 H), 1.94-0.5 (m, 6 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 154, 120.9, 102.9.

Preparation R3cz: 6-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-isothiazolo[4,5-d]pyrimidin-7-one

Using **General Procedure 5** starting from 3-phenyl-6*H*-isothiazolo[4,5-*d*]pyrimidin-7-one as reagent, **Preparation R3cz** was obtained as HCl salt. HRMS calculated for $C_{29}H_{31}N_5O_3S$: 529.2148; found 530.2223 [(M+H)⁺ form].

¹H-NMR (400 MHz, MSM-d6) δ ppm 9.37/8.86 (brs+brs, 2 H), 8.49/8.46 (s, 1 H), 8.43 (m, 2 H), 7.62-7.5 (m, 3 H), 7.39-7.13 (m, 5 H), 5.06/5.03 (s, 1 H), 4.2-2.6 (m, 12 H), 1.98-0.52 (m, 6 H).

Preparation R3da: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one

Using **General Procedure 5** starting from 7-chloro-3*H*-thieno[3,4-*d*]pyrimidin-4-one as reagent, without the deprotection step, the resulted Boc-protected compound reacted with phenylboronic acid using **General Procedure 9**. The resulted phenylated crude product was deprotected according to Step 2 of **General Procedure 5** to give **Preparation R3da** as HCl salt. HRMS calculated for $C_{30}H_{32}N_4O_3S$: 528.2195; found 529.2265 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.14/8.7 (brq+brd, 2 H), 8.51/8.47 (s, 1 H), 8.05/8.04 (m, 2 H), 8.03/7.98 (s, 1 H), 7.52-7.33 (m, 3 H), 7.32-7.1 (m, 5 H), 4.9/4.88 (s, 1 H), 4.02-2.61 (m, 12 H), 1.93-0.58 (m, 6 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 158, 143.5, 134, 127.4.

Preparation R3db: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-5H-pyrrolo[3,2-d]pyrimidin-4-one

Using **General Procedure 5** starting from 7-phenyl-3,5-dihydropyrrolo[3,2-*d*]pyrimidin-4-one as reagent, **Preparation R3db** was obtained as HCl salt. HRMS calculated for $C_{30}H_{33}N_5O_3$: 511.2583; found 512.2647 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 12.35/12.3 (d, 1 H), 9.26/8.79 (brs+brs, 2 H), 8.1/8.05 (s, 1 H), 8.1/8.08 (m, 2 H), 7.92/7.9 (d, 1 H), 7.43-7.08 (m, 8 H), 4.92/4.91 (s, 1 H), 4.07-2.62 (m, 12 H), 1.97-0.63 (m, 6 H).

Preparation R3dc: 7-chloro-3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]thieno[3,4-d]pyrimidin-4-one

Using **General Procedure 5** starting from 7-chloro-3*H*-thieno[3,4-*d*]pyrimidin-4-one as reagent, **Preparation R3dc** was obtained as HCl salt. HRMS calculated for C₂₄H₂₇ClN₄O₃S: 486.1492; found 487.1544 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.16/8.71 (brd+brq, 2 H), 8.44/8.4 (s, 1 H), 8.01/7.96 (s, 1 H), 7.34-7.15 (m, 5 H), 4.87/4.85 (s, 1 H), 4-2.59 (m, 12 H), 1.93-0.52 (m, 6 H).

Preparation R3dd: 6-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-isoxazolo[4,5-d]pyrimidin-7-one

Using **General Procedure 5** starting from 3-phenyl-6*H*-isoxazolo[4,5-*d*]pyrimidin-7-one as reagent, **Preparation R3dd** was obtained as HCl salt. HRMS calculated for C₂₉H₃₁N₅O₄: 513.2376; found 514.2451 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.13/8.76 (brs+brs, 2 H), 8.44/8.4 (s, 1 H), 8.33-8.26 (m, 2 H), 7.67-7.59 (m, 3 H), 7.39-7.18 (m, 5 H), 4.99/4.97 (s, 1 H), 4.19-2.62 (m, 12 H), 1.95-0.52 (m, 6 H).

Preparation R3de: 5-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-1-(4-methoxyphenyl)pyrazolo[3,4-d]pyrimidin-4-one

Using **General Procedure 5** starting from 1-(4-methoxyphenyl)-5*H*-pyrazolo[3,4-*d*]pyrimidin-4-one as reagent, **Preparation R3de** was obtained as HCl salt. HRMS calculated for C₃₀H₃₄N₆O₄: 542.2642; found 543.2711 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ ppm 9.11/8.69 (brs+brm, 2 H), 8.34/8.3 (s/s, 1 H), 8.29/8.25 (s/s, 1 H), 7.9/7.86 (dm/dm, 2 H), 7.37-7.16 (m, 5 H), 7.13/7.12 (m/m, 2 H), 4.91 (brs, 1 H), 4.13-0.53 (m, 16 H), 3.81 (s, 3 H), 3.48/3.42 (m/m, 1 H), 3.22 (m, 1 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 152.6/152.5, 136.3/136.2, 123.8, 114.9/114.8, 55.9, 42.6/42.5, 41.1/40.5.

Preparation R3df: 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]pyrazolo[3,4-d]pyrimidin-4-one

Using **General Procedure 5** starting from 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5*H*-

pyrazolo[3,4-*d*]pyrimidin-4-one as reagent, **Preparation R3df** was obtained as HCl salt. HRMS calculated for C₃₁H₃₄N₆O₅: 570.2591; found 571.2663 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ ppm 9.16/8.74 (brs+brs, 2 H), 8.3/8.26 (s, 1 H), 8.29/8.23 (s, 1 H), 7.53/7.52 (d, 1 H), 7.48/7.47 (dd, 1 H), 7.36-7.15 (m, 5 H), 7.04 (d, 1 H), 4.92/4.9 (s, 1 H), 4.35-4.26 (m, 4 H), 4.1-2.6 (m, 12 H), 1.94-0.58 (m, 6 H).

Preparation R3dg: 6-chloro-7-(4-chloro-3-fluoro-phenyl)-3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2ah** as reagent, **Preparation R3dg** was obtained as HCl salt. HRMS calculated for C₃₀H₃₀N₅O₃FCl₂: 597.171; found 598.1772 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ ppm 8.07/8.03 (s, 1 H), 7.85 (t, 1 H), 7.75 (dd, 1 H), 7.41 (dd, 1 H), 7.3-7.09 (m, 5 H), 6.87/6.84 (s, 1 H), 4.81/4.79 (s, 1 H), 4.06-2.51 (m, 12 H), 1.68-0.74 (m, 6 H).

Preparation R3dh: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-6-methyl-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2de** as reagent, **Preparation R3dh** was obtained as HCl salt. HRMS calculated for C₃₁H₃₅N₅O₃: 525.274; found 526.2827 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ ppm 9.14/8.69 (brs+brs, 2 H), 7.95/7.9 (s, 1 H), 7.61-7.37 (m, 5 H), 7.36-7.15 (m, 5 H), 6.45/6.42 (q, 1 H), 4.84/4.83 (s, 1 H), 4.06-2.61 (m, 12 H), 2.19/2.17 (d, 3 H), 1.95-0.6 (m, 6 H).

Preparation R3di: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-9-methyl-pyrimido[4,5-b]indol-4-one

Using **General Procedure 5** starting from **Preparation R2df** as reagent, **Preparation R3di** was obtained as HCl salt. HRMS calculated for C₂₉H₃₃N₅O₃: 499.2583; found 500.2677 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ ppm 9.19/8.74 (brq+brd, 2 H), 8.38/8.33 (s, 1 H), 8.07/8.02 (dm, 1 H), 7.66/7.65 (dm, 1 H), 7.43/7.42 (m, 1 H), 7.37-7.12 (m, 5 H), 7.32 (m, 1 H), 4.9 (brs, 1 H), 4.21-2.62 (m, 12 H), 3.87/3.86 (s, 3 H), 1.95-0.64 (m, 6 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 158, 152.7, 137.2, 122, 99.

Preparation R3dj: 3-[(4-hydroxy-1-[(3R,4R)-3-phenylpiperidin-4-

yl]carbonyl]piperidin-4-yl)methyl]-6,8-dimethylpyrimido[5,4-*b*]indolizin-4(3*H*)-one

Using **General Procedure 5** starting from **Preparation R2dg** as reagent,

Preparation R3dj was obtained as HCl salt. HRMS calculated for C₂₉H₃₄N₆O₃: 514.2692; found 515.2757 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6): δ ppm 9.25/8.77 (brq+brd, 2 H), 8.18/8.13 (s, 1 H), 7.34-7.1 (m, 5 H), 6.94/6.9 (s, 1 H), 6.71/6.7 (q, 1 H), 4.9 (brs, 1 H), 4.13-2.6 (m, 12 H), 2.47/2.45 (d, 3 H), 2.45/2.44 (s, 3 H), 1.95-0.62 (m, 6 H).

¹³C-NMR (125 MHz, MSM-d6) δ ppm 159.3, 152.6, 140.4, 139, 127.9, 115.4, 108.8, 91.4.

Preparation R3dk: 6-chloro-3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenylpyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2dh** as reagent,

Preparation R3dk was obtained as HCl salt. HRMS calculated for C₃₀H₃₂ClN₅O₃: 545.2194; found 546.2277 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 9.15/8.71 (brd+brq, 2 H), 8.05/8 (s, 1 H), 7.64-7.41 (m, 5 H), 7.37-7.18 (m, 5 H), 6.83/6.8 (s, 1 H), 4.85 (s, 1 H), 4.07-2.61 (m, 12 H), 1.94-0.61 (m, 6 H).

Preparation R3dl: 3-[[4-hydroxy-1-[(3R,4R)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-6-iodo-7-methyl-pyrrolo[2,3-*d*]pyrimidin-4-one

Using **General Procedure 5** starting from **Preparation R2di** as reagent,

Preparation R3dl was obtained as HCl salt. HRMS calculated for C₂₅H₃₀IN₅O₃: 575.1393; found 576.1455 [(M+H)⁺ form].

¹H-NMR (500 MHz, MSM-d6) δ ppm 8.02/7.97 (s/s, 1 H), 7.28-7.02 (m, 5 H), 6.84/6.83 (s/s, 1 H), 4.16-0.65 (m, 16 H), 3.65/3.64 (s/s, 3 H), 3.21/3.16 (m/m, 1 H), 2.88 (m, 1 H)

¹³C-NMR (125 MHz, MSM-d6) δ ppm 147.9/147.8, 111.7/111.6, 80.7/80.6, 46.2, 43.2/42.8, 33.1

Preparation R3dm: 3-[[3,3-difluoro-4-hydroxy-1-[trans-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one

Trimethyl-sulfoxonium iodide (1.11 g, 5 mmol) was dissolved in abs. MSM (10 ml) then sodium-hydride dispersion (60 % in mineral oil, 200 mg, 5 mmol) was added sequentially and stirred for 20 minutes at r.t. *tert*-butyl 3,3-difluoro-4-oxo-piperidine-1-carboxylate (783 mg, 3.33 mmol) solution in MSM (5 ml, abs.) was added to the mixture and stirred for 15 hours at r.t. The reaction mixture was poured into ice-water mixture (40 ml) and extracted with DEE (4 x 15 ml). The combined organic layer was washed with water, brine, then dried over MgSO₄ and evaporated.

The raw epoxide product was reacted with **Preparation R2bu** according to **General Procedure 5**.

The resulted raw HCl salt was reacted with trans-1-*tert*-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid using **General Procedure 7**.

The raw product was deprotected according to Step 2 of **General Procedure 5** to give **Preparation R3dm**. HRMS calculated for C₃₀H₃₁F₂N₅O₃: 547.2394; found 548.2454 and 548.2490 (two diastereomers) [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 9.24/8.82 (m+m, 2 H), 8.19-8.09 (4*s, 1 H), 7.71 (m, 2 H), 7.6-7.5 (4*d, 1 H), 7.56 (m, 2 H), 7.42 (m, 1 H), 7.34-7.16 (m, 5 H), 6.79-6.67 (4*d, 1 H), 6.08 (brs, 1 H), 4.74-2.35 (m, 12 H), 2.06-1.1 (m, 4 H)

Preparation R3dn: 3-[[3,3-difluoro-4-hydroxy-1-[trans-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one

Trimethyl-sulfoxonium iodide (1.11 g, 5 mmol) was dissolved in abs. MSM (10 ml) then sodium-hydride dispersion (60 % in mineral oil, 200 mg, 5 mmol) was added sequentially and stirred for 20 minutes at r.t. *tert*-butyl 3,3-difluoro-4-oxo-piperidine-1-carboxylate (783 mg, 3.33 mmol) solution in MSM (5 ml, abs.) was added to the mixture and stirred for 15 hours at r.t. The reaction mixture was poured into ice-water mixture (40 ml) and extracted with DEE (4 x 15 ml). The combined organic layer was washed with water, brine, then dried over MgSO₄ and evaporated.

The raw epoxide product was reacted with **Preparation R2ax** according to **General Procedure 5**.

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The resulted raw HCl salt was reacted with trans-1-*tert*-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid according to **General Procedure 7**.

The raw product was deprotected according to Step 2 of **General Procedure 5** to give **Preparation R3dn**. HRMS calculated for C₃₁H₃₃F₂N₅O₄: 577.2501; found 578.2547 and 578.2572 (two diastereomers) [(M+H)⁺ form].

¹H NMR (500 MHz, MSM-d₆): δ ppm 9.13/8.74 (m+m, 2 H), 8.16-8.05 (4*s, 1 H), 7.63-7.54 (m, 2 H), 7.48-7.41 (4*d, 1 H), 7.36-7.16 (m, 5 H), 7.14-7.06 (m, 2 H), 6.74-6.63 (4*d, 1 H), 6.17-5.95 (brs, 1 H), 4.69-2.77 (m, 12 H), 3.82/3.81 (s, 3 H), 2.05-1.15 (m, 4 H)

EXAMPLES

The following Examples illustrate the invention but do not limit it in any way.

▪ **3-[(1-{[(3S,4S)-1-benzyl-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 1)**

- 5 Using **General Procedure 6** starting from 3-[(4-hydroxy-1-{[(3S,4S)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (which was obtained according to **General Procedure 5** with *tert*-butyl (3S,4S)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and 3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one) and benzyl bromide as reagents, **EXAMPLE 1** was obtained.
- 10 HRMS calculated for C₃₁H₃₅N₅O₃: 525.2739; found 526.2815 [(M+H)⁺ form].

▪ **7-(2-chlorobenzyl)-3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 2)**

- Using **General Procedure 6** starting from **Preparation R3aa** and **Preparation R1c** as reagents, **EXAMPLE 2** was obtained. HRMS calculated for C₄₁H₄₂ClN₇O₃S: 747.2758; found 374.6457 [(M+2H)²⁺ form].
- 15

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 3)**

- 20 Using **General Procedure 6** starting from **Preparation R3ac** and **Preparation R1c** as reagents, **EXAMPLE 3** was obtained. HRMS calculated for C₄₃H₄₇N₇O₆S: 789.3309; found 395.6734 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 4)**

- 25 Using **General Procedure 6** starting from **Preparation R3ac** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 4** was obtained. HRMS calculated for C₄₃H₄₇N₇O₇S: 805.3257; found 403.6694 [(M+2H)²⁺ form].

▪ **7-(3,5-dichlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 5)**

Using **General Procedure 6** starting from **Preparation R3ad** and **Preparation R1c** as reagents, **EXAMPLE 5** was obtained. HRMS calculated for $C_{40}H_{39}N_7O_3SCl_2$: 767.2212; found 768.2251 [(M+H)⁺ form].

▪ **7-(3,5-dichlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 6)**

Using **General Procedure 6** starting from **Preparation R3ad** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 6** was obtained. HRMS calculated for $C_{40}H_{39}N_7O_4SCl_2$: 783.2161; found 784.2235 [(M+H)⁺ form].

▪ **7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 7)**

Using **General Procedure 6** starting from **Preparation R3ae** and **Preparation R1c** as reagents, **EXAMPLE 7** was obtained. HRMS calculated for $C_{41}H_{42}ClN_7O_4S$: 763.2708; found 764.2766 [(M+H)⁺ form].

▪ **7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 8)**

Using **General Procedure 6** starting from **Preparation R3ae** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 8** was obtained. HRMS calculated for $C_{41}H_{42}ClN_7O_5S$: 779.2657; found 780.2734 [(M+H)⁺ form].

▪ **7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 9)**

Using **General Procedure 6** starting from **Preparation R3af** and **Preparation R1c** as reagents, **EXAMPLE 9** was obtained. HRMS calculated for $C_{42}H_{45}N_7O_5S$: 759.3203; found 760.3244 [(M+H)⁺ form].

5 ▪ **7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 10)**

Using **General Procedure 6** starting from **Preparation R3af** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 10** was obtained. HRMS calculated for $C_{42}H_{45}N_7O_6S$: 775.3152; found 776.32 [(M+H)⁺ form].

10 ▪ **7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 11)**

Using **General Procedure 6** starting from **Preparation R3ah** and **Preparation R1c** as reagents, **EXAMPLE 11** was obtained. HRMS calculated for $C_{40}H_{39}ClFN_7O_3S$: 751.2508; found 752.2564 [(M+H)⁺ form].

15 ▪ **7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 12)**

Using **General Procedure 6** starting from **Preparation R3ah** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 12** was obtained. HRMS calculated for $C_{40}H_{39}ClFN_7O_4S$: 767.2457; found 768.2552 [(M+H)⁺ form].

20 ▪ **7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 13)**

25 Using **General Procedure 6** starting from **Preparation R3ai** and **Preparation R1c** as reagents, **EXAMPLE 13** was obtained. HRMS calculated for $C_{41}H_{42}ClN_7O_4S$: 763.2708; found 764.2792 [(M+H)⁺ form].

▪ **7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 14)**

Using **General Procedure 6** starting from **Preparation R3ai** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 14** was obtained. HRMS calculated for $C_{41}H_{42}ClN_7O_5S$: 779.2657; found 780.2729 [(M+H)⁺ form].

▪ **7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 15)**

Using **General Procedure 6** starting from **Preparation R3aj** and **Preparation R1c** as reagents, **EXAMPLE 15** was obtained. HRMS calculated for $C_{41}H_{42}FN_7O_4S$: 747.3003; found 748.3047 [(M+H)⁺ form].

▪ **7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 16)**

Using **General Procedure 6** starting from **Preparation R3aj** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 16** was obtained. HRMS calculated for $C_{41}H_{42}FN_7O_5S$: 763.2952; found 764.3029 [(M+H)⁺ form].

▪ **7-(3,4-dimethoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 17)**

Using **General Procedure 6** starting from **Preparation R3ak** and **Preparation R1c** as reagents, **EXAMPLE 17** was obtained. HRMS calculated for $C_{42}H_{45}N_7O_5S$: 759.3203; found 380.6691 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 18)**

Using **General Procedure 6** starting from **Preparation R3am** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 18** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_4S$: 729.3096; found 730.3162 $[(M+H)^+$ form].

5 ■ 4-{3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-4-oxo-3,4-dihydro-7H-pyrrolo[2,3-d]pyrimidin-7-yl}benzonitrile (**EXAMPLE 19**)

Using **General Procedure 6** starting from **Preparation R3an** and **Preparation R1c** as reagents, **EXAMPLE 19** was obtained. HRMS calculated for $C_{41}H_{40}N_8O_3S$: 724.2944; found 725.3009 $[(M+H)^+$ form].

10 ■ 4-{3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-4-oxo-3,4-dihydro-7H-pyrrolo[2,3-d]pyrimidin-7-yl}benzonitrile (**EXAMPLE 20**)

Using **General Procedure 6** starting from **Preparation R3an** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 20** was obtained. HRMS calculated for $C_{41}H_{40}N_8O_4S$: 740.2893; found 741.2984 $[(M+H)^+$ form].

15 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(trifluoromethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 21**)

Using **General Procedure 6** starting from **Preparation R3ao** and **Preparation R1c** as reagents, **EXAMPLE 21** was obtained. HRMS calculated for $C_{41}H_{40}N_7O_3F_3S$: 767.2866; found 768.2899 $[(M+H)^+$ form].

20 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(trifluoromethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 22**)

25 Using **General Procedure 6** starting from **Preparation R3ao** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 22** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_4S$: 783.2814; found 784.2887 $[(M+H)^+$ form].

▪ 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 23)

Using **General Procedure 6** starting from **Preparation R3ap** and **Preparation R1c** as reagents, **EXAMPLE 23** was obtained. HRMS calculated for C₄₁H₄₁F₂N₇O₃S: 749.2959; found 750.3017 [(M+H)⁺ form].

▪ 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 24)

Using **General Procedure 6** starting from **Preparation R3ap** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 24** was obtained. HRMS calculated for C₄₁H₄₁F₂N₇O₄S: 765.2909; found 766.297 [(M+H)⁺ form].

▪ 7-[4-(hydroxymethyl)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 25)

Using **General Procedure 6** starting from **Preparation R3aq** and **Preparation R1c** as reagents, **EXAMPLE 25** was obtained. HRMS calculated for C₄₁H₄₃N₇O₄S: 729.3097; found 730.3137 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[4-(hydroxymethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 26)

Using **General Procedure 6** starting from **Preparation R3aq** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 26** was obtained. HRMS calculated for C₄₁H₄₃N₇O₅S: 745.3046; found 746.3142 [(M+H)⁺ form].

▪ 7-(4-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 27)

Using **General Procedure 6** starting from **Preparation R3ar** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 27** was obtained. HRMS calculated for $C_{40}H_{40}ClN_7O_4S$: 749.2551; found 750.2639 $[(M+H)^+]$ form].

5 ■ 3-{[1-({(3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(4-chlorophenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 28**)

Using **General Procedure 6** starting from **Preparation R3ar** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 28** was obtained. HRMS calculated for $C_{34}H_{34}BrClN_6O_3S$: 720.1285; found 721.1355 $[(M+H)^+]$ form].

10 ■ 7-(4-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 29**)

Using **General Procedure 6** starting from **Preparation R3as** and **Preparation R1c** as reagents, **EXAMPLE 29** was obtained. HRMS calculated for $C_{40}H_{40}N_7O_3FS$: 717.2897; found 718.2982 $[(M+H)^+]$ form].

15 ■ 7-(4-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 30**)

Using **General Procedure 6** starting from **Preparation R3as** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 30** was obtained. HRMS calculated for $C_{40}H_{40}FN_7O_4S$: 733.2847; found 734.2907 $[(M+H)^+]$ form].

20 ■ 3-{[1-({(3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(4-fluorophenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 31**)

25 Using **General Procedure 6** starting from **Preparation R3as** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 31** was obtained. HRMS calculated for $C_{34}H_{34}BrFN_6O_3S$: 704.1580; found 705.1642 $[(M+H)^+]$ form].

▪ 7-[4-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 32)

Using **General Procedure 6** starting from **Preparation R3at** and **Preparation R1c** as reagents, **EXAMPLE 32** was obtained. HRMS calculated for $C_{42}H_{46}N_8O_3S$: 742.3414; found 743.3467 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 33)

Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 33** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_5S$: 745.3047; found 746.3124 [(M+H)⁺ form].

▪ 3-{[1-[(3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 34)

Using **General Procedure 6** starting from **Preparation R3ax** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 34** was obtained. HRMS calculated for $C_{35}H_{37}BrN_6O_4S$: 716.1780396; found 717.1836 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-[(3R,4R)-1-[(1-methyl-1H-pyrazol-4-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 35)

Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)-1-methyl-pyrazole as reagents, **EXAMPLE 35** was obtained. HRMS calculated for $C_{36}H_{41}N_7O_4$: 635.3220; found 636.3291 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 36)

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)pyrazine hydrochloride as reagents, **EXAMPLE 36** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3063; found 634.3114 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(5-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 37)**

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-5-methyl-thiazole as reagents, **EXAMPLE 37** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_4S$: 652.2832031; found 653.2891 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-{[1-((3R,4R)-1-[(5-bromopyridin-3-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 38)**

Using **General Procedure 6** starting from **Preparation R3ax** and 3-bromo-5-(chloromethyl)pyridine as reagents, **EXAMPLE 38** was obtained. HRMS calculated for $C_{37}H_{39}BrN_6O_4$: 710.2216; found 711.2297 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-[(4-hydroxy-1-((3R,4R)-3-phenyl-1-(pyridin-3-ylmethyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 39)**

Using **General Procedure 6** starting from **Preparation R3ax** and 3-(chloromethyl)pyridine hydrochloride as reagents, **EXAMPLE 39** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4$: 632.3111; found 633.3167 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[(4-hydroxy-1-((3R,4R)-3-phenyl-1-(1,3-thiazol-5-ylmethyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 40)**

25 Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)thiazole as reagents, **EXAMPLE 40** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4S$: 638.2675; found 639.2738 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(1,3-thiazol-2-ylmethyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 41)**

Using **General Procedure 6** starting from **Preparation R3ax** and
5 2-(chloromethyl)thiazole as reagents, **EXAMPLE 41** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4S$: 638.2675; found 639.2758 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(4-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 42)**

10 Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-4-methyl-thiazole as reagents, **EXAMPLE 42** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_4S$: 652.2832; found 653.2885 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-[(4,5-dimethyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 43)**

15 Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-4,5-dimethyl-thiazole as reagents, **EXAMPLE 43** was obtained. HRMS calculated for $C_{37}H_{42}N_6O_4S$: 666.2988; found 667.3059 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 44)**

20 Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)-2,4-dimethyl-thiazole as reagents, **EXAMPLE 44** was obtained. HRMS calculated for $C_{37}H_{42}N_6O_4S$: 666.2988; found 667.3047 [(M+H)⁺ form].

25 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(1-methyl-1H-pyrazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 45)**

Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)-1-methyl-pyrazole as reagents, **EXAMPLE 45** was obtained. HRMS calculated for $C_{36}H_{41}N_7O_4$: 635.3220; found 636.3288 $[(M+H)^+ \text{ form}]$.

5 ■ **3-([1-((3R,4R)-1-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 46)**

Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)-1,3-dimethyl-pyrazole as reagents, **EXAMPLE 46** was obtained. HRMS calculated for $C_{37}H_{43}N_7O_4$: 649.3376; found 650.3455 $[(M+H)^+ \text{ form}]$.

10 ■ **4-((3R,4R)-4-[(4-hydroxy-4-{[7-(4-methoxyphenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl]-3-phenylpiperidin-1-yl)methyl)pyridine-2-carbonitrile (EXAMPLE 47)**

Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 47** was obtained. HRMS
15 calculated for $C_{38}H_{39}N_7O_4$: 657.3063; found 658.3133 $[(M+H)^+ \text{ form}]$.

■ **3-[4-hydroxy-1-((3R,4R)-1-[(6-methylpyridin-3-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 48)**

Using **General Procedure 6** starting from **Preparation R3ax** and 5-(bromomethyl)-2-methyl-pyridine hydrobromide as reagents, **EXAMPLE 48** was obtained. HRMS
20 calculated for $C_{38}H_{42}N_6O_4$: 646.3267; found 647.3343 $[(M+H)^+ \text{ form}]$.

■ **5-((3R,4R)-4-[(4-hydroxy-4-{[7-(4-methoxyphenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl]-3-phenylpiperidin-1-yl)methyl)pyridine-2-carbonitrile (EXAMPLE 49)**

25 Using **General Procedure 6** starting from **Preparation R3ax** and 5-(bromomethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 49** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_4$: 657.3063; found 658.3138 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(1,3-oxazol-4-ylmethyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 50)**

Using **General Procedure 6** starting from **Preparation R3ax** and
5 4-(chloromethyl)oxazole as reagents, **EXAMPLE 50** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_5$: 622.2903; found 623.2975 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-[(1,5-dimethyl-1H-pyrazol-3-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 51)**

10 Using **General Procedure 6** starting from **Preparation R3ax** and 3-(chloromethyl)-1,5-dimethyl-pyrazole as reagents, **EXAMPLE 51** was obtained. HRMS calculated for $C_{37}H_{43}N_7O_4$: 649.3376; found 650.3431 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(5-methyl-1,3-oxazol-2-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 52)**

15 Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-5-methyl-oxazole as reagents, **EXAMPLE 52** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_5$: 636.3060; found 637.3141 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(2-methyl-1,3-thiazol-4-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 53)**

20 Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)-2-methyl-thiazole as reagents, **EXAMPLE 53** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_4S$: 652.2832; found 653.2896 [(M+H)⁺ form].

25 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(5-methyl-1,2-oxazol-3-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 54)**

Using **General Procedure 6** starting from **Preparation R3ax** and 3-(chloromethyl)-5-methyl-isoxazole as reagents, **EXAMPLE 54** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_5$: 636.3060; found 637.3118 $[(M+H)^+]$ form].

5 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-(1,2-oxazol-3-ylmethyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 55**)

Using **General Procedure 6** starting from **Preparation R3ax** and 3-(chloromethyl)isoxazole as reagents, **EXAMPLE 55** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_5$: 622.2903; found 623.2961 $[(M+H)^+]$ form].

10 ■ 3-{[4-hydroxy-1-[(3R,4R)-1-[(3-methyl-1,2-oxazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 56**)

Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)-3-methyl-isoxazole as reagents, **EXAMPLE 56** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_5$: 636.3060; found 637.3119 $[(M+H)^+]$ form].

15 ■ 3-{[4-hydroxy-1-[(3R,4R)-1-[(5-methyl-1,2-oxazol-4-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 57**)

Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)-5-methyl-isoxazole as reagents, **EXAMPLE 57** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_5$: 636.3060; found 637.3139 $[(M+H)^+]$ form].

20 ■ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[6-(trifluoromethyl)pyridin-3-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 58**)

25 Using **General Procedure 6** starting from **Preparation R3ax** and 5-(bromomethyl)-2-(trifluoromethyl)pyridine as reagents, **EXAMPLE 58** was obtained. HRMS calculated for $C_{38}H_{39}F_3N_6O_4$: 700.2985; found 701.3082 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(trifluoromethoxy)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 59)

5 Using **General Procedure 6** starting from **Preparation R3ay** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 59** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_5S$: 799.2764; found 800.2855 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(trifluoromethoxy)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 60)

Using **General Procedure 6** starting from **Preparation R3ay** and **Preparation R1c** as reagents, **EXAMPLE 60** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_4S$: 783.2814; found 784.2904 [(M+H)⁺ form].

15 ▪ 7-[4-(benzyloxy)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 61)

Using **General Procedure 6** starting from **Preparation R3az** and **Preparation R1c** as reagents, **EXAMPLE 61** was obtained. HRMS calculated for $C_{47}H_{47}N_7O_4S$: 805.3410; found 403.6767 [(M+2H)²⁺ form].

20 ▪ 7-[4-(benzyloxy)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 62)

Using **General Procedure 5** starting from **Preparation R3az** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 62** was obtained. HRMS calculated for $C_{47}H_{47}N_7O_5S$: 821.3359; found 822.3433 [(M+H)⁺ form].

25 ▪ 3-[(1-[(3S,4S)-1-benzyl-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 63)

Using **General Procedure 6** starting from 3-({4-hydroxy-1-[(3*S*,4*S*)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl}-7-methyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (which was obtained according to **General Procedure 5** with *tert*-butyl (3*S*,4*S*)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and **Preparation R2b**) and benzyl bromide as reagents, **EXAMPLE 63** was obtained. HRMS calculated for C₃₂H₃₇N₅O₃: 539.2896; found 540.2984 [(M+H)⁺ form].

▪ 3-[(1-{[(3*R*,4*R*)-1-benzyl-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (**EXAMPLE 64**)

Using **General Procedure 6** starting from **Preparation R3b** and benzyl bromide as reagents, **EXAMPLE 64** was obtained. HRMS calculated for C₃₂H₃₇N₅O₃: 539.2896; found 540.2977 [(M+H)⁺ form].

▪ 3-[(1-{[(3*R*,4*R*)-1-(2-fluorobenzyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (**EXAMPLE 65**)

Using **General Procedure 6** starting from **Preparation R3b** and 1-(bromomethyl)-2-fluoro-benzene as reagents, **EXAMPLE 65** was obtained. HRMS calculated for C₃₂H₃₆FN₅O₃: 557.2802; found 558.2879 [(M+H)⁺ form].

▪ 3-[(1-{[(3*R*,4*R*)-1-(3-fluorobenzyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (**EXAMPLE 66**)

Using **General Procedure 6** starting from **Preparation R3b** and 1-(bromomethyl)-3-fluoro-benzene as reagents, **EXAMPLE 66** was obtained. HRMS calculated for C₃₂H₃₆FN₅O₃: 557.2802; found 558.2902 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-(2-methylbenzyl)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (**EXAMPLE 67**)

Using **General Procedure 6** starting from **Preparation R3b** and 1-(bromomethyl)-2-methyl-benzene as reagents, **EXAMPLE 67** was obtained. HRMS calculated for $C_{33}H_{39}N_5O_3$: 553.3053; found 554.3138 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(3-methylbenzyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 68)**

Using **General Procedure 6** starting from **Preparation R3b** and 1-(bromomethyl)-3-methyl-benzene as reagents, **EXAMPLE 68** was obtained. HRMS calculated for $C_{33}H_{39}N_5O_3$: 553.3052; found 554.3090 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-(3-bromobenzyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 69)**

Using **General Procedure 6** starting from **Preparation R3b** and 1-bromo-3-(bromomethyl)benzene as reagents, **EXAMPLE 69** was obtained. HRMS calculated for $C_{32}H_{36}BrN_5O_3$: 617.2001; found 618.2094 $[(M+H)^+]$ form].

15 ▪ **6-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl]-1-methyl-3,4-dihydroquinolin-2(1H)-one (EXAMPLE 70)**

Using **General Procedure 6** starting from **Preparation R3b** and 6-(chloromethyl)-1-methyl-3,4-dihydroquinolin-2-one as reagents, **EXAMPLE 70** was obtained. HRMS calculated for $C_{36}H_{42}N_6O_4$: 622.3268; found 623.3354 $[(M+H)^+]$ form].

20 ▪ **3-[(1-[(3R,4R)-1-(3-acetylbenzyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 71)**

25 Using **General Procedure 6** starting from **Preparation R3b** and 1-[3-(chloromethyl)phenyl]ethanone as reagents, **EXAMPLE 71** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_4$: 581.3002; found 582.3054 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 72)**

Using **General Procedure 6** starting from **Preparation R3ba** and **Preparation R1c** as reagents, **EXAMPLE 72** was obtained. HRMS calculated for $C_{39}H_{41}N_7O_3S_2$: 719.2712; found 720.2762 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 73)**

Using **General Procedure 6** starting from **Preparation R3ba** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 73** was obtained. HRMS calculated for $C_{39}H_{41}N_7O_4S_2$: 735.2661; found 736.2727 $[(M+H)^+]$ form].

▪ **7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 74)**

Using **General Procedure 6** starting from **Preparation R3bb** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 74** was obtained. HRMS calculated for $C_{38}H_{38}ClN_7O_4S_2$: 755.2115; found 756.219 $[(M+H)^+]$ form].

▪ **7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 75)**

Using **General Procedure 6** starting from **Preparation R3bb** and **Preparation R1c** as reagents, **EXAMPLE 75** was obtained. HRMS calculated for $C_{38}H_{38}N_7O_3S_2Cl$: 739.2166; found 740.2222 $[(M+H)^+]$ form].

▪ **7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 76)**

Using **General Procedure 6** starting from **Preparation R3bc** and **Preparation R1c** as reagents, **EXAMPLE 76** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 758.3125 [(M+H)⁺ form].

5 ■ 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 77**)

10 Using **General Procedure 6** starting from **Preparation R3bc** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 77** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_6S$: 773.2996; found 774.3038 [(M+H)⁺ form].

15 ■ 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 78**)

20 Using **General Procedure 6** starting from **Preparation R3bd** and **Preparation R1c** as reagents, **EXAMPLE 78** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 372.6517 [(M+2H)²⁺ form].

25 ■ 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 79**)

30 Using **General Procedure 6** starting from **Preparation R3bd** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 79** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_6S$: 759.2838; found 380.6487 [(M+2H)²⁺ form].

35 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 80**)

40 Using **General Procedure 6** starting from **Preparation R3bf** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 80** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_4S$: 729.3097; found 730.3189 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 81)

Using **General Procedure 6** starting from **Preparation R3bg** and **Preparation R1c** as reagents, **EXAMPLE 81** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_3S$: 767.2865; found 768.2943 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 82)

Using **General Procedure 6** starting from **Preparation R3bg** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 82** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_4S$: 783.2814; found 784.2897 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[3-[(4-methylpiperazin-1-yl)methyl]phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 83)

Using **General Procedure 6** starting from **Preparation R3bh** and **Preparation R1c** as reagents, **EXAMPLE 83** was obtained. HRMS calculated for $C_{46}H_{53}N_9O_3S$: 811.3992; found 406.7081 [(M+2H)²⁺ form].

▪ 7-[3-(hydroxymethyl)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 84)

Using **General Procedure 6** starting from **Preparation R3bi** and **Preparation R1c** as reagents, **EXAMPLE 84** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_4S$: 729.3098; found 730.3153 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[3-(hydroxymethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 85)

Using **General Procedure 6** starting from **Preparation R3bi** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 85** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_5S$: 745.3046; found 746.313 [(M+H)⁺ form].

5 ▪ **7-(3-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 86)**

Using **General Procedure 6** starting from **Preparation R3bj** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 86** was obtained. HRMS calculated for $C_{40}H_{40}N_7O_4SCl$: 749.2551; found 750.2624 [(M+H)⁺ form].

10 ▪ **3-{[1-[(3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(3-chlorophenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 87)**

Using **General Procedure 6** starting from **Preparation R3bj** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 87** was obtained. HRMS calculated for $C_{34}H_{34}BrClN_6O_3S$: 720.1284; found 721.1336 [(M+H)⁺ form].

15 ▪ **7-(3-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 88)**

Using **General Procedure 6** starting from **Preparation R3bk** and **Preparation R1c** as reagents, **EXAMPLE 88** was obtained. HRMS calculated for $C_{40}H_{40}FN_7O_3S$: 717.2897; found 359.6513 [(M+2H)²⁺ form].

20 ▪ **7-(3-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 89)**

25 Using **General Procedure 6** starting from **Preparation R3bk** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 89** was obtained. HRMS calculated for $C_{40}H_{40}FN_7O_4S$: 733.2847; found 734.2893 [(M+H)⁺ form].

▪ 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 90)

Using **General Procedure 6** starting from **Preparation R3bl** and **Preparation R1c** as reagents, **EXAMPLE 90** was obtained. HRMS calculated for C₄₂H₄₆N₈O₃S: 742.3413; found 372.1784 [(M+2H)²⁺ form].

▪ 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 91)

Using **General Procedure 6** starting from **Preparation R3bl** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 91** was obtained. HRMS calculated for C₄₂H₄₆N₈O₄S: 758.3362; found 380.1752 [(M+2H)²⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 92)

Using **General Procedure 6** starting from **Preparation R3bm** and **Preparation R1c** as reagents, **EXAMPLE 92** was obtained. HRMS calculated for C₄₄H₄₈N₈O₄S: 784.3519; found 785.3594 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 93)

Using **General Procedure 6** starting from **Preparation R3bm** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 93** was obtained. HRMS calculated for C₄₄H₄₈N₈O₅S: 800.3468; found 801.3546 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 94)

Using **General Procedure 6** starting from **Preparation R3bo** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 94** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_5S$: 745.3046; found 746.3117 $[(M+H)^+]$ form].

5 ■ 3-{[1-((3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 95**)

Using **General Procedure 6** starting from **Preparation R3bo** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 95** was obtained. HRMS calculated for $C_{35}H_{37}BrN_6O_4S$: 716.1780; found 717.1825 $[(M+H)^+]$ form].

10 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(trifluoromethoxy)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 96**)

15 Using **General Procedure 6** starting from **Preparation R3bp** and **Preparation R1c** as reagents, **EXAMPLE 96** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_4S$: 783.2814; found 784.2878 $[(M+H)^+]$ form].

20 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(trifluoromethoxy)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 97**)

Using **General Procedure 6** starting from **Preparation R3bp** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 97** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_5S$: 799.2764; found 800.2856 $[(M+H)^+]$ form].

25 ■ 7-[3-(benzyloxy)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 98**)

Using **General Procedure 6** starting from **Preparation R3bq** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 98** was obtained. HRMS calculated for $C_{47}H_{47}N_7O_5S$: 821.3359; found 822.343 $[(M+H)^+ \text{ form}]$.

5 ■ 7-[3-(benzyloxy)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 99**)

Using **General Procedure 6** starting from **Preparation R3bq** and **Preparation R1c** as reagents, **EXAMPLE 99** was obtained. HRMS calculated for $C_{47}H_{47}N_7O_4S$: 805.3410; found 806.3484 $(M+H)^+ \text{ form}]$.

10 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(6-methoxypyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 100**)

Using **General Procedure 6** starting from **Preparation R3bs** and **Preparation R1c** as reagents, **EXAMPLE 100** was obtained. HRMS calculated for $C_{40}H_{42}N_8O_4S$: 730.3049; found 731.3128 $[(M+H)^+ \text{ form}]$.

15 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(6-methoxypyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 101**)

Using **General Procedure 6** starting from **Preparation R3bs** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 101** was obtained. HRMS calculated for $C_{40}H_{42}N_8O_5S$: 746.2998; found 747.308 $[(M+H)^+ \text{ form}]$.

20 ■ 3-[(1-[(3R,4R)-1-benzyl-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 102**)

Using **General Procedure 6** starting from **Preparation R3bu** and benzyl bromide as reagents, **EXAMPLE 102** was obtained. HRMS calculated for $C_{37}H_{39}N_5O_3$: 601.3053; found 602.3155 $[(M+H)^+ \text{ form}]$.

▪ **3-[[1-((3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 103)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 103** was obtained. HRMS calculated for $C_{34}H_{35}N_6O_3SBr$: 686.1675; found 687.1743 [(M+H)⁺ form].

▪ **3-[[1-((3R,4R)-1-[(5-bromopyridin-3-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 104)**

Using **General Procedure 6** starting from **Preparation R3bu** and 3-bromo-5-(chloromethyl)pyridine as reagents, **EXAMPLE 104** was obtained. HRMS calculated for $C_{36}H_{37}BrN_6O_3$: 680.2111; found 681.2179 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyridin-4-ylmethyl)piperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 105)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)pyridine as reagents, **EXAMPLE 105** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3$: 602.3005; found 603.3085 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyridin-3-ylmethyl)piperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 106)**

Using **General Procedure 6** starting from **Preparation R3bu** and 3-(bromomethyl)pyridine hydrobromide as reagents, **EXAMPLE 106** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3$: 602.3005; found 603.3062 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-((3R,4R)-1-[(1-methyl-1H-pyrazol-4-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 107)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)-1-methyl-pyrazole as reagents, **EXAMPLE 107** was obtained. HRMS calculated for $C_{35}H_{39}N_7O_3$: 605.3115; found 606.3188 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 108)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)pyrazine hydrochloride as reagents, **EXAMPLE 108** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_3$: 603.2958; found 604.3021 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(1,3-thiazol-5-ylmethyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 109)**

Using **General Procedure 9** starting from **EXAMPLE 103** and methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carboxylate as reagents, **EXAMPLE 109**
15 was obtained as a result of a dehalogenation during the Suzuki coupling. HRMS calculated for $C_{34}H_{36}N_6O_3S$: 608.2567; found 609.265 $[(M+H)^+ \text{ form}]$.

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(5-methyl-1,3-oxazol-2-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 110)**

20 Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-5-methyl-oxazole as reagents, **EXAMPLE 110** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4$: 606.2955; found 607.3016 $[(M+H)^+ \text{ form}]$.

25 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(1,3-thiazol-2-ylmethyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 111)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)thiazole as reagents, **EXAMPLE 111** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_3S$: 608.2567; found 609.2651 $[(M+H)^+ \text{ form}]$.

▪ 3-{[4-hydroxy-1-((3R,4R)-1-[(5-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 112)

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-5-methyl-thiazole as reagents, **EXAMPLE 112** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2783 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-(1,2-oxazol-3-ylmethyl)-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 113)

Using **General Procedure 6** starting from **Preparation R3bu** and 3-(chloromethyl)isoxazole as reagents, **EXAMPLE 113** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_4$: 592.2798; found 593.2864 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-1-[(3-methyl-1,2-oxazol-5-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 114)

Using **General Procedure 6** starting from **Preparation R3bu** and 5-(chloromethyl)-3-methyl-isoxazole as reagents, **EXAMPLE 114** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4$: 606.2955; found 607.3046 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 115)

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-4-methyl-thiazole as reagents, **EXAMPLE 115** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2782 [(M+H)⁺ form].

▪ 3-{[1-((3R,4R)-1-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 116)

Using **General Procedure 6** starting from **Preparation R3bu** and 5-(chloromethyl)-2,4-dimethyl-thiazole as reagents, **EXAMPLE 116** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_3S$: 636.2883; found 637.2942 $[(M+H)^+]$ form].

5 ▪ **3-{[1-({(3R,4R)-1-[(4,5-dimethyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 117)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-4,5-dimethyl-thiazole as reagents, **EXAMPLE 117** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_3S$: 636.2883; found 637.2965 $[(M+H)^+]$ form].

10 ▪ **3-{[4-hydroxy-1-({(3R,4R)-1-[(5-methyl-1,2-oxazol-4-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 118)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)-5-methyl-isoxazole as reagents, **EXAMPLE 118** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4$: 606.2955; found 607.3009 $[(M+H)^+]$ form].

15 ▪ **3-{[4-hydroxy-1-({(3R,4R)-1-[(1-methyl-1H-pyrazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 119)**

Using **General Procedure 6** starting from **Preparation R3bu** and 5-(chloromethyl)-1-methyl-pyrazole as reagents, **EXAMPLE 119** was obtained. HRMS calculated for $C_{35}H_{39}N_7O_3$: 605.3115; found 606.3186 $[(M+H)^+]$ form].

20 ▪ **3-{[4-hydroxy-1-({(3R,4R)-1-[(5-methyl-1,2-oxazol-3-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 120)**

25 Using **General Procedure 6** starting from **Preparation R3bu** and 3-(chloromethyl)-5-methyl-isoxazole as reagents, **EXAMPLE 120** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4$: 606.2955; found 607.3011 $[(M+H)^+]$ form].

▪ **3- {[4-hydroxy-1-((3R,4R)-1-[(2-methyl-1,3-thiazol-4-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 121)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)-2-methyl-thiazole as reagents, **EXAMPLE 121** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2799 [(M+H)⁺ form].

▪ **4- {[[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl]pyridine-2-carbonitrile (EXAMPLE 122)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 122** was obtained. HRMS calculated for $C_{37}H_{37}N_7O_3$: 627.2958; found 628.3026 [(M+H)⁺ form].

▪ **5- {[[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl]pyridine-2-carbonitrile (EXAMPLE 123)**

Using **General Procedure 6** starting from **Preparation R3bu** and 5-(bromomethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 123** was obtained. HRMS calculated for $C_{37}H_{37}N_7O_3$: 627.2958; found 628.3025 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(1,3-oxazol-4-ylmethyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 124)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)oxazole as reagents, **EXAMPLE 124** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_4$: 592.2797852; found 593.2876 [(M+H)⁺ form].

▪ **3- {[4-hydroxy-1-((3R,4R)-1-[(6-methylpyridin-3-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 125)**

Using **General Procedure 6** starting from **Preparation R3bu** and 5-(bromomethyl)-2-methyl-pyridine hydrobromide as reagents, **EXAMPLE 125** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_3$: 616.3162; found 617.3241 $[(M+H)^+ \text{ form}]$.

5 ■ **3-[(1-[(3S,4S)-1-benzyl-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-ethyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 126)**

Using **General Procedure 6** starting from 7-ethyl-3-({4-hydroxy-1-[(3S,4S)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (which was obtained according to **General Procedure 5** with *tert*-butyl (3*S*,4*S*)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and **Preparation R2c**) and benzyl bromide as reagents, **EXAMPLE 126** was obtained. HRMS calculated for $C_{33}H_{39}N_5O_3$: 553.3053; found 554.312 $[(M+H)^+ \text{ form}]$.

10 ■ **3-[(1-[(3R,4R)-1-benzyl-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-ethyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 127)**

Using **General Procedure 6** starting from **Preparation R3c** and benzyl bromide as reagents, **EXAMPLE 127** was obtained. HRMS calculated for $C_{33}H_{39}N_5O_3$: 553.3053; found 554.3122 $[(M+H)^+ \text{ form}]$.

15 ■ **7-ethyl-3-[(1-[(3R,4R)-1-(2-fluorobenzyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 128)**

20 Using **General Procedure 6** starting from **Preparation R3c** and 1-(bromomethyl)-2-fluoro-benzene as reagents, **EXAMPLE 128** was obtained. HRMS calculated for $C_{33}H_{38}FN_5O_3$: 571.2959; found 572.3022 $[(M+H)^+ \text{ form}]$.

25 ■ **7-ethyl-3-[(1-[(3R,4R)-1-(3-fluorobenzyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 129)**

Using **General Procedure 6** starting from **Preparation R3c** and 1-(bromomethyl)-3-fluoro-benzene as reagents, **EXAMPLE 129** was obtained. HRMS calculated for $C_{33}H_{38}FN_5O_3$: 571.2959; found 572.3037 $[(M+H)^+ \text{ form}]$.

▪ **7-ethyl-3-[(4-hydroxy-1-[(3R,4R)-1-(2-methylbenzyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 130)**

Using **General Procedure 6** starting from **Preparation R3c** and 1-(bromomethyl)-2-methyl-benzene as reagents, **EXAMPLE 130** was obtained. HRMS calculated for $C_{34}H_{41}N_5O_3$: 567.3209; found 568.327 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 131)**

Using **General Procedure 6** starting from **Preparation R3cc** and **Preparation R1c** as reagents, **EXAMPLE 131** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_3S_2$: 705.2556; found 706.262 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 132)**

Using **General Procedure 6** starting from **Preparation R3cc** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 132** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_4S_2$: 721.2505; found 722.2596 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 133)**

Using **General Procedure 6** starting from **Preparation R3cf** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 133** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_4S_2$: 721.2505; found 722.2570 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-1H-imidazol-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 134)**

Using **General Procedure 6** starting from **Preparation R3cg** and **Preparation R1c** as reagents, **EXAMPLE 134** was obtained. HRMS calculated for $C_{38}H_{41}N_9O_3S$: 703.3053; found 352.6599 $[(M+2H)^{2+}$ form].

5 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-1H-imidazol-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 135**)

Using **General Procedure 6** starting from **Preparation R3cg** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 135** was obtained. HRMS calculated for $C_{38}H_{41}N_9O_4S$: 719.3002; found 360.6580 $[(M+2H)^{2+}$ form].

10 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-1H-pyrazol-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 136**)

Using **General Procedure 6** starting from **Preparation R3ch** and **Preparation R1c** as reagents, **EXAMPLE 136** was obtained. HRMS calculated for $C_{38}H_{41}N_9O_3S$: 703.3053; found 704.3095 $[(M+H)^+$ form].

15 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-1H-pyrazol-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 137**)

Using **General Procedure 6** starting from **Preparation R3ch** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 137** was obtained. HRMS calculated for $C_{38}H_{41}N_9O_4S$: 719.3002; found 720.3059 $[(M+H)^+$ form].

20 ▪ 7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 138**)

Using **General Procedure 6** starting from **Preparation R3ci** and **Preparation R1c** as reagents, **EXAMPLE 138** was obtained. HRMS calculated for $C_{38}H_{39}F_2N_9O_3S$: 739.2864; found 740.2936 $[(M+H)^+$ form].

▪ 7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 139)

5 Using **General Procedure 6** starting from **Preparation R3ci** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 139** was obtained. HRMS calculated for $C_{38}H_{39}F_2N_9O_4S$: 755.2814; found 756.287 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(1,3-thiazol-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 140)

10 Using **General Procedure 6** starting from **Preparation R3ck** and **Preparation R1c** as reagents, **EXAMPLE 140** was obtained. HRMS calculated for $C_{37}H_{38}N_8O_3S_2$: 706.2509; found 707.257 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(1,3-thiazol-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 141)

15 Using **General Procedure 6** starting from **Preparation R3ck** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 141** was obtained. HRMS calculated for $C_{37}H_{38}N_8O_4S_2$: 722.2457; found 723.2535 [(M+H)⁺ form].

20 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(prop-2-yn-1-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 142)

25 Using **General Procedure 6** starting from **Preparation R3m** and **Preparation R1c** as reagents, **EXAMPLE 142** was obtained. HRMS calculated for $C_{37}H_{39}N_7O_3S$: 661.2835; found 662.2896 [(M+H)⁺ form].

▪ **3-([1-((3R,4R)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-(2,2,2-trifluoroethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 143)**

Using **General Procedure 6** starting from **Preparation R3o** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 143** was obtained. HRMS calculated for $C_{30}H_{32}BrF_3N_6O_3S$: 692.1392; found 693.1452 [(M+H)⁺ form].

▪ **7-(buta-2,3-dien-1-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 144)**

Using **General Procedure 6** starting from **Preparation R3s** and **Preparation R1c** as reagents, **EXAMPLE 144** was obtained. HRMS calculated for $C_{38}H_{41}N_7O_3S$: 675.2991; found 676.3089 [(M+H)⁺ form].

▪ **7-(4-chlorobenzyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 145)**

Using **General Procedure 6** starting from **Preparation R3x** and **Preparation R1c** as reagents, **EXAMPLE 145** was obtained. HRMS calculated for $C_{41}H_{42}ClN_7O_3S$: 747.2758; found 374.6462 [(M+2H)²⁺ form].

▪ **7-(3-chlorobenzyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 146)**

Using **General Procedure 6** starting from **Preparation R3y** and **Preparation R1c** as reagents, **EXAMPLE 146** was obtained. HRMS calculated for $C_{41}H_{42}ClN_7O_3S$: 747.2758; found 374.645 [(M+2H)²⁺ form].

▪ **7-benzyl-3-([1-([1-benzyl-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 147)**

Using **General Procedure 6** starting from racemic 7-benzyl-3-({4-hydroxy-1-[3-phenylpiperidine-4-carbonyl]piperidin-4-yl)methyl}-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-

one (which was obtained according to **General Procedure 5** with racemic *tert*-butyl 4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and 7-benzyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one) and benzyl bromide as reagents, **EXAMPLE 147** was obtained. HRMS calculated for C₃₈H₄₁N₅O₃: 615.3209; found 616.3308 [(M+H)⁺ form].

▪ **7-benzyl-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (EXAMPLE 148)**

Using **General Procedure 6** starting from **Preparation R3z** and **Preparation R1c** as reagents, **EXAMPLE 148** was obtained. HRMS calculated for C₄₁H₄₃N₇O₃S: 713.3148; found 357.6653 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (EXAMPLE 149)**

Using **General Procedure 7** starting from **Preparation R3ac** and **Preparation R1d** as reagents, **EXAMPLE 149** was obtained. HRMS calculated for C₄₄H₄₇N₇O₇S: 817.3257; found 818.3322 [(M+H)⁺ form].

▪ **7-(3,5-dichlorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (EXAMPLE 150)**

Using **General Procedure 7** starting from **Preparation R3ad** and **Preparation R1d** as reagents, **EXAMPLE 150** was obtained. HRMS calculated for C₄₁H₃₉N₇O₄SCl₂: 795.2161; found 796.225 [(M+H)⁺ form].

▪ **7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (EXAMPLE 151)**

Using **General Procedure 7** starting from **Preparation R3ae** and **Preparation R1d** as reagents, **EXAMPLE 151** was obtained. HRMS calculated for $C_{42}H_{42}N_7O_5SCl$: 791.2657; found 792.2736 $[(M+H)^+$ form].

5 ■ 7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 152)

Using **General Procedure 7** starting from **Preparation R3af** and **Preparation R1d** as reagents, **EXAMPLE 152** was obtained. HRMS calculated for $C_{43}H_{45}N_7O_6S$: 787.3152; found 788.3224 $[(M+H)^+$ form].

10 ■ 7-(3,4-dichlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 153)

Using **General Procedure 7** starting from **Preparation R3ag** and **Preparation R1d** as reagents, **EXAMPLE 153** was obtained. HRMS calculated for $C_{41}H_{39}Cl_2N_7O_4S$: 795.2161; found 796.2221 $[(M+H)^+$ form].

15 ■ 7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
20 (EXAMPLE 154)

Using **General Procedure 7** starting from **Preparation R3ah** and **Preparation R1d** as reagents, **EXAMPLE 154** was obtained. HRMS calculated for $C_{41}H_{39}ClFN_7O_4S$: 779.2457; found 780.2528 $[(M+H)^+$ form].

25 ■ 7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 155)

Using **General Procedure 7** starting from **Preparation R3ai** and **Preparation R1d** as reagents, **EXAMPLE 155** was obtained. HRMS calculated for $C_{42}H_{42}ClN_7O_5S$: 791.2657; found 792.2735 $[(M+H)^+$ form].

5 ■ 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 156)

Using **General Procedure 7** starting from **Preparation R3aj** and **Preparation R1d** as reagents, **EXAMPLE 156** was obtained. HRMS calculated for $C_{42}H_{42}FN_7O_5S$: 775.2952; found 776.3023 $[(M+H)^+$ form].

10 ■ 7-(3,4-dimethoxyphenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 157)

15 Using **General Procedure 7** starting from **Preparation R3ak** and **Preparation R1d** as reagents, **EXAMPLE 157** was obtained. HRMS calculated for $C_{43}H_{45}N_7O_6S$: 787.3152; found 394.6638 $[(M+2H)^{2+}$ form].

20 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(trifluoromethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 158)

Using **General Procedure 7** starting from **Preparation R3ao** and **Preparation R1d** as reagents, **EXAMPLE 158** was obtained. HRMS calculated for $C_{42}H_{40}F_3N_7O_4S$: 795.2814; found 796.2886 $[(M+H)^+$ form].

25 ■ 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 159)

Using **General Procedure 7** starting from **Preparation R3ap** and **Preparation R1d** as reagents, **EXAMPLE 159** was obtained. HRMS calculated for $C_{42}H_{41}F_2N_7O_4S$: 777.2909; found 778.2984 $[(M+H)^+ \text{ form}]$.

5 ▪ **7-[4-(benzyloxy)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 160)**

10 Using **General Procedure 7** starting from **Preparation R3az** and **Preparation R1d** as reagents, **EXAMPLE 160** was obtained. HRMS calculated for $C_{48}H_{47}N_7O_5S$: 833.3359; found 834.3447 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(4-methyl-2-phenyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 161)**

15 Using **General Procedure 7** starting from **Preparation R3b** and 4-methyl-2-phenylthiazole-5-carboxylic acid as reagents, **EXAMPLE 161** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2754 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(3-methyl-1,2-thiazol-4-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 162)**

20 Using **General Procedure 7** starting from **Preparation R3b** and 3-methylisothiazole-4-carboxylic acid as reagents, **EXAMPLE 162** was obtained. HRMS calculated for $C_{30}H_{34}N_6O_4S$: 574.2362; found 575.2434 $[(M+H)^+ \text{ form}]$.

25 ▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(2-phenyl-1,3-thiazol-5-yl)carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 163)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-phenylthiazole-5-carboxylic acid as reagents, **EXAMPLE 163** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2593 $[(M+H)^+ \text{ form}]$.

▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 164)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 164** was obtained. HRMS calculated for $C_{30}H_{34}N_6O_4S$: 574.2362; found 575.2437 [(M+H)⁺ form].

▪ **3-{[1-((3R,4R)-1-[(2-benzyl-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 165)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-benzyl-4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 165** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4S$: 664.2832; found 665.2897 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-(2-methylbenzoyl)-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 166)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-methylbenzoic acid as reagents, **EXAMPLE 166** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_4$: 567.2846; found 568.2904 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-(3-methylbenzoyl)-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 167)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-methylbenzoic acid as reagents, **EXAMPLE 167** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_4$: 567.2846; found 668.2916 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-(4-methylbenzoyl)-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 168)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-methylbenzoic acid as reagents, **EXAMPLE 168** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_4$: 567.2846; found 568.2919 [(M+H)⁺ form].

5 ▪ **3-[(1-[(3R,4R)-1-(2-fluorobenzoyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 169)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-fluorobenzoic acid as reagents, **EXAMPLE 169** was obtained. HRMS calculated for $C_{32}H_{34}FN_5O_4$: 571.2595; found 572.266 [(M+H)⁺ form].

10 ▪ **3-[(1-[(3R,4R)-1-(3-fluorobenzoyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 170)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-fluorobenzoic acid as reagents, **EXAMPLE 170** was obtained. HRMS calculated for $C_{32}H_{34}FN_5O_4$: 571.2595; found 572.265 [(M+H)⁺ form].

15 ▪ **3-[(1-[(3R,4R)-1-(4-fluorobenzoyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 171)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-fluorobenzoic acid as reagents, **EXAMPLE 171** was obtained. HRMS calculated for $C_{32}H_{34}FN_5O_4$: 571.2595; found 572.267 [(M+H)⁺ form].

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(pyridin-4-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 172)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 4-methyl-2-(4-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 172** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.27 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyridin-4-yl)-1,3-thiazol-5-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 173)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-(4-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 173** was obtained. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.254 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[2-(2-fluorophenyl)-4-methyl-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 174)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-(2-fluorophenyl)-4-methyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 174** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_4S$: 668.2581; found 669.2668 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(2-methylphenyl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 175)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-methyl-2-(o-tolyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 175** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4S$: 664.2832; found 665.2917 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(5-bromothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 176)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiophene-2-carboxylic acid as reagents, **EXAMPLE 176** was obtained. HRMS calculated for $C_{30}H_{32}BrN_5O_4S$: 637.1358; found 638.1430 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(1-benzyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 177)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-benzylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 177** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4$: 632.3111; found 633.3184 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(1-methyl-5-phenyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 178)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-methyl-5-phenylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 178** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4$: 632.3111; found 633.3183 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(1H-pyrrol-2-ylcarbonyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 179)**

Using **General Procedure 7** starting from **Preparation R3b** and 1H-pyrrole-2-carboxylic acid as reagents, **EXAMPLE 179** was obtained. HRMS calculated for $C_{30}H_{34}N_6O_4$: 542.2642; found 543.2711 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 180)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-methylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 180** was obtained. HRMS calculated for $C_{31}H_{36}N_6O_4$: 556.2798; found 557.2862 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{1-(pyridin-3-ylmethyl)-1H-pyrrol-2-yl]carbonyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 181)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 1-(3-pyridylmethyl)pyrrole-2-carboxylic acid as reagents, **EXAMPLE 181** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3064; found 317.6602 $[(M+2H)^{2+} \text{ form}]$.

▪ 3-[(1-[(3R,4R)-1-{[5-(2-aminopyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 182)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(2-amino-4-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 182** was obtained. HRMS calculated for C₃₅H₃₇N₇O₄S: 651.2628; found 326.638 [(M+2H)²⁺ form].

▪ 3-[(4-hydroxy-1-{(3R,4R)-1-{[4-methyl-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 183)

Using **General Procedure 7** starting from **Preparation R3b** and 4-methyl-5-(4-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 183** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2676; found 651.2752 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-{(3S,4S)-3-phenyl-1-{[5-(pyridin-4-yl)thiophen-2-yl]carbonyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 184)

Using **General Procedure 7** starting from 3-({4-hydroxy-1-[(3S,4S)-3-phenylpiperidine-4-carbonyl]piperidin-4-yl}methyl)-7-methyl-3*H*,4*H*,7*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (which was obtained according to **General Procedure 5** with *tert*-butyl (3S,4S)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and **Preparation R2b**) and 5-(4-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 184** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.2591 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-{(3R,4R)-1-{[4-nitro-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 185)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1p** as reagents, **EXAMPLE 185** was obtained. HRMS calculated for C₃₅H₃₅N₇O₆S: 681.2369; found 682.2432 [(M+H)⁺ form].

▪ 3- $\{[1-((3R,4R)-1-[(1-ethenyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl\}methyl\}$ -7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 186)

Using **General Procedure 7** starting from **Preparation R3b** and 1-vinylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 186** was obtained. HRMS calculated for $C_{32}H_{36}N_6O_4$: 568.2798; found 569.2884 $[(M+H)^+]$ form].

▪ 3- $\{[4-hydroxy-1-((3R,4R)-3-phenyl-1-([1-(prop-2-en-1-yl)-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl)carbonyl]piperidin-4-yl\}methyl\}$ -7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 187)

Using **General Procedure 7** starting from **Preparation R3b** and 1-allylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 187** was obtained. HRMS calculated for $C_{33}H_{38}N_6O_4$: 582.2955; found 583.3039 $[(M+H)^+]$ form].

▪ 3- $\{[4-hydroxy-1-((3R,4R)-1-[(1-methyl-1H-indol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl\}methyl\}$ -7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 188)

Using **General Procedure 7** starting from **Preparation R3b** and 1-methylindole-2-carboxylic acid as reagents, **EXAMPLE 188** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4$: 606.2955; found 607.3033 $[(M+H)^+]$ form].

▪ 3- $\{[1-((3R,4R)-1-[(4-bromo-1-methyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl\}methyl\}$ -7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 189)

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromo-1-methylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 189** was obtained. HRMS calculated for $C_{31}H_{35}BrN_6O_4$: 634.1903; found 635.1981 $[(M+H)^+]$ form].

▪ 3- $\{[1-((3R,4R)-1-[(2,2-difluoro-1,3-benzodioxol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl\}methyl\}$ -7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 190)

Using **General Procedure 7** starting from **Preparation R3b** and 2,2-difluoro-1,3-benzodioxole-5-carboxylic acid as reagents, **EXAMPLE 190** was obtained. HRMS calculated for $C_{33}H_{33}F_2N_5O_6$: 633.2399; found 634.2475 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(1H-indol-5-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 191)**

Using **General Procedure 7** starting from **Preparation R3b** and 1H-indole-5-carboxylic acid as reagents, **EXAMPLE 191** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_4$: 592.2798; found 593.2881 $[(M+H)^+]$ form].

10 ▪ **tert-butyl 6-[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl]carbonyl]-3,4-dihydroisoquinoline-2(1H)-carboxylate (EXAMPLE 192)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-tert-butoxycarbonyl-3,4-dihydro-1H-isoquinoline-6-carboxylic acid as reagents, **EXAMPLE 192** was obtained.
15 HRMS calculated for $C_{40}H_{48}N_6O_6$: 708.3635; found 709.3717 $[(M+H)^+]$ form].

▪ **3-{[1-[(3R,4R)-1-[(1-acetyl-1,2,3,4-tetrahydroquinolin-6-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 193)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-acetyl-3,4-dihydro-2H-quinoline-6-carboxylic acid as reagents, **EXAMPLE 193** was obtained. HRMS calculated
20 for $C_{37}H_{42}N_6O_5$: 650.3217; found 651.3306 $[(M+H)^+]$ form].

▪ **3-{[1-[(3R,4R)-1-[(4-bromopyridin-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 194)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 4-bromopyridine-2-carboxylic acid as reagents, **EXAMPLE 194** was obtained. HRMS calculated for $C_{31}H_{33}BrN_6O_4$: 632.1747; found 633.1821 $[(M+H)^+]$ form].

▪ **3-[[1-((3R,4R)-1-[(2-bromopyridin-4-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 195)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromopyridine-4-carboxylic acid as reagents, **EXAMPLE 195** was obtained. HRMS calculated for $C_{31}H_{33}BrN_6O_4$: 632.1747; found 633.1824 [(M+H)⁺ form].

▪ **3-[[1-((3R,4R)-1-[(5-bromopyridin-3-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 196)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromopyridine-3-carboxylic acid as reagents, **EXAMPLE 196** was obtained. HRMS calculated for $C_{31}H_{33}BrN_6O_4$: 632.1747; found 633.1827 [(M+H)⁺ form].

▪ **3-[[1-((3R,4R)-1-[(5-bromo-3-fluorothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 197)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-fluorothiophene-2-carboxylic acid as reagents, **EXAMPLE 197** was obtained. HRMS calculated for $C_{30}H_{31}BrFN_5O_4S$: 655.1264; found 656.1341 [(M+H)⁺ form].

▪ **3-[[1-((3R,4R)-1-[(6-bromopyridin-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 198)**

Using **General Procedure 7** starting from **Preparation R3b** and 6-bromopyridine-2-carboxylic acid as reagents, **EXAMPLE 198** was obtained. HRMS calculated for $C_{31}H_{33}BrN_6O_4$: 632.1747; found 633.1822 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(1H-benzotriazol-5-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 199)**

Using **General Procedure 7** starting from **Preparation R3b** and 1*H*-benzotriazole-5-carboxylic acid as reagents, **EXAMPLE 199** was obtained. HRMS calculated for C₃₂H₃₄N₈O₄: 594.2703; found 595.2782 [(M+H)⁺ form].

5 ■ 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-[(trans-2-phenylcyclopropyl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one, diastereoisomer 1
(**EXAMPLE 200**)

10 Using **General Procedure 7** starting from **Preparation R3b** and *trans*-2-phenyl-1-cyclopropanecarboxylic acid as reagents, **EXAMPLE 200** was obtained as pure diastereoisomer after purification on preparative LC (C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MCN, isocratic 37 %). HRMS calculated for C₃₅H₃₉N₅O₄: 593.3002; found 594.3082 [(M+H)⁺ form].

15 ■ 3-[(1-[(3*R*,4*R*)-1-(3-bromobenzoyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (**EXAMPLE 201**)

Using **General Procedure 7** starting from **Preparation R3b** and 3-bromobenzoic acid as reagents, **EXAMPLE 201** was obtained. HRMS calculated for C₃₂H₃₄BrN₅O₄: 631.1794; found 632.1873 [(M+H)⁺ form].

20 ■ 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-[(trans-2-phenylcyclopropyl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one, diastereoisomer 2
(**EXAMPLE 202**)

25 Using **General Procedure 7** starting from **Preparation R3b** and *trans*-2-phenylcyclopropanecarboxylic acid as reagents, **EXAMPLE 202** was obtained as pure diastereoisomer after purification on preparative LC (C-18 Gemini-NX 5μm column, 5 mM aqueous NH₄HCO₃-MCN, isocratic 37 %). HRMS calculated for C₃₅H₃₉N₅O₄: 593.3002; found 594.3084 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(3-nitrobenzoyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 203)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-nitrobenzoic acid as reagents, **EXAMPLE 203** was obtained. HRMS calculated for $C_{32}H_{34}N_6O_6$: 598.2539; found 599.2625 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-benzoyl-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 204)**

Using **General Procedure 7** starting from **Preparation R3b** and benzoic acid as reagents, **EXAMPLE 204** was obtained. HRMS calculated for $C_{32}H_{35}N_5O_4$: 553.2689; found 554.2782 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(3-ethynylbenzoyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 205)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-ethynylbenzoic acid as reagents, **EXAMPLE 205** was obtained. HRMS calculated for $C_{34}H_{35}N_5O_4$: 577.2689; found 578.2776 [(M+H)⁺ form].

▪ **methyl 3-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]benzoate (EXAMPLE 206)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-methoxycarbonylbenzoic acid as reagents, **EXAMPLE 206** was obtained. HRMS calculated for $C_{34}H_{37}N_5O_6$: 611.2744; found 612.2837 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 207)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-(trifluoromethyl)benzoic acid as reagents, **EXAMPLE 207** was obtained. HRMS calculated for $C_{33}H_{34}F_3N_5O_4$: 621.2563; found 622.265 [(M+H)⁺ form].

5 ▪ **3-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzonitrile (EXAMPLE 208)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-cyanobenzoic acid as reagents, **EXAMPLE 208** was obtained. HRMS calculated for $C_{33}H_{34}N_6O_4$: 578.2642; found 579.272 [(M+H)⁺ form].

10 ▪ **3-[(4-hydroxy-1-{(3R,4R)-1-(3-methoxybenzoyl)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 209)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-methoxybenzoic acid as reagents, **EXAMPLE 209** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_5$: 583.2795; found 584.2889 [(M+H)⁺ form].

15 ▪ **3-[(4-hydroxy-1-{(3R,4R)-1-(3-phenoxybenzoyl)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 210)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-phenoxybenzoic acid as reagents, **EXAMPLE 210** was obtained. HRMS calculated for $C_{38}H_{39}N_5O_5$: 645.2951; found 646.3025 [(M+H)⁺ form].

20 ▪ **3-[(1-{(3R,4R)-1-(3-tert-butylbenzoyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 211)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 3-tert-butylbenzoic acid as reagents, **EXAMPLE 211** was obtained. HRMS calculated for $C_{36}H_{43}N_5O_4$: 609.3315; found 610.3382 [(M+H)⁺ form].

▪ **5-bromo-2-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}thiophene-3-carbonitrile (EXAMPLE 212)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-cyanothiophene-2-carboxylic acid as reagents, **EXAMPLE 212** was obtained. HRMS calculated for C₃₁H₃₁BrN₆O₄S: 662.1311; found 663.1384 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(quinolin-6-ylcarbonyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 213)**

Using **General Procedure 7** starting from **Preparation R3b** and quinoline-6-carboxylic acid as reagents, **EXAMPLE 213** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄: 604.2798; found 605.2872 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(2,3-dihydro-1,4-benzodioxin-6-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 214)**

Using **General Procedure 7** starting from **Preparation R3b** and 2,3-dihydro-1,4-benzodioxine-6-carboxylic acid as reagents, **EXAMPLE 214** was obtained. HRMS calculated for C₃₄H₃₇N₅O₆: 611.2744; found 612.2822 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(5,6-dihydro-4H-cyclopenta[b]thiophen-2-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 215)**

Using **General Procedure 7** starting from **Preparation R3b** and 5,6-dihydro-4H-cyclopenta[b]thiophene-2-carboxylic acid as reagents, **EXAMPLE 215** was obtained. HRMS calculated for C₃₃H₃₇N₅O₄S: 599.2567; found 600.2645 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(4,5,6,7-tetrahydro-1-benzothiophen-2-ylcarbonyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 216)**

Using **General Procedure 7** starting from **Preparation R3b** and 4,5,6,7-tetrahydrobenzothiophene-2-carboxylic acid as reagents, **EXAMPLE 216** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_4S$: 613.2723; found 614.2805 $[(M+H)^+]$ form].

5 ▪ **3-{[1-((3R,4R)-1-[(5-bromo-1-methyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 217)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-1-methylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 217** was obtained. HRMS calculated for $C_{31}H_{35}N_6O_4Br$: 634.1903; found 637.1959 $[(M+H)^+]$ form].

10 ▪ **3-{[4-hydroxy-1-((3R,4R)-3-phenyl-1-[(3-phenylcyclobutyl)carbonyl]piperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 218)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-phenylcyclobutanecarboxylic acid as reagents, **EXAMPLE 218** was obtained. HRMS
15 calculated for $C_{36}H_{41}N_5O_4$: 607.3159; found 608.3236 $[(M+H)^+]$ form].

▪ **3-[(1-[(3R,4R)-1-(3-ethoxybenzoyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 219)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-ethoxybenzoic acid as
20 reagents, **EXAMPLE 219** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_5$: 597.2951; found 598.3032 $[(M+H)^+]$ form].

▪ **3-{[4-hydroxy-1-((3R,4R)-1-[3-(4-methylpiperazin-1-yl)benzoyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 220)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 3-(4-methylpiperazin-1-yl)benzoic acid as reagents, **EXAMPLE 220** was obtained. HRMS calculated for $C_{37}H_{45}N_7O_4$: 651.3533; found 652.3604 $[(M+H)^+]$ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-3-phenyl-1-[3-(propan-2-yl)benzoyl]piperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 221)

Using **General Procedure 7** starting from **Preparation R3b** and 3-isopropylbenzoic acid as reagents, **EXAMPLE 221** was obtained. HRMS calculated for $C_{35}H_{41}N_5O_4$: 595.3159; found 596.3251 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-3-phenyl-1-[3-(pyrrolidin-1-ylmethyl)benzoyl]piperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 222)

Using **General Procedure 7** starting from **Preparation R3b** and 3-(pyrrolidin-1-ylmethyl)benzoic acid as reagents, **EXAMPLE 222** was obtained. HRMS calculated for $C_{37}H_{44}N_6O_4$: 636.3424; found 637.3504 [(M+H)⁺ form].

▪ 3-{[1-((3R,4R)-1-[3-(dimethylamino)benzoyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 223)

Using **General Procedure 7** starting from **Preparation R3b** and 3-(dimethylamino)benzoic acid as reagents, **EXAMPLE 223** was obtained. HRMS calculated for $C_{34}H_{40}N_6O_4$: 596.3111; found 597.3194 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-1-[3-(morpholin-4-yl)benzoyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 224)

Using **General Procedure 7** starting from **Preparation R3b** and 3-morpholinobenzoic acid as reagents, **EXAMPLE 224** was obtained. HRMS calculated for $C_{36}H_{42}N_6O_5$: 638.3217; found 639.3282 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-[1-(methylsulfonyl)-1,2,3,4-tetrahydroquinolin-6-yl]carbonyl)-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 225)

Using **General Procedure 7** starting from **Preparation R3b** and 1-methylsulfonyl-3,4-dihydro-2*H*-quinoline-6-carboxylic acid as reagents, **EXAMPLE 225** was obtained. HRMS calculated for C₃₆H₄₂N₆O₆S: 686.2886; found 687.2962 [(M+H)⁺ form].

5 ▪ **3-([4-hydroxy-1-((3*R*,4*R*)-3-phenyl-1-[3-(piperidin-1-yl)benzoyl]piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 226)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-(1-piperidyl)benzoic acid as reagents, **EXAMPLE 226** was obtained. HRMS calculated for C₃₇H₄₄N₆O₄: 636.3424; found 637.3483 [(M+H)⁺ form].

10 ▪ **6-(((3*R*,4*R*)-4-([4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl]carbonyl)-1-methyl-3,4-dihydroquinolin-2(1*H*)-one (EXAMPLE 227)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-methyl-2-oxo-3,4-dihydroquinoline-6-carboxylic acid as reagents, **EXAMPLE 227** was obtained. HRMS
15 calculated for C₃₆H₄₀N₆O₅: 636.3060; found 637.3162 [(M+H)⁺ form].

▪ **3-[(1-(((3*R*,4*R*)-1-[3-[(dimethylamino)methyl]benzoyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 228)**

Using **General Procedure 7** starting from **Preparation R3b** and
20 3-(dimethylaminomethyl)benzoic acid as reagents, **EXAMPLE 228** was obtained. HRMS calculated for C₃₅H₄₂N₆O₄: 610.3268; found 611.335 [(M+H)⁺ form].

▪ **3-([1-((3*R*,4*R*)-1-[(1-ethenyl-1*H*-indol-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 229)**

25 Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1t** as reagents, **EXAMPLE 229** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄: 618.2955; found 619.3002 [(M+H)⁺ form].

▪ **3-{[1-({(3R,4R)-1-[(5-bromo-1-ethenyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 230)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1u** as reagents, **EXAMPLE 230** was obtained. HRMS calculated for $C_{32}H_{35}BrN_6O_4$: 646.1903; found 647.1989 [(M+H)⁺ form].

▪ **3-[(1-({(3R,4R)-1-(2-acetylbenzoyl)-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 231)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-acetylbenzoic acid as reagents, **EXAMPLE 231** was obtained. HRMS calculated for $C_{34}H_{37}N_5O_5$: 595.2795; found 596.2861 [(M+H)⁺ form].

▪ **3-{[1-({(3R,4R)-1-[(3-fluoro-4,5-diiodothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 232)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1h** as reagents, **EXAMPLE 232** was obtained. HRMS calculated for $C_{30}H_{30}FI_2N_5O_4S$: 829.0092; found 830.0159 [(M+H)⁺ form].

▪ **methyl 2-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 233)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-methoxycarbonylbenzoic acid as reagents, **EXAMPLE 233** was obtained. HRMS calculated for $C_{34}H_{37}N_5O_6$: 611.2744; found 612.2823 [(M+H)⁺ form].

▪ **3-{[1-({(3R,4R)-1-[(3-fluoro-4-iodo-5-methylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 234)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1i** as reagents, **EXAMPLE 234** was obtained. HRMS calculated for $C_{31}H_{33}FIN_5O_4S$: 717.1282; found 718.1352 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-{[1-((3R,4R)-1-[(4-bromo-1-ethenyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 235)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1v** as reagents, **EXAMPLE 235** was obtained. HRMS calculated for $C_{32}H_{35}BrN_6O_4$: 646.1903; found 647.198 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-{[1-((3R,4R)-1-[(3-chloro-4-methylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 236)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-chloro-4-methylthiophene-2-carboxylic acid as reagents, **EXAMPLE 236** was obtained. HRMS calculated for $C_{31}H_{34}ClN_5O_4S$: 607.2020; found 608.2107 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-[(1-[(3R,4R)-1-{[3-amino-4-(methylsulfonyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 237)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-amino-4-methylsulfonyl-thiophene-2-carboxylic acid as reagents, **EXAMPLE 237** was obtained. HRMS calculated for $C_{31}H_{36}N_6O_6S_2$: 652.2137; found 653.2224 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(3-iodo-4-methylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 238)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 3-iodo-4-methylthiophene-2-carboxylic acid as reagents, **EXAMPLE 238** was obtained. HRMS calculated for $C_{31}H_{34}IN_5O_4S$: 699.1376; found 700.145 $[(M+H)^+ \text{ form}]$.

▪ **3-([1-((3R,4R)-1-[(5-bromo-3-chloro-4-methylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 239)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-chloro-4-methyl-thiophene-2-carboxylic acid as reagents, **EXAMPLE 239** was obtained. HRMS calculated for $C_{31}H_{33}BrClN_5O_4S$: 685.1125; found 686.1217 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-([1-(methylsulfanyl)methyl]-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 240)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-(methylsulfanylmethyl)pyrrole-2-carboxylic acid as reagents, **EXAMPLE 240** was obtained. HRMS calculated for $C_{32}H_{38}N_6O_4S$: 602.2675; found 603.2756 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(quinoxalin-6-ylcarbonyl)piperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 241)**

Using **General Procedure 7** starting from **Preparation R3b** and quinoxaline-6-carboxylic acid as reagents, **EXAMPLE 241** was obtained. HRMS calculated for $C_{34}H_{35}N_7O_4$: 605.2750; found 606.2831 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-((3R,4R)-1-[(1-methyl-1H-indol-6-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 242)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-methylindole-6-carboxylic acid as reagents, **EXAMPLE 242** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4$: 606.2955; found 607.3035 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-((3R,4R)-1-[(5-oxo-1-phenylpyrrolidin-3-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 243)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-oxo-1-phenylpyrrolidine-3-carboxylic acid as reagents, **EXAMPLE 243** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_5$: 636.3060; found 637.3129 $[(M+H)^+]$ form].

5 ▪ **tert-butyl 7-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-3,4-dihydroquinoxaline-1(2H)-carboxylate (EXAMPLE 244)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-*tert*-butoxycarbonyl-2,3-dihydro-1*H*-quinoxaline-6-carboxylic acid as reagents, **EXAMPLE 244** was obtained. HRMS calculated for $C_{39}H_{47}N_7O_6$: 709.3588; found 710.3667 $[(M+H)^+]$ form].

10 ▪ **tert-butyl 7-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-3,4-dihydroquinoline-1(2H)-carboxylate (EXAMPLE 245)**

Using **General Procedure 7** starting from **Preparation R3b** and 1-*tert*-butoxycarbonyl-3,4-dihydro-2*H*-quinoline-7-carboxylic acid as reagents, **EXAMPLE 245** was obtained.
15 HRMS calculated for $C_{40}H_{48}N_6O_6$: 708.3635; found 709.3715 $[(M+H)^+]$ form].

▪ **3-{{4-hydroxy-1-[(3R,4R)-1-[3-(hydroxyacetyl)benzoyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 246)**

Using **General Procedure 7** starting from **Preparation R3b** and
20 3-(2-chloroacetyl)benzoic acid as reagents, **EXAMPLE 246** was obtained. HRMS calculated for $C_{34}H_{37}N_5O_6$: 611.2744; found 612.2817 $[(M+H)^+]$ form].

▪ **3-{{1-[(3R,4R)-1-[3-(bromothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 247)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 3-bromothiophene-2-carboxylic acid as reagents, **EXAMPLE 247** was obtained. HRMS calculated for $C_{30}H_{32}BrN_5O_4S$: 637.1359; found 638.1428 $[(M+H)^+]$ form].

▪ **3-{{1-((3R,4R)-1-[(4-bromo-1,3-thiazol-2-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 248)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromothiazole-2-carboxylic acid as reagents, **EXAMPLE 248** was obtained. HRMS calculated for $C_{29}H_{31}BrN_6O_4S$: 638.1311; found 639.1389 [(M+H)⁺ form].

▪ **3-{{1-((3R,4R)-1-[(5-bromothiophen-3-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 249)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiophene-3-carboxylic acid as reagents, **EXAMPLE 249** was obtained. HRMS calculated for $C_{30}H_{32}BrN_5O_4S$: 637.1359; found 638.1438 [(M+H)⁺ form].

▪ **3-{{1-((3R,4R)-1-[(2-bromothiophen-3-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 250)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiophene-3-carboxylic acid as reagents, **EXAMPLE 250** was obtained. HRMS calculated for $C_{30}H_{32}BrN_5O_4S$: 637.1359; found 638.1443 [(M+H)⁺ form].

▪ **3-ethoxy-N-(4-{{(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl}carbonyl}benzyl)propanamide (EXAMPLE 251)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-[(3-ethoxypropanoylamino)methyl]benzoic acid as reagents, **EXAMPLE 251** was obtained. HRMS calculated for $C_{38}H_{46}N_6O_6$: 682.3479; found 683.3559 [(M+H)⁺ form].

▪ **tert-butyl (4-{{(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl}carbonyl}benzyl)carbamate (EXAMPLE 252)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-[(*tert*-butoxycarbonylamino)methyl]benzoic acid as reagents, **EXAMPLE 252** was obtained. HRMS calculated for C₃₈H₄₆N₆O₆: 682.3479; found 683.3567 [(M+H)⁺ form].

5 ▪ **3-{{1-[(3R,4R)-1-[(3-chloro-5-iodothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 253)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1j** as reagents, **EXAMPLE 253** was obtained. HRMS calculated for C₃₀H₃₁ClIN₅O₄S: 719.0830; found 720.0905 [(M+H)⁺ form].

10 ▪ **3-[(1-[(3R,4R)-1-(3-acetylbenzoyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 254)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-acetylbenzoic acid as reagents, **EXAMPLE 254** was obtained. HRMS calculated for C₃₄H₃₇N₅O₅: 595.2795; found 596.2875 [(M+H)⁺ form].

15 ▪ **3-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzaldehyde (EXAMPLE 255)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-formylbenzoic acid as reagents, **EXAMPLE 255** was obtained. HRMS calculated for C₃₃H₃₅N₅O₅: 581.2638; found 582.271 [(M+H)⁺ form].

20 ▪ **3-[(1-[(3R,4R)-1-(3-ethenylbenzoyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 256)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 3-vinylbenzoic acid as reagents, **EXAMPLE 256** was obtained. HRMS calculated for C₃₄H₃₇N₅O₄: 579.2845; found 580.2931 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-(3-ethylbenzoyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 257)

Using **General Procedure 7** starting from **Preparation R3b** and 3-ethylbenzoic acid as reagents, **EXAMPLE 257** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_4$: 581.3002; found 582.3077 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-[(3R,4R)-1-[3-(methylsulfonyl)benzoyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 258)

Using **General Procedure 7** starting from **Preparation R3b** and 3-methylsulfonylbenzoic acid as reagents, **EXAMPLE 258** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_6S$: 631.2465; found 632.2549 [(M+H)⁺ form].

▪ 3-{[1-[(3R,4R)-1-[(4,5-dichloro-3-fluorothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 259)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1w** as reagents, **EXAMPLE 259** was obtained. HRMS calculated for $C_{30}H_{30}Cl_2FN_5O_4S$: 645.1379; found 646.1449 [(M+H)⁺ form].

▪ tert-butyl 3-{[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 260)

Using **General Procedure 7** starting from **Preparation R3b** and 3-tert-butoxycarbonylbenzoic acid as reagents, **EXAMPLE 260** was obtained. HRMS calculated for $C_{37}H_{43}N_5O_6$: 653.3214; found 654.3298 [(M+H)⁺ form].

▪ 3-{[1-[(3R,4R)-1-[(5-chloro-3-fluoro-4-methylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 261)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R11** as reagents, **EXAMPLE 261** was obtained. HRMS calculated for $C_{31}H_{33}ClFN_5O_4S$: 625.1926; found 626.1997 $[(M+H)^+ \text{ form}]$.

5 ■ 3-[(1-[(3R,4R)-1-{2,4-bis(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 262**)

Using **General Procedure 7** starting from **Preparation R3b** and 2,4-bis(6-methyl-3-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 262** was obtained. HRMS calculated for $C_{41}H_{42}N_8O_4S$: 742.3049; found 743.3126 $[(M+H)^+ \text{ form}]$.

10 ■ 3-[(1-[(3R,4R)-1-{4-chloro-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 263**)

Using **General Procedure 7** starting from **Preparation R3b** and 4-chloro-2-(6-methyl-3-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 263** was obtained. HRMS
15 calculated for $C_{35}H_{36}ClN_7O_4S$: 685.2238; found 686.2299 $[(M+H)^+ \text{ form}]$.

■ 3-{[1-[(3R,4R)-1-(4-chloro-2-methoxy-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 264**)

Using **General Procedure 7** starting from **Preparation R3b** and 4-chloro-2-methoxy-thiazole-5-carboxylic acid as reagents, **EXAMPLE 264** was obtained. HRMS calculated for
20 $C_{30}H_{33}ClN_6O_5S$: 624.1921; found 625.2 $[(M+H)^+ \text{ form}]$.

■ 3-{[1-[(3R,4R)-1-(4-bromo-2-methoxy-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 265**)

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromo-2-methoxy-thiazole-5-carboxylic acid as reagents, **EXAMPLE 265** was obtained. HRMS calculated for
25 $C_{30}H_{33}BrN_6O_5S$: 668.1417; found 669.1494 $[(M+H)^+ \text{ form}]$.

▪ 6-[[[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]quinazolin-4(3H)-one (EXAMPLE 266)

Using **General Procedure 7** starting from **Preparation R3b** and 4-oxo-3*H*-quinazoline-6-carboxylic acid as reagents, **EXAMPLE 266** was obtained. HRMS calculated for C₃₄H₃₅N₇O₅: 621.2699; found 622.2775 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[[5-(pyridin-2-yl)thiophen-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 267)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(2-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 267** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.2603 [(M+H)⁺ form].

▪ 7-[[[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]-3,4-dihydroisoquinolin-1(2H)-one (EXAMPLE 268)

Using **General Procedure 7** starting from **Preparation R3b** and 1-oxo-3,4-dihydro-2*H*-isoquinoline-7-carboxylic acid as reagents, **EXAMPLE 268** was obtained. HRMS calculated for C₃₅H₃₈N₆O₅: 622.2903; found 623.2977 [(M+H)⁺ form].

▪ 3-[[1-[(3R,4R)-1-[(3-fluoro-5-iodothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 269)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1g** as reagents, **EXAMPLE 269** was obtained. HRMS calculated for C₃₀H₃₁N₅O₄FSI: 703.1125; found 704.1203 [(M+H)⁺ form].

▪ 3-[[1-[(3R,4R)-1-[[4-chloro-2-(2-oxopyridin-1(2H)-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 270)

Using **General Procedure 7** starting from **Preparation R3b** and 4-chloro-2-(2-oxo-1-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 270** was obtained. HRMS calculated for $C_{34}H_{34}ClN_7O_5S$: 687.2031; found 688.2081 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[4-methyl-2-(pyridin-2-yl)methyl]-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 271)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-methyl-2-(2-pyridylmethyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 271** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 666.2862 $[(M+H)^+ \text{ form}]$.

10 ▪ **5-[[[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl]carbonyl]-1H-indole-2,3-dione (EXAMPLE 272)**

Using **General Procedure 7** starting from **Preparation R3b** and 2,3-dioxoindoline-5-carboxylic acid as reagents, **EXAMPLE 272** was obtained. HRMS calculated for $C_{34}H_{34}N_6O_6$: 622.2539; found 623.2633 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[3-(hydroxymethyl)benzoyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 273)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-(hydroxymethyl)benzoic acid as reagents, **EXAMPLE 273** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_5$: 583.2795; found 584.2875 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(2-hydroxybenzoyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 274)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 2-hydroxybenzoic acid as reagents, **EXAMPLE 274** was obtained. HRMS calculated for $C_{32}H_{35}N_5O_5$: 569.2638; found 570.2727 $[(M+H)^+ \text{ form}]$.

▪ **3-[(1-[(3R,4R)-1-{[5-chloro-4-(dimethylamino)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 275)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-chloro-4-(dimethylamino)thiophene-2-carboxylic acid as reagents, **EXAMPLE 275** was obtained. HRMS calculated for $C_{32}H_{37}ClN_6O_4S$: 636.2286; found 637.2358 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-[(5-bromo-4-methoxythiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 276)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methoxythiophene-2-carboxylic acid as reagents, **EXAMPLE 276** was obtained. HRMS calculated for $C_{31}H_{34}BrN_5O_5S$: 667.1464; found 668.153 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-[(4,5-dibromothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 277)**

Using **General Procedure 7** starting from **Preparation R3b** and 4,5-dibromothiophene-2-carboxylic acid as reagents, **EXAMPLE 277** was obtained. HRMS calculated for $C_{30}H_{31}Br_2N_5O_4S$: 715.0463; found 716.053 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(3-oxo-2,3-dihydro-1H-inden-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 278)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-oxoindane-5-carboxylic acid as reagents, **EXAMPLE 278** was obtained. HRMS calculated for $C_{35}H_{37}N_5O_5$: 607.2795; found 608.2871 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 279)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-oxoisindoline-5-carboxylic acid as reagents, **EXAMPLE 279** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_5$: 608.2747; found 609.2814 $[(M+H)^+]$ form].

5 ■ 3-[(1-[(3R,4R)-1-{[4-chloro-2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 280**)

Using **General Procedure 7** starting from **Preparation R3b** and 4-chloro-2-(6-methoxy-3-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 280** was obtained. HRMS calculated for $C_{35}H_{36}N_7O_5S$: 701.2187; found 702.2257 $[(M+H)^+]$ form].

10 ■ methyl 5-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]pyridine-3-carboxylate (**EXAMPLE 281**)

Using **General Procedure 7** starting from **Preparation R3b** and 5-methoxycarbonylpyridine-3-carboxylic acid as reagents, **EXAMPLE 281** was obtained.
15 HRMS calculated for $C_{33}H_{36}N_6O_6$: 612.2697; found 613.2776 $[(M+H)^+]$ form].

■ 3-{[4-hydroxy-1-((3R,4R)-1-[3-(2-hydroxyethyl)benzoyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 282**)

Using **General Procedure 7** starting from **Preparation R3b** and
20 3-(2-hydroxyethyl)benzoic acid as reagents, **EXAMPLE 282** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_5$: 597.2951; found 598.3031 $[(M+H)^+]$ form].

■ 3-{[4-hydroxy-1-((3R,4R)-1-[3-(methylsulfanyl)benzoyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 283**)

25 Using **General Procedure 7** starting from **Preparation R3b** and 3-methylsulfanylbenzoic acid as reagents, **EXAMPLE 283** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_4S$: 599.2567; found 600.2656 $[(M+H)^+]$ form].

▪ **4-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}pyridine-2-carbonitrile (EXAMPLE 284)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-cyanopyridine-4-carboxylic acid as reagents, **EXAMPLE 284** was obtained. HRMS calculated for $C_{32}H_{33}N_7O_4$: 579.2594; found 580.2682 $[(M+H)^+]$ form].

▪ **methyl 3-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-5-nitrobenzoate (EXAMPLE 285)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-methoxycarbonyl-5-nitro-benzoic acid as reagents, **EXAMPLE 285** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_8$: 656.2595; found 657.2679 $[(M+H)^+]$ form].

▪ **dimethyl 5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzene-1,3-dicarboxylate (EXAMPLE 286)**

Using **General Procedure 7** starting from **Preparation R3b** and 3,5-bis(methoxycarbonyl)benzoic acid as reagents, **EXAMPLE 286** was obtained. HRMS calculated for $C_{36}H_{39}N_5O_8$: 669.2798; found 670.2847 $[(M+H)^+]$ form].

▪ **methyl 3-bromo-5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 287)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-bromo-5-methoxycarbonyl-benzoic acid as reagents, **EXAMPLE 287** was obtained. HRMS calculated for $C_{34}H_{36}BrN_5O_6$: 689.1849; found 690.1936 $[(M+H)^+]$ form].

▪ **tert-butyl methyl 5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzene-1,3-dicarboxylate (EXAMPLE 288)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-tert-butoxycarbonyl-5-methoxycarbonyl-benzoic acid as reagents, **EXAMPLE 288** was obtained. HRMS calculated for $C_{39}H_{45}N_5O_8$: 711.3268; found 712.3342 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-4-yl)thiophen-2-**

yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 289)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(4-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 289** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2597 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 290)**

Using **General Procedure 7** starting from **Preparation R3ba** and **Preparation R1d** as reagents, **EXAMPLE 290** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S_2$: 747.2662; found 748.2743 $[(M+H)^+ \text{ form}]$.

▪ **7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 291)**

Using **General Procedure 7** starting from **Preparation R3bb** and **Preparation R1d** as reagents, **EXAMPLE 291** was obtained. HRMS calculated for $C_{39}H_{38}ClN_7O_4S_2$: 767.2115; found 768.2171 $[(M+H)^+ \text{ form}]$.

▪ **7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 292)**

Using **General Procedure 7** starting from **Preparation R3bc** and **Preparation R1d** as reagents, **EXAMPLE 292** was obtained. HRMS calculated for $C_{43}H_{43}N_7O_6S$: 785.2996; found 786.307 [(M+H)⁺ form].

5 ▪ 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 293)

Using **General Procedure 7** starting from **Preparation R3bd** and **Preparation R1d** as reagents, **EXAMPLE 293** was obtained. HRMS calculated for $C_{42}H_{41}N_7O_6S$: 771.2839;
10 found 772.2895 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 294)

15 Using **General Procedure 7** starting from **Preparation R3bg** and **Preparation R1d** as reagents, **EXAMPLE 294** was obtained. HRMS calculated for $C_{42}H_{40}F_3N_7O_4S$: 795.2814; found 796.2883 [(M+H)⁺ form].

20 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[3-(hydroxymethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 295)

Using **General Procedure 7** starting from **Preparation R3bi** and **Preparation R1d** as reagents, **EXAMPLE 295** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 758.3124 [(M+H)⁺ form].

25 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[3-(trifluoromethoxy)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one
(EXAMPLE 296)

Using **General Procedure 7** starting from **Preparation R3bp** and **Preparation R1d** as reagents, **EXAMPLE 296** was obtained. HRMS calculated for $C_{42}H_{40}N_7O_5F_3S$: 811.2764; found 812.2837 $[(M+H)^+$ form].

5 ■ 7-[3-(benzyloxy)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 297)

Using **General Procedure 7** starting from **Preparation R3bq** and **Preparation R1d** as reagents, **EXAMPLE 297** was obtained. HRMS calculated for $C_{48}H_{47}N_7O_5S$: 833.3359; found 834.3436 $[(M+H)^+$ form].

10 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(6-methylpyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 298)

Using **General Procedure 7** starting from **Preparation R3br** and **Preparation R1d** as reagents, **EXAMPLE 298** was obtained. HRMS calculated for $C_{41}H_{42}N_8O_4S$: 742.3049; found 743.313 $[(M+H)^+$ form].

15 ■ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(6-methoxypyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 299)

20 Using **General Procedure 7** starting from **Preparation R3bs** and **Preparation R1d** as reagents, **EXAMPLE 299** was obtained. HRMS calculated for $C_{41}H_{42}N_8O_5S$: 758.2998; found 759.3062 $[(M+H)^+$ form].

25 ■ 3-[(1-[(3R,4R)-1-{[4-chloro-2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 300)

Using **General Procedure 7** starting from **Preparation R3bu** and 4-chloro-2-(6-methoxy-3-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 300** was obtained. HRMS calculated for $C_{40}H_{38}N_7O_5SCl$: 763.2344; found 764.242 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-{[(3S,4S)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 301)**

Using **General Procedure 7** starting from 3-[(4-hydroxy-1-{[(3S,4S)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (which was obtained according to **General Procedure 5** with *tert*-butyl (3S,4S)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and **Preparation R2bu**) and **Preparation R1d** as reagents, **EXAMPLE 301** was obtained. HRMS calculated for C₄₁H₄₁N₇O₄S: 727.2941; found 364.6536 [(M+2H)²⁺ form].

▪ **3-{[1-({(3R,4R)-1-[(2-bromopyridin-4-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 302)**

Using **General Procedure 7** starting from **Preparation R3bu** and 2-bromopyridine-4-carboxylic acid as reagents, **EXAMPLE 302** was obtained. HRMS calculated for C₃₆H₃₅N₆O₄Br: 694.1903; found 695.1969 [(M+H)⁺ form].

▪ **3-{[1-({(3R,4R)-1-[(5-bromopyridin-3-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 303)**

Using **General Procedure 7** starting from **Preparation R3bu** and 5-bromopyridine-3-carboxylic acid as reagents, **EXAMPLE 303** was obtained. HRMS calculated for C₃₆H₃₅N₆O₄Br: 694.1903; found 695.1974 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{(3R,4R)-3-phenyl-1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 304)**

Using **General Procedure 7** starting from **Preparation R3bu** and thiazole-5-carboxylic acid as reagents, **EXAMPLE 304** was obtained. HRMS calculated for C₃₄H₃₄N₆O₄S: 622.2362; found 623.2429 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 305)**

Using **General Procedure 7** starting from **Preparation R3bu** and thiazole-4-carboxylic acid as reagents, **EXAMPLE 305** was obtained. HRMS calculated for $C_{34}H_{34}N_6O_4S$: 622.2362; found 623.2434 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(morpholin-4-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 306)**

Using **General Procedure 7** starting from **Preparation R3bu** and 4-methyl-2-morpholino-thiazole-5-carboxylic acid as reagents, **EXAMPLE 306** was obtained. HRMS calculated for $C_{39}H_{43}N_7O_5S$: 721.3046; found 722.311 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-(4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 307)**

Using **General Procedure 7** starting from **Preparation R3bu** and 4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 307** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2595 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-1-(2-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 308)**

Using **General Procedure 7** starting from **Preparation R3bu** and 2-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 308** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2582 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-(2-chloro-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 309)**

Using **General Procedure 7** starting from **Preparation R3bu** and 2-chlorothiazole-5-carboxylic acid as reagents, **EXAMPLE 309** was obtained. HRMS calculated for $C_{34}H_{33}ClN_6O_4S$: 656.1973; found 657.2041 $[(M+H)^+]$ form].

5 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(1-methyl-1H-indol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 310)**

Using **General Procedure 7** starting from **Preparation R3bu** and 1-methylindole-2-carboxylic acid as reagents, **EXAMPLE 310** was obtained. HRMS calculated for $C_{40}H_{40}N_6O_4$: 668.3111; found 669.3183 $[(M+H)^+]$ form].

10 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(1-methyl-5-phenyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 311)**

Using **General Procedure 7** starting from **Preparation R3bu** and 1-methyl-5-phenylpyrrole-2-carboxylic acid as reagents, **EXAMPLE 311** was obtained. HRMS calculated for $C_{42}H_{42}N_6O_4$: 694.3268; found 695.3331 $[(M+H)^+]$ form].

15 ▪ **methyl 3-{[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 312)**

Using **General Procedure 7** starting from **Preparation R3bu** and 3-methoxycarbonylbenzoic acid as reagents, **EXAMPLE 312** was obtained. HRMS calculated for $C_{39}H_{39}N_5O_6$: 673.2900; found 674.2969 $[(M+H)^+]$ form].

20 ▪ **methyl 5-{[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}pyridine-3-carboxylate (EXAMPLE 313)**

25 Using **General Procedure 7** starting from **Preparation R3bu** and 5-methoxycarbonylpyridine-3-carboxylic acid as reagents, **EXAMPLE 313** was obtained. HRMS calculated for $C_{38}H_{38}N_6O_6$: 674.2853; found 675.291 $[(M+H)^+]$ form].

▪ **methyl 4-[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]pyridine-2-carboxylate (EXAMPLE 314)**

Using **General Procedure 7** starting from **Preparation R3bu** and
5 2-methoxycarbonylpyridine-4-carboxylic acid as reagents, **EXAMPLE 314** was obtained. HRMS calculated for $C_{38}H_{38}N_6O_6$: 674.2853; found 675.2914 [(M+H)⁺ form].

▪ **7-ethyl-3-{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-2-phenyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl]methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 315)**

10 Using **General Procedure 7** starting from **Preparation R3c** and 4-methyl-2-phenylthiazole-5-carboxylic acid as reagents, **EXAMPLE 315** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4S$: 664.2832; found 665.2903 [(M+H)⁺ form].

▪ **7-ethyl-3-{[4-hydroxy-1-((3R,4R)-1-[(3-methyl-1,2-thiazol-4-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl]methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 316)**

15 Using **General Procedure 7** starting from **Preparation R3c** and 3-methylisothiazole-4-carboxylic acid as reagents, **EXAMPLE 316** was obtained. HRMS calculated for $C_{31}H_{36}N_6O_4S$: 588.2519; found 589.2601 [(M+H)⁺ form].

▪ **7-ethyl-3-{[4-hydroxy-1-((3R,4R)-3-phenyl-1-[(2-phenyl-1,3-thiazol-5-yl)carbonyl]piperidin-4-yl]carbonyl)piperidin-4-yl]methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 317)**

20 Using **General Procedure 7** starting from **Preparation R3c** and 2-phenylthiazole-5-carboxylic acid as reagents, **EXAMPLE 317** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2749 [(M+H)⁺ form].

25 ▪ **7-ethyl-3-{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl]methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 318)**

Using **General Procedure 7** starting from **Preparation R3c** and 4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 318** was obtained. HRMS calculated for $C_{31}H_{36}N_6O_4S$: 588.2519; found 589.259 [(M+H)⁺ form].

5 ■ **3-{[1-((3R,4R)-1-[(2-benzyl-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-ethyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 319)**

Using **General Procedure 7** starting from **Preparation R3c** and 2-benzyl-4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 319** was obtained. HRMS calculated for $C_{38}H_{42}N_6O_4S$: 678.2988; found 679.3065 [(M+H)⁺ form].

10 ■ **7-ethyl-3-[(4-hydroxy-1-((3R,4R)-1-(2-methylbenzoyl)-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 320)**

Using **General Procedure 6** starting from **Preparation R3c** and 2-methylbenzoic acid as reagents, **EXAMPLE 320** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_4$: 581.3002; found
15 582.3088 [(M+H)⁺ form].

■ **7-ethyl-3-[(4-hydroxy-1-((3R,4R)-1-(3-methylbenzoyl)-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 321)**

Using **General Procedure 7** starting from **Preparation R3c** and 3-methylbenzoic acid as
20 reagents, **EXAMPLE 321** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_4$: 581.3002; found 582.3075 [(M+H)⁺ form].

■ **7-ethyl-3-[(4-hydroxy-1-((3R,4R)-1-(4-methylbenzoyl)-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 322)**

25 Using **General Procedure 7** starting from **Preparation R3c** and 4-methylbenzoic acid as reagents, **EXAMPLE 322** was obtained. HRMS calculated for $C_{34}H_{39}N_5O_4$: 581.3002; found 582.3073 [(M+H)⁺ form].

▪ 7-ethyl-3-[(1-{[(3R,4R)-1-(2-fluorobenzoyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 323)

Using **General Procedure 7** starting from **Preparation R3c** and 2-fluorobenzoic acid as reagents, **EXAMPLE 323** was obtained. HRMS calculated for $C_{33}H_{36}FN_5O_4$: 585.2751; found 586.282 [(M+H)⁺ form].

▪ 7-ethyl-3-[(1-{[(3R,4R)-1-(3-fluorobenzoyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 324)

Using **General Procedure 7** starting from **Preparation R3c** and 3-fluorobenzoic acid as reagents, **EXAMPLE 324** was obtained. HRMS calculated for $C_{33}H_{36}FN_5O_4$: 585.2751; found 586.2827 [(M+H)⁺ form].

▪ 7-ethyl-3-[(1-{[(3R,4R)-1-(4-fluorobenzoyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 325)

Using **General Procedure 7** starting from **Preparation R3c** and 4-fluorobenzoic acid as reagents, **EXAMPLE 325** was obtained. HRMS calculated for $C_{33}H_{36}FN_5O_4$: 585.2751; found 586.2846 [(M+H)⁺ form].

▪ 7-ethyl-3-[(1-{[(3R,4R)-1-{[2-(2-fluorobenzyl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 326)

Using **General Procedure 7** starting from **Preparation R3c** and 2-[(2-fluorophenyl)methyl]thiazole-5-carboxylic acid as reagents, **EXAMPLE 326** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_4S$: 682.2738; found 683.2804 [(M+H)⁺ form].

▪ 7-ethyl-3-[(4-hydroxy-1-{[(3R,4R)-1-{[4-methyl-2-(2-methylphenyl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 327)

Using **General Procedure 7** starting from **Preparation R3c** and 4-methyl-2-(o-tolyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 327** was obtained. HRMS calculated for $C_{38}H_{42}N_6O_4S$: 678.2988; found 679.3069 $[(M+H)^+]$ form].

5 ▪ **7-ethyl-3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-4-yl)thiophen-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 328)**

Using **General Procedure 7** starting from **Preparation R3c** and 5-(4-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 328** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2755 $[(M+H)^+]$ form].

10 ▪ **7-ethyl-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(pyridin-4-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 329)**

Using **General Procedure 7** starting from **Preparation R3c** and 4-methyl-2-(4-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 329** was obtained. HRMS
15 calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 666.2855 $[(M+H)^+]$ form].

▪ **7-ethyl-3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyridin-4-yl)-1,3-thiazol-5-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 330)**

Using **General Procedure 7** starting from **Preparation R3c** and 2-(4-pyridyl)thiazole-5-
20 carboxylic acid as reagents, **EXAMPLE 330** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.269 $[(M+H)^+]$ form].

▪ **7-ethyl-3-[(1-[(3R,4R)-1-[2-(2-fluorophenyl)-4-methyl-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 331)**

25 Using **General Procedure 7** starting from **Preparation R3c** and 2-(2-fluorophenyl)-4-methyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 331** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_4S$: 682.2738; found 683.2823 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(pyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 332)

Using **General Procedure 7** starting from **Preparation R3ca** and **Preparation R1d** as reagents, **EXAMPLE 332** was obtained. HRMS calculated for C₄₀H₄₀N₈O₄S: 728.2893; found 729.2970 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-1H-imidazol-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 333)

Using **General Procedure 7** starting from **Preparation R3cg** and **Preparation R1d** as reagents, **EXAMPLE 333** was obtained. HRMS calculated for C₃₉H₄₁N₉O₄S: 731.3002; found 732.3086 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-1H-pyrazol-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 334)

Using **General Procedure 7** starting from **Preparation R3ch** and **Preparation R1d** as reagents, **EXAMPLE 334** was obtained. HRMS calculated for C₃₉H₄₁N₉O₄S: 731.3002; found 732.3083 [(M+H)⁺ form].

▪ 7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 335)

Using **General Procedure 7** starting from **Preparation R3ci** and **Preparation R1d** as reagents, **EXAMPLE 335** was obtained. HRMS calculated for C₃₉H₃₉F₂N₉O₄S: 767.2814; found 768.2908 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(pyrimidin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 336)

Using **General Procedure 7** starting from **Preparation R3cj** and **Preparation R1d** as reagents, **EXAMPLE 336** was obtained. HRMS calculated for $C_{39}H_{39}N_9O_4S$: 729.2845; found 730.2922 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1,3-thiazol-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 337)**

Using **General Procedure 7** starting from **Preparation R3ck** and **Preparation R1d** as reagents, **EXAMPLE 337** was obtained. HRMS calculated for $C_{38}H_{38}N_8O_4S_2$: 734.2457; found 735.2523 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methylpiperidin-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 338)**

Using **General Procedure 7** starting from **Preparation R3k** and **Preparation R1d** as reagents, **EXAMPLE 338** was obtained. HRMS calculated for $C_{41}H_{48}N_8O_4S$: 748.3519; found 375.1823 $[(M+2H)^{2+} \text{ form}]$.

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(prop-2-yn-1-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 339)**

Using **General Procedure 7** starting from **Preparation R3m** and **Preparation R1d** as reagents, **EXAMPLE 339** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_4S$: 689.2784; found 690.2847 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-{[1-[(3R,4R)-1-[(3-fluoro-5-iodothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-(2,2,2-trifluoroethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 340)**

25 Using **General Procedure 7** starting from **Preparation R3o** and **Preparation R1g** as reagents, **EXAMPLE 340** was obtained. HRMS calculated for $C_{31}H_{30}F_4IN_5O_4S$: 771.0999; found 772.1074 $[(M+H)^+ \text{ form}]$.

▪ 7-(buta-2,3-dien-1-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 341)

Using **General Procedure 7** starting from **Preparation R3s** and **Preparation R1d** as reagents, **EXAMPLE 341** was obtained. HRMS calculated for $C_{39}H_{41}N_7O_4S$: 703.2941; found 704.3008 [(M+H)⁺ form].

▪ 3-{[1-[(3R,4R)-1-[(5-bromothiophen-2-yl)sulfonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 342)

Using **General Procedure 8** starting from **Preparation R3b** and 5-bromothiophene-2-sulfonyl chloride as reagents, **EXAMPLE 342** was obtained. HRMS calculated for $C_{29}H_{32}BrN_5O_5S_2$: 673.1028; found 674.1114 [(M+H)⁺ form].

▪ 3-{[1-[(3R,4R)-1-[(3-bromophenyl)sulfonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 343)

Using **General Procedure 8** starting from **Preparation R3b** and 3-bromobenzenesulfonyl chloride as reagents, **EXAMPLE 343** was obtained. HRMS calculated for $C_{31}H_{34}BrN_5O_5S$: 667.1464; found 668.153 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(phenylsulfonyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 344)

Using **General Procedure 8** starting from **Preparation R3bu** and benzenesulfonyl chloride as reagents, **EXAMPLE 344** was obtained. HRMS calculated for $C_{36}H_{37}N_5O_5S$: 651.2515; found 652.2577 [(M+H)⁺ form].

▪ 7-(3,4-dichlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 345)

Using **General Procedure 6** starting from **Preparation R3ag** and **Preparation R1c** as reagents, **EXAMPLE 345** was obtained. HRMS calculated for $C_{40}H_{39}Cl_2N_7O_3S$: 767.2212; found 768.2266 $[(M+H)^+$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 346)**

Using **General Procedure 6** starting from **Preparation R3am** and **Preparation R1c** as reagents, **EXAMPLE 346** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_3S$: 713.3148; found 714.3224 $[(M+H)^+$ form].

10 ▪ **7-(4-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 347)**

Using **General Procedure 7** starting from **Preparation R3ar** and **Preparation R1d** as reagents, **EXAMPLE 347** was obtained. HRMS calculated for $C_{41}H_{40}N_7O_4SCl$: 761.2551; found 762.2622 $[(M+H)^+$ form].

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 348)**

Using **General Procedure 7** starting from **Preparation R3ax** and **Preparation R1d** as reagents, **EXAMPLE 348** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 758.3117 $[(M+H)^+$ form].

20 ▪ **3-{[1-[(3R,4R)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 349)**

25 Using **General Procedure 7** starting from **Preparation R3b** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 349** was obtained. HRMS calculated for $C_{30}H_{33}BrN_6O_4S$: 652.1467; found 653.1548 $[(M+H)^+$ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-2-phenyl-1,3-thiazol-5-yl)sulfonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 350)

Using **General Procedure 8** starting from **Preparation R3b** and 2-bromo-4-methyl-1,3-thiazole-5-sulfonyl chloride acid as reagents, the resulted crude bromo-compound was reacted with phenylboronic acid according to **General procedure 9**, to give **EXAMPLE 350**. HRMS calculated for $C_{35}H_{38}N_6O_5S_2$: 686.2345; found 687.2389 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-[(4-methyl-2-(pyridin-4-yl)-1,3-thiazol-5-yl)sulfonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 351)

Using **General Procedure 8** starting from **Preparation R3b** and 2-bromo-4-methyl-1,3-thiazole-5-sulfonyl chloride acid as reagents, the resulted crude bromo-compound was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 351**. HRMS calculated for $C_{34}H_{37}N_7O_5S_2$: 687.2298; found 344.6232 [(M+2H)²⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-[(4-methyl-2-(pyrimidin-5-yl)-1,3-thiazol-5-yl)sulfonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 352)

Using **General Procedure 8** starting from **Preparation R3b** and 2-bromo-4-methyl-1,3-thiazole-5-sulfonyl chloride acid as reagents, the resulted crude bromo-compound was reacted with pyrimidin-5-ylboronic acid according to **General Procedure 9**, to give **EXAMPLE 352**. HRMS calculated for $C_{33}H_{36}N_8O_5S_2$: 688.2250; found 689.2304 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-[(4-methyl-2-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-5-yl)sulfonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 353)

Using **General Procedure 8** starting from **Preparation R3b** and 2-bromo-4-methyl-1,3-thiazole-5-sulfonyl chloride acid as reagents, the resulted crude bromo-compound was

reacted with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 353**. HRMS calculated for $C_{33}H_{38}N_8O_5S_2$: 690.2407; found 691.2481 [(M+H)⁺ form].

5 ▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyrimidin-5-yl)-1,3-thiazol-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 354**)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with pyrimidin-5-ylboronic acid according to **General Procedure 9**, to give **EXAMPLE 354**.
10 HRMS calculated for $C_{33}H_{34}N_8O_4S$: 638.2424; found 639.25 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-3-yl)-1,3-thiazol-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 355**)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 355**. HRMS
15 calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.254 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-4-yl)-1,3-thiazol-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 356**)
20

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 356**. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.252
25 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 357**)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 357**. HRMS calculated for $C_{33}H_{36}N_8O_4S$: 640.2580; found 641.268 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-3-yl)thiophen-2-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 358)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude bromo-compound was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 358**. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2807 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-4-yl)thiophen-2-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 359)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude bromo-compound was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 359**. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2807 [(M+H)⁺ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(5-phenylthiophen-2-yl)methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 360)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude bromo-compound was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 360**. HRMS calculated for $C_{36}H_{39}N_5O_3S$: 621.2773; found 622.2859 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(1-methyl-1H-pyrazol-5-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 361)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude bromo-compound was reacted with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 361**. HRMS calculated for $C_{34}H_{36}N_7O_3S$: 625.2835; found 626.2919 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(5-phenyl-1,3-thiazol-2-yl)carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 362)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 362**. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2592 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[[5-(pyrimidin-5-yl)thiophen-2-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 363)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude bromo-compound was reacted with pyrimidin-5-ylboronic acid according to **General Procedure 9**, to give **EXAMPLE 363**. HRMS calculated for $C_{34}H_{37}N_7O_3S$: 623.2679; found 624.2761 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[[4-methyl-5-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 364)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to

General Procedure 9, to give **EXAMPLE 364**. HRMS calculated for $C_{34}H_{38}N_8O_4S$: 654.2737; found 655.2814 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 365)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo-compound was reacted with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 365**. HRMS calculated for $C_{33}H_{38}N_8O_3S$: 626.2787; found 627.2871 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(4-methyl-5-phenyl-1,3-thiazol-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 366)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 366**. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2756 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(2-phenyl-1,3-thiazol-5-yl)methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 367)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo-compound was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 367**. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2794 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-5-(pyridin-4-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 368)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methyl-thiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 368**. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.2727 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyridin-4-yl)-1,3-thiazol-5-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 369**)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo-compound was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 369**. HRMS calculated for $C_{34}H_{37}N_7O_3S$: 623.2679; found 624.274 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-5-(pyrimidin-5-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 370**)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methyl-thiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with pyrimidin-5-ylboronic acid according to **General Procedure 9**, to give **EXAMPLE 370**. HRMS calculated for $C_{34}H_{36}N_8O_4S$: 652.2580; found 653.2632 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyrimidin-5-yl)-1,3-thiazol-5-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 371**)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo-compound was reacted with pyrimidin-5-ylboronic acid according to **General Procedure 9**, to give **EXAMPLE 371**. HRMS calculated for $C_{33}H_{36}N_8O_3S$: 624.2631; found 625.2706 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[[4-methyl-5-(pyridin-3-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 372)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiazole-2-carboxylic acid as reagents, the resulted crude bromo-compound was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 372**. HRMS calculated for C₃₅H₃₇N₇O₄S: 651.2628; found 652.2723 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[[2-(pyridin-3-yl)-1,3-thiazol-5-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 373)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo-compound was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 373**. HRMS calculated for C₃₄H₃₇N₇O₃S: 623.2679; found 624.2747 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-[[5-chloro-3-fluoro-4-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 374)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1k** as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 374**. HRMS calculated for C₃₆H₃₆ClFN₆O₄S: 702.2191; found 703.2273 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-[[3-fluoro-5-methyl-4-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 375)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1i** as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give

EXAMPLE 375. HRMS calculated for $C_{37}H_{39}FN_6O_4S$: 682.2737; found 683.28 [(M+H)⁺ form].

5 ▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-3-yl)-1,3-thiazol-2-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 376**)

Using **General Procedure 6** starting from **Preparation R3b** and 5-bromo-2-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 376**. HRMS calculated for $C_{34}H_{37}N_7O_3S$: 623.2679; found 624.2737 [(M+H)⁺ form].

10 ▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyrimidin-5-yl)-1,3-thiazol-2-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 377**)

Using **General Procedure 6** starting from **Preparation R3b** and 5-bromo-2-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with pyrimidin-15 5-ylboronic acid according to **General Procedure 9**, to give **EXAMPLE 377**. HRMS calculated for $C_{33}H_{36}N_8O_3S$: 624.2631; found 625.2697 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-4-yl)-1,3-thiazol-2-yl]methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 378**)

20 Using **General Procedure 6** starting from **Preparation R3b** and 5-bromo-2-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 378**. HRMS calculated for $C_{34}H_{37}N_7O_3S$: 623.2679; found 624.274 [(M+H)⁺ form].

25 ▪ 3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(5-phenyl-1,3-thiazol-2-yl)methyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 379**)

Using **General Procedure 6** starting from **Preparation R3b** and 5-bromo-2-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 379**. HRMS calculated for $C_{35}H_{38}N_6O_3S$: 622.2726; found 623.2816 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 380)**

Using **General Procedure 6** starting from **Preparation R3b** and 5-bromo-2-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure**
10 **9**, to give **EXAMPLE 380**. HRMS calculated for $C_{33}H_{38}N_8O_3S$: 626.2787; found 627.2861 $[(M+H)^+]$ form].

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(2-methylpyridin-4-yl)-1,3-thiazol-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 381)**

Using **General Procedure 6** starting from **Preparation R3b** and 5-bromo-2-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General**
20 **Procedure 9**, to give **EXAMPLE 381**. HRMS calculated for $C_{35}H_{39}N_7O_3S$: 637.2835; found 638.2912 $[(M+H)^+]$ form].

25 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[2-(2-methoxy-6-methylpyridin-4-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 382)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with 2-methoxy-6-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General**
25 **Procedure 9**, to give **EXAMPLE 382**. HRMS calculated for $C_{36}H_{41}N_7O_4S$: 667.2940; found 668.3009 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[3-methyl-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 383)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with
5 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 383**. HRMS calculated for $C_{37}H_{40}N_6O_4S$: 664.2832; found 665.291 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methoxypyridin-4-yl)-3-methylthiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 384)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with
10 (2-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 384**. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found 681.2864 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(3-methoxypyridin-4-yl)-3-methylthiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 385)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with
20 (3-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 385**. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found 681.286 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[3-methyl-5-(pyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 386)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with

3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 386**. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2762 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methylpyridin-4-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 387)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 387**. HRMS calculated for $C_{36}H_{40}N_6O_3S$: 636.2883; found 637.2976 $[(M+H)^+]$ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methoxypyridin-4-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 388)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with (2-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 388**. HRMS calculated for $C_{36}H_{40}N_6O_4S$: 652.2832; found 327.1501 $[(M+2H)^{2+}]$ form].

15 ▪ **3-[(1-[(3R,4R)-1-(2,3'-bithiophen-5-ylmethyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 389)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 389**. HRMS calculated for $C_{34}H_{37}N_5O_3S_2$: 627.2338; found 628.2426 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methylpyridin-3-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 390)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 390**. HRMS calculated for C₃₆H₄₀N₆O₃S: 636.2883; found 637.2964 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(3-methoxypyridin-4-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 391)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with (3-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 391**. HRMS calculated for C₃₆H₄₀N₆O₄S: 652.2832; found 653.2935 [(M+H)⁺ form].

▪ **tert-butyl [4-(5-[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl]methyl]thiophen-2-yl)pyridin-2-yl]carbamate (EXAMPLE 392)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with tert-butyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate according to **General Procedure 9**, to give **EXAMPLE 392**. HRMS calculated for C₄₀H₄₇N₇O₅S: 737.3359; found 738.3434 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[5-(6-aminopyridin-3-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 393)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted 5-(4,4,5,5-

tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine according to **General Procedure 9**, to give **EXAMPLE 393**. HRMS calculated for $C_{35}H_{39}N_7O_3S$: 637.2835; found 638.2918 [(M+H)⁺ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methoxy-6-methylpyridin-4-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 394)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted 2-methoxy-6-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General**
10 **Procedure 9**, to give **EXAMPLE 394**. HRMS calculated for $C_{37}H_{42}N_6O_4S$: 666.2988; found 667.3071 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methoxypyridin-3-yl)thiophen-2-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 395)**

15 Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 395**. HRMS calculated for $C_{36}H_{40}N_6O_4S$: 652.2832; found 653.2910 [(M+H)⁺ form].

20 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(4-methyl-2,3'-bithiophen-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 396)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**,
25 to give to give **EXAMPLE 396**. HRMS calculated for $C_{35}H_{37}N_5O_4S_2$: 655.2287; found 656.2362 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-((3R,4R)-1-[(3-methyl-5-phenylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 397)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 397**. HRMS calculated for C₃₇H₃₉N₅O₄S: 649.2723; found 650.2806 [(M+H)⁺ form].

▪ tert-butyl [4-(5-{[(3R,4R)-4-((4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-3-methylthiophen-2-yl)pyridin-2-yl]carbamate (EXAMPLE 398)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with tert-butyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate according to **General Procedure 9**, to give **EXAMPLE 398**. HRMS calculated for C₄₁H₄₇N₇O₆S: 765.3309; found 766.3374 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-[[4-methyl-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 399)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 399**. HRMS calculated for C₃₇H₄₀N₆O₄S: 664.2832; found 665.2922 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-((3R,4R)-1-[[5-(6-methoxypyridin-3-yl)-4-methylthiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 400)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, as reagents, to give

EXAMPLE 400. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found 681.2854 $[(M+H)^+$ form].

▪ **3-[(1-[(3R,4R)-1-{5-(6-aminopyridin-3-yl)-4-methylthiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 401)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine according to **General Procedure 9**, to give **EXAMPLE 401**. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 333.6475 $[(M+2H)^{2+}$ form].

▪ **tert-butyl [4-(5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-4-methylthiophen-2-yl)pyridin-2-yl]carbamate (EXAMPLE 402)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with tert-butyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate according to **General Procedure 9**, to give **EXAMPLE 402**. HRMS calculated for $C_{41}H_{47}N_7O_6S$: 765.3309; found 766.3381 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{5-(2-methoxypyridin-4-yl)-1,3-thiazol-2-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 403)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with (2-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 403**. HRMS calculated for $C_{35}H_{37}N_7O_5S$: 667.2577; found 668.2654 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{5-(3-methoxypyridin-4-yl)-1,3-thiazol-2-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 404)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with (3-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 404**. HRMS calculated for $C_{35}H_{37}N_7O_5S$: 667.2577; found 668.2651 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(6-methoxypyridin-3-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 405)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 405**. HRMS
10 calculated for $C_{35}H_{37}N_7O_5S$: 667.2577; found 668.2649 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(6-methylpyridin-3-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 406)**

15 Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 406**. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.2702 $[(M+H)^+]$ form].

20 ▪ **3-{[1-((3R,4R)-1-[(3-fluoro-5-phenylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 407)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1g** as reagents, the resulted crude product was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 407**. HRMS calculated for $C_{36}H_{36}FN_5O_4S$:
25 653.2472; found 654.2545 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-((3-methyl-5-[2-(trifluoromethyl)pyridin-4-yl]thiophen-2-yl)carbonyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 408)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine according to **General Procedure 9**, to give **EXAMPLE 408**. HRMS calculated for $C_{37}H_{37}F_3N_6O_4S$: 718.2549; found 719.2627 $[(M+H)^+$ form].

▪ **3-{{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-5-phenylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 409)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 409**. HRMS calculated for $C_{37}H_{39}N_5O_4S$: 649.2723; found 650.2803 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-{{(3R,4R)-3-phenyl-1-{{[5-(thiophen-3-yl)-1,3-thiazol-2-yl]carbonyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 410)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 410**. HRMS calculated for $C_{33}H_{34}N_6O_4S_2$: 642.2083; found 643.2166 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-{{(3R,4R)-3-phenyl-1-{{[5-[2-(trifluoromethyl)pyridin-4-yl]-1,3-thiazol-2-yl]carbonyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 411)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine according to **General Procedure 9**, to give **EXAMPLE 411**. HRMS calculated for $C_{35}H_{34}N_7O_4F_3S$: 705.2345; found 706.2421 $[(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({4-methyl-5-[2-(trifluoromethyl)pyridin-4-yl]thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 412)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine according to **General Procedure 9**, to give **EXAMPLE 412**. HRMS calculated for $C_{37}H_{37}N_6O_4F_3S$: 718.2549; found 719.2622 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({5-[2-(trifluoromethyl)pyridin-4-yl]thiophen-2-yl}methyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 413)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiophene as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine according to **General Procedure 9**, to give **EXAMPLE 413**. HRMS calculated for $C_{36}H_{37}F_3N_6O_3S$: 690.2600; found 691.2681 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 414)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 414**. HRMS calculated for $C_{35}H_{39}N_7O_3S$: 637.2835; found 638.2893 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 415)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with [2-(trifluoromethyl)-4-pyridyl]boronic acid according to **General Procedure 9**, to give

EXAMPLE 415. HRMS calculated for $C_{35}H_{36}F_3N_7O_3S$: 691.2552; found 692.2610 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(2-methylpyridin-4-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 416)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 416**. HRMS calculated for $C_{35}H_{39}N_7O_3S$: 637.2835; found 638.2889 $[(M+H)^+$ form].

▪ **3-[(1-[(3R,4R)-1-{3-fluoro-4,5-bis(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 417)**

and

▪ **3-[(1-[(3R,4R)-1-{5-chloro-3-fluoro-4-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 418)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1k** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 417** and **EXAMPLE 418** which were separated by chromatography.

EXAMPLE 417: HRMS calculated for $C_{42}H_{42}FN_7O_4S$: 759.3003; found 760.3079 $[(M+H)^+$ form].

EXAMPLE 418: HRMS calculated for $C_{36}H_{36}ClFN_6O_4$ S: 702.2191; found 703.227 $[(M+H)^+$ form].

▪ **3-[(1-[(3R,4R)-1-{3-fluoro-4,5-di(pyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 419)**

and

3-[(1-[(3R,4R)-1-{[5-chloro-3-fluoro-4-(pyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 420)

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1k** as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 419** and **EXAMPLE 420** which were separated by chromatography.

EXAMPLE 419: HRMS calculated for $C_{40}H_{38}FN_7O_4S$: 731.2690; found 732.275 [(M+H)⁺ form].

EXAMPLE 420: HRMS calculated for $C_{35}H_{34}ClFN_6O_4S$: 688.2035; found 689.212 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[4-(pyridin-4-yl)thiophen-2-yl]carbonyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 421)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromothiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 421**. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2608 (M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[4-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 422)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromothiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 422**. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2778 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[4-(pyridin-3-yl)thiophen-2-yl]carbonyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 423)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromothiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 423**. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2606 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[4-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 424)**

Using **General Procedure 7** starting from **Preparation R3b** and 4-bromothiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**,
10 to give **EXAMPLE 424**. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2763 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[7-(6-methylpyridin-3-yl)-2,3-dihydrothieno[3,4-b][1,4]dioxin-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 425)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-2,3-dihydrothieno[3,4-*b*][1,4]dioxine-7-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to
20 give **EXAMPLE 425**. HRMS calculated for $C_{38}H_{40}N_6O_6S$: 708.2730; found 709.2799 $[(M+H)^+ \text{ form}]$.

25 ▪ **5-(5-[(3R,4R)-4-((4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl)-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl)pyridine-2-carbonitrile (EXAMPLE 426)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiazole as reagents, the resulted crude product was reacted with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carbonitrile according to **General Procedure 9**, to give **EXAMPLE 426**. HRMS calculated for $C_{35}H_{36}N_8O_3S$: 648.2631; found 649.2731 $[(M+H)^+ \text{ form}]$.

▪ 3-[(1-[(3R,4R)-1-({2-[6-(cyclopropylmethoxy)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 427)

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiazole as reagents, the resulted crude product was reacted with 2-(cyclopropylmethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 427**. HRMS calculated for $C_{38}H_{43}N_7O_4S$: 693.3098; found 347.6613 [(M+2H)²⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({4-(methoxymethyl)-5-(6-methoxypyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 428)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-(methoxymethyl)thiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 428**. HRMS calculated for $C_{38}H_{42}N_6O_6S$: 710.2886; found 711.2966 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-({5-(6-aminopyridin-3-yl)-4-(methoxymethyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 429)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-(methoxymethyl)thiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine according to **General Procedure 9**, to give **EXAMPLE 429**. HRMS calculated for $C_{37}H_{41}N_7O_5S$: 695.2890; found 696.2961 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({4-(methylamino)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 430)

and

3-[(4-hydroxy-1-[(3R,4R)-1-[4-(methylamino)-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 431)

Using **General Procedure 7** starting from **Preparation R3b** and 5-chloro-3-(methylamino)thiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 430** (dehalogenated byproduct) and **EXAMPLE 431** which were separated by chromatography.

EXAMPLE 430: HRMS calculated for $C_{31}H_{36}N_6O_4S$: 588.2519; found 589.2593 [(M+H)⁺ form].

EXAMPLE 431: HRMS calculated for $C_{37}H_{41}N_7O_4S$: 679.2941; found 680.3015 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 432)**

Using **General Procedure 6** starting from **Preparation R3b** and 2-bromo-5-(chloromethyl)thiazole as reagents, the resulted crude product was reacted with 6-(dimethylamino)-3-pyridyl]boronic acid according to **General Procedure 9**, to give **EXAMPLE 432**. HRMS calculated for $C_{36}H_{42}N_8O_3S$: 666.3101; found 667.3171 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[3-(6-methylpyridin-3-yl)-4,5,6,7-tetrahydro-2-benzothiophen-1-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 433)**

Using **General Procedure 7** starting from **Preparation R3b** and 3-iodo-4,5,6,7-tetrahydro-2-benzothiophene-1-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 433**. HRMS calculated for $C_{40}H_{44}N_6O_4S$: 704.3145; found 705.3219 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[4-amino-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 434)**

4-Amino-5-bromo-2-thiophenecarboxylic acid (500 mg, 2.25 mmol) was dissolved in PDO (2 ml) and water (2 ml) then sodium-hydroxide (194 mg, 4.86 mmol) was added to the stirred mixture at 0 °C, then Boc₂O (1768 mg, 8.1 mmol) was added. The reaction mixture was stirred for 116 hours while the reaction mixture warmed up to r.t. Aqueous HCl solution (1 N, 4 ml) was added to the mixture, the precipitate was filtered off, washed with water and dried.

The resulted 4-(*tert*-butoxycarbonylamino)-5-methyl-thiophene-2-carboxylic acid (316 mg, 0.93 mmol) and **Preparation R3b** (488 mg, 0.93 mmol, as bis HCl salt) were coupled using **General Procedure 7**.

The resulted product (320 mg, 0.42 mmol) was stirred in PDO (3 ml) and aqueous HCl solution (12.2 M, 103 µl, 1.26 mmol) at 50 °C for 20 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

Using **General Procedure 9** starting from the resulted amino-compound and 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 434** was obtained. HRMS calculated for C₃₆H₃₉N₇O₄S: 665.2784; found 333.648 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(naphthalen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 435)**

Using **General Procedure 7** starting from **Preparation R3be** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 435**. HRMS calculated for C₄₅H₄₃N₇O₄S: 777.3098; found 778.3185 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 436)**

Using **General Procedure 6** starting from **Preparation R3bf** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 436**. HRMS calculated for $C_{41}H_{43}N_7O_3S$: 713.3148; found 714.3205 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(naphthalen-1-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 437)**

Using **General Procedure 7** starting from **Preparation R3bt** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with
10 (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 437**. HRMS calculated for $C_{45}H_{43}N_7O_4S$: 777.3098; found 778.3177 $[(M+H)^+]$ form].

15 ▪ **7-ethyl-3-[(1-[(3R,4R)-1-[3-fluoro-5-(pyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 438)**

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 438**. HRMS calculated for $C_{36}H_{37}FN_6O_4S$: 668.2581; found 669.2654 $[(M+H)^+]$ form].

20 ▪ **7-ethyl-3-[(1-[(3R,4R)-1-[3-fluoro-5-(pyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 439)**

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 439**.
25 HRMS calculated for $C_{36}H_{37}FN_6O_4S$: 668.2581; found 669.2661 $[(M+H)^+]$ form].

▪ 7-ethyl-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 440)

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 440**. HRMS calculated for C₃₇H₃₉FN₆O₄S: 682.2737; found 683.2819 [(M+H)⁺ form].

▪ 7-ethyl-3-{[1-[(3R,4R)-1-[(4-fluoro-2,3'-bithiophen-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 441)

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 441**. HRMS calculated for C₃₅H₃₆FN₅O₄S₂: 673.2193; found 674.2272 [(M+H)⁺ form].

▪ 7-ethyl-3-{[1-[(3R,4R)-1-[(3-fluoro-5-phenylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 442)

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 442**. HRMS calculated for C₃₇H₃₈FN₅O₄S: 667.2629; found 668.2702 [(M+H)⁺ form].

▪ 7-ethyl-3-[(1-[(3R,4R)-1-[(3-fluoro-5-[2-(trifluoromethyl)pyridin-4-yl]thiophen-2-yl]carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 443)

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine according to **General Procedure 9**, to give

EXAMPLE 443. HRMS calculated for $C_{37}H_{36}F_4N_6O_4S$: 736.2455; found 737.2524 ($M+H$)⁺ form].

▪ **7-ethyl-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(2-methoxy-6-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 444)**

Using **General Procedure 7** starting from **Preparation R3c** and **Preparation R1g** as reagents, the resulted crude product was reacted with 2-methoxy-6-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 444**. HRMS calculated for $C_{38}H_{41}FN_6O_5S$: 712.2843; found 713.2916 ($M+H$)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(pyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 445)**

Using **General Procedure 6** starting from **Preparation R3ca** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 445**. HRMS calculated for $C_{39}H_{40}N_8O_3S$: 700.2944; found 701.2986 [$(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(pyridin-3-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 446)**

Using **General Procedure 7** starting from **Preparation R3cb** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 446**. HRMS calculated for $C_{40}H_{40}N_8O_4S$: 728.2893; found 729.2968 [$(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(pyridin-3-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 447)**

Using **General Procedure 6** starting from **Preparation R3cb** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 447**. HRMS calculated for $C_{39}H_{40}N_8O_3S$: 700.2944; found 701.2985 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 448)**

Using **General Procedure 7** starting from **Preparation R3cf** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with
10 (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 448**. HRMS calculated for $C_{39}H_{39}N_7O_4S_2$: 733.2505; found 734.2596 $[(M+H)^+]$ form].

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 449)**

Using **General Procedure 6** starting from **Preparation R3cf** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 449**. HRMS calculated for $C_{38}H_{39}N_7O_3S_2$: 705.2556; found 706.2666 $[(M+H)^+]$ form].

20 ▪ **3-[(1-[(3R,4R)-1-[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(propan-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 450)**

Using **General Procedure 7** starting from **Preparation R3d** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid
25 according to **General Procedure 9**, to give **EXAMPLE 450**. HRMS calculated for $C_{38}H_{41}FN_6O_4S$: 696.2894; found 697.2968 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(propan-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 451)

Using **General Procedure 6** starting from **Preparation R3d** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 451**. HRMS calculated for $C_{37}H_{43}N_7O_3S$: 665.3148; found 333.6636 $[(M+2H)^{2+}$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(propan-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 452)

Using **General Procedure 7** starting from **Preparation R3d** and 2-bromo-4-methylthiazole-5-carboxylic acid as reactants, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 452**. HRMS calculated for $C_{38}H_{43}N_7O_4S$: 693.3098; found 694.3173 $[(M+H)^+$ form].

▪ 7-cyclopropyl-3-[1-[(3R,4R)-1-[(3-fluoro-5-phenylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 453)

Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with phenylboronic acid according to **General Procedure 9**, to give **EXAMPLE 453**. HRMS calculated for $C_{38}H_{38}FN_5O_4$ S: 679.2629; found 680.2696 $[(M+H)^+$ form].

▪ 7-cyclopropyl-3-[(1-[(3R,4R)-1-[3-fluoro-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 454)

Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give

EXAMPLE 454. HRMS calculated for $C_{38}H_{39}FN_6O_4S$: 694.2737; found 695.2808 $[(M+H)^+]$ form].

5 ▪ **7-cyclopropyl-3-[(1-[(3R,4R)-1-[3-fluoro-5-(pyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 455)**

Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 455**. HRMS calculated for $C_{37}H_{37}FN_6O_4S$: 680.2581; found 681.2645 $[(M+H)^+]$ form].

10 ▪ **7-cyclopropyl-3-[(1-[(3R,4R)-1-[3-fluoro-5-(pyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 456)**

Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to
15 **General Procedure 9**, to give **EXAMPLE 456**. HRMS calculated for $C_{37}H_{37}FN_6O_4S$: 680.2581; found 681.2648 $[(M+H)^+]$ form].

 ▪ **7-cyclopropyl-3-[(1-[(3R,4R)-1-[(4-fluoro-2,3'-bithiophen-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 457)**

20 Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 457**. HRMS calculated for $C_{36}H_{36}FN_5O_4S_2$: 685.2193; found 686.2269 $[(M+H)^+]$ form].

25 ▪ **7-cyclopropyl-3-[(1-[(3R,4R)-1-[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 458)**

Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid

according to **General Procedure 9**, to give **EXAMPLE 458**. HRMS calculated for $C_{38}H_{39}FN_6O_4S$: 694.2737; found 695.2812 $[(M+H)^+]$ form].

5 ▪ **7-cyclopropyl-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 459)**

Using **General Procedure 7** starting from **Preparation R3g** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 459**. HRMS calculated for $C_{38}H_{41}N_7O_4S$: 691.2941; found 692.3024 $[(M+H)^+]$ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methylpiperidin-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 460)**

Using **General Procedure 6** starting from **Preparation R3k** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 460**. HRMS calculated for $C_{40}H_{48}N_8O_3S$: 720.3570; found 361.1855 $[(M+2H)^{2+}]$ form].

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(2-methylpropyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 461)**

Using **General Procedure 6** starting from **Preparation R3n** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 461**. HRMS calculated for $C_{38}H_{45}N_7O_3S$: 679.3304; found 340.6733 $[(M+2H)^{2+}]$ form].

20 ▪ **7-(2,2-difluoroethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 462)**

Using **General Procedure 6** starting from **Preparation R3p** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 462**. HRMS calculated for $C_{36}H_{39}F_2N_7O_3S$: 687.2803; found 344.6487 $[(M+2H)^{2+}]$ form].

- 5 ▪ **7-(2,2-difluoroethyl)-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 463)**

Using **General Procedure 7** starting from **Preparation R3p** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 463**. HRMS calculated for $C_{37}H_{37}N_6O_4F_3S$: 718.2549; found 719.2625 $[(M+H)^+]$ form].

10

- **7-(cyclopropylmethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 464)**

Using **General Procedure 6** starting from **Preparation R3q** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 464**. HRMS calculated for $C_{38}H_{43}N_7O_3S$: 677.3149; found 339.6648 $[(M+2H)^{2+}]$ form].

15

- 20 ▪ **7-(cyclopropylmethyl)-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 465)**

Using **General Procedure 7** starting from **Preparation R3q** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 465**. HRMS calculated for $C_{39}H_{41}N_6O_4FS$: 708.2894; found 709.2973 $[(M+H)^+]$ form].

25

- **7-(cyclobutylmethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 466)**

Using **General Procedure 7** starting from **Preparation R3r** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 466**. HRMS calculated for $C_{40}H_{45}N_7O_4S$: 719.3254; found 720.3333 $[(M+H)^+$ form].

▪ **7-(cyclobutylmethyl)-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 467)**

Using **General Procedure 7** starting from **Preparation R3r** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 467**. HRMS calculated for $C_{40}H_{43}FN_6O_4S$: 722.3051; found 723.3125 $[(M+H)^+$ form].

▪ **7-(cyclobutylmethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 468)**

Using **General Procedure 6** starting from **Preparation R3r** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 468**. HRMS calculated for $C_{39}H_{45}N_7O_3S$: 691.3304; found 692.3396 $[(M+H)^+$ form].

▪ **7-(2-fluoroethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 469)**

Using **General Procedure 6** starting from **Preparation R3u** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 469**. HRMS calculated for $C_{36}H_{40}FN_7O_3S$: 669.2897; found 335.6529 $[(M+2H)^{2+}$ form].

▪ 7-(2-fluoroethyl)-3-[(1-[[[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 470)

Using **General Procedure 7** starting from **Preparation R3u** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 470**. HRMS calculated for $C_{37}H_{38}N_6O_4F_2S$: 700.2643; found 701.2725 [(M+H)⁺ form].

▪ 7-(2-hydroxyethyl)-3-[(4-hydroxy-1-[[[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 471)

Using **General Procedure 6** starting from **Preparation R3w** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 471**. HRMS calculated for $C_{36}H_{41}N_7O_4S$: 667.2941; found 334.6543 [(M+2H)²⁺ form].

▪ 3-[(1-[[[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(2-hydroxyethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 472)

Using **General Procedure 7** starting from **Preparation R3w** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 472**. HRMS calculated for $C_{37}H_{39}N_6O_5FS$: 698.2687; found 699.2757 [(M+H)⁺ form].

▪ 3-[(1-[[[(3R,4R)-1-(3-fluorobenzyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 473)

Using **General Procedure 6** starting from **Preparation R1n** and 1-(bromomethyl)-3-fluoro-benzene as reagents, the resulted crude product (35 mg, 0.052 mmol) was reacted with TBAF (1 M in THF, 0.16 ml, 0.156 mmol) in THF (2 ml) at 75 °C for 4 days. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM

aqueous NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 473**. HRMS calculated for $\text{C}_{31}\text{H}_{34}\text{FN}_5\text{O}_3$: 543.2646; found 544.272 $[(\text{M}+\text{H})^+ \text{ form}]$.

5 ▪ **3-[(1-[(3R,4R)-1-(2-fluorobenzyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one**
 (EXAMPLE 474)

Using **General Procedure 6** starting from **Preparation R1n** and 1-(bromomethyl)-2-fluoro-benzene as reagents, the resulted crude product (80 mg, 0.12 mmol) was reacted with TBAF (1 M in THF, 0.24 ml, 0.24 mmol) in THF (3 ml) at 75 °C for 1 day. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μm column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 474**. HRMS calculated for $\text{C}_{31}\text{H}_{34}\text{FN}_5\text{O}_3$: 543.2646; found 544.274 $[(\text{M}+\text{H})^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(3-methylbenzyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one**
15 **(EXAMPLE 475)**

Using **General Procedure 6** starting from **Preparation R1n** and 1-(bromomethyl)-3-methyl-benzene as reagents, the resulted crude product (74 mg, 0.11 mmol) was reacted with TBAF (1 M in THF, 0.22 ml, 0.22 mmol) in THF (3 ml) at 75 °C for 1 day. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μm column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 475**. HRMS calculated for $\text{C}_{32}\text{H}_{37}\text{N}_5\text{O}_3$: 539.2896; found 540.2940 $[(\text{M}+\text{H})^+ \text{ form}]$.

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-(2-methylbenzyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one**
25 **(EXAMPLE 476)**

Using **General Procedure 6** starting from **Preparation R1n** and 1-(bromomethyl)-2-methyl-benzene as reagents, the resulted crude product (88 mg, 0.13 mmol) was reacted with TBAF (1 M in THF, 0.26 ml, 0.26 mmol) in THF (3 ml) at 75 °C for 1 day. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μm column, 5 mM

aqueous NH_4HCO_3 -MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 476**. HRMS calculated for $\text{C}_{32}\text{H}_{37}\text{N}_5\text{O}_3$: 539.2896; found 540.295 [(M+H)⁺ form].

5 **▪ 3-[(1-[(3R,4R)-1-(1-benzofuran-2-ylmethyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 477)**

Using **General Procedure 6** starting from **Preparation R1n** and 2-(chloromethyl)benzofurane as reagents, the resulted crude product (32 mg, 0.046 mmol) was reacted with TBAF (1 M in THF, 0.09 ml, 0.09 mmol) in THF (3 ml) at 75 °C for 1
10 day. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 477**. HRMS calculated for $\text{C}_{33}\text{H}_{35}\text{N}_5\text{O}_4$: 565.2689; found 566.2772 [(M+H)⁺ form].

15 **▪ 3-{[4-hydroxy-1-[(3R,4R)-1-[(4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 478)**

Using **General Procedure 7** starting from **Preparation R1n** and 4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product (87 mg, 0.126 mmol) was reacted with TBAF (1 M in THF, 0.315 ml, 0.315 mmol) in THF (3 ml) at 75 °C for 1 day. The
20 reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 478**. HRMS calculated for $\text{C}_{29}\text{H}_{32}\text{N}_6\text{O}_4\text{S}$: 560.2206; found 561.228 [(M+H)⁺ form].

25 **▪ 3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(2-phenyl-1,3-thiazol-5-yl)carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 479)**

Using **General Procedure 7** starting from **Preparation R1n** and 2-phenylthiazole-5-carboxylic acid as reagents, the resulted crude product (86 mg, 0.11 mmol) was reacted with TBAF (1 M in THF, 0.285 ml, 0.285 mmol) in THF (3 ml) at 75 °C for 1 day. The

reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 479**. HRMS calculated for C₃₄H₃₄N₆O₄S: 622.2362; found 623.2442 [(M+H)⁺ form].

5 ▪ **3-{{[4-hydroxy-1-((3R,4R)-1-[(4-methyl-2-phenyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 480)**

Using **General Procedure 7** starting from **Preparation R1n** and 4-methyl-2-phenylthiazole-5-carboxylic acid as reagents, the resulted crude product (90 mg, 0.117 mmol) was reacted with TBAF (1 M in THF, 0.293 ml, 0.293 mmol) in THF (3 ml)
10 at 75 °C for 1 day. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) then with flash chromatography (MeOH-DCM gradient) to give **EXAMPLE 480**. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.2601 [(M+H)⁺ form].

15 ▪ **3-[(4-hydroxy-1-((3R,4R)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(2-oxopyrrolidin-1-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 481)**

Using **General Procedure 11** starting from **Preparation R2ab** and **Preparation R1m** as reagents, **EXAMPLE 481** was obtained. HRMS calculated for C₃₉H₄₂N₈O₅S: 734.2999; found 735.3045 [(M+H)⁺ form].
20

▪ **3-[(4-hydroxy-1-((3R,4R)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 482)**

Using **General Procedure 11** starting from **Preparation R2am** and **Preparation R1m** as reagents, **EXAMPLE 482** was obtained. HRMS calculated for C₄₂H₄₃N₇O₄S: 741.3098; found 742.3167 [(M+H)⁺ form].
25

▪ **3-[(4-hydroxy-1-((3R,4R)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[4-**

(hydroxymethyl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one

(EXAMPLE 483)

Using **General Procedure 11** starting from **Preparation R2aq** and **Preparation R1m** as reagents, **EXAMPLE 483** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 758.3122 $[(M+H)^+$ form].

▪ 7-(4-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 484**)

Using **General Procedure 11** starting from **Preparation R2as** and **Preparation R1m** as reagents, **EXAMPLE 484** was obtained. HRMS calculated for $C_{41}H_{40}FN_7O_4S$: 745.2847; found 373.6485 $[(M+2H)^{2+}$ form].

▪ 7-[4-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 485**)

Using **General Procedure 11** starting from **Preparation R2at** and **Preparation R1m** as reagents, **EXAMPLE 485** was obtained. HRMS calculated for $C_{43}H_{46}N_8O_4S$: 770.3362; found 771.3439 $[(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(4-methylpiperazin-1-yl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 486**)

Using **General Procedure 11** starting from **Preparation R2au** and **Preparation R1m** as reagents, **EXAMPLE 486** was obtained. HRMS calculated for $C_{46}H_{51}N_9O_4S$: 825.3785; found 413.6974 $[(M+2H)^{2+}$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-

(morpholin-4-yl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one**(EXAMPLE 487)**

Using **General Procedure 11** starting from **Preparation R2av** and **Preparation R1m** as reagents, **EXAMPLE 487** was obtained. HRMS calculated for $C_{45}H_{48}N_8O_5S$: 812.3469; found 813.3555 $[(M+H)^+$ form].

reparation of 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methylpyrimidin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 488)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylic acid as reagents, the resulted crude boronic acid was reacted with 4-bromo-2-methyl-pyrimidine as halo compound according to **General Procedure 9**, to give **EXAMPLE 488**. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.2698 $[(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(5-methylpyrazin-2-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 489)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylic acid as reagents, the resulted crude boronic acid was reacted with 2-bromo-5-methyl-pyrazine as halo compound according to **General Procedure 9**, to give **EXAMPLE 489**. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.2703 $[(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyrazin-2-yl)thiophen-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 490)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylic acid as reagents, the resulted crude boronic acid was reacted with 2-chloropyrazine as halo compound according to **General Procedure 9**, to give **EXAMPLE 490**. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.2547 $[(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methylpyridazin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 491)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylic acid as reagents, the resulted crude boronic acid was reacted with 3-chloro-6-methyl-pyridazine as halo compound according to **General Procedure 9**, to give **EXAMPLE 491**. HRMS calculated for C₃₅H₃₇N₇O₄S: 651.2628; found 652.2709 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methylpyrazin-2-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 492)

Using **General Procedure 7** starting from **Preparation R3b** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylic acid as reagents, the resulted crude boronic acid was reacted with 2-chloro-6-methyl-pyrazine as halo compound according to **General Procedure 9**, to give **EXAMPLE 492**. HRMS calculated for C₃₅H₃₇N₇O₄S: 651.2628; found 652.2699 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 493)

Using **General Procedure 11** starting from **Preparation R2bf** and **Preparation R1m** as reagents, **EXAMPLE 493** was obtained. HRMS calculated for C₄₂H₄₃N₇O₄S: 741.3098; found 742.3171 [(M+H)⁺ form].

▪ 7-(3-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 494)

Using **General Procedure 11** starting from **Preparation R3bj** and **Preparation R1m** as reagents, **EXAMPLE 494** was obtained. HRMS calculated for C₄₁H₄₀N₇O₄SCl: 761.2551; found 762.2622 [(M+H)⁺ form].

▪ 7-(3-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 495)

Using **General Procedure 11** starting from **Preparation R2bk** and **Preparation R1m** as reagents, **EXAMPLE 495** was obtained. HRMS calculated for $C_{41}H_{40}FN_7O_4S$: 745.2847; found 373.6504 [(M+2H)²⁺ form].

▪ 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 496)

Using **General Procedure 11** starting from **Preparation R2bl** and **Preparation R1m** as reagents, **EXAMPLE 496** was obtained. HRMS calculated for $C_{43}H_{46}N_8O_4S$: 770.3362; found 771.3436 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 497)

Using **General Procedure 11** starting from **Preparation R2bm** and **Preparation R1m** as reagents, **EXAMPLE 497** was obtained. HRMS calculated for $C_{45}H_{48}N_8O_5S$: 812.3469; found 813.3544 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 498)

Using **General Procedure 10** starting from **EXAMPLE 297** and boron-tribromide as reagents, **EXAMPLE 498** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 744.2956 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 499)**

Using **General Procedure 11** starting from **Preparation R2bo** and **Preparation R1m** as reagents, **EXAMPLE 499** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 379.6582 $[(M+2H)^{2+}]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(2-methylphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 500)**

Using **General Procedure 11** starting from **Preparation R2bv** and **Preparation R1m** as reagents, **EXAMPLE 500** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_4S$: 741.3098; found 742.3169 $[(M+H)^+]$ form].

▪ **7-(2-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 501)**

Using **General Procedure 11** starting from **Preparation R2bw** and **Preparation R1m** as reagents, **EXAMPLE 501** was obtained. HRMS calculated for $C_{41}H_{40}ClN_7O_4S$: 761.2551; found 762.2633 $[(M+H)^+]$ form].

▪ **7-(2-fluorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 502)**

Using **General Procedure 11** starting from **Preparation R2bx** and **Preparation R1m** as reagents, **EXAMPLE 502** was obtained. HRMS calculated for $C_{41}H_{40}N_7O_4FS$: 745.2847; found 746.2924 $[(M+H)^+]$ form].

▪ **7-[2-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 503)**

Using **General Procedure 11** starting from **Preparation R2by** and **Preparation R1m** as reagents, **EXAMPLE 503** was obtained. HRMS calculated for $C_{43}H_{46}N_8O_4S$: 770.3362; found 771.3447 [(M+H)⁺ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(2-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 504)**

Using **General Procedure 11** starting from **Preparation R2bz** and **Preparation R1m** as reagents, **EXAMPLE 504** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 758.3114 [(M+H)⁺ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 505)**

Using **General Procedure 11** starting from **Preparation R2cc** and **Preparation R1m** as reagents, **EXAMPLE 505** was obtained. HRMS calculated for $C_{39}H_{39}N_7O_4S_2$: 733.2505; found 734.2591 [(M+H)⁺ form].

15 ▪ **7-(furan-3-yl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 506)**

Using **General Procedure 11** starting from **Preparation R2ce** and **Preparation R1m** as reagents, **EXAMPLE 506** was obtained. HRMS calculated for $C_{39}H_{39}N_7O_5S$: 717.2733; found 718.2818 [(M+H)⁺ form].

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1H-indol-1-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 507)**

25 Using **General Procedure 11** starting from **Preparation R2cl** and **Preparation R1m** as reagents, **EXAMPLE 507** was obtained. HRMS calculated for $C_{43}H_{42}N_8O_4S$: 766.3050; found 767.312 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1H-pyrrol-1-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 508)

Using General Procedure 11 starting from Preparation R2cm and Preparation R1m as reagents, EXAMPLE 508 was obtained. HRMS calculated for C₃₉H₄₀N₈O₄S: 716.2893; found 717.2976 [(M+H)⁺ form].

▪ 7-cyclopentyl-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 509)

Using General Procedure 11 starting from Preparation R2i and Preparation R1m as reagents, EXAMPLE 509 was obtained. HRMS calculated for C₄₀H₄₅N₇O₄S: 719.3254; found 718.3195 [(M-H)⁻ form].

▪ 7-cyclohexyl-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 510)

Using General Procedure 11 starting from Preparation R2j and Preparation R1m as reagents, EXAMPLE 510 was obtained. HRMS calculated for C₄₁H₄₇N₇O₄S: 733.3410; found 732.3356 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(tetrahydro-2H-pyran-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 511)

Using General Procedure 11 starting from Preparation R2l and Preparation R1m as reagents, EXAMPLE 511 was obtained. HRMS calculated for C₄₀H₄₅N₇O₅S: 735.3203; found 734.3166 [(M-H)⁻ form].

▪ 3-[(1-[(3R,4R)-1-(3-aminobenzoyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 512)

Using **General Procedure 12** starting from **EXAMPLE 203** and as starting material, **EXAMPLE 512** was obtained. HRMS calculated for $C_{32}H_{36}N_6O_4$: 568.2798; found 569.2855 [(M+H)⁺ form].

5 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[3-(methylamino)benzoyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 513)**

Using **General Procedure 13** starting from **EXAMPLE 512** as amino reagent, **EXAMPLE 513** was obtained. HRMS calculated for $C_{33}H_{38}N_6O_4$: 582.2955; found 583.3036 [(M+H)⁺ form].

10 ▪ **tert-butyl 4-acetyl-7-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-3,4-dihydroquinoxaline-1(2H)-carboxylate (EXAMPLE 514)**

Using **General Procedure 7** starting from **EXAMPLE 244** and acetic acid as reagents, **EXAMPLE 514** was obtained. HRMS calculated for $C_{41}H_{49}N_7O_7$: 751.3693; found 752.3755 [(M+H)⁺ form].

15 ▪ **7-{4-[6-(dimethylamino)pyridin-3-yl]phenyl}-3-[(1-{[(3R,4R)-1-(2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 515)**

20 and

7-(4-chlorophenyl)-3-[(1-{[(3R,4R)-1-(2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 516)

Using **General Procedure 9** starting from **EXAMPLE 28** and [6-(dimethylamino)-3-pyridyl]boronic acid as reagents, **EXAMPLE 515** and **EXAMPLE 516** were obtained and separated by chromatography.

25 **EXAMPLE 515**: HRMS calculated for $C_{48}H_{52}N_{10}O_3S$: 848.3945; found 425.2060 [M+2H]²⁺ form].

EXAMPLE 516: HRMS calculated for $C_{41}H_{43}ClN_8O_3S$: 762.2867; found 382.1494 $[M+2H]^{2+}$ form].

5 ▪ 5-[5-((3R,4R)-4-[(4-{[7-(4-chlorophenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile (**EXAMPLE 517**)

Using **General Procedure 9** starting from **EXAMPLE 28** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carbonitrile as reagents, **EXAMPLE 517** was obtained. HRMS calculated for $C_{40}H_{37}ClN_8O_3S$: 744.2398; found 745.2471 $[M+H]^+$ form].

10 ▪ 7-(4-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 518**)

Using **General Procedure 9** starting from **EXAMPLE 28** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 518** was obtained. HRMS calculated for $C_{40}H_{40}ClN_7O_3S$: 733.2602; found 367.6385 $[(M+2H)^{2+}]$ form].

15 ▪ 5-[5-((3R,4R)-4-[(4-{[7-(4-fluorophenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile (**EXAMPLE 519**)

Using **General Procedure 9** starting from **EXAMPLE 31** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carbonitrile as reagents, **EXAMPLE 519** was obtained. HRMS
20 calculated for $C_{40}H_{37}FN_8O_3S$: 728.2693; found 729.2757 $(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[2-(thiophen-2-yl)-1,3-thiazol-5-yl)methyl]piperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 520**)

Using **General Procedure 9** starting from **EXAMPLE 34** and 2-thienylboronic acid as
25 reagents, **EXAMPLE 520** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_4S_2$: 720.2552; found 721.2612 $[(M+H)^+]$ form].

▪ 3-[(1-[(3R,4R)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 521)

Using **General Procedure 9** starting from **EXAMPLE 34** and [6-(dimethylamino)-3-pyridyl]boronic acid as reagents, **EXAMPLE 521** was obtained. HRMS calculated for $C_{42}H_{46}N_8O_4S$: 758.3362; found 380.1763 $[M+2H]^{2+}$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl}piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 522)

Using **General Procedure 9** starting from **EXAMPLE 34** and [6-(trifluoromethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 522** was obtained. HRMS calculated for $C_{41}H_{40}F_3N_7O_4S$: 783.2814; found 784.2893 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-(pyrimidin-5-yl)-1,3-thiazol-5-yl)methyl}piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 523)

Using **General Procedure 9** starting from **EXAMPLE 34** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 523** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_4S$: 716.2893; found 717.2999 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({2-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 524)

Using **General Procedure 9** starting from **EXAMPLE 34** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 524** was obtained. HRMS calculated for $C_{39}H_{42}N_8O_4S$: 718.3050; found 719.3108 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({2-(1-methyl-1H-pyrazol-4-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 525)

Using **General Procedure 9** starting from **EXAMPLE 34** and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 525** was obtained. HRMS calculated for $C_{39}H_{42}N_8O_4S$: 718.3050; found 719.3131 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(1-methyl-1H-pyrrol-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 526)**

Using **General Procedure 9** starting from **EXAMPLE 34** and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole as reagents, **EXAMPLE 526** was obtained. HRMS calculated for $C_{40}H_{43}N_7O_4S$: 717.3098; found 718.3145 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[2-(thiophen-3-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 527)**

Using **General Procedure 9** starting from **EXAMPLE 34** and 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane as reagents, **EXAMPLE 527** was obtained. HRMS calculated
15 for $C_{39}H_{40}N_6O_4S_2$: 720.2552; found 721.2649 $[(M+H)^+ \text{ form}]$.

▪ **3-[(1-[(3R,4R)-1-{[2-(furan-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 528)**

Using **General Procedure 9** starting from **EXAMPLE 34** and 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as reagents, **EXAMPLE 528** was obtained. HRMS
20 calculated for $C_{39}H_{40}N_6O_5S$: 704.2781; found 705.2852 $[(M+H)^+ \text{ form}]$.

▪ **3-[(1-[(3R,4R)-1-{[2-(furan-2-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 529)**

25 Using **General Procedure 9** starting from **EXAMPLE 34** and 2-furylboronic acid as reagents, **EXAMPLE 529** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_5S$: 704.2781; found 705.2837 $[(M+H)^+ \text{ form}]$.

▪ **5-[5-((3R,4R)-4-[(4-hydroxy-4-{7-(4-methoxyphenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile (EXAMPLE 530)**

Using **General Procedure 9** starting from **EXAMPLE 34** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carbonitrile as reagents, **EXAMPLE 530** was obtained. HRMS calculated for $C_{41}H_{40}N_8O_4S$: 740.2893; found 741.2956 $[M+H]^+$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 531)**

Using **General Procedure 9** starting from **EXAMPLE 34** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 531** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_4S$: 729.3098; found 365.6619 $[(M+2H)^{2+}]$ form].

▪ **3-[(1-[(3R,4R)-1-{5-(furan-2-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 532)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 2-furylboronic acid as reagents, **EXAMPLE 532** was obtained. HRMS calculated for $C_{34}H_{35}N_5O_5S$: 625.2359; found 626.2436 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{5-(1-methyl-1H-pyrazol-5-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 533)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 533** was obtained. HRMS calculated for $C_{34}H_{37}N_7O_4S$: 639.2628; found 640.2696 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{5-(pyridin-3-yl)thiophen-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 534)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 3-pyridylboronic acid as reagents, **EXAMPLE 534** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2582 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[5-(1-methyl-1H-pyrrol-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 535)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole as reagents, **EXAMPLE 535** was obtained. HRMS calculated for $C_{35}H_{38}N_6O_4S$: 638.2675; found 639.2750 $[M+H]^+$ form].

10 ▪ **3-[(1-[(3R,4R)-1-{[5-(4-fluorophenyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 536)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (4-fluorophenyl)boronic acid as reagents, **EXAMPLE 536** was obtained. HRMS calculated for $C_{36}H_{36}FN_5O_4S$:
15 653.2472; found 654.254 $[(M+H)^+]$ form].

▪ **3-[(1-[(3R,4R)-1-{[5-(3-fluorophenyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 537)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (3-fluorophenyl)boronic
20 acid as reagents, **EXAMPLE 537** was obtained. HRMS calculated for $C_{36}H_{36}FN_5O_4S$:
653.2472; found 654.2552 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[5-(3-methylphenyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 538)**

25 Using **General Procedure 9** starting from **EXAMPLE 176** and m-tolylboronic acid as reagents, **EXAMPLE 538** was obtained. HRMS calculated for $C_{37}H_{39}N_5O_4S$: 649.2723; found 650.2793 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[5-(2-methylphenyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 539)**

Using **General Procedure 9** starting from **EXAMPLE 176** and o-tolylboronic acid as reagents, **EXAMPLE 539** was obtained. HRMS calculated for C₃₇H₃₉N₅O₄S: 649.2723; found 650.2793 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[5-(4-methylphenyl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 540)**

Using **General Procedure 9** starting from **EXAMPLE 176** and p-tolylboronic acid as reagents, **EXAMPLE 540** was obtained. HRMS calculated for C₃₇H₃₉N₅O₄S: 649.2723; found 650.2792 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[5-(furan-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 541)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as reagents, **EXAMPLE 541** was obtained. HRMS calculated for: 625.2359; found C₃₄H₃₅N₅O₅S 626.2425 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[5-(pyrimidin-5-yl)thiophen-2-yl]carbonyl}piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 542)**

Using **General Procedure 9** starting from **EXAMPLE 176** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 542** was obtained. HRMS calculated for C₃₄H₃₅N₇O₄S: 637.2471; found 638.2544 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[2-(furan-2-yl)-4-methyl-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 543)**

Using **General Procedure 9** starting from **EXAMPLE 349** and 2-furylboronic acid as reagents, **EXAMPLE 543** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_5S$: 640.2468; found 641.2544 [(M+H)⁺ form].

5 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(pyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 544**)

Using **General Procedure 9** starting from **EXAMPLE 349** and 3-pyridylboronic acid as reagents, **EXAMPLE 544** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.2697 [(M+H)⁺ form].

10 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 545**)

Using **General Procedure 9** starting from **EXAMPLE 349** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 545** was obtained.
15 HRMS calculated for $C_{34}H_{38}N_8O_4S$: 654.2737; found 655.2823 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(1-methyl-1H-pyrrol-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 546**)

Using **General Procedure 9** starting from **EXAMPLE 349** and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole as reagents, **EXAMPLE 546** was obtained.
20 HRMS calculated for $C_{35}H_{39}N_7O_4S$: 653.2784; found 654.2848 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(1-methyl-1H-pyrazol-4-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 547**)

25 Using **General Procedure 9** starting from **EXAMPLE 349** and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 547** was obtained. HRMS calculated for $C_{34}H_{38}N_8O_4S$: 654.2737; found 655.2817 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{2-(furan-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 548)

Using General Procedure 9 starting from EXAMPLE 349 and 2-furylboronic acid as reagents, EXAMPLE 548 was obtained. HRMS calculated for C₃₄H₃₆N₆O₅S: 640.2468; found 641.2541 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(pyrimidin-5-yl)-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 549)

Using General Procedure 9 starting from EXAMPLE 349 and pyrimidin-5-ylboronic acid as reagents, EXAMPLE 549 was obtained. HRMS calculated for C₃₄H₃₆N₈O₄S: 652.2580; found 653.2656 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(3-methylphenyl)-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 550)

Using General Procedure 9 starting from EXAMPLE 349 and m-tolylboronic acid as reagents, EXAMPLE 550 was obtained. HRMS calculated for C₃₇H₄₀N₆O₄S: 664.2832; found 665.2893 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(thiophen-2-yl)-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 551)

Using General Procedure 9 starting from EXAMPLE 349 and 2-thienylboronic acid as reagents, EXAMPLE 551 was obtained. HRMS calculated for C₃₄H₃₆N₆O₄S₂: 656.2239; found 657.2318 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(4-methylphenyl)-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 552)

Using **General Procedure 9** starting from **EXAMPLE 349** and p-tolylboronic acid as reagents, **EXAMPLE 552** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4S$: 664.2832; found 665.2908 $[(M+H)^+]$ form].

5 ■ 3-[(1-[(3R,4R)-1-{2-(4-fluorophenyl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 553**)

Using **General Procedure 9** starting from **EXAMPLE 349** and (4-fluorophenyl)boronic acid as reagents, **EXAMPLE 553** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_4S$: 668.2581; found 669.2656 $[(M+H)^+]$ form].

10 ■ 3-[(1-[(3R,4R)-1-{2-(3-fluorophenyl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 554**)

Using **General Procedure 9** starting from **EXAMPLE 349** and (3-fluorophenyl)boronic acid as reagents, **EXAMPLE 554** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_4S$:
15 668.2581; found 669.2659 $[(M+H)^+]$ form].

■ 3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(thiophen-3-yl)-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 555**)

Using **General Procedure 9** starting from **EXAMPLE 349** and 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane as reagents, **EXAMPLE 555** was obtained. HRMS calculated
20 for $C_{34}H_{36}N_6O_4S_2$: 656.2239; found 657.2300 $[(M+H)^+]$ form].

■ 3-[(1-[(3R,4R)-1-{5-(3-fluoropyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 556**)

25 Using **General Procedure 9** starting from **EXAMPLE 176** and (3-fluoro-4-pyridyl)boronic acid as reagents, **EXAMPLE 556** was obtained. HRMS calculated for $C_{35}H_{35}FN_6O_4S$: 654.2425; found 655.2499 $[(M+H)^+]$ form].

▪ 3-[(1-[(3R,4R)-1-(2,2'-bithiophen-5-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 557)

Using **General Procedure 9** starting from **EXAMPLE 176** and 2-thienylboronic acid as reagents, **EXAMPLE 557** was obtained. HRMS calculated for $C_{34}H_{35}N_5O_4S_2$: 641.2130; found 642.2219 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-(2,3'-bithiophen-5-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 558)

Using **General Procedure 9** starting from **EXAMPLE 176** and 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane as reagents, **EXAMPLE 558** was obtained. HRMS calculated for $C_{34}H_{35}N_5O_4S_2$: 641.2131; found (642.2210 [(M+H)⁺ form]).

▪ 3-[(1-[(3R,4R)-1-{5-(2-fluorophenyl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 559)

Using **General Procedure 9** starting from **EXAMPLE 176** and (2-fluorophenyl)boronic acid as reagents, **EXAMPLE 559** was obtained. HRMS calculated for $C_{36}H_{36}FN_5O_4S$: 653.2472; found 654.2541 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(5-phenylthiophen-2-yl)carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 560)

Using **General Procedure 9** starting from **EXAMPLE 176** and phenylboronic acid as reagents, **EXAMPLE 560** was obtained. HRMS calculated for $C_{36}H_{37}N_5O_4S$: 635.2566; found 636.264 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{5-(1-methyl-1H-pyrazol-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 561)

Using **General Procedure 9** starting from **EXAMPLE 176** and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 561** was obtained. HRMS calculated for $C_{34}H_{37}N_7O_4S$: 639.2628; found 640.2695 $[(M+H)^+]$ form].

5 ▪ **3-[(1-[(3R,4R)-1-{5-(2-chloropyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 562)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (2-chloro-4-pyridyl)boronic acid as reagents, **EXAMPLE 562** was obtained. HRMS calculated for $C_{35}H_{35}ClN_6O_4S$: 670.2129; found 671.2194 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-{5-(3-chloropyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 563)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (3-chloro-4-pyridyl)boronic acid as reagents, **EXAMPLE 563** was obtained. HRMS calculated for $C_{35}H_{35}ClN_6O_4S$:
15 670.2129; found 671.2188 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{5-(3-methylpyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 564)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (3-methyl-4-pyridyl)boronic
20 acid as reagents, **EXAMPLE 564** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$:
650.2675; found 651.2742 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{5-(2-methylpyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 565)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (2-methyl-4-pyridyl)boronic
25 acid as reagents, **EXAMPLE 565** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$:
650.2675; found 651.2724 $[(M+H)^+]$ form].

▪ 3-[(1-[(3R,4R)-1-{[5-(5-chloro-2-fluoropyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 566)

Using General Procedure 9 starting from EXAMPLE 176 and (5-chloro-2-fluoro-4-pyridyl)boronic acid as reagents, EXAMPLE 566 was obtained. HRMS calculated for $C_{35}H_{34}ClFN_6O_4S$: 688.2035; found 689.2135 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[5-(2,5-dichloropyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 567)

Using General Procedure 9 starting from EXAMPLE 176 and 2,5-dichloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, EXAMPLE 567 was obtained. HRMS calculated for $C_{35}H_{34}N_6O_4SCl_2$: 704.1740; found 705.1819 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[5-(2-fluoropyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 568)

Using General Procedure 9 starting from EXAMPLE 176 and (2-fluoro-4-pyridyl)boronic acid as reagents, EXAMPLE 568 was obtained. HRMS calculated for $C_{35}H_{35}N_6O_4S$: 654.2425; found 655.251 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[(5-phenylthiophen-2-yl)sulfonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 569)

Using General Procedure 9 starting from EXAMPLE 342 and phenylboronic acid as reagents, EXAMPLE 569 was obtained. HRMS calculated for $C_{35}H_{37}N_5O_5S_2$: 671.2236; found 672.2297 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[5-(pyridin-4-yl)thiophen-2-yl]sulfonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 570)

Using **General Procedure 9** starting from **EXAMPLE 342** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 570** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_5S_2$: 672.2189; found 337.1169 $[(M+2H)^{2+}$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyrimidin-5-yl)thiophen-2-yl]sulfonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 571)**

Using **General Procedure 9** starting from **EXAMPLE 342** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 571** was obtained. HRMS calculated for $C_{33}H_{35}N_7O_5S_2$: 673.2141; found 674.221 $[(M+H)^+$ form].

10 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[3-(1-methyl-1H-pyrazol-5-yl)benzoyl]-3-phenyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 572)**

Using **General Procedure 9** starting from **EXAMPLE 201** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 572** was obtained.
15 HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3063; found 634.3140 $[(M+H)^+$ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(pyrimidin-5-yl)benzoyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 573)**

Using **General Procedure 9** starting from **EXAMPLE 201** and pyrimidin-5-ylboronic acid
20 as reagents, **EXAMPLE 573** was obtained. HRMS calculated for $C_{36}H_{37}N_7O_4$: 631.2907; found 632.2982 $[(M+H)^+$ form].

▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(pyridin-4-yl)benzoyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 574)**

25 Using **General Procedure 9** starting from **EXAMPLE 201** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 574** was obtained. HRMS calculated for $C_{37}H_{38}N_6O_4$: 630.2955; found 316.1552 $[(M+2H)^{2+}$ form].

▪ **3-([4-hydroxy-1-((3R,4R)-3-phenyl-1-[3-(pyridin-3-yl)benzoyl]piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 575)**

Using **General Procedure 9** starting from **EXAMPLE 201** and 3-pyridylboronic acid as reagents, **EXAMPLE 575** was obtained. HRMS calculated for $C_{37}H_{38}N_6O_4$: 630.2955; found 631.3037 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-(1-methyl-1H-pyrazol-5-yl)pyridin-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 576)**

Using **General Procedure 9** starting from **EXAMPLE 194** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 576** was obtained. HRMS calculated for $C_{35}H_{38}N_8O_4$: 634.3016; found 635.3092 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(4,4'-bipyridin-2-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 577)**

Using **General Procedure 9** starting from **EXAMPLE 194** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 577** was obtained. HRMS calculated for $C_{36}H_{37}N_7O_4$: 631.2907; found 632.2978 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(1-methyl-1H-pyrazol-5-yl)thiophen-2-yl]sulfonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 578)**

Using **General Procedure 9** starting from **EXAMPLE 342** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 578** was obtained. HRMS calculated for $C_{33}H_{37}N_7O_5S_2$: 675.2297; found 676.2372 [(M+H)⁺ form].

▪ **3-([4-hydroxy-1-((3R,4R)-3-phenyl-1-[3-(pyrimidin-5-yl)benzyl]piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 579)**

Using **General Procedure 9** starting from **EXAMPLE 69** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 579** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_3$: 617.3115; found 618.3169 [(M+H)⁺ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(pyrimidin-5-yl)phenyl]sulfonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 580)**

Using **General Procedure 9** starting from **EXAMPLE 343** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 580** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_5S$: 667.2577; found 668.2657 [(M+H)⁺ form].

10 ▪ **3-[(1-[(3R,4R)-1-(biphenyl-3-ylmethyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 581)**

Using **General Procedure 9** starting from **EXAMPLE 69** and phenylboronic acid as reagents, **EXAMPLE 581** was obtained. HRMS calculated for $C_{38}H_{41}N_5O_3$: 615.3209; found 616.3306 [(M+H)⁺ form].

15 ▪ **3-[(1-[(3R,4R)-1-(biphenyl-3-ylsulfonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 582)**

Using **General Procedure 9** starting from **EXAMPLE 343** and phenylboronic acid as reagents, **EXAMPLE 582** was obtained. HRMS calculated for $C_{37}H_{39}N_5O_5S$: 665.2672; found 666.2747 [(M+H)⁺ form].

20 ▪ **3-{[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(pyridin-4-yl)benzyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 583)**

25 Using **General Procedure 9** starting from **EXAMPLE 69** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 583** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_3$: 616.3162; found 309.1648 [(M+2H)²⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 584)**

Using **General Procedure 9** starting from **EXAMPLE 197** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 584** was obtained. HRMS calculated for $C_{35}H_{35}FN_6O_4S$: 654.2425; found (655.2508 [(M+H)⁺ form]).

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(1-methyl-1H-pyrazol-5-yl)pyridin-4-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 585)**

Using **General Procedure 9** starting from **EXAMPLE 195** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 585** was obtained. HRMS calculated for $C_{35}H_{38}N_8O_4$: 634.3016; found 635.3109 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(2,4'-bipyridin-4-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 586)**

Using **General Procedure 9** starting from **EXAMPLE 195** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 586** was obtained. HRMS calculated for $C_{36}H_{37}N_7O_4$: 631.2907; found 632.2999 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[5-(1-methyl-1H-pyrazol-5-yl)pyridin-3-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 587)**

Using **General Procedure 9** starting from **EXAMPLE 196** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 587** was obtained. HRMS calculated for $C_{35}H_{38}N_8O_4$: 634.3016; found 635.3091 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-(3,4'-bipyridin-5-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 588)**

Using **General Procedure 9** starting from **EXAMPLE 196** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 588** was obtained. HRMS calculated for $C_{36}H_{37}N_7O_4$: 631.2907; found 632.2985 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[6-(1-methyl-1H-pyrazol-5-yl)pyridin-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 589)**

Using **General Procedure 9** starting from **EXAMPLE 198** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 589** was obtained. HRMS calculated for $C_{35}H_{38}N_8O_4$: 634.3016; found 635.3110 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-(2,4'-bipyridin-6-ylcarbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 590)**

Using **General Procedure 9** starting from **EXAMPLE 198** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 590** was obtained. HRMS calculated for $C_{36}H_{37}N_7O_4$: 631.2907; found 632.2996 $[(M+H)^+]$ form].

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[[3-(pyridin-4-yl)phenyl]sulfonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 591)**

Using **General Procedure 9** starting from **EXAMPLE 343** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 591** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_5S$: 666.2625; found 667.2711 $[(M+H)^+]$ form].

20 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(1-methyl-4-phenyl-1H-pyrrol-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 592)**

25 Using **General Procedure 9** starting from **EXAMPLE 189** and phenylboronic acid as reagents, **EXAMPLE 592** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_4$: 632.3111; found 633.3178 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-[3-(1-methyl-1H-pyrazol-5-yl)benzyl]-3-phenylpiperidin-4-yl)carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 593)**

Using **General Procedure 9** starting from **EXAMPLE 69** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 593** was obtained. HRMS calculated for C₃₆H₄₁N₇O₃: 619.3271; found 620.3359 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-[3-(1-methyl-1H-pyrazol-5-yl)phenyl]sulfonyl)-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 594)**

Using **General Procedure 9** starting from **EXAMPLE 343** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 594** was obtained. HRMS calculated for C₃₅H₃₉N₇O₅S: 669.2733; found 670.2827 [(M+H)⁺ form].

▪ **3-[(1-((3R,4R)-1-[5-(2,3-dichloropyridin-4-yl)thiophen-2-yl]carbonyl)-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 595)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 2,3-dichloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 595** was obtained. HRMS calculated for C₃₅H₃₄N₆O₄SCl₂: 704.1740; found 705.1807 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-[5-(2-methoxypyridin-4-yl)thiophen-2-yl]carbonyl)-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 596)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (2-methoxy-4-pyridyl)boronic acid as reagents, **EXAMPLE 596** was obtained. HRMS calculated for C₃₆H₃₈N₆O₅S: 666.2625; found 667.2699 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-((3R,4R)-1-[5-(3-methoxypyridin-4-yl)thiophen-2-yl]carbonyl)-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 597)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (3-methoxy-4-pyridyl)boronic acid as reagents, **EXAMPLE 597** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_5S$: 666.2625; found 667.2702 $[(M+H)^+]$ form].

5 ▪ **2-([(3R,4R)-4-((4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl)-3-phenylpiperidin-1-yl)carbonyl]-5-(pyridin-4-yl)thiophene-3-carbonitrile (EXAMPLE 598)**

Using **General Procedure 9** starting from **EXAMPLE 212** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 598** was obtained. HRMS calculated for $C_{36}H_{35}N_7O_4S$: 661.2471; found 662.2543 $[(M+H)^+]$ form].

10 ▪ **3-[(1-([(3R,4R)-1-([3-fluoro-5-(2-methylpyridin-4-yl)thiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 599)**

Using **General Procedure 9** starting from **EXAMPLE 197** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 599** was obtained. HRMS calculated for $C_{36}H_{37}N_6O_4FS$:
15 668.2581; found 669.2662 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-([(3R,4R)-1-([5-(4-methylpyridin-3-yl)thiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 600)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (4-methyl-3-pyridyl)boronic
20 acid as reagents, **EXAMPLE 600** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$:
650.2675; found 651.2756 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-([(3R,4R)-1-([5-(5-methylpyridin-3-yl)thiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 601)**

25 Using **General Procedure 9** starting from **EXAMPLE 176** and (5-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 601** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$:
650.2675; found 651.2774 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 602)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 602** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2757 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 603)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 603** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2768 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[5-(6-aminopyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 604)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine as reagents, **EXAMPLE 604** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 651.2710 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methoxypyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 605)**

Using **General Procedure 9** starting from **EXAMPLE 176** and (6-methoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 605** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_5S$: 666.2625; found 667.2700 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[5-(4-chloropyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 606)**

Using **General Procedure 9** starting from **EXAMPLE 176** and 4-chloro-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 606** was obtained. HRMS calculated for $C_{35}H_{35}ClN_6O_4S$: 670.2129; found 671.2207 ($M+H$)⁺ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(4-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 607)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (4-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 607** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 666.2838 [$(M+H)$]⁺ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(5-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 608)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (5-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 608** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$:
15 665.2784; found 666.2845 [$(M+H)$]⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 609)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (6-methyl-3-pyridyl)boronic
20 acid as reagents, **EXAMPLE 609** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$:
665.2784; found 666.2829 [$(M+H)$]⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(2-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 610)**

25 Using **General Procedure 9** starting from **EXAMPLE 349** and 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 610** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 666.2825 ($M+H$)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{2-(6-aminopyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 611)**

Using **General Procedure 9** starting from **EXAMPLE 349** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine as reagents, **EXAMPLE 611** was obtained. HRMS calculated for C₃₅H₃₈N₈O₄S: 666.2737; found 667.2802 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 612)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (6-methoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 612** was obtained. HRMS calculated for C₃₆H₃₉N₇O₅S: 681.2733; found 682.2797 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{(3R,4R)-1-{1-methyl-5-(2-methylpyridin-4-yl)-1H-pyrrol-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 613)**

Using **General Procedure 9** starting from **EXAMPLE 217** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 613** was obtained. HRMS calculated for C₃₇H₄₁N₇O₄: 647.3220; found 648.3316 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{(3R,4R)-1-{1-methyl-5-(pyridin-3-yl)-1H-pyrrol-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 614)**

Using **General Procedure 9** starting from **EXAMPLE 217** and 3-pyridylboronic acid as reagents, **EXAMPLE 614** was obtained. HRMS calculated for C₃₆H₃₉N₇O₄: 633.3063; found 634.3138 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{(3R,4R)-1-{1-methyl-5-(pyrimidin-5-yl)-1H-pyrrol-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 615)**

Using **General Procedure 9** starting from **EXAMPLE 217** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 615** was obtained. HRMS calculated for $C_{35}H_{38}N_8O_4$: 634.3016; found 635.3092 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(1-[(3R,4R)-1-{2-(5-chloropyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 616)**

Using **General Procedure 9** starting from **EXAMPLE 349** and 3-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 616** was obtained. HRMS calculated for $C_{35}H_{36}ClN_7O_4S$: 685.2238; found 686.2306 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{1-methyl-5-(1-methyl-1H-pyrazol-5-yl)-1H-pyrrol-2-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 617)**

Using **General Procedure 9** starting from **EXAMPLE 217** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 617** was obtained.
15 HRMS calculated for $C_{35}H_{40}N_8O_4$: 636.3173; found 637.3251 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{1-methyl-5-(pyridin-4-yl)-1H-pyrrol-2-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 618)**

Using **General Procedure 9** starting from **EXAMPLE 217** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 618** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3063; found 634.3128 $[(M+H)^+ \text{ form}]$.
20

▪ **3-[(1-[(3R,4R)-1-{3-fluoro-5-(2-methoxypyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 619)**

25 Using **General Procedure 9** starting from **EXAMPLE 197** and (2-methoxy-4-pyridyl)boronic acid as reagents, **EXAMPLE 619** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_5S$: 684.2530; found 685.2594 $[(M+H)^+ \text{ form}]$.

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(3-methoxypyridin-4-yl)-4-methyl-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 620)

Using **General Procedure 9** starting from **EXAMPLE 349** and (3-methoxy-4-pyridyl)boronic acid as reagents, **EXAMPLE 620** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_5S$: 681.2733; found 682.2827 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[5-(5-chloropyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 621)

Using **General Procedure 9** starting from **EXAMPLE 176** and 3-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 621** was obtained. HRMS calculated for $C_{35}H_{35}ClN_6O_4S$: 670.2129; found 671.2200 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-5-(2-methylpyridin-4-yl)-1,3-thiazol-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 622)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with (2-methyl-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 622**. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 666.2863 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(2-methoxypyridin-4-yl)-4-methyl-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 623)

Using **General Procedure 9** starting from **EXAMPLE 349** and (2-methoxy-4-pyridyl)boronic acid as reagents, **EXAMPLE 623** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_5S$: 681.2733; found 682.2807 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[3-fluoro-5-(2-methoxy-6-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 624)

Using **General Procedure 9** starting from **EXAMPLE 269** and 2-methoxy-6-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 624** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_5S$: 698.2687; found 699.2764 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[4-methyl-2-(2-methylpyridin-4-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 625)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 625** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 666.287 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-[[3-fluoro-5-(pyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 626)**

Using **General Procedure 9** starting from **EXAMPLE 269** and 3-pyridylboronic acid as reagents, **EXAMPLE 626** was obtained. HRMS calculated for $C_{35}H_{35}FN_6O_4S$: 654.2424; found 655.2505 $[(M+H)^+]$ form].

15 ▪ **3-[(1-[(3R,4R)-1-[[3-fluoro-5-(3-methoxypyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 627)**

Using **General Procedure 9** starting from **EXAMPLE 269** and (3-methoxy-4-pyridyl)boronic acid as reagents, **EXAMPLE 627** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_5S$: 684.2530; found 685.2598 $[(M+H)^+]$ form].

20 ▪ **tert-butyl [4-(4-fluoro-5-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]thiophen-2-yl)pyridin-2-yl]carbamate (EXAMPLE 628)**

25 Using **General Procedure 9** starting from **EXAMPLE 269** and tert-butyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate as reagents, **EXAMPLE 628** was obtained. HRMS calculated for $C_{40}H_{44}FN_7O_6S$: 769.3058; found 770.3118 $[(M+H)^+]$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[3-methyl-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 629)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to **General Procedure 9**, to give **EXAMPLE 629**. HRMS calculated for $C_{36}H_{38}N_6O_4S$: found 651.2752 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methoxypyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 630)

Using **General Procedure 9** starting from **EXAMPLE 269** and (6-methoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 630** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_5S$: 684.253; found 685.2619 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[5-(6-methoxypyridin-3-yl)-3-methylthiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 631)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 631**. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found 681.2868 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[5-(6-aminopyridin-3-yl)-3-fluorothiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 632)

Using **General Procedure 9** starting from **EXAMPLE 269** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine as reagents, **EXAMPLE 632** was obtained. HRMS calculated for $C_{35}H_{36}FN_7O_4S$: 669.2534; found 335.6352 (M+2H)²⁺ form].

▪ 3-[(1-[(3R,4R)-1-{[5-(6-aminopyridin-3-yl)-3-methylthiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 633)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine according to **General Procedure 9**, to give **EXAMPLE 633**. HRMS calculated for C₃₆H₃₉N₇O₄S: 665.2784; found 333.647 [(M+2H)²⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[3-methyl-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 634)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-3-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 634**. HRMS calculated for C₃₇H₄₀N₆O₄S: 664.2832; found 665.2914 [(M+H)⁺ form].

▪ 3-{[4-hydroxy-1-[(3R,4R)-1-[(3-methyl-2,3'-bithiophen-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 635)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 635**. HRMS calculated for C₃₅H₃₇N₅O₄S₂: 655.2287; found 656.2362 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 636)

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with

(2-methyl-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 636**. HRMS calculated for $C_{37}H_{40}N_6O_4S$: 664.2832; found 665.2913 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(2-methoxypyridin-4-yl)-4-methylthiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 637)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (2-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 637**. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found $[(681.2854 (M+H)^+)]$ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[4-methyl-5-(pyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 638)**

15 Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 638**. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2737 $[(M+H)^+]$ form].

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[5-(3-methoxypyridin-4-yl)-4-methylthiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 639)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-methylthiophene-2-carboxylic acid as reagents, the resulted crude product was reacted with (3-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 639**. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found 681.2859 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({4-methyl-2-[2-(trifluoromethyl)pyridin-4-yl]-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 640)**

Using **General Procedure 9** starting from **EXAMPLE 349** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine as reagents, **EXAMPLE 640** was obtained. HRMS calculated for C₃₆H₃₆F₃N₇O₄S: 719.2502; found 720.2566 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-({3-fluoro-5-[2-(trifluoromethyl)pyridin-4-yl]thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 641)**

Using **General Procedure 9** starting from **EXAMPLE 269** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine as reagents, **EXAMPLE 641** was obtained. HRMS calculated for C₃₆H₃₄F₄N₆O₄S: 722.2299; found 723.2378 [(M+H)⁺ form].

▪ **3-{[1-[(3R,4R)-1-[(4-fluoro-2,3'-bithiophen-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 642)**

Using **General Procedure 9** starting from **EXAMPLE 269** and 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane as reagents, **EXAMPLE 642** was obtained. HRMS calculated for C₃₄H₃₄FN₅O₄S₂: 659.2036; found 660.2108 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({5-(2-methylpyridin-4-yl)-1,3-thiazol-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 643)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with (2-methyl-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 643**. HRMS calculated for C₃₅H₃₇N₇O₄S: 651.26276; found 652.2709 [(M+H)⁺ form].

▪ **tert-butyl [4-(2-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl)-1,3-thiazol-5-yl]pyridin-2-yl]carbamate (EXAMPLE 644)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromothiazole-2-carboxylic acid as reagents, the resulted crude product was reacted with *tert*-butyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate according to **General Procedure 9**, to give **EXAMPLE 644**. HRMS calculated for C₃₉H₄₄N₈O₆S: 752.3104; found 753.318 [(M+H)⁺ form].

▪ **tert-butyl [4-(5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-4-methyl-1,3-thiazol-2-yl)pyridin-2-yl]carbamate (EXAMPLE 645)**

Using **General Procedure 9** starting from **EXAMPLE 349** and *tert*-butyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate as reagents, **EXAMPLE 645** was obtained. HRMS calculated for C₄₀H₄₆N₈O₆S: 766.3261; found 767.3336 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[4-methyl-3,5-bis(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 646)**

and

3-[(1-{[(3R,4R)-1-{[3-chloro-4-methyl-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 647)

Using **General Procedure 9** starting from **EXAMPLE 239** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 646** and **EXAMPLE 647** were obtained and separated by chromatography.

EXAMPLE 646: HRMS calculated for C₄₃H₄₅N₇O₄S: 755.3254; found 756.3331 [(M+H)⁺ form].

EXAMPLE 647: HRMS calculated for C₃₇H₃₉ClN₆O₄S: 698.2442; found 699.253 [(M+H)⁺ form].

▪ **3-{[1-({[(3R,4R)-1-[(3-chloro-4-methyl-5-phenylthiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 648)**

Using **General Procedure 9** starting from **EXAMPLE 239** and phenylboronic acid as reagents, **EXAMPLE 648** was obtained. HRMS calculated for $C_{37}H_{38}ClN_5O_4S$: 683.2333; found 684.241 [(M+H)⁺ form].

5 ▪ **3-[(1-[(3R,4R)-1-{[3-chloro-4-methyl-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 649)**

Using **General Procedure 9** starting from **EXAMPLE 239** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 649** was obtained. HRMS calculated for $C_{36}H_{37}ClN_6O_4S$: 684.2286; found 685.2365 [(M+H)⁺ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({4-methyl-2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 650)**

Using **General Procedure 9** starting from **EXAMPLE 349** and [6-(trifluoromethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 650** was obtained. HRMS calculated for
15 $C_{36}H_{36}F_3N_7O_4S$: 719.2502; found 720.2575 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[2-(2,6-difluoropyridin-3-yl)-4-methyl-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 651)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (2,6-difluoro-3-pyridyl)boronic acid as reagents, **EXAMPLE 651** was obtained. HRMS calculated for
20 $C_{35}H_{35}F_2N_7O_4S$: 687.2440; found 688.2516 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[2-(6-fluoropyridin-3-yl)-4-methyl-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 652)**

25 Using **General Procedure 9** starting from **EXAMPLE 349** and (6-fluoro-3-pyridyl)boronic acid as reagents, **EXAMPLE 652** was obtained. HRMS calculated for $C_{35}H_{36}FN_7O_4S$: 669.25336; found 670.2603 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{3-fluoro-4-(pyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 653)

and

5 3-[(1-[(3R,4R)-1-{3-fluoro-4,5-di(pyridin-4-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 654)

Using General Procedure 9 starting from EXAMPLE 232 and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, EXAMPLE 653 (dehalogenated byproduct) and
10 EXAMPLE 654 were obtained and separated by chromatography.

EXAMPLE 653: HRMS calculated for $C_{35}H_{35}FN_6O_4S$: 654.2424; found 655.2502 [(M+H)⁺ form].

EXAMPLE 654: HRMS calculated for $C_{40}H_{38}FN_7O_4S$: 731.2690; found 732.2764 [(M+H)⁺ form].

15 ▪ 3-[(1-[(3R,4R)-1-{3-chloro-4-methyl-5-(6-methylpyridin-3-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 655)

Using General Procedure 9 starting from EXAMPLE 239 and (6-methyl-3-pyridyl)boronic acid as reagents, EXAMPLE 655 was obtained. HRMS calculated for $C_{37}H_{39}ClN_6O_4S$:
20 698.2442; found 699.2514 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-(3-chloro-4-methyl-5-[2-(trifluoromethyl)pyridin-4-yl]thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 656)

Using General Procedure 9 starting from EXAMPLE 239 and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine as reagents, EXAMPLE 656 was obtained.
25 HRMS calculated for $C_{37}H_{36}ClF_3N_6O_4S$: 752.2159; found 753.2258 [(M+H)⁺ form].

▪ tert-butyl [4-(5-{[(3R,4R)-4-(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]-1,3-thiazol-2-yl)pyridin-2-yl]carbamate (EXAMPLE 657)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with *tert*-butyl *N*-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate according to **General Procedure 9**, to give **EXAMPLE 657**. HRMS calculated for C₃₉H₄₄N₈O₆S: 752.3104; found 753.3187 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[3-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 658)**

Using **General Procedure 9** starting from **EXAMPLE 247** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 658** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2675; found 651.2767 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(pyridin-4-yl)thiophen-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 659)**

Using **General Procedure 9** starting from **EXAMPLE 247** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 659** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.2606 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[3-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 660)**

Using **General Procedure 9** starting from **EXAMPLE 247** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 660** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2675; found 651.2762 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[3-(pyridin-3-yl)thiophen-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 661)**

Using **General Procedure 9** starting from **EXAMPLE 247** and 3-pyridylboronic acid as reagents, **EXAMPLE 661** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2617 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[4-(pyridin-4-yl)-1,3-thiazol-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 662)**

Using **General Procedure 9** starting from **EXAMPLE 248** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 662** was obtained. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.2564 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-(6-methylpyridin-3-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 663)**

Using **General Procedure 9** starting from **EXAMPLE 248** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 663** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$:
15 651.26276; found 652.272 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[4-(pyridin-3-yl)-1,3-thiazol-2-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 664)**

Using **General Procedure 9** starting from **EXAMPLE 248** and 3-pyridylboronic acid as
20 reagents, **EXAMPLE 664** was obtained. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.256 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-(2-methylpyridin-4-yl)-1,3-thiazol-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 665)**

Using **General Procedure 9** starting from **EXAMPLE 248** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 665** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$:
25 651.2628; found 652.2727 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-4-yl)thiophen-3-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 666)**

Using **General Procedure 9** starting from **EXAMPLE 249** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 666** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.2601 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(6-methylpyridin-3-yl)thiophen-3-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 667)**

Using **General Procedure 9** starting from **EXAMPLE 249** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 667** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2675; found 651.2766 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(pyridin-3-yl)thiophen-3-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 668)**

Using **General Procedure 9** starting from **EXAMPLE 249** and 3-pyridylboronic acid as reagents, **EXAMPLE 668** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.26 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[5-(2-methylpyridin-4-yl)thiophen-3-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 669)**

Using **General Procedure 9** starting from **EXAMPLE 249** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 669** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2675; found 651.2756 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyridin-4-yl)thiophen-3-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 670)**

Using **General Procedure 9** starting from **EXAMPLE 250** and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 670** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_4S$: 636.2519; found 637.2615 $[(M+H)^+]$ form].

5 ▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 671**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with 3-pyridylboronic acid according to **General Procedure 9**, to give **EXAMPLE 671**. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.2542 $[(M+H)^+]$ form].

10 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(2-methylpyridin-4-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 672**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (2-methyl-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 672**. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 652.2702 $[(M+H)^+]$ form].

15 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 673**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 673**. HRMS calculated for $C_{35}H_{37}N_7O_5S$: 667.2577; found 668.2648 $[(M+H)^+]$ form].

20 ▪ 3-[(1-[(3R,4R)-1-[2-(6-aminopyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 674**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine according to **General Procedure 9**, to give **EXAMPLE 674**. HRMS calculated for $C_{34}H_{36}N_8O_4S$: 652.2580; found 327.1370 [(M+2H)²⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-[2-(trifluoromethyl)pyridin-4-yl]-1,3-thiazol-5-yl}carbonyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 675**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine according to **General Procedure 9**, to give **EXAMPLE 675**. HRMS calculated for $C_{35}H_{34}F_3N_7O_4S$: 705.2345; found 706.2403 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-({2-(3-methoxypyridin-4-yl)-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 676**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (3-methoxy-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 676**. HRMS calculated for $C_{35}H_{37}N_7O_5S$: 667.2577; found 668.2638 [(M+H)⁺ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-(thiophen-3-yl)-1,3-thiazol-5-yl}carbonyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 677**)

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 677**. HRMS calculated for $C_{33}H_{34}N_6O_4S_2$: 642.2083; found 643.2151 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 678)**

Using **General Procedure 7** starting from **Preparation R3b** and 2-bromothiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 678**. HRMS calculated for C₃₅H₃₇N₇O₄S: 651.2628; found 652.2696 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)thiophen-3-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 679)**

Using **General Procedure 9** starting from **EXAMPLE 250** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 679** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2675; found 651.277 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(pyridin-3-yl)thiophen-3-yl]carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 680)**

Using **General Procedure 9** starting from **EXAMPLE 250** and 3-pyridylboronic acid as reagents, **EXAMPLE 680** was obtained. HRMS calculated for C₃₅H₃₆N₆O₄S: 636.2519; found 637.2603 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(2-methylpyridin-4-yl)thiophen-3-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 681)**

Using **General Procedure 9** starting from **EXAMPLE 250** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 681** was obtained. HRMS calculated for C₃₆H₃₈N₆O₄S: 650.2675; found 651.2761 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[3-chloro-5-(pyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 682)**

Using **General Procedure 9** starting from **EXAMPLE 253** and 3-pyridylboronic acid as reagents, **EXAMPLE 682** was obtained. HRMS calculated for $C_{35}H_{35}ClN_6O_4S$: 670.2129; found 671.2205 $[(M+H)^+]$ form].

5 ▪ **3-[(1-[(3R,4R)-1-{3-chloro-5-(6-methylpyridin-3-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 683)**

Using **General Procedure 9** starting from **EXAMPLE 253** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 683** was obtained. HRMS calculated for $C_{36}H_{37}ClN_6O_4S$: 684.2286; found 685.2368 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-{3-chloro-5-[6-(trifluoromethyl)pyridin-3-yl]thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 684)**

Using **General Procedure 9** starting from **EXAMPLE 253** and [6-(trifluoromethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 684** was obtained. HRMS calculated for $C_{36}H_{34}ClF_3N_6O_4S$: 738.2003; found 739.2071 $[(M+H)^+]$ form].

15 ▪ **3-[(1-[(3R,4R)-1-{5-[6-(dimethylamino)pyridin-3-yl]-3-fluorothiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 685)**

Using **General Procedure 9** starting from **EXAMPLE 269** and [6-(dimethylamino)-3-pyridyl]boronic acid as reagents, **EXAMPLE 685** was obtained. HRMS calculated for $C_{37}H_{40}FN_7O_4S$: 697.2847; found 349.6491 $[(M+2H)^{2+}]$ form].

20 ▪ **3-{[1-[(3R,4R)-1-[(4-chloro-3-fluorothiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 686)**

25 Using **General Procedure 9** starting from **EXAMPLE 259** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 686** was obtained as dehalogenated byproduct. HRMS calculated for $C_{30}H_{31}ClFN_5O_4S$: 611.1769; found 612.1852 $[(M+H)^+]$ form].

▪ 3-[(1-[(3R,4R)-1-({5-[6-(cyclopropylmethoxy)pyridin-3-yl]-3-fluorothiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 687)

Using **General Procedure 9** starting from **EXAMPLE 269** and 2-(cyclopropylmethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 687** was obtained. HRMS calculated for $C_{39}H_{41}FN_6O_5S$: 724.2843; found 363.1484 [(M+2H)²⁺ form].

▪ 3-[(1-[(3R,4R)-1-({5-(6-ethoxypyridin-3-yl)-3-fluorothiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 688)

Using **General Procedure 9** starting from **EXAMPLE 269** and (6-ethoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 688** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_5S$: 698.2687; found 350.1408 [(M+2H)²⁺ form].

▪ 3-[(1-[(3R,4R)-1-({4-chloro-3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 689)

Using **General Procedure 9** starting from **EXAMPLE 259** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 689** was obtained. HRMS calculated for $C_{36}H_{36}ClFN_6O_4S$: 702.2191; found 703.2265 [(M+H)⁺ form].

▪ 5-(4-fluoro-5-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}thiophen-2-yl)pyridine-2-carbonitrile (EXAMPLE 690)

Using **General Procedure 9** starting from **EXAMPLE 269** and (6-cyano-3-pyridyl)boronic acid as reagents, **EXAMPLE 690** was obtained. HRMS calculated for $C_{36}H_{34}FN_7O_4S$: 679.2377; found 680.2461 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-({3-chloro-5-(2-methylpyridin-4-yl)thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 691)

Using **General Procedure 9** starting from **EXAMPLE 253** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 691** was obtained. HRMS calculated for $C_{36}H_{37}ClN_6O_4S$: 684.2286; found 685.2357 [(M+H)⁺ form].

5 ▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-4-methyl-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 692)**

Using **General Procedure 9** starting from **EXAMPLE 261** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 692** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_4S$: 682.2737; found 683.2826 [(M+H)⁺ form].

10 ▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-4-methyl-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 693)**

Using **General Procedure 9** starting from **EXAMPLE 261** and (2-methyl-4-pyridyl)boronic acid as reagents, **EXAMPLE 693** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_4S$:
15 682.2737; found 683.2816 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[4-cyclopropyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 694)**

Using **General Procedure 9** starting from **EXAMPLE 263** and cyclopropyl boronic acid as
20 reagents, **EXAMPLE 694** was obtained. HRMS calculated for $C_{38}H_{41}N_7O_4S$: 691.2941; found 692.3038 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methoxypyridin-3-yl)-4-methylthiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 695)**

25 Using **General Procedure 9** starting from **EXAMPLE 261** and (6-methoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 695** was obtained. HRMS calculated for $C_{37}H_{39}FN_6O_5S$: 698.2687; found 350.1423 [(M+2H)²⁺ form].

▪ 3-[(1-[(3R,4R)-1-(3-fluoro-4-methyl-5-[6-(trifluoromethyl)pyridin-3-yl]thiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 696)

Using **General Procedure 9** starting from **EXAMPLE 261** and [6-(trifluoromethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 696** was obtained. HRMS calculated for $C_{37}H_{36}F_4N_6O_4S$: 736.2455; found 737.2549 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-{3-fluoro-5-(imidazo[1,2-a]pyridin-7-yl)thiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 697)

Using **General Procedure 9** starting from **EXAMPLE 269** and imidazo[1,2-a]pyridin-7-ylboronic acid as reagents, **EXAMPLE 697** was obtained. HRMS calculated for $C_{37}H_{36}FN_7O_4S$: 693.2534; found 694.2616 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-(2-[6-(dimethylamino)pyridin-3-yl]-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 698)

Using **General Procedure 9** starting from **EXAMPLE 349** and [6-(dimethylamino)-3-pyridyl]boronic acid as reagents, **EXAMPLE 698** was obtained. HRMS calculated for $C_{37}H_{42}N_8O_4S$: 694.3050; found 695.3133 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-(3-fluoro-5-[6-(piperazin-1-yl)pyridin-3-yl]thiophen-2-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 699)

Using **General Procedure 9** starting from **EXAMPLE 269** and 1-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]piperazine as reagents, **EXAMPLE 699** was obtained. HRMS calculated for $C_{39}H_{43}FN_8O_4S$: 738.3112; found 739.3183 [(M+H)⁺ form].

▪ 3-[(1-[(3R,4R)-1-(2-[6-(cyclopropylmethoxy)pyridin-3-yl]-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 700)

Using **General Procedure 9** starting from **EXAMPLE 349** and 2-(cyclopropylmethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 700** was obtained. HRMS calculated for $C_{39}H_{43}N_7O_5S$: 721.3046; found 722.3118 $[(M+H)^+]$ form].

5 ▪ **5-(5-([(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl)-4-methyl-1,3-thiazol-2-yl)pyridine-2-carbonitrile (EXAMPLE 701)**

Using **General Procedure 9** starting from **EXAMPLE 349** and (6-cyano-3-pyridyl)boronic acid as reagents, **EXAMPLE 701** was obtained. HRMS calculated for $C_{36}H_{36}N_8O_4S$: 676.2580; found 677.2649 $[(M+H)^+]$ form].

10 ▪ **3-[(4-hydroxy-1-([(3R,4R)-1-({4-(methoxymethyl)-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 702)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-(methoxymethyl)thiophene-2-carboxylic acid as reagents, the resulted crude product was
15 reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 702**. HRMS calculated for $C_{38}H_{42}N_6O_5S$: 694.2938; found 695.302 $[(M+H)^+]$ form].

20 ▪ **3-[(4-hydroxy-1-([(3R,4R)-1-({4-(methoxymethyl)-5-(2-methylpyridin-4-yl)thiophen-2-yl]carbonyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 703)**

Using **General Procedure 7** starting from **Preparation R3b** and 5-bromo-4-(methoxymethyl)thiophene-2-carboxylic acid as reagents. The resulted crude product was
25 reacted with (2-methyl-4-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 703**. HRMS calculated for $C_{38}H_{42}N_6O_5S$: 694.2938; found 695.3030 $[(M+H)^+]$ form].

▪ **3-[(1-([(3R,4R)-1-({3-fluoro-5-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 704)**

Using **General Procedure 9** starting from **EXAMPLE 269** and [6-(2,2,2-trifluoroethoxy)-3-pyridyl]boronic acid as reagents, **EXAMPLE 704** was obtained. HRMS calculated for $C_{37}H_{36}F_4N_6O_5S$: 752.2404; found 753.2476 $[(M+H)^+]$ form].

5 ▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-5-(3-methyl-3H-imidazo[4,5-b]pyridin-6-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 705)**

Using **General Procedure 9** starting from **EXAMPLE 269** and 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[4,5-b]pyridine as reagents, **EXAMPLE 705** was obtained. HRMS calculated for $C_{37}H_{37}FN_8O_4S$: 708.2642; found 709.2708 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-{[4-ethyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 706)**

Using **General Procedure 9** starting from **EXAMPLE 263** and potassium ethyltrifluoroborate as reagents, **EXAMPLE 706** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_4S$: 679.2941; found 680.3022 $[(M+H)^+]$ form].

15 ▪ **3-[(1-[(3R,4R)-1-{[4-(dimethylamino)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 707)**

20 and

3-[(1-[(3R,4R)-1-{[4-(dimethylamino)-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 708)

Using **General Procedure 9** starting from **EXAMPLE 275** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 707** (dehalogenated byproduct) and **EXAMPLE 708** were obtained and separated by chromatography.

25 **EXAMPLE 707**: HRMS calculated for $C_{32}H_{38}N_6O_4S$: 602.2675; found 603.2751 $[(M+H)^+]$ form].

EXAMPLE 708: HRMS calculated for $C_{38}H_{43}N_7O_4S$: 693.3098; found 694.3175 $[(M+H)^+]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methoxy-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 709)**

Using **General Procedure 9** starting from **EXAMPLE 276** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 709** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_5S$: 680.2781; found 681.2860 $[(M+H)^+]$ form].

10 ▪ **3-[(1-[(3R,4R)-1-[4-bromo-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 710)**

and

15 ▪ **3-[(1-[(3R,4R)-1-[4,5-bis(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 711)**

Using **General Procedure 9** starting from **EXAMPLE 277** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 710** and **EXAMPLE 711** were obtained and separated by chromatography.

20 **EXAMPLE 710:** HRMS calculated for $C_{36}H_{37}N_6O_4SBr$: 728.1780; found 729.1856 $[(M+H)^+]$ form].

EXAMPLE 711: HRMS calculated for $C_{42}H_{43}N_7O_4S$: 741.3098; found 742.3166 $[(M+H)^+]$ form].

25 ▪ **methyl 3-[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]-5-(6-methylpyridin-3-yl)benzoate (EXAMPLE 712)**

Using **General Procedure 9** starting from **EXAMPLE 287** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 712** was obtained. HRMS calculated for $C_{40}H_{42}N_6O_6$: 702.3166; found 703.323 $[(M+H)^+]$ form].

▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 713)**

Using **General Procedure 9** starting from **EXAMPLE 269** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 713** was obtained. HRMS calculated for $C_{36}H_{37}FN_6O_4S$: 668.2581; found 669.2661 [(M+H)⁺ form].

▪ **5-[5-((3R,4R)-4-[(4-{[7-(3-chlorophenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl]methyl}-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile (EXAMPLE 714)**

Using **General Procedure 9** starting from **EXAMPLE 87** and (6-cyano-3-pyridyl)boronic acid as reagents, **EXAMPLE 714** was obtained. HRMS calculated for $C_{40}H_{37}ClN_8O_3S$: 744.2398; found 745.2479 [(M+H)⁺ form].

▪ **7-(3-chlorophenyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 715)**

Using **General Procedure 9** starting from **EXAMPLE 87** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 715** was obtained. HRMS calculated for $C_{40}H_{40}ClN_7O_3S$: 733.2602; found 734.2693 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[2-(thiophen-2-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 716)**

Using **General Procedure 9** starting from **EXAMPLE 95** and 2-thienylboronic acid as reagents, **EXAMPLE 716** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_4S_2$: 720.2552; found 721.2616 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[2-(pyrimidin-5-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 717)**

Using **General Procedure 9** starting from **EXAMPLE 95** and pyrimidin-5-ylboronic acid as reagents, **EXAMPLE 717** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_4S$: 716.2893; found 717.2989 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(1-methyl-1H-pyrazol-5-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 718)**

Using **General Procedure 9** starting from **EXAMPLE 95** and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 718** was obtained. HRMS calculated for $C_{39}H_{42}N_8O_4S$: 718.3050; found 719.3109 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(1-methyl-1H-pyrazol-4-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 719)**

Using **General Procedure 9** starting from **EXAMPLE 95** and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 719** was obtained.
15 HRMS calculated for $C_{39}H_{42}N_8O_4S$: 718.3050; found 719.3087 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(1-methyl-1H-pyrrol-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 720)**

Using **General Procedure 9** starting from **EXAMPLE 95** and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole as reagents, **EXAMPLE 720** was obtained.
20 HRMS calculated for $C_{40}H_{43}N_7O_4S$: 717.3098; found 718.3169 $[(M+H)^+ \text{ form}]$.

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-{[2-(thiophen-3-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 721)**

25 Using **General Procedure 9** starting from **EXAMPLE 95** and 4,4,5,5-tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane as reagents, **EXAMPLE 721** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_4S_2$: 720.2552; found 721.2639 $[(M+H)^+ \text{ form}]$.

▪ **3-[(1-[(3R,4R)-1-{2-(furan-3-yl)-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 722)**

Using **General Procedure 9** starting from **EXAMPLE 95** and 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as reagents, **EXAMPLE 722** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_5S$: 704.2781; found 705.2823 $[(M+H)^+$ form].

▪ **3-[(1-[(3R,4R)-1-{2-(furan-2-yl)-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 723)**

Using **General Procedure 9** starting from **EXAMPLE 95** and 2-furylboronic acid as reagents, **EXAMPLE 723** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_5S$: 704.2781; found 705.2846 $[(M+H)^+$ form].

▪ **5-[5-((3R,4R)-4-[(4-hydroxy-4-{7-(3-methoxyphenyl)-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl}methyl)piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl]pyridine-2-carbonitrile (EXAMPLE 724)**

Using **General Procedure 9** starting from **EXAMPLE 95** and (6-cyano-3-pyridyl)boronic acid as reagents, **EXAMPLE 724** was obtained. HRMS calculated for $C_{41}H_{40}N_8O_4S$: 740.2893; found 741.2958 $[(M+H)^+$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 725)**

Using **General Procedure 9** starting from **EXAMPLE 95** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 725** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_4S$: 729.3098; found 365.6635 $[(M+2H)^{2+}$ form].

▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(6'-methyl-3,3'-bipyridin-5-yl)carbonyl]-3-phenylpiperidin-4-yl)carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 726)**

Using **General Procedure 9** starting from **EXAMPLE 303** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 726** was obtained. HRMS calculated for $C_{42}H_{41}N_7O_4$: 707.3220; found 708.329 [(M+H)⁺ form].

5 ▪ **3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 727)**

Using **General Procedure 7** starting from **Preparation R3bu** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 727**. HRMS calculated for $C_{41}H_{39}FN_6O_4S$: 730.2737; found 731.2812 [(M+H)⁺ form].

10 ▪ **3-{[1-[(3R,4R)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 728)**

Using **General Procedure 7** starting from **Preparation R3bu** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 728** was obtained. HRMS calculated for $C_{35}H_{35}N_6O_4SBr$: 714.1624; found 715.1701 [(M+H)⁺ form].

15 ▪ **5-(5-{[(3R,4R)-4-[(4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl]-3-phenylpiperidin-1-yl]carbonyl}-4-methyl-1,3-thiazol-2-yl)pyridine-2-carbonitrile (EXAMPLE 729)**

20 Using **General Procedure 9** starting from **EXAMPLE 728** and (6-cyano-3-pyridyl)boronic acid as reagents, **EXAMPLE 729** was obtained. HRMS calculated for $C_{41}H_{38}N_8O_4S$: 738.2737; found 739.2816 [(M+H)⁺ form].

25 ▪ **3-[(1-[(3R,4R)-1-[(2-[6-(dimethylamino)pyridin-3-yl]-4-methyl-1,3-thiazol-5-yl]carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 730)**

Using **General Procedure 9** starting from **EXAMPLE 728** and [6-(dimethylamino)-3-pyridyl]boronic acid as reagents, **EXAMPLE 730** was obtained. HRMS calculated for $C_{42}H_{44}N_8O_4S$: 756.3206; found 757.3285 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({4-methyl-2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 731)**

Using **General Procedure 9** starting from **EXAMPLE 728** and [6-(trifluoromethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 731** was obtained. HRMS calculated for $C_{41}H_{38}F_3N_7O_4S$: 781.2658; found 782.2735 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 732)**

Using **General Procedure 9** starting from **EXAMPLE 103** and [6-(dimethylamino)-3-pyridyl]boronic acid as reagents, **EXAMPLE 732** was obtained. HRMS calculated for $C_{41}H_{44}N_8O_3S$: 728.3257; found 365.1688 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 733)**

Using **General Procedure 9** starting from **EXAMPLE 103** and (6-methoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 733** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 358.6536 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({2-(6-methoxypyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 734)**

Using **General Procedure 9** starting from **EXAMPLE 728** and (6-methoxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 734** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 744.2969 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({2-[6-(morpholin-4-yl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 735)**

Using **General Procedure 9** starting from **EXAMPLE 103** and (6-morpholino-3-pyridyl)boronic acid as reagents, **EXAMPLE 735** was obtained. HRMS calculated for $C_{43}H_{46}N_8O_4S$: 770.3362; found 386.1758 $[(M+2H)^{2+}]$ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 736)**

Using **General Procedure 9** starting from **EXAMPLE 103** and [6-(trifluoromethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 736** was obtained. HRMS calculated for $C_{40}H_{38}F_3N_7O_3S$: 753.2709; found 754.2786 $[(M+H)^+]$ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-({2-[6-(piperazin-1-yl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 737)**

Using **General Procedure 9** starting from **EXAMPLE 103** and 1-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]piperazine as reagents, **EXAMPLE 737** was obtained.
15 HRMS calculated for $C_{43}H_{47}N_9O_3S$: 769.3522; found 770.3601 $[(M+H)^+]$ form].

▪ **5-(5-[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl)pyridine-2-carbonitrile (EXAMPLE 738)**

Using **General Procedure 9** starting from **EXAMPLE 103** and (6-cyano-3-pyridyl)boronic
20 acid as reagents, **EXAMPLE 738** was obtained. HRMS calculated for $C_{40}H_{38}N_8O_3S$: 710.2787; found 711.2881 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({2-[6-(hydroxymethyl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 739)**

25 Using **General Procedure 9** starting from **EXAMPLE 103** and [6-(hydroxymethyl)-3-pyridyl]boronic acid as reagents, **EXAMPLE 739** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 716.3019 $[(M+H)^+]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[[2-(3-methyl-3H-imidazo[4,5-b]pyridin-6-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 740)**

Using **General Procedure 9** starting from **EXAMPLE 103** and 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[4,5-b]pyridine as reagents, **EXAMPLE 740** was obtained. HRMS calculated for $C_{41}H_{41}N_9O_3S$: 739.3053; found 370.6594 [(M+2H)²⁺ form].

▪ **3-[(1-[(3R,4R)-1-[[2-(5-fluoro-6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 741)**

Using **General Procedure 9** starting from **EXAMPLE 103** and (5-fluoro-6-hydroxy-3-pyridyl)boronic acid as reagents, **EXAMPLE 741** was obtained. HRMS calculated for $C_{39}H_{38}FN_7O_4S$: 719.2690; found 720.2742 [(M+H)⁺ form].

▪ **5-(5-[(3R,4R)-4-((4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl)carbonyl)-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl)pyridine-3-carboxamide (EXAMPLE 742)**

Using **General Procedure 9** starting from **EXAMPLE 103** and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-carboxamide as reagents, **EXAMPLE 742** was obtained. HRMS calculated for $C_{40}H_{40}N_8O_4S$: 728.2893; found 729.296 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-((2-[5-(hydroxymethyl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 743)**

Using **General Procedure 9** starting from **EXAMPLE 103** and [5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-pyridyl]methanol as reagents, **EXAMPLE 743** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 358.6526 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-((2-[6-(tetrahydro-2H-pyran-4-yloxy)pyridin-3-yl]-1,3-thiazol-5-yl)methyl)piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 744)**

Using **General Procedure 9** starting from **EXAMPLE 103** and 2-tetrahydropyran-4-yloxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 744** was obtained. HRMS calculated for $C_{44}H_{47}N_7O_5S$: 785.3359; found 393.6745 $[(M+2H)^{2+}$ form].

5 ▪ **3-[(1-[(3R,4R)-1-{2-(5-amino-6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 745)**

Using **General Procedure 9** starting from **EXAMPLE 103** and 2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-amine as reagents, **EXAMPLE 745** was
10 obtained. HRMS calculated for $C_{40}H_{42}N_8O_4S$: 730.3050; found 366.1585 $[(M+2H)^{2+}$ form].

▪ **methyl 5-(5-[(3R,4R)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl)pyridine-2-carboxylate (EXAMPLE 746)**

15 Using **General Procedure 9** starting from **EXAMPLE 103** and methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carboxylate as reagents, **EXAMPLE 746** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 744.2954 $[(M+H)^{+}$ form].

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-({2-[6-(2-methoxyethoxy)pyridin-3-yl]-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 747)**

Using **General Procedure 9** starting from **EXAMPLE 103** and 2-(2-methoxyethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine as reagents, **EXAMPLE 747** was obtained. HRMS calculated for $C_{42}H_{45}N_7O_5S$: 759.3203; found 760.3268 $[(M+H)^{+}$ form].

25 ▪ **3-{[4-hydroxy-1-[(3R,4R)-1-[(2-{6-[(2-methoxyethyl)amino]pyridin-3-yl}-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 748)**

Using **General Procedure 9** starting from **EXAMPLE 103** and *N*-(2-methoxyethyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine as reagents, **EXAMPLE 748** was obtained. HRMS calculated for C₄₂H₄₆N₈O₄S: 758.3362; found 380.1717 [(M+2H)²⁺ form].

5 ▪ **3-{[4-hydroxy-1-((3R,4R)-1-[(6'-methyl-2,3'-bipyridin-4-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 749)**

Using **General Procedure 9** starting from **EXAMPLE 302** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 749** was obtained. HRMS calculated for C₄₂H₄₁N₇O₄S: 707.3220; found 708.3294 [(M+H)⁺ form].

10 ▪ **3-[(4-hydroxy-1-((3R,4R)-1-[[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 750)**

Using **General Procedure 9** starting from **EXAMPLE 728** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 750** was obtained. HRMS calculated for C₄₁H₄₁N₇O₄S: 727.2941; found 728.3013 [(M+H)⁺ form].

15 ▪ **3-[(4-hydroxy-1-((3R,4R)-1-[[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 751)**

20 Using **General Procedure 9** starting from **EXAMPLE 103** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 751** was obtained. HRMS calculated for C₄₀H₄₁N₇O₃S: 699.2991; found 350.6573 [(M+2H)²⁺ form].

25 ▪ **7-ethyl-3-[(4-hydroxy-1-((3R,4R)-1-[[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 752)**

Using **General Procedure 7** starting from **Preparation R3c** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give

EXAMPLE 752. HRMS calculated for $C_{37}H_{41}N_7O_4S$: 679.2941; found 680.3014 $[(M+H)^+$ form].

5 ▪ **3-[(1-{[(3R,4R)-1-{2-(6-aminopyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-ethyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 753)**

Using **General Procedure 7** starting from **Preparation R3c** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine according to **General Procedure 9**, to give **EXAMPLE 753**. HRMS calculated for $C_{36}H_{40}N_8O_4S$: 680.2893; found 341.1534 $[(M+2H)^{2+}$ form].

10 ▪ **7-ethyl-3-[(4-hydroxy-1-{[(3R,4R)-1-({4-methyl-2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl}carbonyl)-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 754)**

Using **General Procedure 7** starting from **Preparation R3c** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with [6-(trifluoromethyl)-3-pyridyl]boronic acid according to **General Procedure 9**, to give **EXAMPLE 754**. HRMS calculated for $C_{37}H_{38}N_7O_4F_3S$: 733.2658; found 734.2738 $[(M+H)^+$ form].

15 ▪ **7-ethyl-3-[(4-hydroxy-1-{[(3R,4R)-1-{2-(6-methoxypyridin-3-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl}carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 755)**

Using **General Procedure 7** starting from **Preparation R3c** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methoxy-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 755**. HRMS calculated for $C_{37}H_{41}N_7O_5S$: 695.2890; found 696.2959 $[(M+H)^+$ form].

▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(pyridin-4-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 756)

Using **General Procedure 7** starting from **Preparation R3cd** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 756**. HRMS calculated for $C_{40}H_{40}N_8O_4S$: 728.2893; found 729.2971 [(M+H)⁺ form].

▪ 7-cyclopropyl-3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 757)

Using **General Procedure 6** starting from **Preparation R3g** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 757**. HRMS calculated for $C_{37}H_{41}N_7O_3S$: 663.2991; found 332.6581 [(M+2H)²⁺ form].

▪ 7-cyclopropyl-3-[(1-[(3R,4R)-1-({3-fluoro-5-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]thiophen-2-yl}carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 758)

Using **General Procedure 7** starting from **Preparation R3g** and **Preparation R1g** as reagents, the resulted crude product was reacted with [6-(2,2,2-trifluoroethoxy)-3-pyridyl]boronic acid according to **General Procedure 9**, to give **EXAMPLE 758**. HRMS calculated for $C_{39}H_{38}F_4N_6O_5S$: 778.256; found 779.2595 [(M+H)⁺ form].

▪ 7-cyclobutyl-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 759)

Using **General Procedure 7** starting from **Preparation R3h** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 759**. HRMS calculated for $C_{39}H_{43}N_7O_4S$: 705.3098; found 706.3173 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(2-methylpropyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 760)**

Using **General Procedure 6** starting from **Preparation R3n** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 760**. HRMS calculated for C₃₉H₄₅N₇O₄S: 707.3254; found 708.3342 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(2-methylpropyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 761)**

Using **General Procedure 7** starting from **Preparation R3n** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 761**. HRMS calculated for C₃₉H₄₃FN₆O₄S: 710.3051; found 711.3123 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(2,2,2-trifluoroethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 762)**

Using **General Procedure 7** starting from **Preparation R3o** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, **EXAMPLE 762** was obtained. HRMS calculated for C₃₁H₃₂BrF₃N₆O₄S: 720.1341; found 721.1421 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(2,2,2-trifluoroethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 763)**

Using **General Procedure 9** starting from **EXAMPLE 340** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 763** was obtained. HRMS calculated for C₃₇H₃₆F₄N₆O₄S: 736.2455; found 737.253 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(2,2,2-trifluoroethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 764)**

Using **General Procedure 9** starting from **EXAMPLE 762** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 764** was obtained. HRMS calculated for $C_{37}H_{38}F_3N_7O_4S$: 733.2658; found 734.274 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(2,2,2-trifluoroethyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 765)**

Using **General Procedure 9** starting from **EXAMPLE 143** and (6-methyl-3-pyridyl)boronic acid as reagents, **EXAMPLE 765** was obtained. HRMS calculated for $C_{36}H_{38}N_7O_3F_3S$: 705.2709; found 706.2759 [(M+H)⁺ form].

▪ **7-(2,2-difluoroethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 766)**

Using **General Procedure 7** starting from **Preparation R3p** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 766**. HRMS calculated for $C_{37}H_{39}F_2N_7O_4S$: 715.2752; found 716.2836 [(M+H)⁺ form].

▪ **7-(cyclopropylmethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 767)**

Using **General Procedure 7** starting from **Preparation R3q** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 767**. HRMS calculated for $C_{39}H_{43}N_7O_4S$: 705.3098; found 353.6637 [(M+2H)²⁺ form].

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▪ 7-[3-(dimethylamino)propyl]-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 768)

Using **General Procedure 7** starting from **Preparation R3t** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 768**. HRMS calculated for $C_{40}H_{46}FN_7O_4S$: 739.3316; found 370.6742 [(M+2H)²⁺ form].

▪ 7-(2-fluoroethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 769)

Using **General Procedure 7** starting from **Preparation R3u** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 769**. HRMS calculated for $C_{37}H_{40}FN_7O_4S$: 697.2847; found 698.2920 [(M+H)⁺ form].

▪ 7-[2-(dimethylamino)ethyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 770)

Using **General Procedure 7** starting from **Preparation R3v** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 770**. HRMS calculated for $C_{39}H_{46}N_8O_4S$: 722.3362; found 362.1756 [(M+2H)²⁺ form].

▪ 7-[2-(dimethylamino)ethyl]-3-[(1-[(3R,4R)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 771)

Using **General Procedure 7** starting from **Preparation R3v** and **Preparation R1g** as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid

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according to **General Procedure 9**, to give **EXAMPLE 771**. HRMS calculated for $C_{39}H_{44}FN_7O_4S$: 725.3160; found 363.6647 $[(M+2H)^{2+}]$ form].

5 ▪ **7-[2-(dimethylamino)ethyl]-3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 772)**

Using **General Procedure 6** starting from **Preparation R3v** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude product was reacted with (6-methyl-3-pyridyl)boronic acid **General Procedure 9**, to give **EXAMPLE 772**. HRMS calculated for $C_{38}H_{46}N_8O_3S$: 694.3414; found 348.1773 $[(M+2H)^{2+}]$ form].

10 ▪ **7-(2-hydroxyethyl)-3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 773)**

Using **General Procedure 7** starting from **Preparation R3w** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude product was reacted with
15 (6-methyl-3-pyridyl)boronic acid according to **General Procedure 9**, to give **EXAMPLE 773**. HRMS calculated for $C_{37}H_{41}N_7O_5S$: 695.2890; found 696.2960 $[(M+H)^+]$ form].

20 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 774)**

Using **General Procedure 10** starting from **EXAMPLE 160** and boron-tribromide as reagents, **EXAMPLE 774** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 744.2970 $[(M+H)^+]$ form].

25 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 775)**

Using **General Procedure 10** starting from **EXAMPLE 61** and boron-tribromide as reagents, **EXAMPLE 775** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 358.6539 $[(M+2H)^{2+}]$ form].

5 ▪ 3-[(4-hydroxy-1-[(3R,4R)-1-[[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 776**)

and

10 3-[(4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 777**)

Using **General Procedure 10** starting from **EXAMPLE 62** and boron-tribromide as reagents, **EXAMPLE 776** and **EXAMPLE 777** were obtained and separated by chromatography.

15 **EXAMPLE 776**: HRMS calculated for $C_{39}H_{39}N_7O_5S$: 717.2733; found 718.2818 $[(M+H)^+]$ form].

EXAMPLE 777: HRMS calculated for $C_{40}H_{41}N_7O_5S$: 731.2890; found 732.2963 $[(M+H)^+]$ form].

20 ▪ 3-[(1-[(3R,4R)-1-[[5-(2-aminopyridin-4-yl)-3-methylthiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 778**)

Using **General Procedure 14** starting from **EXAMPLE 402** as reactant, **EXAMPLE 778** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 333.6468 $[(M+2H)^{2+}]$ form].

25 ▪ 3-[(1-[(3R,4R)-1-[[4-amino-5-(pyridin-4-yl)thiophen-2-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 779**)

Using **General Procedure 12** starting from **EXAMPLE 185** as reactant, **EXAMPLE 779** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_4S$: 651.2628; found 326.6382 $[(M+2H)^{2+}]$ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-3-phenyl-1-(1,2,3,4-tetrahydroisoquinolin-6-ylcarbonyl)piperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 780)**

Using **General Procedure 14** starting from **EXAMPLE 192** as reactant, **EXAMPLE 780** was obtained. HRMS calculated for $C_{35}H_{40}N_6O_4$: 608.3111; found 305.1639 $[(M+2H)^{2+}]$ form].

▪ **N-(3-[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]phenyl)acetamide (EXAMPLE 781)**

Using **General Procedure 7** starting from **EXAMPLE 512** and acetic acid as reagents, **EXAMPLE 781** was obtained. HRMS calculated for $C_{34}H_{38}N_6O_5$: 610.2903; found 611.2989 $[(M+H)^+]$ form].

▪ **N-(3-[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]phenyl)benzamide (EXAMPLE 782)**

Using **General Procedure 7** starting from **EXAMPLE 512** and benzoic acid as reagents, **EXAMPLE 782** was obtained. HRMS calculated for $C_{39}H_{40}N_6O_5$: 672.30603; found 673.3148 $[(M+H)^+]$ form].

▪ **tert-butyl (2-bromo-5-[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}thiophen-3-yl)carbamate (EXAMPLE 783)**

Using **General Procedure 7** starting from **Preparation R3b** and **Preparation R1o** as reagents, **EXAMPLE 783** was obtained. HRMS calculated for $C_{35}H_{41}BrN_6O_6S$: 752.1992; found 753.2074 $[(M+H)^+]$ form].

▪ **2-chloro-N-(3-[(3R,4R)-4-[(4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl]phenyl)acetamide (EXAMPLE 784)**

EXAMPLE 512 (100 mg, 0.176 mmol), and chloroacetyl chloride (17 μ l, 24 mg, 0.21 mmol) and potassium-carbonate (73 mg, 0.527 mmol) were stirred in DMF (2 ml) at r.t. for 3 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 784**. HRMS calculated for $\text{C}_{34}\text{H}_{37}\text{ClN}_6\text{O}_5$: 644.2514; found 645.2606 [(M+H)⁺ form].

▪ **N-(3-[[[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}phenyl)prop-2-enamide (EXAMPLE 785)**

Using **General Procedure 7** starting from **EXAMPLE 512** and acrylic acid as reagents, **EXAMPLE 785** was obtained. HRMS calculated for $\text{C}_{35}\text{H}_{38}\text{N}_6\text{O}_5$: 622.2903; found 623.2988 [(M+H)⁺ form].

▪ **3-[(1-[[[(3R,4R)-1-{5-(2-aminopyridin-4-yl)-3-fluorothiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 786)**

Using **General Procedure 14** starting from **EXAMPLE 628** as reactant, **EXAMPLE 786** was obtained. HRMS calculated for $\text{C}_{35}\text{H}_{36}\text{FN}_7\text{O}_4\text{S}$: 669.2534; found 335.6337 [(M+2H)²⁺ form].

▪ **3-[(1-[[[(3R,4R)-1-{5-(2-aminopyridin-4-yl)thiophen-2-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 787)**

Using **General Procedure 14** starting from **EXAMPLE 392** as reactant, **EXAMPLE 787** was obtained. HRMS calculated for $\text{C}_{35}\text{H}_{39}\text{N}_7\text{O}_3\text{S}$: 637.2835; found 319.6503 [(M+2H)²⁺ form].

▪ **3-[(4-hydroxy-1-[[[(3R,4R)-3-phenyl-1-(1,2,3,4-tetrahydroquinolin-7-yl)carbonyl]piperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 788)**

Using **General Procedure 14** starting from **EXAMPLE 245** as reactant, **EXAMPLE 788** was obtained. HRMS calculated for $\text{C}_{35}\text{H}_{40}\text{N}_6\text{O}_4$: 608.3111; found 609.3200 [(M+H)⁺ form].

▪ **3-[(1-[(3R,4R)-1-{5-(2-aminopyridin-4-yl)-1,3-thiazol-2-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 789)**

Using **General Procedure 14** starting from **EXAMPLE 644** as reactant, **EXAMPLE 789** was
5 obtained. HRMS calculated for $C_{34}H_{36}N_8O_4S$: 652.2580; found 327.137 [(M+2H)²⁺ form].

▪ **3-[(1-[(3R,4R)-1-{2-(2-aminopyridin-4-yl)-4-methyl-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 790)**

Using **General Procedure 14** starting from **EXAMPLE 645** as reactant, **EXAMPLE 790** was
10 obtained. HRMS calculated for $C_{35}H_{38}N_8O_4S$: 666.2737; found 334.1454 [(M+2H)²⁺ form].

▪ **3-[(1-[(3R,4R)-1-{5-(2-aminopyridin-4-yl)-4-methylthiophen-2-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 791)**

Using **General Procedure 14** starting from **EXAMPLE 398** as reactant, **EXAMPLE 791** was
15 obtained. HRMS calculated for $C_{36}H_{39}N_7O_4S$: 665.2784; found 333.6473 [(M+2H)²⁺ form].

▪ **3-[(1-[(3R,4R)-1-{2-(2-aminopyridin-4-yl)-1,3-thiazol-5-yl}carbonyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 792)**

Using **General Procedure 14** starting from **EXAMPLE 657** as reactant, **EXAMPLE 792** was
20 obtained. HRMS calculated for $C_{34}H_{36}N_8O_4S$: 652.2580; found 653.2646 [(M+H)⁺ form].

▪ **3-{[1-((3R,4R)-1-[4-(aminomethyl)benzoyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 793)**

Using **General Procedure 14** starting from **EXAMPLE 252** as reactant, **EXAMPLE 793** was
25 obtained. HRMS calculated for $C_{33}H_{38}N_6O_4$: 582.2955; found 292.1560 [(M+2H)²⁺ form].

▪ **N-(4-{{(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl}carbonyl}benzyl)prop-2-enamide (EXAMPLE 794)**

Using **General Procedure 7** starting from **EXAMPLE 793** and acrylic acid as reagents,
5 **EXAMPLE 794** was obtained. HRMS calculated for $C_{36}H_{40}N_6O_5$: 636.3060; found 637.3134 [(M+H)⁺ form].

▪ **3-{{[1-{{(3R,4R)-1-[(1-acryloyl-1,2,3,4-tetrahydroquinolin-7-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 795)**

10 Using **General Procedure 7** starting from **EXAMPLE 788** and acrylic acid as reagents, **EXAMPLE 795** was obtained. HRMS calculated for $C_{38}H_{42}N_6O_5$: 662.3217; found 663.3297 [(M+H)⁺ form].

▪ **3-{{(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl}carbonyl}benzamide (EXAMPLE 796)**

15 The mixture of **EXAMPLE 208** (0.23 mmol), acetaldoxime (141 μ l, 137 mg, 2.3 mmol, 10 eq.), and copper(II)-chloride-treated molecular sieve (4Å, 50 mg) was stirred in MeOH (2 ml) for 5 hours at 60 °C. The reaction mixture was filtered, the filtrate was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 796**. HRMS calculated for $C_{33}H_{36}N_6O_5$: 596.2747; found
20 597.283 [(M+H)⁺ form].

▪ **3-{{(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl}carbonyl}benzoic acid (EXAMPLE 797)**

25 The mixture of **EXAMPLE 260** (0.66 mmol), hydrochloric acid (aq. 1 N, 1.33 ml, 2 eq.) in MeCN (2 ml) was stirred at 80 °C for 4 hours. The reaction mixture was injected to preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN,

gradient) to give **EXAMPLE 797**. HRMS calculated for $C_{33}H_{35}N_5O_6$: 597.2587; found 598.2659 [(M+H)⁺ form].

5 ▪ **3-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-N-methylbenzamide (EXAMPLE 798)**

Using **General Procedure 7** starting from **EXAMPLE 797** as carboxylic acid reactant and methylamine hydrochloride as amine reactant, **EXAMPLE 798** was obtained. HRMS calculated for $C_{34}H_{38}N_6O_5$: 610.2903; found 611.2978 [(M+H)⁺ form].

10 ▪ **3-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-N,N-dimethylbenzamide (EXAMPLE 799)**

Using **General Procedure 7** starting from **EXAMPLE 797** as carboxylic acid reactant and dimethylamine hydrochloride as amine reactant, **EXAMPLE 799** was obtained. HRMS calculated for $C_{35}H_{40}N_6O_5$: 624.3060; found 625.3139 [(M+H)⁺ form].

15 ▪ **3-{[4-hydroxy-1-({(3R,4R)-1-[3-(morpholin-4-ylcarbonyl)benzoyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl]methyl}-7-methyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 800)**

Using **General Procedure 7** starting from **EXAMPLE 797** as carboxylic acid reactant and morpholine as amine reactant, **EXAMPLE 800** was obtained. HRMS calculated for $C_{37}H_{42}N_6O_6$: 666.3166; found 334.1668 [(M+2H)²⁺ form].

20 ▪ **5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-2-(6-methylpyridin-3-yl)-1,3-thiazole-4-carbonitrile (EXAMPLE 801)**

25 Mixture of **EXAMPLE 263** (0.15 mmol) and copper(I)-cyanide (156 mg, 1.74 mmol, 12 eq.) in NMP (5 ml) was microwave irradiated for 4 hours at 200 °C. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous formic acid – MeCN, then 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 801**. HRMS calculated for $C_{36}H_{36}N_8O_4S$: 676.2580; found 677.266 [(M+H)⁺ form].

▪ **(3-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}phenyl)(methyl)sulfoniumolate (EXAMPLE 802)**

The mixture of **EXAMPLE 283** (0.267 mmol) and Oxone® (164 mg, 0.267 mmol, 1 eq) in MeOH (5 ml), water (5 ml) and MeCN (5 ml) was stirred at r.t. for 10 hours. Water (30 ml) and MSM (3 ml) was added to the reaction mixture and evaporated. To the residue brine (30 ml) was added and extracted with DCM (4 x 50 ml), the combined organic layers were dried over MgSO₄ and evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 802**. HRMS calculated for C₃₃H₃₇N₅O₅S: 615.2515; found 616.2622 [(M+H)⁺ form].

▪ **methyl 3-amino-5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 803)**

Using **General Procedure 12** starting from **EXAMPLE 285** as reactant, **EXAMPLE 803** was obtained. HRMS calculated for C₃₄H₃₈N₆O₆: 626.2853; found 627.295 [(M+H)⁺ form].

▪ **3-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-N-methoxy-N-methylbenzamide (EXAMPLE 804)**

Using **General Procedure 7** starting from **EXAMPLE 797** as carboxylic acid reactant and N,O-dimethylhydroxylamine hydrochloride as amine reactant, **EXAMPLE 804** was obtained. HRMS calculated for C₃₅H₄₀N₆O₆: 640.3009; found 641.3089 [(M+H)⁺ form].

▪ **methyl 3-(acetylamino)-5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 805)**

Using **General Procedure 7** starting from **EXAMPLE 803** and acetic acid as reactants, **EXAMPLE 805** was obtained. HRMS calculated for C₃₆H₄₀N₆O₇: 668.2958; found 669.3036 [(M+H)⁺ form].

▪ **methyl 3-(benzoylamino)-5-{[(3R,4R)-4-({4-hydroxy-4-[(7-methyl-4-oxo-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate (EXAMPLE 806)**

Using **General Procedure 7** starting from **EXAMPLE 803** and benzoic acid as reagents,
5 **EXAMPLE 806** was obtained. HRMS calculated for $C_{41}H_{42}N_6O_7$: 730.3115; found 731.3194 [(M+H)⁺ form].

▪ **7-(3-chlorophenyl)-3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 807)**

10 Using **General Procedure 10** starting from **EXAMPLE 86** as reactant, **EXAMPLE 807** was obtained. HRMS calculated for $C_{39}H_{38}N_7O_4SCl$: 735.2394; found 736.2464 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 808)**

15 Using **General Procedure 10** starting from **EXAMPLE 99** as reactant, **EXAMPLE 808** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 716.3012 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 809)**

20 Using **General Procedure 10** starting from **EXAMPLE 94** as reactant, **EXAMPLE 809** was obtained. HRMS calculated for $C_{39}H_{39}N_7O_5S$: 717.2733; found 718.2805 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[2-(6-oxo-1,6-dihydropyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(6-methoxypyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 810)**

25 Using **General Procedure 15** starting from **EXAMPLE 101** as reactant, **EXAMPLE 810** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_5S$: 732.2842; found 733.2893 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-1-oxidopyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 811)**

The mixture of **EXAMPLE 750** (0.137 mmol), mCPBA (24 mg, 0.137 mmol, 1 eq.) in DCM (1 ml) was stirred at r.t. for 25 hours. The reaction mixture was evaporated, purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 811**. HRMS calculated for C₄₁H₄₁N₇O₅S: 743.2890; found 744.2959 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 812)**

Using **General Procedure 10** starting from **EXAMPLE 733** as reactant, **EXAMPLE 812** was obtained. HRMS calculated for C₃₉H₃₉N₇O₄S: 701.2784; found 702.2841 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-[(3R,4R)-1-[2-(4-methylpiperazin-1-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 813)**

The mixture of **EXAMPLE 103** (0.391 mmol) and *N*-methylpiperazine (96 μ l, 87 mg, 0.872 mmol, 3 eq.) and PDO (5 ml) was microwave irradiated for altogether 9 hours at 150 °C. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 813**. HRMS calculated for C₃₉H₄₆N₈O₃S: 706.3414; found 707.3487 [(M+H)⁺ form].

▪ **5-(5-[(3R,4R)-4-[(4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl)pyridine-2-carboxylic acid (EXAMPLE 814)**

Using **General Procedure 9** starting from **EXAMPLE 103** and methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-2-carboxylate as reagents, the crude product was dissolved in MeOH (5 ml) and water (5 ml), lithium-hydroxide monohydrate (74 mg, 1.76 mmol) was added and the mixture was stirred for 2 hours at r.t. The reaction mixture

was evaporated to water, neutralized with HCl solution (aq., 1 N), purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 814**. HRMS calculated for C₄₀H₃₉N₇O₅S: 729.2733; found 730.278 [(M+H)⁺ form].

5 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-oxo-1,6-dihydropyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(6-oxo-1,6-dihydropyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 815)**

Using **General Procedure 15** starting from **EXAMPLE 101** as reactant, **EXAMPLE 815** was obtained. HRMS calculated for C₃₈H₃₈N₈O₅S: 718.2686; found 719.2756 [(M+H)⁺ form].

10 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(6-oxo-1,6-dihydropyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 816)**

Using **General Procedure 15** starting from **EXAMPLE 100** as reactant, **EXAMPLE 816** was obtained. HRMS calculated for C₃₉H₄₀N₈O₄S: 716.2893; found 717.2966 [(M+H)⁺ form].

15 ▪ **3-[(4-hydroxy-1-[(3R,4R)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1-methyl-6-oxo-1,6-dihydropyridin-2-yl)-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 817)**

Using **General Procedure 13** starting from **EXAMPLE 816** as reactant and iodomethane as reagent, **EXAMPLE 817** was obtained. HRMS calculated for C₄₀H₄₂N₈O₄S: 730.3050; found 731.3121 [(M+H)⁺ form].

20 ▪ **3-[[1-[(3S,4S)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 818)**

Using **General Procedure 6** starting from 3-[[4-hydroxy-1-[(3S,4S)-3-phenylpiperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (which was obtained according to **General Procedure 5** with *tert*-butyl (3S,4S)-4-(2-oxa-6-azaspiro[2.5]octane-6-carbonyl)-3-phenyl-piperidine-1-carboxylate and 3*H*-thieno[2,3-*d*]pyrimidin-4-one) and benzyl bromide as reagents, **EXAMPLE 818** was obtained. HRMS calculated for C₃₁H₃₄N₄O₃S: 542.2352; found 543.2419 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 819)**

Using **General Procedure 6** starting from **Preparation R3cp** and benzyl bromide as reagents, **EXAMPLE 819** was obtained. HRMS calculated for $C_{31}H_{34}N_4O_3S$: 543.2352; found 543.2401 [(M+H)⁺ form].

▪ **3-[[1-[(3S,4S)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 820)**

Using **General Procedure 6** starting from **Preparation R3cn** and benzyl bromide as reagents, **EXAMPLE 820** was obtained. HRMS calculated for $C_{32}H_{35}N_5O_3$: 537.274; found 538.2837 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 821)**

Using **General Procedure 6** starting from **Preparation R3co** and benzyl bromide as reagents, **EXAMPLE 821** was obtained. HRMS calculated for $C_{32}H_{35}N_5O_4$: 537.2740; found 538.2809 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4S)-1-benzyl-3-(2-thienyl)piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 822)**

Using **General Procedure 5**, starting from 3*H*-pyrido[3,2-*d*]pyrimidin-4-one and **Preparation R1e** as reactants, the resulted crude piperidine product was reacted with **Preparation R1q-(3R,4S)** according to **General Procedure 7**, to give **EXAMPLE 822**. HRMS calculated for $C_{30}H_{33}N_5O_3S$: 544.2304; found 544.2381 [(M+H)⁺ form].

▪ **3-[[1-[(3S,4R)-1-benzyl-3-(2-thienyl)piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 823)**

Using **General Procedure 5**, starting from 3*H*-pyrido[3,2-*d*]pyrimidin-4-one and **Preparation R1e** as reactants, the resulted crude piperidine product was reacted with **Preparation R1q-(3S,4R)** according to **General Procedure 7**, to give **EXAMPLE 823**. HRMS calculated for $C_{30}H_{33}N_5O_3S$: 544.2304; found 544.2394 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(2-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 824)**

Using **General Procedure 6** starting from **Preparation R3cp** and 1-(bromomethyl)-2-fluoro-benzene as reagents, **EXAMPLE 824** was obtained. HRMS calculated for $C_{31}H_{33}FN_4O_3S$: 560.2257; found 561.2301 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(3-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 825)**

Using **General Procedure 6** starting from **Preparation R3cp** and 1-(bromomethyl)-3-fluoro-benzene as reagents, **EXAMPLE 825** was obtained. HRMS calculated for $C_{31}H_{33}FN_4O_3S$: 560.2257; found 561.2331 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(o-tolylmethyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 826)**

Using **General Procedure 6** starting from **Preparation R3cp** and 1-(bromomethyl)-2-methyl-benzene as reagents, **EXAMPLE 826** was obtained. HRMS calculated for $C_{32}H_{36}N_4O_3S$: 556.2508; found 557.2565 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(m-tolylmethyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 827)**

Using **General Procedure 6** starting from **Preparation R3cp** and 1-(bromomethyl)-3-methyl-benzene as reagents, **EXAMPLE 827** was obtained. HRMS calculated for $C_{32}H_{36}N_4O_3S$: 556.2508; found 557.2597 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 828)**

Using **General Procedure 7** starting from **Preparation R3co** and 4-methyl-2-phenyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 828** was obtained. HRMS calculated for $C_{36}H_{36}N_6O_4S$: 648.2519; found 649.2583 [(M+H)⁺ form].

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▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(2-phenylthiazole-5-carbonyl)piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 829)**

Using **General Procedure 7** starting from **Preparation R3co** and 2-phenylthiazole-5-carboxylic acid as reagents, **EXAMPLE 829** was obtained. HRMS calculated for $C_{35}H_{34}N_6O_4S$: 634.2362; found 635.2429 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-6-chloro-pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 830)**

Using **General Procedure 6** starting from **Preparation R3cq** and benzyl bromide as reagents, **EXAMPLE 830** was obtained. HRMS calculated for $C_{32}H_{34}ClN_5O_3$: 571.235; found 572.2416 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-6-methoxy-pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 831)**

Using **General Procedure 6** starting from **Preparation R3cr** and benzyl bromide as reagents, **EXAMPLE 831** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_4$: 567.2846; found 568.2902 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-5H-pyrido[3,2-d]pyrimidine-4,6-dione (EXAMPLE 832)**

Using **General Procedure 6** starting from **Preparation R3cs** and benzyl bromide as reagents, **EXAMPLE 832** was obtained. HRMS calculated for $C_{32}H_{35}N_5O_4$: 553.2689; found 554.2762 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(3-methylisothiazole-4-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 833)**

Using **General Procedure 7** starting from **Preparation R3co** and 3-methylisothiazole-4-carboxylic acid as reagents, **EXAMPLE 833** was obtained. HRMS calculated for $C_{30}H_{32}N_6O_4S$: 572.2206; found 573.2285 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(2-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 834)**

Using **General Procedure 6** starting from **Preparation R3co** and 1-(bromomethyl)-2-fluoro-benzene as reagents, **EXAMPLE 834** was obtained. HRMS calculated for $C_{32}H_{34}FN_5O_3$: 555.2646; found 556.2701 [(M+H)⁺ form].

5 ▪ **3-[[1-[(3R,4R)-1-[(3-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 835)**

Using **General Procedure 6** starting from **Preparation R3co** and 1-(bromomethyl)-3-fluoro-benzene as reagents, **EXAMPLE 835** was obtained. HRMS calculated for $C_{32}H_{34}FN_5O_4$: 555.2647; found 556.2702 [(M+H)⁺ form].

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(o-tolylmethyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 836)**

Using **General Procedure 6** starting from **Preparation R3co** and 1-(bromomethyl)-2-methyl-benzene as reagents, **EXAMPLE 836** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_3$: 551.2896; found 552.2943 [(M+H)⁺ form].

15 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(m-tolylmethyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 837)**

Using **General Procedure 6** starting from **Preparation R3co** and 1-(bromomethyl)-3-methyl-benzene as reagents, **EXAMPLE 837** was obtained. HRMS calculated for $C_{33}H_{37}N_5O_4$: 551.2897; found 552.2990 [(M+H)⁺ form].

20 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 838)**

Using **General Procedure 7** starting from **Preparation R3cp** and 4-methyl-2-phenyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 838** was obtained. HRMS calculated for $C_{35}H_{35}N_5O_4S_2$: 653.2130; found 654.2212 [(M+H)⁺ form].

25 ▪ **3-[[1-[(3R,4R)-1-(2-benzyl-4-methyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 839)**

Using **General Procedure 7** starting from **Preparation R3cp** and 2-benzyl-4-methyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 839** was obtained. HRMS calculated for $C_{36}H_{37}N_5O_4S_2$: 667.2287; found 668.2371 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(3-methylisothiazole-4-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 840)**

Using **General Procedure 7** starting from **Preparation R3cp** and 3-methylisothiazole-4-carboxylic acid as reagents, **EXAMPLE 840** was obtained. HRMS calculated for $C_{29}H_{31}N_5O_4S_2$: 577.1817; found 578.1901 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[[1-[(3R,4R)-1-(benzofuran-2-ylmethyl)-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 841)**

Using **General Procedure 6** starting from **Preparation R3cp** and 2-(chloromethyl)benzofurane as reagents, **EXAMPLE 841** was obtained. HRMS calculated for $C_{33}H_{34}N_4O_4S$: 582.2301; found 583.2376 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-[(3R,4R)-4-[4-hydroxy-4-[(4-oxothieno[2,3-d]pyrimidin-3-yl)methyl]piperidine-1-carbonyl]-3-phenyl-piperidine-1-carbonyl]-1H-indazole-5-carbonitrile (EXAMPLE 842)**

Using **General Procedure 7** starting from **Preparation R3cp** and 5-cyano-1H-indazole-3-carboxylic acid as reagents, **EXAMPLE 842** was obtained. HRMS calculated for $C_{33}H_{31}N_7O_4S$: 621.2158; found 622.2229 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[[1-[(3R,4R)-1-(2-benzyl-4-methyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 843)**

Using **General Procedure 7** starting from **Preparation R3co** and 2-benzyl-4-methyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 843** was obtained. HRMS calculated for $C_{37}H_{38}N_6O_4S$: 662.2675; found 663.2743 $[(M+H)^+ \text{ form}]$.

25

▪ **3-[[1-[(3R,4R)-1-[2-(2-fluorophenyl)-4-methyl-thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 844)**

Using **General Procedure 7** starting from **Preparation R3co** and 2-(2-fluorophenyl)-4-methyl-thiazole-5-carboxylic acid as reagents, **EXAMPLE 844** was obtained. HRMS calculated for $C_{36}H_{35}FN_6O_4S$: 666.2425; found 667.2498 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(o-tolyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 845)**

Using **General Procedure 7** starting from **Preparation R3co** and 4-methyl-2-(o-tolyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 845** was obtained. HRMS calculated for $C_{37}H_{38}N_6O_4S$: 662.2675; found 663.2751 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[2-(4-pyridyl)thiazole-5-carbonyl]piperidine-4-carbonyl]-4-piperidyl)methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 846)**

Using **General Procedure 7** starting from **Preparation R3co** and 2-(4-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 846** was obtained. HRMS calculated for $C_{34}H_{33}N_7O_4S$: 635.2314; found 636.2401 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3S,4S)-3-phenyl-1-[2-(4-pyridyl)thiazole-5-carbonyl]piperidine-4-carbonyl]-4-piperidyl)methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 847)**

Using **General Procedure 7** starting from **Preparation R3cn** and 2-(4-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 847** was obtained. HRMS calculated for $C_{34}H_{33}N_7O_4S$: 635.2315; found 318.6241 $[(M+2H)^{2+}]$ form].

▪ **3-[[1-[(3R,4R)-1-[2-[(2-fluorophenyl)methyl]thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 848)**

Using **General Procedure 7** starting from **Preparation R3co** and 2-[(2-fluorophenyl)methyl]thiazole-5-carboxylic acid as reagents, **EXAMPLE 848** was obtained. HRMS calculated for $C_{36}H_{35}FN_6O_4S$: 666.2425; found 667.2498 $[(M+H)^+]$ form].

▪ **6-(benzylamino)-3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 849)**

Using **General Procedure 6** starting from **Preparation R3ct** and benzyl bromide as reagents, **EXAMPLE 849** was obtained. HRMS calculated for $C_{39}H_{42}N_6O_3$: 642.3318; found 322.1727 [(M+2H)²⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[5-(4-pyridyl)thiophene-2-carbonyl]piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 850)**

Using **General Procedure 7** starting from **Preparation R3co** and 5-(4-pyridyl)thiophene-2-carboxylic acid as reagents, **EXAMPLE 850** was obtained. HRMS calculated for $C_{35}H_{34}N_6O_4S$: 634.2362; found 635.2439 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(4-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 851)**

Using **General Procedure 7** starting from **Preparation R3co** and 4-methyl-2-(4-pyridyl)thiazole-5-carboxylic acid as reagents, **EXAMPLE 851** was obtained. HRMS calculated for $C_{35}H_{35}N_7O_4S$: 649.2471; found 650.2547 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(2-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-6-[(4-methoxyphenyl)methylamino]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 852)**

Using **General Procedure 6** starting from **Preparation R3cu** and 1-(bromomethyl)-2-fluoro-benzene as reagents, **EXAMPLE 852** was obtained. HRMS calculated for $C_{40}H_{43}FN_6O_4$: 690.333; found 346.1732 [(M+2H)²⁺ form].

▪ **6-chloro-3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 853)**

Using **General Procedure 5** Step 1, starting from 6-chloro-3*H*-pyrido[3,2-*d*]pyrimidin-4-one and **Preparation R1s** as epoxide compound, **EXAMPLE 853** was obtained. HRMS calculated for C₃₆H₃₅ClN₆O₄S: 682.2129; found 683.2201 [(M+H)⁺ form].

5 ▪ 3-[[4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(5-pyrimidin-5-ylthiophene-2-carbonyl)piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-*d*]pyrimidin-4-one
(**EXAMPLE 854**)

Using **General Procedure 7** starting from **Preparation R3cp** and 5-bromothiophene-2-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with pyrimidin-5-ylboronic acid to give **EXAMPLE 854**. HRMS
10 calculated for C₃₃H₃₂N₆O₄S₂: 640.1926; found 641.1995 [(M+H)⁺ form].

▪ 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-(4-methyl-2-pyrimidin-5-yl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-*d*]pyrimidin-4-one
(**EXAMPLE 855**)

Using **General Procedure 7** starting from **Preparation R3cp** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude bromo compound was reacted
15 according to **General Procedure 9** with pyrimidin-5-ylboronic acid to give **EXAMPLE 855**. HRMS calculated for C₃₃H₃₃N₇O₄S₂: 655.2035; found 656.2132 [(M+H)⁺ form].

20 ▪ 3-[[4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(5-pyrimidin-5-ylthiophene-2-carbonyl)piperidine-4-carbonyl]-4-piperidyl)methyl]pyrido[3,2-*d*]pyrimidin-4-one
(**EXAMPLE 856**)

Using **General Procedure 7** starting from **Preparation R3co** and 5-bromothiophene-2-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with pyrimidin-5-ylboronic acid to give **EXAMPLE 856**. HRMS
calculated for C₃₄H₃₃N₇O₄S: 635.2315; found 636.2387 [(M+H)⁺ form].

25 ▪ 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[5-(2-methylpyrazol-3-yl)thiophene-2-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-*d*]pyrimidin-4-one
(**EXAMPLE 857**)

Using **General Procedure 7** starting from **Preparation R3cp** and 5-bromothiophene-2-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole to give **EXAMPLE 857**. HRMS calculated for $C_{33}H_{34}N_6O_4S_2$: 642.2083; found 643.2163 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(2-methylpyrazol-3-yl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 858)**

Using **General Procedure 7** starting from **Preparation R3cp** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole to give **EXAMPLE 858**. HRMS calculated for $C_{33}H_{35}N_7O_4S_2$: 657.2192; found 658.2279 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[5-(2-methylpyrazol-3-yl)thiophene-2-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 859)**

Using **General Procedure 7** starting from **Preparation R3co** and 5-bromothiophene-2-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole to give **EXAMPLE 859**. HRMS calculated for $C_{34}H_{35}N_7O_4S$: 637.2471; found 638.2525 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxy-3-pyridyl)-4-methyl-thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one (EXAMPLE 860)**

Using **General Procedure 7** starting from **Preparation R3cp** and 2-bromo-4-methylthiazole-5-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with (6-methoxy-3-pyridyl)boronic acid to give **EXAMPLE 860**. HRMS calculated for $C_{35}H_{36}N_6O_5S_2$: 684.2189; found 685.2269 [(M+H)⁺ form].

▪ 3-[[1-[(3R,4R)-1-[2-(6-amino-3-pyridyl)-4-methyl-thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(EXAMPLE 861)

Using **General Procedure 7** starting from **Preparation R3cp** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine to give **EXAMPLE 861** was obtained. HRMS calculated for $C_{34}H_{35}N_7O_4S_2$: 669.2192; found 670.2245 [(M+H)⁺ form].

▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(EXAMPLE 862)

Using **General Procedure 7** starting from **Preparation R3cp** and 2-bromo-4-methyl-thiazole-5-carboxylic acid as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with (6-methyl-3-pyridyl)boronic acid to give **EXAMPLE 862**. HRMS calculated for $C_{35}H_{36}N_6O_4S_2$: 668.2239; found 669.2306 [(M+H)⁺ form].

▪ 3-[[1-[(3R,4R)-1-[3-fluoro-5-(6-methyl-3-pyridyl)thiophene-2-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(EXAMPLE 863)

Using **General Procedure 7** starting from **Preparation R3cp** and **Preparation R1g** as reagents, the resulted crude iodo compound was reacted according to **General Procedure 9** with (6-methyl-3-pyridyl)boronic acid to give **EXAMPLE 863**. HRMS calculated for $C_{35}H_{34}FN_5O_4S_2$: 671.2036; found 336.6092 [(M+2H)²⁺ form].

▪ 3-[[1-[(3R,4R)-1-[5-(6-amino-3-pyridyl)-3-fluoro-thiophene-2-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(EXAMPLE 864)

Using **General Procedure 7** starting from **Preparation R3cp** and **Preparation R1g** as reagents, the resulted crude iodo compound was reacted according to **General**

Procedure 9 with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine to give **EXAMPLE 864**. HRMS calculated for $C_{34}H_{33}FN_6O_4S_2$: 672.1989; found 671.1926 [(M-H)⁻ form].

5 ▪ 3-[[1-[(3R,4R)-1-[3-fluoro-5-(6-piperazin-1-yl-3-pyridyl)thiophene-2-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one (**EXAMPLE 865**)

Using **General Procedure 7** starting from **Preparation R3cp** and **Preparation R1g** as reagents, the resulted crude iodo compound was reacted according to **General Procedure 9** with 1-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]piperazine
10 to give **EXAMPLE 865**. HRMS calculated for $C_{38}H_{40}FN_7O_4S_2$: 741.2567; found 740.2504 [(M-H)⁻ form].

▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(**EXAMPLE 866**)

15 Using **General Procedure 6** starting from **Preparation R3cp** and **Preparation R1c** as reagents, **EXAMPLE 866** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_3S_2$: 640.2290; found 641.2336 [(M+H)⁺ form].

20 ▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxy-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(**EXAMPLE 867**)

Using **General Procedure 6** starting from **Preparation R3cp** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 867** was obtained. HRMS calculated for $C_{34}H_{36}N_6O_4S_2$: 656.2239; found 657.2343 [(M+H)⁺ form].

25 ▪ 3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-[[2-(6-piperazin-1-yl-3-pyridyl)thiazol-5-yl]methyl]piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[2,3-d]pyrimidin-4-one
(**EXAMPLE 868**)

Using **General Procedure 6** starting from **Preparation R3cp** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo compound was reacted

according to **General Procedure 9** with 1-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]piperazine to give **EXAMPLE 868**. HRMS calculated for $C_{37}H_{42}N_8O_3S_2$: 710.2821; found 356.1477 $[(M+2H)^{2+}$ form].

5 ▪ **3-[[1-[(3R,4R)-1-[[2-(6-amino-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one**
(**EXAMPLE 869**)

Using **General Procedure 6** starting from **Preparation R3cp** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine to give **EXAMPLE 869**. HRMS calculated for $C_{33}H_{35}N_7O_3S_2$: 641.2243; found 642.2342 $[(M+H)^+$ form].

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(3-methylimidazo[4,5-b]pyridin-6-yl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one** (**EXAMPLE 870**)

15 Using **General Procedure 6** starting from **Preparation R3cp** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[4,5-*b*]pyridine to give **EXAMPLE 870**. HRMS calculated for $C_{35}H_{36}N_8O_3S_2$: 680.2352; found 341.1257 $[(M+2H)^{2+}$ form].

20 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-imidazo[1,2-*a*]pyridin-7-ylthiazol-5-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[2,3-d]pyrimidin-4-one**
(**EXAMPLE 871**)

25 Using **General Procedure 6** starting from **Preparation R3cp** and 2-bromo-5-(bromomethyl)thiazole as reagents, the resulted crude bromo compound was reacted according to **General Procedure 9** with imidazo[1,2-*a*]pyridin-7-ylboronic acid to give **EXAMPLE 871**. HRMS calculated for $C_{35}H_{35}N_7O_3S_2$: 665.2243; found 333.6191 $[(M+2H)^{2+}$ form].

▪ **6-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-3-phenyl-triazolo[4,5-d]pyrimidin-7-one (EXAMPLE 872)**

Using **General Procedure 7** starting from **Preparation R3cv** and **Preparation R1d** as reagents, **EXAMPLE 872** was obtained. HRMS calculated for $C_{39}H_{39}N_9O_4S$: 729.2845; found 730.2937 $[(M+H)^+$ form].

▪ **1-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-9-phenyl-purin-6-one (EXAMPLE 873)**

Using **General Procedure 7** starting from **Preparation R3cw** and **Preparation R1d** as reagents, **EXAMPLE 873** was obtained. HRMS calculated for $C_{40}H_{40}N_8O_4S$: 728.2893; found 727.2866 $[(M+H)^+$ form].

▪ **5-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-1-phenyl-pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 874)**

Using **General Procedure 6** starting from **Preparation R3cx** and **Preparation R1c** as reagents, **EXAMPLE 874** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_3S$: 700.2944; found 701.3000 $[(M+H)^+$ form].

▪ **1-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-9-phenyl-purin-6-one (EXAMPLE 875)**

Using **General Procedure 6** starting from **Preparation R3cw** and **Preparation R1c** as reagents, **EXAMPLE 875** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_3S$: 700.2944; found 351.1551 $[(M+2H)^{2+}$ form].

▪ **1-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxy-3-pyridyl)thiazol-5-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-9-phenyl-purin-6-one (EXAMPLE 876)**

Using **General Procedure 6** starting from **Preparation R3cw** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 876** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_4S$: 716.2893; found 359.1535 $[(M+2H)^{2+}$ form].

▪ **5-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxy-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-1-phenyl-pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 877)**

Using **General Procedure 6** starting from **Preparation R3cx** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 877** was obtained. HRMS calculated for $C_{39}H_{40}N_8O_4S$: 716.2893; found 717.2979 $[(M+H)^+$ form].

▪ **5-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-1-phenyl-pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 878)**

Using **General Procedure 7** starting from **Preparation R3cx** and **Preparation R1d** as reagents, **EXAMPLE 878** was obtained. HRMS calculated for $C_{40}H_{40}N_8O_4S$: 728.2893; found 729.2961 $[(M+H)^+$ form].

▪ **7-bromo-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 879)**

Using **General Procedure 6** starting from **Preparation R3cy** and **Preparation R1c** as reagents, **EXAMPLE 879** was obtained. HRMS calculated for $C_{34}H_{36}BrN_7O_3S$: 701.1783; found 702.1856 $[(M+H)^+$ form].

▪ **6-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-isothiazolo[4,5-d]pyrimidin-7-one (EXAMPLE 880)**

Using **General Procedure 6** starting from **Preparation R3cz** and **Preparation R1c** as reagents, **EXAMPLE 880** was obtained. HRMS calculated for $C_{39}H_{39}N_7O_3S_2$: 717.2556; found 718.2602 $[(M+H)^+$ form].

▪ **6-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-isothiazolo[4,5-d]pyrimidin-7-one (EXAMPLE 881)**

Using **General Procedure 7** starting from **Preparation R3cz** and **Preparation R1d** as reagents, **EXAMPLE 881** was obtained. HRMS calculated for $C_{40}H_{39}N_7O_4S_2$: 745.2505; found 746.2575 $[(M+H)^+ \text{ form}]$.

5 ▪ **7-bromo-3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 882)**

Using **General Procedure 7** starting from **Preparation R3cy** and **Preparation R1d** as reagents, **EXAMPLE 882** was obtained. HRMS calculated for $C_{35}H_{36}BrN_7O_4S$: 729.1733; found 730.1797 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one (EXAMPLE 883)**

Using **General Procedure 7** starting from **Preparation R3da** and **Preparation R1d** as reagents, **EXAMPLE 883** was obtained. HRMS calculated for $C_{41}H_{40}N_6O_4S_2$: 744.2552; found 745.2617 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one (EXAMPLE 884)**

Using **General Procedure 6** starting from **Preparation R3da** and **Preparation R1c** as reagents, **EXAMPLE 884** was obtained. HRMS calculated for $C_{40}H_{40}N_6O_3S_2$: 716.2603; found 717.2680 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxy-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one (EXAMPLE 885)**

25 Using **General Procedure 6** starting from **Preparation R3da** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 885** was obtained. HRMS calculated for $C_{40}H_{40}N_6O_4S_2$: 732.2552; found 733.2628 $[(M+H)^+ \text{ form}]$.

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-5H-pyrrolo[3,2-d]pyrimidin-4-one (EXAMPLE 886)**

Using **General Procedure 7** starting from **Preparation R3db** and **Preparation R1d** as reagents, **EXAMPLE 886** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_4S$: 727.2941; found 728.3012 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-5H-pyrrolo[3,2-d]pyrimidin-4-one (EXAMPLE 887)**

Using **General Procedure 6** starting from **Preparation R3db** and **Preparation R1c** as reagents, **EXAMPLE 887** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_3S$: 699.2991; found 700.3065 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxy-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-5H-pyrrolo[3,2-d]pyrimidin-4-one (EXAMPLE 888)**

Using **General Procedure 6** starting from **Preparation R3db** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 888** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 716.3013 $[(M+H)^+]$ form].

▪ **7-chloro-3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[3,4-d]pyrimidin-4-one (EXAMPLE 889)**

Using **General Procedure 7** starting from **Preparation R3dc** and **Preparation R1d** as reagents, **EXAMPLE 889** was obtained. HRMS calculated for $C_{35}H_{35}N_6O_4S_2Cl$: 702.185; found 703.1921 $[(M+H)^+]$ form].

▪ **7-chloro-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[3,4-d]pyrimidin-4-one (EXAMPLE 890)**

Using **General Procedure 6** starting from **Preparation R3dc** and **Preparation R1c** as reagents, **EXAMPLE 890** was obtained. HRMS calculated for $C_{34}H_{35}ClN_6O_3S_2$: 674.1901; found 675.1992 $[(M+H)^+ \text{ form}]$.

5 ▪ **6-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-isoxazolo[4,5-d]pyrimidin-7-one (EXAMPLE 891)**

Using **General Procedure 7** starting from **Preparation R3dd** and **Preparation R1d** as reagents, **EXAMPLE 891** was obtained. HRMS calculated for $C_{40}H_{39}N_7O_5S$: 729.2733; found 730.2806 $[(M+H)^+ \text{ form}]$.

10 ▪ **6-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-3-phenyl-isoxazolo[4,5-d]pyrimidin-7-one (EXAMPLE 892)**

Using **General Procedure 6** starting from **Preparation R3dd** and **Preparation R1c** as reagents, **EXAMPLE 892** was obtained. HRMS calculated for $C_{39}H_{39}N_7O_4S$: 701.2784; found 702.2878 $[(M+H)^+ \text{ form}]$.

15 ▪ **5-[[1-[(3R,4R)-1-[(2-bromothiazol-5-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-1-(4-methoxyphenyl)pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 893)**

Using **General Procedure 6** starting from **Preparation R3de** and 2-bromo-5-(bromomethyl)thiazole as reagents, **EXAMPLE 893** was obtained. HRMS calculated for $C_{34}H_{36}BrN_7O_4S$: 717.1733; found 718.1792 $[(M+H)^+ \text{ form}]$.

20 ▪ **5-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-1-(4-methoxyphenyl)pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 894)**

25 Using **General Procedure 6** starting from **Preparation R3de** and **Preparation R1c** as reagents, **EXAMPLE 894** was obtained. HRMS calculated for $C_{40}H_{42}N_8O_4S$: 730.305; found 731.3146 $[(M+H)^+ \text{ form}]$.

▪ **5-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methoxy-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-1-(4-methoxyphenyl)pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 895)**

Using **General Procedure 6** starting from **Preparation R3de** and 5-(chloromethyl)-2-(6-methoxy-3-pyridyl)thiazole as reagents, **EXAMPLE 895** was obtained. HRMS calculated for $C_{40}H_{42}N_8O_5S$: 746.2999; found 747.3071 $[(M+H)^+]$ form].

▪ **5-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-1-(4-methoxyphenyl)pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 896)**

Using **General Procedure 7** starting from **Preparation R3de** and **Preparation R1d** as reagents, **EXAMPLE 896** was obtained. HRMS calculated for $C_{41}H_{42}N_8O_5S$: 758.2999; found 759.3064 $[(M+H)^+]$ form].

▪ **1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 897)**

Using **General Procedure 7** starting from **Preparation R3df** and **Preparation R1d** as reagents, **EXAMPLE 897** was obtained. HRMS calculated for $C_{42}H_{42}N_8O_6S$: 786.2948; found 787.3016 $[(M+H)^+]$ form].

▪ **1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrazolo[3,4-d]pyrimidin-4-one (EXAMPLE 898)**

Using **General Procedure 6** starting from **Preparation R3df** and **Preparation R1c** as reagents, **EXAMPLE 898** was obtained. HRMS calculated for $C_{41}H_{42}N_8O_5S$: 758.2999; found 759.3077 $[(M+H)^+]$ form].

▪ **6-amino-3-[[1-[(3R,4R)-1-benzyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 899)**

EXAMPLE 830 (8 mg, 0.013 mmol), benzophenone imine (18 mg, 0.1 mmol), cesium-carbonate (11.1 mg, 0.033 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

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(1.3 mg, 0.002 mmol), tris(dibenzylideneacetone)dipalladium(0) (1.1 mg, 0.001 mmol) were stirred in abs. toluene (3 ml) at 110 °C for 5 hours. The reaction mixture was evaporated, to the residue aqueous HCl solution (1 N, 2 ml) and PDO (1 ml) were added and the mixture was stirred at r.t. for 3 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 899**. HRMS calculated for C₃₂H₃₆N₆O₃: 552.2849; found 551.2818 [(M+H)⁺ form].

▪ **6-amino-3-[[1-[(3R,4R)-1-[(2-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one**
(**EXAMPLE 900**)

The solution of **EXAMPLE 852** (110 mg, 0.159 mmol) in TFA (3 ml) was stirred at 70 °C for 90 minutes, then evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 900**. HRMS calculated for C₃₂H₃₅FN₆O₃: 570.2755; found 286.1457 [(M+2H)²⁺ form].

▪ **N-[3-[[1-[(3R,4R)-1-[(2-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-4-oxo-pyrido[3,2-d]pyrimidin-6-yl]-2-(2-oxoindolin-6-yl)acetamide** (**EXAMPLE 901**)

Using **General Procedure 7** starting from **EXAMPLE 900** as amine component and 2-(2-oxoindolin-6-yl)acetic acid as carboxylic acid reactant, **EXAMPLE 901** was obtained. HRMS calculated for C₄₂H₄₂FN₇O₅: 743.3231; found 372.6692 [(M+2H)²⁺ form].

▪ **N-[3-[[1-[(3R,4R)-1-[(2-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-4-oxo-pyrido[3,2-d]pyrimidin-6-yl]-2-(3-hydroxyphenyl)acetamide** (**EXAMPLE 902**)

Using **General Procedure 7** starting from **EXAMPLE 900** as amine component and 3-hydroxyphenylacetic acid as carboxylic acid reactant, **EXAMPLE 902** was obtained. HRMS calculated for C₄₀H₄₁FN₆O₅: 704.3122; found 353.1636 [(M+2H)²⁺ form].

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▪ **3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-6-[(4-methoxyphenyl)methylamino]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 903)**

EXAMPLE 853 (320 mg, 0.468 mmol) was stirred in 4-methoxybenzylamine (7 ml) at 100 °C for 4 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give EXAMPLE 903. HRMS calculated for C₄₄H₄₅N₇O₅S: 783.3203; found 784.326 [(M+H)⁺ form].

▪ **6-amino-3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrido[3,2-d]pyrimidin-4-one (EXAMPLE 904)**

The solution of EXAMPLE 903 (159 mg, 0.203 mmol) in TFA (3 ml) was stirred at 70 °C for 120 minutes, then evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give EXAMPLE 904. HRMS calculated for C₃₆H₃₇N₇O₄S: 663.2628; found 332.6401 [(M+2H)²⁺ form].

▪ **N-[3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-4-oxo-pyrido[3,2-d]pyrimidin-6-yl]-2-(2-oxoindolin-6-yl)acetamide (EXAMPLE 905)**

Using General Procedure 7 starting from EXAMPLE 904 as amine component and 2-(2-oxoindolin-6-yl)acetic acid as carboxylic acid reactant, EXAMPLE 905 was obtained. HRMS calculated for C₄₆H₄₄N₈O₆S: 836.3105; found 837.3173 [(M+H)⁺ form].

▪ **N-[3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-4-oxo-pyrido[3,2-d]pyrimidin-6-yl]-2-(3-hydroxyphenyl)acetamide (EXAMPLE 906)**

Using General Procedure 7 starting from EXAMPLE 904 as amine component and 3-hydroxyphenylacetic acid as carboxylic acid reactant, EXAMPLE 906 was obtained. HRMS calculated for C₄₄H₄₃N₇O₆S: 797.2996; found 798.3073 [(M+H)⁺ form].

▪ **N-[3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-4-oxo-pyrido[3,2-d]pyrimidin-6-yl]-2-phenyl-acetamide (EXAMPLE 907)**

Using **General Procedure 7** starting from **EXAMPLE 904** as amine component and phenylacetic acid as carboxylic acid reactant, **EXAMPLE 907** was obtained. HRMS calculated for $C_{44}H_{43}N_7O_5S$: 781.3046; found 782.3136 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 908)**

Using **General Procedure 9** starting from **EXAMPLE 879** as reactant and phenylboronic acid as reagent, **EXAMPLE 908** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_3S$: 699.2991; found 700.3034 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 909)**

Using **General Procedure 9** starting from **EXAMPLE 882** as reactant and phenylboronic acid as reagents, **EXAMPLE 909** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_4S$: 727.2941; found 728.3013 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-5-methyl-7-phenyl-pyrrolo[3,2-d]pyrimidin-4-one (EXAMPLE 910)**

The suspension of **EXAMPLE 886** (0.052 mmol), iodomethane (6.5 μ l, 0.104 mmol) and K_2CO_3 (14.4 mg, 0.104 mmol) in DMF (1 ml) was stirred at r.t. overnight. The reaction mixture was filtered through syringe filter and purified by preparative LC (on C-18 Gemini-NX 5 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 910**. HRMS calculated for $C_{42}H_{43}N_7O_4S$: 741.3098; found 742.3171 $[(M+H)^+$ form].

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▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(1-methylpyrrol-3-yl)thieno[3,4-d]pyrimidin-4-one (EXAMPLE 911)**

Using **General Procedure 9** starting from **EXAMPLE 890** and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole as reagents, **EXAMPLE 911** was obtained. HRMS calculated for $C_{39}H_{41}N_7O_3S_2$: 719.2712; found 718.2672 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(1-methylpyrazol-4-yl)thieno[3,4-d]pyrimidin-4-one (EXAMPLE 912)**

Using **General Procedure 9** starting from **EXAMPLE 890** and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as reagents, **EXAMPLE 912** was obtained. HRMS calculated for $C_{38}H_{40}N_8O_3S_2$: 720.2665; found 721.2703 [(M+H)⁺ form].

▪ **7-(3-furyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[3,4-d]pyrimidin-4-one (EXAMPLE 913)**

Using **General Procedure 9** starting from **EXAMPLE 890** and 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as reagents, **EXAMPLE 913** was obtained. HRMS calculated for $C_{38}H_{38}N_6O_4S_2$: 706.2396; found 707.2448 [(M+H)⁺ form].

▪ **7-[4-(hydroxymethyl)phenyl]-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[3,4-d]pyrimidin-4-one (EXAMPLE 914)**

Using **General Procedure 9** starting from **EXAMPLE 890** and [4-(hydroxymethyl)phenyl]boronic acid as reagents, **EXAMPLE 914** was obtained. HRMS calculated for $C_{41}H_{42}N_6O_4S_2$: 746.2709; found 747.2782 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(1-methylpyrrol-3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 915)**

Using **General Procedure 9** starting from **EXAMPLE 879** as reactant and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole as reagent, **EXAMPLE 915** was obtained. HRMS calculated for $C_{39}H_{42}N_8O_3S$: 702.3101; found 703.3187 $[(M+H)^+]$ form].

5 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(1-methylpyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 916)**

Using **General Procedure 9** starting from **EXAMPLE 879** as reactant and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole as boron reagent, **EXAMPLE 916** was obtained. HRMS calculated for $C_{38}H_{41}N_9O_3S$: 703.3053; found 704.3159 $[(M+H)^+]$ form].

10 ▪ **7-(3-furyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 917)**

Using **General Procedure 9** starting from **EXAMPLE 879** as reactant and 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as boron reagent, **EXAMPLE 917** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_4S$: 689.2784; found 690.2875 $[(M+H)^+]$ form].

15 ▪ **7-(2-furyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 918)**

Using **General Procedure 9** starting from **EXAMPLE 879** as reactant and 2-furylboronic acid as boron reagent, **EXAMPLE 918** was obtained. HRMS calculated for $C_{38}H_{39}N_7O_4S$: 689.2784; found 690.2865 $[(M+H)^+]$ form].

20 ▪ **7-[4-(hydroxymethyl)phenyl]-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 919)**

Using **General Procedure 9** starting from **EXAMPLE 879** as reactant and [4-(hydroxymethyl)phenyl]boronic acid as boron reagent, **EXAMPLE 919** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_4S$: 729.3098; found 730.3161 $[(M+H)^+]$ form].

▪ **6-chloro-7-(4-chloro-3-fluoro-phenyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 920)**

Using **General Procedure 6** starting from **Preparation R3dg** and **Preparation R1c** as reagents, **EXAMPLE 920** was obtained. HRMS calculated for $C_{40}H_{38}Cl_2FN_7O_3S$: 785.2118; found 786.2163 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-6-methyl-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 921)**

Using **General Procedure 6** starting from **Preparation R3dh** and **Preparation R1c** as reagents, **EXAMPLE 921** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_3S$: 713.3148; found 714.3208 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-9-methyl-pyrimido[4,5-b]indol-4-one (EXAMPLE 922)**

Using **General Procedure 7** starting from **Preparation R3di** and **Preparation R1d** as reagents, **EXAMPLE 922** was obtained. HRMS calculated for $C_{40}H_{41}N_7O_4S$: 715.2941; found 716.3047 [(M+H)⁺ form].

▪ **3-[(4-hydroxy-1-{[(3R,4R)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-6,8-dimethylpyrimido[5',4':4,5]pyrrolo[1,2-b]pyridazin-4(3H)-one (EXAMPLE 923)**

Using **General Procedure 7** starting from **Preparation R3dj** and **Preparation R1d** as reagents, **EXAMPLE 923** was obtained. HRMS calculated for $C_{40}H_{42}N_8O_4S$: 730.305; found 731.3134 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-6-methyl-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 924)**

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Using **General Procedure 7** starting from **Preparation R3dh** and **Preparation R1d** as reagents, **EXAMPLE 924** was obtained. HRMS calculated for $C_{42}H_{43}N_7O_4S$: 741.3098; found 742.3179 $[(M+H)^+]$ form].

5 ▪ **6-chloro-3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 925)**

Using **General Procedure 7** starting from **Preparation R3dk** and **Preparation R1d** as reagents, **EXAMPLE 925** was obtained. HRMS calculated for $C_{41}H_{40}ClN_7O_4S$: 761.2551; found 762.2633 $[(M+H)^+]$ form].

10 ▪ **3-[[1-[(3R,4R)-1-[3-fluoro-5-(2-methyl-4-pyridyl)thiophene-2-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7-methyl-6-(2-thienyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 926)**

Using **General Procedure 9** starting from **Preparation R3dl** as halogenated reactant and 2-thienylboronic acid as boronic acid reagent, 3-[(4-hydroxy-1-{[(3R,4R)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-6-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one was obtained. This intermediate was reacted with **Preparation R1g** according to **General Procedure 7**, and the crude iodo compound was reacted according to **General Procedure 9** with (2-methyl-4-pyridyl)boronic acid to give **EXAMPLE 926**. HRMS calculated for $C_{40}H_{39}FN_6O_4S_2$: 750.2458; found 751.2537 $[(M+H)^+]$ form].

20 ▪ **N-[[3-[[1-[(3R,4R)-1-[(3-fluorophenyl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-4-oxo-7H-pyrrolo[2,3-d]pyrimidin-6-yl]methyl]acetamide (EXAMPLE 927)**

25 2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (3.5 g, 12.3 mmol) was dissolved in abs. THF (55 ml) and cooled to -78 °C, then LDA (2.0 M, 6.8 ml, 13.6 mmol) was added to the mixture and stirred at -78 °C for 40 minutes, then iodine (3.13 g, 12.3 mmol) was added to the mixture, continued stirring at -78 °C for 3 hours. Water (25 ml) was added to the reaction mixture and extracted with EEO (2 x

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30 ml). The combined organic layers were evaporated to Celite and purified by flash chromatography (heptane-EEO, gradient).

A part of the crude product (2.38 g, 5.81 mmol) and lithium-hydroxide hydrate (2.44 g, 58.1 mmol) were dissolved in PDO and water mixture (30 ml, v/v=1:1) and stirred at 100 °C for 70 hours. The reaction mixture was acidified with 1 N aqueous HCl solution. The resulted solid compound was filtered off, washed with water and dried.

The pyrimidone product was reacted using **General Procedure 5** with **Preparation R1e** as epoxide component.

The crude product (3.5 g, 5.79 mmol), copper(I)-cyanide (2.18 g, 24.32 mmol), tetraethylammonium-cyanide (950 mg, 6.08 mmol), tris (dibenzylideneacetone)dipalladium(0) (531 mg, 0.58 mmol), and 1,1'-bis(diphenylphosphino)ferrocene (1.29 g, 2.32 mmol) were dissolved in abs. PDO (45 ml) and the mixture was stirred at 110 °C for 2.3 hours. The reaction mixture was filtered, the filtrate was evaporated, the residue was diluted with MeOH (15 ml) then filtered again. The filtrate was evaporated to Celite and purified by flash chromatography (DCM-MeOH, gradient).

The resulted Boc-protected cyano-product (2.42 g, 4.81 mmol) was deprotected by stirring in mixture of TFA (1.11 ml, 14.47 mmol), formic acid (6.29 ml, 166.6 mmol) and DCM (60 ml) at r.t. for 52 hours. To the reaction mixture K₂CO₃ (25 g) and DCM (180 ml) was added and extracted with water (2 x 160 ml). The organic layer was evaporated.

The crude piperidine product was reacted with (3*R*,4*R*)-1-tert-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid using **General Procedure 7**.

The resulted Boc-protected product (798 mg, 1.16 mmol) was deprotected by stirring in mixture of TFA (266 µl, 3.48 mmol), formic acid (503 µl, 13.3 mmol) and DCM (15 ml) at r.t. for 164 hours. To the reaction mixture K₂CO₃ (2.8 g) was added and extracted with water (2 x 75 ml). The organic layer was evaporated.

The crude piperidine product was reacted with 3-fluoro-benzylchloride according to **General Procedure 6**.

The resulted crude product (534 mg, 0.76 mmol) and Raney-nickel (240 mg) were stirred in ammonia solution in methanol (7 M, 15 ml) under hydrogen atmosphere (2 bar) for 68 hours. The reaction mixture was filtered, the filtrate was evaporated.

The crude aminomethyl product was reacted with acetic acid according to **General Procedure 7**.

The resulted product (85.7 mg, 0.115 mmol) was stirred in TBAF solution (1 M in THF, 223 μ l, 0.223 mmol) and THF (0.5 ml) at 75 °C for 65 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 10 μ m column, 5 mM aqueous NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 927**. HRMS calculated for C₃₄H₃₉FN₆O₄: 614.3017; found 615.3082 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(p-tolylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-6-(2-thienyl)-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 928)**

2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (3.5 g, 12.3 mmol) was dissolved in THF (abs., 55 ml) and cooled to -78 °C, then LDA (2.0 M, 6.8 ml, 13.6 mmol) was added to the mixture and stirred at -78 °C for 40 minutes, then iodine (3.13 g, 12.3 mmol) was added to the mixture, continued stirring at -78 °C for 3 hours. Water (25 ml) was added to the reaction mixture and extracted with EEO (2 x 30 ml). The combined organic layers were evaporated to Celite and purified by flash chromatography (heptane-EEO gradient).

A part of the crude product (2.0 g, 4.88 mmol) and lithium-hydroxide hydrate (2.05 g, 48.8 mmol) were dissolved in PDO and water mixture (30 ml, v/v=1:1) and stirred at 100 °C for 65 hours. The reaction mixture was acidified with 1 N aqueous HCl solution.

The resulted solid compound was filtered off, washed with water and dried.

The pyrimidone product was reacted using **General Procedure 5** with **Preparation R1e** as epoxide component.

The resulted Boc-protected product (930 mg, 1.54 mmol) was deprotected by stirring in mixture of TFA (363 μ l, 4.74 mmol), formic acid (2.06 ml, 54.6 mmol) and DCM (18.6 ml) at r.t. for 46 hours. To the reaction mixture K₂CO₃ (6.5 g) was added and extracted with water (2 x 80 ml). The organic layers were evaporated and the residue was triturated with water (5 ml) to give a solid compound which was filtered off and dried.

The crude piperidine product was reacted with (3R,4R)-1-*tert*-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid using **General Procedure 7**.

The crude Boc-protected product (647 mg, 0.82 mmol) was deprotected by stirring in mixture of TFA (188 μ l, 2.46 mmol), formic acid (356 μ l, 9.43 mmol) and DCM (13 ml) at

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r.t. for 214 hours. To the reaction mixture, K_2CO_3 (1.99 g) was added. The solution was extracted with water (2 x 70 ml) and the organic layer was evaporated.

The crude product was *N*-alkylated with 4-methyl-benzylchloride according to **General Procedure 6**.

5 The crude alkylated compound (165 mg, 0.21 mmol), 2-thienylboronic acid (41 mg, 0.32 mmol), lithium-chloride (27 mg, 0.63 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (15 mg, 0.021 mmol) were dissolved in aqueous Na_2CO_3 solution (2 M, 265 μ l, 0.53 mmol), toluene (4 ml) and EtOH (4 ml) and stirred at 80 °C for 23 hours. The insoluble part was filtered off, the filtrate was
10 evaporated and the residue was purified by preparative LC (on C-18 Gemini-NX 10 μ m column, 25 mM aqueous NH_4HCO_3 -MeCN, gradient).

The resulted product (72 mg, 0.096 mmol) was stirred in TBAF solution (1 M in THF, 144 μ l, 0.144 mmol) and THF (0.5 ml) at 75 °C for 65 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 10 μ m column, 5 mM aqueous
15 NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 928**. HRMS calculated for $C_{36}H_{39}N_5O_3S$: 621.2773; found 622.2846 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(p-tolylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-6-(3-thienyl)-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 929)**

20 2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (3.5 g, 12.3 mmol) was dissolved in THF (abs., 55 ml) and cooled to -78 °C, then LDA (2.0 M, 6.8 ml, 13.6 mmol) was added to the mixture and stirred at -78 °C for 40 minutes, then iodine (3.13 g, 12.3 mmol) was added to the mixture, continued stirring at -78 °C for 3 hours. Water (25 ml) was added to the reaction mixture and extracted with EEO (2 x 30 ml). The combined organic layers were evaporated to Celite and purified by flash
25 chromatography (heptane-EEO gradient).

A part of the crude product (2.0 g, 4.88 mmol) and lithium-hydroxide hydrate (2.05 g, 48.8 mmol) were dissolved in PDO and water mixture (30 ml, v/v=1:1) and stirred at 100 °C for 65 hours. The reaction mixture was acidified with 1 N aqueous HCl solution. The resulted solid compound was filtered off, washed with water and dried.

30 The pyrimidone product was reacted using **General Procedure 5** with **Preparation R1e** as epoxide component.

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The resulted Boc-protected product (930 mg, 1.54 mmol) was deprotected by stirring in mixture of TFA (363 μ l, 4.74 mmol), formic acid (2.06 ml, 54.6 mmol) and DCM (18.6 ml) at r.t. for 46 hours. To the reaction mixture K_2CO_3 (6.5 g) was added and extracted with water (2 x 80 ml). The organic layers were evaporated and the residue was

5 trituated with water (5 ml) to give a solid compound which was filtered off and dried.

The crude piperidine product was reacted with (3R,4R)-1-tert-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid using **General Procedure 7**.

The crude Boc-protected product (647 mg, 0.82 mmol) was deprotected by stirring in mixture of TFA (188 μ l, 2.46 mmol), formic acid (356 μ l, 9.43 mmol) and DCM (13 ml) at

10 r.t. for 214 hours. To the reaction mixture, K_2CO_3 (1.99 g) was added. The solution was extracted with water (2 x 70 ml) and the organic layer was evaporated.

The crude product was *N*-alkylated with 4-methyl-benzylchloride according to **General Procedure 6**.

The crude alkylated compound (170 mg, 0.21 mmol), 4,4,5,5-tetramethyl-2-(3-thienyl)-

15 1,3,2-dioxaborolane (67 mg, 0.32 mmol), lithium-chloride (27 mg, 0.63 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (15 mg, 0.021 mmol) were dissolved in aqueous Na_2CO_3 solution (2 M, 265 μ l, 0.53 mmol), toluene (4 ml) and EtOH (4 ml) and stirred at 80 °C for 23 hours. The insoluble part was filtered off, the filtrate was evaporated and the residue was purified by preparative LC (on C-18 Gemini-NX 5 μ m

20 column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

The resulted product (72 mg, 0.096 mmol) was stirred in TBAF solution (1 M in THF, 144 μ l, 0.144 mmol) and THF (0.5 ml) at 75 °C for 60 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 10 μ m column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient) to give **EXAMPLE 929**. HRMS calculated for $C_{36}H_{39}N_5O_3S$:

25 621.2773; found 622.2834 [(M+H)⁺ form].

▪ **6-(2-fluorophenyl)-3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(p-tolylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 930)**

2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (3.5 g, 12.3 mmol) was dissolved in THF (abs., 55 ml) and cooled to -78 °C, then LDA (2.0 M, 6.8 ml, 13.6 mmol) was added to the mixture and stirred at -78 °C for 40 minutes, then

30 iodine (3.13 g, 12.3 mmol) was added to the mixture, continued stirring at -78 °C for

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3 hours. Water (25 ml) was added to the reaction mixture and extracted with EEO (2 x 30 ml). The combined organic layers were evaporated to Celite and purified by flash chromatography (heptane-EEO gradient).

A part of the crude product (2.0 g, 4.88 mmol) and lithium-hydroxide hydrate (2.05 g, 48.8 mmol) were dissolved in PDO and water mixture (30 ml, v/v=1:1) and stirred at 100 °C for 65 hours. The reaction mixture was acidified with 1 N aqueous HCl solution. The resulted solid compound was filtered off, washed with water and dried.

The pyrimidone product was reacted using **General Procedure 5** with **Preparation R1e** as epoxide component.

The resulted Boc-protected product (930 mg, 1.54 mmol) was deprotected by stirring in mixture of TFA (363 µl, 4.74 mmol), formic acid (2.06 ml, 54.6 mmol) and DCM (18.6 ml) at r.t. for 46 hours. To the reaction mixture K₂CO₃ (6.5 g) was added and extracted with water (2 x 80 ml). The organic layers were evaporated and the residue was triturated with water (5 ml) to give a solid compound which was filtered off and dried.

The crude piperidine product was reacted with (3R,4R)-1-tert-butoxycarbonyl-3-phenyl-piperidine-4-carboxylic acid using **General Procedure 7**.

The crude Boc-protected product (647 mg, 0.82 mmol) was deprotected by stirring in mixture of TFA (188 µl, 2.46 mmol), formic acid (356 µl, 9.43 mmol) and DCM (13 ml) at r.t. for 214 hours. To the reaction mixture, K₂CO₃ (1.99 g) was added. The solution was extracted with water (2 x 70 ml) and the organic layer was evaporated.

The crude product was N-alkylated with 4-methyl-benzylchloride according to **General Procedure 6**.

The crude alkylated compound (170 mg, 0.21 mmol), 2-fluorophenylboronic acid (44 mg, 0.32 mmol), lithium-chloride (27 mg, 0.63 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (15 mg, 0.021 mmol) were dissolved in aqueous Na₂CO₃ solution (2 M, 265 µl, 0.53 mmol), toluene (4 ml) and EtOH (4 ml) and stirred at 80 °C for 22 hours. The insoluble part was filtered off, the filtrate was evaporated and the residue was purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

The resulted product (70 mg, 0.09 mmol) was stirred in TBAF solution (1 M in THF, 138 µl, 0.138 mmol) and THF (0.5 ml) at 75 °C for 60 hours. The reaction mixture was purified by preparative LC (on C-18 Gemini-NX 10µm column, 5 mM aqueous

NH₄HCO₃-MeCN, gradient) to give **EXAMPLE 930**. HRMS calculated for C₃₈H₄₀FN₅O₃: 633.3115; found 634.3194 [(M+H)⁺ form].

5 ▪ **5-fluoro-3-[[4-hydroxy-1-[(3R,4R)-1-(4-methyl-2-phenyl-thiazole-5-carbonyl)-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-methyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 931)**

Using **General Procedure 11** starting from **Preparation R2dj** and (4-methyl-2-phenyl-1,3-thiazol-5-yl)[(3R,4R)-4-(1-oxa-6-azaspiro[2.5]oct-6-ylcarbonyl)-3-phenylpiperidin-1-yl]methanone as reagents, **EXAMPLE 931** was obtained. HRMS calculated for C₃₆H₃₇FN₆O₄S: 668.2581; found 669.2649 [(M+H)⁺ form].

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7,8-dihydro-6H-pyrimido[5,4-b]pyrrolizin-4-one (EXAMPLE 932)**

Using **General Procedure 11** starting from **Preparation R2dk** and **Preparation R1m** as reagents, **EXAMPLE 932** was obtained. HRMS calculated for C₃₈H₄₁N₇O₄S: 691.2941; found 346.6539 [M+2H]²⁺ form].

15 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-6,7,8,9-tetrahydropyrimido[5,4-b]indolizin-4-one (EXAMPLE 933)**

Using **General Procedure 11** starting from **Preparation R2dl** and **Preparation R1m** as reagents, **EXAMPLE 933** was obtained. HRMS calculated for C₃₉H₄₃N₇O₄S: 705.3098; found 706.3172 [(M+H)⁺ form].

20 ▪ **3-[[1-[(3R,4S)-1-benzyl-3-(2-thienyl)piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 934)**

Using **General Procedure 5** starting from 3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one and **Preparation R1e** as epoxide component, the crude product was reacted with **Preparation R1q-(3R,4S)** according to **General Procedure 7** to give **EXAMPLE 934**. HRMS calculated for C₂₉H₃₃N₅O₃S: 531.2304; found 532.2388 [(M+H)⁺ form].

▪ **3-[[1-[(3S,4R)-1-benzyl-3-(2-thienyl)piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 935)**

Using **General Procedure 5** starting from 3H,4H,7H-pyrrolo[2,3-d]pyrimidin-4-one and **Preparation R1e** as epoxide component, the crude product was reacted with **Preparation R1q-(3S,4R)** according to **General Procedure 7** to give **EXAMPLE 935**. HRMS calculated for C₂₉H₃₃N₅O₃S: 531.2304; found 532.2388 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4S)-1-benzyl-3-(2-thienyl)piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-6-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 936)**

2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (600 mg, 2.11 mmol) was dissolved in abs. THF (12 ml) and cooled to -78 °C, then LDA solution (2.0 M, 1.2 ml, 2.4 mmol) was added to the mixture and stirred at -78 °C for 1 hour, then iodomethane (158 µl, 2.53 mmol) was added to the mixture, continued stirring at -78 °C for 3 hours. Water (10 ml) was added to the reaction mixture and extracted with EEO (2 x 20 ml). The combined organic layers were evaporated and purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH₄HCO₃-MeCN, gradient).

A part of the crude product (300 mg, 1.01 mmol) and lithium-hydroxide hydrate (423 mg, 10.1 mmol) were dissolved in PDO and water mixture (4 ml, v/v=1:1) and stirred at 100 °C for 142 hours. The reaction mixture was acidified with aqueous HCl solution (1 N, 9.5 ml). The resulted solid compound was filtered off, washed with water and dried.

Using **General Procedure 5** starting from the crude product and **Preparation R1e** as epoxide component, the resulted product (140 mg, 0.28 mmol) was then stirred in TBAF solution (1 M in THF, 1.4 ml, 1.4 mmol) at 90 °C for 24 hours. Water (5 ml) was added to the reaction mixture and extracted with EEO (2 x 10 ml). The combined organic layers were extracted with water (2 x 10 ml), dried over MgSO₄ and evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 10µm column, 25 mM aqueous NH₄HCO₃-MeCN, ISO39).

The resulted desilylated product (23.5 mg, 0.065 mmol) was stirred in mixture of aqueous HCl solution (0.65 ml) and PDO (0.5 ml) at 60 °C for 4 hours. The reaction mixture was evaporated.

The crude product was reacted with **Preparation R1q-(3R,4S)** according to **General Procedure 7** to give **EXAMPLE 936**. HRMS calculated for $C_{30}H_{35}N_5O_3S$: 545.2460; found 546.2546 [(M+H)⁺ form].

▪ **3-[[1-[(3S,4R)-1-benzyl-3-(2-thienyl)piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-6-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 937)**

2-[(4-chloropyrrolo[2,3-d]pyrimidin-7-yl)methoxy]ethyl-trimethyl-silane (600 mg, 2.11 mmol) was dissolved in abs. THF (12 ml) and cooled to -78 °C, then LDA (2.0 M, 1.2 ml, 2.4 mmol) was added to the mixture and stirred at -78 °C for 1 hour, then iodomethane (158 µl, 2.53 mmol) was added to the mixture, continued stirring at -78 °C for 3 hours. Water (10 ml) was added to the reaction mixture and extracted with EEO (2 x 20 ml). The combined organic layers were evaporated and purified by preparative LC (on C-18 Gemini-NX 5µm column, 5 mM aqueous NH_4HCO_3 -MeCN, gradient).

A part of the crude product (300 mg, 1.01 mmol) and lithium-hydroxide hydrate (423 mg, 10.1 mmol) were dissolved in PDO and water mixture (4 ml, v/v=1:1) and stirred at 100 °C for 142 hours. The reaction mixture was acidified with aqueous HCl solution (1 N, 9.5 ml). The resulted solid compound was filtered off, washed with water and dried.

Using **General Procedure 5** starting from the crude product and **Preparation R1e** as epoxide component, the resulted product (140 mg, 0.28 mmol) was then stirred in TBAF solution (1 M in THF, 1.4 ml, 1.4 mmol) at 90 °C for 24 hours. Water (5 ml) was added to the reaction mixture and extracted with EEO (2 x 10 ml). The combined organic layers were extracted with water (2 x 10 ml), dried over $MgSO_4$ and evaporated. The residue was purified by preparative LC (on C-18 Gemini-NX 10µm column, 25 mM aqueous NH_4HCO_3 -MeCN, ISO39).

The resulted desilylated product (23.5 mg, 0.065 mmol) was stirred in mixture of aqueous HCl solution (0.65 ml) and PDO (0.5 ml) at 60 °C for 4 hours. The reaction mixture was evaporated.

The crude product was reacted with **Preparation R1q-(3S,4R)** according to **General Procedure 7** to give **EXAMPLE 937**. HRMS calculated for $C_{30}H_{35}N_5O_3S$: 545.246; found 546.2527 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(1-methylpyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 938)**

Using **General Procedure 7** starting from **Preparation R3cy** and **Preparation R1d** as reagents, the resulted crude product was reacted with 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 938**. HRMS calculated for C₃₉H₄₁N₉O₄S: 731.3002; found 732.3057 [(M+H)⁺ form].

▪ **7-(3-furyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 939)**

Using **General Procedure 7** starting from **Preparation R3cy** and **Preparation R1d** as reagents, the resulted crude product was reacted with 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 939**. HRMS calculated for C₃₉H₃₉N₇O₅S: 717.2734; found 718.2804 [(M+H)⁺ form].

▪ **7-(3-furyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]thieno[3,4-d]pyrimidin-4-one (EXAMPLE 940)**

Using **General Procedure 7** starting from **Preparation R3dc** and **Preparation R1d** as reagents, the resulted crude product was reacted with 2-(3-furyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane according to **General Procedure 9**, to give **EXAMPLE 940**. HRMS calculated for C₃₉H₃₈N₆O₅S₂: 734.2345; found 735.2417 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(1-methylpyrazol-4-yl)thieno[3,4-d]pyrimidin-4-one (EXAMPLE 941)**

Using **General Procedure 7** starting from **Preparation R3dc** and **Preparation R1d** as reagents, the resulted crude product was reacted with 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give

EXAMPLE 941. HRMS calculated for $C_{39}H_{40}N_8O_4S_2$: 748.2614; found 749.2704 $[(M+H)^+]$ form].

▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-[4-(hydroxymethyl)phenyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (**EXAMPLE 942**)

Using **General Procedure 7** starting from **R3cy** and **R1d** as reagents, the resulted crude product was reacted with [4-(hydroxymethyl)phenyl]boronic acid according to **General Procedure 9**, to give **EXAMPLE 942**. HRMS calculated for $C_{42}H_{43}N_7O_5S$: 757.3046; found 758.3135 $[(M+H)^+]$ form].

▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-[4-(hydroxymethyl)phenyl]thieno[3,4-d]pyrimidin-4-one (**EXAMPLE 943**)

Using **General Procedure 7** starting from **Preparation R3dc** and **Preparation R1d** as reagents, the resulted crude product was reacted with [4-(hydroxymethyl)phenyl]boronic acid according to **General Procedure 9**, to give **EXAMPLE 943**. HRMS calculated for $C_{42}H_{42}N_6O_5S_2$: 774.2658; found 775.2733 $[(M+H)^+]$ form].

▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (**EXAMPLE 944**)

Using **General Procedure 7** starting from **Preparation R3bu** and **Preparation R1x** as reagents, **EXAMPLE 944** was obtained. HRMS calculated for $C_{40}H_{39}N_7O_4S$: 713.2784; found 714.2859 $[(M+H)^+]$ form].

▪ 3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(1-methylpyrrol-3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-one (**EXAMPLE 945**)

Using **General Procedure 7** starting from **Preparation R3cy** and **Preparation R1d** as reagents, the resulted crude product was reacted with 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole according to **General Procedure 9**, to give

EXAMPLE 945. HRMS calculated for $C_{40}H_{42}N_8O_4S$: 730.3050; found 731.3113 $[(M+H)^+ \text{ form}]$.

5 ▪ **7-(3-chlorophenyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 946)**

Using **General Procedure 7** starting from **Preparation R3ar** and **Preparation R1x** as reagents, **EXAMPLE 946** was obtained. HRMS calculated for $C_{40}H_{38}N_7O_4SCl$: 747.2395; found 748.2461 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(3-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 947)**

Using **General Procedure 7** starting from **Preparation R3bo** and **Preparation R1x** as reagents, **EXAMPLE 947** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 744.2968 $[(M+H)^+ \text{ form}]$.

15 ▪ **7-(4-fluorophenyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 948)**

Using **General Procedure 7** starting from **Preparation R3as** and **Preparation R1x** as reagents, **EXAMPLE 948** was obtained. HRMS calculated for $C_{40}H_{38}N_7O_4FS$: 731.2690; found 732.2765 $[(M+H)^+ \text{ form}]$.

20 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 949)**

Using **General Procedure 7** starting from **Preparation R3ax** and **Preparation R1x** as reagents, **EXAMPLE 949** was obtained. HRMS calculated for $C_{41}H_{41}N_7O_5S$: 743.2890; found 744.2951 $[(M+H)^+ \text{ form}]$.

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[2-(6-methoxy-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 950)**

Ethyl 2-(6-methoxy-3-pyridyl)thiazole-5-carboxylate (0.75 mmol) was stirred with lithium-hydroxide hydrate (3 mmol) in mixture of water (2 ml) and methanol (2 ml) at 40 °C for 4 hours. The reaction mixture was neutralized with aqueous 1N HCl solution (3 ml), then evaporated. The resulted crude 2-(6-methoxy-3-pyridyl)thiazole-5-carboxylic acid was reacted with **R3ax** according to **General Procedure 7** to give **EXAMPLE 950**. HRMS calculated for C₄₁H₄₁N₇O₆S: 759.2839; found 760.2908 [(M+H)⁺ form].

▪ **7-(2-furyl)-3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 951)**

Using **General Procedure 7** starting from **Preparation R3cy** and **Preparation R1d** as reagents, the resulted crude product was reacted with 2-furylboronic acid according to **General Procedure 9**, to give **EXAMPLE 951**. HRMS calculated for C₃₉H₃₉N₇O₅S: 717.2734; found 718.2801 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(1-methylpyrrol-3-yl)thieno[3,4-d]pyrimidin-4-one (EXAMPLE 952)**

Using **General Procedure 7** starting from **Preparation R3dc** and **Preparation R1d** as reagents, the resulted crude product was reacted with 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrole according to **General Procedure 9**, to give **EXAMPLE 952**. HRMS calculated for C₄₀H₄₁N₇O₄S₂: 747.2661; found 748.2722 [(M+H)⁺ form].

▪ **3-[[3,3-difluoro-4-hydroxy-1-[trans-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one, enantiomer 1 (EXAMPLE 953)**

and

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3-[[3,3-difluoro-4-hydroxy-1-[trans-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one, enantiomer 2 (EXAMPLE 954)

Using **General Procedure 7** starting from **Preparation R3dm** and **Preparation R1d** as reagents, **EXAMPLE 953** and **EXAMPLE 954** were obtained and separated by liquid chromatography.

EXAMPLE 953: HRMS calculated for $C_{41}H_{39}N_7O_4F_2S$: 763.2752; found 382.6463 [(M+2H)²⁺ form].

EXAMPLE 954: HRMS calculated for $C_{41}H_{39}N_7O_4F_2S$: 763.2752; found 382.6463 [(M+2H)²⁺ form].

▪ **3-[[3,3-difluoro-4-hydroxy-1-[trans-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one, enantiomer 1 (EXAMPLE 955)**
and

3-[[3,3-difluoro-4-hydroxy-1-[trans-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one, enantiomer 2 (EXAMPLE 956)

Using **General Procedure 7** starting from **Preparation R3dn** and **Preparation R1d** as reagents, **EXAMPLE 955** and **EXAMPLE 956** were obtained and separated by liquid chromatography.

EXAMPLE 955: HRMS calculated for $C_{42}H_{41}N_7O_5F_2S$: 793.2858; found 794.2910 [(M+H)⁺ form].

EXAMPLE 956: HRMS calculated for $C_{42}H_{41}N_7O_5F_2S$: 793.2858; found 794.2960 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[4-methyl-2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 957)**

Using **General Procedure 6** starting from **Preparation R3bu** and 5-(chloromethyl)-4-methyl-2-(6-methyl-3-pyridyl)thiazole as reagents, **EXAMPLE 957** was obtained. HRMS calculated for $C_{41}H_{43}N_7O_3S$: 713.3148; found 714.3215 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[[4-methyl-2-(6-methyl-3-pyridyl)thiazol-5-yl]methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 958)**

Using **General Procedure 6** starting from **Preparation R3ax** and 5-(chloromethyl)-4-methyl-2-(6-methyl-3-pyridyl)thiazole as reagents, **EXAMPLE 958** was obtained. HRMS calculated for $C_{42}H_{45}N_7O_4S$: 743.3254; found 744.3323 $[(M+H)^+]$ form].

▪ **7-(3,5-dimethoxyphenyl)-3-[[4-hydroxy-1-[(3S,4S)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 959)**

Using **General Procedure 7** starting from **Preparation R3af** and **Preparation R1d** as reagents, **EXAMPLE 959** was obtained. HRMS calculated for $C_{43}H_{45}N_7O_6S$: 787.3152; found 788.3226 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrimidin-4-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 960)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)pyrimidine as reagents, **EXAMPLE 960** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_3$: 603.2958; found 604.2303 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrimidin-4-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 961)**

Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)pyrimidine as reagents, **EXAMPLE 961** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3064; found 634.3140 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 962)**

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Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)-2-methoxy-pyrimidine as reagents, **EXAMPLE 962** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3064; found 634.3126 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 963)**

Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)-2-methoxy-pyrimidine as reagents, **EXAMPLE 963** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_5$: 663.3169; found 664.3251 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[[1-[(3R,4R)-1-(3-fluorophenyl)sulfonyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 964)**

Using **General Procedure 8** starting from **Preparation R3bu** and 3-fluorobenzenesulfonyl chloride as reagents, **EXAMPLE 964** was obtained. HRMS calculated for $C_{36}H_{36}N_5O_5FS$: 669.2421; found 670.2489 $[(M+H)^+ \text{ form}]$.

15 ▪ **3-[[1-[(3R,4R)-1-(3-fluorophenyl)sulfonyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 965)**

Using **General Procedure 8** starting from **Preparation R3ax** and 3-fluorobenzenesulfonyl chloride as reagents, **EXAMPLE 965** was obtained. HRMS
20 calculated for $C_{37}H_{38}N_5O_6FS$: 699.2527; found 700.2596 $[(M+H)^+ \text{ form}]$.

25 ▪ **3-[[1-[(3R,4R)-1-(2-fluorophenyl)sulfonyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 966)**

Using **General Procedure 8** starting from **Preparation R3bu** and 2-fluorobenzenesulfonyl chloride as reagents, **EXAMPLE 966** was obtained. HRMS
calculated for $C_{36}H_{36}N_5O_5FS$: 669.2421; found 670.2492 $[(M+H)^+ \text{ form}]$.

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▪ **3-[[1-[(3R,4R)-1-(2-fluorophenyl)sulfonyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 967)**

Using **General Procedure 8** starting from **Preparation R3ax** and
5 2-fluorobenzenesulfonyl chloride as reagents, **EXAMPLE 967** was obtained. HRMS calculated for $C_{37}H_{38}N_5O_6FS$: 699.2527; found 700.2598 $[(M+H)^+]$ form].

▪ **3-[[1-[(3R,4R)-1-(4-fluorophenyl)sulfonyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 968)**

Using **General Procedure 8** starting from **Preparation R3bu** and
10 4-fluorobenzenesulfonyl chloride as reagents, **EXAMPLE 968** was obtained. HRMS calculated for $C_{36}H_{36}N_5O_5FS$: 669.2421; found 670.2494 $[(M+H)^+]$ form].

▪ **3-[[1-[(3R,4R)-1-(4-fluorophenyl)sulfonyl-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 969)**

Using **General Procedure 8** starting from **Preparation R3ax** and
15 4-fluorobenzenesulfonyl chloride as reagents, **EXAMPLE 969** was obtained. HRMS calculated for $C_{37}H_{38}N_5O_6FS$: 699.2527; found 700.2598 $[(M+H)^+]$ form].

▪ **7-bromo-3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 970)**

Using **General Procedure 6** starting from **Preparation R3cy** and
20 2-(chloromethyl)pyrazine as reagents, **EXAMPLE 970** was obtained. HRMS calculated for $C_{29}H_{32}N_7O_3Br$: 605.1750; found 606.1826 $[(M+H)^+]$ form].

▪ **7-chloro-3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]thieno[3,4-d]pyrimidin-4-one (EXAMPLE 971)**

Using **General Procedure 6** starting from **Preparation R3dc** and
25 2-(chloromethyl)pyrazine as reagents, **EXAMPLE 971** was obtained. HRMS calculated for $C_{29}H_{31}N_6O_3SCl$: 578.1867; found 579.1947 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazine-2-carbonyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 972)**

Using **General Procedure 7** starting from **Preparation R3bu** and pyrazine-2-carboxylic acid as reagents, **EXAMPLE 972** was obtained. HRMS calculated for C₃₅H₃₅N₇O₄: 617.2751; found 618.2826 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazine-2-carbonyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 973)**

Using **General Procedure 7** starting from **Preparation R3ax** and pyrazine-2-carboxylic acid as reagents, **EXAMPLE 973** was obtained. HRMS calculated for C₃₆H₃₇N₇O₅: 647.2856; found 648.2931 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(6-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 974)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-6-methyl-pyrazine as reagents, **EXAMPLE 974** was obtained. HRMS calculated for C₃₆H₃₉N₇O₃: 617.3114; found 618.3178 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(6-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 975)**

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-6-methyl-pyrazine as reagents, **EXAMPLE 975** was obtained. HRMS calculated for C₃₇H₄₁N₇O₄: 647.3220; found 648.3285 [(M+H)⁺ form].

▪ **3-[[1-[(3R,4R)-1-[(4,6-dimethylpyrimidin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 976)**

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Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-4,6-dimethyl-pyrimidine as reagents, **EXAMPLE 976** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_3$: 631.3271; found 632.3338 $[(M+H)^+]$ form].

5 ▪ **3-[[1-[(3R,4R)-1-[(4,6-dimethylpyrimidin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 977)**

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-4,6-dimethyl-pyrimidine as reagents, **EXAMPLE 977** was obtained. HRMS calculated for $C_{38}H_{43}N_7O_4$: 661.3377; found 662.3424 $[(M+H)^+]$ form].

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 978)**

Using **General Procedure 9** starting from **EXAMPLE 970** and phenylboronic acid as reagents, **EXAMPLE 978** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_3$: 603.2958; found 604.3022 $[(M+H)^+]$ form].

15 ▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,1-f][1,2,4]triazin-4-one (EXAMPLE 979)**

Using **General Procedure 9** starting from **EXAMPLE 970** and (4-methoxyphenyl)boronic acid as reagents, **EXAMPLE 979** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$:
20 633.3064; found 634.3127 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one (EXAMPLE 980)**

Using **General Procedure 9** starting from **EXAMPLE 971** and phenylboronic acid as reagents, **EXAMPLE 980** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_3S$: 620.2570;
25 found 621.2627 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)thieno[3,4-d]pyrimidin-4-one (EXAMPLE 981)**

Using **General Procedure 9** starting from **EXAMPLE 971** and (4-methoxyphenyl)boronic acid as reagents, **EXAMPLE 981** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2676; found 651.2745 $[(M+H)^+]$ form].

5 ▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyridazin-3-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 982)**

Using **General Procedure 6** starting from **Preparation R3bu** and 3-(bromomethyl)pyridazine as reagents, **EXAMPLE 982** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_3$: 603.2958; found 604.3017 $[(M+H)^+]$ form].

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyridazin-3-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 983)**

Using **General Procedure 6** starting from **Preparation R3ax** and 3-(bromomethyl)pyridazine as reagents, **EXAMPLE 983** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3064; found 634.3139 $[(M+H)^+]$ form].

15 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 984)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-5-methyl-pyrazine as reagents, **EXAMPLE 984** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_3$: 617.3114; found 618.3172 $[(M+H)^+]$ form].

20 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 985)**

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-5-methyl-pyrazine as reagents, **EXAMPLE 985** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_4$: 647.3220; found 648.3314 $[(M+H)^+]$ form].

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▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 986)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)pyrimidine as reagents, **EXAMPLE 986** was obtained. HRMS calculated for $C_{35}H_{37}N_7O_3$: 603.2958; found 604.3022 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 987)**

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)pyrimidine as reagents, **EXAMPLE 987** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3064; found 634.3128 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(4-methylpyrimidin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 988)**

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-4-methyl-pyrimidine as reagents, **EXAMPLE 988** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_3$: 617.3114; found 618.3158 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(4-methylpyrimidin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 989)**

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-4-methyl-pyrimidine as reagents, **EXAMPLE 989** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_4$: 647.3220; found 648.3298 $[(M+H)^+$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one (EXAMPLE 990)**

Using **General Procedure 6** starting from **Preparation R3bu** and 4-(chloromethyl)-2-methyl-pyrimidine as reagents, **EXAMPLE 990** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_3$: 617.3114; found 618.3179 $[(M+H)^+ \text{ form}]$.

5 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one**
(**EXAMPLE 991**)

Using **General Procedure 6** starting from **Preparation R3ax** and 4-(chloromethyl)-2-methyl-pyrimidine as reagents, **EXAMPLE 991** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_4$: 647.3220; found 648.3282 $[(M+H)^+ \text{ form}]$.

10 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(6-methoxypyridazin-3-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one**
(**EXAMPLE 992**)

Using **General Procedure 6** starting from **Preparation R3bu** and 3-(chloromethyl)-6-methoxy-pyridazine as reagents, **EXAMPLE 992** was obtained. HRMS calculated for
15 $C_{36}H_{39}N_7O_4$: 633.3064; found 634.3129 $[(M+H)^+ \text{ form}]$.

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(6-methoxypyridazin-3-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one**
(**EXAMPLE 993**)

Using **General Procedure 6** starting from **Preparation R3ax** and 3-(chloromethyl)-6-methoxy-pyridazine as reagents, **EXAMPLE 993** was obtained. HRMS calculated for
20 $C_{37}H_{41}N_7O_5$: 663.3169; found 664.3223 $[(M+H)^+ \text{ form}]$.

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(3-methoxypyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one**
(**EXAMPLE 994**)

25 Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-3-methoxy-pyrazine as reagents, **EXAMPLE 994** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_4$: 633.3064; found 634.3142 $[(M+H)^+ \text{ form}]$.

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(3-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-d]pyrimidin-4-one**
(EXAMPLE 995)

Using **General Procedure 6** starting from **Preparation R3bu** and 2-(chloromethyl)-3-methyl-pyrazine as reagents, **EXAMPLE 995** was obtained. HRMS calculated for $C_{36}H_{39}N_7O_3$: 617.3114; found 618.3214 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(3-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one**
(EXAMPLE 996)

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-3-methyl-pyrazine as reagents, **EXAMPLE 996** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_4$: 647.3220; found 648.3265 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(3-methoxypyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-d]pyrimidin-4-one**
(EXAMPLE 997)

Using **General Procedure 6** starting from **Preparation R3ax** and 2-(chloromethyl)-3-methoxy-pyrazine as reagents, **EXAMPLE 997** was obtained. HRMS calculated for $C_{37}H_{41}N_7O_5$: 663.3169; found 664.3211 [(M+H)⁺ form].

▪ **4-[[[(3R,4R)-4-[4-hydroxy-4-[[4-oxo-7-(2-pyridyl)pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidine-1-carbonyl]-3-phenyl-1-piperidyl)methyl]pyridine-2-carbonitrile**
(EXAMPLE 998)

Using **General Procedure 6** starting from **Preparation R3ca** and 4-(chloromethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 998** was obtained. HRMS calculated for $C_{36}H_{36}N_8O_3$: 628.2910; found 629.2987 [(M+H)⁺ form].

▪ **5-[[[(3R,4R)-4-[4-hydroxy-4-[[7-(1-methylpyrazol-4-yl)-4-oxo-pyrrolo[2,3-d]pyrimidin-3-yl)methyl]piperidine-1-carbonyl]-3-phenyl-1-piperidyl)methyl]pyridine-2-carbonitrile** (EXAMPLE 999)

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Using **General Procedure 6** starting from **Preparation R3ch** and 4-(bromomethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 999** was obtained. HRMS calculated for $C_{35}H_{37}N_9O_3$: 631.3019; found 632.3066 $[(M+H)^+]$ form].

5 ▪ **5-[[[(3R,4R)-4-[4-hydroxy-4-[[4-oxo-7-(2-pyridyl)pyrrolo[2,3-d]pyrimidin-3-yl]methyl]piperidine-1-carbonyl]-3-phenyl-1-piperidyl]methyl]pyridine-2-carbonitrile (EXAMPLE 1000)**

Using **General Procedure 6** starting from **Preparation R3ca** and 4-(bromomethyl)pyridine-2-carbonitrile as reagents, **EXAMPLE 1000** was obtained. HRMS calculated for $C_{36}H_{36}N_8O_3$: 628.2910; found 629.2976 $[(M+H)^+]$ form].

10 ▪ **5-[[[(3R,4R)-4-[4-hydroxy-4-[[7-(1-methylpyrazol-4-yl)-4-oxo-pyrrolo[2,1-f][1,2,4]triazin-3-yl]methyl]piperidine-1-carbonyl]-3-phenyl-1-piperidyl]methyl]pyridine-2-carbonitrile (EXAMPLE 1001)**

Using **General Procedure 6** starting from **Preparation R3cy** and 5-(bromomethyl)pyridine-2-carbonitrile as reagents, the resulted crude product was reacted
15 with 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 1001**. HRMS calculated for $C_{35}H_{37}N_9O_3$: 631.3019; found 632.3068 $[(M+H)^+]$ form].

20 ▪ **4-[[[(3R,4R)-4-[4-hydroxy-4-[[7-(1-methylpyrazol-4-yl)-4-oxo-pyrrolo[2,1-f][1,2,4]triazin-3-yl]methyl]piperidine-1-carbonyl]-3-phenyl-1-piperidyl]methyl]pyridine-2-carbonitrile (EXAMPLE 1002)**

Using **General Procedure 6** starting from **Preparation R3cy** and 4-(chloromethyl)pyridine-2-carbonitrile as reagents, the resulted crude product was reacted
25 with 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 1002**. HRMS calculated for $C_{35}H_{37}N_9O_3$: 631.3019; found 632.3071 $[(M+H)^+]$ form].

▪ **4-[[[(3R,4R)-4-[4-hydroxy-4-[[7-(1-methylpyrazol-4-yl)-4-oxo-thieno[3,4-d]pyrimidin-3-yl]methyl]piperidine-1-carbonyl]-3-phenyl-1-piperidyl]methyl]pyridine-2-carbonitrile (EXAMPLE 1003)**

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Using **General Procedure 6** starting from **Preparation R3dc** and 4-(chloromethyl)pyridine-2-carbonitrile as reagents, the resulted crude product was reacted with 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole according to **General Procedure 9**, to give **EXAMPLE 1003**. HRMS calculated for $C_{35}H_{36}N_8O_3S$:
5 648.2631; found 649.2693 $[(M+H)^+]$ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(**EXAMPLE 1004**)

Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)-5-methyl-pyrazine as reagents, **EXAMPLE 1004** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3S$: 634.2726; found 635.2793 $[(M+H)^+]$ form].
10

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one** (**EXAMPLE 1005**)

Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)pyrimidine as reagents, **EXAMPLE 1005** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_3S$: 620.2570; found 621.2619 $[(M+H)^+]$ form].
15

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(4-methylpyrimidin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(**EXAMPLE 1006**)

Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)-4-methyl-pyrimidine as reagents, **EXAMPLE 1006** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3S$: 634.2726; found 635.2791 $[(M+H)^+]$ form].
20

▪ **3-[[4-hydroxy-1-[(3R,4R)-3-phenyl-1-(pyrimidin-4-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one** (**EXAMPLE 1007**)

Using **General Procedure 6** starting from **Preparation R3da** and 4-(chloromethyl)pyrimidine as reagents, **EXAMPLE 1007** was obtained. HRMS calculated for $C_{35}H_{36}N_6O_3S$: 620.2570; found 621.2656 $[(M+H)^+]$ form].
25

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▪ **3-[[1-[(3R,4R)-1-[(4,6-dimethylpyrimidin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-hydroxy-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(EXAMPLE 1008)

Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)-4,6-dimethyl-pyrimidine as reagents, **EXAMPLE 1008** was obtained. HRMS calculated for $C_{37}H_{40}N_6O_3S$: 648.2883; found 649.2952 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(EXAMPLE 1009)

Using **General Procedure 6** starting from **Preparation R3da** and 4-(chloromethyl)-2-methoxy-pyrimidine as reagents, **EXAMPLE 1009** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2744 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(EXAMPLE 1010)

Using **General Procedure 6** starting from **Preparation R3da** and 4-(chloromethyl)-2-methyl-pyrimidine as reagents, **EXAMPLE 1010** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3S$: 634.2726; found 635.2805 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(6-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(EXAMPLE 1011)

Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)-6-methyl-pyrazine as reagents, **EXAMPLE 1011** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3S$: 634.2726; found 635.2792 [(M+H)⁺ form].

▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(3-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(EXAMPLE 1012)

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Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)-3-methyl-pyrazine as reagents, **EXAMPLE 1012** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_3S$: 634.2726; found 635.2782 $[(M+H)^+]$ form].

5 ▪ **3-[[4-hydroxy-1-[(3R,4R)-1-[(3-methoxypyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl]methyl]-7-phenyl-thieno[3,4-d]pyrimidin-4-one**
(**EXAMPLE 1013**)

Using **General Procedure 6** starting from **Preparation R3da** and 2-(chloromethyl)-3-methoxy-pyrazine as reagents, **EXAMPLE 1013** was obtained. HRMS calculated for $C_{36}H_{38}N_6O_4S$: 650.2675; found 651.2764 $[(M+H)^+]$ form].

PHARMACOLOGICAL STUDY

EXAMPLE A: Evaluation of the inhibition of USP7 by the Fluorescence Intensity (FLINT) readings

USP7 activity was measured using Rhodamine-110 c-terminal labelled Ubiquitin as a substrate (*Viva Biosciences*). Incubation with USP7 results in the release of Rhodamine-110 leading to an increase in fluorescence which can be used in the continuous measurement of USP7 activity.

The USP7 reactions were performed in a 50 μ L volume, in 384 well black solid low binding plates (Corning #3575). The reaction buffer consisted of 100 mM Bicine pH 8.0, 0.01 % TritonX100, 1 mM TCEP, and 10 % DMSO.

0.25 nM His-His-USP7 (aa208-560, [C315A]) was incubated with compound (final concentration 10 % DMSO) for 60 minutes at 30 °C. The reaction was then initiated by the addition of 500 nM Ubiquitin-Rhodamine-110 substrate and the plate read every 3 minutes for 21 minutes to measure the release of Rhodamine-110. Fluorescence Intensity (FLINT) readings were measured using a Biomek Neo plate reader (Ex.485 nm, Em.535 nm).

The inhibition of increasing doses of compound was expressed as a percentage reduction in kinetic rate compared to the kinetic rates established between 'DMSO only' and 'total inhibition' controls (no USP7). The inhibitory concentrations that gave a 50 % reduction in kinetic rate (IC_{50}) were determined, from 11-point dose response curves, in XL-Fit using a 4-Parameter Logistic Model (Sigmoidal Dose-Response Model).

The results presented in Table 1 below show that compounds of the invention inhibit interaction between USP7 protein and the fluorescent peptide described hereinbefore.

EXAMPLE B: *In vitro* cytotoxicity

The cytotoxicity studies were evaluated by MTT assay and carried out on MM1S multiple myeloma or Z138 mantle cell lymphoma tumour cell lines. The cells are distributed onto microplates and exposed to the test compounds for 96 hours. The cell viability is then quantified by a colorimetric assay, the Microculture Tetrazolium Assay (Carmichael et al., *Cancer Res.* 1987, 47, 936-942). The results are expressed in IC₅₀ (the concentration of compound that inhibits cell viability by 50 %) and are presented in Table 1 below.

The results show that the compounds of the invention are cytotoxic.

Table 1: IC₅₀ of USP7 inhibition and of cytotoxicity for MM1S or Z138 cells

Note: IC₅₀ of cytotoxicity for Z138 tumour cell line are underlined.

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
1	1.4E-07	2.8E-06	19	1.2E-08	2.4E-09
2	7.9E-08	NT	20	9.3E-09	NT
3	4.9E-09	3.3E-09	21	5.1E-08	1.9E-08
4	3.3E-09	3.4E-09	22	7.3E-08	NT
5	5.2E-08	2.1E-08	23	7.5E-09	4.8E-09
6	1.2E-07	NT	24	2.3E-08	7.4E-09
7	2.8E-08	5.0E-09	25	6.8E-09	1.1E-09
8	7.3E-08	NT	26	1.5E-08	2.7E-09
9	1.2E-08	4.3E-09	27	1.5E-08	9.1E-09
10	1.5E-08	1.1E-08	28	1.6E-08	1.1E-08
11	1.6E-08	7.6E-09	29	1.2E-08	2.8E-09
12	3.2E-08	1.6E-08	30	1.1E-08	6.5E-09
13	5.9E-09	6.1E-09	31	1.4E-08	1.7E-08
14	1.6E-08	1.5E-08	32	9.4E-09	1.5E-08
15	6.2E-09	2.4E-09	33	9.1E-09	2.4E-09
16	1.3E-08	7.1E-09	34	7.7E-09	9.1E-09
17	2.7E-08	5.9E-09	35	2.5E-08	7.6E-09
18	2.9E-08	4.6E-09	36	1.6E-08	2.6E-09

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
37	2.2E-08	7.7E-09	69	3.6E-08	2.1E-07
38	1.7E-08	5.1E-09	70	1.3E-07	NT
39	1.8E-08	NT	71	9.1E-08	NT
40	9.9E-09	4.23E-09	72	1.6E-08	4.0E-09
41	2.5E-08	NT	73	2.0E-08	7.6E-09
42	3.2E-08	NT	74	3.4E-08	1.7E-08
43	6.6E-08	NT	75	1.2E-08	6.4E-09
44	4.3E-08	5.2E-09	76	7.0E-09	2.8E-09
45	1.0E-07	NT	77	1.1E-08	4.1E-09
46	2.2E-08	NT	78	4.3E-09	2.4E-09
47	1.1E-08	2.56E-09	79	1.2E-08	5.0E-09
48	2.0E-08	NT	80	2.0E-08	8.3E-09
49	2.2E-08	NT	81	2.0E-08	9.5E-09
50	2.9E-08	7.3E-09	82	3.8E-08	1.6E-08
51	3.3E-08	1.0E-08	83	1.7E-09	4.7E-08
52	2.2E-08	9.7E-09	84	4.6E-09	2.5E-09
53	2.3E-08	NT	85	8.2E-09	9.6E-09
54	2.7E-08	5.48E-09	86	1.7E-08	2.1E-08
55	3.3E-08	1.0E-08	87	2.4E-08	3.8E-08
56	1.7E-08	NT	88	1.2E-08	6.1E-09
57	2.3E-08	7,84E-09	89	6.7E-09	1.9E-08
58	7.0E-08	<u>1,42E-08</u>	90	8.3E-09	6.6E-09
59	5.9E-08	NT	91	1.1E-08	2.0E-08
60	4.3E-08	NT	92	5.0E-09	5.3E-09
61	9.3E-09	NT	93	3.8E-09	7.0E-09
62	3.7E-08	NT	94	9.4E-09	6.3E-09
63	8.4E-05	NT	95	1.5E-08	3.2E-08
64	1.0E-07	7.7E-07	96	3.2E-08	1.5E-08
65	7.0E-08	NT	97	7.3E-08	NT
66	1.4E-07	NT	98	7.9E-08	NT
67	1.1E-07	NT	99	3.4E-08	1.7E-08
68	1.1E-07	NT	100	4.7E-08	1.7E-08

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
101	1.0E-07	2.4E-08	133	1.6E-08	6.9E-09
102	5.8E-08	1.2E-08	134	1.7E-08	4.1E-08
103	1.1E-08	6.2E-09	135	1.9E-08	4.8E-08
104	7.9E-09	7.2E-09	136	1.1E-08	4.9E-09
105	1.7E-08	3.6E-09	137	6.7E-09	4.8E-09
106	9.9E-09	9.2E-09	138	1.2E-08	8.3E-09
107	2.5E-08	2.1E-08	139	1.2E-08	1.2E-08
108	2.5E-08	4.3E-09	140	1.7E-08	9.9E-08
109	1.9E-08	7.4E-09	141	4.6E-08	NT
110	3.9E-08	1.3E-08	142	2.4E-08	4.5E-08
111	1.2E-08	1.6E-08	143	8.1E-07	NT
112	2.0E-08	9.0E-09	144	3.2E-08	5.3E-08
113	3.9E-08	1.7E-08	145	8.9E-08	NT
114	5.8E-08	9.3E-09	146	1.0E-07	NT
115	3.6E-08	1.4E-08	147	4.2E-07	3.5E-06
116	3.2E-08	1.0E-08	148	6.2E-08	2.9E-07
117	2.9E-08	1.3E-08	149	4.4E-09	2.4E-09
118	4.2E-08	2.6E-08	150	2.2E-08	1.4E-08
119	3.4E-08	3.8E-08	151	1.7E-08	3.1E-09
120	5.8E-08	1.1E-08	152	9.1E-09	2.3E-09
121	4.8E-08	1.8E-08	153	4.7E-08	8.8E-09
122	5.1E-09	7.67E-09	154	2.0E-08	3.7E-09
123	2.5E-08	5.2E-09	155	1.4E-08	5.5E-09
124	6.3E-08	NT	156	6.7E-09	2.0E-09
125	5.2E-08	1.17E-08/1.93E-08	157	2.1E-08	5.2E-09
126	5.5E-05	NT	158	5.2E-08	1.4E-08
127	1.1E-07	NT	159	6.4E-09	3.3E-09
128	6.4E-08	NT	160	1.6E-08	NT
129	1.3E-07	NT	161	1.5E-08	7.1E-08
130	1.5E-07	NT	162	7.4E-08	NT
131	1.0E-08	8.2E-09	163	3.2E-08	NT
132	1.2E-08	8.7E-09	164	6.1E-08	NT

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
165	3.6E-08	NT	197	1.9E-08	1.3E-07
166	9.3E-08	NT	198	1.4E-07	NT
167	3.7E-08	3.2E-07	199	1.1E-07	NT
168	9.1E-08	NT	200	2.4E-07	NT
169	2.4E-07	NT	201	2.8E-08	NT
170	5.7E-08	NT	202	7.5E-07	NT
171	9.7E-08	NT	203	2.6E-08	6.9E-08
172	1.6E-08	3.9E-08	204	1.5E-07	NT
173	2.5E-08	6.4E-08	205	7.2E-08	1.2E-07
174	2.3E-08	NT	206	4.1E-08	4.4E-08
175	4.1E-08	NT	207	1.5E-07	NT
176	8.4E-08	NT	208	6.5E-08	NT
177	5.8E-07	NT	209	1.2E-07	NT
178	2.7E-08	1.2E-07	210	1.3E-07	NT
179	3.8E-07	NT	211	4.7E-07	NT
180	9.9E-08	NT	212	4.5E-08	NT
181	5.9E-07	NT	213	2.7E-08	1.1E-07
182	1.1E-08	5.3E-08	214	4.1E-08	1.7E-07
183	1.0E-08	3.6E-08	215	8.3E-08	NT
184	1.5E-05	1.3E-05	216	1.2E-07	NT
185	1.6E-08	5.7E-08	217	2.7E-08	1.4E-07
186	9.0E-08	NT	218	1.4E-07	NT
187	1.8E-07	NT	219	5.2E-08	1.6E-07
188	2.3E-08	NT	220	4.5E-08	3.8E-07
189	1.7E-08	1.2E-07	221	6.8E-08	NT
190	1.9E-08	1.7E-07	222	1.9E-07	NT
191	6.4E-08	NT	223	1.4E-07	NT
192	9.5E-08	NT	224	1.5E-07	NT
193	1.1E-07	6.2E-07	225	6.0E-08	NT
194	1.7E-07	NT	226	3.1E-07	NT
195	7.3E-08	NT	227	4.7E-08	NT
196	4.6E-08	NT	228	9.7E-08	NT

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
229	3.4E-07	1.6E-07	261	3.6E-08	1.3E-07
230	3.4E-07	NT	262	1.0E-07	NT
231	9.3E-07	NT	263	2.1E-08	2.8E-08
232	2.2E-07	NT	264	9.6E-08	NT
233	1.2E-06	NT	265	1.3E-07	NT
234	6.3E-08	NT	266	3.0E-08	3.8E-07
235	3.5E-08	4.1E-08	267	4.7E-08	6.5E-08
236	9.3E-08	NT	268	7.4E-08	NT
237	1.1E-07	NT	269	4.4E-08	1.7E-07
238	1.6E-07	NT	270	4.4E-08	4.5E-08
239	4.2E-08	1.0E-07	271	1.5E-07	NT
240	1.1E-06	NT	272	2.6E-08	3.8E-07
241	8.4E-08	NT	273	1.0E-07	NT
242	1.8E-07	NT	274	8.2E-07	NT
243	1.4E-06	NT	275	3.3E-07	NT
244	2.8E-07	NT	276	8.7E-08	NT
245	2.2E-07	NT	277	8.6E-08	NT
246	1.8E-08	4.6E-08	278	5.4E-08	NT
247	8.2E-08	NT	279	1.2E-07	NT
248	3.4E-07	NT	280	5.5E-08	NT
249	1.2E-07	NT	281	2.6E-08	1.8E-07
250	1.8E-07	NT	282	1.2E-07	NT
251	4.3E-07	NT	283	1.0E-07	NT
252	1.6E-07	NT	284	4.1E-08	NT
253	4.6E-08	1.5E-07	285	1.6E-08	NT
254	2.3E-08	1.2E-07	286	1.5E-08	NT
255	2.9E-08	1.8E-07	287	2.5E-08	NT
256	5.5E-08	1.0E-07	288	6.0E-09	2.3E-08
257	8.0E-08	NT	289	1.2E-08	5.4E-08
258	9.7E-08	NT	290	7.4E-09	2.0E-09
259	3.1E-08	1.7E-07	291	8.4E-09	2.5E-09
260	2.2E-08	7.4E-08	292	5.8E-09	2.0E-09

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
293	4.0E-09	2.2E-09	325	8.6E-08	NT
294	9.8E-09	5.6E-09	326	7.9E-08	NT
295	8.0E-09	5.3E-09	327	3.9E-08	9.8E-08
296	2.3E-08	1.1E-08	328	2.0E-08	NT
297	1.4E-08	NT	329	1.8E-08	5.0E-08
298	1.4E-08	1.1E-08	330	2.0E-08	7.6E-08
299	3.9E-08	1.3E-08	331	4.4E-08	NT
300	2.5E-08	NT	332	3.2E-08	8.3E-09
301	1.3E-06	5.5E-07	333	1.9E-08	3.3E-08
302	1.6E-08	7.1E-09	334	7.1E-09	5.1E-09
303	1.5E-08	4.0E-09	335	1.1E-08	8.9E-09
304	5.7E-09	1.5E-08	336	2.4E-08	7.2E-08
305	1.8E-08	3.4E-08	337	2.1E-08	1.1E-07
306	1.1E-08	7.3E-09	338	1.4E-08	1.2E-06
307	1.4E-08	5.4E-09	339	2.5E-08	2.1E-08
308	1.2E-08	5.4E-09	340	5.0E-07	NT
309	1.1E-08	9.1E-09	341	2.6E-08	6.4E-08
310	3.6E-08	1.5E-08	342	2.3E-07	NT
311	1.2E-08	1.4E-08	343	3.3E-08	NT
312	5.5E-09	9.6E-09	344	9.6E-09	1.1E-08
313	8.2E-09	8.2E-09	345	1.1E-07	NT
314	2.1E-08	3.4E-08	346	2.1E-08	2.2E-09
315	4.9E-08	NT	347	1.5E-08	1.6E-09
316	1.2E-07	NT	348	1.2E-08	1.6E-09
317	5.3E-08	NT	349	7.6E-08	NT
318	8.7E-08	NT	350	3.5E-07	NT
319	6.4E-08	NT	351	5.7E-07	NT
320	1.6E-07	NT	352	3.9E-07	NT
321	1.0E-07	NT	353	1.2E-07	NT
322	1.4E-07	NT	354	3.9E-08	2.7E-07
323	2.3E-07	NT	355	4.1E-08	NT
324	7.2E-08	NT	356	1.4E-08	3.3E-08

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
357	6.4E-08	NT	389	1.7E-07	NT
358	4.5E-08	NT	390	3.9E-08	NT
359	4.1E-08	NT	391	6.0E-08	6.9E-08
360	1.1E-07	NT	392	8.0E-08	NT
361	7.2E-08	NT	393	6.2E-08	NT
362	2.9E-08	1.9E-07	394	6.0E-08	NT
363	2.8E-08	7.0E-08	395	6.6E-08	NT
364	3.5E-08	2.8E-07	396	1.7E-08	4.5E-08
365	4.2E-08	1.2E-07	397	2.8E-08	9.4E-08
366	3.8E-08	2.3E-07	398	3.3E-08	6.0E-08
367	2.0E-08	1.4E-07	399	3.6E-08	2.5E-08
368	2.7E-08	1.2E-07	400	4.8E-08	NT
369	2.6E-08	3.8E-08	401	2.9E-08	9.3E-08
370	1.0E-07	NT	402	2.7E-08	3.7E-08
371	5.4E-08	NT	403	1.4E-08	8.8E-08
372	9.4E-08	NT	404	1.9E-08	1.2E-07
373	3.4E-08	4.9E-08	405	3.5E-08	NT
374	2.8E-08	4.5E-08	406	2.3E-08	9.8E-08
375	4.4E-08	4.0E-08	407	2.4E-08	9.0E-08
376	3.1E-08	5.2E-08	408	2.1E-08	4.5E-08
377	3.7E-08	8.6E-08	409	5.2E-08	NT
378	3.1E-08	5.6E-08	410	4.0E-08	1.5E-07
379	9.2E-08	NT	411	4.8E-08	NT
380	9.8E-08	NT	412	2.4E-08	1.1E-07
381	4.3E-08	NT	413	3.5E-08	NT
382	2.1E-08	3.2E-08	414	1.3E-08	NT
383	1.9E-08	1.6E-08	415	2.0E-08	3.0E-08
384	1.6E-08	2.5E-08	416	1.9E-08	2.6E-08
385	2.5E-08	2.8E-08	417	2.5E-08	5.7E-08
386	2.1E-08	2.2E-08	418	3.0E-08	4.7E-08
387	1.5E-08	2.4E-08	419	2.3E-08	1.2E-07
388	5.4E-08	4.3E-08	420	2.3E-08	6.9E-08

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
421	2.6E-08	1.0E-07	453	2.7E-08	6.4E-08
422	2.8E-08	9.2E-08	454	1.1E-08	1.5E-08
423	2.8E-08	8.3E-08	455	1.1E-08	8.4E-09
424	3.1E-08	1.4E-07	456	8.6E-09	1.3E-08
425	8.0E-09	4.5E-08	457	1.7E-08	2.8E-08
426	1.9E-08	1.1E-07	458	1.5E-08	1.2E-08
427	1.9E-08	6.4E-08	459	8.7E-09	1.8E-08
428	4.2E-08	2.5E-07	460	6.1E-09	NT
429	7.3E-08	NT	461	1.9E-07	NT
430	4.2E-07	NT	462	9.9E-08	NT
431	1.1E-07	NT	463	7.6E-08	NT
432	3.8E-08	2.9E-08	464	4.0E-08	4.3E-08
433	1.5E-08	2.0E-08	465	2.1E-08	3.3E-08
434	6.5E-08	2.5E-07	466	3.9E-08	3.7E-08
435	1.6E-08	5.7E-09	467	7.0E-08	NT
436	1.4E-08	2.7E-09	468	9.8E-08	NT
437	6.7E-08	1.3E-08	469	5.0E-08	NT
438	1.3E-08	1.5E-08	470	2.6E-08	2.4E-08
439	2.3E-08	1.5E-08	471	2.7E-08	2.5E-07
440	1.0E-08	1.7E-08	472	2.5E-08	1.3E-07
441	4.1E-08	NT	473	1.2E-07	NT
442	3.6E-08	7.9E-08	474	4.7E-08	NT
443	4.2E-08	NT	475	1.1E-07	NT
444	1.0E-07	NT	476	7.8E-08	NT
445	1.7E-08	1.1E-08	477	8.0E-08	NT
446	1.6E-08	4.0E-09	478	6.1E-08	NT
447	7.1E-09	4.9E-09	479	2.8E-08	NT
448	9.4E-09	1.7E-09	480	1.9E-08	7.6E-08
449	1.8E-08	3.4E-09	481	8.2E-08	NT
450	1.5E-08	1.8E-08	482	1.1E-08	1.9E-09
451	3.7E-08	5.0E-08	483	1.5E-08	5.6E-09
452	2.5E-08	2.2E-08	484	1.5E-08	2.0E-09

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
485	4.6E-08	2.6E-09	517	9.9E-09	6.2E-09
486	5.5E-09	7.1E-09	518	2.6E-08	3.5E-09
487	6.1E-09	8.4E-09	519	4.9E-09	4.0E-09
488	8.2E-08	NT	520	9.7E-09	5.6E-09
489	2.6E-08	6.0E-08	521	3.4E-08	3.1E-09
490	3.1E-08	5.4E-08	522	4.3E-08	9.8E-09
491	4.8E-08	7.0E-08	523	4.7E-09	1.9E-09
492	7.1E-08	NT	524	5.5E-09	2.8E-09
493	1.4E-08	2.6E-09	525	8.8E-09	3.5E-09
494	1.9E-08	4.2E-09	526	1.8E-08	8.6E-09
495	1.3E-08	2.7E-09	527	1.6E-08	9.8E-09
496	5.0E-08	2.6E-09	528	6.6E-09	3.5E-09
497	1.8E-08	2.7E-09	529	6.7E-09	3.0E-09
498	4.3E-09	6.0E-09	530	2.2E-08	3.1E-09
499	1.2E-08	2.0E-09	531	5.5E-09	2.1E-09
500	1.5E-07	NT	532	2.7E-08	1.1E-07
501	7.2E-08	8.8E-09	533	1.3E-08	8.1E-08
502	5.1E-08	7.2E-09	534	2.1E-08	5.0E-08
503	4.3E-07	NT	535	9.0E-08	NT
504	2.0E-07	1.4E-08	536	2.9E-08	NT
505	5.9E-09	2.9E-09	537	4.0E-08	NT
506	5.6E-09	2.1E-09	538	5.3E-08	NT
507	1.2E-07	NT	539	4.5E-08	NT
508	1.9E-08	6.9E-09	540	2.0E-08	NT
509	3.1E-08	1.5E-08	541	2.0E-08	1.0E-07
510	3.3E-08	2.0E-08	542	1.4E-08	7.9E-08
511	4.6E-08	7.8E-08	543	1.6E-08	6.2E-08
512	2.0E-07	NT	544	1.4E-08	4.9E-08
513	1.5E-07	NT	545	1.4E-08	1.3E-07
514	1.1E-07	NT	546	3.5E-08	8.9E-08
515	1.5E-07	NT	547	1.7E-08	1.4E-07
516	4.9E-08	6.5E-09	548	1.2E-08	9.4E-08

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
549	1.9E-08	6.5E-08	581	4.5E-08	NT
550	2.9E-08	NT	582	4.1E-08	NT
551	1.7E-08	4.2E-08	583	2.4E-08	NT
552	1.8E-08	NT	584	1.2E-08	1.4E-08
553	1.3E-08	8.1E-08	585	1.2E-07	NT
554	1.9E-08	4.5E-08	586	5.4E-08	NT
555	3.2E-08	4.2E-08	587	8.0E-08	NT
556	1.1E-08	2.0E-07	588	5.4E-08	NT
557	2.4E-08	NT	589	3.6E-07	NT
558	1.8E-08	6.7E-08	590	2.0E-07	NT
559	2.5E-08	NT	591	1.1E-07	NT
560	2.4E-08	1.4E-07	592	9.0E-08	NT
561	2.4E-08	NT	593	8.9E-08	NT
562	9.6E-09	5.6E-08	594	1.8E-07	NT
563	1.1E-08	8.6E-08	595	1.7E-08	1.1E-07
564	1.1E-08	7.1E-08	596	1.6E-08	4.9E-08
565	9.6E-09	4.5E-08	597	1.8E-08	5.6E-08
566	3.3E-08	NT	598	2.5E-08	8.5E-08
567	2.3E-08	NT	599	6.7E-09	4.0E-08
568	1.4E-08	5.4E-08	600	3.3E-08	7.3E-08
569	3.4E-07	NT	601	3.1E-08	4.8E-08
570	5.0E-07	NT	602	7.7E-09	4.0E-08
571	4.3E-07	NT	603	3.6E-08	7.6E-08
572	2.9E-08	2.8E-07	604	2.0E-08	4.2E-08
573	2.1E-08	2.1E-07	605	2.4E-08	4.7E-08
574	4.8E-08	1.5E-07	606	4.1E-08	9.6E-08
575	6.1E-08	1.2E-07	607	4.4E-08	NT
576	2.2E-07	NT	608	3.1E-08	3.6E-08
577	1.2E-07	NT	609	1.4E-08	2.7E-08
578	1.3E-07	NT	610	3.8E-08	8.6E-08
579	5.2E-08	NT	611	2.1E-08	5.5E-08
580	1.3E-07	NT	612	6.0E-08	3.6E-08

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
613	3.2E-08	6.4E-08	645	2.2E-08	NT
614	5.6E-08	NT	646	7.0E-08	NT
615	6.9E-08	NT	647	3.2E-08	2.6E-08
616	6.1E-08	6.2E-08	648	6.9E-08	NT
617	3.5E-08	8.9E-08	649	1.5E-08	2.7E-08
618	2.0E-08	3.4E-08	650	1.9E-08	3.8E-08
619	3.8E-08	3.0E-08	651	2.8E-08	8.9E-08
620	3.0E-08	5.0E-08	652	1.4E-08	8.2E-08
621	4.1E-08	NT	653	2.4E-08	1.1E-07
622	5.7E-08	NT	654	1.9E-08	8.9E-08
623	2.7E-08	3.5E-08	655	2.7E-08	4.7E-08
624	6.2E-08	NT	656	2.7E-08	8.6E-08
625	3.1E-08	4.0E-08	657	6.2E-08	NT
626	1.2E-08	1.2E-08	658	6.2E-07	NT
627	2.0E-08	1.8E-08	659	5.7E-07	NT
628	4.1E-08	NT	660	7.7E-07	NT
629	1.2E-08	9.2E-09	661	3.8E-07	NT
630	2.5E-08	2.6E-08	662	2.6E-07	NT
631	3.1E-08	3.4E-08	663	1.6E-07	NT
632	1.0E-08	9.4E-09	664	2.2E-07	NT
633	1.9E-08	1.4E-08	665	2.3E-07	NT
634	1.7E-08	1.4E-08	666	3.4E-08	9.7E-08
635	4.0E-08	8.3E-08	667	3.2E-08	8.7E-08
636	2.7E-08	2.8E-08	668	3.1E-08	1.1E-07
637	3.3E-08	5.4E-08	669	2.7E-08	1.1E-07
638	3.8E-08	7.9E-08	670	6.7E-07	NT
639	9.0E-08	NT	671	3.0E-08	5.9E-08
640	3.0E-08	5.4E-08	672	2.8E-08	6.3E-08
641	2.5E-08	5.0E-08	673	1.6E-08	2.8E-08
642	2.0E-08	5.4E-08	674	2.6E-08	1.2E-07
643	3.2E-08	5.4E-08	675	2.7E-08	6.3E-08
644	6.2E-08	NT	676	2.9E-08	5.6E-08

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
677	4.2E-08	NT	709	1.6E-08	2.0E-08
678	1.9E-08	4.1E-08	710	2.9E-08	4.3E-08
679	5.8E-07	NT	711	3.6E-08	NT
680	5.8E-07	NT	712	2.2E-08	NT
681	5.9E-07	NT	713	7.9E-09	1.7E-08
682	1.3E-08	1.5E-08	714	1.1E-08	1.6E-08
683	1.8E-08	1.4E-08	715	1.0E-08	4.1E-09
684	1.2E-08	4.7E-08	716	1.3E-08	5.8E-09
685	7.8E-09	2.1E-08	717	7.1E-09	3.1E-09
686	2.3E-07	NT	718	7.3E-09	2.8E-09
687	1.6E-08	3.3E-08	719	9.4E-09	1.5E-09
688	1.5E-08	3.2E-08	720	8.6E-09	5.0E-09
689	1.7E-08	2.2E-08	721	1.8E-08	7.8E-09
690	1.0E-08	1.6E-08	722	2.2E-08	2.4E-09
691	1.2E-08	1.9E-08	723	1.2E-08	6.5E-09
692	2.0E-08	2.0E-08	724	5.1E-09	3.6E-09
693	3.2E-08	2.6E-08	725	4.4E-08	4.7E-09
694	1.9E-08	4.1E-08	726	3.4E-09	3.9E-09
695	2.0E-08	4.9E-08	727	1.7E-08	1.4E-09
696	2.1E-08	4.5E-08	728	4.0E-08	6.4E-09
697	1.4E-08	1.4E-08	729	2.6E-08	2.7E-09
698	2.0E-08	1.9E-08	730	5.0E-08	2.4E-09
699	8.0E-09	1.2E-08	731	6.9E-08	4.0E-09
700	2.4E-08	3.9E-08	732	1.7E-08	4.3E-09
701	2.2E-08	3.4E-08	733	2.3E-08	5.7E-09
702	2.4E-08	1.8E-07	734	1.5E-08	3.1E-09
703	2.6E-08	1.6E-07	735	1.6E-08	2.3E-09
704	2.9E-08	5.6E-08	736	1.5E-08	1.2E-08
705	7.7E-09	1.1E-08	737	2.0E-09	3.3E-09
706	1.1E-07	NT	738	2.1E-08	2.8E-09
707	2.9E-07	NT	739	6.5E-09	1.7E-09
708	9.9E-08	NT	740	4.3E-09	1.5E-09

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
741	4.5E-09	7.1E-09	773	4.8E-08	NT
742	2.9E-09	6.8E-09	774	1.5E-09	4.1E-09
743	4.9E-09	4.2E-09	775	4.8E-09	4.0E-09
744	1.0E-08	2.9E-09	776	1.8E-09	2.3E-09
745	9.2E-09	3.0E-09	777	5.3E-09	1.1E-08
746	5.1E-09	1.5E-08	778	1.0E-08	1.7E-08
747	5.2E-09	3.7E-09	779	5.5E-08	NT
748	4.8E-09	5.8E-09	780	1.2E-07	NT
749	1.3E-08	7.04E-09	781	2.0E-07	NT
750	7.7E-09	2.3E-09	782	6.5E-08	NT
751	1.3E-08	1.6E-09	783	1.7E-07	NT
752	2.3E-08	4.2E-08	784	7.5E-08	NT
753	2.6E-08	1.0E-07	785	1.7E-07	NT
754	2.4E-08	4.4E-08	786	1.2E-08	4.0E-08
755	2.8E-08	3.8E-08	787	3.9E-08	4.6E-08
756	1.1E-08	1.4E-08	788	1.4E-07	NT
757	1.9E-08	3.5E-08	789	2.4E-08	1.0E-07
758	1.8E-08	6.9E-08	790	2.0E-08	2.3E-07
759	2.3E-08	NT	791	1.5E-08	9.5E-08
760	8.3E-08	NT	792	2.2E-08	9.9E-08
761	5.1E-08	NT	793	1.2E-07	NT
762	5.3E-07	NT	794	2.6E-07	NT
763	2.6E-08	3.0E-07	795	1.4E-07	NT
764	5.4E-08	NT	796	7.2E-08	NT
765	7.6E-08	NT	797	5.7E-07	NT
766	8.5E-08	NT	798	9.8E-08	NT
767	3.5E-08	2.4E-08	799	2.0E-07	NT
768	5.1E-09	6.6E-08	800	5.1E-07	NT
769	2.1E-08	5.2E-08	801	4.9E-08	NT
770	1.1E-08	3.8E-07	802	1.3E-07	NT
771	8.5E-09	1.6E-07	803	3.6E-08	NT
772	3.0E-08	3.8E-07	804	1.5E-07	NT

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
805	3.1E-08	8.9E-06	836	2.6E-07	NT
806	1.8E-08	1.4E-07	837	3.6E-07	NT
807	1.3E-08	6.7E-09	838	7.9E-08	NT
808	9.6E-09	2.5E-09	839	1.2E-07	NT
809	3.3E-09	5.6E-09	840	4.7E-07	NT
810	1.6E-08	1.1E-08	841	3.2E-07	NT
811	7.1E-09	4.2E-09	842	5.6E-07	NT
812	4.9E-09	4.1E-09	843	7.4E-08	NT
813	1.0E-08	5.2E-09	844	3.7E-08	2.8E-07
814	1.4E-08	NT	845	6.5E-08	NT
815	3.6E-08	1.6E-07	846	1.9E-08	1.3E-06
816	3.6E-08	2.3E-08	847	8.3E-06	NT
817	3.0E-08	1.6E-08	848	1.5E-07	NT
818	48.2% @400μM 52.4% @400μM	NT	849	2.9E-07	NT
819	2.2E-07	NT	850	2.1E-08	NT
820	58.5% @400μM 60.9% @400μM	NT	851	2.4E-08	NT
821	1.8E-07	NT	852	1.0E-07	NT
822	68.6% @400μ 66.3% @400μM	NT	853	1.3E-07	NT
823	1.1E-07	NT	854	7.5E-08	NT
824	1.8E-07	NT	855	8.5E-08	NT
825	1.2E-07	NT	856	3.9E-08	3.8E-07
826	4.3E-07	NT	857	8.6E-08	NT
827	2.4E-07	NT	858	1.1E-07	NT
828	4.2E-08	4.3E-07	859	6.5E-08	NT
829	5.7E-08	NT	860	8.2E-08	NT
830	3.4E-07	NT	861	5.6E-08	4.1E-07
831	3.1E-06	NT	862	7.3E-08	1.6E-07
832	1.7E-06	NT	863	2.9E-08	1.1E-07
833	3.2E-07	NT	864	3.1E-08	1.0E-07
834	8.6E-08	NT	865	1.5E-08	6.4E-08
835	1.7E-07	NT	866	8.8E-08	NT

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
867	1.5E-07	NT	899	5.3E-07	NT
868	2.5E-08	1.6E-07	900	1.4E-07	NT
869	7.3E-08	NT	901	1.5E-08	NT
870	4.5E-08	NT	902	2.9E-08	NT
871	5.8E-08	NT	903	1.4E-07	NT
872	3.1E-08	3.1E-08	904	5.5E-08	NT
873	8.6E-09	3.2E-08	905	1.2E-08	NT
874	1.5E-08	6.4E-09	906	2.2E-08	NT
875	2.2E-08	1.8E-08	907	3.8E-08	NT
876	2.7E-08	2.3E-08	908	3.7E-08	5.8E-09
877	1.7E-08	1.5E-08	909	2.4E-08	2.8E-09
878	5.2E-09	4.4E-09	910	4.1E-07	NT
879	1.6E-08	NT	911	2.3E-08	NT
880	3.9E-08	5.5E-08	912	1.1E-08	1.06E-08/ <u>2.01E-08</u>
881	3.9E-08	6.6E-08	913	2.2E-08	<u>2.94E-08</u>
882	4.6E-09	8.2E-09	914	7.9E-09	<u>6.41E-09</u>
883	5.3E-09	3.7E-09	915	3.5E-08	1.69E-08/ <u>2.29E-08</u>
884	9.8E-09	3.1E-09	916	2.5E-08	<u>3.79E-08</u>
885	3.6E-08	1.2E-08	917	2.8E-08	<u>9.48E-08</u>
886	9.1E-09	1.6E-09	918	1.2E-07	NT
887	9.8E-09	2.8E-09	919	3.3E-08	<u>2.86E-09</u>
888	1.1E-08	5.6E-09	920	2.7E-08	2.1E-08
889	3.0E-09	1.3E-08	921	9.7E-09	<u>4.2E-09</u>
890	2.6E-08	NT	922	8.1E-07	NT
891	1.6E-08	<u>3.77E-08</u>	923	2.6E-08	7.5E-09
892	2.6E-08	7.7E-08	924	1.2E-08	<u>2.11E-09</u>
893	8.6E-09	2.3E-08	925	5.6E-09	<u>4.6E-09</u>
894	4.8E-09	6.4E-09	926	1.4E-08	5.3E-08
895	6.3E-09	4.7E-09	927	2.8E-07	NT
896	4.1E-09	3.1E-09	928	6.4E-08	NT
897	3.2E-09	2.0E-09	929	1.5E-07	NT
898	6.4E-09	2.2E-09	930	4.1E-07	NT

EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
931	1.2E-07	NT	963	3.78E-08	1.49E-09
932	1.7E-08	5.7E-08	964	8.61E-08	NT
933	1.1E-08	4.1E-08	965	9.40E-08	NT
934	2.3E-05	NT	966	4.73E-08	4.11E-09
935	1.7E-07	7.9E-07	967	4.23E-08	2.21E-09
936	2.0E-05	NT	968	1.74E-07	NT
937	2.6E-07	NT	969	1.53E-07	NT
938	2.58E-08	1.78E-08	970	3.07E-08	9.92E-08
939	2.91E-08	3.25E-08	971	3.35E-08	2.86E-07
940	1.25E-08	7.48E-09	972	6.09E-08	NT
941	1.43E-08	3.99E-09	973	5.19E-08	9.67E-09
942	1.02E-08	1.56E-09	974	2.79E-08	3.66E-09
943	6.62E-09	1.48E-09	975	2.44E-08	2.92E-09
944	1.01E-08	3.19E-09	976	5.76E-08	6.67E-09
945	5.28E-08	6.32E-09	977	4.70E-08	3.95E-09
946	1.80E-08	6.08E-09	978	5.93E-08	1.20E-08
947	1.44E-08	1.96E-09	979	4.58E-08	7.15E-09
948	8.13E-09	2.73E-09	980	4.44E-08	9.71E-09
949	7.34E-09	2.01E-09	981	4.79E-08	8.68E-09
950	1.22E-08	3.36E-09	982	6.77E-08	1.23E-08
951	3.19E-08	4.66E-08	983	7.25E-08	2.92E-09
952	1.73E-07	NT	984	3.11E-08	1.34E-09
953	2.14E-08	1.51E-09	985	3.25E-08	1.35E-09
954	1.92E-07	NT	986	4.56E-08	2.08E-09
955	1.31E-08	1.18E-09	987	5.15E-08	1.92E-09
956	1.36E-07	NT	988	6.09E-08	6.05E-09
957	1.52E-08	2.75E-09	989	7.86E-08	3.50E-09
958	1.74E-08	2.40E-09	990	4.69E-08	1.99E-09
959	1.19E-06	1.24E-06	991	4.60E-08	8.32E-10
960	5.19E-08	2.81E-09	992	6.29E-08	3.03E-09
961	3.58E-08	2.10E-09	993	6.43E-08	1.52E-09
962	3.78E-08	1.90E-09	994	6.35E-08	9.57E-09

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EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT	EXAMPLE	IC ₅₀ (M) USP7 FLINT	IC ₅₀ (M) MTT
995	8.82E-08	7.82E-09	1005	4.52E-08	8.38E-09
996	5.29E-08	2.81E-09	1006	5.27E-08	1.16E-08
997	3.16E-08	4.21E-09	1007	2.43E-08	1.32E-08
998	6.01E-08	4.48E-08	1008	4.65E-08	1.21E-08
999	3.40E-08	1.62E-08	1009	2.40E-08	7.61E-09
1000	7.97E-08	4.13E-08	1010	2.84E-08	6.27E-09
1001	1.09E-07	NT	1011	2.71E-08	1.09E-08
1002	8.61E-08	1.25E-07	1012	2.75E-08	1.92E-08
1003	3.90E-08	4.07E-08	1013	4.76E-08	2.14E-08
1004	1.81E-08	6.77E-09			

NT: not tested

For partial inhibitors, the percentage fluorescence intensity for a given concentration of the test compound is indicated. Accordingly, 48.2% @400 µM means that 48.2% fluorescence intensity is observed for a concentration of test compound equal to 400 µM.

5 **EXAMPLE C: Anti-tumor activity *in vivo***

The anti-tumour activity of the compounds of the invention is evaluated in a xenograft model of multiple myeloma and/or acute lymphoblastic leukaemia cells.

Human tumour cells are grafted subcutaneously into immunosuppressed mice.

When the tumour volume (TV) reaches about 200 mm³, the mice are treated *per os* with the various compounds once a day for 5 days on/2 days off during 3 weeks. The tumour mass is measured twice weekly from the start of treatment.

The compounds of the invention display anti-tumour activities represented by the TGI (tumor growth inhibition) at the end of the treatment period ranging from 40 to 133.4 %.

The TGI is defined as follows:

$$TGI = \left(1 - \frac{\text{Median (DTV at Dx in treated group)}}{\text{Median (DTV at Dx in control group)}} \right) \times 100 ,$$

with:

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DTV (delta tumoral volume) at Dx = (TV at Dx) – (TV at randomization for each animal).

EXAMPLE D: Pharmaceutical composition: Tablets

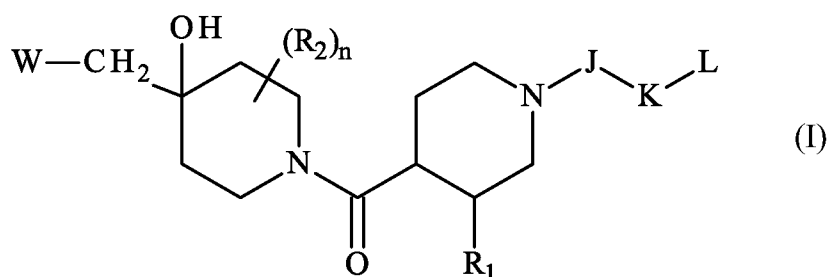
1000 tablets containing a dose of 5 mg of a compound selected from Examples 1 to 1013	5 g
Wheat starch	20 g
Maize starch.....	20 g
Lactose.....	30 g
Magnesium stearate	2 g
Silica	1 g
Hydroxypropylcellulose	2 g

For the avoidance of doubt, any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this specification.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

The claims defining the invention are as follows:

1. Compound of formula (I):



wherein:

- ◆ R_1 represents an aryl group or a heteroaryl group,
- ◆ R_2 represents a hydrogen atom or a halogen atom,
- ◆ n is an integer equal to 0, 1 or 2,
- ◆ J represents a $-C(O)-$ group, a $-CH(R_3)-$ group, or a $-SO_2-$ group,
- ◆ R_3 represents a hydrogen atom or a linear or branched (C_1-C_6) alkyl group,
- ◆ K represents a bond or a $-Cy_1-$ group,
- ◆ L represents a $-Cy_2$ group or a $-CH_2-Cy_2$ group,

- ◆ W represents the group , wherein:

- A represents a heteroaryl ring,
- X represents a carbon atom or a nitrogen atom,
- R_4 represents a hydrogen atom, a halogen atom, a linear or branched (C_1-C_6) alkyl group, a linear or branched (C_2-C_6) alkenyl group, a linear or branched (C_2-C_6) alkynyl group, a $-Y_1-NR_6R_7$ group, a $-Y_1-OR_6$ group, a linear or branched halo (C_1-C_6) alkyl group, an oxo group, a $-Y_1-Cy_3$ group, a $-Cy_3-R_7$ group, a $-Cy_3-OR_7$ group, or a $-Y_1-NR_6-C(O)-R_7$ group,
- R_5 represents a hydrogen atom, a halogen atom, or a linear or branched (C_1-C_6) alkyl group,

- R₆ represents a hydrogen atom or a linear or branched (C₁-C₆)alkyl group,
- R₇ represents a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, or a -Y₂-Cy₄ group,
- Y₁ and Y₂ independently of one another represent a bond or a linear or branched (C₁-C₄)alkylene group,
- ♦ Cy₁ represents a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, which is linked to the group J and to the group L,
- ♦ Cy₂, Cy₃ and Cy₄ independently of one another, represent a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group,

it being understood that:

- “aryl” means a phenyl, naphthyl, or indanyl group,
- “heteroaryl” means any mono- or fused bi-cyclic group composed of from 5 to 10 ring members, having at least one aromatic moiety and containing from 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen,
- “cycloalkyl” means any mono- or fused bi-cyclic non-aromatic carbocyclic group containing from 3 to 7 ring members,
- “heterocycloalkyl” means any non-aromatic mono- or fused bi-cyclic group containing from 3 to 10 ring members, and containing from 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen,

it being possible for the aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups so defined to be substituted by from 1 to 4 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched (C₂-C₆)alkenyl, linear or branched (C₂-C₆)alkynyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', -Y₁-S(O)_m-R', oxo (or *N*-oxide where appropriate), nitro, cyano, -C(O)-R', -C(O)-OR', -O-C(O)-R', -C(O)-NR'R'', -Y₁-NR'-C(O)-R'', -Y₁-NR'-C(O)-OR'', halogen, cyclopropyl, and pyridinyl which can be substituted by a linear or branched (C₁-C₆)alkyl group,

it being understood that R' and R'' independently of one another, represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₂-C₆)alkenyl group, a linear or branched (C₁-C₆)alkoxy group, a linear or branched

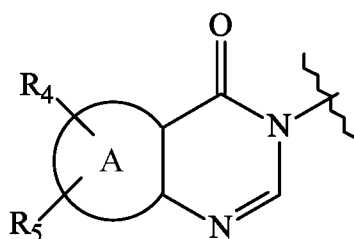
halo(C₁-C₆)alkyl, a linear or branched hydroxy(C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy(C₁-C₆)alkyl group, a phenyl group, a cyclopropylmethyl group, a tetrahydropyranyl group,

or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen, it being understood that the second nitrogen in question may be substituted by from 1 to 2 groups representing a hydrogen atom, or a linear or branched (C₁-C₆)alkyl group,

and it being understood that m is an integer equal to 0, 1 or 2,

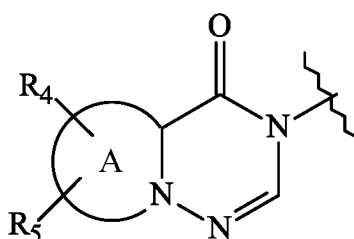
their enantiomers, diastereoisomers and addition salts thereof with a pharmaceutically acceptable acid or base.

2. The compound according to claim 1, wherein W represents the group



wherein R₄, R₅ and A are as defined in claim 1.

3. The compound according to claim 1, wherein W represents the group



wherein R₄, R₅ and A are as defined in claim 1.

4. The compound according to any one of claims 1 to 3, wherein R₁ represents a phenyl group or a thienyl group.

5. The Compound according to any one of claims 1 to 4, wherein R₂ represents a hydrogen atom and a fluorine atom.
6. The compound according to any one of claims 1 to 5, wherein R₃ represents a hydrogen atom or a methyl group.
7. The compound according to any one of claims 1 to 6, wherein J represents a -C(O)- group or a -CH₂- group.
8. The compound according to any one of claims 1 to 7, wherein K represents a bond or a -Cy₁- group selected from a phenyl group, a pyrrolyl group, a thienyl group, a thiazolyl group, a pyridinyl group, a tetrahydrobenzothienyl group, a dihydrothienodioxinyl group, a cyclopropyl group, a cyclobutyl group, or a pyrrolidinyl group.
9. The compound according to any one of claims 1 to 8, wherein L represents a -Cy₂ group.
10. The compound according to any one of claims 1 to 9, wherein Cy₂ represents a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group which are substituted by 1 or 2 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', N-oxide, cyano, -C(O)-OR', -C(O)-NR'R'', halogen, in which R' and R'' independently of one another represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy group, or a tetrahydropyranyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen, it being understood that the second nitrogen in question may be substituted by a linear or branched (C₁-C₆)alkyl group.

11. The compound according to any one of claims 1 to 7, wherein K represents a thienyl group, a thiazolyl group or a pyridinyl group and L represents a pyrrolyl group, a furyl group, a thienyl group, a pyrazolyl group, a pyridinyl group, a pyrimidinyl group, or an imidazopyridinyl group, each said heteroaryl group may be substituted by 1 or 2 groups selected from linear or branched (C₁-C₆)alkyl, linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', *N*-oxide, cyano, -C(O)-NR'R'', halogen, in which R' and R'' independently of one another represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, a linear or branched (C₁-C₆)alkoxy group, a linear or branched (C₁-C₆)alkoxy(C₁-C₆)alkyl group, or a tetrahydropyranyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen.
12. The compound according to any one of claims 1 to 7, wherein K represents a bond and L represents a phenyl group, thiazolyl group, an oxazolyl group, an isoxazolyl group, a pyrazolyl group, a pyridinyl group, a pyrazinyl group, a pyridazinyl group or a pyrimidinyl group, each said heteroaryl group may be substituted by 1 or 2 groups selected from linear or branched (C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', cyano, -C(O)-OR', halogen, it being understood that R' and R'' independently of one another represent a hydrogen atom, a linear or branched (C₁-C₆)alkyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members, which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen, it being understood that the second nitrogen in question may be substituted by from 1 to 2 groups representing a hydrogen atom, or a linear or branched (C₁-C₆)alkyl group.
13. The compound according to any one of claims 1 to 12, wherein R₄ represents a halogen atom, a linear or branched (C₁-C₆)alkyl group, or a -Y₁-Cy₃ group.
14. The compound according to any one of claims 1 to 13, wherein Cy₃ represents a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group which are substituted by from 1 to 3 groups selected from linear or branched (C₁-C₆)alkyl,

linear or branched halo(C₁-C₆)alkyl, -Y₁-OR', -Y₁-NR'R'', cyano, halogen, in which R' and R'' independently of one another represent a hydrogen atom or a linear or branched (C₁-C₆)alkyl group, or the substituents of the pair (R', R'') form together with the nitrogen atom carrying them a non-aromatic ring composed of from 5 to 7 ring members which may contain in addition to the nitrogen a second heteroatom selected from oxygen and nitrogen.

15. The compound according to any one of claims 1 to 14, wherein R₅ represents a hydrogen atom or a methyl group.
16. The compound according to any one of claims 1 to 15, wherein R₆ represents a hydrogen atom or a methyl group.
17. The compound according to any one of claims 1 to 16, wherein R₇ represents a hydrogen atom, a methyl group, or a -CH₂-Cy₄ group.
18. Compounds according to claim 1, which are:
 - 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[3-methyl-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
 - 3-[(1-{[(3*R*,4*R*)-1-{[5-(6-aminopyridin-3-yl)-3-fluorothiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-methyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
 - 7-cyclopropyl-3-[(1-{[(3*R*,4*R*)-1-{[3-fluoro-5-(pyridin-4-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
 - 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
 - 3-[(1-{[(3*R*,4*R*)-1-{[3-fluoro-5-(6-methylpyridin-3-yl)thiophen-2-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(pyridin-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(naphthalen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(furan-3-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(2-fluorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2-chlorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-[4-(4-methylpiperazin-1-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-(1*H*-pyrrol-1-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[1-[(3*R*,4*R*)-1-[(2-bromo-4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-(5-{[(3*R*,4*R*)-4-(4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl]carbonyl)-3-phenylpiperidin-1-yl]carbonyl}-4-methyl-1,3-thiazol-2-yl)pyridine-2-carbonitrile;
- 3-[(1-[(3*R*,4*R*)-1-(2-[6-(dimethylamino)pyridin-3-yl]-4-methyl-1,3-thiazol-5-yl]carbonyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-(4-methyl-2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl]carbonyl)-3-phenylpiperidin-4-yl]carbonyl]piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-4-methyl-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-fluorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-({2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-({2-[6-(morpholin-4-yl)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-(2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(1-[(3*R*,4*R*)-1-(2-[6-(dimethylamino)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-6,8-dimethylpyrimido[5',4':4,5]pyrrolo[1,2-*b*]pyridazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[4-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chlorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-{[4-methyl-2-(6-methyl-1-oxidopyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(2-[6-(piperazin-1-yl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-(2-[6-(trifluoromethyl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]piperidin-4-yl}carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,4-dichlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-(5-{[(3*R*,4*R*)-4-(4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl}-1,3-thiazol-2-yl)pyridine-2-carbonitrile;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(pyridin-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-[4-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,4-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,4-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl)piperidin-4-yl)methyl]-7-(pyridin-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 5-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3,5-dimethoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 4-{3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-4-oxo-3,4-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl} benzonitrile;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(1-methyl-1*H*-pyrazol-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(1-methyl-1*H*-pyrazol-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[3-(hydroxymethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 5-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(1-methyl-1*H*-pyrazol-4-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-fluorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-chloro-5-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-fluoro-3-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chloro-3-methoxyphenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(4-chlorophenyl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(5-chlorothiophen-2-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-bromo-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]pyrrolo[2,1-*f*][1,2,4]triazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(5-methylthiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(hydroxymethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[4-(hydroxymethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylpyrrolo[2,1-*f*][1,2,4]triazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylpyrrolo[2,1-*f*][1,2,4]triazin-4(3*H*)-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-2-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylthieno[3,4-*d*]pyrimidin-4(3*H*)-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenylthieno[3,4-*d*]pyrimidin-4(3*H*)-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,5-dihydro-4*H*-pyrrolo[3,2-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methylphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(thiophen-3-yl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-[3-(morpholin-4-yl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[1-[(3*R*,4*R*)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-[6-(hydroxymethyl)pyridin-3-yl]-1,3-thiazol-5-yl} methyl)-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-7-[3-(trifluoromethyl)phenyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[4-(difluoromethyl)phenyl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[1-(difluoromethyl)-1*H*-pyrazol-4-yl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[1-(difluoromethyl)-1*H*-pyrazol-4-yl]-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-(3-methyl-3*H*-imidazo[4,5-*b*]pyridin-6-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-({2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-[3-(dimethylamino)phenyl]-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(3-fluorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-[2-(5-fluoro-6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-(5-[(3*R*,4*R*)-4-(4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl)methyl]-1,3-thiazol-2-yl)pyridine-3-carboxamide;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-(2-[5-(hydroxymethyl)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(2-[6-(tetrahydro-2*H*-pyran-4-yloxy)pyridin-3-yl]-1,3-thiazol-5-yl)methyl]piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-[2-(5-amino-6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[1-[(3*R*,4*R*)-1-[(2-bromo-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-[2-(thiophen-2-yl)-1,3-thiazol-5-yl]methyl]piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{2-(pyrimidin-5-yl)-1,3-thiazol-5-yl]methyl}}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(1-methyl-1*H*-pyrazol-5-yl)-1,3-thiazol-5-yl]methyl}}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(1-methyl-1*H*-pyrazol-4-yl)-1,3-thiazol-5-yl]methyl}}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(1-methyl-1*H*-pyrrol-3-yl)-1,3-thiazol-5-yl]methyl}}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-{{2-(thiophen-3-yl)-1,3-thiazol-5-yl]methyl}}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{{2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{1-((3*R*,4*R*)-1-[(2-bromopyridin-4-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{{1-((3*R*,4*R*)-1-[(5-bromopyridin-3-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 7-(3-chlorophenyl)-3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-[2-(furan-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-[2-(furan-2-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-[2-(thiophen-2-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-[2-(pyrimidin-5-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(1-methyl-1*H*-pyrazol-5-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(1-methyl-1*H*-pyrazol-4-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-1-[2-(1-methyl-1*H*-pyrrol-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-[2-(thiophen-3-yl)-1,3-thiazol-5-yl]methyl}piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(1-[(3*R*,4*R*)-1-[2-(furan-3-yl)-1,3-thiazol-5-yl]methyl]-3-phenylpiperidin-4-yl]carbonyl]-4-hydroxypiperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-[(1-{[(3*R*,4*R*)-1-{[2-(furan-2-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}-4-hydroxypiperidin-4-yl)methyl]-7-(3-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 7-(1,3-benzodioxol-5-yl)-3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[1-({[(3*R*,4*R*)-1-[(5-bromopyridin-3-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl)-4-hydroxypiperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-(3,4,5-trimethoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-(pyridin-3-ylmethyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(6'-methyl-3,3'-bipyridin-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-3-phenyl-1-(pyridin-4-ylmethyl)piperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-[5-({(3*R*,4*R*)-4-[(4-hydroxy-4-{[7-(3-methoxyphenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl]methyl}piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl}methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- 5-[5-({(3*R*,4*R*)-4-[(4-{[7-(4-chlorophenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl]methyl}-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl}methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- 5-[5-({(3*R*,4*R*)-4-[(4-hydroxy-4-{[7-(4-methoxyphenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl]methyl}piperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl}methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{[4-methyl-2-(morpholin-4-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-({2-[6-(2-methoxyethoxy)pyridin-3-yl]-1,3-thiazol-5-yl}methyl)-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{[2-(4-methylpiperazin-1-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{{(3*R*,4*R*)-1-{[2-(6-hydroxypyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl}carbonyl}piperidin-4-yl)methyl]-7-(3-hydroxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(4-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(2-methyl-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)piperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[1-({(3*R*,4*R*)-1-[(2-chloro-1,3-thiazol-5-yl)carbonyl]-3-phenylpiperidin-4-yl}carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-{[(3*R*,4*R*)-3-phenyl-1-(1,3-thiazol-5-ylmethyl)piperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-[5-({(3*R*,4*R*)-4-[(4-{[7-(4-fluorophenyl)-4-oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl}-4-hydroxypiperidin-1-yl)carbonyl]-3-phenylpiperidin-1-yl}methyl)-1,3-thiazol-2-yl]pyridine-2-carbonitrile;
- methyl 3-{[(3*R*,4*R*)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl}carbonyl)-3-phenylpiperidin-1-yl]carbonyl}benzoate;
- 5-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 5-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[2-(6-methoxypyridin-3-yl)-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 5-[(4-hydroxy-1-{[(3*R*,4*R*)-1-{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl]-3-phenylpiperidin-4-yl]carbonyl}piperidin-4-yl)methyl]-1-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;

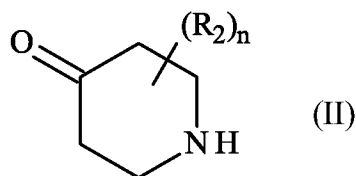
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(2-{6-[(2-methoxyethyl)amino]pyridin-3-yl}-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(1-methyl-1*H*-pyrazol-4-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-({(3*R*,4*R*)-3-phenyl-1-(pyrazin-2-ylmethyl)piperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(5-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[1-({(3*R*,4*R*)-1-[(5-bromopyridin-3-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)-4-hydroxypiperidin-4-yl]methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- methyl 5-{[(3*R*,4*R*)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl} carbonyl)-3-phenylpiperidin-1-yl]carbonyl} pyridine-3-carboxylate;
- 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[(4-hydroxy-1-({(3*R*,4*R*)-1-{{[4-methyl-2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]carbonyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[(4-hydroxy-1-({(3*R*,4*R*)-1-{{[2-(6-methylpyridin-3-yl)-1,3-thiazol-5-yl]methyl}-3-phenylpiperidin-4-yl]carbonyl} piperidin-4-yl)methyl]-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(5-methyl-1,3-thiazol-2-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(3-methyl-1,2-oxazol-5-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl]methyl}-7-phenyl-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;

- 3-{[1-({(3*R*,4*R*)-1-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)-4-hydroxypiperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[(4-hydroxy-1-({(3*R*,4*R*)-1-(1,3-oxazol-4-ylmethyl)-3-phenylpiperidin-4-yl] carbonyl)piperidin-4-yl)methyl]-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-{[4-hydroxy-1-({(3*R*,4*R*)-1-[(5-methyl-1,3-oxazol-2-yl)methyl]-3-phenylpiperidin-4-yl} carbonyl)piperidin-4-yl)methyl}-7-(4-methoxyphenyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 5-{[(3*R*,4*R*)-4-({4-hydroxy-4-[(4-oxo-7-phenyl-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-3-yl)methyl]piperidin-1-yl} carbonyl)-3-phenylpiperidin-1-yl)methyl}pyridine-2-carbonitrile;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-[4-(hydroxymethyl)phenyl]pyrrolo[2,1-*f*][1,2,4]triazin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-[4-(hydroxymethyl)phenyl]thieno[3,4-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(3-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[3,3-difluoro-4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenylpyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[3,3-difluoro-4-hydroxy-1-[(3*R*,4*R*)-1-[4-methyl-2-(6-methyl-3-pyridyl)thiazole-5-carbonyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenylpyrrolo[2,3-*d*]pyrimidin-4-one;

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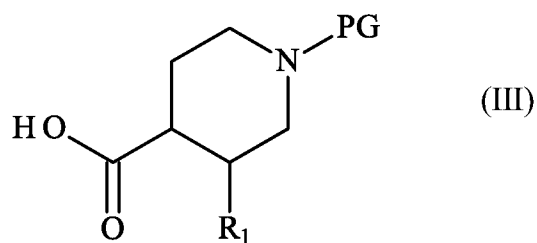
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methoxypyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-3-phenyl-1-(pyrimidin-2-ylmethyl)piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(6-methoxypyridazin-3-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-(4-methoxyphenyl)pyrrolo[2,3-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(5-methylpyrazin-2-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-*d*]pyrimidin-4-one;
- 3-[[4-hydroxy-1-[(3*R*,4*R*)-1-[(2-methylpyrimidin-4-yl)methyl]-3-phenyl-piperidine-4-carbonyl]-4-piperidyl)methyl]-7-phenyl-thieno[3,4-*d*]pyrimidin-4-one.

19. A process for the preparation of a compound of formula (I) according to claim 1, characterized in that there is used as starting material the compound of formula (II):



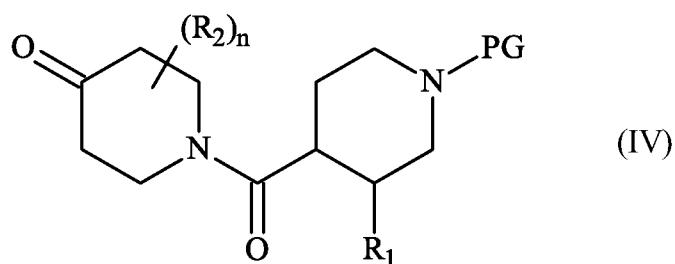
wherein R_2 and n are as defined for formula (I),

which is subjected to coupling with a compound of formula (III):



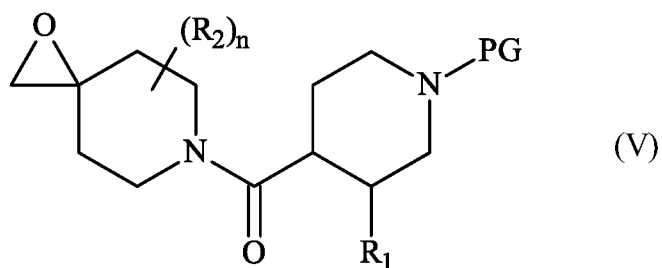
wherein R_1 is as defined for formula (I), and PG represents a protecting group of the amine function,

to yield the compound of formula (IV):



wherein R_1 , R_2 , n and PG are as defined hereinbefore,

compound of formula (IV) which is further converted to an epoxide compound of formula (V):



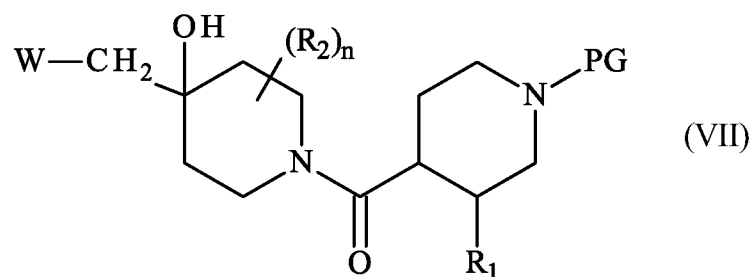
wherein R_1 , R_2 , n and PG are as defined hereinbefore,

compound of formula (V) which is further subjected to coupling with compound of formula (VI):



wherein W is as defined for formula (I),

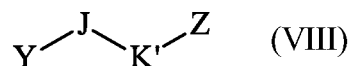
to yield the compound of formula (VII):



wherein R_1 , R_2 , n , W and PG are as defined hereinbefore,

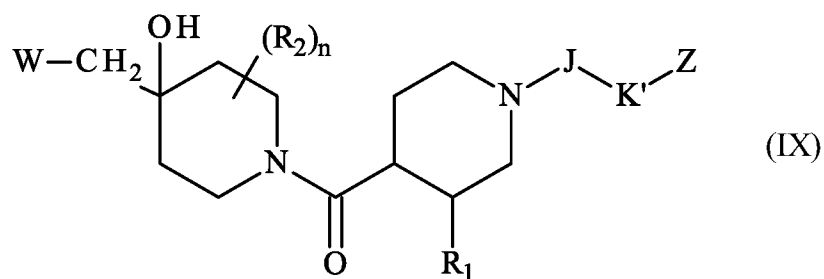
compound of formula (VII) which, after a reaction removing the protecting group PG, is further subjected to:

- **either** coupling with compound of formula (VIII):



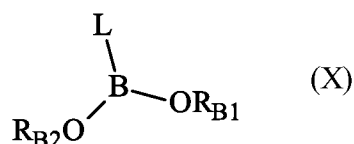
wherein J is as defined in formula (I), K' represents a $-\text{Cy}_1-$ group, Y represents a hydroxy group or a halogen atom, and Z represents a halogen atom,

to yield the compound of formula (IX):



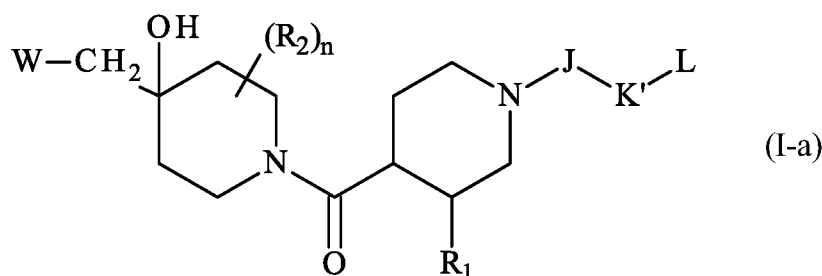
wherein R_1 , R_2 , J, K' , n , W and Z are as defined hereinbefore,

compound of formula (IX) which is further subjected to coupling with compound of formula (X):



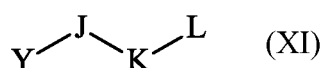
wherein L is as defined for formula (I), and $\text{R}_{\text{B}1}$ and $\text{R}_{\text{B}2}$ represent a hydrogen atom, a linear or branched ($\text{C}_1\text{-C}_6$) alkyl group, or $\text{R}_{\text{B}1}$ and $\text{R}_{\text{B}2}$ are linked together by a linear or branched ($\text{C}_2\text{-C}_6$) alkylene group,

to yield the compound of formula (I-a), a particular case of the compounds of formula (I):



wherein R_1 , R_2 , J, K' , L, n and W are as defined hereinbefore,

- or coupling with compound of formula (XI):



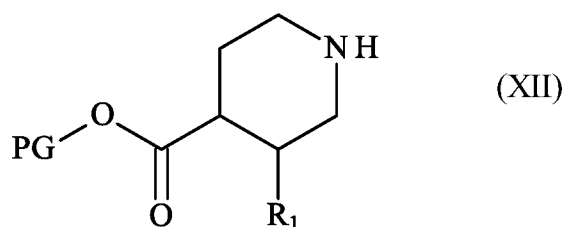
wherein J, K and L are as defined in formula (I), and Y represents a hydroxy group or a halogen atom,

to yield the compound of formula (I),

compound of formula (I) or compound of formula (I-a), which is a particular case of compound of formula (I), may then be purified according to a conventional separation technique, which is converted, if desired, into its addition salts with a pharmaceutically acceptable acid or base and which is optionally separated into its isomers according to a conventional separation technique,

it being understood that at any moment considered appropriate during the course of the process described above, some groups (hydroxy, amino...) of the starting reagents or of the synthesis intermediates can be protected, subsequently deprotected and functionalized, as required by the synthesis.

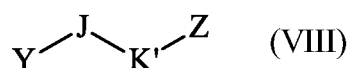
20. A process for the preparation of a compound of formula (I) according to claim 1, characterized in that there is used as starting material the compound of formula (XII):



wherein R₁ is as defined for formula (I), and PG represents a protecting group of the carboxylic acid function,

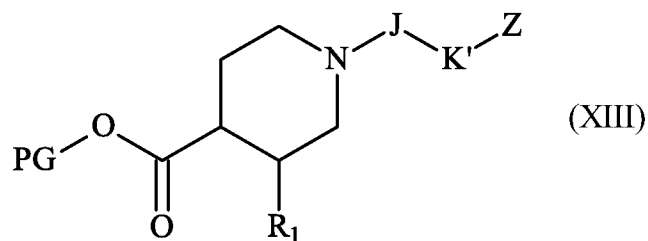
which is subjected to:

- **either** coupling with compound of formula (VIII):



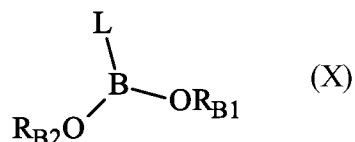
wherein J is as defined in formula (I), K' represents a -Cy₁- group, Y represents a hydroxy group or a halogen atom, and Z represents a halogen atom,

to yield the compound of formula (XIII):



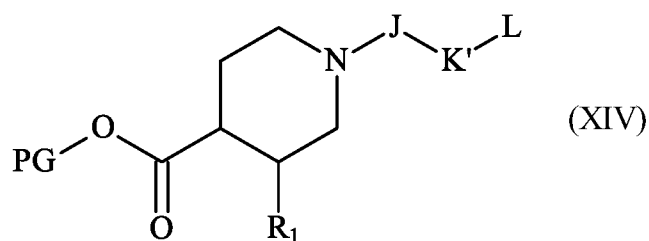
wherein R₁, J, K', Z and PG are as defined hereinbefore,

compound of formula (XIII) which is further subjected to coupling with compound of formula (X):



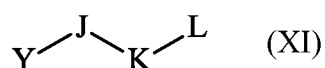
wherein L is as defined for formula (I), and $\text{R}_{\text{B}1}$ and $\text{R}_{\text{B}2}$ represent a hydrogen atom, a linear or branched ($\text{C}_1\text{-C}_6$) alkyl group, or $\text{R}_{\text{B}1}$ and $\text{R}_{\text{B}2}$ are linked together by a linear or branched ($\text{C}_2\text{-C}_6$) alkylene group,

to yield the compound of formula (XIV):



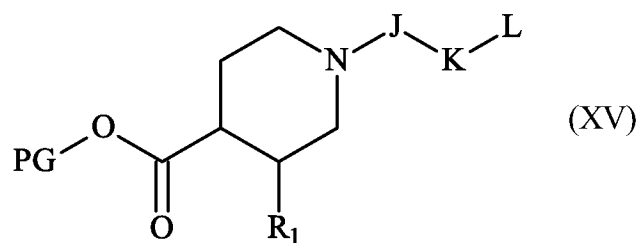
wherein R_1 , J, K' , L and PG are as defined hereinbefore,

- or coupling with compound of formula (XI):



wherein J, K and L are as defined in formula (I), and Y represents a hydroxy group or a halogen atom,

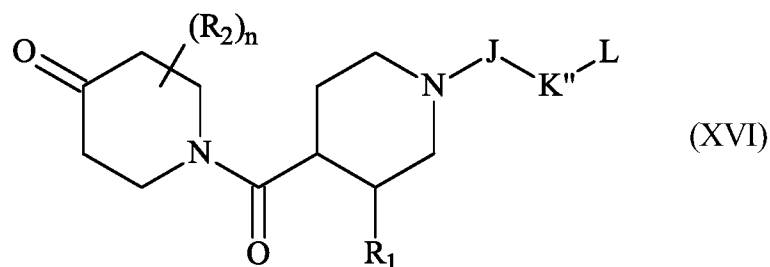
to yield the compound of formula (XV),



wherein R_1 , J, K, L and PG are as defined hereinbefore,

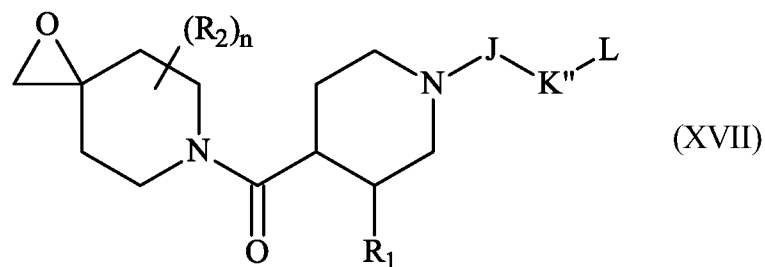
compounds of formula (XIV) and (XV) which, after a reaction removing the protecting group PG, are further subjected to coupling with a compound of formula (II),

to yield the compound of formula (XVI):



wherein R_1 , R_2 , J, L and n are as defined hereinbefore, and K'' is either K' or K as defined hereinbefore,

compound of formula (XVI) which is further converted to an epoxide compound of formula (XVII):



wherein R_1 , R_2 , J, K'' , L and n are as defined hereinbefore,

compound of formula (XVII) which is further subjected to coupling with compound of formula (VI):



wherein W is as defined for formula (I),

to yield the compound of formula (I), which may be purified according to a conventional separation technique, which is converted, if desired, into its addition salts

with a pharmaceutically acceptable acid or base and which is optionally separated into its isomers according to a conventional separation technique, it being understood that at any moment considered appropriate during the course of the process described above, some groups (hydroxy, amino...) of the starting reagents or of the synthesis intermediates can be protected, subsequently deprotected and functionalized, as required by the synthesis.

21. A pharmaceutical composition comprising a compound of formula (I) according to any one of claims 1 to 18 or an addition salt thereof with a pharmaceutically acceptable acid or base in combination with one or more pharmaceutically acceptable excipients.
22. Use of a pharmaceutical composition according to claim 21 in the manufacture of a medicament for use as a pro-apoptotic and/or anti-proliferative agent, wherein the pro-apoptotic or anti-proliferative activity is associated with USP7 inhibition.
23. Use of a pharmaceutical composition according to claim 21 in the manufacture of a medicament for the treatment of cancers or auto-immune and immune system diseases involving USP7 or in which USP7 is implicated.
24. Use of a pharmaceutical composition according to claim 21 in the manufacture of a medicament for the treatment of a disease or condition involving USP7 or in which USP7 is implicated, wherein the disease or condition is selected from cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas, melanomas, malignant haemopathies, myelomas, ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer.
25. A method for the treatment of a disease or condition involving USP7 or in which USP7 is implicated, wherein the disease or condition is selected from cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas,

melanomas, malignant haemopathies, myelomas, ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer, the method comprising administering to a patient in need thereof an effective amount of a compound of formula (I) according to any one of claims 1 to 18 or an addition salt thereof with a pharmaceutically acceptable acid or base, or a pharmaceutical composition according to claim 21.

26. Use of a compound of formula (I) according to any one of claims 1 to 18 or an addition salt thereof with a pharmaceutically acceptable acid or base, in the manufacture of a medicament for the treatment of a disease or condition involving USP7 or in which USP7 is implicated, wherein the disease or condition is selected from cancers of the bladder, brain, breast and uterus, chronic lymphoid leukemia, cancer of the colon, esophagus and liver, lymphoblastic leukemia, acute myeloid leukemia, lymphomas, melanomas, malignant haemopathies, myelomas, ovarian cancer, non-small-cell lung cancer, prostate cancer, pancreatic cancer and small-cell lung cancer.
27. Combination of a compound of formula (I) according to any one of claims 1 to 18 or an addition salt thereof with a pharmaceutically acceptable acid or base, with one or more anti-cancer agents selected from genotoxic agents, mitotic poisons, anti-metabolites, proteasome inhibitors, kinase inhibitors, protein-protein interaction inhibitors, immunomodulators, E3 ligase inhibitors, chimeric antigen receptor T-cell therapy and antibodies.
28. Pharmaceutical composition comprising a combination according to claim 27 in combination with one or more pharmaceutically acceptable excipients.
29. A method for the treatment of cancer involving USP7 or in which USP7 is implicated, the method comprising administering to a patient in need of such treatment an effective amount of a combination according to claim 27 or a pharmaceutical composition according to claim 28.

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30. Use of a combination according to claim 27 in the manufacture of a medicament for the treatment of cancers involving USP7 or in which USP7 is implicated.
31. A method for the treatment of cancers requiring radiotherapy, wherein the cancer involves USP7 or is one in which USP7 is implicated, the method comprising administering to a patient in need of such treatment an effective amount of a compound of formula (I) according to any one of claims 1 to 18 or an addition salt thereof with a pharmaceutically acceptable acid or base, or a pharmaceutical composition according to claim 21.