The present invention is directed to novel compounds of formula (I) and their use in treating metabolic diseases.

\[
\begin{align*}
\text{Ar}^1 - & \quad \text{L}^1 - D - \text{Ar}^2 - \text{L}^2 - \text{N} - \text{Ar}^3 \quad \text{(I)} \\
& \quad \text{R}^1 - \quad \text{L}^2 - \quad \text{R}^2 \\
& \quad \phantom{\text{L}^2} \quad \text{Z}
\end{align*}
\]

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(57) Abstract: The present invention is directed to novel compounds of formula (I) and their use in treating metabolic diseases.
COMPOUNDS, PHARMACEUTICAL COMPOSITION AND METHODS FOR USE IN TREATING METABOLIC DISORDERS

The present invention relates to novel compounds including their pharmaceutically acceptable salts and solvates, which are agonists or partial agonists of G-protein coupled receptor 43 (GPR43) and are useful as therapeutic compounds, particularly in the treatment and/or prevention of Type 2 diabetes mellitus and conditions that are often associated with this disease including, lipid disorders such as dyslipidemia, hypertension, obesity, atherosclerosis and its sequelae.

[BACKGROUND OF THE INVENTION]

Under normal conditions, Free Fatty Acids (FFAs) are implicated in numerous physiological processes by serving as fuel in various metabolic pathways and/or acting as signaling molecules in different tissues such as the heart, liver, skeletal muscle, adipocytes and the pancreas (Newsholme et al., Biochem. J., 80 pp 655-662, 1961; Prentki et al., Endocrine Reviews, PubMed print ahead, 2008). Among FFAs, the short-chain fatty acids (SCFAs, carbon length C2-C6) are generated during anaerobic bacterial fermentation of fiber in the gut (Sellin et al., News. Physiol. ScL, 14, pp 58-64, 1999). Long-chain fatty acids (LCFAs, carbon length C14-C24) are products of dietary intake from adipose tissues and liver (McArthur et al., J. Lipid. Res., 40, pp 1371-1383, 1999).

Obesity is an increasing, worldwide public health problem associated with devastating pathologies such as type 2 diabetes (T2D) and dyslipidemia (Wild et al., Diabetes Care 27, pp 1047-1053, 2004). Dyslipidemia is characterized by high levels of triglycerides and/or LDL (bad cholesterol) or low levels of HDL (good cholesterol). Dyslipidemia is a key independent risk factor for cardiovascular diseases. It has long been suggested that FFAs are implicated in the regulation and/or genesis of these diseases (Fraze et al., J. Clin. Endocrinol. Metab., 61, pp 807-811, 1985). It is well established that regular intake of dietary fiber has several beneficial metabolic effects such as lowering of plasma cholesterol and triglyceride levels (Anderson et al., J. Am. Coll. Nutr., 23, pp 5 -
17, 2004). Specifically, dietary fiber has been shown to increase endogenous levels of SCFAs, leading to the suppression of cholesterol synthesis and improvement in glucose tolerance in rat (Berggren et al., Br. J. Nutr., 76, pp 287-294, 1996), as well as the reduction of hyperglycemia in a diabetic mice model (Sakakibara et al., Biochem. Biophys. Res. Com., 344, pp 597-604, 2006).

Drug therapies are available to address both T2D and dyslipidemia. Specifically, statins, fibrates and nicotinic acid or combinations thereof are often considered as a first line therapy in dyslipidemia whereas metformin, sulphonylureas and thiazolidinediones are three, widely-used classes of oral anti-diabetic drugs (Tenenbaum et al., Cardiovascular Diabetology, 5, pp20-23, 2006). Although theses therapies are widespread in their use, the common appearance of adverse effects or lack of efficacy after long-term use causes concern. Moreover, the growing patient population suffering from T2D, dyslipidemia and associated metabolic diseases creates a demand for new entrants into this therapeutic market.

GPR43 (also named FFA2R) belongs to a subfamily of G-Protein-Coupled Receptors (GPCRs), including GPR40 and GPR41 that have been identified as receptor for FFAs (Le Poul et al., J. Biol Chem. 278, 25481-489, 2003; Covington et al., Biochemical Society transaction 34, 770-773, 2006). The 3 family members share 30 to 40% sequences identity with specificity toward different fatty acids carbon chain lengths, with SCFAs (short chain fatty acids: six carbons molecules or shorter) activating GPR41 and GPR43 and medium and long chain fatty acids (MCFA, LCFA) activating GPR40 (Rayasam et al., Expert Opinion on therapeutic targets, 11 661-671, 2007 ). C2 acetate and C3 propionate are the most potent activators of GPR43. GPR43 is mainly coupled with Gq-proteins, with some evidence for its possible coupling with Gi/o pathways as well.

GPR43 is strongly expressed in adipocytes. Also there is evidence suggesting that GPR43 is overexpressed in pancreatic β-cells in prediabetic states as shown in WO2006/036688A2. Recent papers confirmed the GPR43 expression in pancreatic islets (Ahren, Nature Reviews, 8 pp396-385; 2009; Regard et al., J; Clin. Invst, 117 pp4034-4043, 2007). In adipocyte cells, GPR43 is induced during the differentiation process and increased during the high fat feeding in rodents, suggesting that GPR43 may affect adipocyte functions (Hong et al., Endocrinology, 146 pp5092-5099, 2005). Indeed, it has been reported that acetate
and propionate may stimulate adipogenesis via GPR43. In addition siRNA results hinted that acetate and propionate may inhibit lipolysis in adipocytes via GPR43 activation (Hong et al., Endocrinology, 146 pp5092-5099, 2005). It is interesting to note that the effect of acetate on reducing plasma free fatty acids level has been documented in humans (Suokas et al., Alcoholism, clinical and experimental research, 12 pp52-58, 1988; Laurent et al., European journal of clinical nutrition, 49 pp484-491, 1995). In addition, it has been shown that (i) adipocytes treated with GPR43 endogenous SCFA ligands exhibit a reduction in lipolytic activity and such inhibition of lypolysis is the result of GPR43 activation and (ii) GPR43 activation by acetate results in the reduction of plasma free fatty acids level in vivo (Ge et al., Endocrinology, 149 pp4519-26, 2008). Recently two GPR43 positive allosteric modulator molecules have been shown able to inhibit the lipolysis in adipocytes similarly to that of GPR43 endogenous SCFA ligands (Lee et al., Mol Pharmacol, 74(6) pp1599-1609, 2008). Such results suggest a potential role of GPR43 in regulating plasma lipid profiles and aspects of metabolic syndrome.

On this basis, new agonists or partial agonists of GPR43 may be of therapeutic value for T2D mellitus and conditions that are associated with this disease including, lipid disorders such as dyslipidemia, hypertension, obesity, atherosclerosis and its sequelae.

**[SUMMARY OF THE INVENTION]**

The invention encompasses compounds of general Formula I, their pharmaceutically acceptable salts and solvates as well as methods of use of such compounds or compositions comprising such compounds as modulators of GPR43 activity.

In a general aspect, the invention provides compounds of general formula I:
wherein

Ar₁ is a 5- to 6-membered aryl or heteroaryl group, 3- to 8-membered cycloalkyl group, a 3- to 8-membered heterocycloalkyl group, or a linear or branched C₃-C₆ alkyl group, each of the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, or alkyl groups being optionally substituted by one or more groups selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaryalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocycloxy, aryloxy, amino, alkoxyalkoxy, alkylamino, aminomethyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocycloxy carbonyl, aryloxy carbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxy carbamoyl, alkyl carbamoyl, aryl carbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkyl carbamoylamino, alkyl sulfonamido, haloalkyl sulfonamido, cycloalkyl sulfonamido, heterocyclyl sulfonamido, aryl sulfonamido, heteroaryl sulfonamido, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally
substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, arylxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonetyl;

5. **L**¹ is a single bond, C₁-C₂ alkenylene, C₁-C₂ alkenylene, each optionally being substituted by one or more substituents selected from halo, C₁-C₂ alkyl, C₁-C₂ haloalkyl; or L¹ is -N(R²)-, wherein R² is H or C₁-C₂ alkyl; or L¹ and R¹ together are =CH⁻;

R¹ is H, halo, allyl, or a C₁-C₄ alkyl group, which may optionally be substituted by one or more groups selected from halo or C₁-C₄ alkyl;

10. L² is a C₁-C₃ alkenylene, C₂-C₄ alkenylene, C₃-C₆ cycloalkylene, each of which being optionally substituted by one or more groups selected from halo, alkyl, alkoxy, or haloalkyl; or L² is -0-CH₂⁻; or

R¹ and L² together are =CH⁻, under the condition that - L¹-Ar¹ is H; or

15. R¹ and L² together are a 5- to 6-membered saturated or unsaturated carboyclic or heterocyclic group, preferably a cyclohexenyl group, under the condition that - L¹-Ar¹ is H;

Z is selected from the group consisting of -COOR,
wherein \( R_i \) is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene, \( R_3 \) is H, methyl or ethyl, and \( R_4 \) is hydroxyl -SO\(_2\)CH\(_3\), SC\(^\text{cyclopropyl}\) or -SO\(_2\)CF\(_3\);

\( D \) is CO or SO\(_2\);

\( R^2 \) is H, linear or branched C\(_1\)-C\(_4\) alkyl, C\(_1\)-C\(_4\) hydroxyalkyl, C\(_1\)-C\(_4\) haloalkyl, C\(_2\)-C\(_4\) alkenyl, C\(_2\)-C\(_4\) alkynyl, C\(_3\)-C\(_6\) cycloalkyl, C\(_3\)-C\(_6\) cycloalkylalkyl, aryl, arylalkyl, heteroarylalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, or aralkyloxyalkyl; each of the alkyl, hydroxyalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroarylalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, and aralkyloxyalkyl groups being optionally substituted by one or more substituents selected from halo, cyano, alkyl, hydroxyalkyl,
haloalkyl, alkenyl, alkynyl, heteroalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group;

$\text{Ar}^2$ is a 5- or 6-membered heterocyclic group or a 5- or 6-membered heteroaryl group, optionally substituted by one or more substituents selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, alkenyl, alkynyl, heteroalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group;

$L^3$ is a single bond, $\text{C}_1-\text{C}_3$ alkyne, $\text{C}_1-\text{C}_3$ cycloalkylene $\text{C}_1-\text{C}_3$ alkenylene or carbonylamino;

$\text{Ar}^3$ is an aryl, heteroaryl, or $\text{C}_1-\text{C}_4$ alkyl group, each of which being optionally substituted by one or more groups selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxy carbonyl, heterocyclyloxy carbonyl, aryloxycarbonyl, aryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkoxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl,
heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, cycloalkylaminocarbamoyl, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, haloalkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more cycloalkyl, aryl, heterocycyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkoxyalkyl, alkoxyalkoxy, cycloalkylalkoxy, amino, alkylamino, alkylaminoalkoxy, cycloalkylamino, aralkylamino, alkylaminoalkyl, alkylaminocarbonyl, alkylenecarbonyl, cycloalkylcarbonylamino, alkylheterocycyl, alkylheteroaryl, alkylsulfonyl, alkylsulfonylamino, aralkyl, aralkoxy, aryl, arylamino, arlyoxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryalkyl, heteroarylcyclonyl, heterocyclyl, heterocyclenol, hydroxyl, oxo, or sulfonyl, or L₃-Ar³ form an aryl, preferably phenyl, or heteroaryl group fused to Ar², wherein each of said aryl or heteroaryl groups fused to Ar² are optionally substituted by one or more halo, preferably chloro and fluoro;

with the following provisos:

Ar²-L³-Ar³ is not 4-(4-butylphenyl)thiazol-2-yl, 4-(4-ethylphenyl)thiazol-2-yl, 4-(para-tolyl)thiazol-2-yl, 4-phenylthiazol-2-yl, 4-(4-propylphenyl)thiazol-2-yl, 4-(4-sec-butyl)phenyl)thiazol-2-yl, 4-(4-isopropylphenyl)thiazol-2-yl, 4-(4-tert-butyl)phenyl)thiazol-2-yl, 4-(4-butylphenyl)-5-methylthiazol-2-yl, 4-(4-ethylphenyl)-5-methylthiazol-2-yl, 5-methyl-4-(para-tolyl)thiazol-2-yl, 5-methyl-4-phenylthiazol-2-yl, 5-methyl-4-(4-propylphenyl)thiazol-2-yl, 4-(4-sec-butylphenyl)-5-methylthiazol-2-yl, 4-(4-isopropylphenyl)-5-methylthiazol-2-yl, 4-(4-tert-butyl)phenyl)-5-methylthiazol-2-yl, 4-(4-butyl-3-methylphenyl)thiazol-2-yl, 4-(4-ethyl-3-methylphenyl)thiazol-2-yl, 4-(3,4-dimethylphenyl)thiazol-2-yl, 4-(meta-tolyl)thiazol-2-yl, 4-(3-methyl-4-propylphenyl)thiazol-2-yl, 4-(4-sec-butyl)-3-methylphenyl)thiazol-2-yl, 4-(4-isopropyl-3-methylphenyl)thiazol-2-yl,
4-(4-isobutyl-3-methylphenyl)thiazol-2-yl, 4-(4-(tert-butyl)-3-methylphenyl)thiazol-2-yl, 4-(4-butyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-ethyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(3,4-dimethylphenyl)-5-methylthiazol-2-yl, 5-methyl-4-(meta-tolyl)thiazol-2-yl, 5-methyl-4-(3-methyl-4-propylphenyl)thiazol-2-yl, 4-(4-(sec-butyl)-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-isopropyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-butylphenyl)-5-methylthiazol-2-yl;

$\text{Ar}^3$ is not (7H-pyrrolo[2,3-d]pyrimidin)-4yl;

$\text{Ar}^2$ is not 5-cyano-thiazolyl;

the compound of formula I is none of.

2-[[4-(4-butylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexane carboxylic acid,

6-[[4-(3,4-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,

6-[[4-(3,4-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,

6-[[5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
carboxylic acid
2-[[[5-[(4-chlorophenoxy)methyl]-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[[5-methyl-4-(4-propylphenyl)-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]carbonyl] -cyclohexanecarboxylic acid,
2-[[[[5-methyl-4-(4-chlorophenyl)-2-thiazolyl]amino]carbonyl] -cyclohexanecarboxylic acid,
6-[[4-[4-(l,l-dimethylethyl)phenyl]-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-ethyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid-1-methylethyl ester
2-[[5-methyl-4-phenyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-4-[4-(2-methylpropyl)phenyl]-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-cyclopropyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-(cyclopentylmethyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[4-(4-chlorophenyl)5-ethyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[4-(3-methoxyphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-methyl-4-(4-methylphenyl)-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-cyclopropyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(4-chlorophenyl)-5-ethyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[4-(2,5-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-phenyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[6-carboxy-3-cyclohexen-1-yl]carbonyl]amino]-4-phenyl-5-thiazolecarboxylic acid-5-ethyl ester,
2-[[4,5-dimethyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-cyclopropyl-1,3,4-oxadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-methyl-4-[4-(2-methylpropyl)phenyl]-2-thiazolyl]amino]carbonyl]-3-
cyclohexene-1-carboxylic acid,
6-[[4,5-diphenyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(2,4-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-
cyclohexene-1-carboxylic acid,
2-[[4-(2,4-dimethylpenty1)-5-methyl-2-thiazolyl]amino]carbonyl]-
cyclohexanecarboxylic acid,
2-[[5-(2-thienyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[(4,5-diphenyl-2-thiazolyl)amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(4-ethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-
carboxylic acid,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-methyl-5-thiazolecarboxylic acid-5-
methyl ester,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-methyl-5-thiazolecarboxylic acid-5-
ethyl ester,
2-[[5-ethyl-4-phenyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
acid,
2-[[5-cyclopropyl-1,3,4-oxadiazol-2-yl]amino]carbonyl-cyclohexanecarboxylic acid,
2-[[[4-(4-fluorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-methyl-5-thiazoleacetic acid-5-ethyl ester,
2-[[4-(2,4-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(3-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-((5-cyclohexyl-1,3,4-thiadiazol-2-yl)carbamoyl)cyclohexanecarboxylic acid
2-[[5-methyl-4-(4-methylphenyl)-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-(2-thienyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[4,5-diphenyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(4-ethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-dimethylamino]carbonyl]-4-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-ethyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-phenyl-5-thiazolecarboxylic acid-5-ethyl ester,
6-[[5-ethyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-ethyl-5-methyl-2-thiazolyl]amino] carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-4-[4-(1-methylethyl)phenyl]-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-acetyl-4-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(2,4-dichlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[4-(4-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-cyclohexyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(4-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl-cyclohexanecarboxylic acid,
6-[[4-(4-fluorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[6-carboxy-3-cyclohexen-1-yl]carbonyl-4-methyl-5-thiazolecarboxylic acid-5-methyl ester,
2-[[4-(1,1-dimethylethyl)phenyl]-5-methyl-2-thiazolyl]amino]carbonyl-cyclohexanecarboxylic acid,
2-[[5(dimethylethylamino)carbonyl]-4-methyl-2-thiazolyl]amino]carbonyl-cyclohexanecarboxylic acid,
6-[[5-methyl-4-phenyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]carbonyl] -cyclohexanecarboxylic acid,
and
6-[[5-(2-thienyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid.

In another aspect, the present invention provides a pharmaceutical composition comprising at least one compound according to the invention or a pharmaceutically acceptable salt or solvate thereof.

The invention also relates to the use of the above compounds or their pharmaceutically acceptable salts and solvates as modulators of GPR43, preferably as agonists or partial agonists of GPR43.

The invention further provides methods of treatment and/or prevention of type II diabetes, obesity, dyslipidemia such as mixed or diabetic
dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH) comprising the administration of a therapeutically effective amount of a compound or pharmaceutically acceptable salt or solvate of formula (I), to a patient in need thereof. Preferably the patient is a warm-blooded animal, more preferably a human.

The invention also provides the use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as a medicament. Preferably, the medicament is used for the treatment and/or prevention of type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH).

In a preferred embodiment the disease is type II diabetes, a lipid disorder such as dyslipidemia, hypertension, obesity, or atherosclerosis and its sequelae.

[DETAILED DESCRIPTION OF THE INVENTION]

As noted above, the invention relates to compounds of formula I, as well as their pharmaceutically acceptable salts and solvates.
Preferred compounds of formula I and pharmaceutically acceptable salts and solvates thereof are those wherein

D is CO; and/or

Z is -COOR, wherein R is defined as above in respect to formula I, preferably Z is COOH; and/or

R^1 is hydrogen, halogen, or a group selected from C_{1-4} alkyl optionally substituted by one or more substituents selected from halogen, allyl or alkyl; preferably R^1 is selected from hydrogen, fluoro, methyl, or ethyl, the methyl or ethyl group being optionally substituted with one or more substituents selected from fluoro or alkyl, more preferably R^1 is hydrogen, fluoro or methyl, and most preferably R^1 is hydrogen, and L^2 is as defined above in respect to formula I, preferably L^2 is cyclopropylene, ethylene, n-propylene, -CH_2C(R'R")- or -C(R'R")-, wherein R' and R" are independently selected from H, halogen, methyl, and ethyl, more preferably L^2 is cyclopropylene, ethylene, methylene, -CHMe-, -CHF-; even more preferably L^2 is methylene, or R^1 and L^2 together are =CH-; and/or

R^2 is H, linear or branched C_{1-4} alkyl, C_{1-4} hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentylmethyl, cyclopropylmethyl, 1,1,1-trifluoroethyl, -C_2H_4CO_2CH_3, -CH_2CO_2CH_3, or -CH_2CONH_2, benzyl, benzoyloxyethyl, methoxyethyl, preferably R^2 is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, -C_2H_4CO_2CH_3, -CH_2CO_2CH_3, -CH_2CONH_2, more preferably R^2 is methyl or cyclopropyl; and/or

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, or a 5- to 6-membered cycloalkyl or heterocycloalkyl group, each of which may optionally be substituted by one or more groups selected from halogen, trifluoromethyl, cyano, methoxy, trifluoromethoxy, and methoxyethoxy, and L^1 is a single bond, C_{1-2} alkyne, or C_2 alkenylene, each optionally being substituted by one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} haloalkyl, preferably L^1 is a single bond, C_{1-2} alkyne, optionally substituted by C_{1-2} alkyl, preferably Ar^1 is phenyl or cyclohexyl and L^1 is methylene, optionally substituted by methyl; or Ar^1 is a
linear or branched C₃-C₆ alkyl group, optionally substituted by one or more groups selected from halogen, trifluoromethyl, cyano, and methoxy, and L¹ is a single bond, C₁-C₂ alkylene, or C₂ alkenylene, preferably C₁-C₂ alkylene or C₂ alkenylene, and even more preferably C₁-C₂ alkylene, (Z)-ethenylene, or (E)-ethenylene, each optionally being substituted by one or more substituents selected from halo, C₁-C₂ alkyl, C₁-C₂ haloalkyl, preferably L¹ is a single bond or C₁-C₂ alkylene, optionally substituted by C₁-C₂ alkyl or one or more fluoro, more preferably L¹ is CH₂₂; preferably Ar¹ is isopropyl, butyl, isobutyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl, phenyl, furanyl, thiophenyl, thiazolyl or pyridyl, and L¹ is CH₂, more preferably Ar¹ is cyclopentyl, tetrahydrofuranyl, tetrahydropyranyl, phenyl or furanyl and L¹ is CH₂; and/or

Ar² is selected from the group consisting of thiazolene, 1,2,4-thiadiazolylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, oxazolylene, 1,2,4-oxadiazolylene, pyrazolylene, each of which being optionally substituted by one or more substituents selected from halo, cyano, hydroxyl, linear or branched C₁-C₃ alkyl, C₁-C₃ hydroxyalkyl, C₁-C₃ haloalkyl, preferably F, Cl, CH₃, or CF₃, preferably Ar² is thiazolylene, 1,2,4-thiadiazolylene, pyridinylene, more preferably Ar² is thiazolylene linked to the nitrogen of N-R² at position 2 and to L³ of L³-Ar³ at position 4, 1,2,4-thiadiazolylene linked to the nitrogen of N-R² at position 5 and to L³ of L³-Ar³ at position 3, pyridinylene linked to the nitrogen of N-R² at position 2 and to L³ of L³-Ar³ at position 5; and/or

Ar³ is an aryl or heteroaryl group, optionally substituted by one or more substituents selected from halo, C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, cyano, 5 or 6 membered heteroaryl such as pyridinyl, pyrazinyl, and pyridazinyl, phenyl, methylcarbonylamino, -NH-SO₂CF₃, methylenedioxy and L³ is a single bond or C₁-C₂ alkylene; Ar³ is a C₁-C₄ alkyl group and L³ is a single bond; or -L³-Ar³ is a phenyl group fused to Ar²; preferably Ar³ is an aryl, preferably phenyl, or heteroaryl group, preferably thiophenyl, more preferably thiophen-2-yl, furanyl, more preferably furan-2-yl, each of said aryl or heteroaryl being optionally substituted by one or more substituents selected from halo, C₁-C₄ alkyl, cyclopropyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, 5 or 6 membered aryl, preferably phenyl, 5 or
6 membered heteroaryl, preferably furanyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, more preferably furan-3-yl, thiophen-3-yl, pyridinyl, still more preferably pyridin-3-yl, each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl being optionally fused to one or more 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents selected from halo, hydroxyl, oxo, alkyl, and/or each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally substituted by one or more substituents selected from cyano, halo, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, alkyaminooxy, alkylaminoalkyl, cycloalkylaminooxy, aryloxymethylene, aralkylamino, aralkyloxyalkyl, alkylaminocarbonyl, heteroarylmethoxycarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylaminooxy, arylaminooxy, aralkylaminooxy, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl; more preferably Ar^3 is phenyl, thiophenyl, preferably thiophen-2-yl, furanyl, preferably furan-2-yl, each of said phenyl, thiophenyl, furanyl, being optionally substituted by one or more substituents selected from halo, C_1-C_4 alkyl, cyclopropyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, phenyl, pyridin-3-yl, each of said phenyl or pyridin-3-yl being optionally fused to one or more 5 or 6 membered heterocyclyl, phenyl, or heteroaryl moiety, preferably oxopyrrolidinyl, imidazolinyl, piperidinyl, morpholynyl, pyrrolidinyl, imidazoyl, or pyridinyl, more preferably 2-oxopyrrolidinyl 2-oxoimidazolyl, 2-oxopiperidinyl or pyrrolidinyl, thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, and/or each of said phenyl or pyridin-3-yl groups being optionally substituted by one or more substituents selected from halo, alkyl, heterocyclyl, heteroaryl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy,
aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, aralkylamino, alkyaminocarbonyl, alkylcarbonylamino, each of said heterocyclyl, heteroaryl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl.

Other preferred compounds of formula I are those wherein R\textsubscript{1} and L\textsubscript{2} together are a 5- to 6-membered saturated or unsaturated carbocyclic or heterocyclic group, preferably a cyclohexenyl group, under the condition that -L\textsubscript{1}-Ar\textsubscript{1} is H; and Ar\textsubscript{2}, Ar\textsubscript{3}, R\textsubscript{2}, and L\textsubscript{3} are as defined above.

Still other preferred compounds of formula I are those wherein D is SO\textsubscript{2} and Ar\textsubscript{1}, Ar\textsubscript{2}, Ar\textsubscript{3}, R\textsubscript{1}, R\textsubscript{2}, L\textsubscript{1}, L\textsubscript{2}, L\textsubscript{3}, and Z are as defined above in respect to formula I.

In one embodiment, preferred compounds of Formula I are those of formula Ia:

![Chemical structure](image)

Ia

and pharmaceutically acceptable salts, and solvates thereof, wherein

R is H or linear or branched C\textsubscript{1}-C\textsubscript{4} alkyl; and

Ar\textsubscript{1}, Ar\textsubscript{2}, Ar\textsubscript{3}, R\textsubscript{1}, R\textsubscript{2}, L\textsubscript{1}, L\textsubscript{2} and L\textsubscript{3} are as defined above in respect to formula I.

Preferred compounds of formula Ia are those wherein
R\textsuperscript{1} is hydrogen and L\textsuperscript{2} is ethenylene, ethylene, n-propylene, -CH(Me)-, -CH\textsubscript{2}-, -CHF-, -CF\textsubscript{2}-, or cyclopropylene; or R\textsuperscript{1} and L\textsuperscript{2} together are =CH-; and

Ar\textsuperscript{1}, Ar\textsuperscript{2}, Ar\textsuperscript{3}, R\textsuperscript{2}, L\textsuperscript{1} and L\textsuperscript{3} are as defined above in respect to formula I.

In another embodiment, preferred compounds of Formula I are those of formula Ib:

Ib

and pharmaceutically acceptable salts, and solvates thereof, wherein

X is S or O, preferably X is S;

Y is CH or N, preferably Y is CH;

L\textsuperscript{3} is attached to the heterocyclic group either in position 4 or 5, preferably in position 4; and

if Y is CH, R\textsuperscript{5} is H, halo, cyano, hydroxyl, linear or branched C\textsubscript{1}-C\textsubscript{3} alkyl, C\textsubscript{1}-C\textsubscript{3} hydroxyalkyl, C\textsubscript{1}-C\textsubscript{3} haloalkyl, preferably H, methyl, F, Cl, or CF\textsubscript{3}, more preferably H or F and R\textsuperscript{5} is attached to the heterocyclic group either in position 4, if L\textsuperscript{3} is attached in position 5, or in position 5, if L\textsuperscript{3} is attached in position 4; preferably R\textsuperscript{5} is attached in position 5;
if Y is N, R^5 is absent and L^3 is attached in position 5; and

Ar^1 and L^1 are as defined above in respect to formula I, preferably Ar^1 is a 5- to 6-membered aryl, preferably phenyl, or heteroaryl group, preferably furanyl, thiophenyl, oxazolyl, isoxazolyl, or thiazolyl optionally substituted by one or more groups selected from halogen, trifluoromethyl, cyano, methoxy trifluoromethoxy, and methoxyethoxy, and L^1 is a single bond, C_1-C_2 alkyne, or C_2 alkenylene, each optionally being substituted by one or more substituents selected from halo, C_1-C_2 alkyl, C_1-C_2 haloalkyl, preferably L^1 is a single bond, or C_1-C_2 alkenylene, optionally substituted by C_1-C_2 alkyl, more preferably L^1 is -CH_2-; or Ar^1 is a linear or branched C_3-C_6 alkyl group, preferably isopropyl, butyl, isobutyl, optionally substituted by one or more groups selected from halogen, trifluoromethyl, cyano, and methoxy, and L^1 is a single bond; or Ar^1 is cycloalkyl, preferably cyclopropyl, cyclopentyl, cyclohexyl, bicyclo[2.2.1]heptan-2-yl, more preferably cyclopentyl, or heterocycloalkyl, preferably tetrahydroturanil or tetrahydropyranyl and L^1 is C_1-C_2 alkenylene or C_2 alkenylene, preferably C_1-C_2 alkenylene or C_2 alkenylene, and even more preferably -CH_2-; (Z)-ethenylene, or (E)-ethenylene, each optionally being substituted by one or more substituents selected from halo, C_1-C_2 alkyl, C_1-C_2 haloalkyl, preferably L^1 is a single bond or C_1-C_2 alkenylene, optionally substituted by C_1-C_2 alkyl, even more preferably L^1 is methylene;

Ar^3 is as defined above in respect to formula I, preferably Ar^3 is an aryl or heteroaryl group, optionally substituted by one or more substituents selected from halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, cyano, 5 or 6 membered heteroaryl such as pyridinyl, phenyl, methylecarbonylamino, -NH-SO_2CF_3, and L^3 is a single bond or C_1-C_2 alkenylene; or Ar^3 is a C_1-C_4 alkyl group and L^3 is a single bond, more preferably Ar^3 is an aryl, preferably phenyl, or heteroaryl group, preferably thiophenyl, more preferably thiophen-2-yl, furanyl, more preferably furan-2-yl, each of said aryl or heteroaryl being optionally substituted by one or more substituents selected from halo, C_1-C_4 alkyl, cyclopropyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, 5 or 6 membered aryl, preferably phenyl, 5 or 6 membered heteroaryl, preferably
furanyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, more preferably furan-3-yl, thiophen-3-yl, pyridinyl, still more preferably pyridinyl, each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl being optionally fused to one or more 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents selected from halo, hydroxyl, oxo, alkyl, and/or each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally substituted by one or more substituents selected from cyano, halo, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, aralkylamino, alkenyl, cycloalkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonfyl, haloalkylsulfonfyl, alkylsulfonlamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl; still more preferably Ar³ is phenyl, thiophenyl, preferably thiophen-2-yl, furanyl, preferably furan-2-yl, each of said phenyl, thiophenyl, furanyl, being optionally substituted by one or more substituents selected from halo, C₁-C₄ alkyl, cyclopropyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, phenyl, pyridin-3-yl, each of said phenyl or pyridin-3-yl being optionally fused to one or more 5 or 6 membered heterocyclyl, phenyl, or heteroaryl moiety, preferably oxopyrrolidinyl, imidazolinyl, piperidinyl, morpholinyl, pyrrolyl, imidazolyl, or pyridyl, more preferably 2-oxopyrrolidinyl 2-oximidazolinyl, 2-oxopiperidinyl or pyrrolyl, thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, and/or each of said phenyl or pyridin-3-yl groups being optionally substituted by one or more substituents selected from halo, alkyl, heterocyclyl, heteroaryl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino,
aralkylamino, alkylaminocarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, each of said heterocyclyl, heteroaryl, cycloalkylalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl;

R₁ is as defined above in respect to formula I, preferably R₁ is hydrogen, halogen, allyl, or a group selected from C₁₋₄ alkyl optionally substituted by one or more substituents selected from halogen or alkyl; more preferably R₁ is selected from hydrogen, fluoro, or methyl or ethyl, the methyl or ethyl group being optionally substituted with one or more substituents selected from fluoro or alkyl, even more preferably R₁ is hydrogen, fluoro or methyl, and most preferably R₁ is hydrogen, and L² is as defined above in respect to formula I, preferably L² is cyclopropylene, ethylene, n-propylene, -C(R'R'")-, wherein R' and R" are independently selected from H, halogen, methyl, and ethyl, more preferably L² is cyclopropylene, ethylene, methylene, -CHMe-, -CHF-, even more preferably L² is methylene; or R¹ and L² together are =CH-;

Z is as defined above in respect to formula I, preferably Z is -COOR, wherein R is defined as above in respect to formula I, more preferably Z is COOH; and

R³ is as defined above in respect to formula I, preferably R³ is H, linear or branched C₁₋₄ alkyl, C₁₋₂ hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentylmethyl, cyclopropylmethyl, benzyl, benzyloxyethyl, methoxyethyl, 1,1,1-trifluoroethyl, -C₂H₄CO₂CH₃, -CH₂CO₂CH₃, or -CH₂CONH₂, more preferably R³ is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, -C₂H₄CO₂CH₃, -CH₂CO₂CH₃, or -CH₂CONH₂, more preferably R³ is methyl or cyclopropyl.

Preferred compounds of formula Ib are those wherein Z is -COOR, preferably COOH, and R, Ar¹, Ar², Ar³, R¹, R², L¹, L² and L³ are as defined above in respect to formula I.
Particularly preferred compounds of formula Ib are those of formula Ib-1

\[
\begin{align*}
R^6, R^7, R'^6, R'^7 \text{ and } R^8 & \text{ are independently selected from } H, \text{ halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaryalkyl, } \\
& \text{ hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, } \\
& \text{ heterocyclyloxycarbonyl, arlyoxycarbonyl, heteroaryloxycarbonyl, alkycarbonyloxy, cycloalkyl carbonyloxy, heterocyclyl carbonyloxy, } \\
& \text{ arylcarbonyloxy, heteroarylcarnbonyloxy, arylalkyloxy, alkyl carbonylamino, } \\
& \text{ haloalkyl carbonylamino, cycloalkyl carbonylamino, heterocycl carbonylamino, aryl carbonylamino, heteroarylcarnbonylamino, alkyl carbonylamino, acylamino, cycloalkyl carbonylamino, carbamoyl, hydroxycarbamoyl, alkyl carbamoyl, heteroaryl carbamoyl, carbamoylalkyl, carbamoylamino, alkyl carbamoylamino, } \\
& \text{ alkylsulfonil, haloalkyl sulfonil, cyclalkylsulfonil, heterocyclic sulfonil, } \\
& \text{ arylsulfonil, heteroarylsulfonil sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroaryl sulfamoyl, alkylsulfonilamino, cycloalkyl sulfonilamino, heterocyclic sulfonilamino, aryl sulfonilamino, heteroarylsulfonilamino, haloalkyl sulfonilamino, or } R^6 \text{ and } R^7 \text{ or } R^8 \text{ or } R'^6 \text{ and } R'^7 \text{ or } R^7 \text{ and } R^8
\end{align*}
\]
together form an alkylenedioxy group or a haloalkylenedioxy group, or \( R^6 \) and \( R^7 \) or \( R^7 \) and \( R^8 \) or \( R'^6 \) and \( R'^7 \) or \( R'^7 \) and \( R^8 \) together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the phenyl group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloaryl, heteroaryl, heteroarylalkyl, heteroarylcycloalkyl, heterocyclyl, hydroxyl, oxo, or sulfonyle, preferably \( R^6, R^7, R'^6, R'^7 \) and \( R^8 \) are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyle, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyle, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, more preferably \( R'^6, R'^7 \) and \( R^8 \) are independently selected from H, hydroxyl, halo, alkyl, haloalkyl, alkoxy, alkoxyalkyl preferably methoxyethyl, haloalkoxy preferably -OCF₃, alkylsulfonyle, haloalkylsulfonyl and cyano, even more preferably from H, halo, \( CF₃ \), C1-C2 alkyl, C1-C2 alkoxy, and cyano, still more preferably from H, F, Cl, CF₃, methyl, methoxy, and cyano, still more preferably \( R^6, R^7, R'^6, R'^7 \) are H and \( R^8 \) is selected from H, Cl, methyl, hydroxyl and methoxy, and most preferably \( R^6, R^7, R'^6, R'^7 \) are H and \( R^8 \) is selected from H, Cl, methyl, and methoxy.

Preferred compounds of formula Ib-I are those of formula Ib-Ia

![Ib-Ia](image-url)
wherein $L^2$, $L^3$, $Ar^3$, $X$, $Y$, $R^2$, $R^5$, $R^6$, $R'^6$, $R'^7$ and $R^8$ are as defined above in respect to formula Ib-I.

Other preferred compounds of formula Ib are selected form the group consisting of formulae Ib-2a, Ib-2b, Ib-2c, Ib-2d, Ib-2e and Ib-2f:

Ib-2a

Ib-2b

Ib-2c
wherein $L_1$, $L_2$, $L_3$, $A_r^3$, $X$, $Y$, $Z$, $R_1$, $R_2$, and $R_5$ are as defined above in respect to
formula Ib, preferably $L^1$ is methylene;

$B^1$, $B^2$ and $B^3$ are independently $CF_2$, O, NR, CO, or SO$_2$, wherein $R^x$ is H or alkyl, preferably linear or branched $C_1$-$C_4$ alkyl; $C_1$-$C_4$ alkylsulfonil, $C_1$-$C_4$ alkylaminocarbonil, $C_3$-$C_6$ cycloalkyl; $C_3$-$C_6$ cycloalkylcarbonyl, $C_3$-$C_6$ cycloalkylsulfonyl, $C_3$-$C_6$ cycloalkylaminocarbonil, aryl, arylcarbonyl, arylsulfonil or arylaminocarbonil, heteroaryl, heteroarylcariyl, heteroarylsulfonyl or heteroarylamino-carbonil; preferably $B^1$, $B^2$ and $B^3$ are O and

$R^9$, $R^{10}$, $R^{11}$, $R^{12}$, $R^{13}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, $R'^{13}$ and $R''^{13}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkylnyl, heteroalkyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxy, haloxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminocycloalkyl, carboxy, alkoxycarbonyl, cycloalkylxocarbonyl, heterocyclyloxycarbonyl, aryloxyacarbonyl, heteroaryloxyacarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxy carbamoyl, alkyl carbamoyl, aminocycloalkyl, heteroarylmocarboyl, carbamoylalkyl, carbamoylamino, alkyl carbamoylamino, alkylsulfonil, haloalkylsulfonil, cycloalkylsulfonil, heterocyclylsulfonil, arylsulfonil, heteroarylsulfonil sulfamoyl, alkyl sulfamoyl, heteroarylsulfamoyl, alkylsulfonilamino, cycloalkylsulfonilamino, heterocyclylsulfonilamino, arylsulfonilamino, heteroarylsulfonilamino, haloalkylsulfonilamino, or one of $R^9$ or $R^{10}$ and one of $R^{11}$, $R^{12}$, $R^{13}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, $R'^{13}$ or $R''^{13}$, or one of $R^{11}$ or $R^{12}$ and one of $R^9$, $R^{10}$, $R^{13}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, $R'^{13}$ or $R''^{13}$, or one of $R^{13}$ or $R'^{13}$ and one of $R^9$, $R^{10}$, $R^{11}$, $R^{12}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, or $R''^{13}$ together form an alkylendioxy group or a haloalkylenedioxy group, or one of $R^9$ or $R^{10}$ and one of $R^{11}$, $R^{12}$, $R^{13}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, $R'^{13}$ or $R''^{13}$, or one of $R^{11}$ or $R^{12}$ and one of $R^9$, $R^{10}$, $R^{13}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, $R'^{13}$ or $R''^{13}$, or one of $R^{13}$ or $R'^{13}$ and one of $R^9$, $R^{10}$, $R^{11}$, $R^{12}$, $R'^9$. 


R’\textsuperscript{10}, R’\textsuperscript{11}, R’\textsuperscript{12}, or R’\textsuperscript{13} together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, arilloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryllalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably R’\textsuperscript{9}, R’\textsuperscript{10}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13}, R’\textsuperscript{9}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13} and R’\textsuperscript{13} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkyllalkyl, heteroalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroaryllalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, arilloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyle, haloalkylsulfonyle, cycloalkylsulfonyle, heterocyclylsulfonyle, arylsulfonyle, heteroarylsulfonyle, alkylsulfonylamino, cycloalkylsulfonylamino, or one of R’\textsuperscript{9} or R’\textsuperscript{10} and one of R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13}, R’\textsuperscript{9}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13} or R’\textsuperscript{13}, or one of R’\textsuperscript{11} or R’\textsuperscript{12} and one of R’\textsuperscript{9}, R’\textsuperscript{10}, R’\textsuperscript{13}, R’\textsuperscript{9}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13} or R’\textsuperscript{13}, or one of R’\textsuperscript{13} or R’\textsuperscript{13} and one of R’\textsuperscript{9}, R’\textsuperscript{10}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13}, or R’\textsuperscript{13} together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, arilloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryllalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyle, more preferably R’\textsuperscript{9}, R’\textsuperscript{10}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13}, R’\textsuperscript{9}, R’\textsuperscript{11}, R’\textsuperscript{12}, R’\textsuperscript{13} and R’\textsuperscript{13} are independently selected from H, hydroxyl, Ci-C\textsubscript{3}-alkyl, halo, haloalkyl, alkoxy, haloalkoxy, alkylsulfonyl, haloalkylsulfonyl and cyano, even more preferably from H, Ci-C\textsubscript{3}-alkyl, halo, CF\textsubscript{3}, C1-C2 alkoxy, and cyano, and still more preferably from H, F, Cl, methyl, CF\textsubscript{3}, methoxy, and cyano, and most preferably H or methyl.

Particularly preferred compounds of formula Ib-2a are
wherein A is -(CH$_2$)$_n$-O-, -(CH$_2$)$_m$-NR$_a$-, -(CH$_2$)$_n$-SO$_2$-, or -(CH$_2$)$_m$-, wherein n is
equal to 0 or 1, m is equal to 1 or 2, and Rₐ is as defined above in respect to formula Ib-2b, preferably Rₐ is H or alkyl, preferably linear or branched C₁-C₄ alkyl; C₁-C₄ alkylcarbonyl, C₁-C₄ alkylsulfanyl, more preferably linear or branched C₁-C₄ alkyl; and

\[ \text{L}^1, \text{L}^2, \text{L}^3, \text{Ar}^3, \text{X}, \text{Y}, \text{Z}, \text{R}^1, \text{R}^2 \text{ and } \text{R}^5 \text{ are as defined above in respect to formula Ib-2a.} \]

Even more preferred compounds of formula Ib-2a are selected from

![Chemical Structures](image-url)

and
wherein $A$ is $-(\text{CH}_2)_n\text{-O-}$, $-(\text{CH}_2)_n\text{-NR}_a\text{-}$, $-(\text{CH}_2)_n\text{-SO}_2\text{-}$, or $-(\text{CH}_2)_m\text{-}$, wherein $n$ is equal to $0$ or $1$, $m$ is equal to $1$ or $2$, and $R_a$ is as defined above in respect to formula Ib-2b, preferably $R_a$ is H or alkyl, preferably linear or branched C$_1$-C$_4$ alkyl; C$_1$-C$_4$ alkylcarbonyl, C$_1$-C$_4$ alkylsulfonfonyl, more preferably linear or branched C$_1$-C$_4$ alkyl; and

$L_2$, $L_3$, $Ar_3$, $X$, $Y$, $R$, $R^1$, $R^2$ and $R^5$ are as defined above in respect to formula Ib-2a.

Further preferred compounds of formula Ib are those of formula Ib-3,

preferably
Ib-3a,

wherein $L_2$, $L_3$, $A_{r_3}$, $X$, $Y$, $R$, $R_1$, $R_2$ and $R_5$ are as defined above in respect to formula Ib; and

$R_{16}$, $R_{17}$, $R_{18}$ and $R_{19}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminooalkyl, carboxy, alkoxy carbonyl, cycloalkyloxy carbonyl, heterocyclyloxy carbonyl, aryloxy carbonyl, heteroaryloxy carbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylamino alkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroaryliminocarbonyl, carbamoylalkyl, carbamoylaminocarbonyl, alkylcarbamoylaminocarbonyl, alkylsulfonamido, haloalkylsulfonamido, cycloalkylsulfonamido, heterocyclylsulfonamido, arylsulfonamido, heteroarylsulfonamido, sulfonylamido, alkylsulfamido, arylsulfamido, heteroarylsulfamido.

$R_{16}$ and $R_{17}$ or $R_{17}$ and $R_{18}$ or $R_{18}$ and $R_{19}$ together form an alkylenedioxy group or a haloalkylenedioxy group, or $R_{16}$ and $R_{17}$ or $R_{17}$ and $R_{18}$ or $R_{18}$ and $R_{19}$ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the phenyl
group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably R^{16}, R^{17}, R^{18} and R^{19} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroaryalkyl, hydroxyl, alkoxy, alkoxyalkyl, preferably methoxyethyl, haloalkoxy, preferably trifluoromethoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, more preferably R^{16}, R^{17}, R^{18} and R^{19} are independently selected from H, hydroxyl, halo, haloalkyl, alkoxy, haloalkoxy, preferably trifluoromethoxy, alkylsulfonyl, haloalkylsulfonyl and cyano, even more preferably from H, halo, CF_3, methyl, C_1-C_2 alkoxy, and cyano, and most preferably from H, F, Cl, CF_3, methyl, methoxy, and cyano.

Further preferred compounds of formula Ib are those of formula Ib-4

- Ar^1, Ar^3, L^1, L^2, R^1, R^2, R^5, X, Y and Z are as defined above in respect to
Preferred compounds of formula Ib-4 are those of formula Ib-4a

wherein

$\text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{X}, \text{Y} \text{ and } \text{Z}$ are as defined above in respect to formula Ib-4,

$\text{R}^{20}$ and $\text{R}^{20}$ are independently selected from halo (preferably -F and -Cl), cyano, C$_1$-C$_3$ alkyl, cyclopropyl, haloalkyl, alkoxy, haloalkoxy, alkoxy carbonylamino, or the two substituents form an alkylenedioxy group or a haloalkylenedioxy group, preferably $\text{R}^{20}$ and $\text{R}^{20}$ are halo preferably fluoro or chloro, haloalkyl, preferably -CF$_3$ or -CHF$_2$, alkoxy preferably methoxy, haloalkoxy preferably -OCF$_3$ or -OCHF$_2$;

$\text{Ar}^4$ is 5 or 6 membered aryl, preferably phenyl, 5 or 6 membered heteroaryl, preferably furanyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, more preferably furan-3-yl, thiophen-3-yl, pyridinyl, still more preferably pyridin-3-yl, each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally fused to one or more 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents
selected from halo, hydroxyl, oxo, alkyl, and/or each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally substituted by one or more substituents selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylmethyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxoy, heterocyclylalkoxy, arlyloxy, aralkyloxy, alkylamino, alkyllaminoalkyl, cycloalkylaminio, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylmethyl, alkylaminocarbonyl, cycloalkylaminocarbonyl, alkylaminocarbonyl, haloalkylhaloalkyl, alkylsulfonlamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylmethyl, cycloalkyloxoy, heterocyclylalkoxy, arlyloxy, aralkyloxy, heteroarylmethyl, cycloalkylaminio, arylamino, aralkylamino, cycloalkylaminocarbonyl being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl; preferably Ar^4 is phenyl or pyridin-3-yl, each of said phenyl or pyridin-3-yl being optionally fused to one or more 5 or 6 membered heterocyclyl, phenyl, or 5 or 6 membered heteroaryl moiety, preferably oxopyrrolidinyl, imidazolinyl, piperidinyl, morpholinyl, pyrrolyl, imidazolyl, or pyridyl more preferably 2-oxopyrrolidinyl, 2-oximidazolinyl, 2-oxopiperidinyl, or pyrrolyl, thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, and/or each of said phenyl or pyridin-3-yl groups being optionally substituted by one or more substituents selected from halo, alkyl, heterocyclyl, heteroaryl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, cycloalkyloxoy, heterocyclylalkoxy, arlyloxy, aralkyloxy, alkylaminoalkyl, cycloalkylaminio, arylamino, alkyllaminoalkyl, alkyllaminoalkyl, alkylaminocarbonyl, alkylaminocarbonyl, cycloalkylaminocarbonyl, each of said heterocyclyl, heteroaryl, cycloalkyloxoy, cycloalkyloxoy, heterocyclylalkoxy, arlyloxy, cycloalkylaminio, arylamino, cycloalkylaminocarbonyl being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl.
Preferred compounds of formula Ib-4a are those of formula Ib-4b

\[
\begin{align*}
\text{Ib-4b} & \\
\text{wherein} & \\
5 & \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{and} \ Z \text{ are as defined above in respect to formula Ib, and} \\
& \text{Ar}^4, \text{R}^{20} \text{ and} \ R^{120}, \text{are as defined above in respect to formula Ib-4a.} \\
\text{Preferred compounds of formula Ib-4b are those of formula Ib-4c}
\end{align*}
\]
wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{and Z} \] are as defined above in respect to formula Ib;

\[ \text{R}^{20} \text{ and R}^{120}, \text{are as defined above in respect to formula Ib-4a;} \]

\[ \text{R}^{21} \text{ and R}^{22} \text{ are independently selected from H, halo, preferably fluoro or chloro, alkoxy, preferably methoxy, preferably R}^{21} \text{ and R}^{22} \text{ are H;} \]

\[ \text{R}^{23} \text{ is selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, preferably dimethylaminoethoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, preferably C}_1-C}_3 alkylsulfonyl, more preferably methylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino preferably N-methyl(methylsulfonyl)amino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, cycloalkylamine.} \]
arylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl preferably R^{23} is selected from halo, preferably chloro or fluoro, alkyl, preferably linear or branched C_{1}-C_{5} alkyl, more preferably methyl or isopropyl, 5 or 6-membered heterocyclyl, preferably pyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 1-methyl-2-oxoimidazolin-3-yl, 1-methylpiperazin-4-yl, morpholin-4-yl, heteroaryl, preferably 1,3,4-triazol-1-yl, haloalkyl, C_{1}-C_{3} alkoxy, preferably methoxy, haloalkoxy, alkoxyalkyl, preferably methoxymethyl, alkoxyalkoxy, preferably methoxyethoxy, cycloalkyloxy, cycloalkylalkyloxy, preferably cyclopropylmethylthio, heterocyclyloxy, preferably (tetrahydropyran-4-yl)oxy, aralkyloxy, preferably benzyloxy, C_{1}-C_{3} alkyloxy, preferably dimethylamino, alkylaminoalkyl, cycloalkylamino, preferably N-methylcyclohexylamino, aralkylamino, preferably N-methylbenzylamino, C_{1}-C_{6} alkylaminocarbonyl preferably dimethylaminocarbonyl, C_{1}-C_{6} alkylcarbonylamino, preferably methylcarbonylamino, cycloalkylcarbonylamino, each of said 5 or 6-membered heterocyclyl, heteroaryl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl, even more preferably R^{23} is selected from chloro, fluoro, isopropyl, 5 or 6-membered heterocyclyl preferably pyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, morpholin-4-yl, 1-methyl-2-oxoimidazolin-3-yl, C_{1}-C_{3} alkoxy preferably methoxy, alkylalkyloxy, preferably methoxyethoxy, aralkyloxy, preferably benzylamino, C_{1}-C_{3} alkylamino preferably dimethylamino, each of said 5 or 6-membered heterocyclyl, aralkyloxy being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo, or methyl;

Y^{1} is N or C-R^{24} where R^{24} is H, halo, alkoxy, alkyl, heterocyclyl, preferably pyrrolidinyl, imidazoliny1, piperidinyl, morpholinyl, more preferably 2-oxopyrrolidin-1-yl, 2-oxoimidazolin-1-yl, 2-oxopiperidin-1-yl, or morpholin-4-yl, each of said substituents being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, preferably R^{24} is H, halo, methoxy, more preferably H, chloro or fluoro, or

Y^{1} is C-R^{24} and R^{24} and R^{23} together form a 5 or 6 membered cycloalkyl, aryl,
heterocyclyl or heteroaryl moiety, preferably 2-oxopyrrolidinyl, morpholinyl, 2-oxopiperidinyl, furanyl, pyrrolyl, imidazolyl, thus forming a fused ring system, the latter fused ring system being optionally substituted by one or more group selected from oxo, alkyl or halo; and

5 Y² is N or C-R²⁵ where R²⁵ is H, halo, alkoxy, alkyl, heterocyclyl, preferably pyrrolidinyl, imidazoliny, piperidinyl or morpholinyl, more preferably 2-oxopyrrolidin-1-yl, 2-oximidazolin-1-yl, 2-oxopiperidin-1-yl or morpholin-4-yl, each of said substituents being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, preferably R²⁵ is H, halo, methoxy, more preferably H, chloro or fluoro, or

10 Y² is C-R²⁵ and R²⁵ and R²³ together form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, preferably 2-oxopyrrolidinyl, morpholinyl, 2-oxopiperidinyl, furanyl, pyrrolyl, imidazolyl, furanyl, thus forming a fused ring system, the latter fused ring system being optionally substituted by one or more group selected from oxo, alkyl or halo, under the condition that R²⁴ and R²³ together do not form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety.

Preferred compounds of formula Ib-4c are those of formula Ib-4d
Ib-4d,

wherein,

\( \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \) and \( Z \) are as defined above in respect to formula Ib;

\( \text{R}^{20} \) and \( \text{R}'^{20} \), are as defined above in respect to formula Ib-4a; and

\( \text{R}^{21}, \text{R}^{22}, \text{R}^{23} \) and \( \text{R}^{25} \) are as defined above in respect to formula Ib-4c.

Preferred compounds of formula Ib-4d are those of formula Ib-4e.
Ib-4e,

wherein,

\( \text{Ar}^1, L^1, L^2, R^1, R^2, R^5, \text{and } Z \) are as defined above in respect to formula Ib;

\( R^{20} \) and \( R^{*20} \), are as defined above in respect to formula Ib-4a; and

\( R^{21}, R^{22}, R^{23} \) and \( R^{25} \) are as defined above in respect to formula Ib-4c.

Other preferred compounds of formula Ib-4d are those of Ib-4f
Ib-4f,

wherein

\[ \text{Ar}_1, \text{L}_1, \text{L}_2, \text{R}_1, \text{R}_2, \text{R}_5, \text{and } Z \] are as defined above in respect to formula Ib;

\[ \text{R}_2^0 \text{ and } \text{R}'_2^0, \] are as defined above in respect to formula Ib-4a; and

\[ \text{R}^2_1, \text{R}^2_2, \text{R}^2_3 \text{ and } \text{R}^2_5 \] are as defined above in respect to formula Ib-4c.

Still other preferred compounds of formula Ib-4d are those of formula Ib-4g.
Ib-4g,

wherein

\( \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \) and \( \text{Z} \) are as defined above in respect to formula Ib;

\( \text{R}^{20} \) and \( \text{R}'^{20} \), are as defined above in respect to formula Ib-4a; and

\( \text{R}^{21}, \text{R}^{22}, \text{R}^{23} \) and \( \text{R}^{25} \) are as defined above in respect to formula Ib-4c.

Other preferred compounds of formula Ib-4c are those of formula Ib-4d'
Ib-4d',

wherein

\( \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \) and \( \text{Z} \) are as defined above in respect to formula Ib;

\( \text{R}^{20} \) and \( \text{R}'^{20} \), are as defined above in respect to formula Ib-4c; and

\( \text{R}^{21}, \text{R}^{22}, \text{R}^{23}, \text{and} \text{R}^{25} \) are as defined above in respect to formula Ib-4c.

Preferred compounds of formula Ib-4d' are those of formula Ib-4e'.
Ib-4e'

wherein

$A_{r1}$, $L_1$, $L_2$, $R_1$, $R_2$, $R_5$, and $Z$ are as defined above in respect to formula Ib;

$R > 20$ and $R' > 20$, are as defined above in respect to formula Ib-4a; and

$R^{21}$, $R^{22}$, $R^{23}$ and $R^{25}$ are as defined above in respect to formula Ib-4c.

Other preferred compounds of formula Ib-4d' are those of formula Ib-4f
Ib-4f

wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{and Z} \text{ are as defined above in respect to formula Ib;} \]

\[ \text{R}^{20} \text{ and R}^{120}, \text{ are as defined above in respect to formula Ib-4a;} \text{ and} \]

\[ \text{R}^{21}, \text{R}^{22}, \text{R}^{23} \text{ and } \text{R}^{25} \text{ are as defined above in respect to formula Ib-4c.} \]

Still other preferred compounds of formula Ib-4d' are those of formula Ib-4g'
wherein,

\( \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \) and \( \text{Z} \) are as defined above in respect to formula Ib;

\( \text{R}^{20} \) and \( \text{R}^{120} \), are as defined above in respect to formula Ib-4a;

\( \text{R}^{21}, \text{R}^{22}, \text{R}^{23} \) and \( \text{R}^{25} \) are as defined above in respect to formula Ib-4c.

In another embodiment of the invention, preferred compounds of formula Ib-4a are those of formula Ib-4h.
Ib-4h,

wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{and } Z \text{ are as defined above in respect to formula Ib; and} \]

\[ \text{Ar}^4, \text{R}^{20} \text{ and } \text{R}'^{20}, \text{ are as defined above in respect to formula Ib-4a.} \]

Preferred compounds of formula Ib-4h are those of formula Ib-4i
wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{and Z are as defined above in respect to formula Ib;} \]

\[ \text{R}^{20} \text{ and } \text{R}^{20}, \text{are as defined above in respect to formula Ib-4a;} \text{ and} \]

\[ \text{R}^{21}, \text{R}^{22}, \text{R}^{23}, \text{Y}^1 \text{ and } \text{Y}^2 \text{ are as defined above in respect to formula Ib-4c.} \]

Preferred compounds of formula Ib-4i are those of formula Ib-4j
Ib-4j,

wherein

$\text{Ar}^1, L^1, L^2, R^1, R^2, R^5, \text{and } Z$ are as defined above in respect to formula Ib;

$R^2 > 20$ and $R'^2 > 20$, are as defined above in respect to formula Ib-4a; and

$R^{20}$ and $R'^{20}$, are as defined above in respect to formula Ib-4c.

$R^{31}, R^{22}, R^{23}$ and $R^{25}$ are as defined above in respect to formula Ib-4c.

Other preferred compounds of formula Ib-4 are those of formula Ib-4k,
wherein

\[ I_b \text{-} 4k \]

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{X}, \text{Y}, \text{and Z are as defined above in respect to formula I}_b; \]

\[ \text{R}^{26}, \text{R}^{26}', \text{R}^{27}, \text{R}^{27}', \text{R}^{28} \text{ are independently selected from H, halo, cyano, alkyl, } \]

\[ \text{haloalkyl, cycloalkyl, cycloalkylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, alkyamino, carboxy, alkoxy carbonyl—} \text{alkylcarbonylamino, } \]

\[ \text{haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, alkoxy carbamoyl, cycloalkyl carbamoyl, alkyl carbamoylamino, } \]

\[ \text{cycloalkylaminocarbamoyl, alkylsulfonil, haloalkylsulfonil, sulfamoyl, alkylsulfamoyl, alkylsulfonilylamino, haloalkylsulfonilylamino, or two substituents } \]

\[ \text{form an alkylenedioxy group or a haloalkylenedioxy group, preferably R}^{26}, \text{R}^{26}', \text{R}^{27}, \text{R}^{27}', \text{R}^{28} \text{ are independently selected from H, halo, preferably chloro or fluoro, more preferably chloro, cyano, alkyl, preferably methyl, haloalkyl, preferably -CF}_3 \text{ or -CHF}_2, \text{ cycloalkyl, preferably cyclopropyl, alkoxy, preferably methoxy or isopropoxy, haloalkoxy, preferably -OCF}_3 \text{ or -OCHF}_2, \text{ alkoxy carbamoyl, or two substituents form an methylenedioxy group, more preferably R}^{26}, \text{R}^{26}', \text{R}^{27}, \text{R}^{27}', \text{R}^{28} \text{ are independently selected from H, halo, preferably chloro or fluoro,} \]
more preferably chloro, haloalkyl, preferably -CF₃ or -CHF₂, alkoxy, preferably methoxy.

Preferred compounds of formula Ib-4k are those of formula Ib-41

wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5 \text{ and Z are as defined above in respect to formula Ib; and} \]

\[ \text{R}^{26}, \text{R}^{26'}, \text{R}^{27}, \text{R}^{27'} \text{ and } \text{R}^{28} \text{ are as defined above in respect to formula Ib-4k.} \]

Preferred compounds of formula Ib-41 are those of formula Ib-4m
wherein,

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5 \text{ and } Z \] 
are as defined above in respect to formula \( \text{Ib} \); and

\[ \text{R}^\prime_{26} \text{ and } \text{R}^\prime_{27} \] 
are as defined above in respect to formula \( \text{Ib-4k} \), preferably \( \text{R}^\prime_{26} \) and \( \text{R}^\prime_{27} \) are independently selected from \( \text{H}, \text{halo}, \text{haloalkyl}, \text{haloalkoxy}, \text{preferably} \text{chloro, fluoro} \text{CF}_3, \text{CHF}_2, \text{OCF}_3 \text{ or OCHF}_2, \text{preferably} \text{ R}^\prime_{26} \) is chloro and \( \text{R}^\prime_{27} \) is selected from \( \text{H}, \text{halo}, \text{CF}_3, \text{CHF}_2, \text{OCF}_3 \text{ or OCHF}_2, \text{preferably} \text{chloro and fluoro.} \)

Other preferred compounds of formula \( \text{Ib-41} \) are those of formula \( \text{Ib-4n}, \)
wherein,

\[ \text{Ar}^1, L^1, L^2, R^1, R^2, R^5 \] and \( Z \) are as defined above in respect to formula Ib; and

\[ R'^{26}, R^{27} \] and \( R^{28} \) are as defined above in respect to formula Ib-4k, preferably \( R'^{26}, R^{27} \) and \( R^{28} \) are independently selected from \( H, \) halo, haloalkyl, haloalkoxy, preferably chloro, fluoro, \( C_F^3 \), or \( CHF_2 \), preferably \( OCF_3 \) or \( OCHF_2 \).

Other preferred compounds of formula Ib-4l are those of formula Ib-4o

\[ \text{Ib-4n} \]
wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5 \text{ and } \text{Z} \text{ are as defined above in respect to formula Ib; and} \]

\[ R^{27} \text{ and } R^{127} \text{ are as defined above in respect to formula Ib-4k, preferably } R^{27} \text{ and} \]

\[ R^{127} \text{ are independently selected from H, halo, haloalkyl, haloalkoxy, preferably chloro, fluoro, CF}_3, \text{CHF}_2\text{OCF}_3 \text{ or OCHF}_2. \]

Other preferred compounds of formula Ib-41 are those of formula Ib-4p
Ib-4p

wherein,

$\textbf{Ar}^1$, $\textbf{L}^1$, $\textbf{L}^2$, $\textbf{R}^1$, $\textbf{R}^2$, $\textbf{R}^5$ and $\textbf{Z}$ are as defined above in respect to formula Ib; and

$\textbf{R}^{27}$ and $\textbf{R}^{28}$ are as defined above in respect to formula Ib-4k, preferably $\textbf{R}^{27}$ and $\textbf{R}^{28}$ are independently selected from H, halo, haloalkyl, alkoxy, haloalkoxy, preferably chloro, fluoro, CF$_3$, CHF$_2$, methoxy, OCF$_3$ or OCHF$_2$.

Still other preferred compounds of formula Ib-41 are those of formula Ib-4q
Ib-4q

wherein,

\( \text{Ar}^1, L^1, L^2, R^1, R^2, R^5 \) and \( Z \) are as defined above in respect to formula Ib; and

\( R_{26} \) and \( R_{27} \) are as defined above in respect to formula Ib-4k, preferably \( R_{26} \) and \( R_{27} \) are independently selected from H, halo, haloalkyl, alkoxy, haloalkoxy, preferably chloro, fluoro, CF\(_3\), or CHF\(_2\), methoxy, OCF\(_3\) or OCHF\(_2\).

In yet another embodiment, preferred compounds of formula I are those of formula Ic.
and pharmaceutically acceptable salts, and solvates thereof, wherein

wherein $\text{Ar}^2$, $\text{Ar}^3$, $\text{R}^1$, $\text{R}^2$, $\text{L}^1$, $\text{L}^2$, $\text{L}^3$ and $Z$ are as defined above in respect to formula I; and

$R^6$, $R^7$, $R^6'$, $R^7'$ and $R^8$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylamino, heterocyclyloxy, heterocyclyloxyalkyl, hydroxy, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, haloalkoxy, cycloalkylalkoxy, haloalkylcarbonylamino, haloalkylcarbonyloxy, cycloalkylcarbonylamino, cycloalkylcarbonyloxy, alkylcarbonylamino, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcycloalkylcarbonyloxy, alkylcarbonyloxy, heterocyclylcarbonyloxy, haloalkylcarbonyloxy, alkylcarbonyl, haloalkylsulfonylamino, haloalkylsulfonyloxy, alkylsulfonyl, heteroarylsulfonylamino, arylsulfonyl, heteroarylsulfonyloxy, alkylsulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfamoylamino, alkylsulfamoylamino, cycloalkylsulfonylamino, cycloalkylsulfonyloxy, cycloalkylsulfonyl, heteroarylsulfonylamino, haloalkylsulfonylamino, haloalkylsulfonyloxy, haloalkylsulfonyl, or $R^6$ and $R^7$ or $R^7'$ and $R^8$ or $R^6'$ and $R^7$ or $R^7$ and $R^8$ together form an alkylenedioxy group or a haloalkylenedioxy group, or $R^6$ and $R^7$ or $R^7$ and $R^8$ or $R^6'$ and $R^7$ or $R^7$ and $R^8$ together form a heterocyclyl, ary1, heterocyclyl or heteroaryl moiety fused to the phenyl group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, amino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylamino, heterocyclyl, heteroarylcycloalkyl, heterocyclyloxy, hydroxyl, oxo, or sulfonyl, preferably $R^6$, $R^7$, $R^6'$, $R^7'$ and $R^8$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylcycloalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino.
acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, more preferably $R^6$, $R^7$, $R'^6$, and $R'^7$ are independently selected from H, hydroxyl, halo, alkyl, haloalkyl, alkoxy, alkoxyalkyl preferably methoxyethyl, haloalkoxy, preferably $-OCF_3$, alkylsulfonyl, haloalkylsulfonyl and cyano, even more preferably from H, halo, C1-C2 alkyl, CF$_3$, C1-C2 alkoxy, and cyano, still more preferably from H, F, Cl, CF$_3$, methyl, methoxy, and cyano, even more preferably $R^6$, $R^7$, $R'^6$, $R'^7$ are H and $R^8$ is selected from H, Cl, methyl, hydroxyl, and methoxy, and most preferably $R^6$, $R^7$, $R'^6$, $R'^7$ are H and $R^8$ is selected from H, Cl, methyl, and methoxy.

Preferred compounds of formula Ic are those wherein

$Z$ is -COOH;

$R^1$ is H;

$L^2$ is cyclopropylene, ethylene, methylene, -CHMe-, -CHF-;

$L^1$ is as defined above in respect to formula I, preferably methylene, ethylene, or a single bond; and

$Ar^2$, $Ar^3$, $R^2$, $R^6$, $R^7$, $R'^6$, $R'^7$, $R^8$ and $L^3$ are as defined above in respect to formula I.

Particularly preferred compounds of formula Ic are those of formula Ic-I
and pharmaceutically acceptable salts, and solvates thereof, wherein

\( \text{Ar}_2, \text{Ar}_3, \text{R}_2, \text{R}_6, \text{R}_7, \text{R}_7', \text{R}_8, \text{L}_2, \text{L}_3, \) and \( \text{Z} \) are as defined above in respect to formula Ic.

Preferred compounds of formula Ic-I are those wherein

\( \text{Z} \) is \(-\text{COOH};\)

\( \text{L}_2 \) is cyclopropylene, ethylene, methylene, \(-\text{CHMe}-, \ -\text{CHF}-; \) and

\( \text{Ar}_2, \text{Ar}_3, \text{R}_2, \text{R}_6, \text{R}_7, \text{R}_7', \text{R}_8, \) and \( \text{L}_3 \) are as defined above in respect to formula Ic.

In yet another embodiment, preferred compounds of formula I are those of formula Id

Id
and pharmaceutically acceptable salts, esters, esters, amides, phosphates, and solvates thereof, wherein

the dotted line is present or absent; and

Ar\textsuperscript{2}, Ar\textsuperscript{3}, R, R\textsuperscript{2} and L\textsuperscript{3} are as defined above in respect to formula I.

In one variant of the compounds of formula Id the dotted line is present.

Preferred compounds of formula Id are those of formula Id-I

wherein

the dotted line is present or absent, preferably the dotted line is present;

X is S or O;

Y is CH or N;

L\textsuperscript{3} is attached to the heterocyclic group either in position 4 or 5, preferably in position 4;

If Y is CH, R\textsuperscript{5} is halo, cyano, hydroxyl, linear or branched C\textsubscript{1}-C\textsubscript{3} alkyl, C\textsubscript{1}-C\textsubscript{3}
hydroxyalkyl, C_{1}-C_{3} haloalkyl, preferably F, Cl, or CF_{3} and R^{5} is attached to the heterocyclic group either in position 4, if L^{3} is attached in position 5, or in position 5, if L^{3} is attached in position 4; preferably R^{5} is attached in position 5;

If Y is N, R^{5} is absent and L^{3} is attached in position 5; and

5 \quad \text{Ar}^{3} \text{ is as defined above in respect to formula I, preferably Ar}^{3} \text{ is an aryl or heteroaryl group, optionally substituted by one or more substituents selected from halogen, C}_{1}-C_{4} \text{ alkyl, C}_{1}-C_{4} \text{ haloalkyl, C}_{1}-C_{4} \text{ alkoxy, cyano, 5 or 6 membered heteroaryl such as pyridinyl, phenyl, methylcarbonylamino, -NH-SO_{2}CF_{3}, and L}^{3} \text{ is a single bond or C}_{1}-C_{2} \text{ alkylene; or Ar}^{3} \text{ is a C}_{1}-C_{4} \text{ alkyl group and L}^{3} \text{ is a single bond, more preferably Ar}^{3} \text{ is an aryl, preferably phenyl, or heteroaryl group, preferably thiophenyl, more preferably thiophen-2-yl, furanyl, more preferably furan-2-yl, each of said aryl or heteroaryl being optionally substituted by one or more substituents selected from halo, C}_{1}-C_{4} \text{ alkyl, cyclopropyl, C}_{1}-C_{4} \text{ haloalkyl, C}_{1}-C_{4} \text{ alkoxy, C}_{1}-C_{4} \text{ haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, 5 or 6 membered aryl, preferably phenyl, 5 or 6 membered heteroaryl, preferably furanyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, more preferably furan-3-yl, thiophen-3-yl, pyridinyl, still more preferably pyridin-3-yl each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl being optionally fused to one or more 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, and the latter fused ring being optionally substituted by one or more further substituents selected from halo, hydroxyl, oxo, alkyl, and/or each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally substituted by one or more substituents selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaryalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamine, arylamine, aralkylamine, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonlamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaryalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamine, arylamine, aralkylamine, cycloalkylcarbonylamino being optionally substituted}
by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl; still more preferably $\text{Ar}^3$ is phenyl, thiophenyl, furanyl, preferably phenyl, thiophen-2-yl, furan-2-yl, each of said phenyl, thiophenyl, furanyl, being optionally substituted by one or more substituents selected from halo, $\text{C}_1-\text{C}_4$ alkyl, cyclopropyl, $\text{C}_1-\text{C}_4$ haloalkyl, $\text{C}_1-\text{C}_4$ alkoxy, $\text{C}_1-\text{C}_4$ haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, phenyl, pyridin-3-yl, each of said phenyl or pyridin-3-yl being optionally fused to one or more 5 or 6 membered heterocyclyl, phenyl, or 5 or 6 membered heteroaryl moiety, preferably oxopyrrolidinyl, imidazoliny1, piperidinyl, morpholinyl, pyrrolyl, imidazolyl, or pyridyl, more preferably 2-oxopyrrolidinyl, 2-oxoimidazoliny1, 2-oxopiperidinyl or pyrrolyl, thus forming a fused ring system, and the latter fused ring being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, and/or each of said phenyl or pyridin-3-yl groups being optionally substituted by one or more substituents selected from halo, alkyl, heterocyclyl, heteroaryl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, aralkylamino, alkylaminocarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, each of said heterocyclyl, heteroaryl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl;

$R$ is as defined above in respect to formula I; and

$R^2$ is as defined above in respect to formula I, preferably $R^2$ is H, linear or branched $\text{C}_1-\text{C}_4$ alkyl, $\text{C}_1-\text{C}_2$ hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentylmethyl, cyclopropylmethyl, benzyl, benzyloxyethyl, methoxyethyl, 1,1,1-trifluoroethyl, $-\text{C}_2\text{H}_4\text{CO}_2\text{CH}_3$, $-\text{CH}_2\text{CO}_2\text{CH}_3$, $-\text{CH}_2\text{CONH}_2$, more preferably $R^2$ is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, $-\text{C}_2\text{H}_4\text{CO}_2\text{CH}_3$, $-\text{CH}_2\text{CO}_2\text{CH}_3$, or $-\text{CH}_2\text{CONH}_2$, more preferably $R^2$ is methyl or cyclopropyl.

In still another embodiment, preferred compounds of Formula I are
those of formula Ie:

\[
\begin{align*}
&\text{Ar}^1 - \text{L}^1 - \text{O} - \text{N} - \text{Y} - \text{L}^2 - \text{R}^1 - \text{L}^3 - \text{Ar}^3 \\
&\text{R}^{14} - \text{Y} - \text{L}^2 - \text{R}^{15}
\end{align*}
\]

\text{Ie}

wherein

- \( Y \) is CH or N; and
- \( R^{14} \) and \( R^{15} \) are independently H, halo, cyano, hydroxyl, linear or branched \( C_1-C_3 \) alkyl, \( C_1-C_3 \) hydroxyalkyl, \( C_1-C_3 \) haloalkyl, preferably H, F, Cl, or CF₃, more preferably H;
- \( \text{Ar}^1 \) and \( \text{L}^1 \) are as defined above in respect to formula I, preferably as defined in respect to formula Ib, more preferably \( \text{Ar}^1 \) is a 5- to 6-membered aryl or heteroaryl group, optionally substituted by one or more groups selected from halogen, trifluoromethyl, cyano, and methoxy, and \( \text{L}^1 \) is a methylene group, \( C_1-C_2 \) alkyne, or \( C_2 \) alkenylene; or \( \text{Ar}^1 \) is a linear or branched \( C_3-C_6 \) alkyl group, optionally substituted by one or more groups selected from halogen, trifluoromethyl, cyano, and methoxy, and \( \text{L}^1 \) is a methylene group;
- \( \text{Ar}^3 \) is as defined above in respect to formula I, preferably \( \text{Ar}^3 \) is an aryl or heteroaryl group, optionally substituted by one or more substituents selected from halogen, \( C_1-C_4 \) alkyl, \( C_1-C_4 \) haloalkyl, \( C_1-C_4 \) alkoxy, cyano, 5 or 6 membered heteroaryl such as pyridinyl, phenyl, methylcarbonylamino, -NH-SO₂CF₃, and \( \text{L}^3 \)
is a single bond or C₁-C₂ alkylene; or Ar³ is a C₁-C₄ alkyl group and L³ is a single bond, more preferably Ar³ is an aryl, preferably phenyl, or heteroaryl group, preferably thiophenyl, more preferably thiophen-2-yl, furanyl, more preferably furan-2-yl, each of said aryl or heteroaryl being optionally substituted by one or more substituents selected from halo, C₁-C₄ alkyl, cyclopropyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, 5 or 6 membered aryl, preferably phenyl, 5 or 6 membered heteroaryl, preferably furanyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, more preferably furan-3-yl, thiophen-3-yl, pyridinyl, still more preferably pyridin-3-yl, each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl being optionally fused to one or more 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, and the latter fused ring being optionally substituted by one or more further substituents selected from halo, hydroxyl, o xo, alkyl, and/or each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally substituted by one or more substituents selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylcycloalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminalkoxy, cycloalkylalkoxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylaminocycloalkylamine, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylcycloalkyl, cycloalkylalkoxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcycloalkylamine, arylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, o xo or alkyl, preferably methyl; still more preferably Ar³ is phenyl, thiophenyl, furanyl, preferably phenyl, thiophen-2-yl, furan-2-yl, each of said phenyl, thiophenyl, furanyl, being optionally substituted by one or more substituents selected from halo, C₁-C₄ alkyl, cyclopropyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, cyano, ethoxycarbamoyl, methylenedioxy, phenyl, pyridin-3-yl, each of said phenyl or pyridin-3-yl being optionally fused to one or more 5 or 6 membered heterocyclyl, phenyl, or 5 or 6 membered heteroaryl moiety, preferably oxopyrrolidinyl, imidazolyl, piperidinyl, morpholinyl, pyrrolyl, imidazolyl, or pyridyl, more preferably 2-oxopyrrolidinyl, 2-
oxoimidazolinyl 2-oxopiperidinyl, or pyrrolyl, thus forming a fused ring system, and the latter fused ring being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo, alkyl, preferably methyl, and/or each of said phenyl or pyridin-3-yl groups being optionally substituted by one or more substituents selected from halo, alkyl, heterocyclyl, heteroaryl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, alkylamino, alkyaminoalkyl, cycloalkylamine, aralkylamino, alkylaminocarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, each of said heterocyclyl, heteroaryl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamine, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl;

R¹ is as defined above in respect to formula I, preferably R¹ is hydrogen, halogen, or a group selected from C₁⁻₄ alkyl optionally substituted by one or more substituents selected from halogen or alkyl; more preferably R¹ is selected from hydrogen, fluoro, or methyl or ethyl, the methyl or ethyl group being optionally substituted with one or more substituents selected from fluoro or alkyl, even more preferably R¹ is hydrogen, fluoro or methyl, and most preferably R¹ is hydrogen, and L² is as defined above in respect to formula I, preferably L² is cyclopropylene, ethylene, n-propylene, or -C(R'R")-, wherein R' and R" are independently selected from H, halogen, methyl, and ethyl, more preferably L² is cyclopropylene, ethylene, methylene, -CHMe-, -CHF-, even more preferably L² is methylene; or R¹ and L² together are =CH-under the condition that L¹-Ar¹ is H.;

Z is as defined above in respect to formula I, preferably Z is -COOR, wherein R is defined as above in respect to formula I; preferably Z is COOH and

R² is as defined above in respect to formula I, preferably R² is H, linear or branched C₁⁻⁴ alkyl, C₁⁻₂ hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentymethyl, cyclopropymethyl, benzyl, benzyloxyethyl, methoxyethyl, 1,1,1-trifluoroethyl, -C₂H₄CO₂CH₃, -CH₂CO₂CH₃, or -CH₂CONH₂,
more preferably $R^2$ is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, $-\text{C}_2\text{H}_4\text{CO}_2\text{CH}_3$, $-\text{CH}_2\text{CO}_2\text{CH}_3$, or $-\text{CH}_2\text{CONH}_2$, most preferably $R^2$ is methyl or cyclopropyl.

Preferred compounds of formula Ie are those wherein $Z$ is $-\text{COOR}$ and $R$, $A_{r1}$, $A_{r2}$, $A_{r3}$, $R^1$, $R^2$, $L^1$, $L^2$ and $L^3$ are as defined above in respect to formula I, preferably $L^1$ is a methylene group and $A_{r1}$ is phenyl.

In still another embodiment, preferred compounds of Formula I are those of formula If if,

$$
\begin{array}{c}
\text{L}^1
\end{array}
\begin{array}{c}
\text{R}^2
\end{array}
\begin{array}{c}
\text{N}
\end{array}
\begin{array}{c}
\text{R}^3
\end{array}
\begin{array}{c}
\text{L}^3
\end{array}
\begin{array}{c}
\text{Ar}^3
\end{array}
$$

wherein

$A_{r1}$, $A_{r3}$, $L^1$, $L^2$, $L^3$, $R^1$, $R^2$, $R^{14}$, $R^{15}$, $Y$ and $Z$ are as defined above in respect to formula Ie.

In still another embodiment, preferred compounds of Formula I are those of formula Ig:
wherein

B\textsuperscript{4} is O or S or N-R\textsuperscript{b} where R\textsuperscript{b} is H or alkyl, preferably linear or branched C\textsubscript{1}-C\textsubscript{4} alkyl; C\textsubscript{1}-C\textsubscript{4} alkylcarbonyl, C\textsubscript{1}-C\textsubscript{4} alkylsulfonyl, C\textsubscript{1}-C\textsubscript{4} alkylaminocarbonyl, C\textsubscript{3}-C\textsubscript{6} cycloalkyl; preferably O or S, more preferably O,

R\textsuperscript{9}, R\textsuperscript{9}', and R\textsuperscript{11} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaryalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminooalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclyl carbonyloxy, ary lacarbenyl ox y, heteroarylc arboxyl ox y, ary lacarboxylox y, alky lacar bonyl amin o, cyclo alkylcar bonylam ino, cy cloalkylcar bonylam ino, hetero cyclyl carb onylam ino a rylcarbonylam ino, heteroary lacar bonylam ino, alkylcarb onylamine alkyl, acylamino, carbamoyl, hydroxycarbamoyl, alky carbamoyl, ary lacarbam o y, hetero a rly carbamoyl, carb amoylalkyl, car bamoylam ino, alkyl carbamoyl amino, alkyl sulfonyl, haloalkyl sulfonyl, cycloalkyl sulfonyl, heterocyclyl sulfonyl, aryl sulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, aryl sulphamoyl, heteroarylsulfonyl, alkyl sulfonyl amino, cycloalkyl sulfonyl amino, heterocyclyl sulfonyl amino, aryl sulfonyl amino, heteroarylsulfonyl amino, or one of R\textsuperscript{9} or R\textsuperscript{9}' and R\textsuperscript{11} together form an
alkylenedioxy group or a haloalkylenedioxy group, or one of R⁹ or R⁹‘ and R₁¹ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably R⁹, R⁹‘, and R₁¹ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylcyclyl, heterocyclyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or one of R⁹ or R⁹‘ and R₁¹ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, more preferably R⁹, R⁹‘, and R₁¹ are independently selected from H, hydroxyl, C₁-C₃-alkyl, halo, preferably chloro or fluoro, haloalkyl, alkoxy, alkoxyalkyl preferably methoxymethyl, haloalkoxy, preferably -OCF₃, alkylsulfonyl, haloalkylsulfonyl and cyano, even more preferably from H, C₁-C₃-alkyl, halo, CF₃, C₁-C₂ alkoxy, and cyano, and still more preferably from H, F, Cl, methyl, CF₃, methoxy, and cyano, and most preferably H, F or methyl; and

\[ \text{Ar}^2, \text{Ar}^3, \text{L}^1, \text{L}^2, \text{L}^3, \text{R}^1, \text{R}^2, \text{and Z are as defined above in respect to formula I.} \]
those of formula Ih:

\[
\begin{align*}
&\text{Ih} \\
&\text{wherein} \\
&B^5 \text{ is CH}_2 \text{ or O preferably O;} \\
&R^9, R^{10}, R'^9, R^{11}, R^{12} \text{ and } R''^{13} \text{ are independently selected from H, halo,} \\
&\text{cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl,} \\
&\text{alkynyl, heteroalkyl, heterocycyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl,} \\
&\text{heteroaryalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy,} \\
&\text{heterocyclyloxy, aryloxy, amino, alkylamino, aminocarbonyl, carboxy,} \\
&\text{alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl,} \\
&\text{aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy,} \\
&\text{cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy,} \\
&\text{heteroarylcarnbonyloxy, arylalkyloxy, alkylcarbonylamino,} \\
&\text{haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino,} \\
&\text{arylcarbonylamino, heteroarylcarnbonylamino, alkylcarbonylaminoalkyl,} \\
&\text{acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, aryldarbamoyl,} \\
&\text{heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino,} \\
&\text{alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl,} \\
&\text{arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl,} \\
&\text{heteroarylsulfamoyl, alkylsulfonlamino, cycloalkylsulfonlamino,} \\
&\text{heterocyclylsulfonlamino, arylsulfonlamino, heteroarylsulfonlamino,}
\end{align*}
\]
haloalkylsulfonylamino, or one of $R^{11}$ or $R^{12}$ and one of $R^9$, $R^{10}$, $R^{19}$ or $R^{10}$, or $R^{13}$ and one of $R^{9}$ or $R^{10}$ together form an alkylenedioxy group or a haloalkylenedioxy group, or one of $R^{11}$ or $R^{12}$ and one of $R^9$, $R^{10}$, $R^{19}$ or $R^{10}$, or $R^{13}$ and one of $R^{9}$ or $R^{10}$ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryllalkyl, heteroarylsulfonyl, heterocyclyl, hydroxyl, oxo, or sulfonyle, preferably $R^9$, $R^{10}$, $R^{11}$, $R^{12}$, $R^{19}$, $R^{10}$, and $R^{13}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclylalkyl, hydroxyl, alkyl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkylhydroxy, heterocyclyloxoy, aryloxy, carboxyl, alkylnlamino, haloalkylsulfonylamino, cycloalkylcarbamoylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcocabamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or one of $R^{11}$ or $R^{12}$ and one of $R^9$, $R^{10}$, $R^{19}$ or $R^{10}$, or $R^{13}$ and one of $R^{19}$ or $R^{10}$ together form an alkylenedioxy group or a haloalkylenedioxy group, or one of $R^{11}$ or $R^{12}$ and one of $R^9$, $R^{10}$, $R^{19}$ or $R^{10}$, or $R^{13}$ and one of $R^{19}$ or $R^{10}$ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryllalkyl, heteroarylcobamoyl, heterocyclyl, hydroxyl, oxo, or sulfonyle, more preferably $R^9$, $R^{10}$, $R^{11}$, $R^{12}$, $R^{19}$, $R^{10}$, $R^{11}$, $R^{12}$, $R^{13}$ and $R^{13}$ are independently selected from H, hydroxyl, Cy-C$_3$-alkyl, halo, preferably chloro or fluoro, haloalkyl, alkoxy, alkyloalkyl preferably methoxyethyl, haloalkoxy, preferably -OCF$_3$, alkylsulfonyl, haloalkylsulfonyl and cyano, even more preferably from H, C$_1$-C$_2$-alkyl, halo, CF$_3$, C$_1$C$_2$ alkoxy, preferably methoxy, and cyano, and still more preferably from H, F, Cl, methyl, CF$_3$, methoxy, and cyano, and most preferably H or methyl; and

$\text{Ar}^2, \text{Ar}^3, L^1, L^2, L^3, R^1, R^2$, and $Z$ are as defined above in respect to formula 1.
In still another embodiment, preferred compounds of Formula I are those of formula II

![Chemical Structure](image)

wherein

\( B^4 \) is as defined above in respect to formula Ig.

\( R^9, R^{10} \) and \( R^{12} \) are independently selected from \( H, \) halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaryalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryl oxycarbonyl, heteroaryl oxycarbonyl, alkyl carbonyloxy, alkyl carbonylamino, halo alkyl carbonylamino, cyclo alkyl carbonylamino, heterocyclyl carbonylamino, hetero ary l carbonylamino, alkyl carbonyl amino alkyl, acyl amino, carbamoyl, hydroxy carbamoyl, alkyl carbamoyl, aryl carbamoyl, hetero ary l carbamoyl, carbamoyl alkyl, carbamoyl amino, alkyl carbamoylamino, alkyl sulfonyl, haloalkyl sulfonyl, cyclo alkyl sulfonyl, heterocyclyl sulfonyl, aryl sulfonyl, heteroaryl sulfonyl, sulfamoyl, alkyl sulfamoyl, aryl sulfamoyl, heteroaryl sulfamoyl,
alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino,
aryl sulfonyleamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or R^9 and
R^{12} together form an alklynedioxy group or a haloalkynedioxy group, or R^9 and
R^{12} together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together
with the cyclic group they are attached to, each of said substituents being
optionally substituted by one or more further substituents selected from halo,
alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl,
aryl, arylamino, ariloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl,
heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyle, preferably R^9, R'^9,
and R^{12}, are independently selected from H, halo, cyano, alkyl, hydroxyalkyl,
haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclyl,
heterocyclylalkyl, aryl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy,
haloalkoxy, cycloalkyloxy, heterocyclyloxy, arylxy, carboxy,
alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino,
acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl,
heteroarylcramoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino,
alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl,
aryl sulfonamido, heteroarylsulfonylamino, or R^9 and R^{12} together form an alklynedioxy group or a haloalkynedioxy group, or
R^9 and R^{12} together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety
together with the cyclic group they are attached to, each of said substituents being
optionally substituted by one or more further substituents selected from halo,
alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl,
aryl, arylamino, ariloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl,
heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyle, preferably R^9,
R'^9, and R^{12}, are independently selected from H, hydroxyl, Ci-C_3-alkyl, halo,
preferably chloro or fluoro, haloalkyl, alkoxy, alkoxyalkyl preferably
methoxyethyl, haloalkoxy, preferably -OCF_3, alkylsulfonyl, haloalkylsulfonyl and
cyano, even more preferably from H, Ci-C_3-alkyl, halo, CF_3, C_1-C_2 alkoxy,
preferably methoxy, and cyano, and still more preferably from H, F, Cl, methyl,
CF_3, methoxy, and cyano, and most preferably H or methyl; and
\( \text{Ar}^2, \text{Ar}^3, L^1, L^2, L^3, R^1, R^2, \text{and } Z \text{ are as defined above in respect to formula I.} \)

In still another embodiment, preferred compounds of Formula I are those of formula \( I_j \):

![Chemical structure](image)

wherein

\( B^5 \) is as defined above in respect to formula \( I_h \),

\( R^9, R'^9, R^{10}, R'^{10}, R^{11}, R'^{11}, R^{12} \text{ and } R'^{12} \) are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaryalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylnicarbonyloxy, arylcarbonyloxy, alkylcarbonylamino, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylicarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylicarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl,
heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or one of R\textsuperscript{11} or R\textsuperscript{12} and one of R\textsuperscript{9}, R\textsuperscript{10}, R\textsuperscript{'9} or R\textsuperscript{'10}, or one of R\textsuperscript{9} or R\textsuperscript{'10} and R\textsuperscript{''13} together form an alkenedioxy group or a haloalkylenedioxy group, or one of R\textsuperscript{11} or R\textsuperscript{12} and one of R\textsuperscript{9}, R\textsuperscript{10}, R\textsuperscript{'9} or R\textsuperscript{'10}, or one of R\textsuperscript{9} or R\textsuperscript{'10} and R\textsuperscript{''13} together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryllalkyl, heteroarylcyanobenzyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably R\textsuperscript{9}, R\textsuperscript{'9}, R\textsuperscript{10}, R\textsuperscript{11}, R\textsuperscript{'12} and R\textsuperscript{''13} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroaryllalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxy carbamoyl, alkyl carbamoyl, aryl carbamoyl, heteroaryl carbamoyl, carbamoylalkyl, carbamoylamino, alkyl carbamoylamino, alkylsulfonyl, haloalkyl sulfonyl, cycloalkyl sulfonyl, heterocyclyl sulfonyl, aryl sulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or one of R\textsuperscript{11} or R\textsuperscript{12} and one of R\textsuperscript{9}, R\textsuperscript{10}, R\textsuperscript{'9} or R\textsuperscript{'10}, or one of R\textsuperscript{9} or R\textsuperscript{'10} and R\textsuperscript{''13} together form an alkenedioxy group or a haloalkylenedioxy group, or one of R\textsuperscript{11} or R\textsuperscript{12} and one of R\textsuperscript{9}, R\textsuperscript{10}, R\textsuperscript{'9} or R\textsuperscript{'10}, or one of R\textsuperscript{9} or R\textsuperscript{'10} and R\textsuperscript{''13} together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkyl carbonyl, alkyl heteroaryl, alkyl sulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryllalkyl, heteroarylcyanobenzyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, more preferably R\textsuperscript{9}, R\textsuperscript{'9}, R\textsuperscript{10}, R\textsuperscript{'10}, R\textsuperscript{11}, R\textsuperscript{'12} and R\textsuperscript{''13} are independently selected from H, hydroxyl, Ci-C<sub>3</sub>-alkyl, halo, preferably chloro or fluoro, haloalkyl, alkoxy, alkoxyalkyl preferably methoxyethyl, haloalkoxy, preferably -OCF<sub>3</sub>, alkyl sulfonyl, haloalkyl sulfonyl and cyano, even more preferably from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, halo, CF<sub>3</sub>, C<sub>1</sub>-C<sub>2</sub> alkoxy, preferably methoxy, and cyano, and still more preferably from H, F, Cl, methyl,
CF$_3$, methoxy, and cyano, and most preferably H or methyl; and

$\text{Ar}^2, \text{Ar}^3, \text{L}^1, \text{L}^2, \text{L}^3, \text{R}^1, \text{R}^2,$ and $Z$ are as defined above in respect to formula I.

In still another embodiment, preferred compounds of Formula I are those of formula I$_k$:

\[
\text{Ik}
\]

wherein

$R^{29}$ is H, halo, alkyl, haloalkyl preferably -CF$_3$ or -CF$_2$H, alkoxy, haloalkoxy preferably -OCF$_3$ or -OCF$_2$H, cyano, preferably $R^{29}$ is H, F, -CF$_3$, alkyl preferably methyl, more preferably $R^{29}$ is H, F or methyl; and

$\text{Ar}^2, \text{Ar}^3, \text{L}^1, \text{L}^2, \text{L}^3, \text{R}^1, \text{R}^2,$ and $Z$ are as defined above in respect to formula I.

In still another embodiment, preferred compounds of Formula I are those of formula II:
II,
wherein

$R^9$ and $R^{10}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminocarbonyl, carboxyl, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, aminocarbonyl, alkylaminoalkyl, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfamoyl, haloalkylsulfamoyl, cycloalkylsulfamoyl, heterocyclylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonamoyl, cycloalkylsulfonamoyl, heterocyclylsulfonamoyl, arylsulfonamino, heteroarylsulfonamino, haloalkylsulfonamino, or $R^9$ and $R^{10}$ together form an alkylenedioxy group or a haloalkylenedioxy group, or $R^9$ and $R^{10}$ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonil, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylcycloalkyl, heteroarylcarbonyl,
heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably \( R^9 \) and \( R^{10} \) are independently selected from \( H \), halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonfyl, haloalkylsulfonfyl, cycloalkylsulfonfyl, heterocyclylsulfonfyl, arylsulfonfyl, heteroarylsulfonfyl, alkylsulfonfylamino, cycloalkylsulfonfylamino, or \( R^9 \) and \( R^{10} \) together form an alkylenedioxy group or a haloalkylenedioxy group, or one of \( R^9 \) and \( R^{10} \) together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonfyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcycloalkyl, heterocyclyl, hydroxyl, oxo, or sulfonfyl, more preferably \( R^9 \) and \( R^{10} \) are independently selected from \( H \), hydroxyl, \( \text{C}_1-\text{C}_3 \)-alkyl, halo, preferably chloro or fluoro, haloalkyl, alkoxy, alkoxyalkyl preferably methoxyethyl, haloalkoxy, preferably \(-\text{OCF}_3\), alkylsulfonfyl, haloalkylsulfonfyl and cyano, even more preferably from \( H \), \( \text{C}_1-\text{C}_3 \)-alkyl, halo, \( \text{CF}_3 \), \( \text{C}_1-\text{C}_2 \) alkoxy, preferably methoxy, and cyano, and still more preferably from \( H \), \( \text{F}, \text{Cl}, \text{methyl}, \text{CF}_3 \), methoxy, and cyano, and most preferably \( \text{H} \) or methyl; and

\[ \text{Ar}^2, \text{Ar}^3, \text{L}^1, \text{L}^2, \text{L}^3, \text{R}^1, \text{R}^2, \text{and Z} \] are as defined above in respect to formula 1.

Particularly preferred compounds of the invention are those listed in Table 1 hereafter:

**Table 1:**

<table>
<thead>
<tr>
<th>Compound number</th>
<th>Compound name</th>
<th>(M+H)+</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)cyclohex-3-enecarboxylic acid</td>
<td>363.83</td>
</tr>
<tr>
<td>2</td>
<td>(R)-3-benzyl-4-(((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>401.88</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td>(R)-3-benzyl-4-(((4-(2,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>436.3</td>
</tr>
<tr>
<td>4</td>
<td>(R)-3-benzyl-4-(((4-(2-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>385.4</td>
</tr>
<tr>
<td>5</td>
<td>(R)-3-benzyl-4-(((4-(3,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>436.3</td>
</tr>
<tr>
<td>8</td>
<td>(R)-3-benzyl-4-(((4-(4-cyanophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>392.4</td>
</tr>
<tr>
<td>9</td>
<td>(S)-4-(((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-phenylbutanoic acid</td>
<td>387.9</td>
</tr>
<tr>
<td>10</td>
<td>(Z)-4-(((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobut-2-enoic acid</td>
<td>309.7</td>
</tr>
<tr>
<td>11</td>
<td>(R)-3-benzyl-4-oxo-4-(((3-phenyl-1,2,4-thiadiazol-5-yl)amino)butanoic acid</td>
<td>368.4</td>
</tr>
<tr>
<td>12</td>
<td>(R)-3-benzyl-4-(((4-(3-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>401.9</td>
</tr>
<tr>
<td>13</td>
<td>(R)-3-benzyl-4-oxo-4-(((4-(3-(trifluoromethyl)phenyl)thiazol-2-yl)amino)butanoic acid</td>
<td>435.4</td>
</tr>
<tr>
<td>14</td>
<td>(R)-3-benzyl-4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>415.9</td>
</tr>
<tr>
<td>15</td>
<td>(R)-3-benzyl-4-(((5-(2-chlorophenyl)pyridin-2-yl)amino)-4-oxobutanoic acid</td>
<td>395.9</td>
</tr>
<tr>
<td>16</td>
<td>(R)-3-(((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)heptanoic acid</td>
<td>367.9</td>
</tr>
<tr>
<td>17</td>
<td>(R)-4-(((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-fluorobenzyl)-4-oxobutanoic acid</td>
<td>419.9</td>
</tr>
<tr>
<td>18</td>
<td>(R)-4-(((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid</td>
<td>407.9</td>
</tr>
<tr>
<td>19</td>
<td>(R)-3-(((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)-5-methylhexanoic acid</td>
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<td>450.4</td>
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<td>(R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid</td>
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<td>23</td>
<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxy-2-oxoethyl)amino)-4-oxobutanoic acid</td>
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<td>24</td>
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<td>(R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid</td>
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<td>(S)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid</td>
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<td>28</td>
<td>(R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-(4-(trifluoromethyl)benzyl)butanoic acid</td>
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<td>(R)-3-benzyl-4-oxo-4-(4-(2,4,6-trichlorophenyl)thiazol-2-ylamino)butanoic acid</td>
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<td>(S)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid</td>
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<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid</td>
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<td>46</td>
<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-methoxybenzyl)-4-oxobutanoic acid</td>
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<td>48</td>
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<td>52</td>
<td>(R)-3-((3-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>53</td>
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<td>54</td>
<td>(3S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-1H-inden-1-yl)-4-oxobutanoic acid</td>
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<td>55</td>
<td>(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-1H-inden-2-yl)-4-oxobutanoic acid</td>
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<td>56</td>
<td>(R)-4-(benzo[d]thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid</td>
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<td>(R)-4-(benzo[d]oxazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid</td>
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<td>(R)-2-(((1H-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-phenylpropanamide</td>
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<td>59</td>
<td>(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide</td>
<td>455.9</td>
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<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>61</td>
<td>(S)-4-((2-chlorophenyl)thiazol-2-ylaminio)-3-cyclohexyl-4-oxobutanoic acid</td>
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<td>62</td>
<td>(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-cyclohexyl-4-oxobutanoic acid</td>
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<td>63</td>
<td>(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-phenylbutanoic acid</td>
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<td>64</td>
<td>(3R)-3-[(4-(2-Chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylpentanoic acid</td>
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<tr>
<td>65</td>
<td>(R)-2-[[1H-Tetrazol-5-yl]methyl]-N-(4-(2-Chlorophenyl)thiazol-2-yl)-3-phenylpropanamide</td>
<td>425.9</td>
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<td>66</td>
<td>(R)-2-Benzyl-N-(4-(2-Chlorophenyl)thiazol-2-yl)-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide</td>
<td>441.9</td>
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<td>68</td>
<td>(3R)-3-Benzyl-4-(4-(2-Chlorophenyl)thiazol-2-ylamino)-2-methyl-4-oxobutanoic acid</td>
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<td>69</td>
<td>(R)-2-Benzyl-N-(4-(2-Chlorophenyl)thiazol-2-yl)-3-(3-Hydroxyisoxazol-5-yl)propanamide</td>
<td>440.9</td>
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<td>70</td>
<td>(R)-3-Benzyl-4-(4-(2-Chlorophenyl)pyrimidin-2-ylamino)-4-oxobutanoic acid</td>
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<td>71</td>
<td>(R)-3-Benzyl-4-(6-(2-Chlorophenyl)pyridin-2-ylamino)-4-oxobutanoic acid</td>
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<td>72</td>
<td>(E)-3-[(4-(2-Chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylbut-3-enoic acid</td>
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<td>74</td>
<td>(Z)-4-<a href="methyl">(4-(2-Chlorophenyl)thiazol-2-yl)</a>amino)-4-oxo-3-phenylbut-2-enoic acid</td>
<td>399.9</td>
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<td>75</td>
<td>(R)-3-[(N-(4-(2-Chlorophenyl)thiazol-2-yl)]-N-methylsulfamoyl)-4-phenylbutanoic acid</td>
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<td>(S)-3-[(N-(4-(2-Chlorophenyl)thiazol-2-yl)]-N-methylsulfamoyl)-4-phenylbutanoic acid</td>
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<td>(R)-3-Benzyl-4-(4-(2-Chlorophenyl)thiazol-2-ylamino)-3-fluoro-4-oxobutanoic acid</td>
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<td>81</td>
<td>(E)-3-<a href="methyl">(4-(2-Chlorophenyl)thiazol-2-yl)</a>carbamoyl)-4-phenylbut-3-enoic acid</td>
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<td>82</td>
<td>(3S)-3-<a href="methyl">(4-(2-Chlorophenyl)thiazol-2-yl)</a>carbamoyl)-4-phenylpentanoic acid</td>
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<td>83</td>
<td>(R)-3-Benzyl-4-<a href="methyl">(3-(2-Chlorophenyl)-1,2,4-thiadiazol-5-yl)</a>amino)-4-oxobutanoic acid</td>
<td>416.9</td>
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84 (R)-3-benzyl-4-((3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)(methyl)amino)-4-oxobutanoic acid 400.8

85 (R)-3-benzyl-4-((1-(2-chlorophenyl)-1H-pyrazol-3-yl)(methyl)amino)-4-oxobutanoic acid 398.9

86 (R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxyisoxazol-5-yl)-N-methylpropanamide 454.9

89 (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid 422

90 (R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-5-methylhexanoic acid 381.9

91 (R)-3-benzyl-4-((4-(2-cyanophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid 406.5

92 (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-phenylbutanoic acid 387.9

93 (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(3-fluorobenzyl)-4-oxobutanoic acid 419.9

94 (S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-methylpentanoic acid 367.9

95 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid 423.9

96 (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(ethyl)amino)-4-oxobutanoic acid 429.9

97 (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid 441.9

98 cis-6-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)cyclohex-3-enecarboxylic acid 363.8

99 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid 445.9

100 cis-6-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohex-3-enecarboxylic acid 377.9

101 cis-2-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohexanecarboxylic acid 379.9
<p>| 102 | (R)-3-benzyl-4-(4-(2,5-dimethylthiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid | 401.5 |
| 103 | 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid | 422.0 |
| 105 | 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid | 407.9 |
| 106 | (3S,4R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid | 429.9 |
| 107 | (R)-3-benzyl-4-(methyl(2-(thiophen-3-yl)phenyl)thiazol-2-ylamino)-4-oxobutanoic acid | 463.6 |
| 108 | (R)-3-benzyl-4-((4-((2-(6-chloropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 493.0 |
| 109 | (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(phenylamino)butanoic acid | 416.9 |
| 110 | 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methylbenzyl)-4-oxobutanoic acid | 429.9 |
| 111 | (R)-4-((4-([1,1’-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid | 457.6 |
| 112 | (R)-3-benzyl-4-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid | 442.4 |
| 113 | 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopropylmethyl)-4-oxobutanoic acid | 379.9 |
| 114 | 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiazol-4-ylmethyl)butanoic acid | 422.9 |
| 115 | (R)-3-benzyl-4-((4-(2-(6-dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 501.6 |
| 116 | (R)-3-benzyl-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 488.6 |
| 117          | (R)-3-benzyl-4-(((4-(2-(methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 488.6 |
| 118          | (R)-3-benzyl-4-(((4-(2-((ethoxycarbonyl)amino)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 468.5 |
| 119          | (R)-3-benzyl-4-(((4-(2-(6-fluoropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 476.5 |
| 120          | (R)-3-benzyl-4-((methyl(4-(2-(6-methylpyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 472.6 |
| 121          | (R)-4-((2-amino-2-oxoethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid | 458.9 |
| 122          | (R)-3-benzyl-4-oxo-4-(((4-(3-trifluoromethoxy)phenyl)thiazol-2-yl)amino)butanoic acid | 451.4 |
| 123          | (R)-3-benzyl-4-(((4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 436.3 |
| 124          | (R)-3-benzyl-4-(((4-(3-chloro-4-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 419.9 |
| 125          | (R)-3-benzyl-4-(((4-(3-chloro-4-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 431.9 |
| 126          | (R)-3-benzyl-4-(((4-(2-chlorophenyl)thiazol-2-yl)(3-methoxy-3-oxopropyl)amino)-4-oxobutanoic acid | 488.0 |
| 127          | 3-(bicyclo[2.2.1]heptan-2-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 434.0 |
| 128 | (R)-3-benzyl-4-((4-(2-(6-ethoxypyrindin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 502.6 |
| 129 | (R)-3-benzyl-4-((4-(4'-methoxy-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 487.6 |
| 130 | (R)-3-benzyl-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 450.4 |
| 131 | (R)-1-(5-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)phenyl)pyridin-2-yl)pyrrolidin-1-ium 2,2,2-trifluoroacetate | 641.7 |
| 132 | (R)-4-(2''-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)-[1,1'-biphenyl]-4-yl)morpholin-4-ium 2,2,2-trifluoroacetate | 656.7 |
| 133 | (R)-3-benzyl-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 543.6 |
| 134 | (R)-3-benzyl-4-((4-(3'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 492.0 |
| 135 | (R)-3-benzyl-4-((4-(2-(furan-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 447.5 |
| 136 | (R)-3-benzyl-4-((4-(2-(6-(2-methoxyethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 532.6 |
| 138 | (R)-3-benzyl-4-((4-(4'-isopropyl-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 499.6 |
| 139 | (R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyrindin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid | 480.6 |</p>
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<td>(R)-3-benzyl-4-(((4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(methyl((4-(2-(6-(((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>476.4</td>
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<td>143</td>
<td>4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>144</td>
<td>(R)-3-benzyl-4-(((4-(2-cyclopropylphenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>421.5</td>
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<tr>
<td>145</td>
<td>(R)-3-benzyl-4-(((4-(4'-(dimethylamino) [-1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>146</td>
<td>(R)-3-benzyl-4-(((4-(3'-fluoro-[-1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>147</td>
<td>(R)-3-benzyl-4-(((4-(3',5'-difluoro-[-1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>493.5</td>
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<td>148</td>
<td>(R)-3-benzyl-4-(((4-(2-chloro-6-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>419.9</td>
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<td>149</td>
<td>(R)-3-benzyl-4-(((4-(4'-chloro-[-1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>492.0</td>
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<td>150</td>
<td>(R)-3-benzyl-4-(methyl((4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>541.6</td>
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<td>151</td>
<td>(R)-3-benzyl-4-((4-(4-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>523.0</td>
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<td>152</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>153</td>
<td>(R)-3-benzyl-4-((4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>506.6</td>
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<td>154</td>
<td>(3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-2-yl)methyl)butanoic acid</td>
<td>409.9</td>
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<td>155</td>
<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid</td>
<td>445.9</td>
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<td>156</td>
<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(3-hydroxypropyl)amino)-4-oxobutanoic acid</td>
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<td>157</td>
<td>(R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>158</td>
<td>(R)-3-benzyl-4-((4-(2-(6-(benzyloxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>564.7</td>
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<td>159</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>442.4</td>
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<td>160</td>
<td>(R)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>496.6</td>
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<td>161</td>
<td>(R)-3-benzyl-4-(((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>162</td>
<td>(R)-3-benzyl-4-(((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(((4-(3,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(((4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>165</td>
<td>(R)-4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>166</td>
<td>(R)-3-((cyclopentylmethyl)-4-((cyclopropyl)(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>468.4</td>
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<td>167</td>
<td>(R)-4-((cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)oxobutanoic acid</td>
<td>484.4</td>
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<td>168</td>
<td>(R)-4-(((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)oxobutanoic acid</td>
<td>458.4</td>
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<td>169</td>
<td>(R)-3-((cyclopentylmethyl)-4-((cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>506.6</td>
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<td>170</td>
<td>(R)-3-benzyl-4-(((2-hydroxyethyl)(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>171</td>
<td>(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>172</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid</td>
<td>472.4</td>
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<td>173</td>
<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>423.9</td>
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<td>174</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<tr>
<td>175</td>
<td>(R)-3-benzyl-4-(methyl(4-(2,3,5-trichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>176</td>
<td>(R)-3-benzyl-4-((4-(4-chloro-[1,1'-biphenyl]-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>177</td>
<td>(R)-3-benzyl-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>178</td>
<td>(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>179</td>
<td>(R)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>180</td>
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<td>181</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>182</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yI)amino)-4-oxobutanoic acid</td>
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<td>183</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>559.7</td>
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<tr>
<td>184</td>
<td>(R)-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>185</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>465.5</td>
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<td>186</td>
<td>(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
<td>452.0</td>
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<td>187</td>
<td>(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>533.7</td>
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<tr>
<td>188</td>
<td>(R)-3-benzyl-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>473.5</td>
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<tr>
<td>189</td>
<td>(R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid</td>
<td>459.9</td>
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<td>190</td>
<td>(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>191</td>
<td>(R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid</td>
<td>509.9</td>
</tr>
<tr>
<td>192</td>
<td>(R)-3-benzyl-4-((4-(2-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>447.5</td>
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<td>193</td>
<td>(R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>194</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>547.7</td>
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<tr>
<td>195</td>
<td>(3R,4S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid</td>
<td>429.9</td>
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<td>196</td>
<td>(R)-2-(2-benzyl-3-carboxypropanamido)-5-(2-chlorophenyl)pyridine 1-oxide</td>
<td>411.9</td>
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<td>197</td>
<td>(R)-3-benzyl-4-((5-(2-chlorophenyl)pyrazin-2-yl)amino)-4-oxobutanoic acid</td>
<td>396.8</td>
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<td>198</td>
<td>4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(morpholinomethyl)-4-oxobutanoic acid</td>
<td>424.9</td>
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<td>199</td>
<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxyethyl)amino)-4-oxobutanoic acid</td>
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<td>200</td>
<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylamino)-4-oxobutanoic acid</td>
<td>408.9</td>
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<td>201</td>
<td>(R)-3-benzyl-4-((2-(benzylxy)ethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>202</td>
<td>(R)-3-benzyl-4-(((4-(5-methylfuran-2-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>371.4</td>
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<td>203</td>
<td>(R)-3-benzyl-4-oxo-4-(((3-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)amino)butanoic acid</td>
<td>418.4</td>
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<td>204</td>
<td>(R)-3-benzyl-4-(((4-(5-chloro-2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>431.9</td>
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<td>205</td>
<td>4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-hydroxybenzyl)-4-oxobutanoic acid</td>
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<td>206</td>
<td>(R)-3-benzyl-4-(((4-(4'-cyano-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>207</td>
<td>(3R)-3-benzyl-4-(((3-carbamoyl-4-(2,4-dichlorophenyl)-5-methylthiophen-2-yl)amino)-4-oxobutanoic acid</td>
<td>492.4</td>
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<td>208</td>
<td>(R)-3-benzyl-4-(((4-(3'-methoxy-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>487.6</td>
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<td>209</td>
<td>4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid</td>
<td>436.9</td>
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<td>210</td>
<td>4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid</td>
<td>420.9</td>
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<td>211</td>
<td>(R)-3-benzyl-4-(((4-(2'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>212</td>
<td>(R)-3-benzyl-4-(((4-(2-(2-methoxypyrimidin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>489.6</td>
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<tr>
<td>213</td>
<td>(R)-3-benzyl-4-(((4-(2,5-difluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>403.4</td>
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<td>214</td>
<td>4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(oxazol-4-ylmethyl)-4-oxobutanoic acid</td>
<td>406.9</td>
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<tr>
<td>215</td>
<td>(3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-3-yl) methyl)butanoic acid</td>
<td>409.9</td>
</tr>
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<td>216</td>
<td>(R)-3-benzyl-4-(methyl(4-((2-(8-methyl-7-o xo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl) phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>541.6</td>
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<td>217</td>
<td>(R)-3-benzyl-4-(methyl(4-((2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>511.6</td>
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<td>218</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-((2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>519.7</td>
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<td>219</td>
<td>(R)-4-((4-((2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
<td>541.1</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-((2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>221</td>
<td>(R)-3-benzyl-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>222</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>557.5</td>
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<td>223</td>
<td>(R)-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>224</td>
<td>(R)-4-(((5-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>225</td>
<td>(S)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>227</td>
<td>(R)-3-benzyl-4-((4-benzylthiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>381.5</td>
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<td>229</td>
<td>(R)-3-benzyl-4-oxo-4-((5-phenyl-4H-1,2,4-triazol-3-yl)amino)butanoic acid</td>
<td>351.4</td>
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<td>230</td>
<td>3-[[1,1'-biphenyl]-4-ylmethyl]-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>231</td>
<td>(R)-3-benzyl-4-((4-(1-methyl-1H-pyrazol-4-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>232</td>
<td>(R)-3-benzyl-4-((4-(4-methyl-1,2,5-oxadiazol-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((methyl(4-(2-(1-methyl-1H-pyrazol-4-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>461.5</td>
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<td>(3R)-3-benzyl-4-((4-(2-(3,5-dimethylisoxazol-4-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)carbamoyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>236</td>
<td>(R)-3-benzyl-4-((6-(2-chlorophenyl)pyridazin-3-yl)amino)-4-oxobutanoic acid</td>
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<td>237</td>
<td>(R)-3-benzyl-4-((methyl(4-(2-(2-oxopyrrolidin-1-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>464.5</td>
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<td>238</td>
<td>(S)-2-(((1-(4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)oxy)acetic acid</td>
<td>431.9</td>
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<td>239</td>
<td>(R)-3-benzyl-4-((1-methyl-5-phenyl-1H-imidazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>240</td>
<td>(R)-3-benzyl-4-((4-(2-(1-(2-methoxyethyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>241</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>242</td>
<td>4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoic acid</td>
<td>434.9</td>
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<td>243</td>
<td>4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid</td>
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<td>244</td>
<td>(R)-3-benzyl-4-((4-(2-(6-hydroxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((S)-2-hydroxypropyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((R)-2-hydroxypropyl)amino)-4-oxobutanoic acid</td>
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<td>247</td>
<td>(R)-3-(cyclohexylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(((4-(4,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>251</td>
<td>(R)-4-(((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>252</td>
<td>(R)-4-(((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>253</td>
<td>(R)-3-(furan-2-ylmethyl)-4-(((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>254</td>
<td>(S)-4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid</td>
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<td>255</td>
<td>(R)-4-(((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>256</td>
<td>(R)-3-benzyl-4-((cyclopropyl(4-2-(6-2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-ylamino)-4-oxobutanoic acid</td>
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<td>257</td>
<td>(R)-3-benzyl-4-(((4-(2,3-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>258</td>
<td>(R)-3-benzyl-4-((methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>261</td>
<td>(R)-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>262</td>
<td>(R)-3-benzyl-4-(cyclopropyl(4-((3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>263</td>
<td>(R)-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>264</td>
<td>(R)-3-benzyl-4-((4-(2-(6-isopropoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>265</td>
<td>(R)-3-benzyl-4-((4-(2-(6-(cyclopropylmethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>266</td>
<td>(R)-3-benzyl-4-((4-(2-(6-(methoxymethyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(2-(6-(dimethylamino)methyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>268</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(6-(N-methylcyclopropanecarboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>269</td>
<td>(R)-3-benzyl-4-((4-(2-(6-(dimethylcarbamoyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>270</td>
<td>(R)-4-((4-(2-(6-(4H-1,2,4-triazol-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid</td>
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<td>271</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>272</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>273</td>
<td>(R)-3-benzyl-4-(methyl(4-(2-(3-methyl-3H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(2-(6-(benzyl(methyl)amino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>275</td>
<td>(R)-3-benzyl-4-((4-(2-(6-(cyclohexyl(methyl)amino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(methyl(4-(2-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>277</td>
<td>(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopopyl)amino)-3-(cyclopentanyl)methyl)-4-oxobutanoic acid</td>
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<td>278</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>524.6</td>
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<td>279</td>
<td>(R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)-3-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>541.0</td>
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<td>280</td>
<td>(R)-3-benzyl-4-((4-(3-fluoro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>524.6</td>
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<td>281</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(3,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>283</td>
<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((S)-tetrahydrofuran-2-yl)methyl)butanoic acid</td>
<td>409.9</td>
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<td>284</td>
<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((R)-tetrahydrofuran-2-yl)methyl)butanoic acid</td>
<td>409.9</td>
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<td>285</td>
<td>(R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
<td>473.9</td>
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<td>286</td>
<td>(R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>287</td>
<td>(R)-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
<td>471.9</td>
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<td>288</td>
<td>(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
<td>431.9</td>
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<td>289</td>
<td>(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>290</td>
<td>(R)-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>293</td>
<td>(R)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
<td>544.5</td>
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<td>294</td>
<td>(R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
<td>466.4</td>
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<td>295</td>
<td>(R)-4-(((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
<td>449.9</td>
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<td>296</td>
<td>(R)-4-(((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>297</td>
<td>(R)-4-(((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-4-(((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid</td>
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<td>4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylfuran-2-yl)methyl)-4-oxobutanoic acid</td>
<td>419.9</td>
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<td>300</td>
<td>4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((4,5-dimethylfuran-2-yl)methyl)-4-oxobutanoic acid</td>
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<td>301</td>
<td>3-(benzofuran-2-ylmethyl)-4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>302</td>
<td>(R)-4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyridin-2-ylmethyl)butanoic acid</td>
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<td>303</td>
<td>(R)-4-(((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyrimidin-2-ylmethyl)butanoic acid</td>
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<td>304</td>
<td>((3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-2-yl)methyl)butanoic acid)</td>
<td>458.4</td>
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<td>305</td>
<td>((3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-3-yl)methyl)butanoic acid)</td>
<td>458.4</td>
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<td>306</td>
<td>((R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R,3R)-2-methyltetrahydro-2H-pyran-3-yl)methyl)-4-oxobutanoic acid)</td>
<td>472.4</td>
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<td>307</td>
<td>((3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R)-2-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid)</td>
<td>472.4</td>
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<td>308</td>
<td>((3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid)</td>
<td>486.4</td>
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<td>309</td>
<td>((3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((3S)-3-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid)</td>
<td>472.4</td>
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<td>310</td>
<td>((3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((3R,5S)-3,5-dimethyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid)</td>
<td>486.4</td>
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<td>311</td>
<td>((R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(4-hydroxy-1,2,5-thiadiazol-3-yl)-N-methylpropanamide)</td>
<td>472.0</td>
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<td>312</td>
<td>((R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxy-5-methylisoxazol-4-yl)-N-methylpropanamide)</td>
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<td>313</td>
<td>(R)-4-(((4-(5-chloro-2-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>314</td>
<td>(R)-4-(((4-(5-chloro-2-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-((6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>557.1</td>
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<td>316</td>
<td>(R)-4-(((4-(5-chloro-2-((6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>317</td>
<td>(R)-4-(((4-(5-chloro-2-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>318</td>
<td>(R)-4-(((4-(5-chloro-2-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>628.1</td>
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<td>319</td>
<td>(R)-4-((cyclopropyl)(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-((cyclopropyl(4-(5-((difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid)</td>
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<td>(R)-4-((cyclopropyl(4-(5-((difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid)</td>
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<td>(R)-4-((cyclopropyl(4-(5-((difluoromethoxy)-2-(6-2-oxypyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid)</td>
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<td>(R)-4-((cyclopropyl(4-(5-((difluoromethoxy)-2-(6-2-oxypyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid)</td>
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<td>326</td>
<td>(R)-4-((cyclopropyl(5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid)</td>
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<td>329</td>
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<td>390</td>
<td>(R)-4-(((4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>633.7</td>
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<td>391</td>
<td>(R)-4-((methyl(4-(2-6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>563.7</td>
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<td>392</td>
<td>(R)-4-(((5-fluoro-4-(2-6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>581.7</td>
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<tr>
<td>393</td>
<td>(R)-4-(((5-fluoro-4-(2-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>514.6</td>
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<td>394</td>
<td>(R)-4-((methyl(4-(2-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>549.7</td>
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<td>395</td>
<td>(R)-4-(((5-fluoro-4-(2-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>567.6</td>
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<td>396</td>
<td>(R)-4-(((4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>397</td>
<td>(R)-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>599.7</td>
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<td>398</td>
<td>(R)-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>514.6</td>
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<td>399</td>
<td>(R)-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>532.6</td>
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<td>(R)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>401</td>
<td>(R)-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>585.6</td>
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<td>402</td>
<td>(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
<td>582.1</td>
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<td>403</td>
<td>(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
<td>600.1</td>
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<td>404</td>
<td>(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>407</td>
<td>(R)-4-(((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>408</td>
<td>(R)-3-(cyclopentylmethyl)-4-(((4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(((4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>411</td>
<td>(R)-3-(cyclopentylmethyl)-4-(((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>415</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>416</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(6-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>551.6</td>
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<td>419</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>422</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>423</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>424</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>425</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>590.1</td>
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<td>426</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>608.1</td>
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<td>427</td>
<td>(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-chloro-2-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>431</td>
<td>(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-((6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>554.6</td>
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<td>(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-((6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>434</td>
<td>(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>607.6</td>
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<td>(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>436</td>
<td>(R)-3-benzyl-4-((methyl(4-(2-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>555.7</td>
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<td>437</td>
<td>(R)-3-benzyl-4-((5-fluoro-4-(2-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>506.6</td>
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<td>439</td>
<td>(R)-3-benzyl-4-((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>442</td>
<td>(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>445</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>551.6</td>
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<td>446</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>577.7</td>
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<td>447</td>
<td>(R)-4-((4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>567.6</td>
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<td>448</td>
<td>(R)-4-(cyclopropyl(4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>593.7</td>
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<td>449</td>
<td>(R)-3-benzyl-4-((4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>451</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>537.6</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-((4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>454</td>
<td>(R)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>456</td>
<td>(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>571.6</td>
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<td>457</td>
<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>539.6</td>
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<td>458</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>459</td>
<td>(R)-4-((4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>461</td>
<td>(R)-3-benzyl-4-((4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-y1)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>547.6</td>
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<td>462</td>
<td>(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-y1)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>573.7</td>
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<td>463</td>
<td>(R)-3-((cyclopentylmethyl)-4-((4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-y1)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-((4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-y1)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-y1)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-((4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>474</td>
<td>(R)-3-benzyl-4-(cyclopropyl)(4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-((4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrlo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>476</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-benzyl-4-(((5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>486</td>
<td>(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(((5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>488</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>489</td>
<td>(R)-4-(((5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td><strong>490</strong></td>
<td>(R)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td><strong>491</strong></td>
<td>(R)-3-benzyl-4-((4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-benzyl-4-(((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-(((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-benzyl-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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511  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid  538.1

512  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid  564.1

513  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid  554.1

514  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid  580.1

515  (R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid  546.1

516  (R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid  572.1

517  (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid  533.7

518  (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid  559.7
<p>| 519 | (R)-4-(methyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 549.7 |
| 520 | (R)-4-(cyclopropyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 575.7 |
| 521 | (R)-3-benzyl-4-(cyclopropyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 567.7 |
| 522 | (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 519.6 |
| 523 | (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 545.7 |
| 524 | (R)-4-(methyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 535.6 |
| 525 | (R)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 561.7 |
| 526 | (R)-3-benzyl-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 553.6 |
| 527 | (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 521.6 |
| 528 | (R)-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 537.6 |
| 529 | (R)-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 563.7 |
| 530 | (R)-3-benzyl-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 555.7 |
| 531 | (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 503.6 |
| 532 | (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 529.7 |
| 533 | (R)-4-(methyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 519.6 |
| 534 | (R)-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid | 545.7 |
| 535 | (R)-3-benzyl-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid | 537.6 |</p>
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<td>(R)-3-benzyl-4-(((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid</td>
<td>608.1</td>
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<tr>
<td>602</td>
<td>(R)-4-(((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
<td>556.1</td>
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<td>603</td>
<td>(R)-4-(((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
<td>582.1</td>
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<td>604</td>
<td>(R)-4-(((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>572.1</td>
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<td>605</td>
<td>(R)-4-(((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>598.1</td>
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<td>606</td>
<td>(R)-3-benzyl-4-(((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>564.0</td>
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<td>607</td>
<td>(R)-3-benzyl-4-(((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid</td>
<td>590.1</td>
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<td>608</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
<td>551.6</td>
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<tr>
<td>609</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>577.7</td>
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<td>610</td>
<td>(R)-4-((5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>567.6</td>
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<td>611</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>612</td>
<td>(R)-3-benzyl-4-((5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>613</td>
<td>(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>614</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<tr>
<td>616</td>
<td>(R)-4-((5-fluoro-4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>553.6</td>
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<td>617</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>618</td>
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<td>620</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>565.7</td>
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<td>622</td>
<td>(R)-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>623</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>547.6</td>
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<td>625</td>
<td>(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>573.7</td>
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<td>626</td>
<td>(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>547.7</td>
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<td>628</td>
<td>(R)-4-((5-fluoro-4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
<td>537.6</td>
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<td>629</td>
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<td>630</td>
<td>(R)-3-benzyl-4-((5-fluoro-4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>631</td>
<td>(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>555.6</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[3,2-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>633</td>
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<td>634</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>560.7</td>
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<tr>
<td>635</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[3,2-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<tr>
<td>636</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methyl-5-oxo-5,6,7,8-tetrahydro-1,6-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<tr>
<td>637</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1,3-dimethyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>638</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(7-methyl-8-oxo-5,6,7,8-tetrahydro-1,7-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methyl-5-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<tr>
<td>640</td>
<td>(R)-4-((4-(2-(5-chloro-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(3-methyl-3H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methyl-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>646</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-1H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>648</td>
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<td>649</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-1,2,3,4-tetrahydro-1,5-naphthyridin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(3-methyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>651</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>652</td>
<td>(R)-4-(cyclopropyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-((cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>581.7</td>
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<td>(R)-3-((cyclopentylmethyl)-4-((5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-((cyclopentylmethyl)-4-((methyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td>589.6</td>
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<td>(R)-3-benzyl-4-(cyclopropyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-((5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-benzyl-4-(methyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxobutanoic acid</td>
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<td>664</td>
<td>(R)-3-benzyl-4-(cyclopropyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxobutanoic acid</td>
<td>568.7</td>
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<td>665</td>
<td>(R)-3-(cyclopentylmethyl)-4-(methyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxobutanoic acid</td>
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<td>667</td>
<td>(R)-4-(methyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-4-(cyclopropyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-5-(trifluoromethyl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-5-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(pyridin-2-ylmethyl)butanoic acid</td>
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<td>(R)-2-(2-(carboxymethyl)-3-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-oxopropyl)pyridine 1-oxide</td>
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<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((R)-tetrahydro-2H-pyran-2-yl)methyl)butanoic acid</td>
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<td>(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid</td>
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<td>720</td>
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<td>(3R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(((2S)-2-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((S)-tetrahydro-2H-pyran-2-yl)methyl)butanoic acid</td>
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<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((R)-tetrahydrofuran-2-yl)methyl)butanoic acid</td>
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<tr>
<td>744</td>
<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(3-methyltetrahydrofuran-3-yl)methyl)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>745</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyltetrahydrofuran-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>746</td>
<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(3-methyltetrahydrofuran-3-yl)methyl)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>747</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluoroacetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>748</td>
<td>(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(3-fluoroacetan-3-yl)methyl)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>749</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>750</td>
<td>(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(3-fluoroacetan-3-yl)methyl)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>751</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyltetrahydrofuran-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>752</td>
<td>(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(3-fluoroacetan-3-yl)methyl)-4-oxobutanoic acid</td>
<td></td>
</tr>
<tr>
<td>753</td>
<td>(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluoroacetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid</td>
<td></td>
</tr>
</tbody>
</table>
The compounds of formula I can be prepared by different ways with reactions known by the person skilled in the art. Reaction schemes as described in the example section illustrate by way of example different possible approaches.

The invention further provides the use of the compounds of the invention or pharmaceutically acceptable salts, or solvates thereof as agonists or partial agonists of G-protein coupled receptor 43 (GPR43).

Accordingly, in a particularly preferred embodiment, the invention relates to the use of compounds of formula I and subformulae in particular those of table 1 above, or pharmaceutically acceptable salts and solvates thereof, as GPR43 agonists or partial agonists.

[APPLICATIONS]

The compounds of the invention are therefore useful in the prevention or in the prevention and/or treatment of type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH).

Preferred diseases are type II diabetes, lipid disorders such as dyslipidemia, hypertension, obesity, atherosclerosis and its sequelae.

In a particular preferred embodiment the diseases are type II
diabetes and a lipid disorder such as dyslipidemia.

The invention also provides for a method for delaying in patient the onset of type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia, hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH) comprising the administration of a pharmaceutically effective amount of a compound of formula (I) or pharmaceutically acceptable salt thereof to a patient in need thereof.

Preferably, the patient is a warm-blooded animal, more preferably a human.

The invention further provides the use of a compound of formula (I) or a pharmaceutically acceptable salt or solvates thereof for the manufacture of a medicament for use in treating a patient and/or preventing a patient from developing a disease selected from the group consisting of type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia, hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH).
Preferably, the patient is a warm-blooded animal, more preferably a human.

According to a further feature of the present invention there is provided a method for modulating GPR43 receptor activity, in a patient, preferably a warm-blooded animal, and even more preferably a human, in need of such treatment, which comprises administering to said animal an effective amount of compound of the present invention, or a pharmaceutically acceptable salt or solvate thereof.

According to one embodiment, the compounds of the invention, their pharmaceutical acceptable salts or solvates may be administered as part of a combination therapy. Thus, are included within the scope of the present invention embodiments comprising coadministration of, and compositions and medicaments which contain, in addition to a compound of the present invention, a pharmaceutically acceptable salt or solvate thereof as active ingredient, additional therapeutic agents and/or active ingredients. Such multiple drug regimens, often referred to as combination therapy, may be used in the treatment and/or prevention of any of the diseases or conditions mediated by or associated with GPR43 receptor modulation, particularly type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia, hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH). The use of such combinations of therapeutic agents is especially pertinent with respect to the treatment of the above-mentioned list of diseases within a patient in need of treatment or one at risk of becoming such a patient.
In addition to the requirement of therapeutic efficacy, which may necessitate the use of active agents in addition to the GPR43 agonist or partial agonist compounds of Formula I or their pharmaceutical acceptable salts or solvates thereof, there may be additional rationales which compel or highly recommend the use of combinations of drugs involving active ingredients which represent adjunct therapy, i.e., which complement and supplement the function performed by the GPR43 receptor agonist or partial agonist compounds of the present invention. Suitable supplementary therapeutic agents used for the purpose of auxiliary treatment include drugs which, instead of directly treating or preventing a disease or condition mediated by or associated with GPR43 receptor modulation, treat diseases or conditions which directly result from or indirectly accompany the basic or underlying GPR43 receptor modulated disease or condition.

Thus, the methods of treatment and pharmaceutical compositions of the present invention may employ the compounds of Formula I or their pharmaceutical acceptable salts or solvates thereof in the form of monotherapy, but said methods and compositions may also be used in the form of multiple therapy in which one or more compounds of Formula I or their pharmaceutically acceptable salts or solvates are coadministered in combination with one or more other therapeutic agents such as those described in detail further herein.

Examples of other active ingredients that may be administered in combination with a compound of Formula I or a pharmaceutically acceptable salt or solvate thereof, and either administered separately or in the same pharmaceutical composition, include but are not limited to:

(a) PPARγ agonists and partial agonists, including both glitazones and non-glitazones (e.g. troglitazone, pioglitazone, englitazone, MCC-555, rosiglitazone, balaglitazone, netoglitazone, T-131, LY-300512 and LY-818;

(b) Biguanides such as metformin and phenformin;
(c) Protein tyrosine phosphatase-IB (PTP-IB) inhibitors,
(d) Dipeptidyl peptidase IV (DP-IV) inhibitor, such as MK-0431 and LAF-237;
(e) Insulin or insulin mimetics;
(f) Sulfonylureas such as tolbutamide and glipizide or related materials;
(g) α-glucosidase inhibitors (such as acarbose);
(h) agents which improve a patient's lipid profile such as (i) HMG-CoA reductase inhibitors (lovastatin, simvastatin, rosvastatin, pravastatin, fluvastatin, atorvastatin, rivastatin, itavastatin, ZD-4522 and other statins),
(ii) bile acid sequestrants (cholestyramine, colestipol and dialkylaminoalkyl derivatives of a cross-linked dextran), (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPARα agonists such as fenofibrin acid derivatives (gemfibrozil, clofibrate, fenofibrate and bezafibrate), (v) cholesterol absorption inhibitors such as for example ezetimibe, (vi) acyl CoA:cholesterol acyltransferase (ACAT)inhibitors such as avasimibe, (vii) CETP inhibitors such as torcetrapib and (viii) phenolic anti-oxidants such as probucol;
(i) PPAR α/γ dual agonists such as muraglitazar, tesaglitazar, farglitazar and JT-501;
Q) PPAR δ agonists such those disclosed in WO97/28 149;
(k) Antiobesity compounds such as fenfluramine, dextenfluramine, phentiramine, subitramine, orlistat, neuropeptide Y5 inhibitors, MC4R agonists, cannabinoid receptor 1 antagonists/inverse agonists and β3 adrenergic receptor agonists;
(l) Ileal bile acid transporter inhibitors;
(m)Agents intended for use in inflammatory conditions such as aspirin, non-steroidal, anti-inflammatory drugs, glucocorticoids, azulfidine and cyclooxygenase 2 selective inhibitors;
(n) Glucagon receptor antagonists;
(o) GLP-I;
(p) GIP-I;
(q) GLP-I analogs, such as exendins, for example exenitide, and

(i) Hydroxysterol dehydrogenase-1 (HSD-I) inhibitors.

The above combinations include combinations of a compound of the present invention or a pharmaceutically acceptable salt or solvate not only with one other active compound but also with two or more active compounds. Non-limiting examples include combinations of compounds having Formula I with two or more active compounds selected from biguanides, sulfonylureas, HMG-CoA reductase inhibitors, other PPAR agonists, PTP-IB inhibitors, DP-IV inhibitors and anti-obesity compounds.

In the above-described embodiment combinations of the present invention, the compound of Formula I, a pharmaceutically acceptable salt or solvate thereof and other therapeutic active agents may be administered in terms of dosage forms either separately or in conjunction with each other, and in terms of their time of administration, either serially or simultaneously. Thus, the administration of one component agent may be prior to, concurrent with, or subsequent to the administration of the other component agent(s).

The invention also provides pharmaceutical compositions comprising a compound of formula I or a pharmaceutically acceptable salt or solvate thereof and at least one pharmaceutically acceptable carrier, diluent, excipient and/or adjuvant. As indicated above, the invention also covers pharmaceutical compositions which contain, in addition to a compound of the present invention, a pharmaceutically acceptable salt or solvate thereof as active ingredient, additional therapeutic agents and/or active ingredients.

Another object of this invention is a medicament comprising at least one compound of the invention, or a pharmaceutically acceptable salt or solvate thereof, as active ingredient.

The invention also provides the use of a compound of formula I or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a
medicament. Preferably, the medicament is used for the treatment and/or prevention of type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH).

Preferred diseases are type II diabetes, lipid disorders such as dyslipidemia, hypertension, obesity, atherosclerosis and its sequelae.

In a particular preferred embodiment the disease are type II diabetes and a lipid disorder such as dyslipidemia.

According to a further feature of the present invention there is provided the use of a compound of formula I or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for modulating GPR43 receptor activity, in a patient, in need of such treatment, which comprises administering to said patient an effective amount of compound of the present invention, or a pharmaceutically acceptable salt or solvate thereof.

Preferably, the patient is a warm-blooded animal, more preferably a human.

As set forth above, the compounds of the invention, their pharmaceutically acceptable salts or solvates may be used in monotherapy or in combination therapy. Thus, according to one embodiment, the invention provides the use of a compound of the invention for the manufacture of a medicament for at least one of the purposes described above, wherein said medicament is administered to a patient in need thereof, preferably a warm-blooded animal, and
even more preferably a human, in combination with at least one additional therapeutic agent and/or active ingredient. The benefits and advantages of such a multiple drug regimen, possible administration regimens as well as suitable additional therapeutic agents and/or active ingredients are those described above.

Generally, for pharmaceutical use, the compounds of the inventions may be formulated as a pharmaceutical preparation comprising at least one compound of the invention and at least one pharmaceutically acceptable carrier, diluent, excipient and/or adjuvant, and optionally one or more further pharmaceutically active compounds.

By means of non-limiting examples, such a formulation may be in a form suitable for oral administration, for parenteral administration (such as by intravenous, intramuscular or subcutaneous injection or intravenous infusion), for topical administration (including ocular), for administration by inhalation, by a skin patch, by an implant, by a suppository, etc. Such suitable administration forms - which may be solid, semi-solid or liquid, depending on the manner of administration - as well as methods and carriers, diluents and excipients for use in the preparation thereof, will be clear to the skilled person; reference is made to the latest edition of Remington's Pharmaceutical Sciences.

Some preferred, but non-limiting examples of such preparations include tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols, ointments, cremes, lotions, soft and hard gelatin capsules, suppositories, drops, sterile injectable solutions and sterile packaged powders (which are usually reconstituted prior to use) for administration as a bolus and/or for continuous administration, which may be formulated with carriers, excipients, and diluents that are suitable per se for such formulations, such as lactose, dextrose, sucrose, sorbitol, mannitol, starches, gum acacia, calcium phosphate, alginates, tragacanth, gelatin, calcium silicate, microcrystalline cellulose, polyvinylpyrrolidone, polyethylene glycol, cellulose, (sterile) water, methylcellulose, methyl- and propylhydroxybenzoates, talc,
magnesium stearate, edible oils, vegetable oils and mineral oils or suitable mixtures thereof. The formulations can optionally contain other substances that are commonly used in pharmaceutical formulations, such as lubricating agents, wetting agents, emulsifying and suspending agents, dispersing agents, desintegrants, bulking agents, fillers, preserving agents, sweetening agents, flavoring agents, flow regulators, release agents, etc.. The compositions may also be formulated so as to provide rapid, sustained or delayed release of the active compound(s) contained therein.

The pharmaceutical preparations of the invention are preferably in a unit dosage form, and may be suitably packaged, for example in a box, blister, vial, bottle, sachet, ampoule or in any other suitable single-dose or multi-dose holder or container (which may be properly labeled); optionally with one or more leaflets containing product information and/or instructions for use. Generally, such unit dosages will contain between 0.05 and 1000 mg, and usually between 1 and 500 mg, of the at least one compound of the invention, e.g. about 10, 25, 50, 100, 200, 300 or 400 mg per unit dosage.

Usually, depending on the condition to be prevented or treated and the route of administration, the active compound of the invention will usually be administered between 0.01 to 100 mg per kilogram, more often between 0.1 and 50 mg, such as between 1 and 25 mg, for example about 0.5, 1, 5, 10, 15, 20 or 25 mg, per kilogram body weight day of the patient per day, which may be administered as a single daily dose, divided over one or more daily doses, or essentially continuously, e.g. using a drip infusion.

[DEFINITIONS]

The definitions and explanations below are for the terms as used throughout the entire application, including both the specification and the claims.
When describing the compounds of the invention, the terms used are to be construed in accordance with the following definitions, unless indicated otherwise.

Where groups may be substituted, such groups may be substituted with one or more substituents, and preferably with one, two or three substituents. Substituents may be selected from but not limited to, for example, the group comprising halogen, hydroxyl, oxo, nitro, amido, carboxy, amino, cyano haloalkoxy, and haloalkyl.

As used herein the terms such as "alkyl, aryl, or cycloalkyl, each being optionally substituted with..." or "alkyl, aryl, or cycloalkyl, optionally substituted with..." encompasses "alkyl optionally substituted with...", "aryl optionally substituted with..." and "cycloalkyl optionally substituted with...".

The term "halo" or "halogen" means fluoro, chloro, bromo, or iodo. Preferred halo groups are fluoro and chloro.

The term "alkyl" by itself or as part of another substituent refers to a hydrocarbyl radical of Formula \(C_nH_{2n+1}\) wherein \(n\) is a number greater than or equal to 1. Generally, alkyl groups of this invention comprise from 1 to 6 carbon atoms, preferably from 1 to 4 carbon atoms, more preferably from 1 to 3 carbon atoms, still more preferably 1 to 2 carbon atoms. Alkyl groups may be linear or branched and may be substituted as indicated herein.

Suitable alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl and t-butyl, pentyl and its isomers (e.g. n-pentyl, iso-pentyl), and hexyl and its isomers (e.g. n-hexyl, iso-hexyl). Preferred alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl and t-butyl.

When the suffix "ene" ("alkylene") is used in conjunction with an alkyl group, this is intended to mean the alkyl group as defined herein having two single bonds as points of attachment to other groups. The term "alkylene" includes
methylene, ethylene, methylmethylene, propylene, ethylethylene, and 1,2-dimethylethylene.

The term "alkenyl" as used herein refers to an unsaturated hydrocarbyl group, which may be linear or branched, comprising one or more carbon-carbon double bonds. Suitable alkenyl groups comprise between 2 and 6 carbon atoms, preferably between 2 and 4 carbon atoms, still more preferably between 2 and 3 carbon atoms. Examples of alkenyl groups are ethenyl, 2-propenyl, 2-butenyl, 3-butenyl, 2-pentenyl and its isomers, 2-hexenyl and its isomers, 2,4-pentadienyl and the like.

The term "alkynyl" as used herein refers to a class of monovalent unsaturated hydrocarbyl groups, wherein the unsaturation arises from the presence of one or more carbon-carbon triple bonds. Alkynyl groups typically, and preferably, have the same number of carbon atoms as described above in relation to alkenyl groups. Non-limiting examples of alkynyl groups are ethynyl, 2-propynyl, 2-butynyl, 3-butylnyl, 2-pentynyl and its isomers, 2-hexynyl and its isomers-and the like. The terms "alkenylene" and "alkynylene" respectively mean an alkenyl group or an alkynyl group as defined above having two single bonds as points of attachment to other groups.

The term "haloalkyl" alone or in combination, refers to an alkyl radical having the meaning as defined above wherein one or more hydrogens are replaced with a halogen as defined above. Non-limiting examples of such haloalkyl radicals include chloromethyl, 1-bromoethyl, fluoromethyl, difluoromethyl, trifluoromethyl, 1,1,1-trifluoroethyl and the like.

The term "cycloalkyl" as used herein is a cyclic alkyl group, that is to say, a monovalent, saturated, or unsaturated hydrocarbyl group having 1 or 2 cyclic structures. Cycloalkyl includes monocyclic or bicyclic hydrocarbyl groups. Cycloalkyl groups may comprise 3 or more carbon atoms in the ring and generally, according to this invention comprise from 3 to 10, more preferably
from 3 to 8 carbon atoms still more preferably from 3 to 6 carbon atoms. Examples of cycloalkyl groups include but are not limited to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, with cyclopropyl being particularly preferred.

When the suffix "ene" is used in conjunction with a cyclic group, this is intended to mean the cyclic group as defined herein having two single bonds as points of attachment to other groups.

Therefore, "cycloalkylene" herein refers to a saturated homocyclic hydrocarbyl biradical of Formula C\textsubscript{n}H\textsubscript{2n-2}. Suitable cycloalkylene groups are C\textsubscript{3-6} cycloalkylene group, preferably a C\textsubscript{3-5} cycloalkylene (i.e. 1,3-cyclopropylene, 1,1-cyclopropylene, 1,1-cyclobutylene, 1,2-cyclobutylene, 1,3-cyclopentylene), more preferably a C\textsubscript{3-4} cycloalkylene (i.e. 1,3-cyclopropylene, 1,1-cyclobutylene, 1,1-cyclobutylene).

Where at least one carbon atom in a cycloalkyl group is replaced with a heteroatom, the resultant ring is referred to herein as "heterocycloalkyl" or "heterocyclyl".

The terms "heterocycl"l, "heterocycloalkyl" or "heterocyclo" as used herein by itself or as part of another group refer to non-aromatic, fully saturated or partially unsaturated cyclic groups (for example, 3 to 7 member monocyclic, 7 to 11 member bicyclic, or containing a total of 3 to 10 ring atoms) which have at least one heteroatom in at least one carbon atom-containing ring. Each ring of the heterocyclic group containing a heteroatom may have 1, 2, 3 or 4 heteroatoms selected from nitrogen, oxygen and/or sulfur atoms, where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. Any of the carbon atoms of the heterocyclic group may be substituted by oxo (for example piperidone, pyrrolidinone). The heterocyclic group may be attached at any heteroatom or carbon atom of the ring or ring system, where valence allows. The rings of multi-ring heterocycles may be fused, bridged and/or joined through one or more spiro
atoms. Non limiting exemplary heterocyclic groups include oxetanyl, piperidinyl, azetidinyl, 2-imidazolinyl, pyrazolidinyl imidazolidinyl, isoxazolyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, piperidinyl, 3H-indolyl, indolyl, isoindolinyl, 2-oxopiperazinyl, piperazinyl, homopiperazinyl, 2-pyrazolyl, 3-pyrazolyl, tetrahydro-2H-pyranyl, 2H-pyranyl, 4H-pyranyl, 3,4-dihydro-2H-pyranyl, 3-dioxolanyl, 1,4-dioxanyl, 2,5-dioximidazolidinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, indolyl, tetrahydropyranyl, tetrahydrofuranyl, tetrahydroquinolinyl, tetrahydroisoquinolin-1-yl, tetrahydroisoquinolin-2-yl, tetrahydroisoquinolin-3-yl, tetrahydroisoquinolin-4-yl, thiomorpholin-4-yl, thiomorpholin-4-ylsulf oxide, thiomorpholin-4-ylsulfone, 1,3-dioxolanyl, 1,4-oxathianyl, 1H-pyrrolizinyl, tetrahydro-1,1-dioxothiophenyl, N-formylpiperazinyl, and morpholin-4-yl.

The ring atoms of heterocyclyl and heterocyclylene moieties are numbered based on scheme below

The term "aryl" as used herein refers to a polyunsaturated, aromatic hydrocarbyl group having a single ring (i.e. phenyl) or multiple aromatic rings fused together (e.g. naphtyl) or linked covalently, typically containing 5 to 12
atoms; preferably 6 to 10, wherein at least one ring is aromatic. The aromatic ring may optionally include one to two additional rings (either cycloalkyl, heterocyclyl or heteroary1) fused thereto. Aryl is also intended to include the partially hydrogenated derivatives of the carbocyclic systems enumerated herein. Non-limiting examples of aryl comprise phenyl, biphenylyl, biphenylenyl, 5- or 6-tetralinyl, naphthalen-1- or -2-yl, 4-, 5-, 6 or 7-indenyl, 1- 2-, 3-, 4- or 5-acenaphtylenyl, 3-, 4- or 5-acenaphtenyl, 1- or 2-pentalenyl, 4- or 5-indany1, 5-, 6-, 7- or 8-tetrahydronapthyl, 1,2,3,4-tetrahydronapthyl, 1,4-dihydronapthyl, 1-, 2-, 3-, 4- or 5-pyrenyl.

The term "arylene" as used herein is intended to include divalent carbocyclic aromatic ring systems such as phenylene, biphenylylene, naphthylene, indenylene, pentalenylene, azulenylene and the like. Arylene is also intended to include the partially hydrogenated derivatives of the carbocyclic systems enumerated above. Non-limiting examples of such partially hydrogenated derivatives are 1,2,3,4-tetrahydronaphthylene, 1,4-dihydronapthylene and the like.

Where at least one carbon atom in an aryl group is replaced with a heteroatom, the resultant ring is referred to herein as a heteroaryl ring.

The term "heteroaryl" as used herein by itself or as part of another group refers but is not limited to 5 to 12 carbon-atom aromatic rings or ring systems containing 1 to 2 rings which are fused together or linked covalently, typically containing 5 to 6 atoms; at least one of which is aromatic, in which one or more carbon atoms in one or more of these rings is replaced by oxygen, nitrogen and/or sulfur atoms where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. Such rings may be fused to an aryl, cycloalkyl, heteroaryl or heterocyclyl ring. Non-limiting examples of such heteroaryl, include: furanyl, thiophenyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, oxatiazolyl, thiatiazolyl, pyridinyl,
pyrimidyl, pyrazinyl, pyridazinyl, oxazinyl, dioxinyl, thiazinyl, triazinyl, imidazo[2, 1-b][1,3]thiazolyl, thieno[3,2-b]furanyl, thieno[3,2-b]thiophenyl, thieno[2,3-d][1,3]thiazolyl, thieno[2,3-d]imidazolyl, tetrazolo[1,5-a]pyridinyl, indolyl, indolizinyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzothiophenyl, isobenzothiophenyl, indazolyl, benzimidazolyl, 1,3-benzoazolyl, 1,2-benzisoxazolyl, 2,1-benzisoxazolyl, 1,3-benzothiazolyl, 1,2-benzoisothiazolyl, 2,1-benzoisothiazolyl, benzotriazolyl, 1,2,3-benoxadiazolyl, 2,1,3-benoxadiazolyl, 1,2,3-benzothiadiazolyl, 2,1,3-benzothiadiazolyl, thienopyridinyl, purinyl, imidazo[1,2-a]pyridinyl, 6-oxo-pyridazin-l(6H)-yl, 2-oxopyridin-l(2H)-yl, 6-oxo-pyridazin-l(6H)-yl, 2-oxopyridin-l(2H)-yl, 1,3-benzodioxolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, quinoxalinyl.

The term "heteroarylene" as used herein means divalent carbocyclic aromatic ring systems including pyridinylene and the like.

The ring atoms of heteroaryl or heteroarylene moieties are numbered on scheme below:
The term "biaryl" as used herein designates two aryl moieties as defined herein linked via a single bond. Non-limiting examples of such biaryl moieties include biphenyl.

The term "heterobiaryl" as used herein designates two heteroaryl moieties as defined herein or a heteroaryl moiety and an aryl moiety as defined
herein linked via a single bond. Non-limiting examples of such heterobiaryl moieties include pyridinylphenyl which is meant to include (2-pyridinyl)phenyl, (3-pyridinyl)phenyl and (4-pyridinyl)phenyl, bipyridinyl.

\[
\begin{align*}
&\text{(2-pyridinyl)phenyl} & \text{(3-pyridinyl)phenyl} & \text{(4-pyridinyl)phenyl} \\
&\text{bipyridinyl}
\end{align*}
\]

The term "alkylamino" as used herein means an amino group substituted with one or two alkyl groups. This includes monoalkylamino and dialkylamino groups.

The compounds of Formula I and subformulae thereof contain at least one asymmetric center and thus may exist as different stereoisomeric forms. Accordingly, the present invention includes all possible stereoisomers and includes not only racemic compounds but the individual enantiomers and their non racemic mixtures as well. When a compound is desired as a single enantiomer, such may be obtained by stereospecific synthesis, by resolution of the final product or any convenient intermediate, or by chiral chromatographic methods as each are known in the art. Resolution of the final product, an intermediate, or a starting material may be effected by any suitable method known in the art. See, for example, Stereochemistry of Organic Compounds by E. L. Eliel, S. H. Wilen, and L. N. Mander (Wiley- Interscience, 1994), incorporated by reference with regard to stereochemistry.

The bonds from an asymmetric carbon in compounds of the present
invention may be depicted herein using a solid line (—), a zigzag line (—···), a solid wedge (→"), or a dotted wedge (····). The use of a solid line to depict bonds from an asymmetric carbon atom is meant to indicate that all possible stereoisomers are meant to be included, unless it is clear from the context that a specific stereoisomer is intended. The use of either a solid or dotted wedge to depict bonds from an asymmetric carbon atom is meant to indicate that only the stereoisomer shown is meant to be included.

The compounds of the invention may also contain more than one asymmetric carbon atom. In those compounds, the use of a solid line to depict bonds from asymmetric carbon atoms is meant to indicate that all possible stereoisomers are meant to be included, unless it is clear from the context that a specific stereoisomer is intended.

The compounds of the invention may be in the form of pharmaceutically acceptable salts. Pharmaceutically acceptable salts of the compounds of formula I include the acid addition and base salts thereof. Suitable acid addition salts are formed from acids which form non-toxic salts. Examples include the acetate, adipate, aspartate, benzoate, besylate, bicarbonate/carbonate, bisulphate/sulphate, borate, camsylate, citrate, cyclamate, edisylate, esylate, formate, fumarate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactate, maleate, maleate, malonate, mesylate, methylsulphate, naphthylate, 2-napsylate, nicotinate, nitrate, orotate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, pyroglutamate, saccharate, stearate, succinate, tannate, tartrate, tosylate, trifluoroacetate and xinofoate salts. Suitable base salts are formed from bases which form non-toxic salts. Examples include the aluminium, arginine, benzathine, calcium, choline, diethylamine, diolamine, glycine, lysine, magnesium, meglumine, olamine, potassium, sodium, tromethamine, 2-(diethylamino)ethanol, ethanolamine, morpholine, 4-(2-hydroxyethyl)morpholine and zinc salts. Hemisalts of acids and bases may also be formed, for example, hemisulphate and hemicalcium salts. Preferred,
pharmaceutically acceptable salts include hydrochloride/chloride, hydrobromide/bromide, bisulphate/sulphate, nitrate, citrate, and acetate.

When the compounds of the invention contain an acidic group as well as a basic group the compounds of the invention may also form internal salts, and such compounds are within the scope of the invention. When the compounds of the invention contain a hydrogen-donating heteroatom (e.g. NH), the invention also covers salts and/or isomers formed by transfer of said hydrogen atom to a basic group or atom within the molecule.

Pharmaceutically acceptable salts of compounds of Formula I may be prepared by one or more of these methods:

(i) by reacting the compound of Formula I with the desired acid;

(ii) by reacting the compound of Formula I with the desired base;

(iii) by removing an acid- or base-labile protecting group from a suitable precursor of the compound of Formula I or by ring-opening a suitable cyclic precursor, for example, a lactone or lactam, using the desired acid; or

(iv) by converting one salt of the compound of Formula I to another by reaction with an appropriate acid or by means of a suitable ion exchange column.

All these reactions are typically carried out in solution. The salt, may precipitate from solution and be collected by filtration or may be recovered by evaporation of the solvent. The degree of ionization in the salt may vary from completely ionized to almost non-ionized.

The term "solvate" is used herein to describe a molecular complex comprising the compound of the invention and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is
employed when said solvent is water.

All references to compounds of formula I include references to salts, solvates, multi-component complexes and liquid crystals thereof.

The compounds of the invention include compounds of formula I as hereinbefore defined, including all polymorphs and crystal habits thereof, prodrugs and isomers thereof (including optical, geometric and tautomeric isomers) and isotopically-labeled compounds of formula I.

In addition, although generally, with respect to the salts of the compounds of the invention, pharmaceutically acceptable salts are preferred, it should be noted that the invention in its broadest sense also included non-pharmaceutically acceptable salts, which may for example be used in the isolation and/or purification of the compounds of the invention. For example, salts formed with optically active acids or bases may be used to form diastereoisomeric salts that can facilitate the separation of optically active isomers of the compounds of Formula I above.

The invention also generally covers all pharmaceutically acceptable predrugs and prodrugs of the compounds of Formula I.

The term "prodrug" as used herein means the pharmacologically acceptable derivatives of compounds of formula I such as esters whose in vivo biotransformation product is the active drug. Prodrugs are characterized by increased bio-availability and are readily metabolized into the active compounds in vivo. Suitable prodrugs for the purpose of the invention include carboxylic esters, in particular alkyl esters, aryl esters, acyloxyalkyl esters, and dioxolene carboxylic esters; ascorbic acid esters as well as compounds of formula I in which Z is a substituent selected from the table 2 below.
Table 2

<table>
<thead>
<tr>
<th>Z</th>
<th>Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>-C(O)SQ</td>
<td>Alkyl or aryl</td>
</tr>
<tr>
<td>-C(O)NQ₁Q²</td>
<td>H, alkyl, aryl, OH or NH₂</td>
</tr>
</tbody>
</table>
| -C(O)OCHQ₁O(O)CQ² | Q₁= H or phenyl  
|            | Q₂= alkyl or aryl  |
| -C(O)OCHQCl | H or aryl          |
| -C(OQ)₃   | Alkyl              |
| -C(O)OC(O)OQ | Alkyl or aryl     |
| -C(O)CH₂Q | SMe, SOMe, SO₂Me   |

The term "predrug", as used herein, means any compound that will be modified to form a drug species, wherein the modification may take place either inside or outside of the body, and either before or after the predrug reaches the area of the body where administration of the drug is indicated.

The term "patient" refers to a warm-blooded animal, more preferably a human, who/which is awaiting or receiving medical care or is or will be the object of a medical procedure.

The term "human" refers to subject of both genders and at any stage of development (i.e. neonate, infant, juvenile, adolescent, adult).

The terms "treat", "treating" and "treatment, as used herein, are meant to include alleviating or abrogating a condition or disease and/or its attendant symptoms.

The terms "prevent", "preventing" and "prevention", as used herein, refer to a method of delaying or precluding the onset of a condition or disease and/or its attendant symptoms, barring a patient from acquiring a condition or disease, or reducing a patient's risk of acquiring a condition or
disease.

The term "therapeutically effective amount" (or more simply an "effective amount") as used herein means the amount of active agent or active ingredient (e.g. GPR43 agonist or partial agonist) which is sufficient to achieve the desired therapeutic or prophylactic effect in the individual to which it is administered.

The term "administration", or a variant thereof (e.g."administering"), means providing the active agent or active ingredient (e.g. a GPR43 agonist or partial agonist), alone or as part of a pharmaceutically acceptable composition, to the patient in whom/which the condition, symptom, or disease is to be treated or prevented.

By "pharmaceutically acceptable" is meant that the ingredients of a pharmaceutical composition are compatible with each other and not deleterious to the patient thereof.

The term "agonist" as used herein means a ligand that activates an intracellular response when it binds to a receptor. An agonist according to the invention may promote internalization of a cell surface receptor such that the cell surface concentration of a receptor is decreased or remove.

The term "partial agonist" as used herein means an agonist which is unable to induce maximal activation of a receptor, regardless of the amount of compound applied on the receptor.

The term "pharmaceutical vehicle" as used herein means a carrier or inert medium used as solvent or diluent in which the pharmaceutically active agent is formulated and/or administered. Non-limiting examples of pharmaceutical vehicles include creams, gels, lotions, solutions, and liposomes.
The term "lipid disorder" as used herein means any plasma lipid disorder including but not limited to dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia and hypertriglyceridemia.

The present invention will be better understood with reference to the following examples. These examples are intended to representative of specific embodiments of the invention, and are not intended as limiting the scope of the invention.

CHEMISTRY EXAMPLES

All temperatures are expressed in °C and all reactions were carried out at room temperature (RT) unless otherwise stated.

Analytical thin layer chromatography (TLC) was used to monitor reactions, establish flash chromatography conditions and verify purity of intermediates or final products. TLC plates used were Merck TLC aluminium sheet silica gel 60 F254 purchased from VWR International. TLC plates were revealed using ultraviolet irradiation (wavelength=254nm) at room temperature or bromocresol green spray reagent at 0.1% in propan-2-ol purchased from VWR International upon heating at 160°C or KMnO4 revelator upon heating at 160°C. The KMnO4 revelator was prepared by dissolving 3g of potassium permanganate, 20g of sodium carbonate, 0.5g of sodium hydroxide in 100mL of distilled water.

HPLC-MS spectra were obtained on Agilent LC-MS using Electrospray ionization (ESI). The Agilent instrument includes an Autosampler 1200, a binary pump 1100, a 5 wave length detector 1100 and a 6100 Single Quad. The column used was an XBridge C18, 4.6 x 50 mm, 3.5 µm.

Eluent was a mixture of solution A (0.1% TFA in H2O) and solution B (0.1% TFA in ACN). Gradient was applied at a flow rate of 2 mL min⁻¹ as follows: gradient A: held the initial conditions of 5% solution B for 1 min, increased linearly to
95% solution B in 4 min, held at 95% during 1 min, returned to initial conditions in 0.5 min and maintained for 1 min; gradient B: held the initial conditions of 5% solution B for 1 min, increased linearly to 60% in 10 min, increased linearly to 95% in 0.5 min, held at 95% during 3 min, returned to initial conditions in 0.5 min and maintained for 1 min.

Determination of ee was performed on an Agilent 1100 (binary pump and 5 wavelengths detector) with manual or automatic (Autosampler 1100) injection. Columns used were CHIRALPAK IA CHIRALPAK IB or CHIRALPAK IC in isocratic mode. Mixtures of eluents were selected depending on the separation obtained of enantiomers or diastereosiomers. Usual mixtures were:

- Hexane and Ethanol (0.1% TFA)
- Hexane and Propanol (0.1% TFA)
- Hexane and Ethyl acetate (0.1% TFA)
- Hexane and Dichloromethane (0.1% TFA)
- Hexane and tert-butyl methyl ether (0.1% TFA)

Selected specific methods A, B and C are reported below. Method A: compound was characterized on a CHIRALPAK IA column (isocratic mode) using a mixture of hexane and dichloromethane (65/35) acidified by 0.4% of TFA at a flow rate of 1.2 mL/min, and confirmed on a CHIRALPAK IC column (isocratic mode) using a mixture of heptane and Ethyl acetate (75/25) acidified by 0.1% of TFA at 1 mL/min. Method B: compound was characterized on a CHIRALPAK IC column (isocratic mode) using a mixture of heptane and ethyl acetate (70/30) acidified by 0.1% of TFA at a flow rate of 1 mL/min. Method C: compound was characterized on a CHIRALPAK IC column (isocratic mode) using a mixture of heptane and ethanol (95/5) acidified by 0.1% of TFA at a flow rate of 1.5 mL/min.

Preparative HPLC purifications were carried out on Fractionlynx instrument, from Waters. This instrument consists of a Fraction Collector, a 2767 Sample Manager, a pump control a module II, a 515 HPLC Pump, a 2525 Binary Gradient Module, a Switching Valve, a 2996 Photodiode Array Detector and a
Micromass ZQ. The column used was a Waters Sunfire C18 Eluent was a mixture of solution A (0.1% TFA in H₂O) and solution B (0.1% TFA in ACN). The gradient was adapted depending on impurities present in samples, to allow sufficient separation between impurities and target compound.

Chiral preparative HPLC purification were performed on an Agilent 1100 instrument (binary pump and 5 wavelengths detector) with manual injection using a CHIRALPAK IA or a CHIRALPAK IB column in isocratic mode. Mixtures of eluents were selected depending on the separation of enantiomers or diastereoisomers obtained with the analytical method. Usual mixtures were the same as those used for the determination of ee.

¹H and ¹³C NMR spectra were recorded on a Bruker ARX 300MHz. Chemical shifts are expressed in parts per million, (ppm, δ units). Coupling constants are expressed in Hertz units (Hz). Splitting patterns describe apparent multiplicities and are described as s (singlet), d (doublet), t (triplet), q (quintet), m (multiplet), or br (broad).

Solvents, reagents and starting materials were purchased from well known chemical suppliers such as for example Sigma Aldrich, Acros Organics, Fluorochem, Eurisotop, VWR International, Sopachem and Polymer labs and the following abbreviations are used:

ACN: Acetonitrile,
DCM: Dichloromethane,
DMF: N,N-dimethylformamide,
EtOAc: Ethyl acetate,
EtOH: Ethanol,
MeOH: Methanol,
RT: Room temperature,
DIEA: N,N-diisopropylethylamine,
HATU: O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium
hexafluorophosphate ,
Y: Yield,
g: Grams,
mg: Milligrams,
L: Liters,
 mL: Milliliters,
µL: Microliters,
mol: Moles,
mmol: Millimoles,
h: Hours,
min: Minutes,
TLC: Thin layer chromatography,
MW: Molecular weight,
eq: Equivalent,
µW: Microwave,
THF: Tetrahydrofuran,
TFA: Trifluoroacetic acid,
Ac: Acetyl,
NaHMDS: Sodium hexamethyldisilazane,
DCA: Dicyclohexylamine,
TCA: Trichloroacetimidate,
CDI: Carbonyl diimidazole,
e: Enantiomeric excess,
DPP: Diphenylphosphino,
BINAP: l,l'-Binaphtyl,
tBu: tert-Butyl
P: UV purity at 254nm determined by HPLC-MS,
SPE: Solid phase extraction,
Rt: Retention time,
TMSCl: Chlorotrimethylsilane,
BuLi: Butyllithium,
MCPBA: 3-Chloroperbenzoic acid,
MOM: Methoxymethyl,
NCS: N-chlorosuccinimide,
NBS: N-bromosuccinimide.

**General synthetic scheme**

Most compounds of the invention are synthesized according to Scheme 1.

*Scheme 1*: General synthetic route for most of the compounds in the present invention

**Synthesis of intermediates 1**

Chiral syntheses of intermediates 1 were carried out using Evans' chiral auxiliary approach (Evans et al. *J. Org. Chem.* 1999, 64, 6411-6417; Tararov et al. *J. Chem. Soc. Perkin Trans. 1*, 1997, 3101-3106) *(Scheme 2).*
Scheme 2: General scheme for the preparation of intermediates 1 using Evans’ chiral auxiliary approach

This methodology was also used for the synthesis of (R)-cycloalkylalkylsuccinic acid, (R)-heterocyclicalkylsuccinic acid, (R)-arylalkylsuccinic acid and (R)-heteroarylalkylsuccinic acid monoester intermediates 1.

As depicted on Scheme 3, (R)-benzylsuccinic acid monoester intermediates 1 can also be made starting from maleic anhydride followed by the application of Wittig reaction, asymmetric hydrogenation (Wallace et al. Org. Proc. Res. & Dev. 2004, 8, 738-743), tBu ester protection and selective saponification of the methyl ester (Atkinson et al. J. Org. Chem. 1999, 64, 3467).
Scheme 3: Synthesis of (R)-benzyl-succinic acid monoester intermediates 1 using Wittig approach

This methodology was also used for the synthesis of (R)-cycloalkylalkylsuccinic acid, (R)-heterocyclylalkylsuccinic acid, (R)-arylalkylsuccinic acid and (R)-heteroarylalkylsuccinic acid monoester intermediates 1.

Synthesis of intermediates 2

Scheme 4: General scheme for the preparation of 4-aryl-2-amino-thiazoles using Hantzsch-type synthetic approach

Alternatively, synthesis of N-substituted-4-aryl-2-amino-thiazoles can be achieved through the method described by Rudolph (Rudolph, J. Tetrahedron 2000, 56, 3161)

Scheme 5: General scheme for the preparation of N-substituted-4-aryl-2-amino-thiazoles using Rudolph's synthetic approach

Synthetic Schemes for the Preparation of the Carboxylic Acid Bioisosteres

Synthetic routes for the preparation of selected bioisosteres of the carboxylic acid moiety are given hereunder. Isosterism is a concept defined by I. Langmuir in J. Am. Chem. Soc. 1919, 41, 1549 and developed by H.L. Friedman in Symposium on Chemical-Biological correlations, National Council Publication, Washington, DC (1951). As used herein the term "bioisosteres" refers to "groups or molecules which have chemical and physical similarities producing similar biological effects" (as defined in Chem. Soc. Rev. 1979, 8, 563). Suitable well-known bioisosteric replacements of carboxylic acid groups and synthetic routes are reported in The Practice of Medicinal Chemistry, 2nd edition, by CG. Wermuth. It is obvious to the person skilled in the art to synthesize carboxylic acid isosteres, selected useful references are Drysdale et al. J. Med. Chem. 1992,
Synthesis of tetrazole and hydroxy-oxadiazole isosteres


![Scheme](image)

Treatment of the aforesaid nitrile intermediate with sodium azide can be used to afford the tetrazole isostere (see Scheme below). (Matthews et al. J. Comb. Chem. 2000, 2, 19-23)

![Scheme](image)

Treatment of the aforesaid nitrile intermediate with hydroxylamine, followed by dehydrative cyclization can be used to yield the hydroxy-oxadiazole isostere (see Scheme below) (Peretto et al. J. Med. Chem. 2005, 48, 5705-5720).
In addition, synthetic approaches to the preparation of other well-recognized carboxylic acid isosteres are outlined below.

A suggested synthetic approach for the preparation of hydroxy-thiadiazole isosteres:

![Chemical Reaction Diagram]

1) NH$_4$Cl, KCN
2) H$_2$O$_2$, NaOH

$\text{H$_2$O}_2$  

LIOH

An alternative suggested synthetic approach for the preparation of hydroxy-isoxazole isosteres
Additional synthetic schemes

An alternative approach towards synthesis of intermediates 1 (see Scheme 2) can be envisioned through Stobbe condensation as depicted in Scheme 6.

**Scheme 6:** A suggested synthetic approach for the preparation of benzylsuccinic acid monoester intermediates through Stobbe condensation

**Synthesis of compound n°68 (Scheme 7):**

**Scheme 7:** Synthesis of compound 68

As shown in Scheme 7, upon treatment of (R)-benzylsuccinic acid t-butyl ester with excess LiHMDS in the presence of MeI, the desired monomethylated intermediate was isolated as an epimeric mixture, which was used in turn to furnish the final target structure (as epimeric mixture), as per the general procedure outlined on Scheme 1.
Synthesis of aryl-pyridine and aryl-pyrimidines intermediates 2 (Scheme 8):

A suggested synthesis of compound n°74 (Scheme 9):
Suggested syntheses of compounds n°75 and n°76 (Scheme 10):

\[
\text{Scheme 10: Suggested syntheses of compounds n°75 and n°76}
\]
Suggested syntheses of compounds n°79 and n°80 (Scheme 11):

Scheme 11: Suggested syntheses of compounds n°79 and n°80
Suggested syntheses of compounds n°83 to n°85 (Scheme 12):
Synthesis of intermediates 1 using Horner-Wadsworth Emmons approach (HWE) (Scheme 13):

\[
\text{MeO-PO-CH}_2\text{CO}_2\text{R} \xrightarrow{\text{NaH, THF}} \text{MeO-PO-CH}_2\text{CO}_2\text{Bu} \xrightarrow{n-\text{BuLi, THF}} \text{Ar}^-\text{CHO} \xrightarrow{\text{Ar}^-\text{CO}_2\text{Bu}} 
\]

\[
\text{LiOH} \xrightarrow{\text{THF/H}_2\text{O}} \xrightarrow{\text{or}} \text{Bu}_4\text{N-OH} \xrightarrow{\text{THF/H}_2\text{O}} \text{Ar}^-\text{CH}==\text{CH}_2 \xrightarrow{\text{Pd/C, H}_2} \text{Ar}^-\text{CH}==\text{CH}_2\text{CO}_2\text{Bu} \xrightarrow{\text{or asymmetric hydrogenation, e.g.:}} \text{MeOH} \xrightarrow{[\text{RuCl}_2[[\text{S}-\text{BINAP}]]]} \text{H}_2, 10 \text{ bars, 55°C} \xrightarrow{\text{DIC}} \text{Ar}^-\text{CH}==\text{CH}_2\text{CO}_2\text{Bu}
\]

Scheme 13: Synthesis of intermediates 1 using Horner-Wadsworth Emmons approach (HWE)

The HWE methodology as depicted in Scheme 13 is the preferred methodology of the invention for the synthesis of intermediates 1.
**Synthesis of compounds 98, 100 and 101 (Scheme 14):**

![Scheme 14](image)

**Scheme 14**: Synthesis of compounds 98, 100 and 101

**General scheme for the preparation of biaryl- or heterobiaryl-thiazole amine intermediates using Suzuki approach (Scheme 15):**

![Scheme 15](image)

**Scheme 15**: General scheme for the preparation of biaryl- or heterobiaryl-thiazole amine intermediates using Suzuki approach
Synthesis of intermediates 2n and 2r3 (Scheme 16):

Scheme 16: Synthesis of intermediates 2n and 2r3

Alternative general scheme for the preparation of biaryl- or heterobiaryl-thiazole amine intermediates using Suzuki approach (Scheme 17):

Scheme 17: Alternative general scheme for the preparation of biaryl- or heterobiaryl-thiazole amine intermediates using Suzuki approach
Synthesis of compound n°198 (Scheme 18):

![Synthesis diagram](image)

**Scheme 18**: Synthesis of compound n°198

General synthetic scheme for the preparation of substituted acetophenone reagents through Weinreb amide approach (Scheme 20):

![General scheme diagram](image)

**Scheme 20**: General synthetic scheme for the preparation of substituted acetophenone reagents through Weinreb amide approach
Synthesis of intermediate 2p3 (Scheme 21):

\[
\begin{align*}
\text{EtO} & \quad \text{CO} \quad \text{N} \quad \text{NH}_2 \\
\text{Boc}_2O & \quad \text{DIEA} \quad \text{DMAP} \quad \text{DCM} \\
\text{EtO} & \quad \text{CO} \quad \text{N} \quad \text{NH}_2 \\
\text{NaOH} & \quad \text{EtOH}
\end{align*}
\]

\[
\begin{align*}
\text{H} & \quad \text{O} \quad \text{N} \\
\text{NH}_2 & \quad \text{HATU} \quad \text{DIEA} \quad \text{ACN} \\
\text{Cl} & \quad \text{H} \quad \text{N} \quad \text{O} \\
\text{TFA} & \quad \text{DCM}
\end{align*}
\]

\[
\text{2p3}
\]

Scheme 21: Synthesis of intermediate 2p3

Synthesis of compound n°238 (Scheme 22):

\[
\begin{align*}
\text{C} & \quad \text{H} \quad \text{O} \\
\text{H} & \quad \text{OH} \\
\text{H} & \quad \text{N} \quad \text{N} \quad \text{Cl} \\
\text{H} & \quad \text{O} \quad \text{N} \quad \text{Cl} \\
\text{Br} & \quad \text{O} \quad \text{N} \quad \text{Cl} \\
\text{NaHMDS} & \quad \text{THF} \\
\text{C} & \quad \text{H} \quad \text{O} \quad \text{N} \quad \text{Cl} \\
\text{HO} & \quad \text{O} \\
\text{compound n°238}
\end{align*}
\]

Scheme 22: Synthesis of compound n°238
General synthetic scheme for the preparation of substituted thiourea reagents
(Scheme 23):

\[
\text{Scheme 23: General synthetic scheme for the preparation of substituted thiourea reagents}
\]

**General method A:** synthesis of intermediate **1a** (S)-4-tet/-butoxy-4-oxo-2-phenylbutanoic acid

**Step 1:** synthesis of (S)-4-benzyl-3-(2-phenylacetyl)oxazolidin-2-one

(S)-4-benzyl-oxazolidin-2-one (0.011 mol) was dissolved in THF (50 mL). A 1.6 M solution of n-BuLi (0.0124 mol) was added dropwise at -78 °C. A solution of 2-phenylacetyl chloride (0.011 mol) in THF (20 mL) was added dropwise to the obtained dark solution at the same temperature. The reaction mixture was stirred for 1 h at -78 °C. Then a saturated solution of NH₄Cl (2 mL) and a solution of NaHCO₃ (4 mL) were added dropwise, and the reaction mixture was warmed to RT. The organic layer was separated, and the aqueous one was extracted with diethyl ether (3 x 25 mL). The combined extracts were washed with water, brine, dried over Na₂SO₄, and evaporated. The residue was purified by chromatography (silica gel, hexane/ether, 2/1) to yield title compound. Y: 2.1 g (64.7%).

**Step 2:** synthesis of (S)-tert-buty 4-((S)-4-benzyl-2-oxooxazolidin-3-yl)-4-oxo-3-phenylbutanoate

A 1M solution of NaHMDS (7.8 mmol) in THF was added to a solution of (S)-4-benzyl-3-(2-phenylacetyl)oxazolidin-2-one (7.1 mmol) in THF at
-78 °C in a flow of argon. After keeping for 1.5 h at the same temperature tert-butyl bromoacetate (21.3 mmol) was added. The reaction mixture was stirred for 2 h at -78 °C and warmed to RT. A saturated solution of NH₄Cl (15 mL) and ethyl acetate (12 mL) were added. The organic layer was separated, and the aqueous one was extracted with ethyl acetate (3 x 30 mL). The combined extracts were washed with brine, dried over Na₂SO₄, and evaporated to give title compound. Y: 1.64 g (57%).

**Step 3:** synthesis of intermediate Ia (S)-4-tert-butoxy-4-oxo-2-phenylbutanoic acid

(S)-Tert-butyl 4-((S)-4-benzyl-2-oxooxazolidin-3-yl)-4-oxo-3-phenylbutanoate (4 mmol) was dissolved in THF, and a 35% solution of H₂O₂ in water (16 mmol) was added dropwise at 0 °C. Then a solution of LiOH (8 mmol) in H₂O (19 mL) was added. The reaction mixture was stirred for 1.5 h at 0 °C (TLC: CCl₄/ethyl acetate= 7/3) indicated reaction was complete. A solution of Na₂SO₃ (15 mL) and NaHCO₃ (15 mL) were added at 0 °C. The reaction mixture was evaporated in a rotary evaporator by one half. Water (50 mL) was added to the residue, and the mixture was extracted with CH₂Cl₂ (3 x 45 mL). The aqueous layer was acidified with 6M HCl to pH=2 at 0 °C. The product was extracted with ethyl acetate (3 x 50 mL). Combined extracts were washed with brine, dried over Na₂SO₄, and evaporated. The residue was recrystallized from hexane to give title compound. Y: 0.75 g (75%).

The following intermediates were synthesized or may be synthesized using general method B adapting the oxazolidinone chirality and starting materials to targeted intermediate:

- intermediate Ie: (R)-4-tert-butoxy-4-oxo-2-phenethylbutanoic acid,
- intermediate If: (S)-4-tert-butoxy-4-oxo-2-phenethylbutanoic acid,
- intermediate Io: (R)-2-benzyl-5-methoxy-5-oxopentanoic acid; step 2 being replaced by a Michael addition on methyl acrylate using Ti(OiPr)₂Cl₂ and DIEA in DCM at 0°C as described in WO1996/33176,
intermediate Ip: (S)-2-benzyl-5-methoxy-5-oxopentanoic acid; step 2 being replaced by a Michael addition on methyl acrylate using Ti(OiPr)$_2$Cl$_2$ and DIEA in DCM at 0°C as described in WO1996/33176, intermediate It: (2S)-4-te/t-butoxy-2-(2,3-dihydro-1H-inden-1-yl)-4-oxobutanoic acid, intermediate Iu: (S)-4-te/t-butoxy-2-(2,3-dihydro-1H-inden-2-yl)-4-oxobutanoic acid, intermediate Iv: (S)-4-tert-butoxy-2-cyclohexyl-4-oxobutanoic acid, intermediate Iw: (R)-4-tert-butoxy-2-(cyclohexylmethyl)-4-oxobutanoic acid, intermediate Ix: (R)-4-tert-butoxy-4-oxo-2-phenylbutanoic acid, intermediate Iz: (S)-4-tert-butoxy-4-oxo-2-((R)-1-phenylethyl)butanoic acid, intermediate IeI: (2R)-4-(tert-butoxy)-4-oxo-2-((tetrahydrofuran-2-yl)methyl)butanoic acid, intermediate IfI: (R)-4-(tert-butoxy)-2-(cyclopentylmethyl)-4-oxobutanoic acid, intermediate IgI: (R)-4-(tert-butoxy)-4-oxo-2-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid, intermediate IhI: (R)-4-(tert-butoxy)-4-oxo-2-((S)-1-phenylethyl)butanoic acid, intermediate Iol: (2R)-4-(tert-butoxy)-4-oxo-2-((tetrahydrofuran-3-yl)methyl)butanoic acid, intermediate IiI: (R)-4-(fert-butoxy)-2-(furan-2-ylmethyl)-4-oxobutanoic acid, intermediate IuI: (S)-4-(tert-butoxy)-4-oxo-2-(thiophen-2-ylmethyl)butanoic acid.

General method B: synthesis of intermediate Ib (R)-2-benzyl-4-te/t-butoxy-4-oxobutanoic acid
Step 1: synthesis of 3-(triphenylphosphoranylidene)dihydrofuran-2,5-dione

A solution of maleic anhydride (105 g, 1.07 mol) was added dropwise to a solution of triphenylphosphine (270 g, 1.03 mol) in acetone (1.2 L). The reaction mixture was stirred overnight at room temperature, cooled to 5°C, and filtered. The product was washed with acetone (2 x 100 mL), diethyl ether (100 mL), and dried under vacuum to give title compound. Y: 360 g (97%), rt=3.21 min (gradient A), (M+H)+ = 379.

Step 2: synthesis of 4-methoxy-4-oxo-3-(triphenylphosphoranylidene)butanoic acid

A solution of 3-(triphenylphosphoranylidene)dihydrofuran-2,5-dione (110 g, 0.305 mol) in methanol (600 mL) was stirred overnight at room temperature and evaporated. The residue was recrystallized from ethyl acetate (500 mL) to give title compound. Y: 98 g (81%) rt=3.32 min (gradient A), (M+H)+ = 393.

Step 3: synthesis of (3E)-3-(methoxycarbonyl)-4-phenylbut-3-enoic acid

4-methoxy-4-oxo-3-(triphenylphosphoranylidene)butanoic acid (50 g, 0.127 mol) was suspended in benzene (100 mL). A solution of benzaldehyde (14.8 g, 0.14 mol) in a mixture of dichloromethane (30 mL) and benzene (7.5 mL) was added dropwise. The reaction mixture was stirred at RT for 20 h, diluted with diethyl ether (200 mL), and extracted with a solution of potassium bicarbonate (0.23 mol) in water (300 mL). The organic layer was discarded and the aqueous one was washed with a mixture of benzene (200 mL) and ether (100 mL). The aqueous solution was acidified with HCl (30 mL) under cooling and extracted with an ethyl acetate/benzene mixture, 1:2 (2 x 400 mL). The organic layer was washed with water (50 mL) and brine (50 mL), dried over sodium sulfate, and evaporated. The obtained crude product (28 g) was purified by column chromatography (silica gel, CCl4/ethyl acetate, 1:0 → 9:1) to give title compound. Y: 18.9 g (67.5%) rt=3.49 min (gradient A), (M+H)+ = 221.
Step 4: synthesis of (3R)-3-benzyl-4-methoxy-4-oxobutanoic acid

A mixture of (3E)-3-(methoxycarbonyl)-4-phenylbut-3-enoic acid (10.75 g, 48.8 mmol), dicyclohexylamine (18.62 g, 102.6 mmol), water (10 mL), and dichloro ((S)-(-)-2,2-bis(diphenylphosphino)-1,1-binaphthyl)rhenium(I) (40 mg) in methanol (90 mL) was hydrogenated in a Parr apparatus at 60 °C and 60 psi for 30 h. The resulting mixture was evaporated in a rotary evaporator by Å. Acetonitrile (90 mL) was added to the residue, and the mixture was evaporated again by Å. This operation was repeated once more, and the solution was left at RT overnight. The formed precipitate was filtered off and washed with cold acetonitrile. The product (9 g) was dissolved in water (150 mL) and acidified with concentrated HCl to pH=3 under cooling. The product was extracted with an ethyl acetate/benzene 1:2 mixture (300 mL). The organic layer was washed with water, brine, dried over Na₂SO₄, and evaporated to give title compound. Y: 6.35 g (58.6%) P>95%, rt= 3.54 min (gradient A), (M+H)+ =222, ee: 96% (method C).

Step 5: synthesis of (R)-4-tert-butyl-1-methyl 2-benzysuccinate

tert-butyl-2,2,2-trichloroacetimidate (9 mmol, 1.61 mL) and boron trifluoride diethyl etherate (0.675 mmol, 85 µL) was added to a solution of (3R)-3-Benzyl-4-methoxy-4-oxobutanoic acid (4.5 mmol, 1 g) in anhydrous THF (10 mL) at RT. The mixture stirred at RT under nitrogen for 3h. TLC (cyclohexane/AcOEt=1/1) indicated reaction was complete. Reaction mixture was diluted with sat. aq. NaHCO₃ (10 mL) and extracted with AcOEt (2x20 mL). Combined organic layers were washed with water, dried over MgSO₄, evaporated. Crude was purified by flash chromatography (cyclohexane/AcOEt=9/1) to give title compound as a very light yellow oil. Y: 1.25 g (62%), P>90% rt=4.65 mn (gradient A), (M+H)+ =222 (-*Bu) by 1H NMR.

Step 6: synthesis of intermediate 1b (R)-2-benzyl-4-tert-butoxy-4-oxobutanoic acid

To a solution of (R)-4-tert-butyl 1-methyl 2-benzysuccinate (308 mg, 1.11 mmol) in THF (3mL) was added a solution of lithium hydroxide (107 mg, 4.44
mmol) in water (3 mL). The mixture was stirred at RT overnight. TLC (cyclohexane/AcOEt=7/3) indicated reaction was complete. Reaction mixture was acidified to pH=1 with 2M HCl and extracted with DCM (2x20 mL). Combined organic layers were passed through a phase separator and evaporated. Crude was purified by flash chromatography (cyclohexane/AcOEt= 9/1->7/3) (loading as solution in starting eluent) to yield title compound as a colorless oil. Y: 274mg (94%), P>95%, rt=4.17 mn (gradient A), (M+H)+=209 (-/Bu).

The following intermediates were or may be synthesized using general method B:

intermediate Ic: (R)-4-tert-butoxy-2-(4-fluorobenzyl)-4-oxobutanoic acid,
intermediate Id: (R)-4-tert-butoxy-2-(cyclohexylmethyl)-4-oxobutanoic acid,
intermediate Ig: (R)-4-tert-butoxy-2-(4-(trifluoromethyl)benzyl)butanoic acid,
intermediate Ih: (R)-4-tert-butoxy-2-(3-(trifluoromethyl)benzyl)butanoic acid,
intermediate II: (R)-4-tert-butoxy-2-(2-cyanobenzyl)-4-oxobutanoic acid
intermediate Ij: (R)-4-tert-butoxy-2-(3-cyanobenzyl)-4-oxobutanoic acid,
intermediate Ik: (R)-4-tert-butoxy-2-(4-cyanobenzyl)-4-oxobutanoic acid,
intermediate Il: (R)-4-tert-butoxy-2-(4-methoxybenzyl)-4-oxobutanoic acid,
intermediate Im: (R)-4-tert-butoxy-2-(3-methoxybenzyl)-4-oxobutanoic acid,
intermediate In: (R)-4-tert-butoxy-2-(2-methoxybenzyl)-4-oxobutanoic acid,
intermediate Iq: (R)-4-tert-butoxy-2-(4-chlorobenzyl)-4-oxobutanoic acid,
intermediate Ir: (R)-4-tert-butoxy-2-(3-chlorobenzyl)-4-oxobutanoic acid,
intermediate Is: (R)-4-tert-butoxy-2-(2-chlorobenzyl)-4-oxobutanoic acid,
intermediate Iy: (R)-4-tert-butoxy-2-(3-fluorobenzyl)-4-oxobutanoic acid.
**General method C**: synthesis of intermediate 2a 4-(2-chlorophenyl)thiazol-2-amine

Thiourea (2.1 g, 27.45 mmol) was added to a solution 2-bromo-l-(2-chlorophenyl)ethanone (7 g, 27.45 mmol) in ethanol (10 mL) and reaction mixture was stirred at RT for 18 h. The solvent was evaporated and refluxed for 5 minutes in DCM. Suspension was filtered to yield 7.84 g of 4-(2-chlorophenyl)thiazol-2-amine hydrobromide as a white powder. This powder was stirred in a mixture of aq. sat. Na₂CO₃ and AcOEt. Phases are separated and organic layer dried over MgSO₄, concentrated in vacuo to yield title compound as a yellow oil which solidifies spontaneously. Y: 5.37 g (93%), P=100%, rt=2.84 mn (gradient A), (M+H)+ = 211.

The following intermediates were or may be synthesized from the appropriate bromoketone (for which synthesis is described in **Scheme 20**) and thiourea (for which synthesis is described in **Scheme 23**) using general method C:

- intermediate 2c: 4-(2-chlorophenyl)-N-methylthiazol-2-amine, using N-methylthiourea instead of thiourea,
- intermediate 2f: 4-(2,4,6-trichlorophenyl)thiazol-2-amine,
- intermediate 2g: N-benzyl-4-(2-chlorophenyl)thiazol-2-amine,
- intermediate 2i: 2-(2-(methylamino)thiazol-4-yl)benzonitrile
- intermediate 2j: 4-(2-chlorophenyl)-N-ethylthiazol-2-amine,
- intermediate 2l: 4-(2-bromophenyl)-N-methylthiazol-2-amine,
- intermediate 2o: N-methyl-4-(2-nitrophenyl)thiazol-2-amine,
- intermediate 2s: 4-(3-(trifluoromethoxy)phenyl)thiazol-2-amine
- intermediate 2w: N-cyclopropyl-4-(2,5-dichlorophenyl)thiazol-2-amine,
- intermediate 2al: 4-(2,5-dichlorophenyl)-N-methylthiazol-2-amine,
- intermediate 2yl: 4-(2-chloro-5-(trifluoromethyl)phenyl)-N-methylthiazol-2-amine,
- intermediate 2zl: 4-(2-chloro-5-fluorophenyl)-N-methylthiazol-2-amine
- intermediate 2a2: 4-(3,5-dichlorophenyl)-N-methylthiazol-2-amine,
- intermediate 2b2: 4-(3-(difluoromethoxy)phenyl)-N-methylthiazol-2-
amine,
intermediate 2e2: 4-(5-chloro-2-(trifluoromethyl)phenyl)-N-methylthiazol-2-amine,
intermediate 2f2: N-methyl-4-(2,3,5-trichlorophenyl)thiazol-2-amine,
intermediate 2l2: N-methyl-4-(2-(trifluoromethoxy)phenyl)thiazol-2-amine,
intermediate 2m2: 4-(2-choro-5-fluorophenyl)-N-cyclopropythiazol-2-amine,
intermediate 2n2: N-cyclopropyl-4-(3-(difluoromethoxy)phenyl)thiazol-2-amine,
intermediate 2o2: 4-(2-choro-5-(trifluoromethyl)phenyl)-N-cyclopropylthiazol-2-amine,
intermediate 2v3: (S)-l-((4-(2-chlorophenyl)thiazol-2-yl)amino)propan-2-ol,
intermediate 2w3: (R)-l-((4-(2-chlorophenyl)thiazol-2-yl)amino)propan-2-ol,
intermediate 2z3: 4-(2,3-dichlorophenyl)-N-methylthiazol-2-amine,
intermediate 2a4: N-methyl-4-(3-(trifluoromethoxy)phenyl)thiazol-2-amine,
intermediate 2b4: N-cyclopropyl-4-(3-(trifluoromethoxy)phenyl)thiazol-2-amine
intermediate 2c4: (4-(2-(difluoromethoxy)phenyl)-N-methylthiazol-2-amine).

General method D: synthesis of intermediate 2b 4-(2-chlorophenyl)-N-(cyclopropylmethyl)thiazol-2-amine
2-bromo-l-(2-chlorophenyl)ethanone (0.5 mmol, 116 mg) and dry sodium thiocyanate (0.55 mmol, 45 mg) were stirred in 1 mL ethanol for 3 h at 50°C. A solution of cyclopropane methyl amine (0.55 mmol, 39 mg) in 0.5 mL of ethanol was added at once and the reaction mixture was stirred for 12 h. The ethanol was distilled off, and ethyl acetate and water were added. The aqueous phase was extracted twice with ethyl acetate, the combined organic phases were dried over Na₂SO₄, and the solvent was removed \textit{in vacuo}. Crude was purified by flash chromatography (cyclohexane/DCM=6/4) to give title compound as a dark yellow oil. Y: 40 mg (30%), P=100%, rt=3.5 min (gradient A), (M+H)+=264.8.

The following intermediates were or may be synthesized from the appropriate bromoketone (for which synthesis is described in Scheme 20) and amine reagents using general method D:

- intermediate 2d: N-allyl-4-(2-chlorophenyl)thiazol-2-amine,
- intermediate 2e: methyl 2-(4-(2-chlorophenyl)thiazol-2-ylamino)acetate,
- intermediate 2h: 4-(2-chlorophenyl)-N-(2,2,2-trifluoroethyl)thiazol-2-amine,
- intermediate 2k: 4-(2-chlorophenyl)-N-cyclopropylthiazol-2-amine,
- intermediate 2r: 2-((4-(2-chlorophenyl)thiazol-2-yl)amino)acetamide,
- intermediate 2x: methyl 3-((4-(2-chlorophenyl)thiazol-2-yl)amino)propanoate,
- intermediate 2ul: N-(2-(benzyloxy)ethyl)-4-(2-chlorophenyl)thiazol-2-amine,
- intermediate 2vl: N-(3-(benzyloxy)propyl)-4-(2-chlorophenyl)thiazol-2-amine,
- intermediate 2s2: 4-(2-chlorophenyl)-N-(2-methoxyethyl)thiazol-2-amine,
- intermediate 2t2: N-(2-(benzyloxy)ethyl)-4-(2-chlorophenyl)thiazol-2-amine.
**General method E**: synthesis of Example 1: compound n°2: (R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid

**Step 1**: synthesis of (R)-tert-butyl 3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxobutanoate

To a solution of (R)-2-benzyl-4-tert-butoxy-4-oxobutanoic acid Ib (1.21 mmol, 320 mg) in anhydrous DMF (5 mL) was added HATU (1.33 mmol, 505 mg). After 5 min was added 4-(2-chlorophenyl)thiazol-2-amine 2a (1.33 mmol, 279 mg) and DIEA (1.815 mmol, 300 µL). Reaction mixture was stirred at RT for 4 days. TLC (cyclohexane/AcOEt=8/2) indicated reaction was complete. Reaction mixture (rm) was diluted with AcOEt (20 mL) and washed with sat. aq. NaHCO₃ (10 mL) and water (3x10 mL). The organic phase was dried over MgSO₄ and evaporated. Crude was purified by flash chromatography (cyclohexane/AcOEt=9/1) (loading onto silica) to yield title compound as a yellow gum. Y: 370 mg (67%), P>95%, rt=5.24 min (gradient A), (M+H)+ =457.1. ACN was also used instead of DMF.

**Step 2**: synthesis of Example 1: compound n°2: (R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid

To a solution of (R)-tert-butyl 3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxobutanoate (0.7 mmol, 320 mg) in DCM (8 mL) was added TFA (2 mL). Rm was stirred at RT overnight. TLC (cyclohexane/AcOEt=7/3) indicated reaction was complete. Reaction mixture was evaporated and residue purified using a Biotage PEAX SPE cartridge. The oil obtained was triturated in diethyl ether/pentane=2/8 to yield title compound as a colorless solid. Y: 280 mg (99%), P>99% rt=9.32 min (gradient B), (M+H)+ =401.1, ee=96% (method B). ¹H NMR (CDCl₃): δ=12.2 (br s, 1H), 7.39-7.33 (m, 9H), 7.14 (s, 1H), 3.36 (q, 1H), 3.14 (m, 1H), 2.89-2.77 (m, 2H), 2.57 (dd, 1H).

Examples 2 to 18 were synthesized using general method E and intermediates described above or commercially available.
Example 2: compound n°9: (S)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-phenylbutanoic acid was synthesized using intermediates 1a and 2a. P=99%, (M+H)+=387, ee=98% (method A), ¹H NMR (DMSO-d₆): δ=7.78 (d, J=2.8Hz, IH), 7.5 (m, 2H), 7.4-7.1 (m, 9H), 4.3 (q, IH), 3.18 (dd, J=17Hz, J=27Hz, IH), 2.66 (dd, J=4.8Hz, J=22Hz, IH).

Example 3: compound n°3: (R)-3-benzyl-4-(4-(2,4-dichlorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate Ib and 4-(2,4-dichlorophenyl)thiazol-2-amine.

Example 4: compound n°4: (R)-3-benzyl-4-(4-(2-fluorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate Ib and 4-(2-fluorophenyl)thiazol-2-amine.

Example 5: compound n°5: (R)-3-benzyl-4-(4-(3,4-dichlorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate Ib and 4-(3,4-dichlorophenyl)thiazol-2-amine.

Example 8: compound n°8: (R)-3-benzyl-4-(4-(4-cyanophenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate Ib and 4-(2-aminothiazol-4-yl)benzonitrile.

Example 9: compound n°12: (R)-3-benzyl-4-(4-(3-chlorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate Ib and 4-(3-chlorophenyl)thiazol-2-amine.

Example 10: compound n°13: (R)-3-benzyl-4-oxo-4-(4-(3-(trifluoromethyl)phenyl)thiazol-2-ylamino)butanoic acid was synthesized using intermediate Ib and 4-(3-(trifluoromethyl)phenyl)thiazol-2-amine.
Example 1: compound n°14: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized using intermediates Ib and 2c. Y: 142 mg (80%), P>99% rt=10.5 mn (gradient B), (M+H)^+ =414.8, ee=96% (method B), ^1^HNMR (CDCl_3): δ= 7.92 (d, IH), 7.54 (s, IH), 7.45 (d, IH), 7.34-7.13 (m, 7H), 3.62 (s, 3H), 3.47 (m, IH), 3.15-3.01 (m, 2H), 2.61-2.54 (m, IH), 2.53-2.51 (dd, IH).

Example 2: compound n°17: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(4-fluorobenzyl)-4-oxobutanoic acid was synthesized using intermediates Ic and 2a.

Example 3: compound n°18: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(cyclohexylmethyl)-4-oxobutanoic acid was synthesized using intermediates Id and 2a. Y: 15 mg (30%), P>90% rt=10.76 mn (gradient B), (M+H)^+ =401.1, ee=96% (method B), ^1^HNMR (CDCl_3): δ= 12.26 (br s, IH), 7.35-7.45 (m, 2H), 7.15-7.30 (m, 4H), 3.15-3.25 (m, IH), 2.7 (dd, IH), 2.5 (dd, IH), 1.45-1.8 (m, 6H), 1.1-1.4 (m, 5H), 0.8-1.0 (m, 2H).

Example 4: compound n°22: (R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid was synthesized using intermediates Ib and 2d.

Example 5: compound n°23: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxy-2-oxoethyl)amino)-4-oxobutanoic acid was synthesized using intermediate Ib and 2e.

**Example 18:** compound n°21: (R)-3-benzyl-4-((5-chloro-4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized using intermediate Ib and 5-chloro-4-(2-chlorophenyl)-N-methylthiazol-2-amine which was prepared by reacting intermediate 2c with N-chlorosuccinimide and triethylamine in chloroform.

**Example 19:** compound n°15: (R)-3-benzyl-4-(5-(2-chlorophenyl)pyridin-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate I b and 5-iodopyridin-2-amine. Amide coupling such as in general method E, subsequent Suzuki coupling with 2-chlorophenylboronic acid using PdCl$_2$(PPh$_3$)$_4$ catalyst and K$_2$CO$_3$ in dioxane/H$_2$O followed by tBu deprotection as described in general method E provided title compound.

**Example 20:** compound n°10: (Z)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxobut-2-enoic acid was synthesized using intermediate 2a and (Z)-4-methoxy-4-oxobut-2-enoic acid. Amide coupling such as in general method E followed by saponification such as in step 6 of general method B provided title compound.

**Example 21:** compound n°16: (R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)heptanoic acid was synthesized using intermediate 2a and (R)-2-(2-tert-butoxy-2-oxoethyl)hexanoic acid. (R)-2-(2-tert-butoxy-2-oxoethyl)hexanoic acid was prepared from (R)-3-(methoxycarbonyl)heptanoic acid as done in steps 5 and 6 of general method B.

**Example 22:** compound n°19: (R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-methylhexanoic acid was synthesized using intermediate 2a and (R)-2-(2-tert-butoxy-2-oxoethyl)-4-methylpentanoic acid. (R)-2-(2-tert-butoxy-2-oxoethyl)-4-methylpentanoic acid was prepared from (R)-3-(methoxycarbonyl)-5-methylhexanoic acid as done in steps 5 and 6 of general method B.
Example 23: compound n°1: 6-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)cyclohex-3-enecarboxylic acid was synthesized using intermediate 2a and 6-(methoxycarbonyl)cyclohex-3-enecarboxylic acid. Amide coupling such as in general method E followed by saponification such as in step 6 of general method B provided title compound.

Example 24: compound n°24: (R)-methyl 3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxobutanoate may be synthesized by treating compound n°2 with TMSCl in MeOH.

Example 26: compound n°26: (R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid may be synthesized from intermediates Ie and 2a using general method E.

Example 27: compound n°27: (S)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid may be synthesized from intermediates If and 2a using general method E.

Example 28: compound n°28: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-(4-(trifluoromethyl)benzyl)butanoic acid was synthesized from intermediates Ig and 2a using general method E.

Example 29: compound n°29: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-(3-(trifluoromethyl)benzyl)butanoic acid was synthesized from intermediates Ih and 2a using general method E.

Example 30: compound n°30: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(2-cyanobenzyl)-4-oxobutanoic acid may be synthesized from intermediates Ii and 2a using general method E.

Example 31: compound n°31: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(3-cyanobenzyl)-4-oxobutanoic acid may be synthesized from intermediates Ij and 2a using general method E.
Example 32: compound n°32: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(4-cyanobenzyl)-4-oxobutanoic acid may be synthesized from intermediates Ik and 2a using general method E.

Example 33: compound n°33: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(4-methoxybenzyl)-4-oxobutanoic acid may be synthesized from intermediates 11 and 2a using general method E.

Example 34: compound n°34: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(3-methoxybenzyl)-4-oxobutanoic acid may be synthesized from intermediates Im and 2a using general method E.

Example 35: compound n°35: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(2-methoxybenzyl)-4-oxobutanoic acid may be synthesized from intermediates In and 2a using general method E.

Example 36: compound n°36: (R)-3-benzyl-4-(4-(2-methoxyphenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized from intermediate 1b and 4-(2-methoxyphenyl)thiazol-2-amine using general method E.

Example 37: compound n°37: ((R)-3-benzyl-4-oxo-4-(4-(2,4,6-trichlorophenyl)thiazol-2-ylamino)butan-2-yl)butanoic acid may be synthesized from intermediates 1b and 2f using general method E.

Example 38: compound n°38: (R)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid may be synthesized from intermediates Io and 2c using general method E, replacing the TFA tBu ester deprotection by a methyl ester saponification using LiOH in THF/H₂O.

Example 39: compound n°39: (S)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid was synthesized from intermediates Ip and 2c using general method E, replacing the TFA tBu ester deprotection by a methyl ester saponification using LiOH in THF/H₂O.
Example 40: compound n°40: (R)-methyl 4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate may be synthesized from intermediates 1o and 2a using general method E.

Example 41: compound n°41: (S)-methyl 4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate may be synthesized from intermediates 1p and 2a using general method E.

Example 42: compound n°42: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropylmethyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2b using general method E.

Example 43: compound n°43: (R)-3-benzyl-4-(benzyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2g using general method E.

Example 44: compound n°44: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2,2,2-trifluoroethyl)amino)-4-oxobutanoic acid may be synthesized from intermediates 1b and 2h using general method E.

Example 45: compound n°45: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid was synthesized from 4-(tert-butoxy)-2-(4-methoxybenzyl)-4-oxobutanoic acid and intermediate 2c using general method E and chiral preparative HPLC purification. 4-(tert-butoxy)-2-(4-methoxybenzyl)-4-oxobutanoic acid was synthesized from commercially available 4-methoxybenzaldehyde using the HWE methodology (Scheme 13).

Example 46: compound n°46: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-methoxybenzyl)-4-oxobutanoic acid may be synthesized from intermediates 1m and 2c using general method E.

Example 47: compound n°47: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-methoxybenzyl)-4-oxobutanoic acid may be synthesized from intermediates 1n and 2c using general method E.
Example 48: compound n°48: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-cyanobenzyl)-4-oxobutanoic acid was synthesized from 4-(tert-butoxy)-2-(4-cyanobenzyl)-4-oxobutanoic acid and intermediate 2c using general method E and chiral preparative HPLC purification. 4-(tert-butoxy)-2-(4-cyanobenzyl)-4-oxobutanoic acid was synthesized from commercially available 4-cyanobenzaldehyde using the HWE methodology (Scheme 13).

Example 49: compound n°49: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-cyanobenzyl)-4-oxobutanoic acid may be synthesized from intermediates Ij and 2c using general method E.

Example 50: compound n°50: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-cyanobenzyl)-4-oxobutanoic acid may be synthesized from intermediates Ii and 2c using general method E.

Example 51: compound n°51: (R)-3-(4-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from 4-(tert-butoxy)-2-(4-chlorobenzyl)-4-oxobutanoic acid and intermediate 2c using general method E and chiral preparative HPLC purification. 4-(tert-butoxy)-2-(4-chlorobenzyl)-4-oxobutanoic acid was synthesized from commercially available 4-chlorobenzaldehyde using the HWE methodology (Scheme 13).

Example 52: compound n°52: (R)-3-(3-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid may be synthesized from intermediates Ir and 2c using general method E.

Example 53: compound n°53: (R)-3-(2-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid may be synthesized from intermediates Is and 2c using general method E.

Example 54: compound n°54: (3S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-lH-inden-1-yl)-4-oxobutanoic acid may be synthesized from intermediates It and 2c using general method E. It may be synthesized using Stobbe's condensation (Scheme 6).
Example 55: compound n°55: (S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-1H-inden-2-yl)-4-oxobutanoic acid may be synthesized from intermediates 1u and 2c using general method E. 1u may be synthesized using Stobbe's condensation (Scheme 6).

Example 56: compound n°56: (R)-4-(benzo[d]thiazol-2-yl(methyl)amino)-3-benzyl-4-oxobutanoic acid may be synthesized from intermediate Ib and N-methylbenzo[d]thiazol-2-amine using general method E. N-methylbenzo[d]thiazol-2-amine may be prepared by Eischweiler-Clarke methylation of benzo[d]thiazol-2-amine.

Example 57: compound n°57: (R)-4-(benzo[d]oxazol-2-yl(methyl)amino)-3-benzyl-4-oxobutanoic acid may be synthesized from intermediate Ib and N-methylbenzo[d]oxazol-2-amine using general method E. N-methylbenzo[d]oxazol-2-amine may be prepared by Eischweiler-Clarke methylation of benzo[d]oxazol-2-amine.

Example 58: compound n°58: (R)-2-((IH-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-phenylpropanamide may be synthesized from compound n°14 using methodologies described in the isosteres synthetic schemes section.

Example 59: compound n°59: (R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide may be synthesized from compound n°14 using methodologies described in the isosteres synthetic schemes section.

Example 60: compound n°60: (R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized using intermediate 1b and 4-(2-chlorophenyl)-5-fluoro-N-methylthiazol-2-amine which was prepared in one step from intermediate 2c as described in Chem. Res. Toxicol. 2007, 1954-1965.

Example 61: compound n°61: (S)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-cyclohexyl-4-oxobutanoic acid may be synthesized from intermediates Iv and 2a
using general method E.

Example 62: compound n°62: (S)-4-((4-(2-chlorophenyl)thiazol-2-y1)(methyl)amino)-3-cyclohexyl-4-oxobutanoic acid was synthesized from (S)-4-(tert-butoxy)-2-cyclohexyl-4-oxobutanoic acid and intermediate 2c using general method E. (S)-4-(tert-butoxy)-2-cyclohexyl-4-oxobutanoic acid was synthesized from commercially available (S)-3-cyclohexyl-4-methoxy-4-oxobutanoic acid as described in steps 5 and 6 of general method B.

Example 63: compound n°63: (S)-4-((4-(2-chlorophenyl)thiazol-2-y1)(methyl)amino)-4-oxo-3-phenylbutanoic acid may be synthesized from intermediates 1a and 2c using general method E.

Example 64: compound n°64: (3R)-3-(4-(2-chlorophenyl)thiazol-2-y1carbamoyl)-4-phenylpentanoic acid may be synthesized from intermediate 2a and (2R)-4-tert-butoxy-4-oxo-2-(1-phenylethyl)butanoic acid using general method E. (2R)-4-tert-butoxy-4-oxo-2-(1-phenylethyl)butanoic acid may be obtained by Stobbe condensation (Scheme 6).

Example 65: compound n°65: (R)-2-((lH-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-phenylpropanamide was synthesized from compound n°2 using methodologies described in the isosteres synthetic schemes section.

Example 66: compound n°66: (R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide was synthesized from compound n°2 using methodologies described in the isosteres synthetic schemes section.

Example 68: compound n°68: (3R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-2-methyl-4-oxobutanoic acid was synthesized as described in Scheme 7.

Example 69: compound n°69: (R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxyisoxazol-5-yl)propanamide may be synthesized using methodologies described in the isosteres synthetic schemes section.
Example 70: compound n°70: (R)-3-benzyl-4-(4-(2-chlorophenyl)pyrimidin-2-ylamino)-4-oxobutanoic acid was synthesized from intermediate 1b and 4-(2-chlorophenyl)pyrimidin-2-amine using general method E. 4-(2-chlorophenyl)pyrimidin-2-amine was synthesized as described in Scheme 8.

Example 71: compound n°71: (R)-3-benzyl-4-(6-(2-chlorophenyl)pyridin-2-ylamino)-4-oxobutanoic acid was synthesized from intermediate 1b and 6-(2-chlorophenyl)pyridin-2-amine using general method E. 6-(2-chlorophenyl)pyridin-2-amine was synthesized as described in Scheme 8.

Example 72: compound n°72: (E)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylbut-3-enoic acid may be synthesized from (E)-2-benzylidene-4-tert-butoxy-4-oxobutanoic acid and intermediate 2a using general method E. (E)-2-benzylidene-4-tert-butoxy-4-oxobutanoic acid was synthesized from maleic anhydride following steps 1, 2, 3, 5 and 6 of general method B.

Example 74: compound n°74: (Z)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-phenylbut-2-enoic acid may be synthesized as described in Scheme 9.

Example 75: compound n°75: (R)-3-(N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methylsulfamoyl)-4-phenylbutanoic acid may be synthesized as described in Scheme 10.

Example 76: compound n°76: (S)-3-(N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methylsulfamoyl)-4-phenylbutanoic acid may be synthesized as described in Scheme 10.

Example 79: compound n°79: (R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-fluoro-4-oxobutanoic acid may be synthesized as described in Scheme 11.

Example 80: compound n°80: (R)-3-benzyl-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)hex-5-enoic acid may be synthesized as described in Scheme 11.
Example 81: compound n°81: (E)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylbut-3-enoic acid was synthesized from (E)-2-benzylidene-4-tert-butoxy-4-oxobutanoic acid and intermediate 2c using general method E. (E)-2-benzylidene-4-tert-butoxy-4-oxobutanoic acid was synthesized from maleic anhydride following steps 1, 2, 3, 5 and 6 of general method B.

Example 82: compound n°82: (3S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid may be synthesized from intermediate 2c and (2R)-4-tert-butoxy-4-oxo-2-(1-phenylethyl)butanoic acid using general method E. (2R)-4-tert-butoxy-4-oxo-2-(1-phenylethyl)butanoic acid may be obtained by Stobbe condensation (Scheme 6).

Example 83: compound n°83: (R)-3-benzyl-4-((3-(2-chlorophenyl)-1,2,4-thiadiazol-5-yl)(methyl)amino)-4-oxobutanoic acid was synthesized as described in Scheme 12.

Example 84: compound n°84: (R)-3-benzyl-4-((3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)(methyl)amino)-4-oxobutanoic acid may be synthesized as described in Scheme 12.

Example 85: compound n°85: (R)-3-benzyl-4-((1-(2-chlorophenyl)-1H-pyrazol-3-yl)(methyl)amino)-4-oxobutanoic acid may be synthesized as described in Scheme 12.

Example 86: compound n°86: (R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxyisoxazol-5-yl)-N-methylpropanamide was synthesized using methodologies described in the isosteres synthetic schemes section.

Example 89: compound n°89: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid was synthesized from intermediates Iw and 2c using general method E. Intermediate Iw was synthesized by hydrogenation of intermediate Ib using PtO₂ in MeOH.

Example 90: compound n°90: (R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-5-methylhexanoic acid was synthesized from intermediate
2c and (R)-2-(2-?ert-butoxy-2-oxoethyl)-4-methylpentanoic acid using general method E. (R)-2-(2-te/t-butoxy-2-oxoethyl)-4-methylpentanoic acid was synthesized from (R)-3-(methoxycarbonyl)-5-methylhexanoic acid using methodology described in steps 5 and 6 of general method B.

Example 91: compound n°91: (R)-3-benzyl-4-((4-(2-cyanophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2i using general method E.

Example 92: compound n°92: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-phenylbutanoic. Phenylacetic acid was converted to its tBu ester using tBuTCA. Treatment of this tBu ester with LiHMDS followed by the addition of t-butyl bromoacetate provided 1-tert-butyl 4-methyl 2-phenylsuccinate. tBu deprotection with TFA yielded 4-methoxy-4-oxo-2-phenylbutanoic acid. HATU coupling of this acid with intermediate 2a and subsequent methyl ester saponification using LiOH yielded 4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-phenylbutanoic. Chiral preparative HPLC purification of this racemic mixture allowed isolating compound n°92.

Example 93: compound n°93: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(3-fluorobenzyl)-4-oxobutanoic acid was synthesized from intermediates Iy and 2a using general method E and preparative HPLC purification.

Example 94: compound n°94: (S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-methylpentanoic acid was synthesized from (S)-4-tert-butoxy-2-isopropyl-4-oxobutanoic acid and intermediate 2c using general method E. (S)-4-tert-butoxy-2-isopropyl-4-oxobutanoic acid was synthesized from commercially available (S)-3-(methoxycarbonyl)-4-methylpentanoic acid using reactions described in steps 5 and 6 of general method B.

Example 95: compound n°95: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from (R)-4-tert-butoxy-4-oxo-2-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid and intermediate 2c using general method E. (R)-4-tert-butoxy-4-oxo-2-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from commercially
available tetrahydro-2H-pyran-4-carbaldehyde using the HWE methodology (Scheme 13).

**Example 96:** compound n°96: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(ethyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2j using general method E.

**Example 97:** compound n°97: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2k using general method E.

**Example 98:** compound n°98: cis-6-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)cyclohex-3-enecarboxylic acid was synthesized from cis-3a,4,7,7a-tetrahydroisobenzofuran-1,3-dione and intermediate 2a as described in Scheme 14.

**Example 99:** compound n°99: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid was synthesized from 4-te/t-butoxy-2-(4-methoxybenzyl)-4-oxobutanoic acid and intermediate 2c using general method E. 4-te/t-butoxy-2-(4-methoxybenzyl)-4-oxobutanoic acid was synthesized from 4-methoxybenzaldehyde using the HWE methodology (Scheme 13).

**Example 100:** compound n°100: cis-6-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohex-3-enecarboxylic acid was synthesized from cis-3a,4,7,7a-tetrahydroisobenzofuran-1,3-dione and intermediate 2c as described in Scheme 14.

**Example 101:** compound n°101: cis-2-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohexanecarboxylic acid was synthesized from cis-hexahydroisobenzofuran-1,3-dione and intermediate 2c as described in Scheme 14.

**Example 102:** compound n°102: (R)-3-benzyl-4-((4-(2,5-dimethylthiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized from intermediate Ib and commercially available 4-(2,5-dimethylthiophen-3-yl)thiazol-2-amine using
Example 103: compound n°103: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid was synthesized from 4-tert-butoxy-2-(cyclohexylmethyl)-4-oxobutanoic acid and intermediate 2c using general method E. 4-tert-butoxy-2-(cyclohexylmethyl)-4-oxobutanoic acid was synthesized by hydrogenation of (E)-4-tert-butyl 1-methyl 2-benzylidenesuccinate using PtO₂ in MeOH.

Example 105: compound n°105: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from 4-tert-butoxy-2-(cyclopentylmethyl)-4-oxobutanoic acid and intermediate 2c using general method E. 4-tert-butoxy-2-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from commercially available cyclopentanecarbaldehyde using the HWE methodology (Scheme 13).

Example 106: compound n°106: (3S,4R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid from intermediates I₂ and 2c using general method E.

Example 107: compound n°107: (R)-3-benzyl-4-(methyl(4-(2-(thiophen-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediate Ib and N-methyl-4-(2-(thiophen-3-yl)phenyl)thiazol-2-amine using general method E. N-methyl-4-(2-(thiophen-3-yl)phenyl)thiazol-2-amine was synthesized from commercially available thiophen-3-ylboronic acid using the methodology shown in Scheme 15.

Example 108: compound n°108: (R)-3-benzyl-4-((4-(2-(6-chloropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediate Ib and 4-(2-(6-chloropyridin-3-yl)phenyl)-N-methylthiazol-2-amine using general method E. 4-(2-(6-chloropyridin-3-yl)phenyl)-N-methylthiazol-2-amine was synthesized from commercially available 6-chloropyridin-3-ylboronic acid using the methodology shown in Scheme 15.

Example 109: compound n°109: (R)-4-((4-(2-chlorophenyl)thiazol-2-
yl)(methyl)amino)-4-oxo-3-(phenylamino)butanoic acid was synthesized from (R)-4-tert-butoxy-4-oxo-2-(phenylamino)butanoic acid and intermediate 2c using general method E. (R)-4-tert-butoxy-4-oxo-2-(phenylamino)butanoic acid was synthesized from commercially available (R)-2-amino-4-tert-butoxy-4-oxobutanoic acid and iodobenzene using CuI catalyzed coupling as described in *J. Am. Chem. Soc.* 1998, 120, 12459.

**Example 110:** compound n°110: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methylbenzyl)-4-oxobutanoic acid was synthesized from 4-tert-butoxy-2-(4-methylbenzyl)-4-oxobutanoic acid and intermediate 2c using general method E. 4-tert-butoxy-2-(4-methylbenzyl)-4-oxobutanoic acid was synthesized from 4-methylbenzaldehyde using the HWE methodology (Scheme 13).

**Example 111:** compound n°111: (R)-4-((4-((l,l'-biphenyl)-2-yl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid was synthesized from intermediate Ib and 4-((l,l'-biphenyl)-2-yl)-N-methylthiazol-2-amine using general method E. 4-((l,l'-biphenyl)-2-yl)-N-methylthiazol-2-amine was synthesized from commercially available phenylboronic acid using the methodology shown in Scheme 15.

**Example 112:** compound n°112: (R)-3-benzyl-4-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized from intermediate Ib and commercially available 4-(2,5-dichlorothiophen-3-yl)thiazol-2-amine using general method E.

**Example 113:** compound n°113: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopropylmethyl)-4-oxobutanoic acid was synthesized from intermediates IaI (4-(tert-butoxy)-2-(cyclopropylmethyl)-4-oxobutanoic acid) and 2c using general method E. IaI was synthesized from cyclopropanecarbaldehyde using the HWE methodology (Scheme 13).

**Example 114:** compound n°114: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiazol-4-ylmethyl)butanoic acid was synthesized from intermediates IbI (4-(tert-butoxy)-4-oxo-2-(thiazol-4-ylmethyl)butanoic
acid) and 2c using general method E. IbI was synthesized from thiazole-4-carbaldehyde using the HWE methodology (Scheme 13).

**Example 115:** compound n°115: (R)-3-benzyl-4-\((4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)\)-4-oxobutanoic acid was synthesized from intermediate 1b and 4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine using general method E. 4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine was synthesized from (6-(dimethylamino)pyridin-3-yl)boronic acid and 21 using the methodology shown in Scheme 15.

**Example 116:** compound n°116: (R)-3-benzyl-4-\((4-(2-(6-methoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino\)-4-oxobutanoic acid was synthesized from intermediate 1b and intermediate 2m (4-(2-(6-methoxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2m was synthesized from (6-methoxy)pyridin-3-yl)boronic acid and 21 using the methodology shown in Scheme 15.

**Example 117:** compound n°117: (R)-3-benzyl-4-\((4-(2-(6-methoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino\)-4-oxobutanoic acid was synthesized from intermediate 1b and (4-(2-(6-methoxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. (4-(2-(6-methoxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) was synthesized from (2-methoxy)pyridin-3-yl)boronic acid and 21 using the methodology shown in Scheme 15.

**Example 118:** compound n°118: (R)-3-benzyl-4-\((4-(2-((ethoxycarbonyl)amino)phenyl)thiazol-2-yl)(methyl)amino\)-4-oxobutanoic acid was synthesized from intermediates 1b and 2n (ethyl (2-(2-(methylamino)thiazol-4-yl)phenyl)carbamate) using general method E. Intermediate 2n was synthesized using the methodology described in Scheme 16.

**Example 119:** compound n°119: (R)-3-benzyl-4-\((4-(2-(6-fluoropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino\)-4-oxobutanoic acid was synthesized from intermediates 1b and 2p (4-(2-(6-fluoropyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate
2p was synthesized from (6-fluoropyridin-3-yl)boronic acid and 21 using the methodology described in Scheme 15.

**Example 120:** compound n°120: (R)-3-benzyl-4-methyl(4-(2-(6-methylpyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2q (N-methyl-4-(2-(6-methylpyridin-3-yl)phenyl)thiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2q was synthesized from (6-methylpyridin-3-yl)boronic acid and 21 using the methodology described in Scheme 15.

**Example 121:** compound n°121: (R)-4-(2-oxoethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid was synthesized from intermediates 1b and 2r using general method E.

**Example 122:** compound n°122: (R)-3-benzyl-4-oxo-4-(4-(3-trifluoromethoxy)phenyl)thiazol-2-yl)amino)butanoic acid was synthesized from intermediates 1b and commercially available 2s (4-(3-trifluoromethoxy)phenyl)thiazol-2-amine) using general method E.

**Example 123:** compound n°123: (R)-3-benzyl-4-(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2t (4-(2,5-dichlorophenyl)thiazol-2-amine) using general method E.

**Example 124:** compound n°124: (R)-3-benzyl-4-(4-(3-chloro-4-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2u (4-(3-chloro-4-fluorophenyl)thiazol-2-amine) using general method E.

**Example 125:** compound n°125: (R)-3-benzyl-4-(4-(3-chloro-4-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2v (4-(3-chloro-4-methoxyphenyl)thiazol-2-amine) using general method E.

**Example 126:** compound n°126: (R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2w (4-(2-chlorophenyl)thiazol-2-amine) using general method E.
yl)(3-methoxy-3-oxopropyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2x using general method E.

**Example 127:** compound n°127: 3-(bicyclo[2.2.1]heptan-2-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates IcI (2-(bicyclo[2.2.1]heptan-2-ylmethyl)-4-(tert-butoxy)-4-oxobutanoic acid) and 2c using general method E. IcI was synthesized from bicyclo[2.2.1]heptane-2-carbaldehyde using the HWE methodology (Scheme 13).

**Example 128:** compound n°128: (R)-3-benzyl-4-((4-(2-(6-ethoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2y (4-(2-(6-ethoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2y was synthesized from (6-ethoxypyridin-3-yl)boronic acid and 21 using the methodology described in Scheme 15.

**Example 129:** compound n°129: (R)-3-benzyl-4-((4-(4′-methoxy-[1,1′-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2z (4-(4′-methoxy-[1,1′-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2z was synthesized from (4-methoxyphenyl)boronic acid and 21 using the methodology described in Scheme 15.

**Example 130:** compound n°130: (R)-3-benzyl-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2al using general method E.

**Example 131:** compound n°131: (R)-l-(5-(2-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)phenyl)pyrrolidin-2-yl)pyrrolidin-1-ium 2,2,2-trifluoroacetate was synthesized from intermediates 1b and 2bl (N-methyl-4-(2-(6-(pyrrolidin-1-yl)pyrrolidin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2bl was synthesized from 2-(pyrrolidin-1-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine and 21 by Suzuki coupling with the conditions described in Scheme 15.
**Example 132:** compound n°132: (R)-4-(2’-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)-[1,1'-biphenyl]-4-yl)morpholin-4-ium 2,2,2-trifluoroacetate was synthesized from intermediates 1b and 2cl (N-methyl-4-(4'-morpholino-[1',1'-biphenyl]-2-yl)thiazol-2-amine) using general method E. Intermediate 2cl was synthesized from 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)morpholine and 2l by Suzuki coupling with the conditions described in **Scheme 15**.

**Example 133:** compound n°133: (R)-3-benzyl-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2dl (N-methyl-4-(2-(6-morpholino-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2dl was synthesized from 4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)morpholine and 2l using the methodology described in **Scheme 15**.

**Example 134:** compound n°134: (R)-3-benzyl-4-(4-(3'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2el (4-(3'-chloro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2el was synthesized from (3-chlorophenyl)boronic acid and 2l by Suzuki coupling with the conditions described in **Scheme 15**.

**Example 135:** compound n°135: (R)-3-benzyl-4-((4-(2-(furan-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2fl (4-(2-(furan-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2fl was synthesized from furan-3-ylboronic acid and 2l by Suzuki coupling with the conditions described in **Scheme 15**.

**Example 136:** compound n°136: (R)-3-benzyl-4-((4-(2-(6-(2-methoxyethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2gl (4-(2-(6-(2-methoxyethoxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2gl was synthesized from 5-bromo-2-(2-methoxyethoxy)pyridine and 2l using the methodology described in **Scheme 17**.
Example 138: compound n°138: (R)-3-benzyl-4-((4-(4'-isopropyl-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2hl (4-(4'-isopropyl-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2hl was synthesized from (4-isopropylphenyl)boronic acid and 21 by Suzuki coupling with the conditions described in Scheme 15.

Example 139: compound n°139: (R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid (ee=50%) and intermediate 2m using general method E and chiral preparative HPLC purification. (R)-4-tert-butoxy-2-(cyclopentylmethyl)-4-oxobutanoic acid (ee=50%) was synthesized from commercially available cyclopentanecarbaldehyde using the HWE methodology as described in Scheme 13.

Example 140: compound n°140: (R)-3-benzyl-4-((4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2il (4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2il was synthesized from 5-bromo-3-fluoro-2-methoxypyridine using the methodology described in Scheme 17.

Example 141: compound n°141: (R)-3-benzyl-4-(methyl(4-(2-(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2jl (N-methyl-4-(2-(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2jl was synthesized from 5-bromo-2-(((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine and 21 using the methodology described in Scheme 17.

Example 142: compound n°142: (R)-3-benzyl-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid from intermediates 1b and 2w using general method E.

Example 143: compound n°143: 4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid from intermediates 1b and 2w using general method E.
yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid was synthesized from intermediates IdI (4-(?ert-butoxy)-2-(furan-2-ylmethyl)-4-oxobutanoic acid) and 2c using general method E. IdI was synthesized from furan-2-carbaldehyde using the HWE methodology described Scheme 13.

Example 144: compound n°144: (R)-3-benzyl-4-(4-(2-cyclopropylphenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2kl (4-(2-cyclopropylphenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2kl was synthesized from cyclopropylboronic acid and 21 using the methodology described in Scheme 15.

Example 145: compound n°145: (R)-3-benzyl-4-(4-(4'-dimethylamino)-[l,l'-biphenyl]-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 211 (4-(4'-dimethylamino)-[l,l'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E. Intermediate 211 was synthesized from N,N-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline using the methodology described in Scheme 15.

Example 146: compound n°146: (R)-3-benzyl-4-(4-(3'-fluoro-[l,l'-biphenyl]-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2ml (4-(3'-fluoro-[l,l'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2ml was synthesized from (3-fluorophenyl)boronic acid and 4-(2-bromophenyl)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15.

Example 147: compound n°147: (R)-3-benzyl-4-(4-(3',5'-difluoro-[l,l'-biphenyl]-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2nl (4-(3',5'-difluoro-[l,l'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E. Intermediate 2nl was synthesized from (3,5-difluorobiphenyl)boronic acid and 21 by Suzuki coupling with the conditions described in Scheme 15.

Example 148: compound n°148: (R)-3-benzyl-4-(4-(2-chloro-6-
fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates I b and commercially available 2ol (4-(2-chloro-6-fluorophenyl)thiazol-2-amine) using general method E.

Example 149: compound n°149: (R)-3-benzyl-4-((4-(4'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates I b and 2pl (4-(4'-chloro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2pl was synthesized from (4-chlorophenyl)boronic acid and 21 by Suzuki coupling with the conditions described in Scheme 15.

Example 150: compound n°150: (R)-3-benzyl-4-(methyl(4-(2-(6-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates I b and 2ql (l-(5-(2-(2-(methylamino)thiazol-4-yl)phenyl)pyrrolidin-2-one) using general method E. Intermediate 2ql was synthesized from l-(5-bromopyridin-2-yl)pyrrolidin-2-one and 21 using the methodology described in Scheme 17.

Example 151: compound n°151: (R)-3-benzyl-4-((4-(4-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates I b and 2rl (4-(4-chloro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2rl was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-4-chlorophenyl)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromo-4-chlorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.

Example 152: compound n°152: (R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates I b and 2sl (4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2sl was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-5-chlorophenyl)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromo-5-chlorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.
Example 153: compound n°153: (R)-3-benzyl-4-((4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2tl (4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2tl was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-3-fluorophenyl)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromo-3-fluorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.

Example 154: compound n°154: (3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-2-yl)methyl)butanoic acid was synthesized from intermediates 1cl and 2c using general method E.

Example 155: compound n°155: (3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-2-yl)methyl)butanoic acid was synthesized from intermediates 1b and 2ul using general method E followed by debenzylolation with FeCl₃ in DCM.

Example 156: compound n°156: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(3-hydroxypropyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2vl using general method E followed by debenzylolation with FeCl₃ in DCM.

Example 157: compound n°157: (R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2wl (4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2wl was synthesized from 5-bromo-3-chloro-2-methoxypyridine and 2i using the methodology described in Scheme 17.

Example 158: compound n°158: (R)-3-benzyl-4-((4-(2-(6-(benzyloxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2xl (4-(2-(6-(benzyloxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2xl was synthesized from (6-benzyloxy)pyridin-3-
yl)boronic acid and 21 by Suzuki coupling with the conditions described in 
Scheme 15.

**Example 159**: compound n°159: (R)-3-(cyclopentylmethyl)-4-((4-(2,5-
dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized 
from intermediates **IfI** and **2al** using general method E.

**Example 160**: compound n°160: (R)-4-(((4-(2-(6-methoxypyridin-3-
yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-
yl)methyl)butanoic acid was synthesized from intermediates **IfG** and **2c** using 
general method E.

**Example 161**: compound n°161: (R)-3-benzyl-4-((4-(2-chloro-5-
(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was 
synthesized from intermediates **Ib** and **2yl** using general method E.

**Example 162**: compound n°162: (R)-3-benzyl-4-((4-(2-chloro-5-
fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **Ib** and **2zl** using general method E.

**Example 163**: compound n°163: (R)-3-benzyl-4-((4-(3,5-dichlorophenyl)thiazol-
2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **Ib** and **2a2** using general method E.

**Example 164**: compound n°164: (R)-3-benzyl-4-((4-(3-
(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **Ib** and **2b2** using general method E.

**Example 165**: compound n°165: (R)-4-(((4-(2-chlorophenyl)thiazol-2-
yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from intermediates **IfI** and **2c** using general method E.

**Example 166**: compound n°166: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-
(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from 
intermediates **IfI** and **2w** using general method E.
Example 167: compound n°167: (R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates IgI and 2w using general method E.

Example 168: compound n°168: (R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates IgI and 2al using general method E.

Example 169: compound n°169: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2c2 (N-cyclopropyl-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2c2 was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-4-chlorophenyl)-N-cyclopropylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromo-4-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

Example 170: compound n°170: (R)-3-benzyl-4-((2-hydroxyethyl)(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2d2 (N-(2-(benzyloxy)ethyl)-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-amine) using general method E followed by debenzylation with FeCl₃ in DCM. Intermediate 2d2 was synthesized from (6-methoxypyridin-3-yl)boronic acid and N-(2-(benzyloxy)ethyl)-4-(2-bromophenyl)thiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. N-(2-(benzyloxy)ethyl)-4-(2-bromophenyl)thiazol-2-amine was synthesized using general method C.

Example 171: compound n°171: (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2dl using general method E.

Example 172: compound n°172: (R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2d3 using general method E followed by
debenzylation with \( \text{FeCl}_3 \) in DCM.

**Example 173**: compound \( \text{n}^\circ 173 \): \((R)-4-((4-(2\text{-chlorophenyl})\text{thiazol-2-yl})(\text{methyl})\text{amino})-4\text{-oxo}-3-((\text{tetrahydro}-2\text{H}\text{-pyran-4-yl})\text{methyl})\text{butanoic acid was synthesized from intermediates IgI and 2c using general method E.}

**Example 174**: compound \( \text{n}^\circ 174 \): \((R)-3\text{-benzyl-4-}((4-(2\text{-chloro-5-}(\text{trifluoromethyl})\text{phenyl})\text{thiazol-2-yl})(\text{methyl})\text{amino})-4\text{-oxobutanoic acid was synthesized from intermediates Ib and 2e2 using general method E.}

**Example 175**: compound \( \text{n}^\circ 175 \): \((R)-3\text{-benzyl-4-}(\text{methyl}(4-(2,3,5\text{-trichlorophenyl})\text{thiazol-2-yl})\text{amino})-4\text{-oxobutanoic acid was synthesized from intermediates Ib and 2f2 using general method E.}

**Example 176**: compound \( \text{n}^\circ 176 \): \((R)-3\text{-benzyl-4-}((4-(4\text{-chloro-}[1,1\text{-biphenyl}]\text{-3-yl})\text{thiazol-2-yl})(\text{methyl})\text{amino})-4\text{-oxobutanoic acid was synthesized from intermediates Ib and 2g2 (4-(4-chloro-[1,1\text{-biphenyl}]\text{-3-yl})\text{N-methylthiazol-2-amine) using general method E. Intermediate 2g2 was synthesized from phenylboronic acid and 4-(5-bromo-2-chlorophenyl)\text{-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(5-bromo-2-chlorophenyl)\text{-N-methylthiazol-2-amine was synthesized using general method C.}

**Example 177**: compound \( \text{n}^\circ 177 \): \((R)-3\text{-benzyl-4-}((4-(2\text{-chloro-5-(6\text{-methoxypyridin-3-yl})phenyl})\text{thiazol-2-yl})(\text{methyl})\text{amino})-4\text{-oxobutanoic acid was synthesized from intermediates Ib and 2h2 (4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)\text{-N-methylthiazol-2-amine) using general method E. Intermediate 2h2 was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(5-bromo-2-chlorophenyl)\text{-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(5-bromo-2-chlorophenyl)\text{-N-methylthiazol-2-amine was synthesized using general method C.}

**Example 178**: compound \( \text{n}^\circ 178 \): \((R)-3\text{-benzyl-4-}(\text{cyclopropyl}(4-(2-(6\text{-methoxypyridin-3-yl})\text{phenyl})\text{thiazol-2-yl})\text{amino})-4\text{-oxobutanoic acid was synthesized from intermediates Ib and 2c2 using general method E.}
Example 179: compound n°179: (R)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates IgI and 2c2 using general method E.

Example 180: compound n°180: (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2i2 (N-cyclopropyl-4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2i2 was synthesized from 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)morpholine and 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

Example 181: compound n°181: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2i2 using general method E.

Example 182: compound n°182: (R)-3-benzyl-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2j2 (N-methyl-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2j2 was synthesized from commercially available 7-bromo-4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazine and 21 using the methodology described in Scheme 17.

Example 183: compound n°183: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyrindin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2k2 (l-(5-(2-(cyclopropylamino)thiazol-4-yl)phenyl)pyrrolidin-2-one) using general method E. Intermediate 2k2 was synthesized from l-(5-bromopyridin-2-yl)pyrrolidin-2-one and 4-(2-bromo-4-chlorophenyl)-N-cyclopropylthiazol-2-amine using the methodology described in Scheme 17. l-(5-bromopyridin-2-
yl)pyrrolidin-2-one was synthesized by reacting 5-bromopyridin-2-amine with Na$_2$HPO$_4$ in CHCl$_3$, 4-bromobutyryl chloride and NaOMe in MeOH as described in *Tetrahedron* 1957, 1, 9635. 4-(2-bromo-4-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

**Example 184:** compound n°184: (R)-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates IgI and 2i2 using general method E.

**Example 185:** compound n°185: (R)-3-benzyl-4-(methyl(4-(2-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 212 using general method E.

**Example 186:** compound n°186: (R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from intermediates Ib and 2m2 using general method E and preparative HPLC purification.

**Example 187:** compound n°187: (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2q1 using general method E.

**Example 188:** compound n°188: (R)-3-benzyl-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2n2 using general method E and preparative HPLC purification.

**Example 189:** compound n°189: (R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2m2 using general method E and preparative HPLC purification.

**Example 190:** compound n°190: (R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
was synthesized from intermediates IgI and 2m2 using general method E and preparative HPLC purification.

Example 191: compound n°191: (R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2o2 using general method E and preparative HPLC purification.

Example 192: compound n°192: (R)-3-benzyl-4-((4-(2-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2c4 using general method E.

Example 193: compound n°193: (R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates IgI and 2o2 using general method E.

Example 194: compound n°194: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyridin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2p2 (N-cyclopropyl-4-(2-(4-methyl-3,4-dihydro-2H-pyridin-7-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2p2 was synthesized from commercially available 7-bromo-4-methyl-3,4-dihydro-2H-pyridin-2-amine and 2q2 using the methodology described in Scheme 17. 4-(2-bromo-4-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

Example 195: compound n°195: (3R,4S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid was synthesized from intermediates IhI and 2c using general method E.

Example 196: compound n°196: (R)-2-(2-benzyl-3-carboxypropanamido)-5-(2-chlorophenyl)pyridine 1-oxide was synthesized from intermediates Ib and 2q2 (2-amino-5-(2-chlorophenyl)pyridine) using general method E followed by oxidation with MCPBA. 2q2 was made from commercially available 5-bromopyridin-2-
amine and (2-chlorophenyl)boronic acid using Suzuki coupling.

**Example 197**: compound n°197: (R)-3-benzyl-4-((5-(2-chlorophenyl)pyrazin-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2r2 (5-(2-chlorophenyl)pyrazin-2-amine) using general method E. 2r2 was made from commercially available 5-bromopyrazin-2-amine and (2-chlorophenyl)boronic acid using Suzuki coupling.

**Example 198**: compound n°198: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(morpholinomethyl)-4-oxobutanoic acid was synthesized as described in Scheme 18.

**Example 199**: compound n°199: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxyethyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2s2 using general method E.

**Example 200**: compound n°200: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylamino)-4-oxobutanoic acid was synthesized from intermediates IjI ((R)-4-(fert-butoxy)-2-(cyclopentylamino)-4-oxobutanoic acid) and 2c using general method E. IjI was made from (R)-2-amino-4-(te/t-butoxy)-4-oxobutanoic acid and cyclopentanone by reductive amination using sodium cyanoborohydride in methanol.

**Example 201**: compound n°201: (R)-3-benzyl-4-((2-(benzyloxy)ethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2ul using general method E.

**Example 202**: compound n°202: (R)-3-benzyl-4-((4-(5-methylfuran-2-yl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2u2 (4-(5-methylfuran-2-yl)thiazol-2-amine) using general method E.

**Example 203**: compound n°203: (R)-3-benzyl-4-oxo-4-((3-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)amino)butanoic acid was synthesized from intermediates 1b and commercially available 2v2 (3-(3-
Example 204: compound n°204: (R)-3-benzyl-4-((4-(5-chloro-2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2w2 (4-(5-chloro-2-methoxyphenyl)thiazol-2-amine) using general method E.

Example 205: compound n°205: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-hydroxybenzyl)-4-oxobutanoic acid was synthesized from intermediates IkI (4-(?ert-butoxy)-2-(4-(methoxymethoxy)benzyl)-4-oxobutanoic acid) and 2c using general method E, the MOM group was deprotected with TFA in DCM. IkI was synthesized from A-(methoxymethoxy)benzaldehyde using the HWE methodology (Scheme 13).

Example 206: compound n°206: (R)-3-benzyl-4-((4-(4'-cyano-[l,l'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2x2 (2'-(2-(methylamino)thiazol-4-yl)-[l,l'-biphenyl]-4-carbonitrile) using general method E. Intermediate 2x2 was synthesized from (4-cyanophenyl)boronic acid and 21 by Suzuki coupling with the conditions described in Scheme 15.

Example 207: compound n°207: (3R)-3-benzyl-4-((3-carbamoyl-4-(2,4-dichlorophenyl)-5-methylthiophen-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2y2 (2-amino-4-(2,4-dichlorophenyl)-5-methylthiophene-3-carbonitrile) using general method E.

Example 208: compound n°208: (R)-3-benzyl-4-((4-(3'-methoxy-[l,l'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2z2 (4-(3'-methoxy-[l,l'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E. Intermediate 2z2 was synthesized from (3-methoxyphenyl)boronic acid and 21 by Suzuki coupling with the conditions described in Scheme 15.

Example 209: compound n°209: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid was
synthesized from intermediates 111 (4-(te/t-butoxy)-2-((2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid) and 2c using general method E. III was synthesized from 2-methylthiazole-5-carbaldehyde using the HWE methodology (Scheme 13).

Example 210: compound n°210: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid was synthesized from intermediates ImI (4-(te/t-butoxy)-2-((5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid) and 2c using general method E. ImI was synthesized from 5-methylisoxazole-3-carbaldehyde using the HWE methodology (Scheme 13).

Example 211: compound n°211: (R)-3-benzyl-4-((4-(2'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2a3 (4-(2'-chloro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate 2a3 was synthesized from (2-chlorophenyl)boronic acid and 21 by Suzuki coupling with the conditions described in Scheme 15.

Example 212: compound n°212: (R)-3-benzyl-4-((4-(2-(2-methoxypyrimidin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2b3 (4-(2-(2-methoxypyrimidin-5-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2b3 was synthesized from 5-bromo-2-methoxypyrimidine and 21 using the methodology described in Scheme 17.

Example 213: compound n°213: (R)-3-benzyl-4-((4-(2,5-difluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 2c3 (4-(2,5-difluorophenyl)thiazol-2-amine) using general method E.

Example 214: compound n°214: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(oxazol-4-ylmethyl)-4-oxobutanoic acid was synthesized from intermediates ImI (4-(?ert-butoxy)-2-(oxazol-4-ylmethyl)-4-oxobutanoic acid) and 2c using general method E. ImI was synthesized from oxazole-4-
carbaldehyde using the **HWE** methodology (Scheme 13).

**Example 215:** compound n°215: (3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-3-yl)methyl)butanoic acid was synthesized from intermediates \( \text{lol} \) and 2c using general method E.

**Example 216:** compound n°216: (R)-3-benzyl-4-(methyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2e3 (1-methyl-6-(2-(methylamino)thiazol-4-yl)phenyl)-3,4-dihydro-1,8-naphthyridin-2(1H)-one) using general method E.

Intermediate 2e3 was synthesized from 6-bromo-1-methyl-3,4-dihydro-1,8-naphthyridin-2(1H)-one (which was obtained by treatment of 6-bromo-3,4-dihydro-1,8-naphthyridin-2(1H)-one with NaH in DMF and MeI) and 21 using the methodology described in Scheme 17. Intermediate 1b was synthesized using the **HWE** methodology (Scheme 13):

38.125 mmol of (E)-2-benzylidene-4-(tert-butoxy)-4-oxobutanoic acid, 75 mL of methanol and 38.125 mmol of DCA were successively introduced into a Schlenck tube under Ar. The solution was degassed using three argon/vacuum cycles, and subsequently transferred into the reaction vessel under inert atmosphere. To this degassed solution was added, under argon flow, 0.121 mmol of the RuCl\(_2\)-L(S)-BINAP] catalyst. The reaction vessel was then transferred into a Parr autoclave, under Ar flow. The Parr vessel was purged 3 times with H\(_2\) with a pressure up to 20 sbars; the pressure was then adjusted to 10 bars. The Parr autoclave was put into an oil bath at 55°C. The reaction mixture was stirred at this temperature for 3 days. The reaction mixture was allowed to cool to RT and the hydrogen pressure was released carefully and the Parr vessel opened. The crude reaction mixture was concentrated to dryness using rotary evaporator to afford 16.74 g of a colored solid. An aliquot of the solid was diluted with water and acidified with HCl 6N to pH 1; then, the solution was extracted with EtOAc. The organic layer was dried over magnesium sulfate, concentrated using rotary evaporator to yield the desired intermediate (ee= 82.6%, determined by chiral HPLC).
Solid (16.74 g) was recrystallized from an ACN/water mixture. Recrystallized product was diluted with water and acidified with 6N HCl to pH 1, the solution was extracted with EtOAc. The organic layer was dried over magnesium sulfate, concentrated at rotavap to yield the desired intermediate Ib (ee= 96.6%, determined by chiral HPLC).

**Example 217**: compound n°217: (R)-3-benzyl-4-(methyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2f3 (N-methyl-4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-amine) using general method E. Intermediate 2f3 was synthesized from 5-bromo-1-methyl-1H-pyrrolo[2,3-b]pyridine (which was obtained by treatment of 5-bromo-1H-pyrrolo[2,3-b]pyridine with NaH in DMF and MeI) and 21 using the methodology described in Scheme 17.

**Example 218**: compound n°218: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IfI and 2g3 (N-cyclopropyl-4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-amine) using general method E and preparative HPLC purification. 2g3 was synthesized from 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine and 6-(dimethylamino)pyridin-3-ylboronic acid by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

**Example 219**: compound n°219: (R)-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from intermediates IfI and 2h3 (4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)-N-cyclopropylthiazol-2-amine) using general method E. 2g3 was synthesized from 5-bromo-3-chloro-2-methoxypyridine and A-(2-bromophenyl)-N-cyclopropylthiazol-2-amine using the methodology described in Scheme 17. 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.
Example 220: compound n°220: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates $\text{Iff}$ and 2i3 (N-cyclopropyl-4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-amine) using general method E. 2i3 was synthesized from 5-bromo-3-fluoro-2-methoxypyridine and 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine using the methodology described in Scheme 17. 4-(2-bromophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

Example 221: compound n°221: (R)-3-benzyl-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2j3 using general method E.

Example 222: compound n°222: (R)-3-benzyl-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2k3 (4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. 2k3 was synthesized from 5-bromo-3-chloro-2-methoxypyridine and 4-(2-bromo-5-chlorophenyl)-N-methylthiazol-2-amine using the methodology described in Scheme 17. 4-(2-bromo-5-chlorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.

Example 223: compound n°223: (R)-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from intermediates $\text{Iff}$ and 213 (4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)-N-cyclopropylthiazol-2-amine) using general method E. 213 was synthesized from 5-bromo-3-chloro-2-methoxypyridine and 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine using the methodology described in Scheme 17. 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.
Example 224: compound n°224: (R)-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from intermediates IfI and 2m3 (4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)-N-cyclopropylthiazol-2-amine) using general method E. 2m3 was synthesized from 5-bromo-3-fluoro-2-methoxypyridine and 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine using the methodology described in Scheme 17. 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

Example 225: compound n°225: (S)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates IPI ((S)-2-benzyl-4-(tert-butoxy)-4-oxobutanoic acid) and 2a using general method E. IPI was synthesized from (S)-3-benzyl-4-methoxy-4-oxobutanoic acid using the chemistry described in steps 5 and 6 of general method B.

Example 227: compound n°227: (R)-3-benzyl-4-((4-benzylthiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available 4-benzylthiazol-2-amine using general method E.

Example 229: compound n°229: (R)-3-benzyl-4-oxo-4-((5-phenyl-4H-1,2,4-triazol-3-yl)amino)butanoic acid was synthesized from intermediates 1b and commercially available 5-phenyl-4H-1,2,4-triazol-3-amine using general method E.

Example 230: compound n°230: 3-([I',l'-biphenyl]-4-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates IQI (2-([I',l'-biphenyl]-4-ylmethyl)-4-(tert-butoxy)-4-oxobutanoic acid) and 2c using general method E. IQI was synthesized from [I',l'-biphenyl]-4-carbaldehyde using the HWE methodology described in Scheme 13.
Example 231: compound n°231: (R)-3-benzyl-4-((4-(1-methyl-1H-pyrazol-4-yl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and commercially available 4-(1-methyl-1H-pyrazol-4-yl)thiazol-2-amine using general method E.

Example 232: compound n°232: ((R)-3-benzyl-4-((4-(4-methyl-1,2,5-oxadiazol-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and commercially available 4-(4-methyl-1,2,5-oxadiazol-3-yl)thiazol-2-amine using general method E.

Example 233: compound n°233: (R)-3-benzyl-4-(methyl(4-(2-(1-methyl-1H-pyrazol-4-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2n3 (N-methyl-4-(2-(1-methyl-1H-pyrazol-4-yl)phenyl)thiazol-2-amine) using general method E. 2n3 was synthesized from commercially available l-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and 21 using the methodology described in Scheme 15.

Example 234: compound n°234: (3R)-3-benzyl-4-((4-(2-(3,5-dimethylisoxazol-4-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2o3 (4-(2-(3,5-dimethylisoxazol-4-yl)phenyl)-N-methylthiazol-2-amine) using general method E. 2o3 was synthesized from commercially available 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoxazole and 21 using the methodology described in Scheme 15.

Example 235: compound n°235: (R)-3-benzyl-4-((4-((2-chlorophenyl)carbamoyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2p3 using general method E and preparative HPLC purification. 2p3 was synthesized as described in Scheme 21.

Example 236: compound n°236: (R)-3-benzyl-4-((6-(2-chlorophenyl)pyridazin-3-yl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2q3 (6-
(2-chlorophenyl)pyridazin-3-amine) using general method E. 2q3 was synthesized from 6-bromopyridazin-3-amine and 2-chlorophenylboronic acid by Suzuki coupling with the conditions described in **Scheme 8**.

**Example 237**: compound n°237: (R)-3-benzyl-4-((methyl(4-(2-oxopyrrolidin-1-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2r3 (l-(2-(2-(methylamino)thiazol-4-yl)phenyl)prrrolidin-2-one) using general method E. 2r3 was synthesized as described in **Scheme 16**.

**Example 238**: compound n°238: (S)-2-((l-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-l-oxo-3-phenylpropan-2-yl)oxy)acetic acid was synthesized as described in **Scheme 22**.

**Example 239**: compound n°239: (R)-3-benzyl-4-((l-methyl-5-phenyl-lH-imidazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and commercially available l-methyl-5-phenyl-lH-imidazol-2-amine using general method E.

**Example 240**: compound n°240: (R)-3-benzyl-4-((4-(2-((l-(2-methoxyethyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2s3 (l-(2-methoxyethyl)-5-(2-(2-(methylamino)thiazol-4-yl)phenyl)pyridin-2(lH)-one) using general method E. 2s3 was synthesized from 5-bromo-l-(2-methoxyethyl)pyridin-2(lH)-one and 21 using the methodology described in **Scheme 17**.

**Example 241**: compound n°241: (R)-3-benzyl-4-((methyl(4-(2-((l-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2t3 (l-methyl-5-(2-(methylamino)thiazol-4-yl)phenyl)pyridin-2(lH)-one) using general method E. 2t3 was synthesized from 5-bromo-l-methylpyridin-2(lH)-one and 21 using the methodology described in **Scheme 17**.
Example 242: compound n°242: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoic acid was synthesized from intermediates IrI (tert-butyl 4-amino-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoate) and 2c using general method E. IrI was synthesized from 2,5-dimethyloxazole-4-carbaldehyde using the HWE methodology described in Scheme 13.

Example 243: compound n°243: 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid was synthesized from intermediates IsI (4-(te/t-butoxy)-2-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid) and 2c using general method E. IsI was synthesized from 1-methyl-1H-pyrazole-5-carbaldehyde using the HWE methodology described in Scheme 13.

Example 244: compound n°244: (R)-3-benzyl-4-((4-(2-(6-hydroxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized by debenzylation of compound n°158 with FeCl3 in DCM and preparative HPLC purification.

Example 245: compound n°245: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((S)-2-hydroxypropyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2w3 using general method E and preparative HPLC purification.

Example 246: compound n°246: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((R)-2-hydroxypropyl)amino)-4-oxobutanoic acid was synthesized from intermediates Ib and 2w3 using general method E and preparative HPLC purification.

Example 247: compound n°247: (R)-3-(cyclohexylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was
synthesized from intermediates 1w and 2c2 using general method E and preparative HPLC purification.

**Example 248**: compound n°248: (R)-3-benzyl-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2u3 (4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2u3 was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-5-fluorophenyl)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromo-5-fluorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.

**Example 250**: compound n°250: (R)-3-benzyl-4-((4-(4,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates 1b and 2x3 (4-(4,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate 2x3 was synthesized from (6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-4,5-difluorophenyl)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in Scheme 15. 4-(2-bromo-4,5-difluorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.

**Example 251**: compound n°251: (R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid was synthesized from intermediates 1t1 and 2al using general method E.

**Example 252**: compound n°252: (R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid was synthesized from intermediates 1t1 and 2zl using general method E.

**Example 253**: compound n°253: (R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was
synthesized from intermediates \textit{Ii} and 2m using general method E.

\textbf{Example 254}: compound \textnumero 254: \((S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid was synthesized from intermediates \textit{Ii} and 2c using general method E.

\textbf{Example 255}: compound \textnumero 255: \((R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid was synthesized from intermediates I\textsubscript{b} and 2y3 \((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-N-cyclopropylthiazol-2-amine) using general method E. Intermediate 2y3 was synthesized from \((6-methoxypyridin-3-yl)boronic acid and 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine by Suzuki coupling with the conditions described in \textbf{Scheme 15}. 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

\textbf{Example 256}: compound \textnumero 256: \((R)-3-benzyl-4-(cyclopropyl(4-(2-(6-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates I\textsubscript{b} and 2k2 using general method E.

\textbf{Example 257}: compound \textnumero 257: \((R)-3-benzyl-4-((4-(2,3-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates I\textsubscript{b} and 2z3 using general method E.

\textbf{Example 258}: compound \textnumero 258: \((R)-3-benzyl-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates I\textsubscript{b} and 2a4 using general method E.

\textbf{Example 259}: compound \textnumero 259: \((R)-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates IgI and 2n2 using
Example 260: compound n°260: \( (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic \) acid was synthesized from intermediates \text{ItI} \text{ and } 2c \text{ using general method E.}

Example 261: compound n°261: \( (R)-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic \) acid was synthesized from intermediates \text{IgI} \text{ and } 2a4 \text{ using general method E.}

Example 262: compound n°262: \( (R)-3-benzyl-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic \) acid was synthesized from intermediates \text{1b} \text{ and } 2b4 \text{ using general method E.}

Example 263: compound n°263: \( (R)-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic \) acid was synthesized from intermediates \text{IgI} \text{ and } 2b4 \text{ using general method E.}

BIOLOGY EXAMPLES

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 represents the effect of compound 9 on glucose-uptake measured in 3T3-L1 adipocyte cells in response to 10nM of insulin.

Figure 2 represents the effect of compound 9 on glucose-uptake measured in adipocytes isolated from High-fat diet fed mice.

Figure 3 represents the effect of compound 9 on isoprenaline-induced lipolysis in adipocytes from high-fat diet fed mice.

Figure 4 represents the inhibition of \textit{in-vivo} lipolysis following the injection of compound 2 in mice.
Figure 5 represents the inhibition of in-vivo lipolysis following the injection of compound 9 in mice.

Figure 6 represents the effect of compound 89 on isoprenaline-induced lipolysis in adipocytes isolated from normal rats.

Figure 7 represents the effect of compounds 14, 89, 126, 139, 142, 155, 169 and 183 on isoprenaline-induced lipolysis in adipocytes isolated from normal rats.

Figure 8 represents the inhibition of in-vivo lipolysis following the injection of compound 14, 169 or 183 in mice.

Figure 9 represents the effect of compound 169 on the GLP-I release from NCI-H716 cells.

Membrane binding assay: GTPγS binding assay.
The following assay can be used for determination of GPR43 activation. When a GPCR is in its active state, either as a result of ligand binding or constitutive activation, the receptor couples to a G protein and stimulates the release of GDP and subsequent binding of GTP to the G protein. The alpha subunit of the G protein-receptor complex acts as a GTPase and slowly hydrolyses the GTP to GDP, at which point the receptor normally is deactivated. Activated receptors continue to exchange GDP for GTP. The non-hydrolysable GTP analog, [35S]GTPγS, was used to demonstrate enhance binding of [35S]GTPγS to membranes expressing receptors. The assay uses the ability of GPCR to stimulate [35S]GTPγS binding to membranes expressing the relevant receptors. The assay can, therefore, be used in the direct identification method to screen candidate compounds to endogenous or not endogenous GPCR.

Preparation of membrane extracts:
Membrane extracts were prepared from cells expressing the human GPR43 receptor (hGPR43) as follows: the medium was aspirated and the cells were scraped from the plates in Ca++ and Mg++-free Phosphate-buffered saline (PBS). The cells were then centrifuged for 3 min at 1500 g and the pellets were resuspended in buffer A (15 mM Tris-HCl pH 7.5, 2 mM MgCl₂, 0.3 mM EDTA, 1 mM EGTA) and homogenized in a glass homogenizer. The crude membrane fraction was collected by two consecutive centrifugation steps at 40,000 x g for 25 min separated by a washing step in buffer A. The final pellet was resuspended in 500 µl of buffer B (75 mM Tris-HCl pH 7.5, 12.5 mM MgCl₂, 0.3 mM EDTA,
ImM EGTA, 250 nM sucrose) and flash frozen in liquid nitrogen. Protein content was assayed by the Folin method.

GTPγS assay (SPA method):

The assay was performed in the presence of SCFA, and was used to determine the activity of the compounds of the invention. The [35S]GTPγS assay was incubated in 20 mM HEPES pH7.4, 100 mM NaCl, 10 µg/ml saponin, 30 mM of MgCl2, 10 µM of GDP, 5 µg membrane-expressing hGPR43, 250µg of wheatgerm agglutinin beads (Amersham, ref: RPNQ001), a range concentration of compounds (from 30 µM to 1 nM) in a final volume of 100 µl for 30 min at room temperature. The SCFA propionate was used at 1 mM final concentration as positive control. The plates were then centrifuged for 10 minutes at 2000 rpm, incubated for 2 hours at room temperature and counted for 1 min in a scintillation counter (TopCount, PerkinElmer). The results of the tested compounds are reported as the concentration of the compound required to reach 50% (EC50) of the maximum level of the activation induced by these compounds.

When tested in the assay described above and by way of illustration the compounds in Table 3 activate GPR43 receptor with an EC50 ranging from 13 nM to 2910 nM.

Table 3: Compounds EC50 values in GTPγ35S assay.

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<thead>
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<th>Compound n°</th>
<th>EC50 (nM)</th>
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Cell based assay: Calcium flux. The Aequorin-based assay
The following assay can be used for determination of GPR43 activation. The aequorin assay uses the responsiveness of mitochondrial apoaequorin to intracellular calcium release induced by the activation of GPCRs (Stables et al., 1997, Anal. Biochem. 252:115-126; Detheux et al., 2000, J. Exp. Med., 192 1501-1508). Briefly, GPCR-expressing clones are transfected to coexpress mitochondrial apoaequorin and Gαδ6. Cells expressing GPR43 receptor are incubated with 5 μM Coelenterazine H (Molecular Probes) for 4 hours at room temperature, washed in DMEM-F12 culture medium and resuspended at a
concentration of 0.5 x 10^6 cells/ml (the amount can be changed for optimization). Cells are then mixed with test compounds and light emission by the aequorin is recorded with a luminometer for 30 sec. Results are expressed as Relative Light Units (RLU). Controls include assays using cells not expressing GPR43 (mock transfected), in order to exclude possible non-specific effects of the candidate compound.

Aequorin activity or intracellular calcium levels are "changed" if light intensity increases or decreases by 10% or more in a sample of cells, expressing a GPR43 and treated with a compound of the invention, relative to a sample of cells expressing the GPR43 but not treated with the compound of the invention or relative to a sample of cells not expressing the GPR43 (mock-transfected cells) but treated with the compound of the invention.

**Cell based assay: Intracellular Inositol-Phosphate accumulation assay. (Gq-associated receptor)**

The following assay can be used for determination of GPR43 activation. On day 1, GPR43-expressing cells in mid-log phase are detached with PBS-EDTA, centrifuged at 2000 x g for 2 min and resuspended in medium without antibiotics. After counting, cells are resuspended at 4 x 10^5 cells/ml (the amount can be changed for optimization) in medium without antibiotics, distributed in a 96 well plate (100 µl/well) and the plate is incubated overnight at 37°C with 5% CO₂. On day 2, the medium is removed and the compounds of the invention, at increasing concentrations, are added (24 µl/well) and the plate is incubated for 30 min. at 37°C in a humidified atmosphere of 95% air with 5% CO₂. The IPl concentrations are then estimated using the IPl-HTRF assay kit (Cisbio international, France) following the manufacturer recommendations.

**Cell based assay: cAMP accumulation assay (G_{i/o} associated receptor)**

The following assay can be used for determination of GPR43 activation. Cells expressing GPR43 in mid-log phase and grown in media without antibiotics are detached with PBS-EDTA, centrifuged and resuspended in media without antibiotics. Cells are counted and resuspended in assay buffer at 4.2 x 10^5 cells/ml. 96 well plates are filled with 12 µl of cells (5 x 10^3 cells/well), 6 µl of compound
of the invention at increasing concentrations and 6 µl of Forskolin (final concentration of 10 µM). The plate is then incubated for 30 min. at room temperature. After addition of the lysis buffer, cAMP concentrations are estimated, according to the manufacturer specification, with the HTRF kit from Cis-Bio International.

**In vitro assays to assess compound activity in 3T3-L1 cell line**

3T3-L1 adipocytes cell line has been described as cellular model to assess compounds mimicking insulin-mediated effect such as inhibition of lipolysis and activation of glucose uptake.

**Lipolysis.**

3T3-L1 cells (ATCC) are cultured in Dulbecco's modified eagle's medium (DMEM) containing 10% (v/v) bovine serum (fresh regular medium) in 24 well plate. On day 0 (2 days after 3T3-L1 preadipocytes reached confluence), cells are induced to differentiate by insulin (10 µg/ml), IBMX (0.5 mM) and dexamethasone (1 µM). On day 3 and every other 3rd day thereafter, fresh regular medium is substituted until day 14. On day 14, the medium is removed and cells are washed twice with 1 ml of a wash buffer (Hank's balanced salt solution). The wash solution is removed and the SCFA or the compounds of the invention, or a combination of both, are added at the desired concentration in Hank's buffer supplemented with 2% BSA-FAF and incubated for 10 minutes at 37°C. Then, isoproterenol (100 nM) is added to induce lipolysis and incubate for 30 minutes at 37°C. The supernatants are collected in a glycerol-free container. 25 µl (the amount can be changed for optimization) of cell-free supernatants are dispensed in 96-well microtiter plate, 25 µl of free glycerol assay reagent (Chemicon, the amount can be changed for optimization) is added in each well and the assay plate is incubated for 15 minutes at room temperature. The absorbance is recorded with a spectrophotometer at 540 or 560 nm. Using the supernatants, the free fatty acids amount can be assessed using the NEFA assay kit (Wako) according the manufacturer's recommendations.

**Glucose Uptake.**

3T3-L1 cells are differentiated as described previously with or without of 30 µM
of compound of the invention (the concentration can be changed for optimization) during the 14 days of differentiation. The day of the experiment, the cells are washed twice with a KREBS-Ringer bicarbonate (pH 7.3) supplemented with 2 mM sodium pyruvate and starved for 30 minutes in the same buffer at 37°C in an atmosphere containing 5% CO2 and 95% O2. Various amount of SCFA, compounds of the invention or combination of both are then added with or without 10 nM of insulin (the amount can be changed for optimization) for 30 minutes at 37°C in an atmosphere containing 5% CO2 and 95% O2. Then, D-(3H)-2 deoxyglucose (0.2 µCi/well) and D-2-deoxyglucose (0.1 mM) is added for 30 minutes. To stop the reaction, the cells are immersed in ice-cold saline buffer, washed for 30 min, and then dissolved in NaOH 1 M at 55°C for 60 minutes. NaOH is neutralized with HCl 1 M. The 3H labeled radioactivity of an aliquot of the extract is counted in the presence of a scintillation buffer.

When tested in the glucose-uptake assay described above and by way of illustration the compound n^0 9 significantly increases the glucose-uptake in response to 10nM of insulin (Figure 1).

It is important to note that in the above-mentioned assay the positive allosteric modulators (PAMs) disclosed in Lee et al., (MoI. Pharmacol. 74(6) pp 1599-1609, 2008) do not increase the glucose uptake. This lack of effect on glucose uptake could be explained by the weak affinity (~1 µM) of the PAMs disclosed by Lee et al.

**In vitro assays to assess compound activity in NCI-H716 cell line**

Human intestinal cell line NCI-H716 has been described as cellular model to assess compounds mimicking nutrient-mediated effect such as glucagon-like peptide-1 (GLP-I) secretion.

**GLP-I release.**

NCI-H716 cells (ATCC, Manassas) are cultured in Dulbecco’s modified eagle’s medium (DMEM) containing 10% (v/v) bovine serum, 2 mM L-glutamine, 100 IU/ml penicillin and 100 µg/ml streptomycin in 75 ml flask. Cell adhesion and endocrine differentiation is initiated by growing cells in 96-well plate coated with matrigel in High Glucose DMEM containing 10% (v/v) bovine serum, 2 mM L-glutamine, 100 IU/ml penicillin and 100 µg/ml streptomycin for 2 days.

On day 2, the medium is removed and cells are washed once with a pre-warmed
wash buffer (Phosphate Buffered salt solution). The wash solution is removed and
the SCFA or the compounds of the invention, or a combination of both, are added
at the desired concentration in High Glucose DMEM containing 0.1% (v/v)
bovine serum and incubated for 2 hours at 37°C. The supernatants are collected in
a container. Using the cell-free supernatants, the GLP-I amount is assessed using
a GLP-I specific ELISA assay kit according the manufacturer’s recommendations
(ALPCON).

When tested in the GLP-I release assay described above and by way of
illustration the compound n0 169 significantly increases the GLP-I secretion from
NCI-H7 I6 cells (Figure 9).

**Ex vivo assays to assess compound activity in adipocytes from normal and
High-fat diet fed mice**

Mice C56Black6 male were housed in Makrolon type IV group housing cages (56
x 35 x 20 cm3) throughout the experimental phase. Animals' cages litters were
changed once a week. They were housed in groups of 10 animals at 12 light dark
(at 8h30 pm lights off), 22 +/- 2 °C and 50 +/- 5 % relative humidity. Animals
were acclimated one week. During the whole phase, standard diet or diet high in
energy from fat (Research Diets, New Brunswick, NJ) and tap water were
provided *ad libitum*. The animals were 16 weeks old at the time of the study.

For keeping only mice that have responded to the high fat diet, fasted glycemia
was measured in these mice just before performing the ex-vivo study.

**Glucose uptake assay in isolated adipocytes.**

Animals were killed by cervical dislocation and epididymal fat pads were
removed and digested in collagenase buffer at 37°C/120rpm for approximately 50
minutes. The digest was filtered through gauze to recover the adipocytes, which
were washed and resuspended in Krebs-Ringer Hepes (KRH) buffer containing
1% BSA, 20OnM adenosine and 2mM glucose.

Isolated adipocytes were washed in glucose-free KRH-buffer and resuspended to
30%. Adipocytes were then incubated at 37°C/80 rpm with either compound of
the invention (30µM, 1µM and 1µM) in the presence or absence of insulin
(10nM) for 30 min. 2-deoxyglucose and 2-deoxy-D-[l- ³H]-glucose (³H-2-DOG)
were added and incubation continued for 10 min. The reactions were then stopped
by addition of cytochalasin B followed by centrifugation through dinonylphthalate to recover the adipocytes. The uptake of $^3$H-2-DOG- was measured by scintillation. Each data point was investigated in triplicates in two independent experiments.

When tested in the assay described above and by way of illustration the compound n°9 significantly increase the glucose uptake in adipocytes isolated from High-fat diet fed mice (Figure 2).

Lipolysis assay in isolated adipocytes.

Isolated adipocytes were diluted to 5% in KRH-buffer and were pre-treated with compound of the invention (30µM, 10µM and 1µM) for 30 min at 37°C/120rpm. After the pre-treatment, Isoprenaline (1µM) was added to the adipocytes followed by 30 min incubation at 37 °C/150 rpm. The reactions were put on ice and the buffer was assayed spectrophotometrically for the production of NADH+ from glycerol breakdown in reactions catalyzed by glycerol kinase and glycerol-3-phosphate dehydrogenase and/or Non Esterified Fatty Acid (NEFA). Each data point was investigated in triplicates in two independent experiments.

According to the method described above and by way of illustration the compound n°9 dose-dependently inhibits isoprenaline-induced lipolysis in adipocytes from high-fat diet fed mice (Figure 3).

Compounds n° 14, 89, 126, 139, 142, 155, 169 and 183 inhibit isoprenaline-induced lipolysis in adipocytes isolated from normal rats according to the method described above (Figures 6 and 7).

It is important to note that in the above-mentioned assay the positive allosteric modulators (PAMs) disclosed in Lee et al., (MoI. Pharmacol. 74(6) pp 1599-1609, 2008) do not display an anti-lipolytic effect on rat adipocytes. This lack of effect could be explained by the weak affinity (~1µM) of the PAMs disclosed by Lee et al.
**In vivo** assay to assess compound activity in rodent diabetes model

**Genetic rodent models:**
Rodent models of T2D associated with obesity and insulin resistance have been developed. Genetic models such as db/db and ob/ob in mice and fa/fa in Zucker rats have been developed for understanding the pathophysiology of disease and testing candidate therapeutic compounds as compound of the invention. The homozygous animals, C57 Black/6-db/db mice developed by Jackson Laboratory are obese, hyperglycemic, hyperinsulinemic and insulin resistant ([J Clin Invest, 1990, 85:962-967](#)), whereas heterozygotes are lean and normoglycemic. In the db/db model, mice progressively develop insulinopenia with age, a feature commonly observed in late stages of human T2D when sugar levels are insufficiently controlled. Since this model resembles that of human T2D, the compounds are tested for activities including, but not limited to, lowering of plasma glucose and triglycerides. Zucker (fa/fa) rats are severely obese, hyperinsulinemic, and insulin resistant, and the fa/fa mutation may be the rat equivalent of the murine db mutation.

Genetically altered obese diabetic mice (db/db) (male, 7-9 weeks old) are housed under standard laboratory conditions at 22°C and 50% relative humidity, and maintained on a diet of Purina rodent chow and water *ad libitum*. Prior to treatment, blood is collected from the tail vein of each animal and blood glucose concentrations are determined using one touch basic glucose monitor system (Lifescan). Mice that have plasma glucose levels between 250 to 500 mg/dl are used. Each treatment group consists of several mice that are distributed so that the mean of glucose levels are equivalent in each group at the start of the study. Db/db mice are dosed by micro-osmotic pumps, inserted using isoflurane anesthesia, to provide compounds of the invention, saline, or an irrelevant compound to the mice intravenously (i.v). Blood is sampled from the tail vein at intervals thereafter and analyzed for blood glucose concentrations. Significant differences between groups (comparing compounds of the invention to saline-treated) are evaluated using Student t-test.
The high-fat diet fed mouse:
This model was originally introduced by Surwit et al. in 1988. The model has shown to be accompanied by insulin resistance, as determined by intravenous glucose tolerance tests, and of insufficient islet compensation to the insulin resistance. The model has, accordingly, been used in studies on pathophysiology of impaired glucose tolerance (IGT) and type 2 diabetes and for development of new treatments.

C57BL/6J mice are maintained in a temperature-controlled room (22°C) on a 12-h light-dark cycle. One week after arrival, mice are divided into two groups and are fed either a high-fat diet or received continuous feeding of a normal diet for up to 12 months. On caloric basis, the high-fat diet consist of 58% fat from lard, 25.6% carbohydrate, and 16.4% protein (total 23.4 kJ/g), whereas the normal diet contains 11.4% fat, 62.8% carbohydrate, and 25.8% protein (total 12.6 kJ/g). Food intake and body weight are measured once a week, and blood samples are taken at indicated time points from the intraorbital retrobulbar plexus from nonfasted anesthetized mice.

For intravenous glucose tolerance tests (IVGTTs), 4-h fasted mice are anesthetized with 7.2 mg/kg fluanison/fenlanyl and 15.3 mg/kg midazolam. Thereafter a blood sample is taken from the retrobulbar, intraorbital, capillary plexus, after which D-glucose (1 g/kg) is injected intravenously in a tail vein (volume load 10 v g). Additional blood samples are taken at 1, 5, 10, 20, 50, and 75 min after injection. Following immediate centrifugation at 4°C, plasma is separated and stored at -20°C until analysis. For oral glucose tolerance tests (OGTTs), 16-h fasted anesthetized mice are given 150 mg glucose by gavage through a gastric tube (outer diameter 1.2 mm), which is inserted in the stomach. Blood samples are taken at 0, 15, 30, 60, 90, and 120 min after glucose administration and handled as above.

Administration of the compounds: Five-week-old mice are fed a high-fat or a normal diet for 8 weeks. After 4 weeks, the mice are additionally given the compound of the invention in their drinking water (0.3 mg/ml, the amount can be changed for optimization. Control groups are given tap water without compound. After another 4 weeks, the mice are subjected to an OGTT as described above.
Insulin and glucose measurements: Insulin is determined enzymatically using an ELISA assay kit (Linco Research, St. Charles, MO). Plasma glucose is determined by the glucose oxidase method.

5 **In vivo** assay to assess compound anti-obesity activity in rodent model

Mouse acute food intake and weight change:
Male C57BL/6N wild-type mice are weighed and vehicle or compounds of the invention are administered by oral gavage to male mice approximately 30 min prior to the onset of the dark phase of the light cycle. Mice are fed *ad libitum* in the dark phase following dosing. A preweighed aliquot of a highly palatable medium high fat diet is provided in the food hopper of the cage 5 min prior to the onset of the dark phase of the light cycle and weighed 2 and 18h after the onset of the dark phase of the light cycle.

15 Acute studies in Diet-induced obesity (DIO) rats:
For acute experiments, male Sprague-Dawley DIO rats from Charles River Laboratories are raised from 4 weeks of age on a diet moderately high fat (32% kcal) and high in sucrose (25% kcal). Animals are used at 12 weeks of age and are maintained on a 12/12h light dark cycle. The rats are randomized into groups (n=6/group) for compounds of the invention and vehicle dosing. Rats are weighed 17h after dosing to determine effects on overnight body weight gain. Compounds of the invention are administered orally or s.c. at amount desired 1h before the start of the dark cycle. Powdered food is provided in food cups which are weighed continuously at 5 min intervals over 18h and the data are recorded using a computerized system.

Chronic studies in Diet-induced obesity rats:
For the 14-day chronic experiment, male Sprague-Dawley DIO rats are obtained as described above. Animals are used at 15 weeks of age and are maintained on a 12/12 hour light-dark cycle. Rats are conditioned to dosing for 4 days prior to baseline measurements, using an oral gavage or a s.c. route of vehicle. Thereafter, animals are dosed daily with vehicle or compound by oral gavage or s.c. Compound of the invention or vehicle is administered 1h before the dark cycle for 14 days. Body composition is measured by dual energy X-ray densitometry.
(DEXAscan) 5 days prior to the study and at the end of the 14-day study. Daily endpoints included body weight and food intake.

**In vivo assay to assess compound anti-lipolytic activity in rodent model**

Male C57BL/6N wild-type are housed one per cage in a room maintained on a 12h light/dark cycle under constant temperature (22-25°C) with *ad libitum* access to food and water. The anti-lipolytic effects of the compounds of the invention are studied in awake mice. Animals are fasted overnight before experimental use. On the day of the experiment, animals are put in metabolic cages and left undisturbed to acclimate to the environment for 1-2h. blood samples are taken at indicated time points from the intraorbital retrobulbar plexus. A 1% sodium citrate saline solution is used to flush the lines. A pre-treatment blood sample is obtained from each animal to determine baseline values for free fatty acids (FFA) and triglycerides (TG). Compounds of the invention are given via oral gavage, sc injection, iv injection or ip injection for each different series of experiments. Blood samples are collected into pre-cooled tubes pre-coated with heparin (200µl blood, Li-heparin, Sarstedt) for determination triglycerides and glycerol and in tris-potassium EDTA added sodium fluoride (200 µl blood, K₃-EDTA, 1.6 mg/mL + 1% NaF, Sarstedt) for determination of plasma free fatty acids. The tubes are placed on wet ice pending processing. Blood samples will be centrifuged at 4000 x g, at 4°C, 15 min the resulting plasma will be transferred into non-coated tubes and stored at -80°C until analyses. The plasma is thawed at 4°C for determinations of FFA and TG using commercial kits (Wako Chemicals).

According to the method described above and by way of illustration the compounds n⁰ 2 and 9 administered by ip injection, inhibit, 15 minutes following the injection, *in vivo* FFA baseline at the concentration of 15mg/kg from normal diet fed mice in comparison to the vehicle (Figures 4 and 5). The compounds n⁰ 14, 169 and 183 orally administered, inhibit, 15 minutes following the dosing, *in vivo* FFA baseline at the concentration of 50mg/kg from normal diet fed mice in comparison to the vehicle (Figure 8).
While embodiments of the invention have been illustrated and described, it is not intended that these embodiments illustrate and describe all possible forms of the invention. Rather, the words used in the specification are words of description rather than limitation and it is understood that various changes may be made without departing from the spirit and scope of the invention.
CLAIMS

1. A compound of formula I:

(I),

Ar<sup>1</sup> is a 5- to 6-membered aryl or heteroaryl group, 3- to 8-membered cycloalkyl group, a 3- to 8-membered heterocycloalkyl group, or a linear or branched C<sub>1</sub>-C<sub>6</sub> alkyl group, each of the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, or alkyl groups being optionally substituted by one or more groups selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxy, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkoxyalkoxy, alkylamino, alkoxyalkyl, carboxy, alkoxyacyl, cycloalkyloxyacyl, heterocyclyloxyacyl, arylacyl, heteroarylacyl, alkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino, arylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroaryl sulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroaryl sulfamoyl, alkylsulfamoylamino, cycloalkylsulfamoylamino, heterocyclylsulfamoylamino, arylsulfamoylamino, heteroaryl sulfamoylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl,
heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyle; L \textsuperscript{1} is a single bond, C\textsubscript{1}-C\textsubscript{2} alkylenne, each optionally being substituted by one or more substituents selected from halo, C\textsubscript{1}-C\textsubscript{2} alkyl, C\textsubscript{1}-C\textsubscript{2} haloalkyl; or L\textsuperscript{1} is -N(R\textsuperscript{N})-, wherein R\textsuperscript{N} is H or C\textsubscript{1}-C\textsubscript{2} alkyl; or L\textsuperscript{1} and R\textsuperscript{1} together are =CH-; R\textsuperscript{1} is H, halo, allyl, or a C\textsubscript{1}-C\textsubscript{4} alkyl group, which may optionally be substituted by one or more groups selected from halo or C\textsubscript{1}-C\textsubscript{4} alkyl; L\textsuperscript{2} is a C\textsubscript{1}-C\textsubscript{3} alkylenne, C\textsubscript{2}-C\textsubscript{4} alkenylene, C\textsubscript{3}-C\textsubscript{6} cycloalkylene, each of which being optionally substituted by one or more groups selected from halo, alkyl, alkoxy, or haloalkyl; or L\textsuperscript{2} is -0-CH\textsubscript{2}-; R\textsuperscript{1} and L\textsuperscript{2} together are =CH-, under the condition that -L\textsuperscript{1}-Ar\textsuperscript{1} is H; or R\textsuperscript{1} and L\textsuperscript{2} together are a 5- to 6-membered saturated or unsaturated carbocyclic or heterocyclic group, preferably a cyclohexenyl group, under the condition that -L\textsuperscript{1}-Ar\textsuperscript{1} is H; Z is selected from the group consisting of -COOR,
wherein \( R \) is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene, \( R_3 \) is H, methyl or ethyl, and \( R_4 \) is hydroxyl -SO\(_2\)CH\(_3\), -SC\(^{\text{cyclopropyl}}\) or -SO\(_2\)CF\(_3\);

\( D \) is CO or SO\(_2\);

\( R_2 \) is H, linear or branched C\(_1\)-C\(_4\) alkyl, C\(_1\)-C\(_4\) hydroxyalkyl, C\(_1\)-C\(_4\) haloalkyl, C\(_2\)-C\(_4\) alkenyl, C\(_2\)-C\(_4\) alkynyl, C\(_3\)-C\(_6\) cycloalkyl, C\(_3\)-C\(_6\) cycloalkylalkyl, aryl, arylalkyl, heteroarylalkyl, alkoxy carbonylalkyl, aminocarbonylalkyl, or aralkyloxyalkyl; each of the alkyl, hydroxyalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroarylalkyl, alkoxy carbonylalkyl, aminocarbonylalkyl, and aralkyloxyalkyl groups being optionally substituted by one or more substituents selected from halo, cyano, alkyl, hydroxyalkyl,
haloalkyl, alkenyl, alkynyl, heteroalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylosulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group,

$\text{Ar}^2$ is a 5- or 6-membered heterocyclic group or a 5- or 6-membered heteroaryl group, optionally substituted by one or more substituents selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, alkenyl, alkynyl, heteroalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylosulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group,

$L^3$ is a single bond, $\text{C}_1$-$\text{C}_3$ alkyne, $\text{C}_1$-$\text{C}_3$ alkenylene or carbonylamino;

$\text{Ar}^3$ is an aryl, heteroaryl, or $\text{C}_1$-$\text{C}_4$ alkyl group, each of which being optionally substituted by one or more groups selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxy carbonyl, heterocyclyloxy carbonyl, aryl oxy carbonyl, heteroaryloxy carbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkoxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl,
heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, cycloalkylaminocarbamoyl, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkoxyalkyl, alkoxyalkoxy, cycloalkylalkyloxy, amino, alkylamino, alkylaminoalkoxy, cycloalkylamino, aralkylamino, alkylaminooalkyl, alkylaminocarbonyl, alkylcarbonyl, cycloalkylcarbonylamino, alkylheterocyclyl, alkylheteroaryl, alkylsulfonyl, alkylsulfonylamino, aralkyl, aralkyloxy, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroaryalkyl, heteroarylcarbonyl, heterocyclyl, heterocyclyloxy, hydroxyl, oxo, or sulfonyl, or \(L_3^-\text{Ar}_3\) form an aryl, preferably phenyl, or heteroaryl group fused to \(Ar^2\), wherein each of said aryl or heteroaryl groups fused to \(Ar^2\) are optionally substituted by one or more halo, preferably chloro and fluoro;

with the following provisos:

\[Ar^2-L_3^-\text{Ar}_3\] is not 4-(4-(butylphenyl)thiazol-2-yl, 4-(4-ethylphenyl)thiazol-2-yl, 4-(4-(sec-butyl)phenyl)thiazol-2-yl, 4-(4-isobutylphenyl)thiazol-2-yl, 4-(4-tert-butylphenyl)thiazol-2-yl, 4-(4-propylphenyl)thiazol-2-yl, 4-(4-isopropylphenyl)thiazol-2-yl, 4-(4-butylnphenyl)thiazol-2-yl, 4-(4-(sec-butyl)phenyl)thiazol-2-yl, 4-(4-(4-methyl-2-ethylphenyl)thiazol-2-yl, 5-methyl-4-(para-tolyl)thiazol-2-yl, 5-methyl-4-phenylthiazol-2-yl, 5-methyl-4-(4-propylphenyl)thiazol-2-yl, 4-(4-(sec-butyl)phenyl)thiazol-2-yl, 4-(4-propylphenyl)thiazol-2-yl, 4-(4-isopropylphenyl)thiazol-2-yl, 4-(4-tert-butylphenyl)thiazol-2-yl, 4-(4-sec-butylphenyl)thiazol-2-yl, 4-(4-(4-butyl-3-methylphenyl)thiazol-2-yl, 4-(4-ethyl-3-methylphenyl)thiazol-2-yl, 4-(4-(3,4-dimethylphenyl)thiazol-2-yl, 4-(meta-tolyl)thiazol-2-yl, 4-(3-methyl-4-propylphenyl)thiazol-2-yl, 4-(4-(sec-butyl)-3-methylphenyl)thiazol-2-yl, 4-(4-isopropyl-3-methylphenyl)thiazol-2-yl,
4-(4-isobutyl-3-methylphenyl)thiazol-2-yl, 4-(4-(tert-butyl)-3-methylphenyl)thiazol-2-yl, 4-(4-butyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(3,4-dimethylphenyl)-5-methylthiazol-2-yl, 5-methyl-4-(meta-tolyl)thiazol-2-yl, 5-methyl-4-(3-methyl-4-propylphenyl)thiazol-2-yl, 4-(4-(sec-butyl)-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-isopropyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-ethyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-isobutyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-isopropyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-ethyl-3-methylphenyl)-5-methylthiazol-2-yl; Ar^3 is not (7H-pyrrolo[2,3-d]pyrimidin)-4yl; Ar^2 is not 5-cyano-thiazolyl;

the compound of formula I is none of.

2-[[[4-(4-butylphenyl)-5-methyl-2-thiazolyl] amino]carbonyl]-cyclohexane carboxylic acid,
6-[[4,5-dimethyl-2-thiazolyl) amino] carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-(cyclopentylmethyl)-1,3,4-thiadiazol-2-y]l amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-acetyl-4-methyl-2-thiazolyl] amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(4-methoxyphenyl)-5-methyl-2-thiazolyl] amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(3,4-dimethylphenyl)-5-methyl-2-thiazolyl] amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-methyl-4-(4-propylphenyl)-2 thiazolyl] amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(2,4-dichlorophenyl)-5-methyl-2-thiazolyl] amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[4-(2,5-dimethylphenyl)-5-methyl-2 thiazolyl] amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-(2-chlorophenyl)-1,3,4-thiadiazol-2-y]l amino]carbonyl]-3-cyclohexene-1-
carboxylic acid,
2-[[5-[(4-chlorophenoxy)methyl]-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-4-(4-propylphenyl)-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]carbonyl] -cyclohexanecarboxylic acid,
6-[[4-[4-(1,1-dimethylethyl)phenyl]-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1 -carboxylic acid,
6-[[5-ethyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1 -carboxylic acid-1-methylethyl ester
2-[[5-methyl-4-phenyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-4-[4-(2-methylpropyl)phenyl]-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-cyclopropyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3 —cyclohexene-1-carboxylic acid,
2-[[5-(cyclopentylmethyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[4-(4-chlorophenyl)5-ethyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[4-(3-methoxyphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-methyl-4-(4-methylphenyl)-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-cyclopropyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(4-chlorophenyl)-5-ethyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-(6-carboxy-3-cyclohexen-1-yl)carbonyl]amino]-4-phenyl-5-thiazolecarboxylic acid-5-ethyl ester,
2-[[4,5-dimethyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-cyclopropyl-1,3,4-oxadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-methyl-4-[4-(2-methylpropyl)phenyl]-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-ethyl-4-phenyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[4-(2,4-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(3-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-(1-ethylphenyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(3,4-dimethylpentyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-(2-thienyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[4,5-diphenyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(4-ethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-methyl-5-thiazolecarboxylic acid-5-methyl ester,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-methyl-5-thiazolecarboxylic acid-5-ethyl ester,
2-[[5-ethyl-4-phenyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[(5-cyclopropyl-1,3,4-oxadiazol-2-yl)amino]carbonyl-cyclohexanecarboxylic acid,
2-[[4-(4-fluorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[(2-carboxycyclohexyl)carbonyl]amino]-4-methyl-5-thiazoleacetic acid-5-ethyl ester,
2-[[4-(2,4-dimethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(3-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-((5-cyclohexyl-1,3,4-thiadiazol-2-yl)carbamoyl)cyclohexanecarboxylic acid,
2-[[5-methyl-4-(4-methylphenyl)-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-(2-thienyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[4,5-diphenyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(4-ethylphenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[5-dimethylamino]carbonyl]-4-methyl-2-thiazolyl]amino] carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-ethyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[2-carboxycyclohexyl]carbonyl]amino]-4-phenyl-5-thiazolecarboxylic acid-5-ethyl ester,
6-[[5-ethyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-ethyl-5-methyl-2-thiazolyl]amino] carbonyl]-cyclohexanecarboxylic acid,
2-[[5-methyl-4-[4-(l-methylethyl)phenyl]-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
2-[[5-acetyl-4-methyl-2-thiazolyl]amino]carbonyl]-cyclohexanecarboxylic acid,
6-[[4-(2,4-dichlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[4-(4-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
6-[[5-cyclohexyl-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[4-(4-chlorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl-cyclohexanecarboxylic acid,
6-[[4-(4-fluorophenyl)-5-methyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[6-carboxy-3-cyclohexen-1-yl]carbonyl-4-methyl-5-thiazolecarboxylic acid-5-methyl ester,
2-[[4-(1,1-dimethylethyl)phenyl]-5-methyl-2-thiazolyl]amino]carbonyl-cyclohexanecarboxylic acid,
2-[[5(dimethylethylamino)carbonyl]4-methyl-2-thiazolyl]amino]carbonyl-cyclohexanecarboxylic acid,
6-[[5-methyl-4-phenyl-2-thiazolyl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,
2-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]carbonyl] -cyclohexanecarboxylic acid, and
6-[[5-(2-thienyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid;

and pharmaceutically acceptable salts, and solvates thereof.
2. The compound according to claim 1 having the formula Ib:

wherein Z, Ar¹, Ar³, L¹, L², L³, and R and as defined in claim 1;

5 X is S or O;

Y is CH or N;

L³ is attached to the heterocyclic group either in position 4 or 5, preferably in position 4; and

if Y is CH, R⁵ is H, halo, cyano, hydroxyl, linear or branched C₁-C₃ alkyl, C₁-C₃ hydroxyalkyl, C₁-C₃ haloalkyl, preferably methyl and F, Cl, or CF₃ and R⁵ is attached to the heterocyclic group either in position 4, if L³ is attached in position 5, or in position 5, if L³ is attached in position 4; preferably R⁵ is attached in position 5;

if Y is N, R⁵ is absent and L³ is attached in position 5;

and pharmaceutically acceptable salts, and solvates thereof.
3. The compound according to claim 2 having the formula Ib-Ia:

\[
\text{Ib-Ia}
\]

wherein \(X, Y, \text{Ar}^3, \text{L}^2, \text{L}^3, R^2\) and \(R^5\) and as defined in claim 1;

\(R\) is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene;

\(R^6, R^7, R'^6, R'^7\) and \(R^8\) are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylmethylenyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylmethylenyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, alkylaminocarbonyl, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl, alkylaminocarbonyl, aminoalkyl, carboxy, alkoxy, carbonyl, cycloalkyloxy, heteroarylmethylenyl,}
together form an alkylenedioxy group or a haloalkylenedioxy group, or \( R^6 \) and \( R^7 \) or \( R^7 \) and \( R^8 \) or \( R'^6 \) and \( R'^7 \) or \( R'^7 \) and \( R^8 \) together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the phenyl group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl;

and pharmaceutically acceptable salts, and solvates thereof.

4. The compound according to claim 2 selected form the group consisting of formulae Ib-2a, Ib-2b, Ib-2c, Ib-2d, Ib-2e and Ib-2f:

![Diagram](image)

Ib-2a

![Diagram](image)

Ib-2b
wherein $X$, $Y$, $Z$, $\text{Ar}^3$, $L^2$, $L^3$, $R^1$, $R^2$, and $R^5$ are as defined in claim 2;

$B^1$, $B^2$ and $B^3$ are independently $\text{CF}_2$, $\text{O}$, $\text{NR}^a$, $\text{CO}$, or $\text{SO}_2$, wherein $R^a$ is $\text{H}$ or alkyl, preferably linear or branched $\text{C}_{1-4}$ alkyl; $\text{C}_{1-4}$ alky carbonyl, $\text{C}_{1-4}$ alkyl sulfon yl, $\text{C}_{1-4}$ alkylaminocarbonyl, aryl, arylcarbonyl, arylsulfon yl or arylaminocarbonyl; and

$R^9$, $R^{10}$, $R^{11}$, $R^{12}$, $R^{13}$, $R'^9$, $R'^{10}$, $R'^{11}$, $R'^{12}$, $R'^{13}$ and $R''^{13}$ are independently selected from $\text{H}$, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroaryl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxy, haloxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryl oxycarbonyl, alkyl carbonyloxy, cycloalkyl carbonyloxy, heterocyclyl carbonyloxy, aryl carbonyloxy, heteroaryl carbonyloxy, aryloxycarbonyl, alkyl carbonyl amino, haloalkyl carbonylamino, cycloalkyl carbonylamino, heterocyclyl carbonylamino, aryl carbonylamino, heteroaryl carbonylamino, alkyl carbonylaminoalkyl, acylamino, car bamo yl, hydroxycarbamoyl, alkyl carbamoyl, aryl carbamoyl, heteroaryl carbamoyl, carbamo yl alkyl, carbamo yl amino, alkyl carbamoylamino, alkyl sulfon yl, haloalkyl sulfon yl, cycloalkyl sulfon yl, heterocyclyl sulfon yl, ary lsulfon yl, heteroaryl sulfon yl, sulfamoyl, alkyl sulfamoyl, aryl sulfamoyl,
heteroarylsulfamoyl, alklysulfonylamino, cycloalkylsulfonylamino, heterocyclysulfonlamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or one of \( R^9 \) or \( R^{10} \) and one of \( R^{11}, R^{12}, R^{13}, R'^9, R'^{10}, R'^{11}, R'^{12}, R'^{13} \) or \( R''^{13} \), or one of \( R^{11} \) or \( R^{12} \) and one of \( R^9, R^{10}, R^{13}, R'^9, R'^{10}, R''^{11}, R''^{12}, R''^{13} \) or \( R'^{13} \), or one of \( R^9 \) or \( R^{10} \) and one of \( R^{13}, R^{12}, R'^9, R'^{10}, R''^{10}, R''^{12}, R''^{13} \) or \( R'^{13} \) together form an alkylenedioxy group or a haloalkylenedioxy group, or one of \( R^9 \) or \( R^{10} \) and one of \( R^{11}, R^{12}, R^{13}, R'^9, R'^{10}, R''^{11}, R''^{12}, R''^{13} \) or \( R'^{13} \), or one of \( R^{11} \) or \( R^{12} \) and one of \( R^9, R^{10}, R^{13}, R'^9, R'^{10}, R''^{11}, R''^{12}, R''^{13} \) or \( R'^{13} \), or one of \( R^{13} \) or \( R'^{13} \) and one of \( R^9, R^{10}, R^{11}, R^{12}, R'^9, R'^{10}, R''^{11}, R''^{12}, R''^{13} \) or \( R'^{13} \) together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety together with the cyclic group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkysulfonyl, aralkyl, aryl, alylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl;

and pharmaceutically acceptable salts, and solvates thereof.

5. The compound according to claim 2 having the formula Ib-3:
wherein $L_2$, $L_3$, $Ar_3$, $X$, $Y$, $R$, $R_1$, $R_2$, and $R_5$ are as defined in claim 2;

$R$ is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene; and

$R_{16}$, $R_{17}$, $R_{18}$ and $R_{19}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkyaminio, aminoalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcycloalkyloxy, arylcarbonyloxy, heteroarylcycloalkyl, alkyloxycarbonyl, haloalkyloxycarbonyl, cycloalkylcarbonyloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxyalkyl, alkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino, arylcarbonylamino, cycloalkylcarbonylaminoalkyl, acylaminio, carbamoyl, hydroxycarbamoyl, alkylcarbamoiylo, arylcarbamoioylo, heteroarylcarbamoioylo, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonlamino, cycloalkylsulfonlamino, heterocyclylsulfonlamino, arylsulfonlamino, heteroarylsulfonlamino, haloalkylsulfonlamino, or $R_{16}$ and $R_{17}$ or $R_{17}$ and $R_{18}$ or $R_{18}$ and $R_{19}$ together form an alkylendioxy group or a haloalkylenedioxy group, or $R_{16}$ and $R_{17}$ or $R_{17}$ and $R_{18}$ or $R_{18}$ and $R_{19}$ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the phenyl group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alky carbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylkyl, hetero Aryl carbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl;

and pharmaceutically acceptable salts, and solvates thereof.
6. The compound according to claim 2 having the formula Ib-4:

\[
\text{Ib-4,}
\]

wherein

\[
\begin{align*}
\text{Ar}^1, \text{Ar}^3, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^3, \text{R}^5, \text{X}, \text{Y} \text{ and } Z & \text{ are as defined in claim 2;} \\
	ext{and pharmaceutically acceptable salts, and solvates thereof.}
\end{align*}
\]

7. The compound according to claim 6 having the formula Ib-4a:
wherein

$\text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5,$ and $Z$ are as defined in claim 2;

$\text{R}^{20}$ and $\text{R'}^{20}$ are independently selected from halo, cyano, $\text{C}_1\text{C}_3$ alkyl, cyclopropyl, haloalkyl, alkoxy, haloalkoxy, alkoxyacetamino, or the two substituents form an alkylenedioxy group or a haloalkylenedioxy group;

$\text{Ar}^4$ is 5 or 6 membered aryl, 5 or 6 membered heteroaryl, each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally fused to one or more 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, and the latter fused ring system being optionally substituted by one or more further substituents selected from halo, hydroxyl, oxo, alkyl, and/or each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl groups being optionally substituted by one or more further substituents selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylmethyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, arloxy, aralkyloxy, alkylamino, alkylaminomethyl, cycloalkylaminomethyl, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylmethyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylmethyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, arloxy, aralkyloxy, heteroarylmethyl, cycloalkyloxy, arloxy, aralkyloxy, heteroarylmethyl, cycloalkyloxy, arloxy, aralkyloxy, heteroarylmethyl, cycloalkymethyl, arylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, oxo or alkyl;

and pharmaceutically acceptable salts, and solvates thereof.

8. The compound according to claim 6 having the formula Ib-4c:
wherein

\[ \text{Ar}^1, \text{L}^1, \text{L}^2, \text{R}^1, \text{R}^2, \text{R}^5, \text{and Z} \text{ are as defined in claim 2,} \]

\[ \text{R}^{20} \text{ and } \text{R}^{120} \text{, are as defined in claim 7,} \]

\[ \text{R}^{21} \text{ and } \text{R}^{22} \text{ are independently selected from H, halo, alkoxy;} \]

\[ \text{R}^{23} \text{ is selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, haloalkyl, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, preferably dimethylaminoethoxy,} \]

cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, alkyminocarbonyl, heteroarylcarbonyl, alkylcarbonylamin, cycloalkylcarbonylamin, alkylsulfonl, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, alkymino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, oxo or alkyl;

\[ \text{Y}^1 \text{ is N or C-}\text{R}^{24} \text{ where } \text{R}^{24} \text{ is H, halo, alkoxy, alkyl, heterocyclyl, or} \]
Y¹ is C-R²⁴ and R²⁴ and R²³ together form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, the latter fused ring system being optionally substituted by one or more group selected from oxo, alkyl or halo; and

5 Y² is N or C-R²⁵ where R²⁵ is H, halo, alkoxy, alkyl, heterocyclyl, or

Y² is C-R²⁵ and R²⁵ and R²³ together form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, the latter fused ring system being optionally substituted by one or more group selected from oxo, alkyl or halo, under the condition that R²⁴ and R²³ together do not form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety;

9. The compound according to claim 2 having the formula Ib-4i:

Ib-4i,

wherein

Ar¹, L¹, L², R¹, R², R⁵, and Z are as defined in respect claim 2;
Ar\(^4\), R\(^{20}\) and R\(^{20}'\), are as defined in claim 7; and

R\(^{21}\), R\(^{22}\), R\(^{23}\), Y\(^1\) and Y\(^2\) are as defined in claim 8;

and pharmaceutically acceptable salts, and solvates thereof.

10. The compound according to claim 2 having the formula Ib-4m:

\[
\begin{array}{c}
\text{R}^{27} \\
\text{Ar}\stackrel{\text{L}^1}{\longrightarrow} \text{O} \\
\text{R}^{26} \\
\text{Z} \\
\end{array}
\]

\[
\begin{array}{c}
\text{Ar}^1 \\
\text{L}^2 \\
\text{R}^1 \\
\text{R}^2 \\
\end{array}
\]

wherein

Ar\(^1\), L\(^1\), L\(^2\), R\(^1\), R\(^2\), R\(^5\), and Z are as defined in respect claim 2; and

R\(^{126}\) and R\(^{27}\) are independently selected from H, halo, cyano, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, alkylamino, carboxy, alkoxy carbonyl, alkylcarbonylamino, haloalkyl carbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, alkoxy carbamoyl, cycloalkyl carbamoyl, alkyl carbamoyl amino, cycloalkylaminocarbamoyl, alkylsulfonyl, haloalkyl sulfonyl, sulfamoyl, alkyl sulfamoyl, alkyl sulfonylamino, haloalkyl sulfonylamino, or the two substituents form an alkylenedioxy group or a haloalkylenedioxy group; and
pharmaceutically acceptable salts, and solvates thereof.

11. The compound according to claim 1 having the formula Ic:

\[
\text{R}^6, \text{R}^7, \text{R}^6', \text{R}^7' \text{ and } \text{R}^8 \text{ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxy carbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylicarbonylamino, heteroarylicarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxy carbamoyl, alkyl carbamoyl, arylicarbamoyl, heteroarylicarbamoyl, carbamoyl alkyl, carbamoylamino, alkyl carbamoylamino, alkylsulfonfonyl, haloalkyl sulfonyl, cycloalkyl sulfonyl, heterocyclyl sulfonyl, aryl sulfonyl, heteroaryl sulfonyl, sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonfonyl, cycloalkyl sulfonylamino, heterocyclyl sulfonylamino,}
\]
aryl sulfonlamino, heteroaryl sulfonlamino, haloalkyl sulfonlamino, or R₆ and R₇ or R₈ or R'₆ and R'₇ or R'₈ together form an alkylenedioxy group or a haloalkylenedioxy group, or R₆ and R₇ or R₈ or R'₆ and R'₇ or R'₈ together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the phenyl group they are attached to, each of said substituents being optionally substituted by one or more further substituents selected from halo, alkoxy, alkyl, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylmethy, heteroarylsulfonyl, heterocyclyl, hydroxyl, oxo, or sulfonlamino; and

12. The compound according to claim 1 having the formula Id:

![Diagram](attach:formulaId.png)

Id

wherein the dotted line is present or absent;

13. The compound according to claim 1 having the formula Ie:
I e

wherein

Y is CH or N;

R$^{14}$ and R$^{15}$ are independently H, halo, cyano, hydroxyl, linear or branched C$_1$-C$_3$ alkyl, C$_1$-C$_3$ hydroxyalkyl, C$_1$-C$_3$ haloalkyl; and

Ar$^1$, Ar$^3$, L$^1$, R$^1$, R$^2$, and Z are as defined in claim 1;

and pharmaceutically acceptable salts, and solvates thereof.

14. The compound according to claim 1 selected from the group consisting of:

1. 6-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)cyclohex-3-ene-carboxylic acid
2. (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
3. (R)-3-benzyl-4-((4-(2,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
4. (R)-3-benzyl-4-((4-(2-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(3,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(4-cyanophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-phenylbutanoic acid
(Z)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobut-2-enolic acid
(R)-3-benzyl-4-oxo-4-((3-phenyl-1,2,4-thiadiazol-5-yl)amino)butanoic acid
(R)-3-benzyl-4-((4-(3-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-oxo-4-((4-(3-(trifluoromethyl)phenyl)thiazol-2-yl)amino)butanoic acid
(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((5-(2-chlorophenyl)pyridin-2-yl)amino)-4-oxobutanoic acid
(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)heptanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-fluorobenzyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid
(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)-5-methylhexanoic acid
(R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((5-chloro-4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxy-2-oxoethyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid
(R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxy-2-oxoethyl)amino)-4-oxobutanoic acid
(R)-methyl-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoate
(R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid
(S)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid
(R)-4-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-(4-(trifluoromethyl)benzyl)butanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-(3-(trifluoromethyl)benzyl)butanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(2-cyanobenzyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(3-cyanobenzyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-cyanobenzyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(3-methoxybenzyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(2-methoxybenzyl)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-oxo-4-(4-(2,4,6-trichlorophenyl)thiazol-2-ylamino)butanoic acid
(R)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid
(S)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid
(R)-methyl-4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate
(S)-methyl-4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate
(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropylmethyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(benzyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2,2,2-trifluoroethyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-methoxybenzyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-methoxybenzyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-cyanobenzyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-cyanobenzyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-cyanobenzyl)-4-oxobutanoic acid

(R)-3-(4-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(3-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(2-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-IH-inden-1-yl)-4-oxobutanoic acid

(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-IH-inden-2-yl)-4-oxobutanoic acid

(R)-4-(benzo[d]thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid

(R)-4-(benzo[d]oxazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid

(R)-2-((IH-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-phenylpropanamide
(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide

(R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(S)-4-((4-(2-chlorophenyl)thiazol-2-ylamino)-3-cyclohexyl-4-oxobutanoic acid

(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-cyclohexyl-4-oxobutanoic acid

(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-phenylbutanoic acid

(3R)-3-((4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylpentanoic acid

(R)-2-((1H-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-phenylpropanamide

(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide

(3R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-ylamino)-2-methyl-4-oxobutanoic acid

(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxyisoxazol-5-yl)propanamide

(R)-3-benzyl-4-((4-(2-chlorophenyl)pyrimidin-2-ylamino)-4-oxobutanoic acid

(R)-3-benzyl-4-((6-(2-chlorophenyl)pyridin-2-ylamino)-4-oxobutanoic acid

(E)-3-((4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylbut-3-enoic acid

(Z)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-phenylbut-2-enoic acid

(R)-3-(N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methylsulfamoyl)-4-phenylbutanoic acid

(S)-3-(N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methylsulfamoyl)-4-phenylbutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-ylamino)-3-fluoro-4-oxobutanoic acid
(R)-3-benzyl-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)hex-5-enoic acid

(E)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylbut-3-enolic acid

(3S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid

(R)-3-benzyl-4-((3-(2-chlorophenyl)-1,2,4-thiadiazol-5-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((1-(2-chlorophenyl)-1H-pyrazol-3-yl)(methyl)amino)-4-oxobutanoic acid

(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxyisoxazol-5-yl)-N-methylpropanamide

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid

(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-5-methylhexanoic acid

(R)-3-benzyl-4-((2-cyanophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-phenylbutanoic acid

(R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(3-fluorobenzyl)-4-oxobutanoic acid

(S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-methylpentanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(ethyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

cis-6-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)cyclohex-3-ene-carboxylic acid
4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid

cis-6-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohex-3-ene carboxylic acid

cis-2-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohexanecarboxylic acid

(R)-3-benzyl-4-(4-(2,5-dimethylthiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid

(R)-3-benzyl-4-(4-(2,5-dimethylthiophen-3-yl)thiazol-2-yl)(methyl)carbamoyl)cyclohexanecarboxylic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3S,4R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(thiophen-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-chloropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(phenylamino)butanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methylbenzyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid

(R)-3-benzyl-4-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopropylmethyl)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiazol-4-ylmethyl)butanoic acid

(R)-3-benzyl-4-((4-(2-(2-methylpropyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(2-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-((ethoxycarbonyl)amino)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-fluoropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(6-methylpyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((2-amino-2-oxoethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid

(R)-3-benzyl-4-oxo-4-((4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)butanoic acid

(R)-3-benzyl-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3-chloro-4-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3-chloro-4-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(3-methoxy-3-oxopropyl)amino)-4-oxobutanoic acid

3-(bicyclo[2.2.1]heptan-2-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-ethoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4'-methoxy-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-1-(5-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)phenyl)pyridin-2-yl)pyrrolidin-1-ium 2,2,2-trifluoroacetate

(R)-4-(2'-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)-[1,1'-biphenyl]-4-yl)morpholin-4-ium 2,2,2-trifluoroacetate

(R)-3-benzyl-4-(methyl(4-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(furan-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-methoxyethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4'-isopropyl-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-cyclopropylphenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4'-(dimethylamino)-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3'-fluoro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
147  (R)-3-benzyl-4-((4-(3',5'-difluoro-[1,r-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
148  (R)-3-benzyl-4-((4-(2-chloro-6-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
149  (R)-3-benzyl-4-((4-(4'-chloro-[1,l'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
150  (R)-3-benzyl-4-(methyl(4-(2-(6-(2-oxopyrrolidin-l-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
151  (R)-3-benzyl-4-((4-(4-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
152  (R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
153  (R)-3-benzyl-4-((4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
154  (3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-2-yl)methyl)butanoic acid
155  (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid
156  (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(3-hydroxypropyl)amino)-4-oxobutanoic acid
157  (R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
158  (R)-3-benzyl-4-((4-(2-(6-(benzyloxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
159  (R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
160  (R)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
161  (R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl) (methyl) amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((2-hydroxyethyl)(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-chloro-2-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2,3,5-trichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4-chloro-[1,1'-biphenyl]-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-methoxy-pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-methoxy-pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-morpholino-pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-morpholino-pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-((2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-morpholino-pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-(difluoromethoxy)phenyl)thiazol-2-yl) (methyl) amino) -4-oxobutanoic acid

(R)-4-((4-(2-cmoro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R,4S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid

(R)-2-(2-benzyl-3-carboxypropanamido)-5-(2-chlorophenyl)pyridine 1-oxide

(R)-3-benzyl-4-((5-(2-chlorophenyl)pyrazin-2-yl)amino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(morpholinomethyl)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxyethyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylamino)-4-oxobutanoic acid

(R)-3-benzyl-4-((2-(benzyloxy)ethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-methylfuran-2-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((3-(3-(trifluoromethyl)phenyl)-IH-pyrazol-5-yl)amino)butanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-hydroxybenzyl)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(4'-cyano-1,1'-biphenyl)-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3R)-3-benzyl-4-((3-carbamoyl-4-(2,4-dichlorophenyl)-5-methylthiophen-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3'-methoxy-1,1'-biphenyl)-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chloro-1,1'-biphenyl)-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(2-methoxypyrimidin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl) (methyl) amino) -4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(S)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-benzylthiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-oxo-4-((5-phenyl-4H-1,2,4-triazol-3-yl)amino)butanoic acid

3-([l,l'-biphenyl]-4-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(1-methyl-lH-pyrazol-4-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4-methyl-1,2,5-oxadiazol-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4-methyl-1,2,5-oxadiazol-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(l-methyl-lH-pyrazol-4-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-benzyl-4-((4-(2-(3,5-dimethylisoxazol-4-yl)phenyl)thiazol-2-yl) (methyl) amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)carbamoyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((6-(2-chlorophenyl)pyridazin-3-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(2-oxopyrrolidin-l-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(S)-2-((1-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)oxy)acetic acid

(R)-3-benzyl-4-((1-methyl-5-phenyl-1H-imidazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(((2-(1-(2-methoxyethyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoic acid

4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-hydroxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-cmorophenyl)thiazol-2-yl)((S)-2-hydroxypropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((R)-2-hydroxypropyl)amino)-4-oxobutanoic acid

(R)-3-(cyclohexylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(4,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxy pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2,3-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(6-(6-isopropoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-(cyclopropylmethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(6-(methoxymethyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-((dimethylamino)methyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(6-(N-methylcyclopropane carboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(2-(6-(dimethylcarbamoyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-(6-(4H-1,2,4-triazol-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid

(R)-3-benzyl-4-((methyl(4-(2-(6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((methyl(4-(2-(6-(benzyl(methyl)amino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((methyl(4-(2-(6-(cyclohexyl(methyl)amino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(2-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)-3-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3-fluoro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(3,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((S)-tetrahydrofuran-2-yl)methyl)butanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((R)-tetrahydrofuran-2-yl)methyl)butanoic acid

(R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid
(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyridin-2-ylmethyl)butanoic acid

(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyrimidin-2-ylmethyl)butanoic acid

(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-2-yl)methyl)butanoic acid

(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-3-yl)methyl)butanoic acid

(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R,3R)-2-methyltetrahydro-2H-pyran-3-yl)methyl)-4-oxobutanoic acid

(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R)-2-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((3S)-3-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((3R,5S)-3,5-dimethyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(4-hydroxy-1,2,5-thiadiazol-3-yl)-N-methylpropanamide
(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxy-5-methylisoxazol-4-yl)-N-methylpropanamide

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
<table>
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<th>Chemical Structure</th>
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<td>322</td>
<td>(R)-4-(cyclopropyl(4-((5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>323</td>
<td>(R)-4-(cyclopropyl(4-((5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>324</td>
<td>(R)-4-(cyclopropyl(4-((5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>325</td>
<td>(R)-4-(cyclopropyl(4-((2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>326</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-((2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>327</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-((2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>328</td>
<td>(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>329</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-((2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>330</td>
<td>(R)-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
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<td>331</td>
<td>(R)-4-(cyclopropyl(5-fluoro-4-((2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid</td>
</tr>
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(R)-4-(cyclopropyl(4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopentyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopentyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopentyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopentyl(5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopentyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((methyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((5-fluoro-4-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(((5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-IH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-IH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-IH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-((4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-3-benzyl-4-((4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid
(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-napthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-napthyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-napthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-napthyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid
(R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(methyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-3-benzyl-4-(cyclopropyl(4-(2-(l-methyl-2-oxo-2,3-dihydro-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(methyl(4-(2-(4-methyl-3,4-dihydro-2H-pyridopyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyridopyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyridopyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(l-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(l-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(4-methyl-3,4-dihydro-2H-pyridopyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(8-methyl-7-oxo,6,7,8-tetrahydro-1, 8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(l-methyl-2-oxo-2,3-dihydro-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(5-fluoro-2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
567 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-
  (fluoromethoxy)-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-
  b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
568 (R)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-2,3-
  dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-
  yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-
  yl)methyl)butanoic acid
569 (R)-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(1-
  methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-
  yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
570 (R)-3-benzyl-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-2-oxo-
  2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-
  yl)(methyl)amino)-4-oxobutanoic acid
571 (R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(1-
  methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-
  yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
572 (R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(4-
  methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-
  2-yl)(methyl)amino)-4-oxobutanoic acid
573 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-
  (fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-
  b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
574 (R)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-
  pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-
  oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
575 (R)-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(4-methyl-3,4-
  dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-
  yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
576 (R)-3-benzyl-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(4-methyl-3,4-
  dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-
  yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-(fluoromethoxy)-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)methyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid
597  (R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-
b]1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl) -4-oxobutanoic acid

598  (R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-
b]1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

599  (R)-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-
b]1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

600  (R)-3-benzyl-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b]1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

601  (R)-3-benzyl-4-((4-(5-chloro-2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b]1,4]oxazin-7-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

602  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

603  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

604  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

605  (R)-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

606  (R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-((4-(5-chloro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(8-methyl-7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(l-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(l-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(l-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(2-(l-methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(R)-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(4-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(4-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((5-fluoro-4-(2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-lH-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-lH-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methyl-5-oxo-5,6,7,8-tetrahydro-1,6-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1,3-dimethyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(7-methyl-8-oxo-5,6,7,8-tetrahydro-1,7-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methyl-5-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(2-(5-chloro-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(3-methyl-3H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2,3-dihydro-LH-imidazo[4,5-b][l,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(7-methyl-6-oxo-5,6,7,8-tetrahydro-1,7-naphthyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methyl-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1,3-dimethyl-2-oxo-2,3-dihydro-LH-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-LH-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(5-fluoro-6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-1,2,3,4-tetrahydro-1,5-naphthyridin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(3-methyl-2-oxo-1,2,3,4-tetrahydropyrido[3,2-d]pyrimidin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(methyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(methyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-((5-fluoro-4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(methyl(4-(5-methyl-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(cyclopropyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxobutanoic acid

(R)-4-(methyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(3-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-1,2,4-thiadiazol-5-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid
(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-((4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3R)-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(3R)-4-((4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(R)-4-((4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

(3R)-3-benzyl-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-benzyl-4-((4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3R)-3-benzyl-4-(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3R)-3-benzyl-4-((4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
(R)-3-benzyl-4-(cyclopropyl(4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-benzyl-4-(((4-(2,5-dimethyl-4-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)furan-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-((cyclopropyl(4-(2-(6-(1-methyl-6-oxopiperidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxopiperidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyl-2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(N-methylacetamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1,3-dimethyl-2-oxohexahydropyrimidin-5-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(5-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(pyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

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(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(4-methyl-2,5-dioxopiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(dimethylcarbamoyl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyl-2-oxohexahydropyrimidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-isoproxyopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-6-oxopiperidin-2-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-5-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyl-2-oxotetrahydropyrimidin-1(2H)-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxotetrahydropyrimidin-1(2H)-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1,3-dimethyl-2-oximidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1,3-dimethyl-2-oxohexahydropyrimidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxohexahydropyrimidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(N-methylcyclopropanecarboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxopiperidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(methoxymethyl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxohexahydropyrimidin-5-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(5-oxopyrrolidin-2-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-5-(trifluoromethyl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(fluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)-5-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(pyridin-2-ylmethyl)butanoic acid

(R)-2-(2-(carboxymethyl)-3-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-oxopropyl)pyridine 1-oxide

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((R)-tetrahydro-2H-pyran-2-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((S)-tetrahydro-2H-pyran-3-yl)methyl)butanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((S)-tetrahydro-2H-pyran-3-yl)methyl)butanoic acid
(3R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(((2S)-2-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((R)-tetrahydro-2H-pyran-3-yl)methyl)butanoic acid

(3R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(((3R,5S)-3,5-dimethyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(((2R,3R)-2-methyltetrahydro-2H-pyran-3-yl)methyl)-4-oxobutanoic acid

(3R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(((3S)-3-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((S)-tetrahydro-2H-pyran-2-yl)methyl)butanoic acid

(R)-3-(benzofuran-2-ylmethyl)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((R)-tetrahydrofuran-2-yl)methyl)butanoic acid

(R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((5-methylfuran-2-yl)methyl)-4-oxobutanoic acid

(3R)-4-(cyclpropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-3-yl)methyl)butanoic acid
(3R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

(3R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-2-yl)methyl)butanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(oxetan-3-ylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(oxetan-3-ylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyl-2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(oxetan-3-ylmethyl)-4-oxobutanoic acid

(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluoro-2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-(3-methyloxetan-3-ylmethyl)-4-oxobutanoic acid
15. A pharmaceutical composition comprising a compound according to any of Claims 1 to 14 or a pharmaceutically acceptable salt or solvate thereof and at least one pharmaceutically acceptable carrier, diluent, excipient...
16. Medicament comprising a compound according to any of Claims 1 to 14.

17. Use of a compound according to any of Claims 1 to 14 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment and/or prevention of type II diabetes, obesity, dyslipidemia such as mixed or diabetic dyslipidemia, hypercholesterolemia, low HDL cholesterol, high LDL cholesterol, hyperlipidemia, hypertriglyceridemia, hypoglycemia, hyperglycemia, glucose intolerance, insulin resistance, hyperinsulinemia, hypertension, hyperlipoproteinemia, metabolic syndrome, syndrome X, thrombotic disorders, cardiovascular disease, atherosclerosis and its sequelae including angina, claudication, heart attack, stroke and others, kidney diseases, ketoacidosis, nephropathy, diabetic neuropathy, diabetic retinopathy, nonalcoholic fatty liver diseases such as steatosis or nonalcoholic steatohepatitis (NASH).

18. Use of a compound according to any of Claims 1 to 14 or a pharmaceutically acceptable salt or solvate thereof as a modulator of GPR43 receptor activity.

19. Use according to Claim 18, wherein the compound is an agonist or partial agonist of GPR43 receptor activity.
**Figure 1**

- Compound 9 (µM): - 30 10 1

*p< 0.01 vs control (ANOVA)*

**Figure 2**

- Compound 9 (µM): - 1 10 30

* p< 0.05 vs control (ANOVA)*
Figure 3

Compound 9 (µM): - 1 10 30

***: p < 0.001 vs control (ANOVA)

Figure 4

Statistics: One-way ANOVA followed by Dunnett post-hoc
**p < 0.01 for treatment vs vehicle. N = 10 mice/group
Statistics: One-way ANOVA followed by Dunnett post-hoc
**p<0.01 for treatment vs vehicle. N= 5 mice/group

Figure 5

*** p<0.001 for treatment vs control (Student t test).

Figure 6
**Figure 7**

NEFA Release (% of isoproterenol response)

**Figure 8**

FFA (% of Baseline)

**p<0.01 treatment vs control.**
One-way ANOVA and Dunnett's post-hoc
*** $p < 0.001$ vehicle vs treatment

*Student t test*

Figure 9
**INTERNATIONAL SEARCH REPORT**

International application No
PCT/EP2009/066536

A. CLASSIFICATION OF SUBJECT MATTER

| INV. | C07D213/75 | C07D231/40 | C07D239/42 | C07D239/69 | C07D263/48 |
| C07D263/58 | C07D271/06 | C07D277/46 | C07D277/82 | C07D285/08 |
| C07D417/12 | A61K31/426 | A61K31/44 | A61P3/10 |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>1-3, 6-11, 14-19</td>
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<td>WAGNER GERHARD [US]; CHOREV MICHAEL [US]</td>
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<td>MOERRE 27 July 2006 (2006-07-27) compounds o and p - page 91; page 29, line 8 - page 34, line 15; claims; figures</td>
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<td>KANNO H ET AL: &quot;Synthesis and evaluation of 2-(biphenylmethyl)glutaric acid amide derivatives as neutral endopeptidase inhibitors&quot; BIOORGANIC &amp; MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 6, no. 13, 9 July 1996 (1996-07-09), pages 1487-1490, XP004175738</td>
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Further documents are listed in the continuation of Box C

See patent family annex

- Special categories of cited documents
  - "A" document defining the general state of the art which is not considered to be of particular relevance
  - "E" earlier document but published on or after the international filing date
  - "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  - "O" document referring to an oral disclosure use, exhibition or other means
  - "P" document published prior to the international filing date but later than the priority date claimed

Date of the actual completion of the international search
26 April 2010

Date of mailing of the international search report
04/05/2010

Name and mailing address of the ISA/
European Patent Office, P B 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040,
Fax (+31-70) 340-3016

Authorized officer
Gavril iu, Daniel a
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/066536

Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

1  ☐  Claims Nos because they relate to subject matter not required to be searched by this Authority, namely

2  ☐  Claims Nos because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically

3  ☐  Claims Nos because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)

Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows

see additional sheet

1  ☐  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims

2  ☐  As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees

3  ☑  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos 3, 8

4  ☑  No required additional search fees were timely paid by the applicant Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos

Remark on Protest

☐  The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee

☐  The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation

☒  No protest accompanied the payment of additional search fees

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2005)
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 3(completely); 1, 2, 6-11, 14-19(partially)

   Compounds of formula Ib-Ia and their uses as anti-diabetes agents.

2. claims: 4(completely); 1, 2, 14-19(partially)

   Compounds of formulae Ib-2a-2f and their uses as anti-diabetes agents.

3. claims: 5(completely); 1, 2, 14-19(partially)

   Compounds of formula Ib-3 and their uses as anti-diabetes agents.

4. claims: 7(completely); 1, 2, 14-19(partially)

   Compounds of formula Ib-4b and their uses as anti-diabetes agents.

5. claims: 8(completely); 1, 2, 14-19(partially)

   Compounds of formula Ib-4c and their uses as anti-diabetes agents.
### INTERNATIONAL SEARCH REPORT

#### Information on patent family members

**PCT/EP2009/066536**

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