(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 June 2010 (17.06.2010)

PCT

(10) International Publication Number
WO 2010/066682 A1

(51) International Patent Classification:

C07D 213/75 (2006.01)	*C07D 277/46* (2006.01)
C07D 231/40 (2006.01)	*C07D 277/82* (2006.01)
C07D 239/42 (2006.01)	*C07D 285/08* (2006.01)
C07D 239/69 (2006.01)	*C07D 417/12* (2006.01)
C07D 263/48 (2006.01)	*A61K 31/426* (2006.01)
C07D 263/58 (2006.01)	*A61K 31/44* (2006.01)
C07D 271/06 (2006.01)	*A61P 3/10* (2006.01)

(21) International Application Number:
PCT/EP2009/066536

(22) International Filing Date:
7 December 2009 (07.12.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

08305896.6	8 December 2008 (08.12.2008)	EP
61/205,735	23 January 2009 (23.01.2009)	US
61/152,294	13 February 2009 (13.02.2009)	US
61/168,159	9 April 2009 (09.04.2009)	US

(71) Applicant *(for all designated States except US)*: **EUROSCREEN S.A.** [BE/BE]; Route de Lennik 802, B-1070 Brussels (BE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HOVEYDA, Hamid** [CA/BE]; Rue Berkendael, 124, B-1050 Bruxelles (BE). **BRANTIS, Cyrille Evangelos** [FR/BE]; Rue des Clercs 39, B-7000 Mons (BE). **DUTHEUIL, Guillaume** [FR/BE]; Rue du haut Flénu, 29C, B-7012 Flenu (BE). **ZOUTE, Ludivine** [FR/BE]; Rue du haut Flénu, 29C, B-7012 Flenu (BE). **SCHILS, Didier** [BE/BE]; Chaussée de Charleroi 31, B-1471 Loupoigne (BE). **BERNARD, Jérôme** [FR/FR]; 79 avenue de Verdun, F-59300 Valenciennes (FR).

(74) Agents: **TOUATI, Catherine** et al.; Cabinet Plasseraud, 52 rue de la Victoire, F-75440 Paris Cedex 09 (FR).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

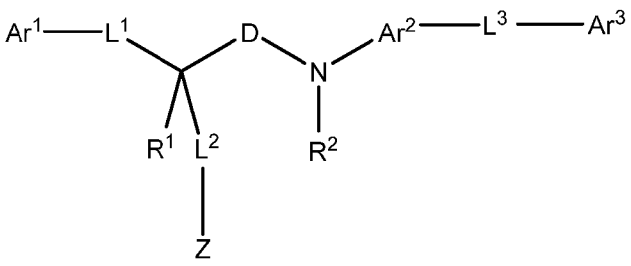
— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: COMPOUNDS, PHARMACEUTICAL COMPOSITION AND METHODS FOR USE IN TREATING METABOLIC DISORDERS



(I)

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

WO 2010/066682 A1

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. Sci., 14, pp 58-64, 1999). Long-chain fatty acids (LCFAs, carbon length C_{14}-C_{24}) 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 (Ahrén, 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., Endrocrinology, 146 pp5092-5099, 2005). Indeed, it has been reported that acetate

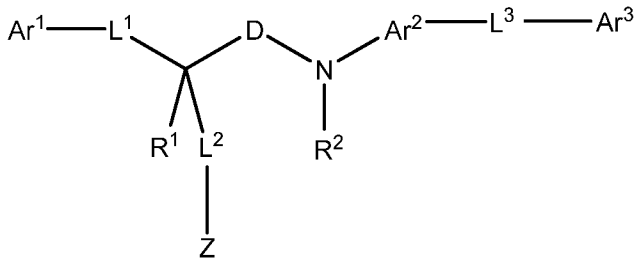
and propionate may stimulate adipogenesis via GPR43. In addition siRNA results hinted that acetate and propionate may inhibit lipolysis in adipocytes via GPR43 activation (Hong et al., Endocrinology, 146 pp5092-5099, 2005). It is interesting to note that the effect of acetate on reducing plasma free 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:



(I),

wherein

Ar^1 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_3-C_6 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, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkoxyalkoxy, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, 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, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl;

L^1 is a single bond, C_1-C_2 alkylene, C_1-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; or L^1 is $-N(R^N)-$, wherein R^N is H or C_1-C_2 alkyl; or **L^1** and **R^1** together are =CH-;

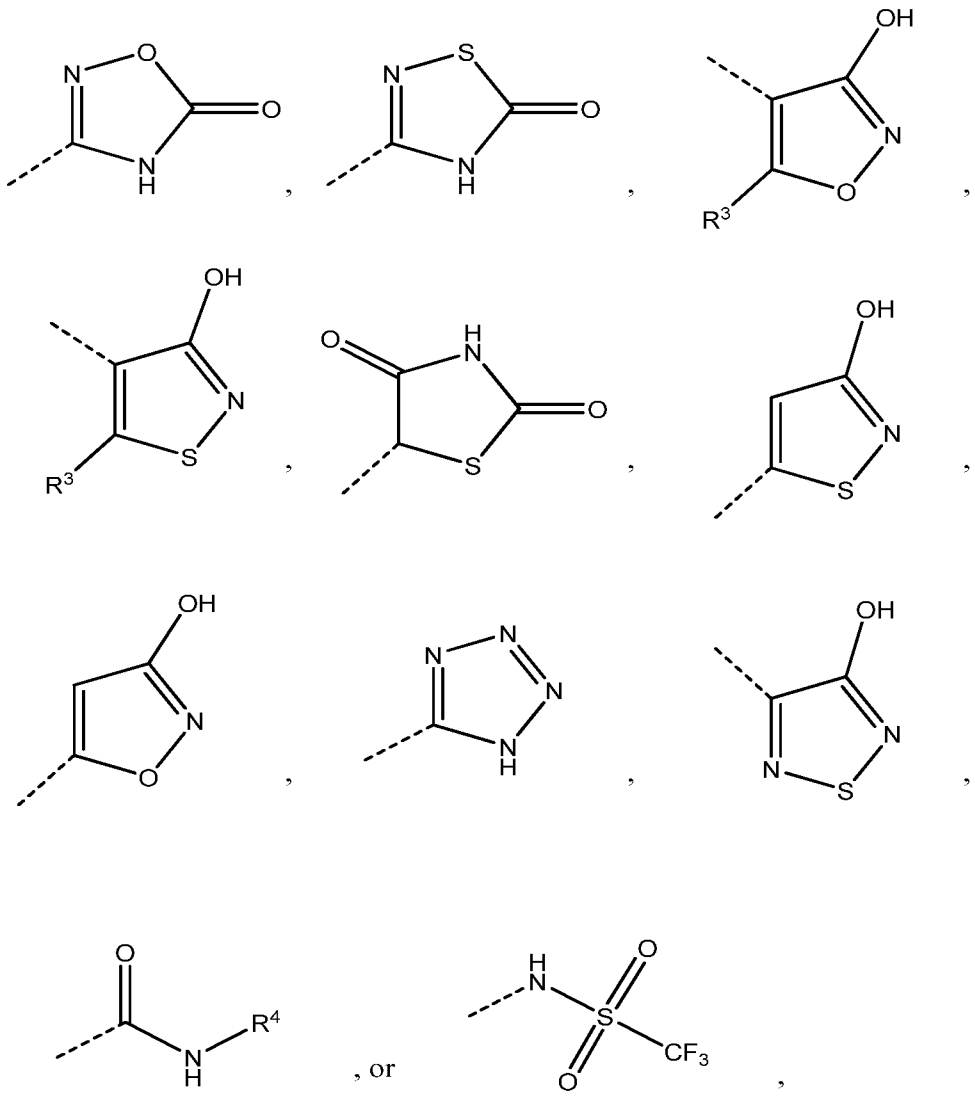
R^1 is H, halo, allyl, or a C_1-C_4 alkyl group, which may optionally be substituted by one or more groups selected from halo or C_1-C_4 alkyl;

L^2 is a C_1-C_3 alkylene, C_2-C_4 alkenylene, C_3-C_6 cylcloalkylene, each of which being optionally substituted by one or more groups selected from halo, alkyl, alkoxy, or haloalkyl; or **L^2** is -O-CH_2-; or

R^1 and **L^2** together are =CH-, under the condition that **$-L^1$-Ar^1** is H; or

R^1 and **L^2** together are a 5- to 6-membered saturated or unsaturated carbocyclic or heterocyclic group, preferably a cyclohexenyl group, under the condition that **$-L^1$-Ar^1** is H;

Z is selected from the group consisting of -COOR,



wherein **R** is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene, $\mathbf{R^3}$ is H, methyl or ethyl, and $\mathbf{R^4}$ is hydroxyl $-SO_2CH_3$, $-SO_2$cyclopropyl or $-SO_2CF_3$;

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, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group;

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, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group;

L^3 is a single bond, C_1-C_3 alkylene, C_1-C_3 cycloalkylene C_1-C_3 alkenylene or carbonylamino;

Ar^3 is an aryl, heteroaryl, or C_1-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, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, 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, alkylaminoalkyl, alkylaminocarbonyl, alkylcarbonyl, cycloalkylcarbonylamino, alkylheterocyclyl, alkylheteroaryl, alkylsulfonyl, alkylsulfonylamino, aralkyl, aralkyloxy, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, heterocyclyloxy, hydroxyl, oxo, or sulfonyl, or $\mathbf{L^3}$-$\mathbf{Ar^3}$ form an aryl, preferably phenyl, or heteroaryl group fused to $\mathbf{Ar^2}$, wherein each of said aryl or heteroaryl groups fused to $\mathbf{Ar^2}$ are optionally substituted by one or more halo, preferably chloro and fluoro;

with the following provisos:

$\mathbf{Ar^2}$-$\mathbf{L^3}$-$\mathbf{Ar^3}$ 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-isobutylphenyl)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-butyl)phenyl)-5-methylthiazol-2-yl, 4-(4-isopropylphenyl)-5-methylthiazol-2-yl, 4-(4-isobutylphenyl)-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-isobutyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-(tert-butyl)-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-yl]amino]carbonyl]-3-cyclohexene-1-carboxylic acid,

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

2-[[[4-(4-methoxyphenyl)-5-methyl-2-thiazolyl] amino]carbonyl]-cyclohexanecarboxylic acid,

6-[[[4-(3,4-dimethylpheny1)-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-yl]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]-cyclohexanecarboxybic 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-l-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-carboxybic 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-2yl]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-[[(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]-cyclohexanecarboxybic 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]-cyclohexanecarboxybic 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)carbony1]-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[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

$\mathbf{R^1}$ 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 $\mathbf{R^1}$ 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 $\mathbf{R^1}$ is hydrogen, fluoro or methyl, and most preferably $\mathbf{R^1}$ is hydrogen, and $\mathbf{L^2}$ is as defined above in respect to formula I, preferably $\mathbf{L^2}$ is cyclopropylene, ethenylene, 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 $\mathbf{L^2}$ is cyclopropylene, ethenylene, methylene, –CHMe-, –CHF-; even more preferably $\mathbf{L^2}$ is methylene, or $\mathbf{R^1}$ and $\mathbf{L^2}$ together are =CH-; and/or

$\mathbf{R^2}$ is H, linear or branched C_1-C_4 alkyl, C_1-C_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, benzyloxyethyl, methoxyethyl, preferably $\mathbf{R^2}$ is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, $-C_2H_4CO_2CH_3$, $-CH_2CO_2CH_3$, $-CH_2CONH_2$, more preferably $\mathbf{R^2}$ is methyl or cyclopropyl; and/or

$\mathbf{Ar^1}$ 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 $\mathbf{L^1}$ is a single bond, C_1-C_2 alkylene, 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 $\mathbf{L^1}$ is a single bond, C_1-C_2 alkylene, optionally substituted by C_1-C_2 alkyl, preferably $\mathbf{Ar^1}$ is phenyl or cyclohexyl and $\mathbf{L^1}$ is methylene, optionally substituted by methyl; or $\mathbf{Ar^1}$ 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 $\mathbf{L^1}$ is a single bond, C_1-C_2 alkylene, or C_2 alkenylene, preferably C_1-C_2 alkylene or C_2 alkenylene, and even more preferably C_1-C_2 alkylene, (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 $\mathbf{L^1}$ is a single bond or C_1-C_2 alkylene, optionally substituted by C_1-C_2 alkyl or one or more fluoro, more preferably $\mathbf{L^1}$ is CH_2; preferably $\mathbf{Ar^1}$ is isopropyl, butyl, isobutyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl, tetrahydropyranyl, phenyl, furanyl, thiophenyl, thiazolyl or pyridyl, and $\mathbf{L^1}$ is CH_2, more preferably $\mathbf{Ar^1}$ is cyclopentyl, tetrahydrofuranyl, tetrahydropyranyl, phenyl or furanyl and $\mathbf{L^1}$ is CH_2; and/or

$\mathbf{Ar^2}$ is selected from the group consisting of thiazolylene, 1,2,4-thiadiazolylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, triazinylene, 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 C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, preferably F, Cl, CH_3, or CF_3, preferably $\mathbf{Ar^2}$ is thiazolylene, 1,2,4-thiadiazolylene, pyridinylene, more preferably $\mathbf{Ar^2}$ is thiazolylene linked to the nitrogen of N-$\mathbf{R^2}$ at position 2 and to $\mathbf{L^3}$ of $\mathbf{L^3}$-$\mathbf{Ar^3}$ at position 4, 1,2,4-thiadiazolylene linked to the nitrogen of N-$\mathbf{R^2}$ at position 5 and to $\mathbf{L^3}$ of $\mathbf{L^3}$-$\mathbf{Ar^3}$ at position 3, pyridinylene linked to the nitrogen of N-$\mathbf{R^2}$ at position 2 and to $\mathbf{L^3}$ of $\mathbf{L^3}$-$\mathbf{Ar^3}$ at position 5; and/or

$\mathbf{Ar^3}$ 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, pyrazinyl, and pyridazinyl, phenyl, methylcarbonylamino, -NH-SO_2CF_3, methylenedioxy and $\mathbf{L^3}$ is a single bond or C_1-C_2 alkylene; $\mathbf{Ar^3}$ is a C_1-C_4 alkyl group and $\mathbf{L^3}$ is a single bond; or **–** $\mathbf{L^3}$**-**$\mathbf{Ar^3}$ is a phenyl group fused to $\mathbf{Ar^2}$**;** preferably $\mathbf{Ar^3}$ 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

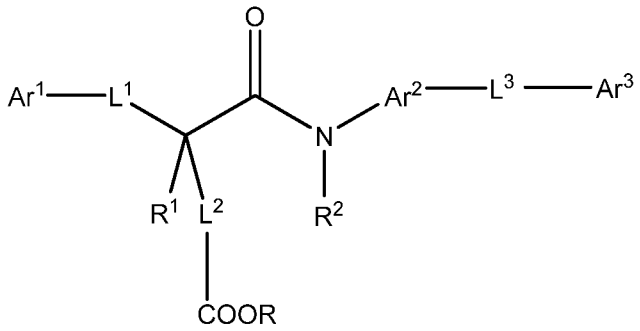
6 membered heteroaryl, preferably furanyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, more preferably furan-3-yl, thiophen-3-yl, pyridinyl, still more preferably pyridin-3-yl, each of said 5 or 6 membered aryl or 5 or 6 membered heteroaryl being optionally fused to one or more 5 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, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, arylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl; more preferably $\mathbf{Ar^3}$ 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, morpholinyl, pyrrolyl, imidazolyl, or pyridinyl, more preferably 2-oxopyrrolidinyl 2-oxoimidazolinyl, 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, 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^1** and **L^2** together are a 5- to 6-membered saturated or unsaturated carbocyclic or heterocyclic group, preferably a cyclohexenyl group, under the condition that **$-L^1$-Ar^1** is H; and **Ar^2**, **Ar^3**, **R^2**, and **L^3** are as defined above.

Still other preferred compounds of formula I are those wherein **D** is SO_2 and **Ar^1**, **Ar^2**, **Ar^3**, **R^1**, **R^2**, **L^1**, **L^2**, **L^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:



Ia

and pharmaceutically acceptable salts, and solvates thereof, wherein

R is H or linear or branched C_1-C_4 alkyl; and

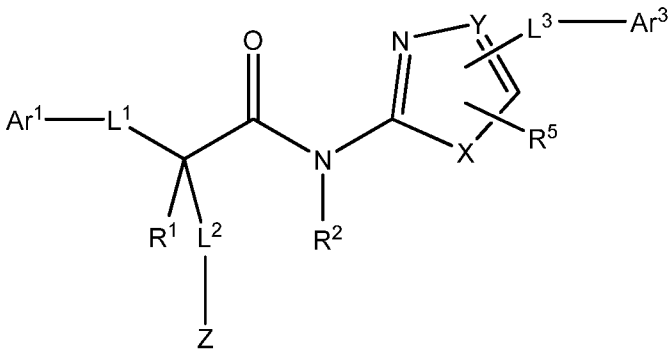
Ar^1, **Ar^2**, **Ar^3**, **R^1**, **R^2**, **L^1**, **L^2** and **L^3** are as defined above in respect to formula I.

Preferred compounds of formula Ia are those wherein

R^1 is hydrogen and **L^2** is ethenylene, ethylene, n-propylene, -CH(Me)-, -CH_2-, -CHF-, -CF_2-, or cyclopropylene; or **R^1** and **L^2** together are =CH-; and

Ar^1, **Ar^2**, **Ar^3**, **R^2**, **L^1** and **L^3** are as defined above in respect to formula I.

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

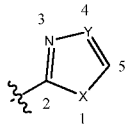


Ib

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^3 is attached to the heterocyclic group  either in position 4 or 5, preferably in position 4; and

if **Y** is CH, **R^5** is H, halo, cyano, hydroxyl, linear or branched C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, preferably H, methyl, F, Cl, or CF_3, more preferably H or F 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, $\mathbf{R^5}$ is absent and $\mathbf{L^3}$ is attached in position 5; and

$\mathbf{Ar^1}$ and $\mathbf{L^1}$ are as defined above in respect to formula I, preferably $\mathbf{Ar^1}$ 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 $\mathbf{L^1}$ is a single bond, C_1-C_2 alkylene, 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 $\mathbf{L^1}$ is a single bond, or C_1-C_2 alkylene, optionally substituted by C_1-C_2 alkyl, more preferably $\mathbf{L^1}$ is -CH_2; or $\mathbf{Ar^1}$ 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 $\mathbf{L^1}$ is a single bond; or $\mathbf{Ar^1}$ is cycloalkyl, preferably cyclopropyl, cyclopentyl, cyclohexyl, bicyclo[2.2.1]heptan-2-yl, more preferably cyclopentyl, or heterocycloalkyl, preferably tetrahydrofuranyl or tetrahydropyranyl and $\mathbf{L^1}$ is C_1-C_2 alkylene or C_2 alkenylene, preferably C_1-C_2 alkylene 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 $\mathbf{L^1}$ is a single bond or C_1-C_2 alkylene, optionally substituted by C_1-C_2 alkyl, even more preferably $\mathbf{L^1}$ is methylene;

$\mathbf{Ar^3}$ is as defined above in respect to formula I, preferably $\mathbf{Ar^3}$ 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-SO_2CF_3, and $\mathbf{L^3}$ is a single bond or C_1-C_2 alkylene; or $\mathbf{Ar^3}$ is a C_1-C_4 alkyl group and $\mathbf{L^3}$ is a single bond, more preferably $\mathbf{Ar^3}$ 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, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, arylamino, 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 **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, 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 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, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from fluoro, chloro, oxo or methyl;

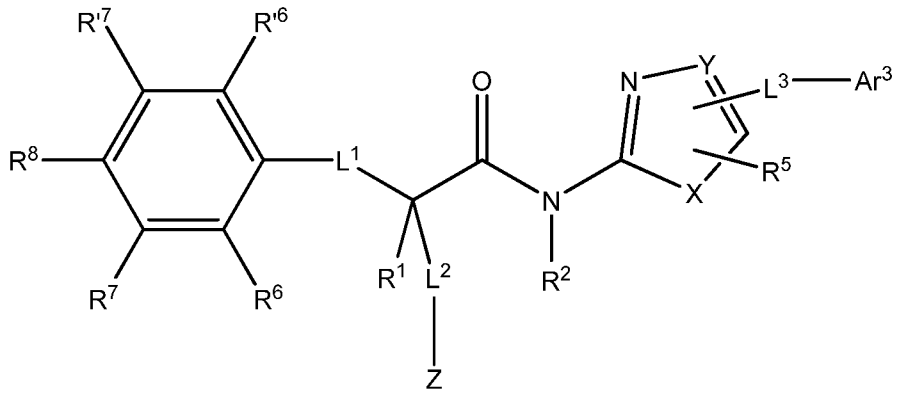
$\mathbf{R^1}$ is as defined above in respect to formula I, preferably $\mathbf{R^1}$ is hydrogen, halogen, allyl, or a group selected from C_{1-4} alkyl optionally substituted by one or more substituents selected from halogen or alkyl; more preferably $\mathbf{R^1}$ is selected from hydrogen, fluoro, 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 $\mathbf{R^1}$ is hydrogen, fluoro or methyl, and most preferably $\mathbf{R^1}$ is hydrogen, and $\mathbf{L^2}$ is as defined above in respect to formula I, preferably $\mathbf{L^2}$ is cyclopropylene, ethenylene, n-propylene, –C(R'R'')-, wherein R' and R'' are independently selected from H, halogen, methyl, and ethyl, more preferably $\mathbf{L^2}$ is cyclopropylene, ethenylene, methylene, –CHMe-, –CHF-, even more preferably $\mathbf{L^2}$ is methylene; or $\mathbf{R^1}$ and $\mathbf{L^2}$ 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

$\mathbf{R^2}$ is as defined above in respect to formula I, preferably $\mathbf{R^2}$ is H, linear or branched C_1-C_4 alkyl, C_1-C_2 hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentylmethyl, cyclopropylmethyl, benzyl, benzyloxyethyl, methoxyethyl, 1,1,1-trifluoroethyl, $-C_2H_4CO_2CH_3$, $-CH_2CO_2CH_3$, or $-CH_2CONH_2$, more preferably $\mathbf{R^2}$ is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, $-C_2H_4CO_2CH_3$, $-CH_2CO_2CH_3$, or $-CH_2CONH_2$, more preferably $\mathbf{R^2}$ is methyl or cyclopropyl.

Preferred compounds of formula Ib are those wherein **Z** is –COOR, preferably COOH, and **R**, $\mathbf{Ar^1}$, $\mathbf{Ar^2}$, $\mathbf{Ar^3}$, $\mathbf{R^1}$, $\mathbf{R^2}$, $\mathbf{L^1}$, $\mathbf{L^2}$ and $\mathbf{L^3}$ are as defined above in respect to formula I.

Particularly preferred compounds of formula Ib are those of formula Ib-1



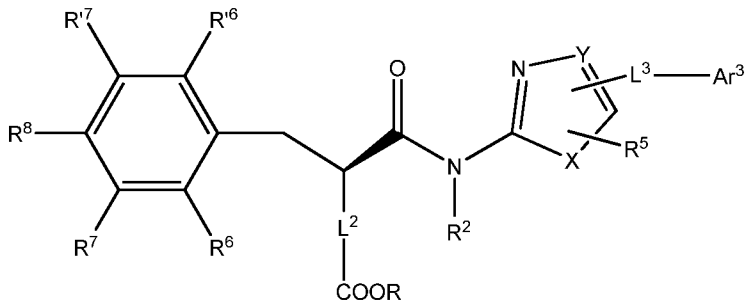
Ib-1

wherein **L^1, L^2, L^3, Ar^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, optionally substituted by C_1-C_2 alkyl or halo, preferably by methyl or fluoro, even more preferably **L^1** is methylene; 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, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, 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 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, 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, heteroarylalkyl, 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**, **R'^7** and **R^8** 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, CF_3, C1-C2 alkyl, C1-C2 alkoxy, and cyano, still more preferably from H, F, Cl, CF_3, 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.

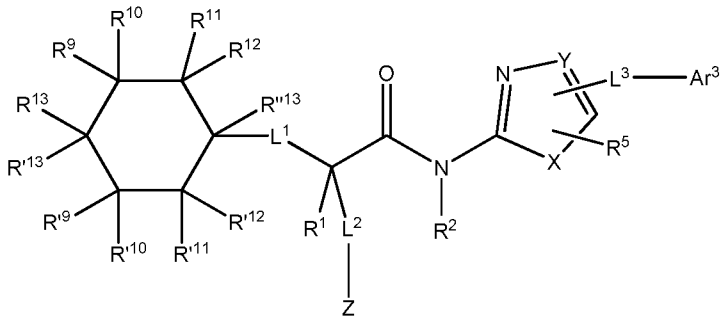
Preferred compounds of formula Ib-1 are those of formula Ib-1a



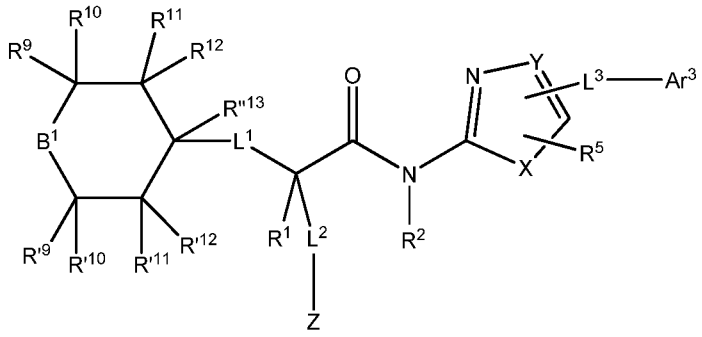
Ib-1a

wherein **L^2, L^3, Ar^3, X, Y, R^2, R^5, R^6, R^7, R'^6, R'^7** and **R^8** are as defined above in respect to formula Ib-1.

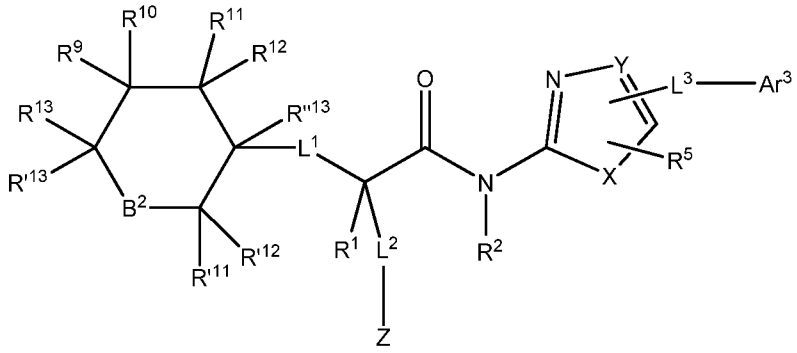
Other preferred compounds of formula Ib are selected form the group consisting of formulae Ib-2a, Ib-2b, Ib-2c, Ib-2d, Ib-2e and Ib-2f:



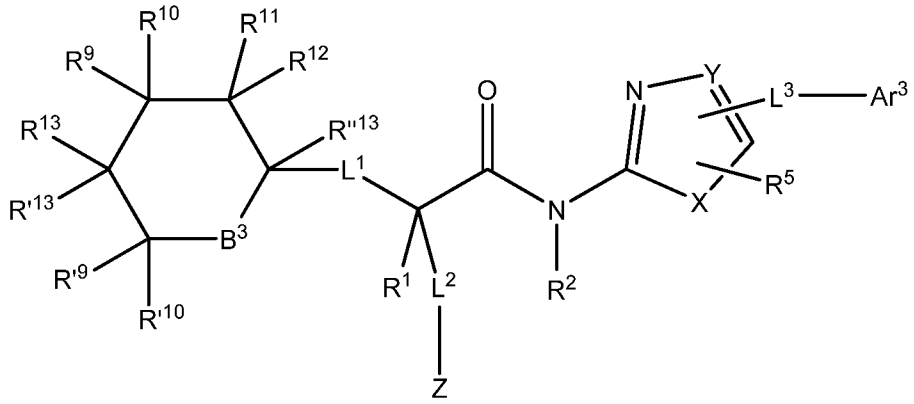
Ib-2a



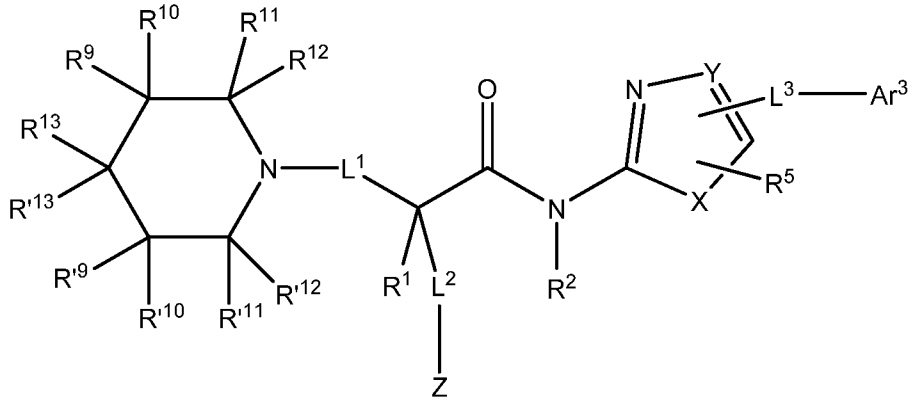
Ib-2b



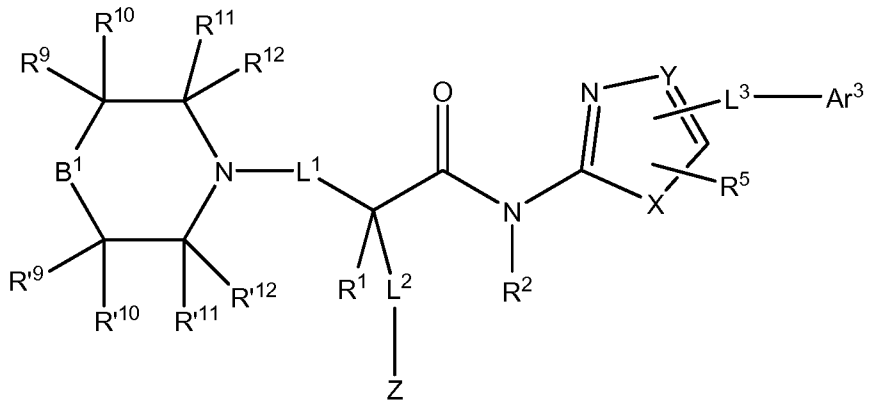
Ib-2c



Ib-2d



Ib-2e



Ib-2f

wherein **L^1, L^2, L^3, Ar^3, X, Y, Z, R^1, R^2** and **R^5** are as defined above in respect to

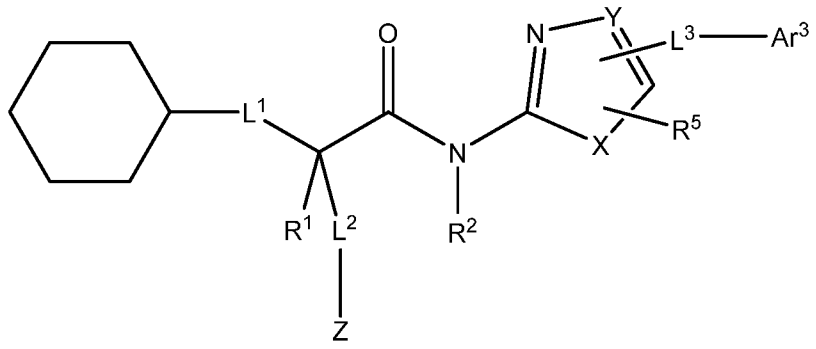
formula Ib, preferably L^1 is methylene;

B^1, B^2 and B^3 are independently CF_2, O, NR^a, CO, or SO_2, wherein R^a is H or alkyl, preferably linear or branched C_1-C_4 alkyl; C_1-C_4 alkylcarbonyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylaminocarbonyl, C_3-C_6 cycloalkyl; C_3-C_6 cycloalkylcarbonyl, C_3-C_6 cycloalkylsulfonyl, C_3-C_6 cycloalkylaminocarbonyl, aryl, arylcarbonyl, arylsulfonyl or arylaminocarbonyl, heteroaryl, heteroarylcarbonyl, heteroarylsulfonyl or heteroarylaminocarbonyl; preferably B^1, B^2 and B^3 are O and

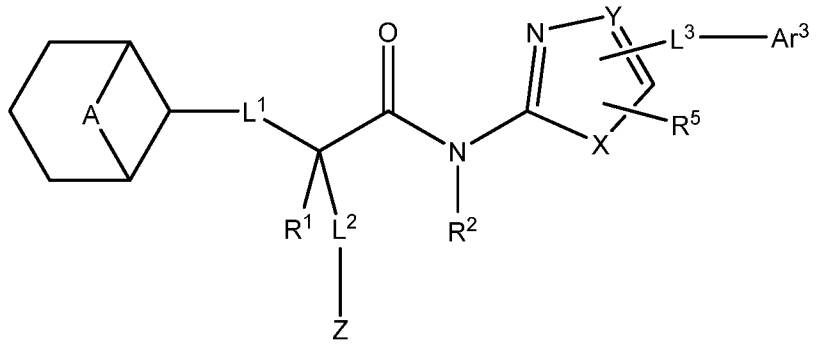
R^9, R^{10}, R^{11}, R^{12}, R^{13}, R'^9, R'^{10}, R'^{11}, R'^{12}, R'^{13} and R''^{13} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, 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^{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 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}, 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, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably **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, 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, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, 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 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 **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, hydroxyl, C_1-C_3-alkyl, halo, haloalkyl, alkoxy, haloalkoxy, alkylsulfonyl, haloalkylsulfonyl and cyano, even more preferably from H, C_1-C_3-alkyl, halo, CF_3, C1-C2 alkoxy, and cyano, and still more preferably from H, F, Cl, methyl, CF_3, methoxy, and cyano, and most preferably H or methyl.

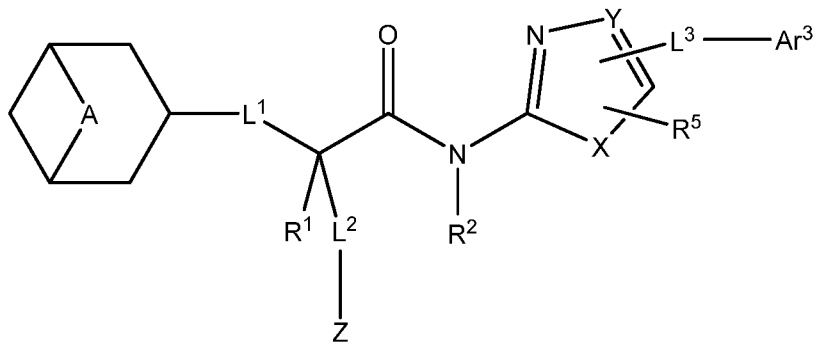
Particularly preferred compounds of formula Ib-2a are



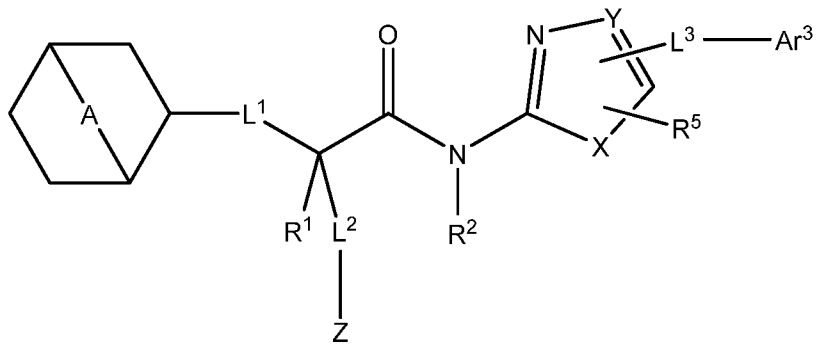
,



,



,



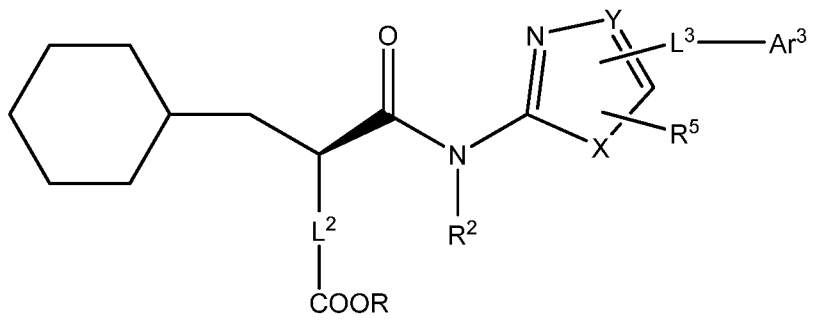
,

wherein **A** is $-(CH_2)_n-O-$, $-(CH_2)_n-NR^a-$, $-(CH_2)_n-SO_2-$, or $-(CH_2)_m-$, wherein n is

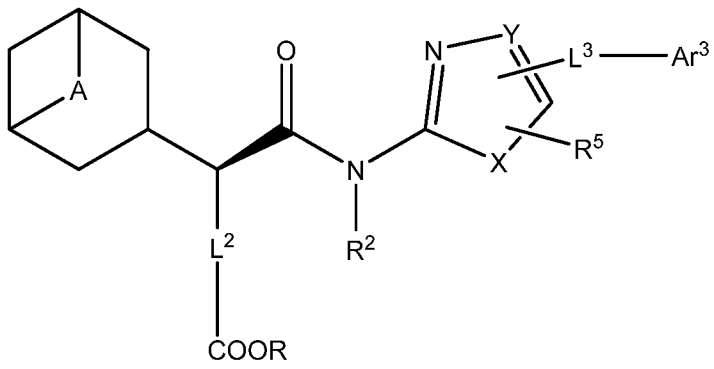
equal to 0 or 1, m is equal to 1 or 2, and R^a is as defined above in respect to formula Ib-2b, preferably R^a is H or alkyl, preferably linear or branched C_1-C_4 alkyl; C_1-C_4 alkylcarbonyl, C_1-C_4 alkylsulfonyl, more preferably linear or branched C_1-C_4 alkyl; and

L^1, L^2, L^3, Ar^3, X, Y, Z, R^1, R^2 and **R^5** are as defined above in respect to formula Ib-2a.

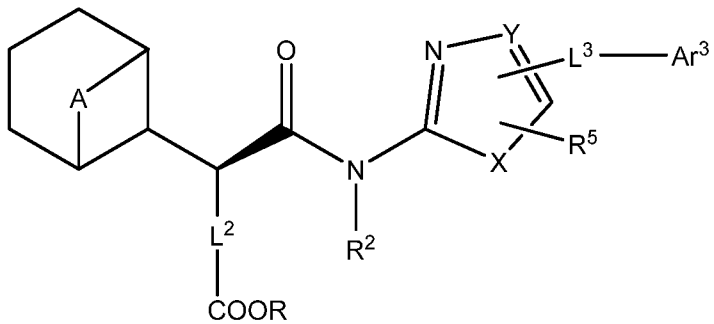
Even more preferred compounds of formula Ib-2a are selected from



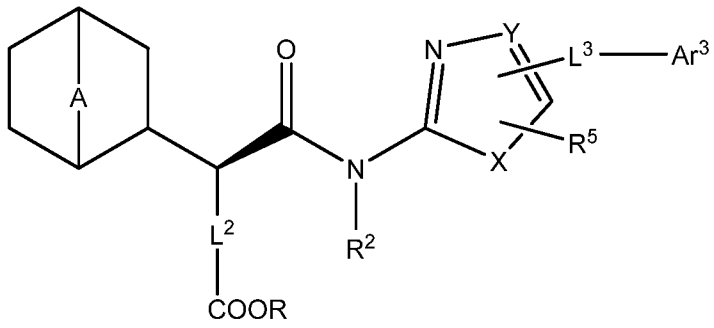
,



,



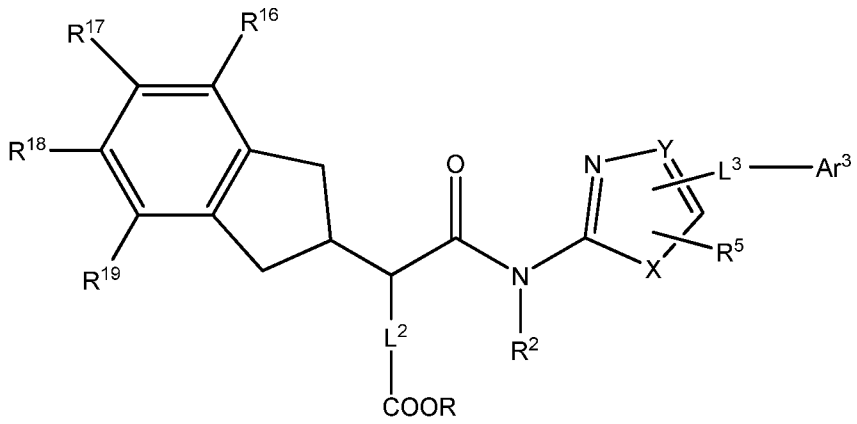
, and



wherein **A** is $-(CH_2)_n-O-$, $-(CH_2)_n-NR^a-$, $-(CH_2)_n-SO_2-$, or $-(CH_2)_m-$, wherein n is equal to 0 or 1, m is equal to 1 or 2, and 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 alkylsulfonyl, more preferably linear or branched C_1-C_4 alkyl; and

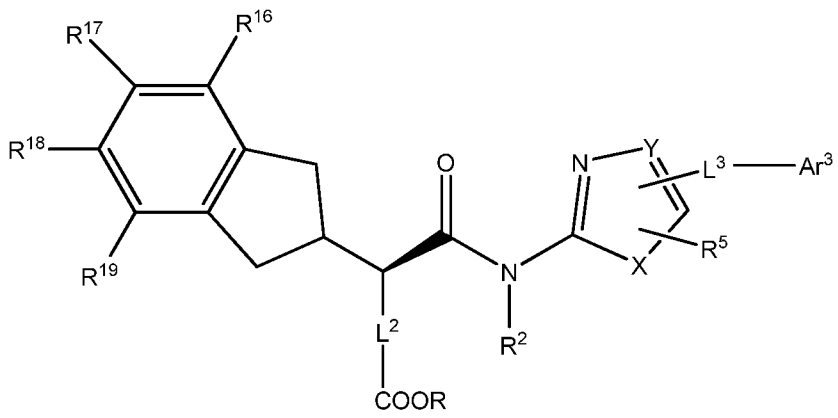
L^2, L^3, Ar^3, X, Y, R, R^1, R^2 and **R^5** are as defined above in respect to formula Ib-2a.

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



Ib-3,

preferably



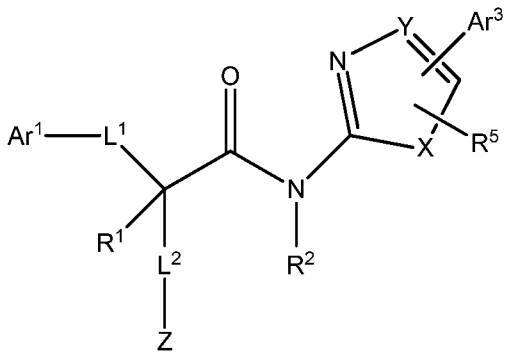
Ib-3a,

wherein **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; 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, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or 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, heteroarylalkyl, 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, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylalkyl, 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



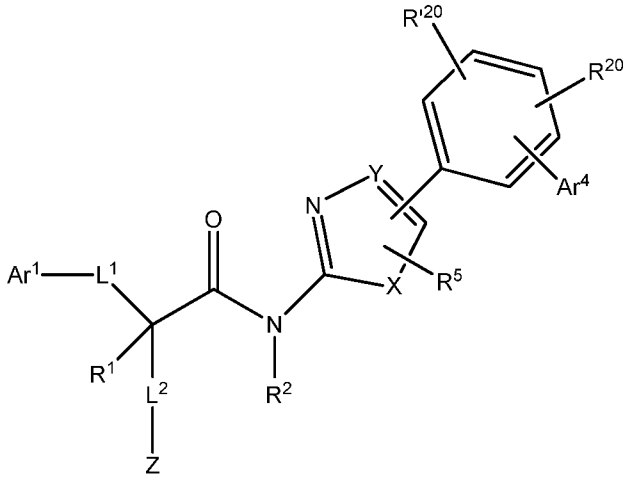
Ib-4,

wherein

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

formula Ib.

Preferred compounds of formula Ib-4 are those of formula Ib-4a



Ib-4a

wherein

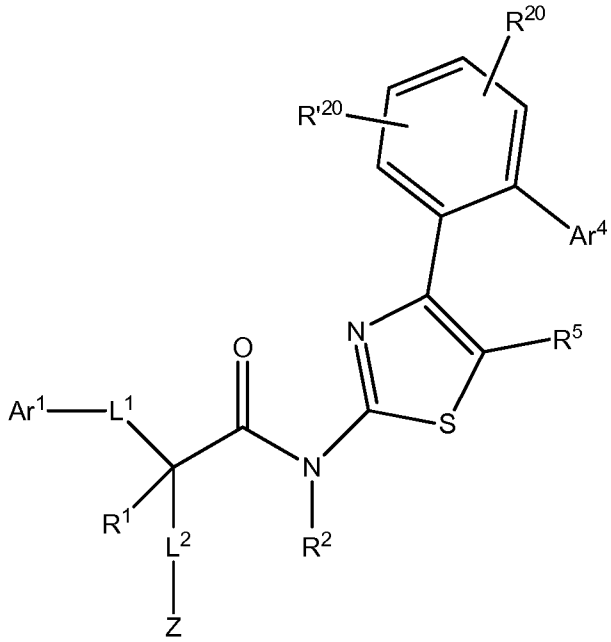
Ar^1, **L^1**, **L^2**, **R^1**, **R^2**, **R^5**, **X**, **Y** and **Z** are as defined above in respect to formula Ib-4,

R^{20} and **R'^{20}** are independently selected from halo (preferably –F and –Cl), cyano, C_1-C_3 alkyl, cyclopropyl, haloalkyl, alkoxy, haloalkoxy, alkoxycarbonylamino, or the two substituents form an alkylenedioxy group or a haloalkylenedioxy group, , preferably **R^{20}** and **R'^{20}** are halo preferably fluoro or chloro, haloalkyl, preferably -CF_3 or -CHF_2, alkoxy preferably methoxy, haloalkoxy preferably -OCF_3 or -$OCHF_2$;

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, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, 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 $\mathbf{Ar^4}$ 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-oxoimidazolinyl, 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, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aralkyloxy, cycloalkylamino, aralkylamino, cycloalkylcarbonylamino 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

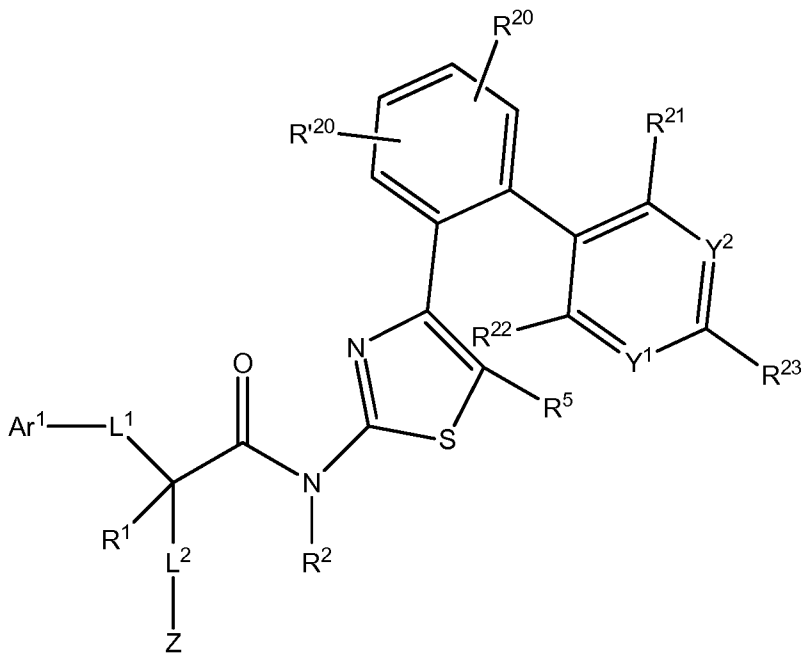


Ib-4b

wherein

Ar^1, **L^1**, **L^2**, **R^1**, **R^2**, **R^5**, and **Z** are as defined above in respect to formula Ib, and **Ar^4**, **R^{20}** and **R'^{20}**, are as defined above in respect to formula Ib-4a.

Preferred compounds of formula Ib-4b are those of formula Ib-4c



Ib-4c

wherein

Ar^{1}, **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;

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

R^{23} 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,

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 $\mathbf{R^{23}}$ 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 cyclopropylmethyloxy, heterocyclyloxy, preferably (tetrahydropyran-4-yl)oxy, aralkyloxy, preferably benzyloxy, C_1-C_3 alkylamino, 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 $\mathbf{R^{23}}$ 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, alkyloxyalkoxy, preferably methoxyethoxy, aralkyloxy, preferably benzyloxy, 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;

$\mathbf{Y^1}$ is N or C-$\mathbf{R^{24}}$ where $\mathbf{R^{24}}$ is H, halo, alkoxy, alkyl, heterocyclyl, preferably pyrrolidinyl, imidazolinyl, 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 $\mathbf{R^{24}}$ is H, halo, methoxy, more preferably H, chloro or fluoro, or

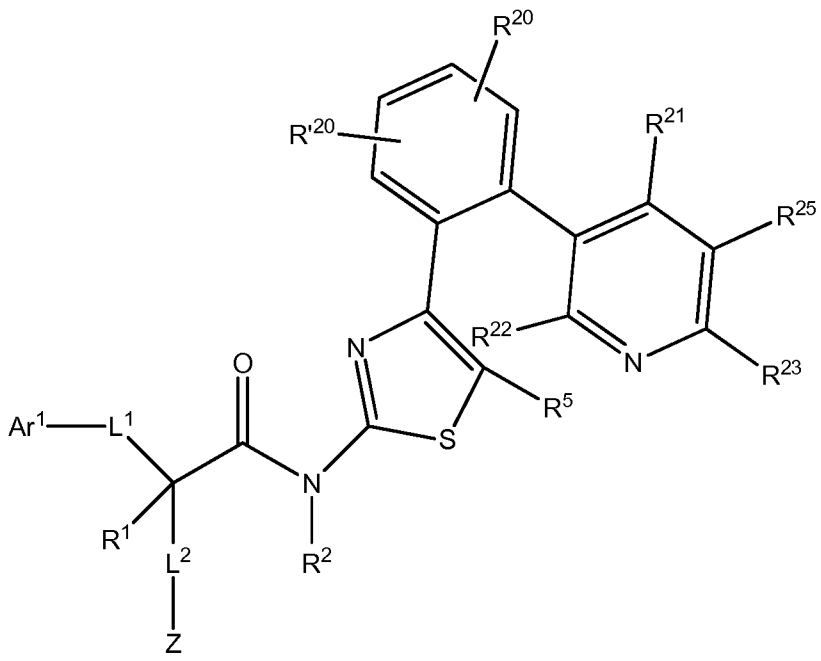
$\mathbf{Y^1}$ is C-$\mathbf{R^{24}}$ and $\mathbf{R^{24}}$ and $\mathbf{R^{23}}$ together form a 5 or 6 membered cycloalkyl, aryl,

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

$\mathbf{Y^2}$ is N or C-$\mathbf{R^{25}}$ where $\mathbf{R^{25}}$ is H, halo, alkoxy, alkyl, heterocyclyl, preferably pyrrolidinyl, imidazolinyl, piperidinyl or morpholinyl, more preferably 2-oxopyrrolidin-1-yl, 2-oxoimidazolin-1-yl, 2-oxopiperidin-1yl 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 $\mathbf{R^{25}}$ is H, halo, methoxy, more preferably H, chloro or fluoro, or

$\mathbf{Y^2}$ is C-$\mathbf{R^{25}}$ and $\mathbf{R^{25}}$ and $\mathbf{R^{23}}$ 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 $\mathbf{R^{24}}$ and $\mathbf{R^{23}}$ 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,

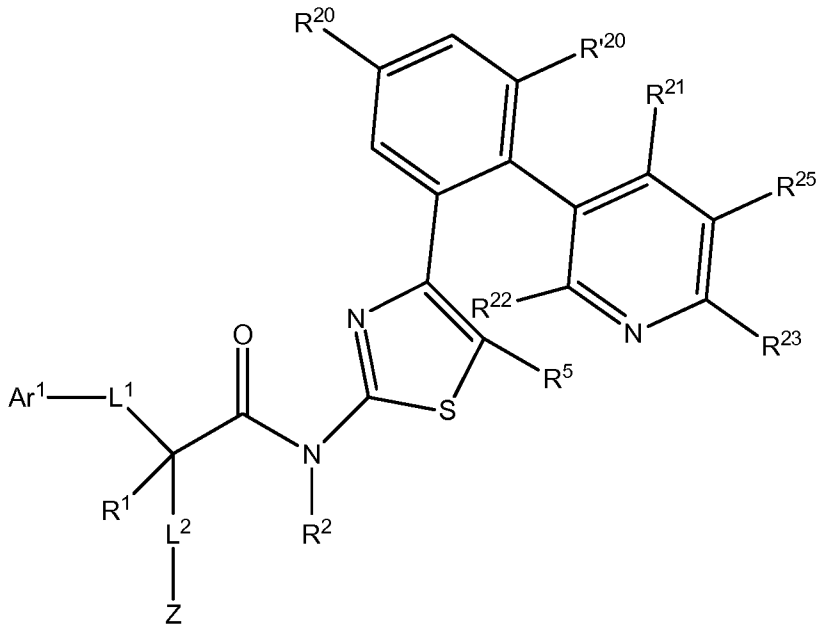
wherein,

Ar^{1}, **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.

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



Ib-4e,

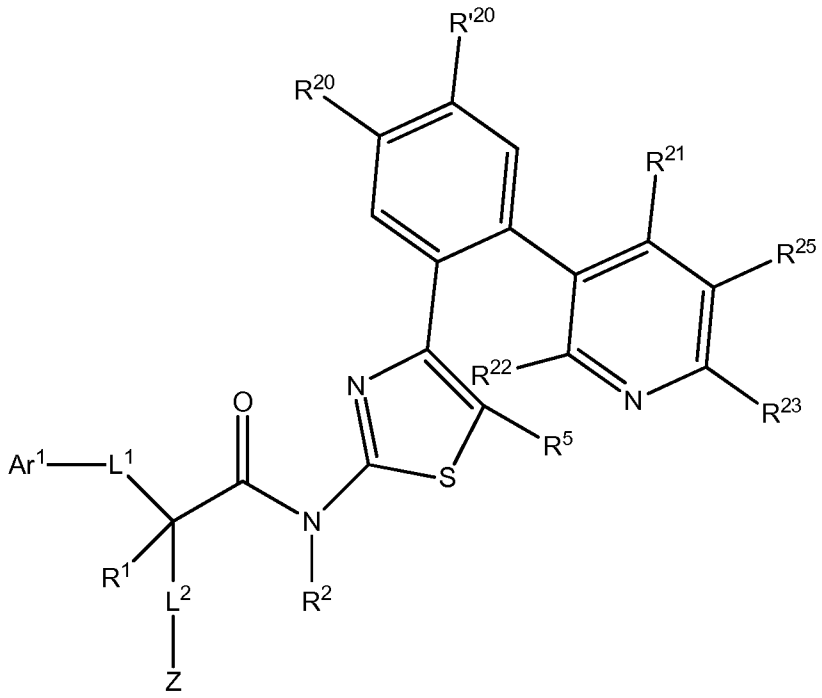
wherein,

Ar^{1}, **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 Ib-4f



Ib-4f,

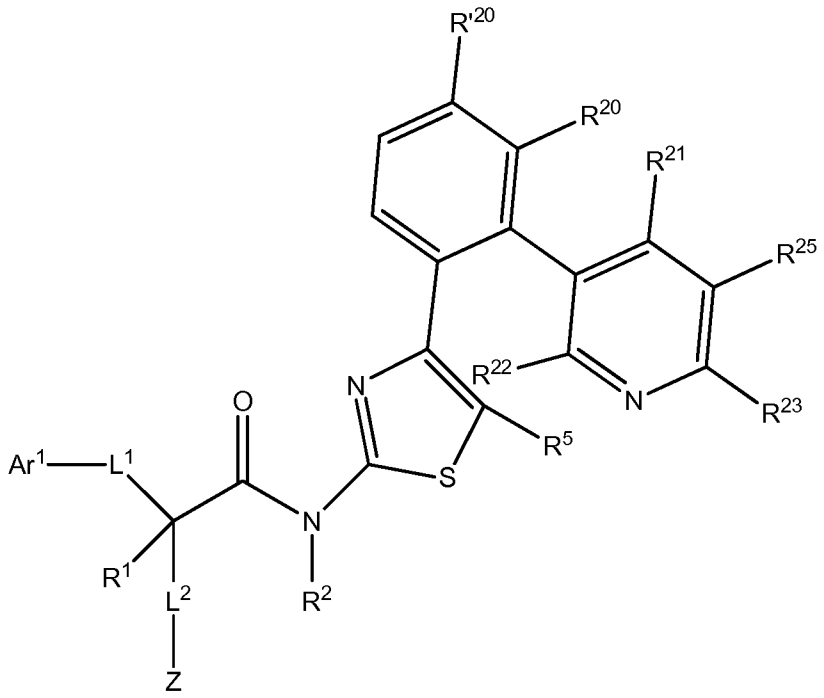
wherein

Ar^{1}, **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.

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



Ib-4g,

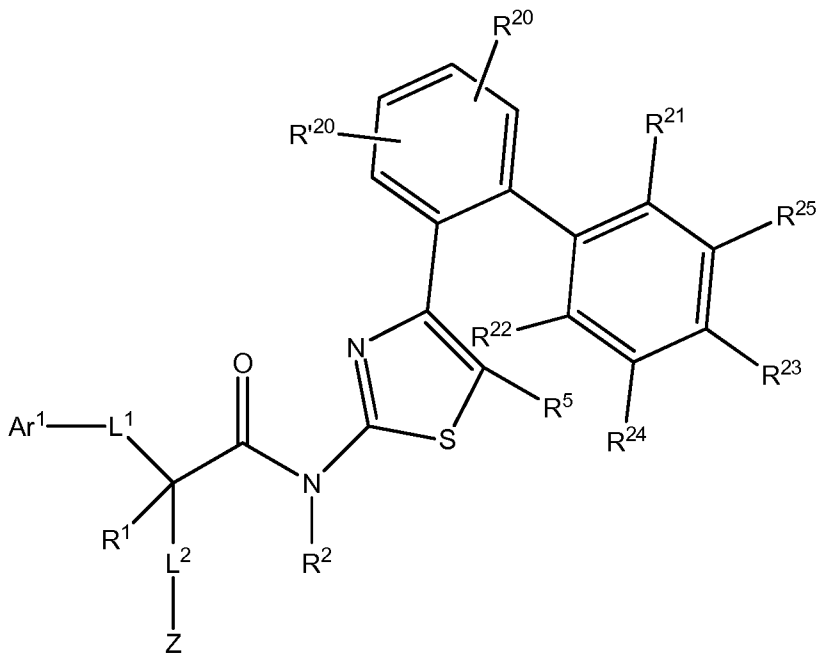
wherein

Ar^{1}, **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-4c are those of formula Ib-4d'



Ib-4d',

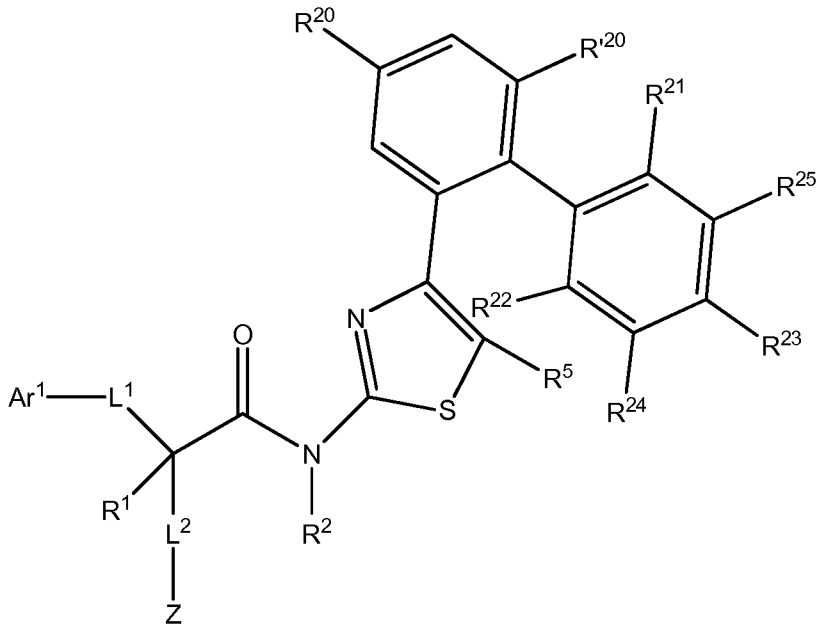
wherein

Ar^{1}, **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.

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



Ib-4e'

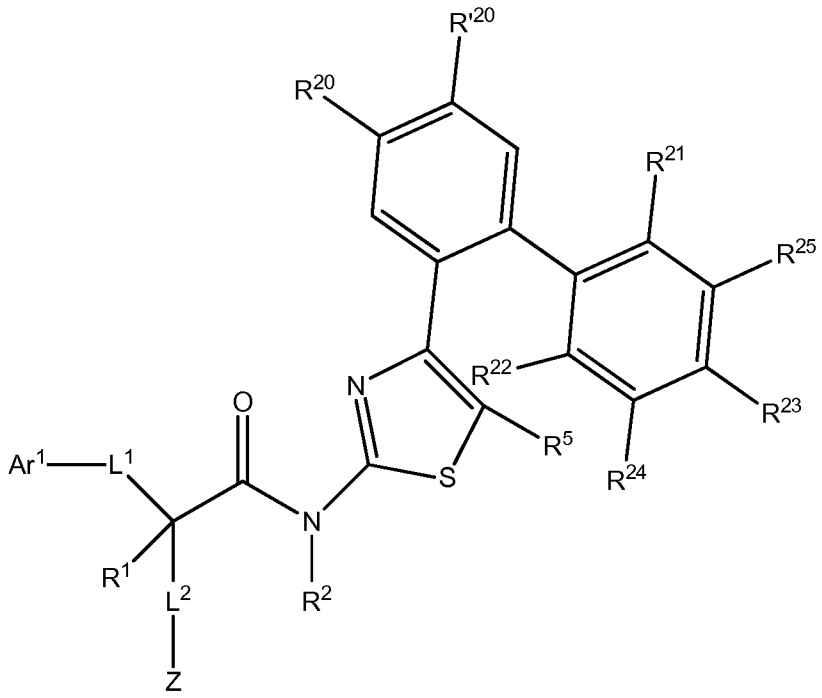
wherein

Ar^{1}, **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'

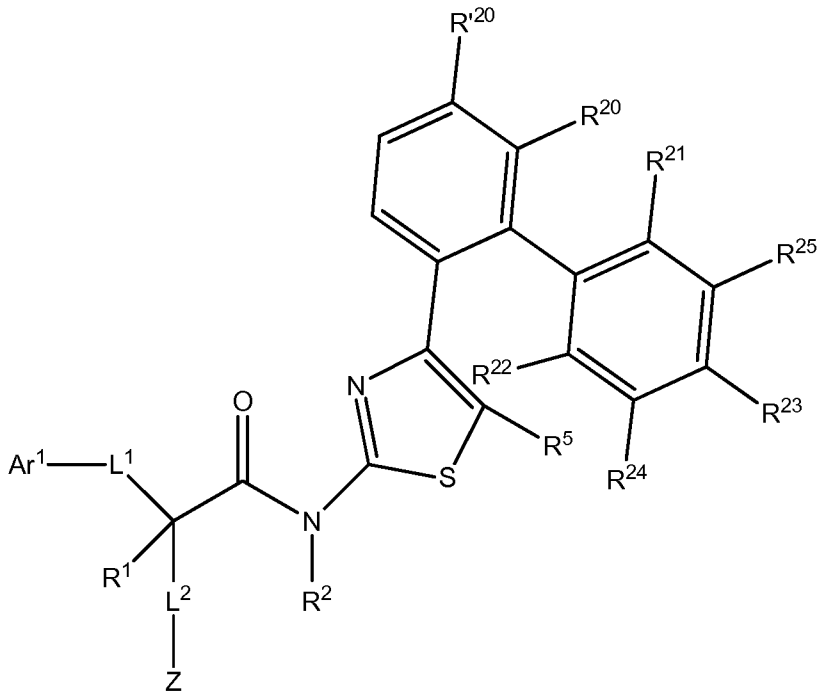
wherein

Ar^{1}, **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.

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



Ib-4g'

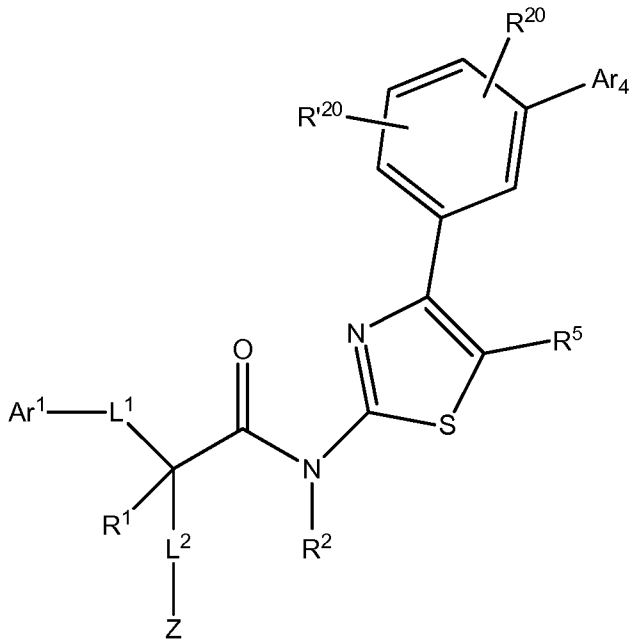
wherein,

Ar^1, **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;

R^{21}, **R^{22}**, **R^{23}** and **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,



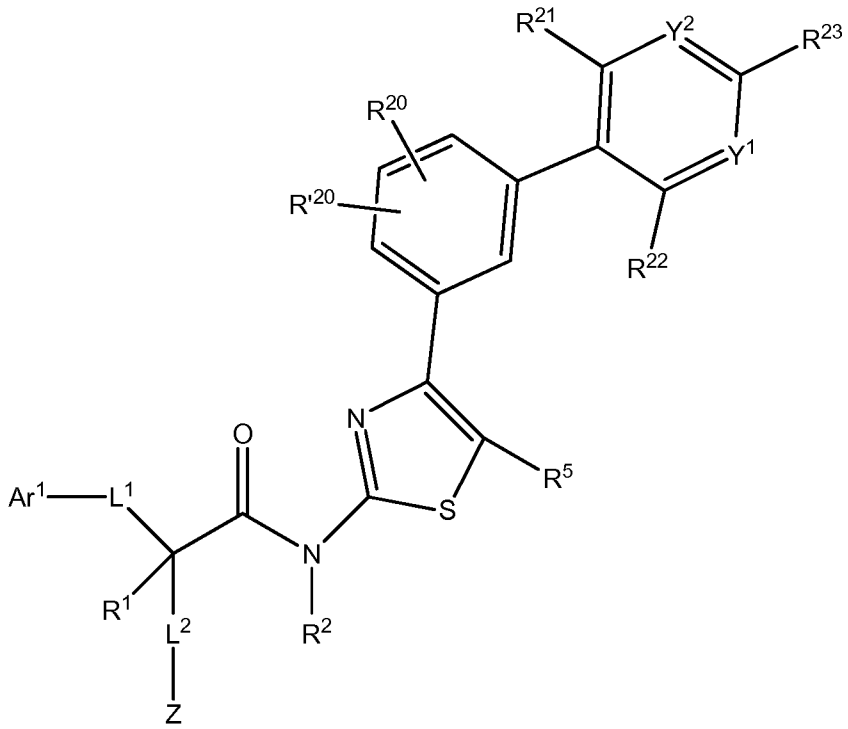
Ib-4h,

wherein

Ar^1, **L^1**, **L^2**, **R^1**, **R^2**, **R^5**, and **Z** are as defined above in respect to formula Ib; and

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

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



Ib-4i,

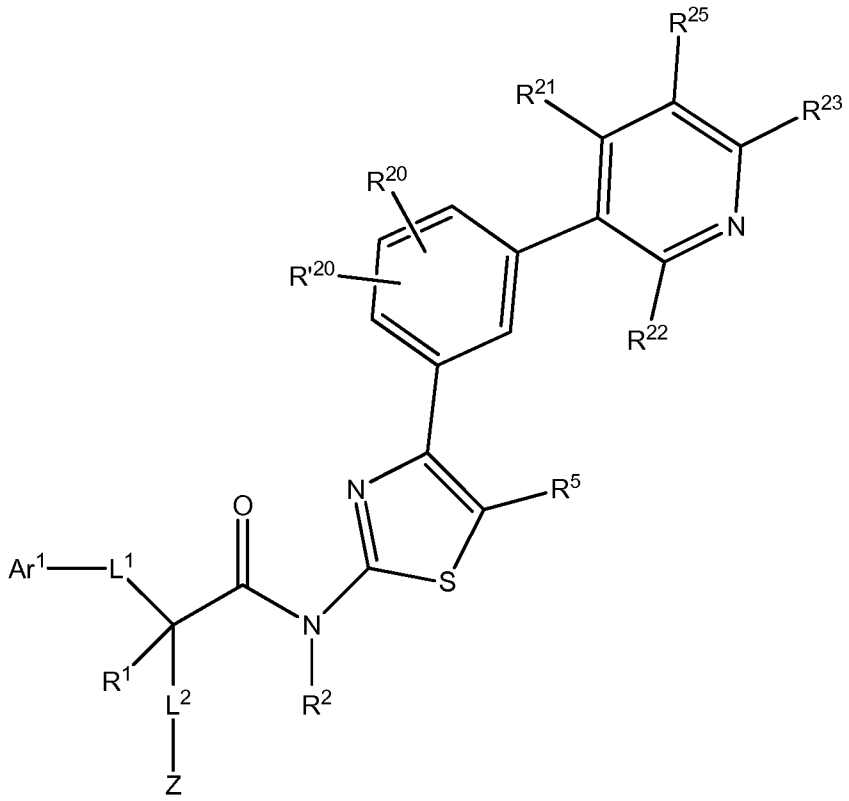
wherein

Ar^{1}, **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}, **Y**^{1} and **Y**^{2} are as defined above in respect to formula Ib-4c.

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



Ib-4j,

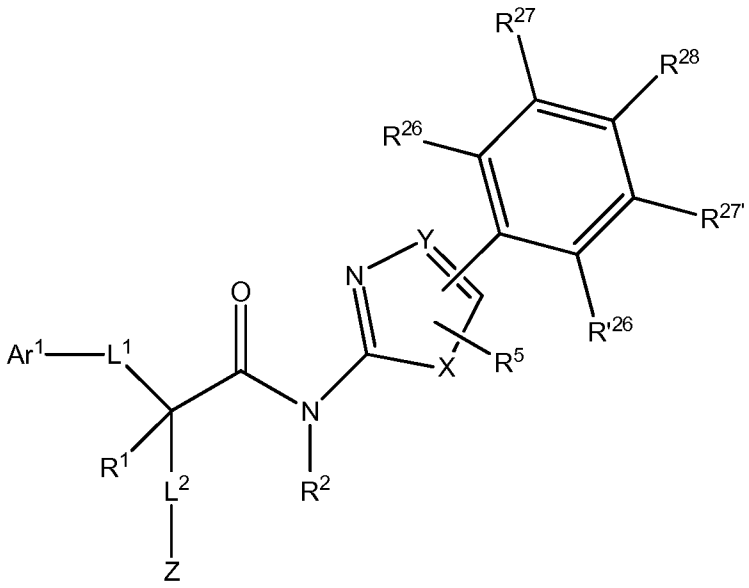
wherein

Ar^{1}, **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-4 are those of formula Ib-4k,



Ib-4k

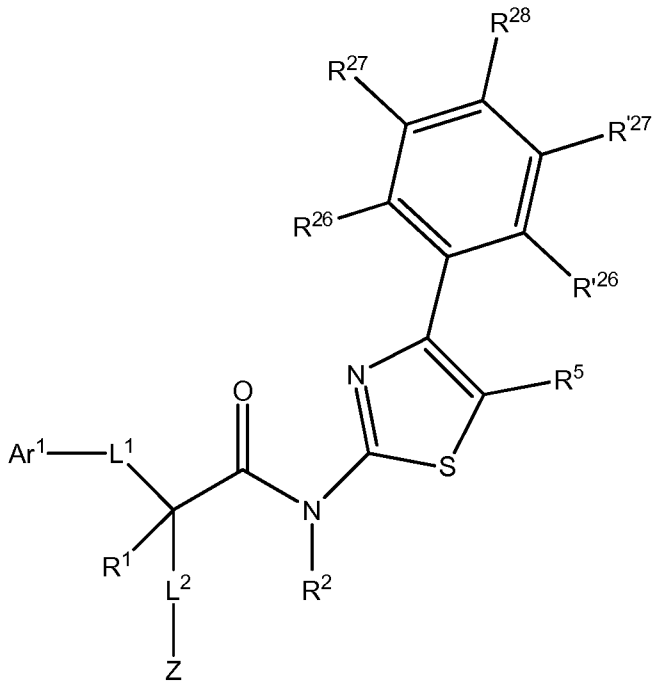
wherein

Ar^{1}, **L**^{1}, **L**^{2}, **R**^{1}, **R**^{2}, **R**^{5}, **X**, **Y**, and **Z** are as defined above in respect to formula Ib;

R^{26}, **R'**^{26}, **R**^{27}, **R'**^{27}, **R**^{28} are independently selected from H, halo, cyano, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, alkylamino, carboxy, alkoxycarbonyl,═alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, alkoxycarbamoyl, cycloalkylcarbamoyl, alkylcarbamoylamino, cycloalkylaminocarbamoyl, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, preferably **R**^{26}, **R'**^{26}, **R**^{27}, **R'**^{27}, **R**^{28} are independently selected from H, halo, preferably chloro or fluoro, more preferably chloro, cyano, alkyl, preferably methyl, haloalkyl, preferably –CF_3 or –CHF_2, cycloalkyl, preferably cyclopropyl, alkoxy, preferably methoxy or isopropyloxy, haloalkoxy, preferably –OCF_3 or –$OCHF_2$, alkoxycarbamoyl, or two substituents form an methlenedioxy group, more preferably **R**^{26}, **R'**^{26}, **R**^{27}, **R'**^{27}, **R**^{28} are independently selected from H, halo, preferably chloro or fluoro,

more preferably chloro, haloalkyl, preferably $-CF_3$ or $-CHF_2$, alkoxy, preferably methoxy.

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



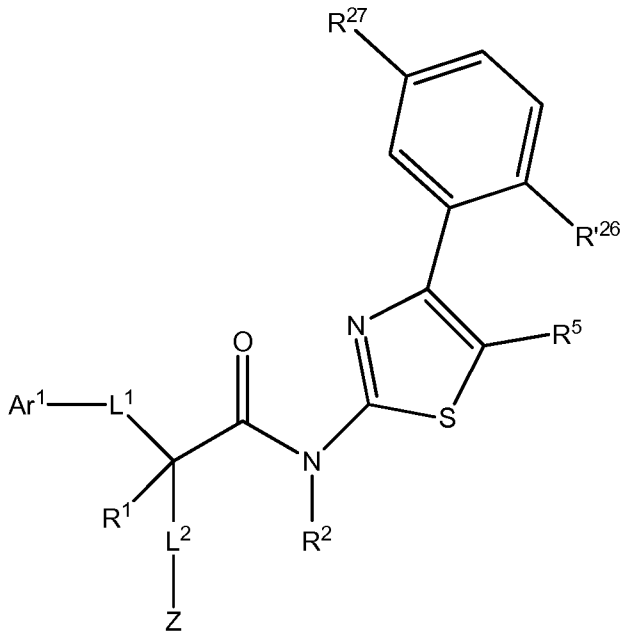
Ib-4l

wherein

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

Preferred compounds of formula Ib-4l are those of formula Ib-4m



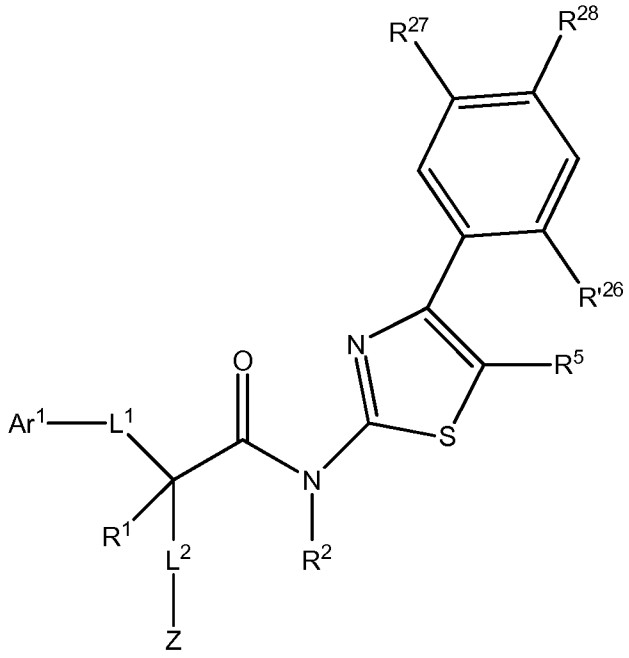
Ib-4m

wherein,

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, haloalkoxy, preferably chloro, fluoro CF_3, CHF_2, OCF_3 or $OCHF_2$, preferably **R'**^{26} is chloro and **R**^{27} is selected from H, halo, CF_3, CHF_2, OCF_3 or $OCHF_2$, preferably chloro and fluoro.

Other preferred compounds of formula Ib-4l are those of formula Ib-4n,



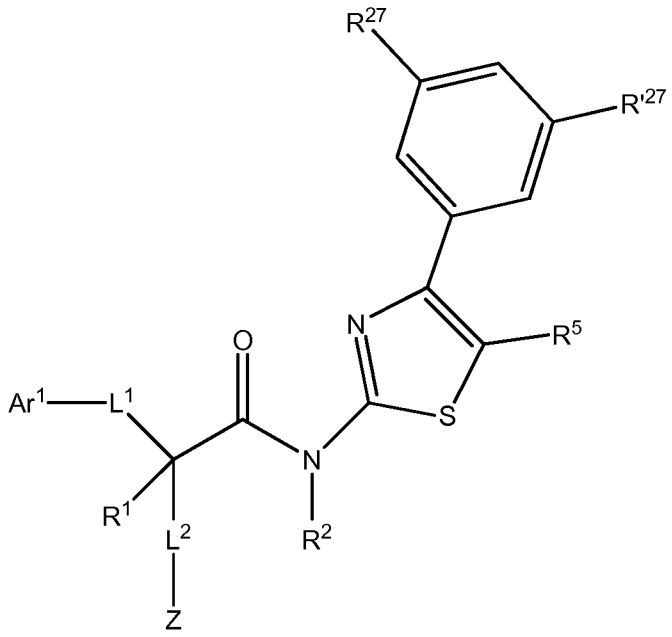
Ib-4n

wherein,

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, CF_3, or CHF_2, preferably OCF_3 or $OCHF_2$.

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



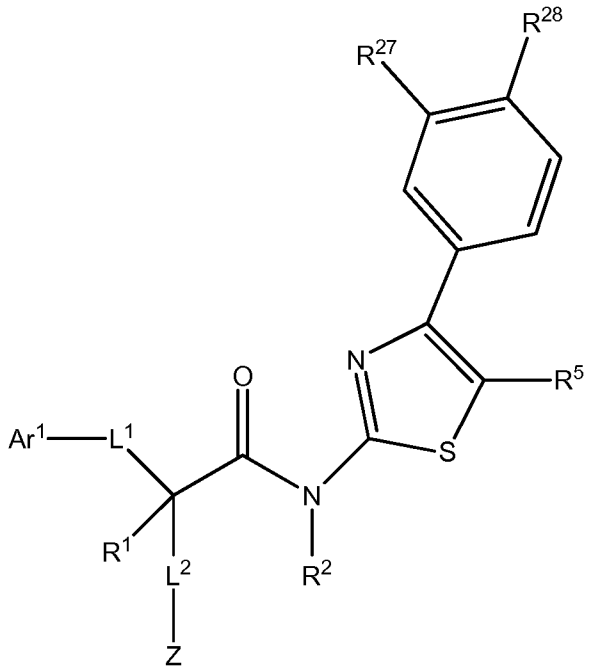
Ib-4o

wherein

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^{27} and **R'**^{27} are as defined above in respect to formula Ib-4k, preferably **R**^{27} and **R'**^{27} are independently selected from H, halo, haloalkyl, haloalkoxy, preferably chloro, fluoro, CF_3, CHF_2OCF_3 or $OCHF_2$.

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



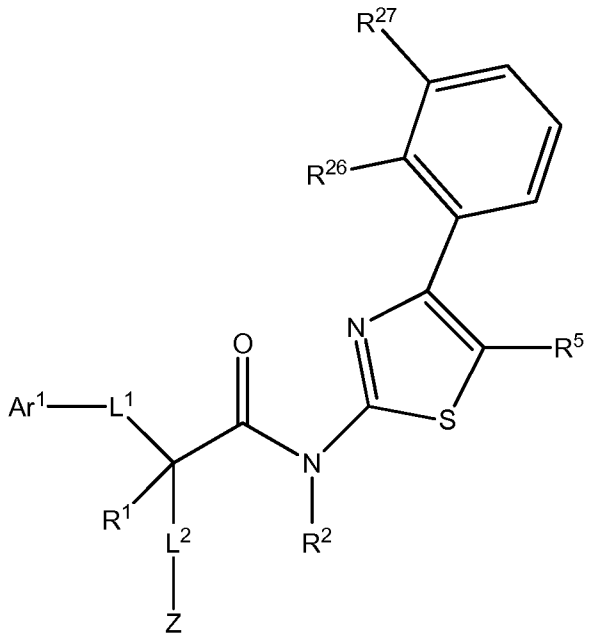
Ib-4p

wherein,

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^{27} and **R**^{28} are as defined above in respect to formula Ib-4k, preferably **R**^{27} and **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-4l are those of formula Ib-4q



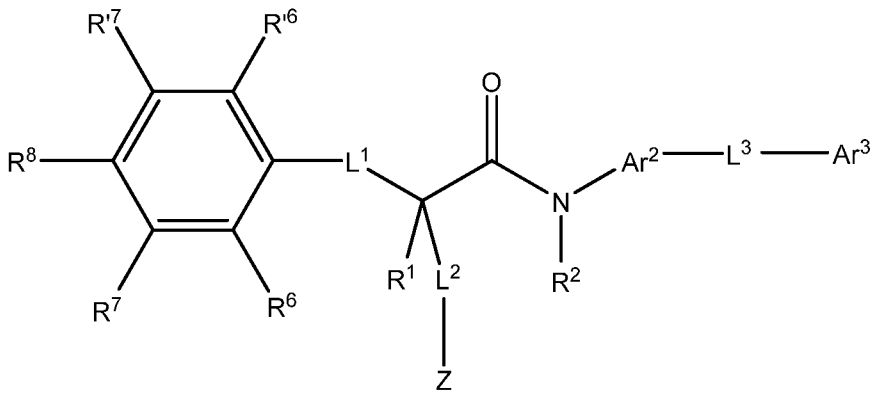
Ib-4q

wherein,

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



Ic

and pharmaceutically acceptable salts, and solvates thereof, wherein

wherein Ar^2, Ar^3, R^1, R^2, L^1, L^2, 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, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, 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 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, 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, heteroarylalkyl, 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}, **R'**^{7} and **R**^{8} 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;

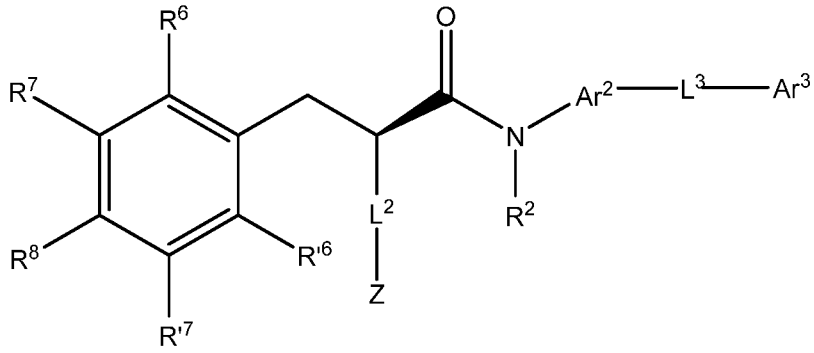
L^{2} is cyclopropylene, ethenylene, methylene, –CHMe-, –CHF-;

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-1

60



Ic-1

and pharmaceutically acceptable salts, and solvates thereof, wherein

Ar^2, **Ar^3**, **R^2**, **R^6**, **R^7**, **R'^{6}**, **R'^{7}** **R^8**, **L^2**, **L^3**, and **Z** are as defined above in respect to formula Ic.

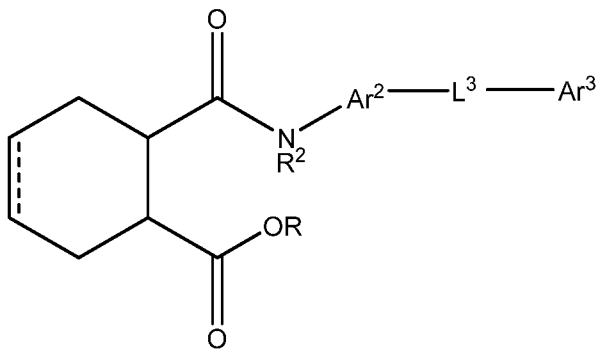
Preferred compounds of formula Ic-1 are those wherein

Z is –COOH;

L^2 is cyclopropylene, ethenylene, methylene, –CHMe-, –CHF-; 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 Ic.

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



Id

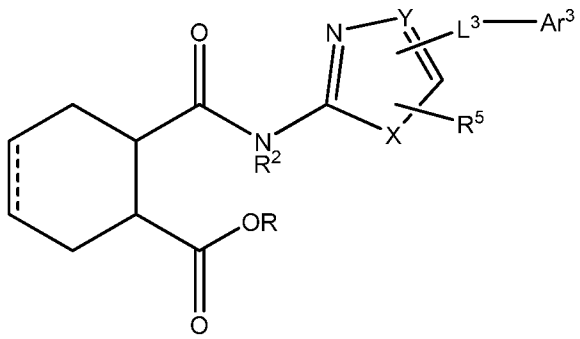
and pharmaceutically acceptable salts, esters, esters, amides, phosphates, and solvates thereof, wherein

the dotted line is present or absent; and

Ar^2, **Ar^3**, **R**, **R^2** and **L^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-1



Id-1

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^3 is attached to the heterocyclic group either in position 4 or 5, preferably in position 4;

If **Y** is CH, **R^5** is halo, cyano, hydroxyl, linear or branched C_1-C_3 alkyl, C_1-C_3

hydroxyalkyl, C_1-C_3 haloalkyl, preferably F, Cl, or CF_3 and $\mathbf{R^5}$ is attached to the heterocyclic group either in position 4, if $\mathbf{L^3}$ is attached in position 5, or in position 5, if $\mathbf{L^3}$ is attached in position 4; preferably $\mathbf{R^5}$ is attached in position 5;

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

$\mathbf{Ar^3}$ is as defined above in respect to formula I, preferably $\mathbf{Ar^3}$ 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-SO_2CF_3, and $\mathbf{L^3}$ is a single bond or C_1-C_2 alkylene; or $\mathbf{Ar^3}$ is a C_1-C_4 alkyl group and $\mathbf{L^3}$ is a single bond, more preferably $\mathbf{Ar^3}$ 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 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, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, arylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted

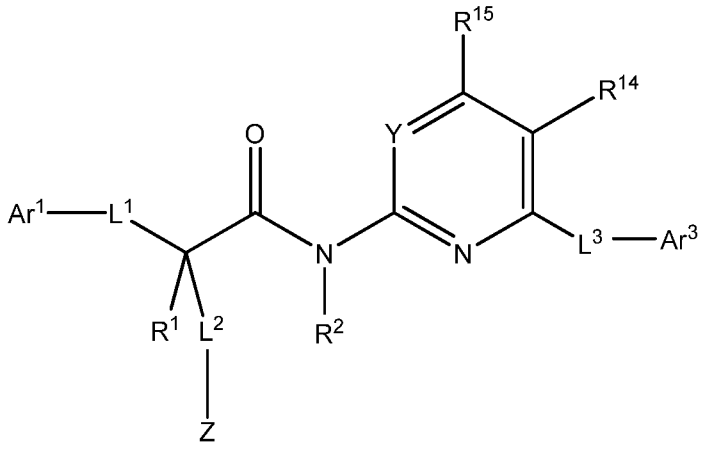
by one or more further substituents selected from halo, preferably chloro or fluoro, oxo or alkyl, preferably methyl; still more preferably **Ar**^{3} is phenyl, thiophenyl, furanyl, preferably phenyl, thiophen-2-yl, furan-2-yl, each of said phenyl, thiophenyl, furanyl, being optionally substituted by one or more substituents selected from halo, 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 5 or 6 membered heteroaryl moiety, preferably oxopyrrolidinyl, imidazolinyl, 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, 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 C_1-C_4 alkyl, C_1-C_2 hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentylmethyl, cyclopropylmethyl, benzyl, benzyloxyethyl, methoxyethyl, 1,1,1-trifluoroethyl, -$C_2H_4CO_2CH_3$, -$CH_2CO_2CH_3$, or -CH_2CONH_2, more preferably **R**^{2} is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, -$C_2H_4CO_2CH_3$, -$CH_2CO_2CH_3$, or -CH_2CONH_2, more preferably **R**^{2} is methyl or cyclopropyl.

In still another embodiment, preferred compounds of Formula I are

those of formula Ie:



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 CF_3, more preferably H;

Ar^1 and **L^1** are as defined above in respect to formula I, preferably as defined in respect to formula Ib, more preferably **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 **L^1** is a methylene group, C_1-C_2 alkylene, or C_2 alkenylene; or **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 **L^1** is a methylene group;

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, methylcarbonylamino, -NH-SO_2CF_3, and **L^3**

is a single bond or C_1-C_2 alkylene; or $\mathbf{Ar^3}$ is a C_1-C_4 alkyl group and $\mathbf{L^3}$ is a single bond, more preferably $\mathbf{Ar^3}$ 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 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, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, arylamino, 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 $\mathbf{Ar^3}$ 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, 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 5 or 6 membered heteroaryl moiety, preferably oxopyrrolidinyl, imidazolinyl, 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, 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^1 is as defined above in respect to formula I, preferably **R^1** is hydrogen, halogen, or a group selected from C_{1-4} alkyl optionally substituted by one or more substituents selected from halogen or alkyl; more preferably **R^1** 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 **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, ethenylene, n-propylene, or –C(R'R'')-, wherein R' and R'' are independently selected from H, halogen, methyl, and ethyl, more preferably **L^2** is cyclopropylene, ethenylene, methylene, –CHMe-, –CHF-, even more preferably **L^2** is methylene; or **R^1** and **L^2** together are =CH-under the condition that **L^1-Ar^1** is H.;

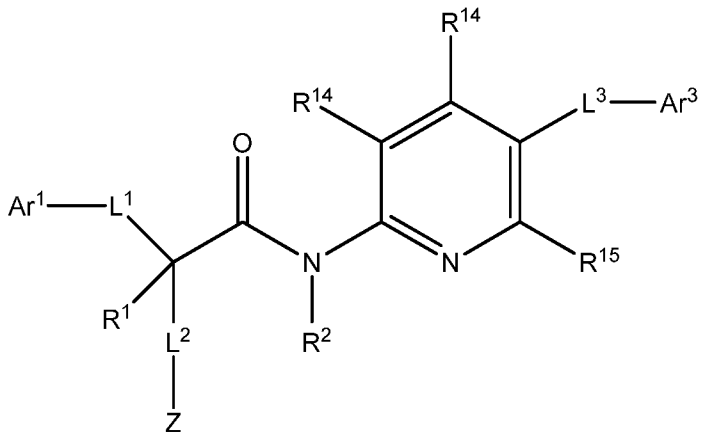
Z is as defined above in respect to formula I, preferably **Z** is –COOR, wherein **R** is defined as above in respect to formula I; preferably **Z** is COOH and

R^2 is as defined above in respect to formula I, preferably **R^2** is H, linear or branched C_1-C_4 alkyl, C_1-C_2 hydroxyalkyl, allyl, propargyl, cyclopropyl, cyclopentyl, cyclopentylmethyl, cyclopropylmethyl, benzyl, benzyloxyethyl, methoxyethyl, 1,1,1-trifluoroethyl, -$C_2H_4CO_2CH_3$, -$CH_2CO_2CH_3$, or -CH_2CONH_2,

more preferably **R^2** is H, methyl, ethyl, allyl, cyclopropyl, hydroxyethyl, -$C_2H_4CO_2CH_3$, -$CH_2CO_2CH_3$, or -CH_2CONH_2, most preferably **R^2** is methyl or cyclopropyl.

Preferred compounds of formula Ie are those wherein **Z** is –COOR and **R**, **Ar^1**, **Ar^2**, **Ar^3**, **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 **Ar^1** is phenyl.

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

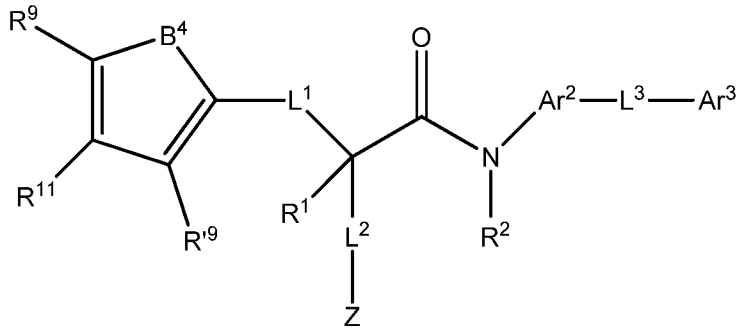


If,

wherein

Ar^1, **Ar^3**, **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:



Ig

wherein

B^4 is O or S or N-R^b where **R^b** is H or alkyl, preferably linear or branched C_1-C_4 alkyl; C_1-C_4 alkylcarbonyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylaminocarbonyl, C_3-C_6 cycloalkyl; preferably O or S, more preferably O,

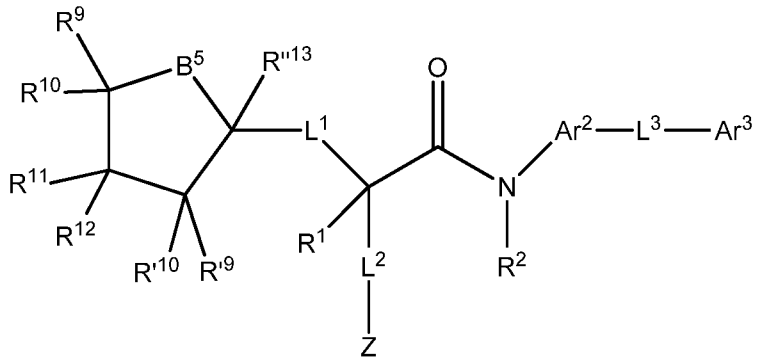
R^9, **R'^9**, and **R^{11}** are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or one of R^9 or R'^9 and R^{11} together form an

alkylenedioxy group or a haloalkylenedioxy group, or one of R^9 or R'^9 and R^{11} 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 $\mathbf{R^9}$, $\mathbf{R'^9}$, and $\mathbf{R^{11}}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, 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, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or one of R^9 or R'^9 and R^{11} 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 $\mathbf{R^9}$, $\mathbf{R'^9}$, and $\mathbf{R^{11}}$ are independently selected from H, hydroxyl, C_1-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, C_1-C_3-alkyl, halo, CF_3, C_1-C_2 alkoxy, and cyano, and still more preferably from H, F, Cl, methyl, CF_3, methoxy, and cyano, and most preferably H, F or methyl; and

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

In still another embodiment, preferred compounds of Formula I are

those of formula Ih:



Ih

wherein

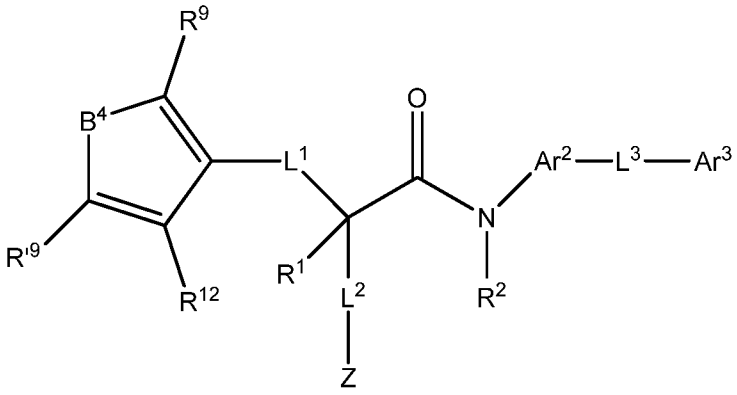
$\mathbf{B^5}$ is CH_2 or O preferably O;

$\mathbf{R^9}$, $\mathbf{R^{10}}$, $\mathbf{R'^9}$, $\mathbf{R'^{10}}$, $\mathbf{R^{11}}$, $\mathbf{R^{12}}$ and $\mathbf{R''^{13}}$ 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, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

haloalkylsulfonylamino, or one of R^{11} or R^{12} and one of R^9, R^{10}, R'^9 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'^9 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, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably $\mathbf{R^9}$, $\mathbf{R^{10}}$, $\mathbf{R^{11}}$, $\mathbf{R^{12}}$, $\mathbf{R'^9}$, $\mathbf{R'^{10}}$, and $\mathbf{R''^{13}}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, 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, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or one of R^{11} or R^{12} and one of R^9, R^{10}, R'^9 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'^9 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, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, more preferably $\mathbf{R^9}$, $\mathbf{R^{10}}$, $\mathbf{R^{11}}$, $\mathbf{R^{12}}$, $\mathbf{R^{13}}$, $\mathbf{R'^9}$, $\mathbf{R'^{10}}$, $\mathbf{R'^{11}}$, $\mathbf{R'^{12}}$, $\mathbf{R'^{13}}$ and $\mathbf{R''^{13}}$ are independently selected from H, hydroxyl, C_1-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, C_1-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

$\mathbf{Ar^2}$, $\mathbf{Ar^3}$, $\mathbf{L^1}$, $\mathbf{L^2}$, $\mathbf{L^3}$, $\mathbf{R^1}$, $\mathbf{R^2}$, 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

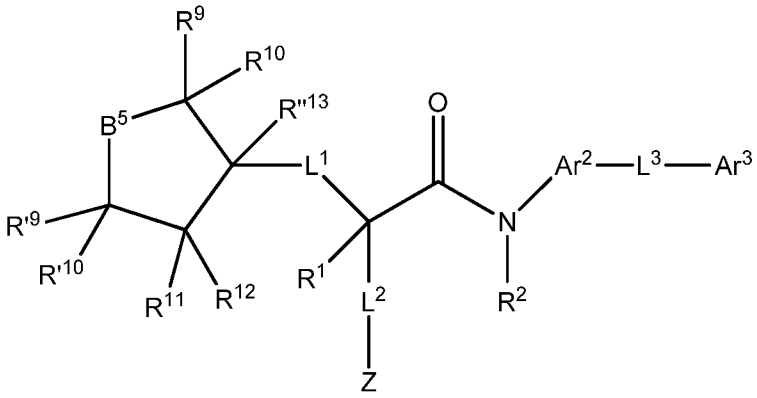
B^4 is as defined above in respect to formula Ig,

R^9, **R'^9** and **R^{12}** 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, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl,

alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or R^9 and R^{12} together form an alkylenedioxy group or a haloalkylenedioxy 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, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably $\mathbf{R^9}$, $\mathbf{R'^9}$, and $\mathbf{R^{12}}$, are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, carboxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or R^9 and R^{12} together form an alkylenedioxy group or a haloalkylenedioxy 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, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, more preferably $\mathbf{R^9}$, $\mathbf{R'^9}$, and $\mathbf{R^{12}}$, are independently selected from H, hydroxyl, C_1-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, C_1-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

Ar^2, **Ar^3**, **L^1**, **L^2**, **L^3**, **R^1**, **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 Ij:



Ij

wherein

B^5 is as defined above in respect to formula Ih,

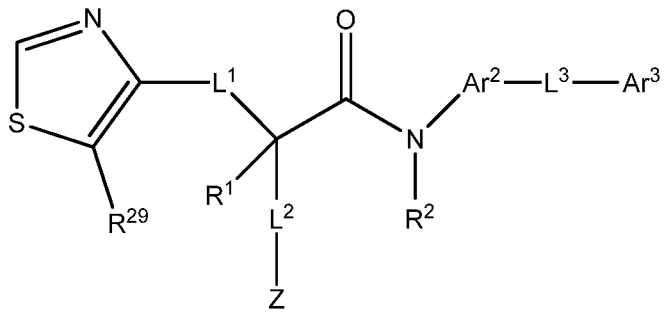
R^9, **R'^{9}**, **R^{10}**, **R'^{10}**, **R^{11}**, **R^{12}** and **R''^{13}** are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, heteroalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkoxyalkyl, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl,

heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or one of R^{11} or R^{12} and one of R^9, R^{10}, R'^9 or R'^{10}, or one of R'^9 or R'^{10} and R''^{13} 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'^9 or R'^{10}, or one of R'^9 or R'^{10} and 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, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably $\mathbf{R^9}$, $\mathbf{R'^9}$, $\mathbf{R^{10}}$, $\mathbf{R'^{10}}$, $\mathbf{R^{11}}$, $\mathbf{R^{12}}$ and $\mathbf{R''^{13}}$ are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, 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, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, or one of R^{11} or R^{12} and one of R^9, R^{10}, R'^9 or R'^{10}, or one of R'^9 or R'^{10} and R''^{13} 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'^9 or R'^{10}, or one of R'^9 or R'^{10} and 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, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, more preferably $\mathbf{R^9}$, $\mathbf{R'^9}$, $\mathbf{R^{10}}$, $\mathbf{R'^{10}}$, $\mathbf{R^{11}}$, $\mathbf{R^{12}}$ and $\mathbf{R''^{13}}$ are independently selected from H, hydroxyl, C_1-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, C_1-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

Ar^2, **Ar^3**, **L^1**, **L^2**, **L^3**, **R^1**, **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 Ik:



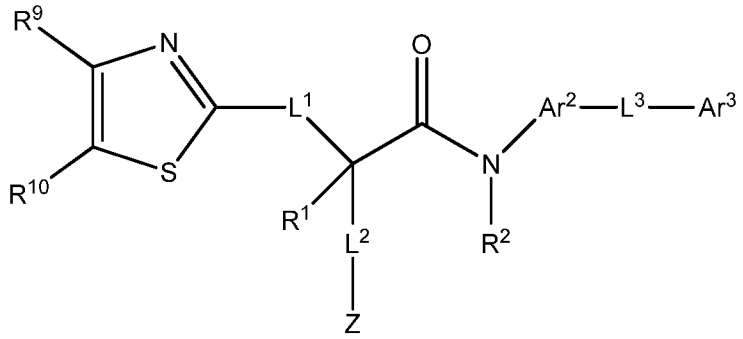
Ik

wherein

R^{29} is H, halo, alkyl, haloalkyl preferably $-CF_3$ or $-CF_2H$, alkoxy, haloalkoxy preferably $-OCF_3$ or $-OCF_2H$, cyano, preferably **R^{29}** is H, F, $-CF_3$, alkyl preferably methyl, more preferably **R^{29}** is H, F or methyl; and

Ar^2, **Ar^3**, **L^1**, **L^2**, **L^3**, **R^1**, **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 Il:



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, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, 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, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl,

heterocyclyl, hydroxyl, oxo, or sulfonyl, preferably **R**^{9} and **R**^{10} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, 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, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonylamino, cycloalkylsulfonylamino, 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, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl, more preferably **R**^{9} and **R**^{10} are independently selected from H, hydroxyl, C_1-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, C_1-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

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

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

Table 1:

Compound number	**Compound name**	**(M+H)+**
1	6-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)cyclohex-3-enecarboxylic acid	**363.83**

2	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**401.88**
3	(R)-3-benzyl-4-((4-(2,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**436.3**
4	(R)-3-benzyl-4-((4-(2-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**385.4**
5	(R)-3-benzyl-4-((4-(3,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**436.3**
8	(R)-3-benzyl-4-((4-(4-cyanophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**392.4**
9	(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-phenylbutanoic acid	**387.9**
10	(Z)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobut-2-enoic acid	**309.7**
11	(R)-3-benzyl-4-oxo-4-((3-phenyl-1,2,4-thiadiazol-5-yl)amino)butanoic acid	**368.4**
12	(R)-3-benzyl-4-((4-(3-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**401.9**
13	(R)-3-benzyl-4-oxo-4-((4-(3-(trifluoromethyl)phenyl)thiazol-2-yl)amino)butanoic acid	**435.4**
14	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**415.9**
15	(R)-3-benzyl-4-((5-(2-chlorophenyl)pyridin-2-yl)amino)-4-oxobutanoic acid	**395.9**
16	(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)heptanoic acid	**367.9**
17	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-fluorobenzyl)-4-oxobutanoic acid	**419.9**
18	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid	**407.9**
19	(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)-5-methylhexanoic acid	**367.9**

20	(R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid	**419.9**
21	(R)-3-benzyl-4-((5-chloro-4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**450.4**
22	(R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid	**441.9**
23	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxy-2-oxoethyl)amino)-4-oxobutanoic acid	**473.9**
24	(R)-methyl-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoate	**415.9**
26	(R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid	**415.9**
27	(S)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid	**415.9**
28	(R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-(4-(trifluoromethyl)benzyl)butanoic acid	**469.9**
29	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-(3-(trifluoromethyl)benzyl)butanoic acid	**469.9**
30	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(2-cyanobenzyl)-4-oxobutanoic acid	**426.9**
31	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(3-cyanobenzyl)-4-oxobutanoic acid	**426.9**
32	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-cyanobenzyl)-4-oxobutanoic acid	**426.9**
33	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid	**431.9**
34	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(3-methoxybenzyl)-4-oxobutanoic acid	**431.9**
35	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(2-methoxybenzyl)-4-oxobutanoic acid	**431.9**
36	(R)-3-benzyl-4-((4-(2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**397.5**
37	(R)-3-benzyl-4-oxo-4-(4-(2,4,6-trichlorophenyl)thiazol-2-ylamino)butanoic acid	**470.8**

38	(R)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid	**429.9**
39	(S)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid	**429.9**
40	(R)-methyl 4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate	**429.9**
41	(S)-methyl 4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate	**429.9**
42	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropylmethyl)amino)-4-oxobutanoic acid	**456.0**
43	(R)-3-benzyl-4-(benzyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**492.0**
44	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2,2,2-trifluoroethyl)amino)-4-oxobutanoic acid	**483.9**
45	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid	**445.9**
46	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-methoxybenzyl)-4-oxobutanoic acid	**445.9**
47	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-methoxybenzyl)-4-oxobutanoic acid	**445.9**
48	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-cyanobenzyl)-4-oxobutanoic acid	**440.9**
49	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(3-cyanobenzyl)-4-oxobutanoic acid	**440.9**
50	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2-cyanobenzyl)-4-oxobutanoic acid	**440.9**

51	(R)-3-(4-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**450.4**
52	(R)-3-(3-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**450.4**
53	(R)-3-(2-chlorobenzyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**450.4**
54	(3S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-1H-inden-1-yl)-4-oxobutanoic acid	**441.9**
55	(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-1H-inden-2-yl)-4-oxobutanoic acid	**441.9**
56	(R)-4-(benzo[d]thiazol-2-yl(methyl)amino)-3-benzyl-4-oxobutanoic acid	**355.4**
57	(R)-4-(benzo[d]oxazol-2-yl(methyl)amino)-3-benzyl-4-oxobutanoic acid	**339.4**
58	(R)-2-((1H-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methyl-3-phenylpropanamide	**439.9**
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	**455.9**
60	(R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**433.9**
61	(S)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-cyclohexyl-4-oxobutanoic acid	**393.9**
62	(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-cyclohexyl-4-oxobutanoic acid	**407.9**
63	(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-phenylbutanoic acid	**401.9**

64	(3R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylpentanoic acid	**415.9**
65	(R)-2-((1H-tetrazol-5-yl)methyl)-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-phenylpropanamide	**425.9**
66	(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)propanamide	**441.9**
68	(3R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-2-methyl-4-oxobutanoic acid	**415.9**
69	(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxyisoxazol-5-yl)propanamide	**440.9**
70	(R)-3-benzyl-4-(4-(2-chlorophenyl)pyrimidin-2-ylamino)-4-oxobutanoic acid	**396.8**
71	(R)-3-benzyl-4-(6-(2-chlorophenyl)pyridin-2-ylamino)-4-oxobutanoic acid	**395.9**
72	(E)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylbut-3-enoic acid	**399.9**
74	(Z)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-phenylbut-2-enoic acid	**399.9**
75	(R)-3-(N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methylsulfamoyl)-4-phenylbutanoic acid	**452.0**
76	(S)-3-(N-(4-(2-chlorophenyl)thiazol-2-yl)-N-methylsulfamoyl)-4-phenylbutanoic acid	**452.0**
79	(R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-fluoro-4-oxobutanoic acid	**419.9**
80	(R)-3-benzyl-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)hex-5-enoic acid	**441.9**
81	(E)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylbut-3-enoic acid	**413.9**
82	(3S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid	**429.9**
83	(R)-3-benzyl-4-((3-(2-chlorophenyl)-1,2,4-thiadiazol-5-yl)(methyl)amino)-4-oxobutanoic acid	**416.9**

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-ylcarbamoyl)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**

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(4-(2-(thiophen-3-yl)phenyl)thiazol-2-yl)amino)-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-(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-ethoxypyridin-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-(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-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**480.6**

140	(R)-3-benzyl-4-((4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**506.6**
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	**558.7**
142	(R)-3-benzyl-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**476.4**
143	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**405.9**
144	(R)-3-benzyl-4-((4-(2-cyclopropylphenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**421.5**
145	(R)-3-benzyl-4-((4-(4'-(dimethylamino)-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**500.6**
146	(R)-3-benzyl-4-((4-(3'-fluoro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**475.5**
147	(R)-3-benzyl-4-((4-(3',5'-difluoro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**493.5**
148	(R)-3-benzyl-4-((4-(2-chloro-6-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**419.9**
149	(R)-3-benzyl-4-((4-(4'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**492.0**
150	(R)-3-benzyl-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**541.6**

151	(R)-3-benzyl-4-((4-(4-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**523.0**
152	(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**523.0**
153	(R)-3-benzyl-4-((4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**506.6**
154	(3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-2-yl)methyl)butanoic acid	**409.9**
155	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid	**445.9**
156	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(3-hydroxypropyl)amino)-4-oxobutanoic acid	**460.0**
157	(R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**523.0**
158	(R)-3-benzyl-4-((4-(2-(6-(benzyloxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**564.7**
159	(R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**442.4**
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	**496.6**

161	(R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**483.9**
162	(R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**433.9**
163	(R)-3-benzyl-4-((4-(3,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**450.4**
164	(R)-3-benzyl-4-((4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**447.5**
165	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**407.9**
166	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**468.4**
167	(R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**484.4**
168	(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**458.4**
169	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**506.6**
170	(R)-3-benzyl-4-((2-hydroxyethyl)(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**518.6**

171	(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**535.7**
172	(R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid	**472.4**
173	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**423.9**
174	(R)-3-benzyl-4-((4-(5-chloro-2-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**483.9**
175	(R)-3-benzyl-4-(methyl(4-(2,3,5-trichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**484.8**
176	(R)-3-benzyl-4-((4-(4-chloro-[1,1'-biphenyl]-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**492.0**
177	(R)-3-benzyl-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**523.0**
178	(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**514.6**
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	**522.6**
180	(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**569.7**

181	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**561.7**
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	**529.6**
183	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**559.7**
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	**577.7**
185	(R)-3-benzyl-4-(methyl(4-(2-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**465.5**
186	(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**452.0**
187	(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**533.7**
188	(R)-3-benzyl-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**473.5**
189	(R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid	**459.9**
190	(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**468.0**

191	(R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid	**509.9**
192	(R)-3-benzyl-4-((4-(2-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**447.5**
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	**518.0**
194	(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	**547.7**
195	(3R,4S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid	**429.9**
196	(R)-2-(2-benzyl-3-carboxypropanamido)-5-(2-chlorophenyl)pyridine 1-oxide	**411.9**
197	(R)-3-benzyl-4-((5-(2-chlorophenyl)pyrazin-2-yl)amino)-4-oxobutanoic acid	**396.8**
198	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(morpholinomethyl)-4-oxobutanoic acid	**424.9**
199	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxyethyl)amino)-4-oxobutanoic acid	**460.0**
200	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylamino)-4-oxobutanoic acid	**408.9**
201	(R)-3-benzyl-4-((2-(benzyloxy)ethyl)(4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**536.1**

202	(R)-3-benzyl-4-((4-(5-methylfuran-2-yl)thiazol-2-yl)amino)-4-oxobutanoic acid	**371.4**
203	(R)-3-benzyl-4-oxo-4-((3-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)amino)butanoic acid	**418.4**
204	(R)-3-benzyl-4-((4-(5-chloro-2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**431.9**
205	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-hydroxybenzyl)-4-oxobutanoic acid	**431.9**
206	(R)-3-benzyl-4-((4-(4'-cyano-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**482.6**
207	(3R)-3-benzyl-4-((3-carbamoyl-4-(2,4-dichlorophenyl)-5-methylthiophen-2-yl)amino)-4-oxobutanoic acid	**492.4**
208	(R)-3-benzyl-4-((4-(3'-methoxy-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**487.6**
209	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid	**436.9**
210	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid	**420.9**
211	(R)-3-benzyl-4-((4-(2'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**492.0**
212	(R)-3-benzyl-4-((4-(2-(2-methoxypyrimidin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**489.6**
213	(R)-3-benzyl-4-((4-(2,5-difluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**403.4**

214	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(oxazol-4-ylmethyl)-4-oxobutanoic acid	**406.9**
215	(3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-3-yl)methyl)butanoic acid	**409.9**
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	**541.6**
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	**511.6**
218	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**519.7**
219	(R)-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**541.1**
220	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**524.6**
221	(R)-3-benzyl-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**481.9**
222	(R)-3-benzyl-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**557.5**
223	(R)-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**575.5**

224	(R)-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**559.1**
225	(S)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**401.9**
227	(R)-3-benzyl-4-((4-benzylthiazol-2-yl)amino)-4-oxobutanoic acid	**381.5**
229	(R)-3-benzyl-4-oxo-4-((5-phenyl-4H-1,2,4-triazol-3-yl)amino)butanoic acid	**351.4**
230	3-([1,1'-biphenyl]-4-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**492.0**
231	(R)-3-benzyl-4-((4-(1-methyl-1H-pyrazol-4-yl)thiazol-2-yl)amino)-4-oxobutanoic acid	**371.4**
232	(R)-3-benzyl-4-((4-(4-methyl-1,2,5-oxadiazol-3-yl)thiazol-2-yl)amino)-4-oxobutanoic acid	**373.4**
233	(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-1H-pyrazol-4-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**461.5**
234	(3R)-3-benzyl-4-((4-(2-(3,5-dimethylisoxazol-4-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**476.6**
235	(R)-3-benzyl-4-((4-((2-chlorophenyl)carbamoyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**444.9**
236	(R)-3-benzyl-4-((6-(2-chlorophenyl)pyridazin-3-yl)amino)-4-oxobutanoic acid	**396.8**
237	(R)-3-benzyl-4-(methyl(4-(2-(2-oxopyrrolidin-1-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**464.5**

238	(S)-2-((1-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)oxy)acetic acid	**431.9**
239	(R)-3-benzyl-4-((1-methyl-5-phenyl-1H-imidazol-2-yl)amino)-4-oxobutanoic acid	**364.4**
240	(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	**532.6**
241	(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**488.6**
242	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoic acid	**434.9**
243	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid	**419.9**
244	(R)-3-benzyl-4-((4-(2-(6-hydroxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**474.5**
245	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((S)-2-hydroxypropyl)amino)-4-oxobutanoic acid	**460.0**
246	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((R)-2-hydroxypropyl)amino)-4-oxobutanoic acid	**460.0**
247	(R)-3-(cyclohexylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**520.7**

248	(R)-3-benzyl-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**506.6**
250	(R)-3-benzyl-4-((4-(4,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**524.6**
251	(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**440.3**
252	(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**423.9**
253	(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**478.5**
254	(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid	**421.9**
255	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**541.1**
256	(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**567.7**
257	(R)-3-benzyl-4-((4-(2,3-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**450.4**
258	(R)-3-benzyl-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**465.5**

259	(R)-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**481.5**
260	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**405.9**
261	(R)-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**473.5**
262	(R)-3-benzyl-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**491.5**
263	(R)-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**499.5**
264	(R)-3-benzyl-4-((4-(2-(6-isopropoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**516.6**
265	(R)-3-benzyl-4-((4-(2-(6-(cyclopropylmethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**528.6**
266	(R)-3-benzyl-4-((4-(2-(6-(methoxymethyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**502.6**
267	(R)-3-benzyl-4-((4-(2-(6-((dimethylamino)methyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**515.6**
268	(R)-3-benzyl-4-(methyl(4-(2-(6-(N-methylcyclopropanecarboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**555.7**

269	(R)-3-benzyl-4-((4-(2-(6-(dimethylcarbamoyl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**529.6**
270	(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	**525.6**
271	(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	**556.6**
272	(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	**527.6**
273	(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	**512.6**
274	(R)-3-benzyl-4-((4-(2-(6-(benzyl(methyl)amino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**577.7**
275	(R)-3-benzyl-4-((4-(2-(6-(cyclohexyl(methyl)amino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**569.7**
276	(R)-3-benzyl-4-(methyl(4-(2-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**556.7**
277	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**541.1**

278	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**524.6**
279	(R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)-3-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**541.0**
280	(R)-3-benzyl-4-((4-(3-fluoro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**524.6**
281	(R)-3-benzyl-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**541.0**
282	(R)-3-benzyl-4-((4-(3,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**524.6**
283	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((S)-tetrahydrofuran-2-yl)methyl)butanoic acid	**409.9**
284	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((R)-tetrahydrofuran-2-yl)methyl)butanoic acid	**409.9**
285	(R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**473.9**
286	(R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**489.9**

287	(R)-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**471.9**
288	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**431.9**
289	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**513.0**
290	(R)-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**513.0**
291	(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**546.5**
292	(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**562.5**
293	(R)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**544.5**
294	(R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**466.4**

295	(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**449.9**
296	(R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**499.9**
297	(R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**515.9**
298	(R)-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid	**497.9**
299	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylfuran-2-yl)methyl)-4-oxobutanoic acid	**419.9**
300	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((4,5-dimethylfuran-2-yl)methyl)-4-oxobutanoic acid	**433.9**
301	3-(benzofuran-2-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**455.9**
302	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyridin-2-ylmethyl)butanoic acid	**416.9**
303	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyrimidin-2-ylmethyl)butanoic acid	**417.9**

304	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-2-yl)methyl)butanoic acid	**458.4**
305	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-3-yl)methyl)butanoic acid	**458.4**
306	(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R,3R)-2-methyltetrahydro-2H-pyran-3-yl)methyl)-4-oxobutanoic acid	**472.4**
307	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R)-2-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid	**472.4**
308	(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	**486.4**
309	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((3S)-3-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid	**472.4**
310	(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	**486.4**
311	(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(4-hydroxy-1,2,5-thiadiazol-3-yl)-N-methylpropanamide	**472.0**
312	(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxy-5-methylisoxazol-4-yl)-N-methylpropanamide	**469.0**

313	(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	**624.2**
314	(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	**642.2**
315	(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	**557.1**
316	(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	**575.1**
317	(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	**610.1**
318	(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	**628.1**
319	(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	**655.7**

320	(R)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**673.7**
321	(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	**588.6**
322	(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	**606.6**
323	(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	**641.7**
324	(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	**659.7**
325	(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	**589.7**
326	(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	**607.7**
327	(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	**540.6**

328	(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	**575.7**
329	(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	**593.7**
330	(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	**607.7**
331	(R)-4-(cyclopropyl(5-fluoro-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	**625.7**
332	(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	**540.6**
333	(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	**558.6**
334	(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	**593.7**
335	(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	**611.7**

336	(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	**608.2**
337	(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	**626.2**
338	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**559.1**
339	(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	**594.1**
340	(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	**612.1**
341	(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	**639.7**
342	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid	**657.7**
343	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**572.6**

344	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid	**590.6**
345	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**625.7**
346	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid	**643.7**
347	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**573.7**
348	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**591.7**
349	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**524.6**
350	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**577.7**
351	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**591.7**
352	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**609.7**

353	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**524.6**
354	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**542.6**
355	(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	**577.7**
356	(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	**595.7**
357	(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	**616.1**
358	(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	**634.1**
359	(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid	**549.1**
360	(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid	**567.0**
361	(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	**602.1**
362	(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	**620.1**

363	(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	**647.7**
364	(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid	**665.7**
365	(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**580.6**
366	(R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid	**598.6**
367	(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	**633.7**
368	(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	**651.7**
369	(R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**581.7**
370	(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	**599.7**
371	(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**532.6**
372	(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**585.7**

373	(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	**599.7**
374	(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	**617.7**
375	(R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**532.6**
376	(R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**550.6**
377	(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	**585.7**
378	(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	**603.7**
379	(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	**598.1**
380	(R)-4-((4-(5-chloro-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	**616.1**
381	(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	**531.0**

382	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**549.0**
383	(R)-4-((4-(5-chloro-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	**584.1**
384	(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	**602.1**
385	(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	**629.7**
386	(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	**647.7**
387	(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	**562.6**
388	(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	**580.6**

389	(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	**615.7**
390	(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	**633.7**
391	(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	**563.7**
392	(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	**581.7**
393	(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	**514.6**
394	(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	**549.7**
395	(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	**567.6**
396	(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	**581.7**

397	(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	**599.7**
398	(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	**514.6**
399	(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	**532.6**
400	(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	**567.6**
401	(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	**585.6**
402	(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	**582.1**
403	(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	**600.1**
404	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**515.0**

405	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**533.0**
406	(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	**568.1**
407	(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	**586.1**
408	(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	**613.7**
409	(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	**631.7**
410	(R)-3-(cyclopentylmethyl)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**546.6**
411	(R)-3-(cyclopentylmethyl)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**564.6**

412	(R)-3-(cyclopentylmethyl)-4-((4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**599.7**
413	(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	**617.7**
414	(R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**547.7**
415	(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	**565.7**
416	(R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**480.6**
417	(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**498.6**
418	(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	**551.6**
419	(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	**565.7**

420	(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	**583.7**
421	(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**498.6**
422	(R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**516.6**
423	(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	**551.6**
424	(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	**569.6**
425	(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	**590.1**
426	(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	**608.1**
427	(R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**541.0**
428	(R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**576.1**

429	(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	**594.1**
430	(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	**621.7**
431	(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	**639.7**
432	(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**554.6**
433	(R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**572.6**
434	(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	**607.6**
435	(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	**625.6**
436	(R)-3-benzyl-4-(methyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**555.7**
437	(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	**573.7**

438	(R)-3-benzyl-4-((5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**506.6**
439	(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	**559.6**
440	(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	**573.7**
441	(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	**591.6**
442	(R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**524.6**
443	(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	**559.6**
444	(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	**577.6**
445	(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	**551.6**
446	(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	**577.7**

447	(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	**567.6**
448	(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	**593.7**
449	(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	**559.6**
450	(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	**585.7**
451	(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	**537.6**
452	(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	**563.7**
453	(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	**553.6**

454	(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	**579.7**
455	(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	**545.6**
456	(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)amino)-4-oxobutanoic acid	**571.6**
457	(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	**539.6**
458	(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	**565.7**
459	(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	**555.6**
460	(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	**581.7**

461	(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	**547.6**
462	(R)-3-benzyl-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	**573.7**
463	(R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid	**521.6**
464	(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	**547.7**
465	(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	**537.6**
466	(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	**563.7**
467	(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	**529.6**
468	(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	**555.6**

469	(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	**581.7**
470	(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	**607.7**
471	(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	**597.7**
472	(R)-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-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**623.7**
473	(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	**589.6**
474	(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	**615.7**
475	(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	**567.6**

476	(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	**593.7**
477	(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	**583.6**
478	(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	**609.7**
479	(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	**575.6**
480	(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	**601.7**
481	(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	**569.7**
482	(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	**595.7**

483	(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	**585.7**
484	(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	**611.7**
485	(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	**577.6**
486	(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	**603.7**
487	(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	**551.6**
488	(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	**577.7**
489	(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	**567.6**

490	(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	**593.7**
491	(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	**559.6**
492	(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	**585.7**
493	(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	**568.1**
494	(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	**594.1**
495	(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	**584.1**
496	(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	**610.1**

497	(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)(methyl)amino)-4-oxobutanoic acid	**576.1**
498	(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	**602.1**
499	(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	**554.1**
500	(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	**580.1**
501	(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	**570.1**
502	(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	**596.1**
503	(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	**562.1**

504	(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	**588.1**
505	(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	**556.1**
506	(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	**582.1**
507	(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	**572.1**
508	(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	**598.1**
509	(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	**564.1**
510	(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	**590.1**

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**

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**

536	(R)-3-(cyclopentylmethyl)-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	**569.6**
537	(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	**595.7**
538	(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	**585.6**
539	(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	**611.7**
540	(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	**577.6**
541	(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	**603.7**
542	(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	**555.6**

543	(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	**581.6**
544	(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	**571.6**
545	(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	**597.6**
546	(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	**563.6**
547	(R)-3-benzyl-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	**589.6**
548	(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	**557.6**
549	(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	**583.7**

550	(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	**573.6**
551	(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)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**599.7**
552	(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)(methyl)amino)-4-oxobutanoic acid	**565.6**
553	(R)-3-benzyl-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	**591.6**
554	(R)-3-(cyclopentylmethyl)-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	**539.6**
555	(R)-3-(cyclopentylmethyl)-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	**565.6**
556	(R)-4-((5-fluoro-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	**555.6**
557	(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	**581.6**

558	(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	**547.6**
559	(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	**573.6**
560	(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	**599.7**
561	(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	**625.7**
562	(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	**615.7**
563	(R)-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-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**641.7**
564	(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	**607.6**
565	(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	**633.7**

566	(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	**585.6**
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	**611.7**
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	**601.6**
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	**627.7**
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	**593.6**
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	**619.7**
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	**587.7**

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	**613.7**
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	**603.6**
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	**629.7**
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	**595.6**
577	(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	**621.7**
578	(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	**569.6**
579	(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	**595.7**

580	(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	**585.6**
581	(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)butanoic acid	**611.7**
582	(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	**577.6**
583	(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	**603.7**
584	(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-(cyclopentylmethyl)-4-oxobutanoic acid	**586.1**
585	(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-(cyclopentylmethyl)-4-oxobutanoic acid	**612.1**
586	(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	**602.1**

587	(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	**628.1**
588	(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	**594.1**
589	(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	**620.1**
590	(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	**572.1**
591	(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	**598.1**
592	(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)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**588.1**
593	(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)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**614.1**

594	(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	**580.0**
595	(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	**606.1**
596	(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	**574.1**
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	**600.1**
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	**590.1**
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	**616.1**
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)(methyl)amino)-4-oxobutanoic acid	**582.1**

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	**608.1**
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	**556.1**
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	**582.1**
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	**572.1**
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	**598.1**
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	**564.0**
607	(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	**590.1**

608	(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	**551.6**
609	(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	**577.7**
610	(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	**567.6**
611	(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	**593.7**
612	(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	**559.6**
613	(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	**585.7**
614	(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	**537.6**

615	(R)-3-(cyclopentylmethyl)-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)amino)-4-oxobutanoic acid	**563.7**
616	(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	**553.6**
617	(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)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid	**579.7**
618	(R)-3-benzyl-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	**545.6**
619	(R)-3-benzyl-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)amino)-4-oxobutanoic acid	**571.6**
620	(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	**539.6**
621	(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	**565.7**

622	(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	**555.6**
623	(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	**581.7**
624	(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	**547.6**
625	(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	**573.7**
626	(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	**521.6**
627	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**547.7**
628	(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	**537.6**

629	(R)-4-(cyclopropyl(5-fluoro-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	**563.7**
630	(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	**529.6**
631	(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	**555.6**
632	(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	**529.7**
633	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**546.7**
634	(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	**560.7**
635	(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	**545.7**
636	(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	**559.7**

637	(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	**574.7**
638	(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	**559.7**
639	(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	**545.7**
640	(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	**594.1**
641	(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	**530.7**
642	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**547.7**
643	(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	**546.7**
644	(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	**559.7**
645	(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	**545.7**

646	(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	**560.7**
647	(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	**530.7**
648	(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	**577.7**
649	(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	**559.7**
650	(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	**560.7**
651	(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	**597.7**
652	(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	**579.7**
653	(R)-4-((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	**571.6**

654	(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	**553.6**
655	(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	**581.7**
656	(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	**563.7**
657	(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	**555.6**
658	(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	**537.6**
659	(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	**589.6**
660	(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	**571.7**
661	(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	**563.6**
662	(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	**545.6**
663	(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	**542.6**

664	(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	**568.7**
665	(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	**534.6**
666	(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	**560.7**
667	(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	**550.6**
668	(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	**576.7**
669	(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	**595.7**
670	(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	**569.7**
671	(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	**577.7**
672	(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	**551.7**

673	(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	**611.7**
674	(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	**585.7**
675	(R)-4-(cyclopropyl(4-(2,5-dimethyl-4-(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	**593.7**
676	(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	**567.7**
677	(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	**603.7**
678	(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	**577.6**
679	(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	**585.7**
680	(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	**559.6**

681	(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	**587.7**
682	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxopiperidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**587.7**
683	(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	**574.7**
684	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(N-methylacetamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**547.7**
685	(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	**602.8**
686	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(5-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**559.7**
687	(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	**574.7**
688	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(pyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**545.7**
689	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**560.7**

690	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-5-oxopyrrolidin-2-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**573.7**
691	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(4-methyl-3-oxopiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**588.7**
692	(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	**602.7**
693	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(dimethylcarbamoyl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**547.7**
694	(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	**588.7**
695	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-isopropoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**534.7**
696	(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	**587.7**
697	(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	**573.7**
698	(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	**588.7**

699	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxotetrahydropyrimidin-1(2H)-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**574.7**
700	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1,3-dimethyl-2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**588.7**
701	(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	**602.8**
702	(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	**588.7**
703	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(N-methylcyclopropanecarboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**573.7**
704	(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	**573.7**
705	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(cyclopropylmethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**546.7**
706	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**559.7**
707	(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	**587.7**

708	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(methoxymethyl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**520.7**
709	(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	**588.7**
710	(3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(5-oxopyrrolidin-2-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**559.7**
711	(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	**627.7**
712	(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	**607.7**
713	(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	**643.7**
714	(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	**568.7**
715	(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	**584.7**
716	(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	**575.7**

717	(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(pyrimidin-2-ylmethyl)butanoic acid	**569.6**
718	(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	**573.7**
719	(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((S)-tetrahydrofuran-2-yl)methyl)butanoic acid	**561.7**
720	(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	**575.7**
721	(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	**589.7**
722	(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-3-yl)methyl)butanoic acid	**575.7**
723	(3R)-4-(cyclopropyl(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	**603.7**
724	(R)-4-(cyclopropyl(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	**589.7**

725	(3R)-4-(cyclopropyl(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	**589.7**
726	(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	**575.7**
727	(R)-3-(benzofuran-2-ylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**607.7**
728	(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	**561.7**
729	(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((5-methylfuran-2-yl)methyl)-4-oxobutanoic acid	**571.7**
730	(3R)-4-(cyclopropyl(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	**575.7**
731	(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	**603.7**
732	(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	**557.6**
733	(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	**575.7**

734	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**506.6**
735	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid	**541.1**
736	(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	**547.6**
737	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**532.7**
738	(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	**547.6**
739	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**546.7**
740	(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	**547.6**
741	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**550.7**
742	(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-methyloxetan-3-yl)methyl)-4-oxobutanoic acid	**561.7**
743	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**532.7**

744	(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-methyloxetan-3-yl)methyl)-4-oxobutanoic acid	**561.7**
745	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**546.7**
746	(R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-methyloxetan-3-yl)methyl)-4-oxobutanoic acid	**561.7**
747	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**550.7**
748	(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-fluorooxetan-3-yl)methyl)-4-oxobutanoic acid	**565.6**
749	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**532.7**
750	(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-fluorooxetan-3-yl)methyl)-4-oxobutanoic acid	**565.6**
751	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**546.7**
752	(S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-fluorooxetan-3-yl)methyl)-4-oxobutanoic acid	**565.6**
753	(R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	**550.7**

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-1B (PTP-1B) 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, rosuvastatin, 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 fenofibric 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) PPARα/γ dual agonists such as muraglitazar, tesaglitazar, farglitazar and JT-501;

(j) PPARδ agonists such those disclosed in WO97/28149;

(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 cyclo-oxygenase 2 selective inhibitors;

(n) Glucagon receptor antagonists;

(o) GLP-1;

(p) GIP-1;

(q) GLP-1 analogs, such as exendins, for example exenitide, and

(r) Hydroxysterol dehydrogenase-1 (HSD-1) 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-1B 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-butynyl, 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 alkinyl 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.

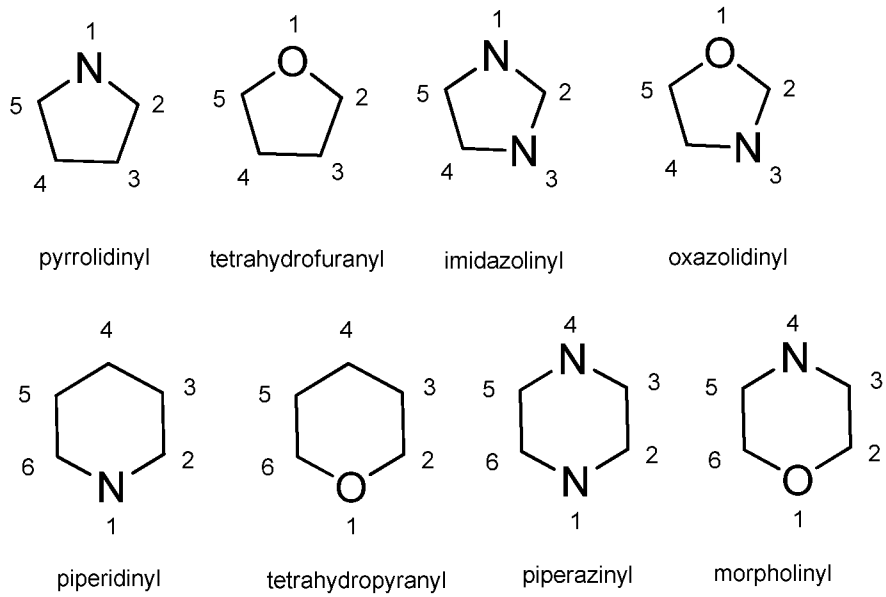
Therefore, "cycloalkylene" herein refers to a saturated homocyclic hydrocarbyl biradical of Formula C_nH_{2n-2}. Suitable cycloalkylene groups are C_{3-6} cycloalkylene group, preferably a C_{3-5} cycloalkylene (i.e. 1,3-cyclopropylene, 1,1-cyclopropylene, 1,1-cyclobutylene, 1,2-cyclobutylene, 1,3-cyclopentylene,or 1,1-cyclopentylene), more preferably a C_{3-4} cycloalkylene (i.e. 1,3-cyclopropylene, 1,1-cyclopropylene, 1,1-cyclobutylene, 1,2-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 "heterocyclyl", “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, isoxazolinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, piperidinyl, 3H-indolyl, indolinyl, isoindolinyl, 2-oxopiperazinyl, piperazinyl, homopiperazinyl, 2-pyrazolinyl, 3-pyrazolinyl, tetrahydro-2H-pyranyl, 2H-pyranyl, 4H-pyranyl, 3,4-dihydro-2H-pyranyl, 3-dioxolanyl, 1,4-dioxanyl, 2,5-dioximidazolidinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, indolinyl, tetrahydropyranyl, tetrahydrofuranyl, tetrahydroquinolinyl, tetrahydroisoquinolin-1-yl, tetrahydroisoquinolin-2-yl, tetrahydroisoquinolin-3-yl, tetrahydroisoquinolin-4-yl, thiomorpholin-4-yl, thiomorpholin-4-ylsulfoxide, 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 heteroaryl) 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-indanyl, 5-, 6-, 7- or 8-tetrahydronaphthyl, 1,2,3,4-tetrahydronaphthyl, 1,4-dihydronaphthyl, 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-dihydronaphthylene and the like.

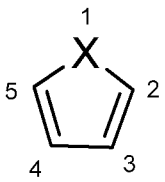
Where at least one carbon atom in an aryl group is replaced with a heteroatom, the resultant ring is referred to herein as a heteroaryl ring.

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, oxatriazolyl, thiatriazolyl, 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-benzoxazolyl, 1,2-benzisoxazolyl, 2,1-benzisoxazolyl, 1,3-benzothiazolyl, 1,2-benzoisothiazolyl, 2,1-benzoisothiazolyl, benzotriazolyl, 1,2,3-benzoxadiazolyl, 2,1,3-benzoxadiazolyl, 1,2,3-benzothiadiazolyl, 2,1,3-benzothiadiazolyl, thienopyridinyl, purinyl, imidazo[1,2-a]pyridinyl, 6-oxo-pyridazin-1(6H)-yl, 2-oxopyridin-1(2H)-yl, 6-oxo-pyridazin-1(6H)-yl, 2-oxopyridin-1(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.

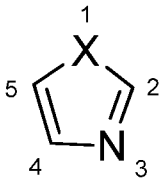
The ring atoms of heteroaryl or heteroarylene moieties are numbered on scheme below:



X is selected from:
N, O or S

Examples:

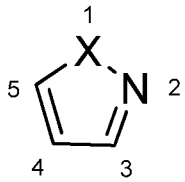
pyrrolyl
furanyl
thiophenyl



X is selected from:
N, O or S

Examples:

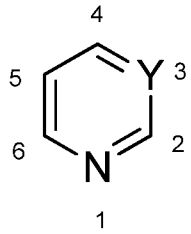
imidazolyl
oxazolyl
thiazolyl



X is selected from:
N, O or S

Examples:

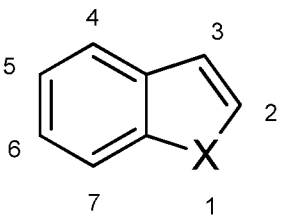
pyrazolyl
isooxazolyl
isothiazolyl



Y is selected from:
C, N

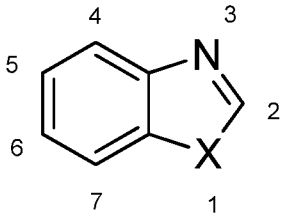
Examples:

pyridyl
pyrimidinyl



X is selected from:
N, O or S

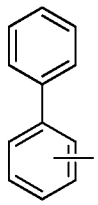
Examples:
indolyl
benzofuranyl
benzothiophenyl



X is selected from:
N, O or S

Examples:
benzimidazolyl
benzoxazolyl
benzothiazolyl

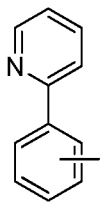
The term "biaryl" as used herein designates two aryl moieties as defined herein linked via a single bond. Non-limiting examples of such biaryl moieties include biphenyl.



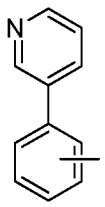
biphenyl

The term "heterobiaryl" as used herein designates two heteroaryl moieties as defined herein or a heteroaryl moiety and an aryl moity as defined

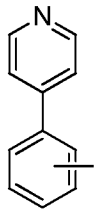
herein linked via a single bond. Non-limiting examples of such heterobiaryl moieties include pyridinylphenyl which is meant to include (2-pyridinyl)phenyl, (3-pyridinyl)phenyl and (4-pyridinyl)phenyl, bipyridinyl.



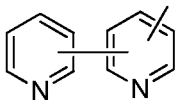
(2-pyridinyl)phenyl



(3-pyridinyl)phenyl



(4-pyridinyl)phenyl



bipyridinyl

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, malate, 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

Z	Q
-C(O)SQ	Alkyl or aryl
$-C(O)NQ^1Q^2$	H, alkyl, aryl, OH or NH_2
$-C(O)OCHQ^1O(O)CQ^2$	Q^1= H or phenyl Q^2= alkyl or aryl
-C(O)OCHQCl	H or aryl
$-C(OQ)_3$	Alkyl
-C(O)OC(O)OQ	Alkyl or aryl
$-C(O)CH_2Q$	SMe, SOMe, SO_2Me

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 suject 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 F_{254} 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 $KMnO_4$ revelator upon heating at 160°C. The $KMnO_4$ 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 LCMS using Electropsray 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 H_2O) 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 1ml/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 1ml/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 1.5ml/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 H_2O) 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 diastereosiomers obtained with the analytical method. Usual mixtures were the same as those used for the determination of ee.

^{1}H and ^{13}C 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'-tretramethyluronium

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,

ee: Enantiomeric excess,

DPP: Diphenylphosphino,

BINAP: 1,1'-Binaphtyl,

tBu: tert-Butyl

P: UV purity at 254nm determined by HPLC-MS,

SPE: Sold phase extraction,

Rt: Retention time,

TMSCl: Chlorotrimethylsilane,

BuLi: Butyllithium,

MCPBA: 3-Chloroperbenzoic acid,

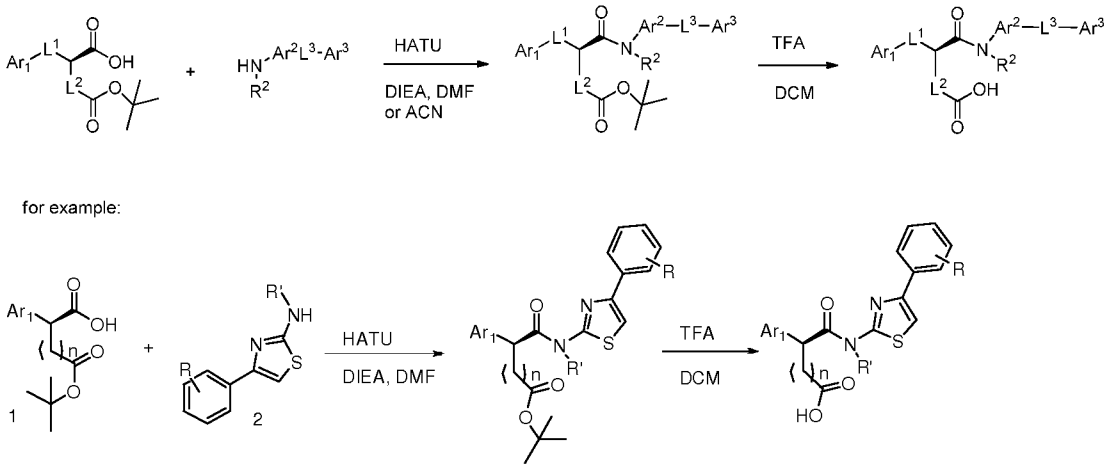
MOM: Methoxymethyl,

NCS: N-chlorosuccinimide,

NBS: N-bromosuccinimide.

General synthetic scheme

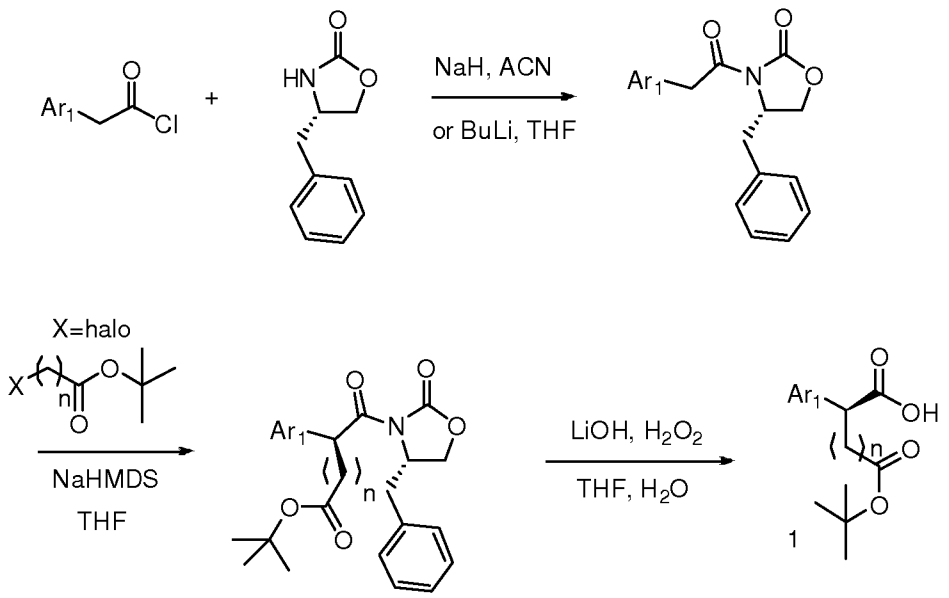
Most compounds of the invention are synthesized according to Scheme 1.



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

Synthesis of intermediates **1**

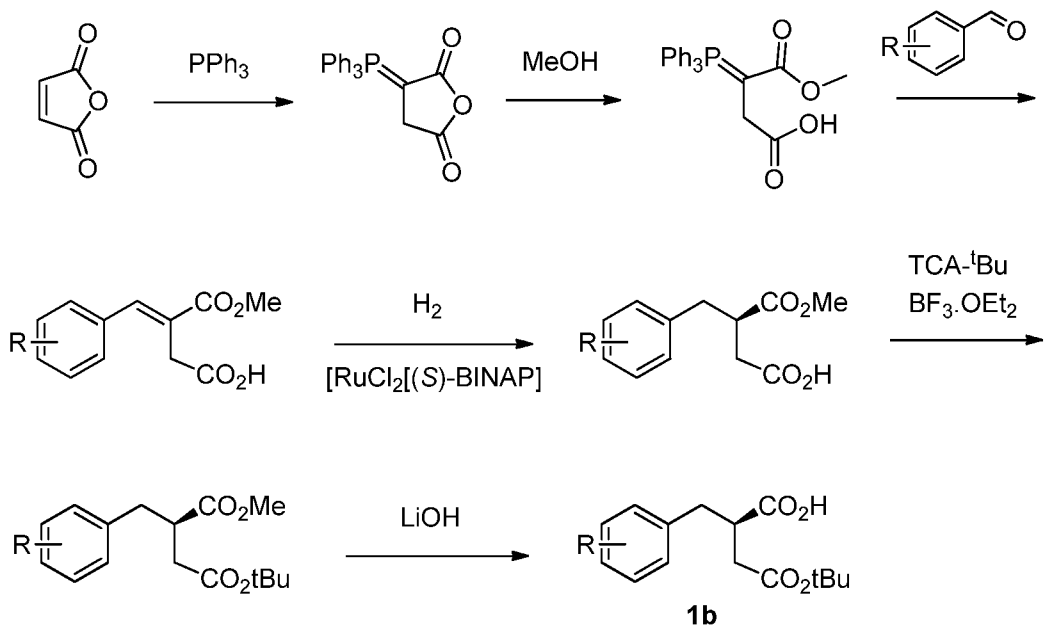
Chiral syntheses of intermediates **1** were carried out using Evans' chiral auxiliary approach (Evans et al. *J. Org. Chem.* **1999**, *64*, 6411-6417; Tararov et al. *J. Chem. Soc. Perkin Trans. 1*, **1997**, 3101-3106) (Scheme 2).



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*)-heterocyclylalkylsuccinic 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).

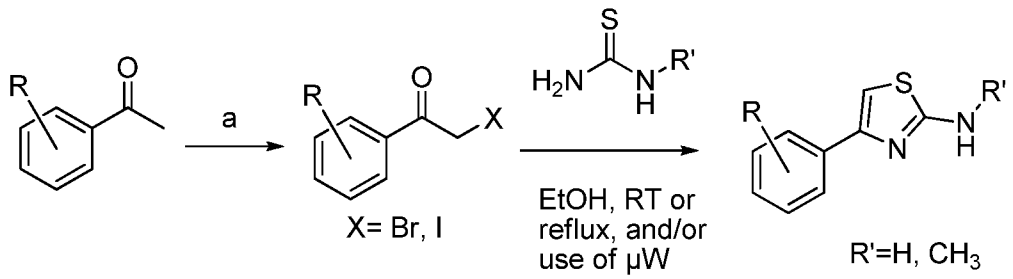


Scheme 3: Synthesis of (R)-benzyl-succinic acid monoester intermediates **1** using Wittig approach

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.**

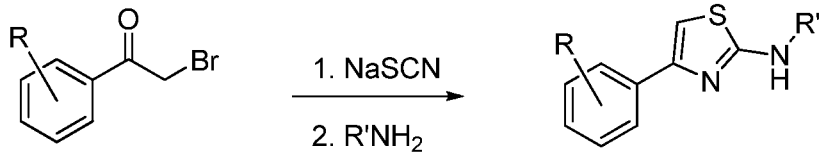
Synthesis of intermediates **2**

4-aryl-2-amino-thiazoles can be made using Hantzsch-type synthetic methodology as shown in Scheme 4. Thus, halogenation of substituted acetophenones (Larock, R. C. *Comprehensive Org Transf* 2nd Ed., Wiley, **1999**, pp 709-719; White et al. *J. Med. Chem.* **1996**, *39*, 4382-95) and subsequent condensation with thiourea (Swain et al. *J. Med. Chem.* **1991**, *34*, 140-151; Bartoli et al. *J. Med. Chem.* **1998**, *41*, 1855-68) will furnish 4-aryl-2-amino-thiazoles.



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

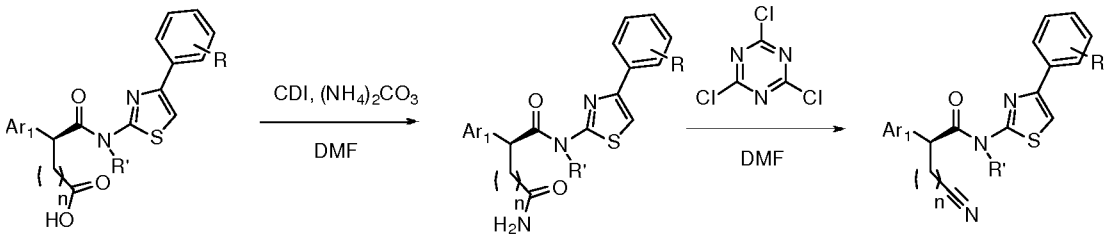
Synthetic Schemes for the Preparation of the Carboxylic Acid Bioisosteres

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 C.G. 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**,

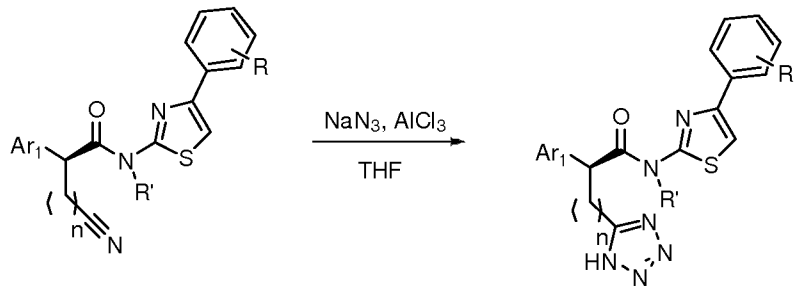
35, 2573-2581, Liljebris et al. *J. Med. Chem.* **2002**, *45*, 1785-1798.

Synthesis of tetrazole and hydroxy-oxadiazole isosteres

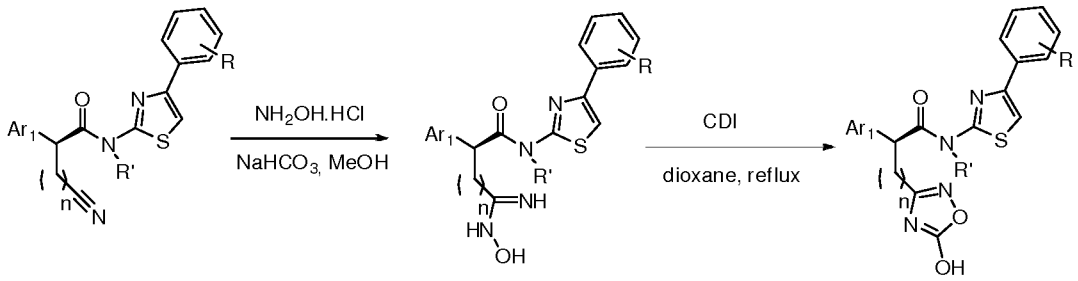
The tetrazole and hydroxy-oxadiazole isosteres can be synthesized using a common nitrile intermediate (see Scheme below). (Arienti et al. *J. Med. Chem.* **2005**, *48*, 6, 1882; Rodriguez et al. *Tetrahedron* **1997**, *38*, 24, 4221; Claremon et al. *Tet. Lett.* **1988**, 28, 2155).



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)

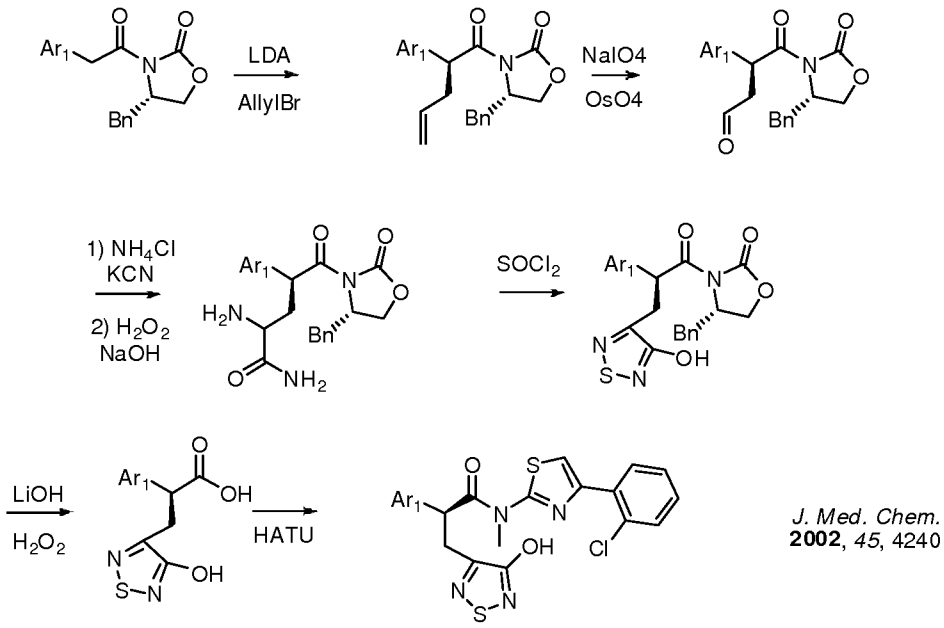


Treatment of the aforesaid nitrile intermediate with hydroxylamine, followed by dehydrative cyclization can be used to yield the hydroxy-oxadiazole isostere (see Scheme below) (Peretto et al. *J. Med. Chem.* 2005, *48*, 5705-5720).



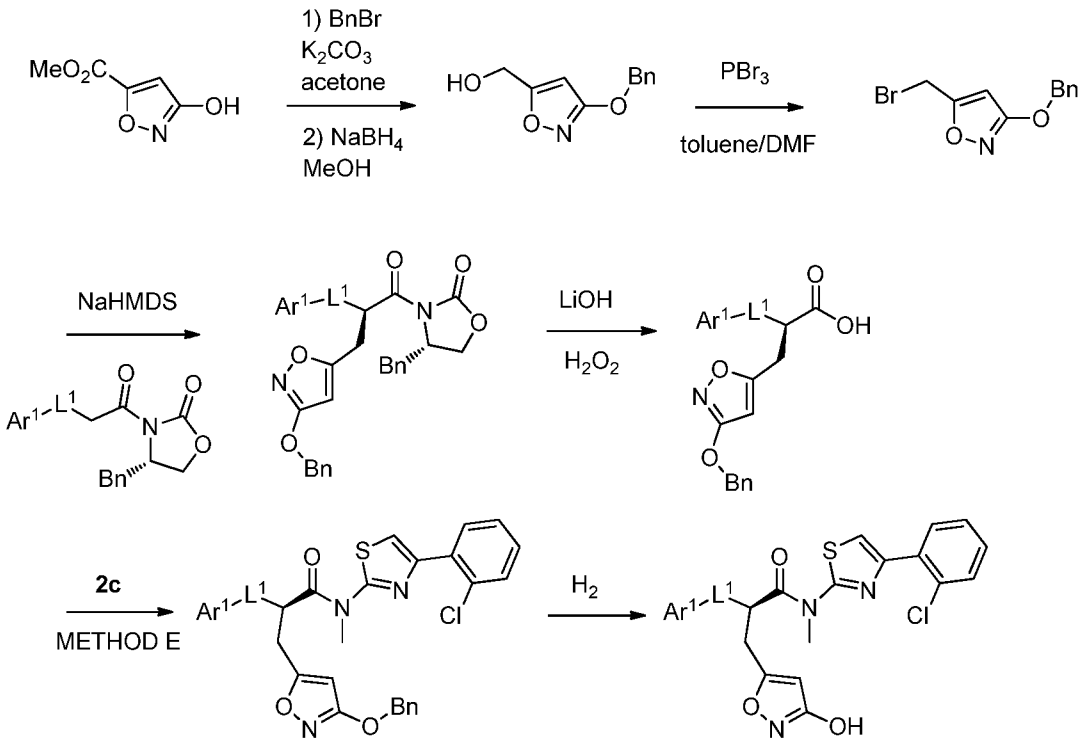
In addition, synthetic approaches to the preparation of other well-recognized carboxylic acid isosteres are outlined below.

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



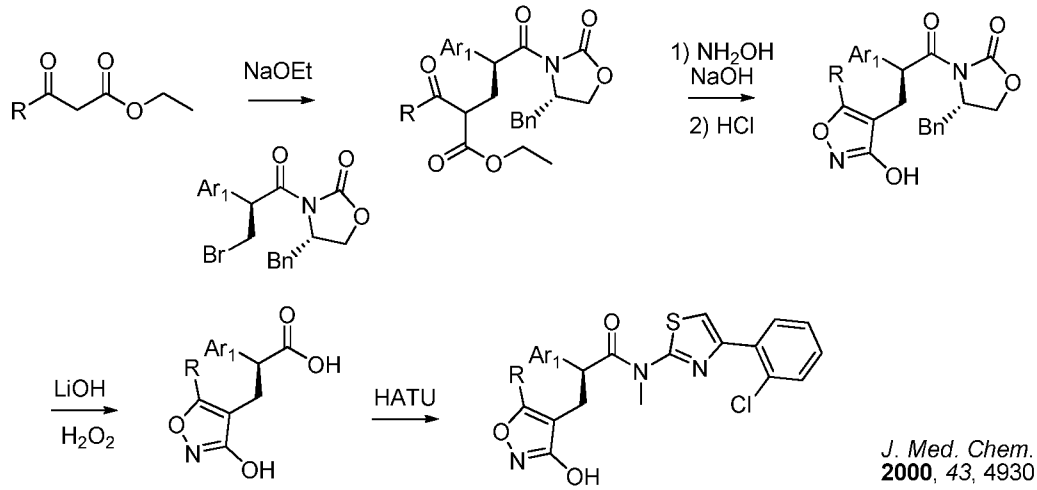
J. Med. Chem. **2002**, *45*, 4240

Synthesis of hydroxy-isoxazole isosteres



Eur. J. Org. Chem. **1998**, 473

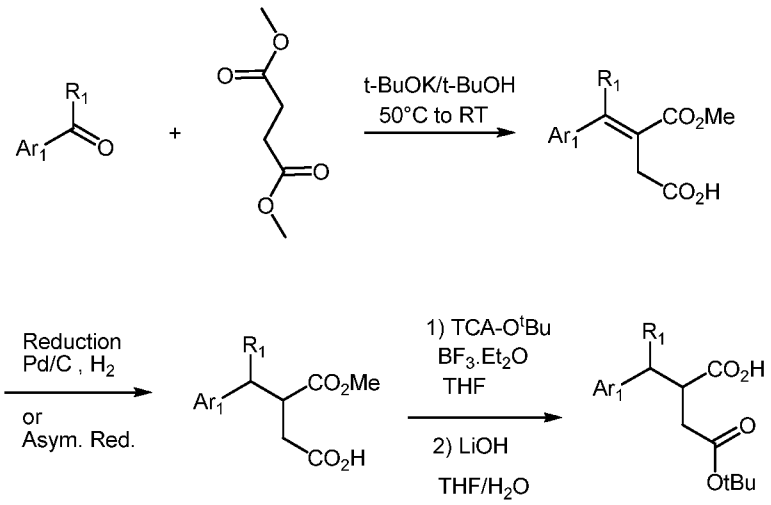
An alternative suggested synthetic approach for the preparation of hydroxy-isoxazole isosteres



J. Med. Chem. **2000**, *43*, 4930

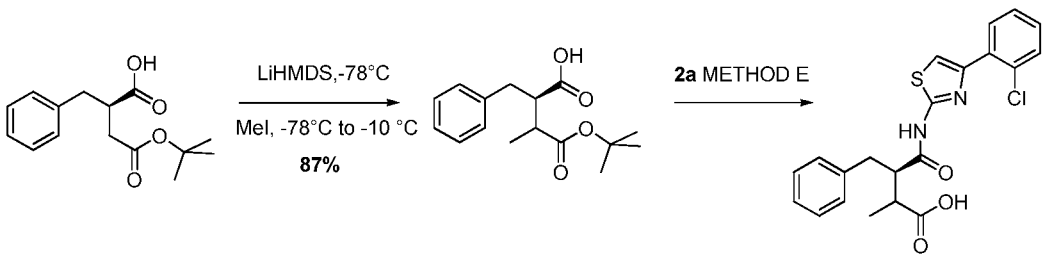
Additional synthetic schemes

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

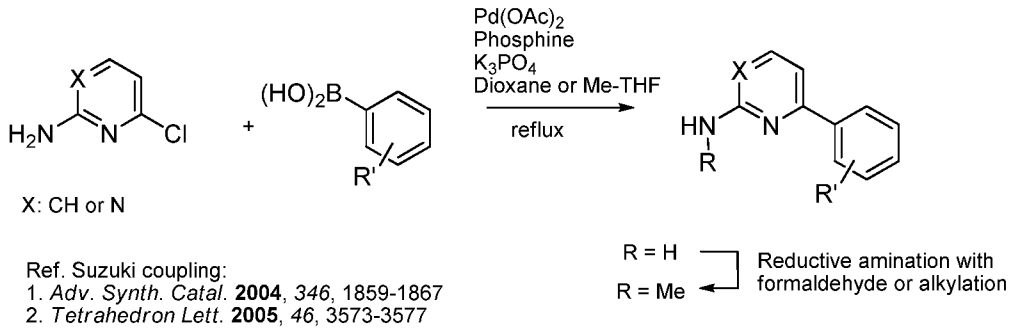
Synthesis of compound n°68 (**Scheme 7**):



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**):

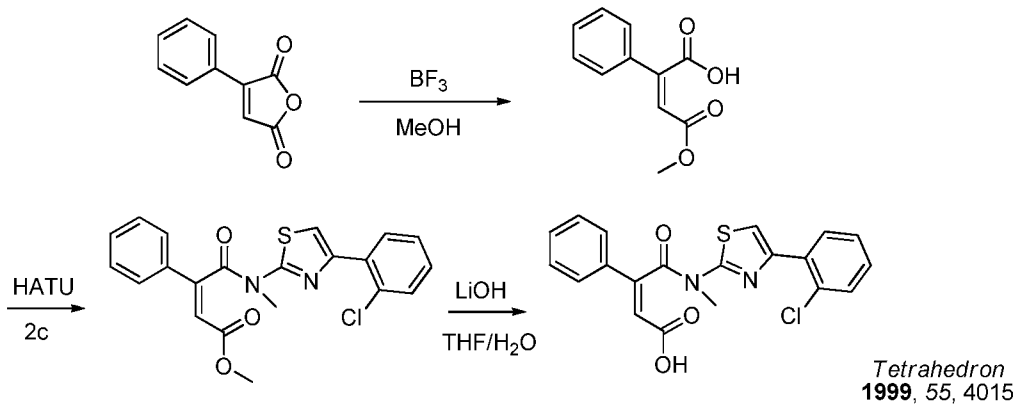


Ref. Suzuki coupling:
1. *Adv. Synth. Catal.* **2004**, *346*, 1859-1867
2. *Tetrahedron Lett.* **2005**, *46*, 3573-3577

Scheme 8: synthesis of aryl-pyridines and pyrimidines

Suzuki coupling between pyridinyl or pyrimidinyl chloride and phenylboronic acid reagents allowed synthesizing the aryl-pyridine and aryl-pyrimidines intermediates **2.**

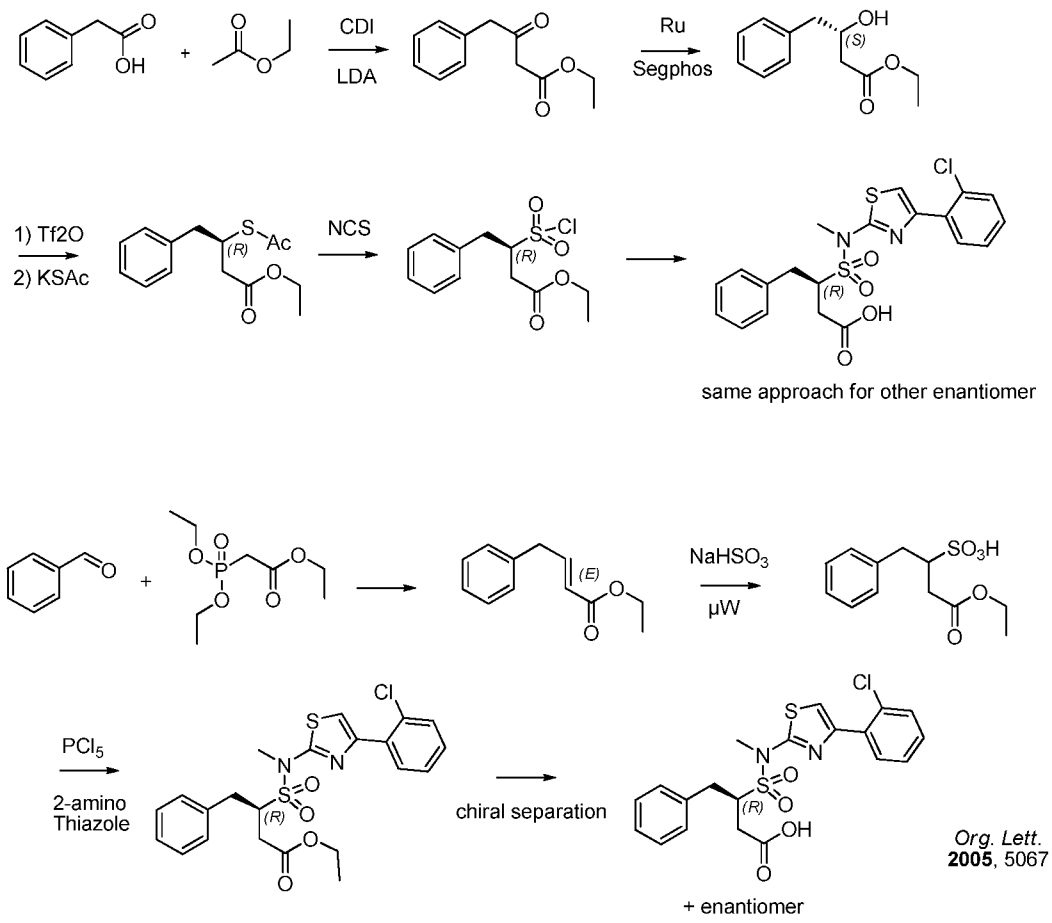
A suggested synthesis of compound n°74 (**Scheme 9**):



compound 74

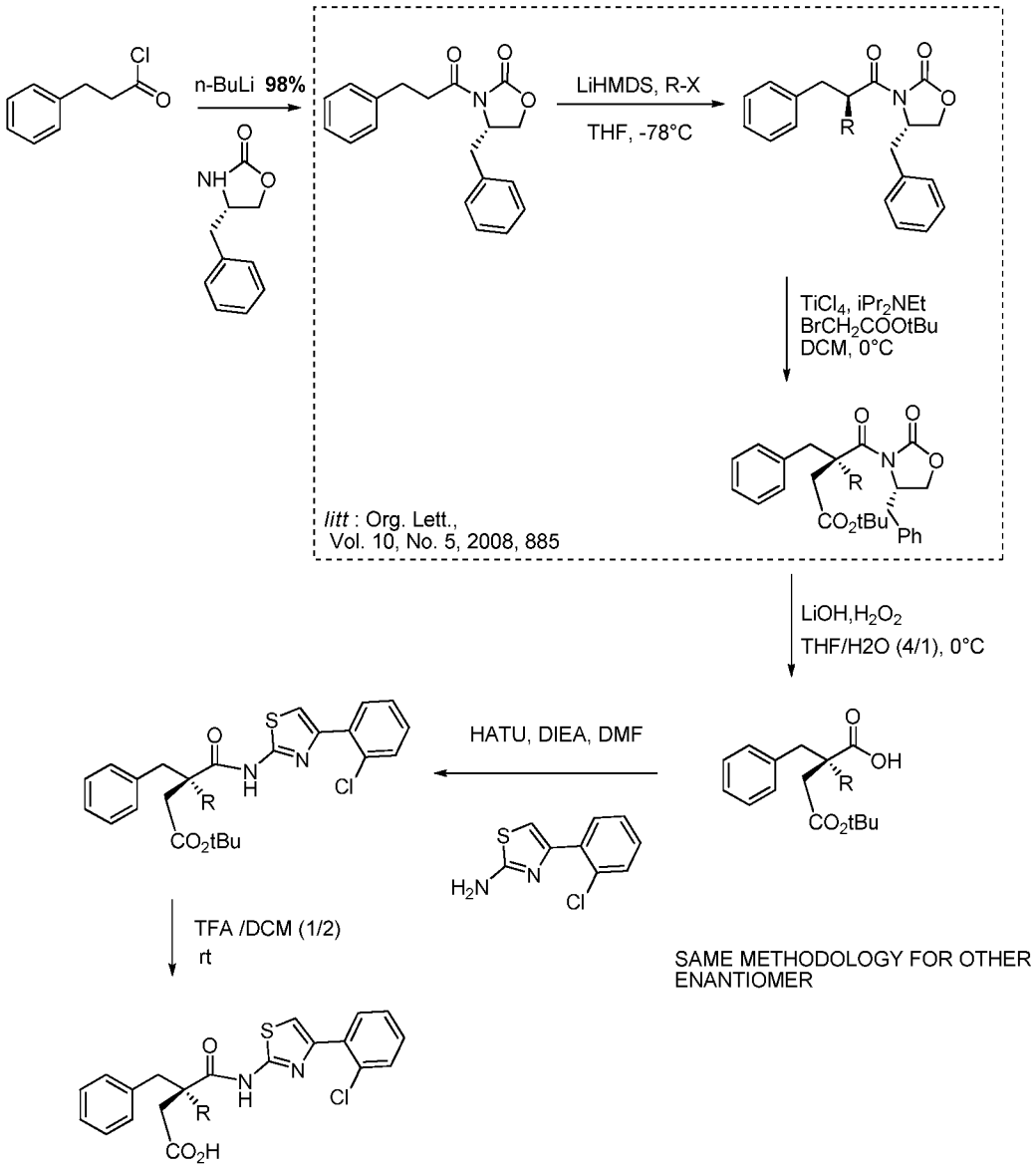
Scheme 9: A suggested synthesis of compound n°74

Suggested syntheses of compounds n°75 and n°76 (**Scheme 10**):



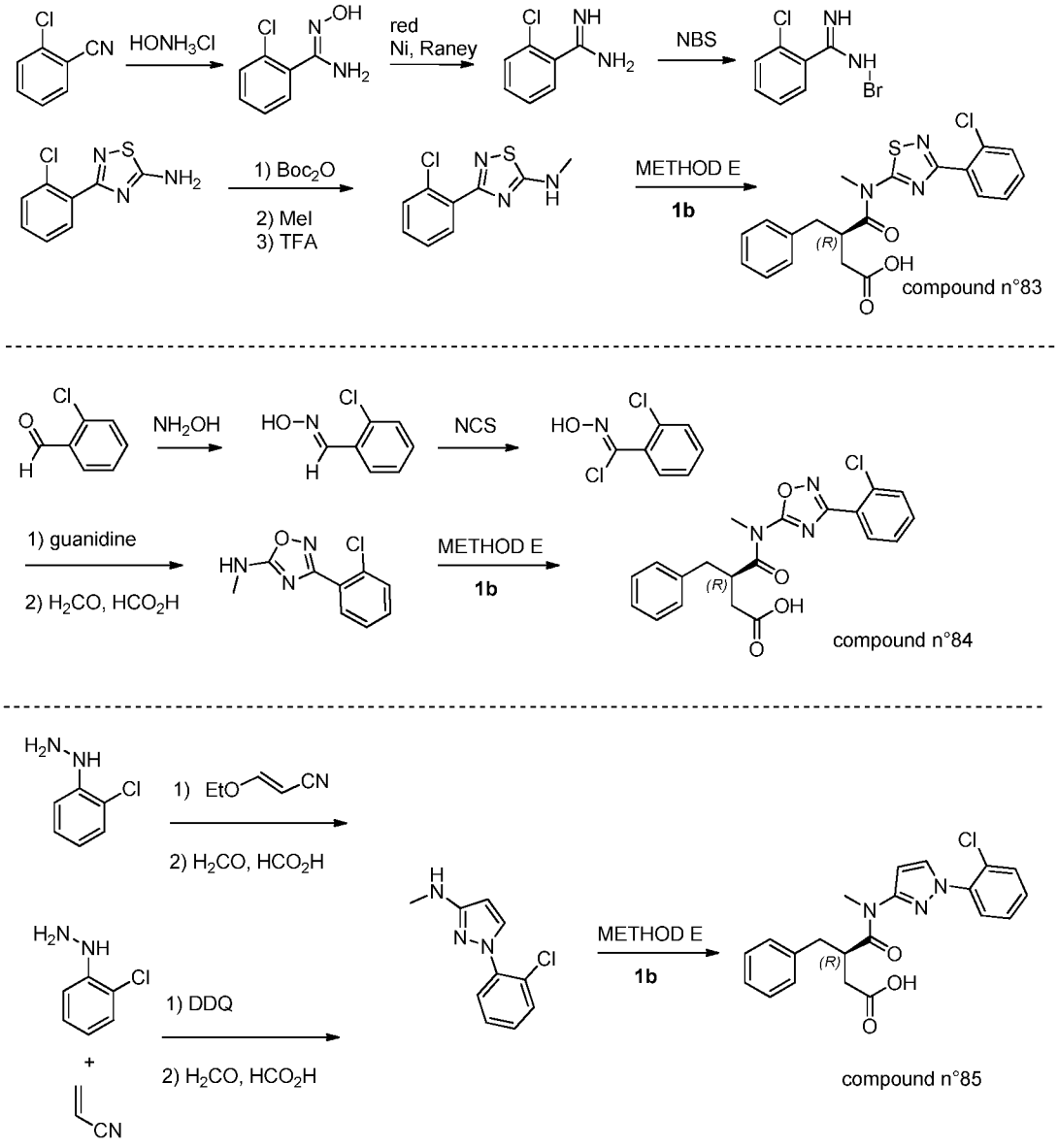
Scheme 10: Suggested syntheses of compounds n°75 and n°76

Suggested syntheses of compounds n°79 and n°80 (**Scheme 11**):



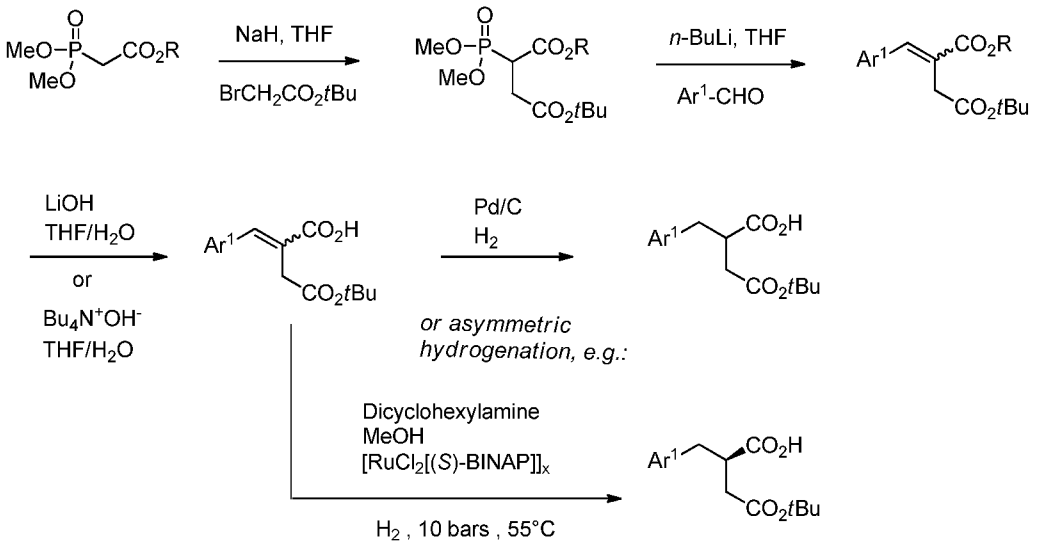
Scheme 11: Suggested syntheses of compounds n°79 and n°80

Suggested syntheses of compounds n°83 to n°85 (**Scheme 12**):



Scheme 12: Suggested syntheses of compounds n°83 to n°85

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

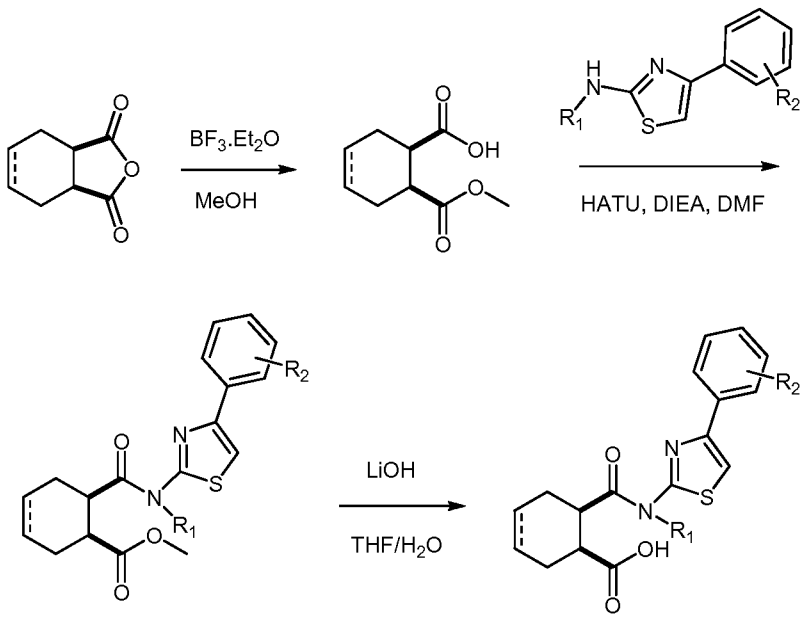


Org. Proc. Res. Dev. **2004**, *8*, 738-743

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

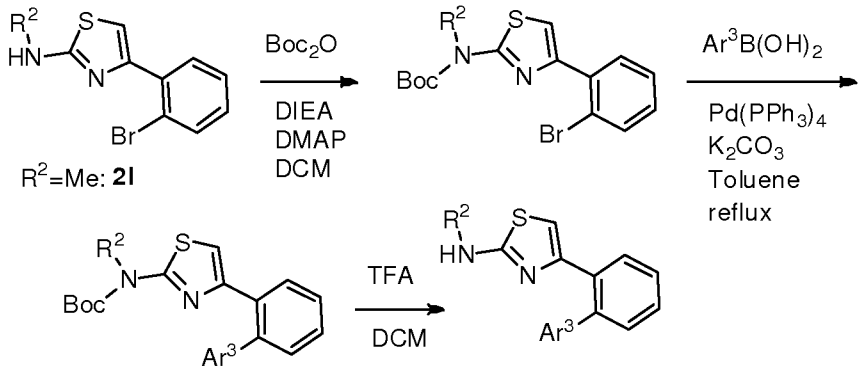
The HWE methodology as depicted in Scheme 13 is the preferred methodology of the invention for the synthesis of intermediates **1**.

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



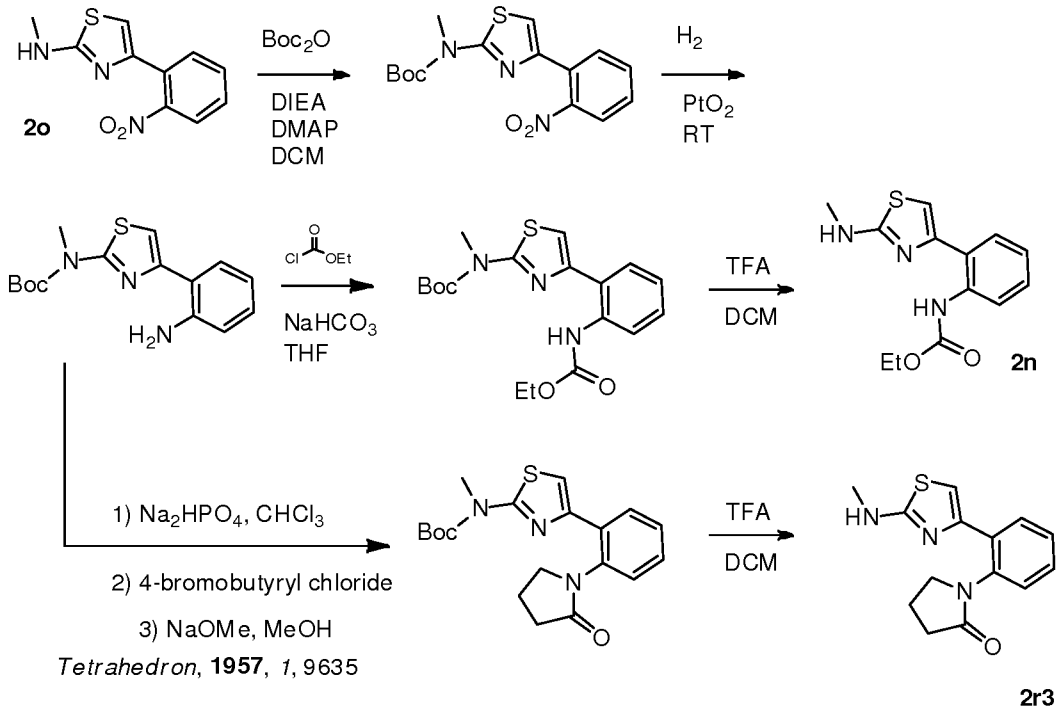
Scheme 14: Synthesis of compounds 98, 100 and 101

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



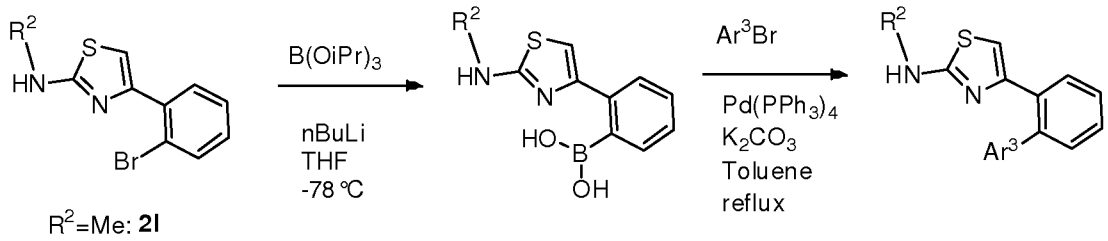
Scheme 15: General scheme for the preparation of biaryl- or heterobiaryl-thiazole amine intermediates using Suzuki approach

Synthesis of intermediates **2n** and **2r3** (**Scheme 16**):



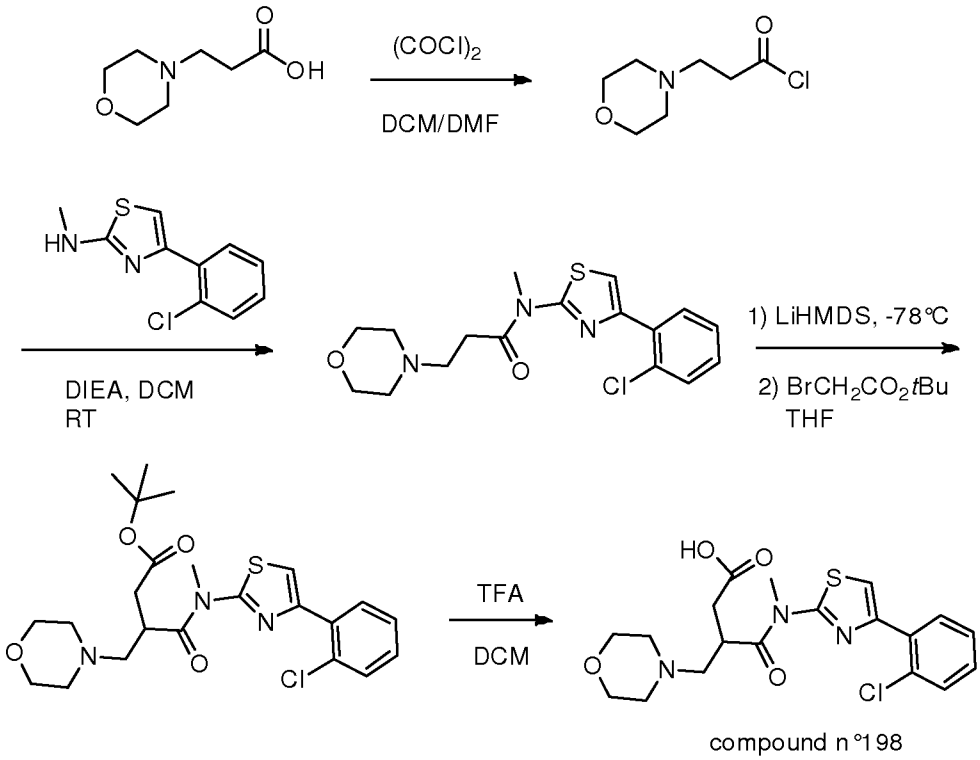
Scheme 16: Synthesis of intermediates **2n** and **2r3**

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



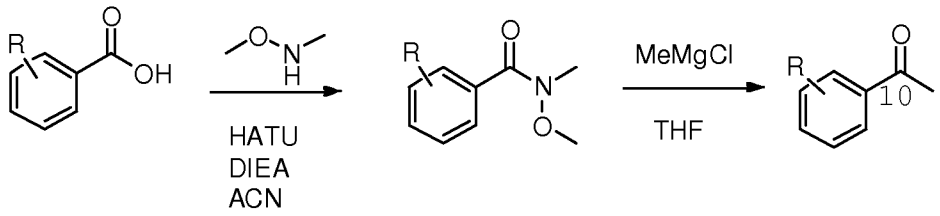
Scheme 17: Alternative general scheme for the preparation of biaryl- or heterobiaryl-thiazole amine intermediates using Suzuki approach

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



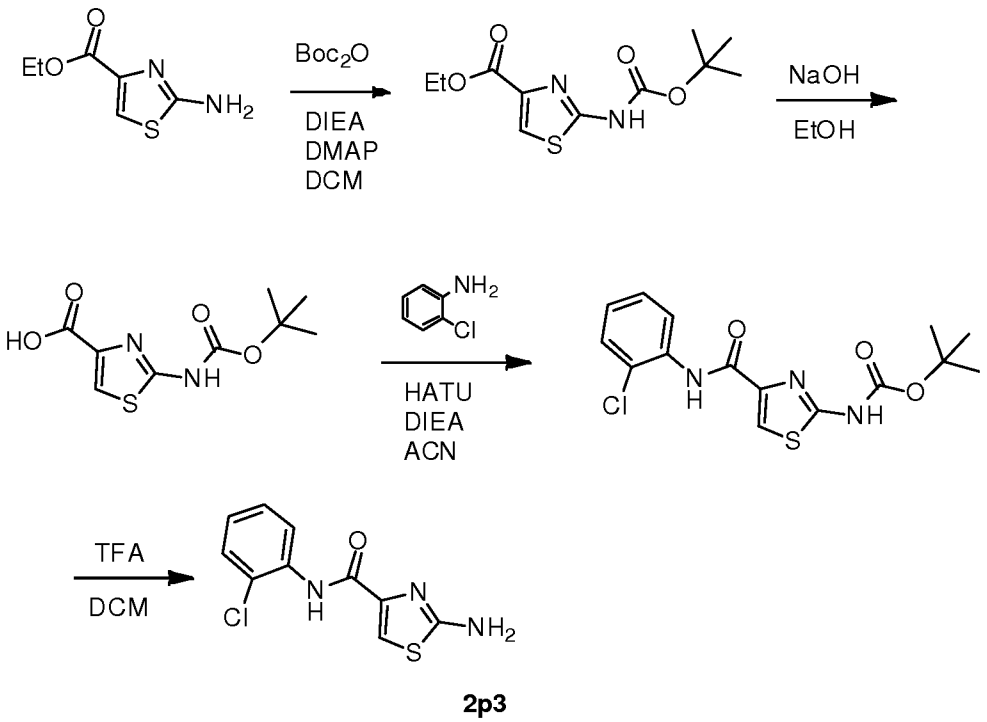
Scheme 18: Synthesis of compound n°198

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



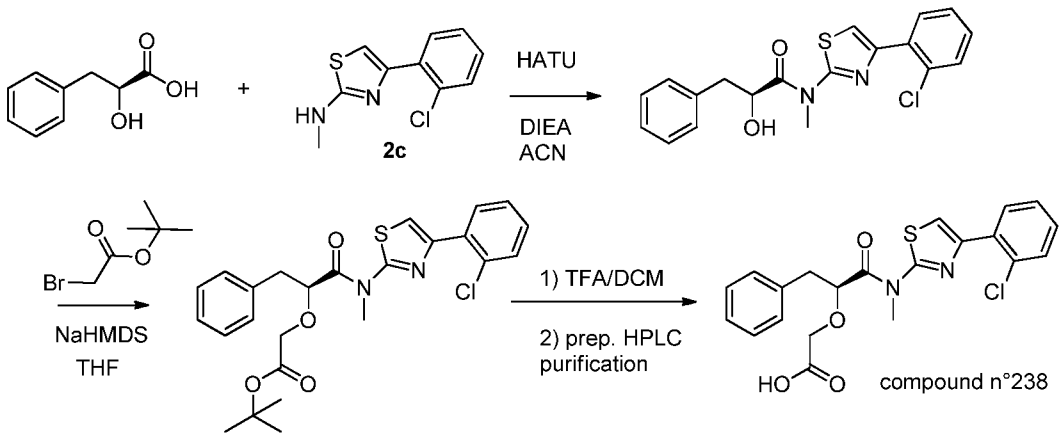
Scheme 20: General synthetic scheme for the preparation of substituted acetophenone reagents through Weinreb amide approach

Synthesis of intermediate **2p3** (**Scheme 21**):



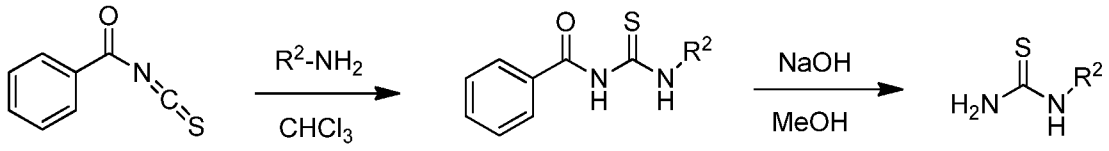
Scheme 21: Synthesis of intermediate **2p3**

Synthesis of compound n°238(**Scheme 22**):



Scheme 22: Synthesis of compound n°238

General synthetic scheme for the preparation of substituted thiourea reagents (**Scheme 23**):



Scheme 23: General synthetic scheme for the preparation of substituted thiourea reagents

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

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

(S)-4-benzyloxazolidin-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 NH_4Cl (2 mL) and a solution of $NaHCO_3$ (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 × 25 mL). The combined extracts were washed with water, brine, dried over Na_2SO_4, 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*-butyl 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 NH_4Cl (15 mL) and ethyl acetate (12 mL) were added. The organic layer was separated, and the aqueous one was extracted with ethyl acetate (3 × 30 mL). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated to give title compound. Y: 1.64 g (57%).

Step 3: synthesis of intermediate **1a** (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 H_2O_2 in water (16 mmol) was added dropwise at 0 °C. Then a solution of LiOH (8 mmol) in H_2O (19 mL) was added. The reaction mixture was stirred for 1.5 h at 0 °C (TLC: CCl_4/ethyl acetate= 7/3) indicated reaction was complete. A solution of Na_2SO_3 (15 mL) and $NaHCO_3$ (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 CH_2Cl_2 (3 × 45 mL). The aqueous layer was acidified with 6M HCl to pH=2 at 0 °C. The product was extracted with ethyl acetate (3 × 50 mL). Combined extracts were washed with brine, dried over Na_2SO_4, 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 **1e**: (R)-4-*tert*-butoxy-4-oxo-2-phenethylbutanoic acid,

intermediate **1f**: (S)-4-*tert*-butoxy-4-oxo-2-phenethylbutanoic acid,

intermediate **1o**: (R)-2-benzyl-5-methoxy-5-oxopentanoic acid; step 2 being replaced by a Michael addition on methyl acrylate using $Ti(OiPr)_2Cl_2$ and DIEA in DCM at 0°C as described in WO1996/33176,

intermediate **1p**: (S)-2-benzyl-5-methoxy-5-oxopentanoic acid; step 2 being replaced by a Michael addition on methyl acrylate using $Ti(OiPr)_2Cl_2$ and DIEA in DCM at 0°C as described in WO1996/33176,

intermediate **1t**: (2S)-4-*tert*-butoxy-2-(2,3-dihydro-1H-inden-1-yl)-4-oxobutanoic acid,

intermediate **1u**: (S)-4-*tert*-butoxy-2-(2,3-dihydro-1H-inden-2-yl)-4-oxobutanoic acid,

intermediate **1v**: (S)-4-*tert*-butoxy-2-cyclohexyl-4-oxobutanoic acid

intermediate **1w**: (R)-4-*ter*t-butoxy-2-(cyclohexylmethyl)-4-oxobutanoic acid,

intermediate **1x**: (R)-4-tert-butoxy-4-oxo-2-phenylbutanoic acid,

intermediate **1z**: (S)-4-*tert*-butoxy-4-oxo-2-((R)-1-phenylethyl)butanoic acid,

intermediate **1e1**: (2R)-4-(*tert*-butoxy)-4-oxo-2-((tetrahydrofuran-2-yl)methyl)butanoic acid,

intermediate **1f1:** (R)-4-(*tert*-butoxy)-2-(cyclopentylmethyl)-4-oxobutanoic acid,

intermediate **1g1:** (R)-4-(*tert*-butoxy)-4-oxo-2-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid ,

intermediate **1h1**: (R)-4-(*tert*-butoxy)-4-oxo-2-((S)-1-phenylethyl)butanoic acid

intermediate **1o1**: (2R)-4-(*tert*-butoxy)-4-oxo-2-((tetrahydrofuran-3-yl)methyl)butanoic acid

intermediate **1t1**: (R)-4-(*tert*-butoxy)-2-(furan-2-ylmethyl)-4-oxobutanoic acid

intermediate **1u1**: (S)-4-(*ter*t-butoxy)-4-oxo-2-(thiophen-2-ylmethyl)butanoic acid.

General method B: synthesis of intermediate **1b** (R)-2-benzyl-4-*tert*-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 × 100 mL), diethyl ether (100 mL), and dried under vacuum to give title compound. Y: 360 g (97%), rt=3.21min (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 (3*E*)-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 × 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, CCl_4/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 (3*R*)-3-benzyl-4-methoxy-4-oxobutanoic acid

A mixture of (3*E*)-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)ruthenium(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 ½. Acetonitrile (90 mL) was added to the residue, and the mixture was evaporated again by ½. 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 Na_2SO_4, 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-benzylsuccinate

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 (3*R*)-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. $NaHCO_3$ (10 mL) and extracted with AcOEt (2x20 mL). Combined organic layers were washed with brine, dried over $MgSO_4$, 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 (-*t*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-benzylsuccinate (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 (-*t*Bu).

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

intermediate **1c**: (R)-4-*tert*-butoxy-2-(4-fluorobenzyl)-4-oxobutanoic acid,

intermediate **1d**: (R)-4-*tert*-butoxy-2-(cyclohexylmethyl)-4-oxobutanoic acid,

intermediate **1g**: (R)-4-*tert*-butoxy-4-oxo-2-(4-(trifluoromethyl)benzyl)butanoic acid,

intermediate **1h**: (R)-4-*tert*-butoxy-4-oxo-2-(3-(trifluoromethyl)benzyl)butanoic acid,

intermediate **1i**: (R)-4-*tert*-butoxy-2-(2-cyanobenzyl)-4-oxobutanoic acid

intermediate **1j**: (R)-4-*tert*-butoxy-2-(3-cyanobenzyl)-4-oxobutanoic acid,

intermediate **1k**: (R)-4-*tert*-butoxy-2-(4-cyanobenzyl)-4-oxobutanoic acid,

intermediate **1l**: (R)-4-*tert*-butoxy-2-(4-methoxybenzyl)-4-oxobutanoic acid,

intermediate **1m**: (R)-4-*tert*-butoxy-2-(3-methoxybenzyl)-4-oxobutanoic acid,

intermediate **1n**: (R)-4-*tert*-butoxy-2-(2-methoxybenzyl)-4-oxobutanoic acid,

intermediate **1q**: (R)-4-*tert*-butoxy-2-(4-chlorobenzyl)-4-oxobutanoic acid,

intermediate **1r**: (R)-4-*tert*-butoxy-2-(3-chlorobenzyl)-4-oxobutanoic acid,

intermediate **1s**: (R)-4-*tert*-butoxy-2-(2-chlorobenzyl)-4-oxobutanoic acid,

intermediate **1y**: (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-1-(2-chlorophenyl)ethanone (7 g, 27.45 mmol) in ethanol (10 mL) and reaction mixture was stirred at RT for 18h. 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. Na_2CO_3 and AcOEt. Phases are separated and organic layer dried over $MgSO_4$, 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 **2a1**: 4-(2,5-dichlorophenyl)-N-methylthiazol-2-amine,

intermediate **2y1**: 4-(2-chloro-5-(trifluoromethyl)phenyl)-N-methylthiazol-2-amine,

intermediate **2z1**: 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-chloro-5-fluorophenyl)-N-cyclopropylthiazol-2-amine,
intermediate **2n2**: N-cyclopropyl-4-(3-(difluoromethoxy)phenyl)thiazol-2-amine,
intermediate **2o2**: 4-(2-chloro-5-(trifluoromethyl)phenyl)-N-cyclopropylthiazol-2-amine,
intermediate **2d3**: N-(2-(benzyloxy)ethyl)-4-(2,5-dichlorophenyl)thiazol-2-amine,
intermediate **2e3**: 4-(2-chloro-5-(difluoromethyl)phenyl)-N-methylthiazol-2-amine,
intermediate **2j3**: (4-(2-chloro-5-(difluoromethoxy)phenyl)-N-methylthiazol-2-amine),
intermediate **2v3**: (S)-1-((4-(2-chlorophenyl)thiazol-2-yl)amino)propan-2-ol,
intermediate **2w3**: (R)-1-((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-1-(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 Na_2SO_4, and the solvent was removed *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 mn (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 **2u1**: N-(2-(benzyloxy)ethyl)-4-(2-chlorophenyl)thiazol-2-amine,

intermediate **2v1**: 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 **1b** (1.21 mmol, 320 mg) in anhydrous DMF (5mL) was added HATU (1.33mmol, 505mg). 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 (20mL) and washed with sat. aq. $NaHCO_3$ (10mL) and water (3x10 mL). The organic phase was dried over $MgSO_4$ 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 mn (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 mn (gradient B), $(M+H)^+$ =401.1, ee=96% (method B), ^{1}HNMR ($CDCl_3$): 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), ^{1}HNMR (DMSO-d_6): δ=7.78 (d, J=2.8Hz, 1H), 7.5 (m, 2H), 7.4-7.1 (m, 9H), 4.3 (q, 1H), 3.18 (dd, J=17Hz, J=27Hz, 1H), 2.66 (dd, J=4.8Hz, J=22Hz, 1H).

Example **3**: compound n°3: (R)-3-benzyl-4-(4-(2,4-dichlorophenyl)thiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate **1b** 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 **1b** 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 **1b** 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 **1b** 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 **1b** 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 **1b** and 4-(3-(trifluoromethyl)phenyl)thiazol-2-amine.

Example **11**: compound n°14: (R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized using intermediates **1b** 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, 1H), 7.54 (s, 1H), 7.45 (d, 1H), 7.34-7.13 (m, 7H), 3.62 (s, 3H), 3.47 (m, 1H), 3.15-3.01 (m, 2H), 2.61-2.54 (m, 1H), 2.53-2.51 (dd, 1H).

Example **12**: compound n°17: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(4-fluorobenzyl)-4-oxobutanoic acid was synthesized using intermediates **1c** and **2a**.

Example **13**: compound n°18: (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-3-(cyclohexylmethyl)-4-oxobutanoic acid was synthesized using intermediates **1d** 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, 1H), 7.35-7.45 (m, 2H), 7.15-7.30 (m, 4H), 3.15-3.25 (m, 1H), 2.7 (dd, 1H), 2.5 (dd, 1H), 1.45-1.8 (m, 6H), 1.1-1.4 (m, 5H), 0.8-1.0 (m, 2H).

Example **14**: compound n°22: (R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid was synthesized using intermediates **1b** and **2d**.

Example **15**: 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 **1b** and **2e**.

Example **16**: compound n°11: (R)-3-benzyl-4-oxo-4-(3-phenyl-1,2,4-thiadiazol-5-ylamino)butanoic acid was synthesized using intermediate **1b** and 3-phenyl-1,2,4-thiadiazol-5-amine.

Example **17**: compound n°20: (R)-3-benzyl-4-(4-(2-chlorophenyl)-5-fluorothiazol-2-ylamino)-4-oxobutanoic acid was synthesized using intermediate **1b** and 4-(2-chlorophenyl)-5-fluorothiazol-2-amine which was prepared in one

step from intermediate **2a** as described in *Chem. Res. Toxicol.* 2007, 1954-1965.

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 **1b** 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 **1b** 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_2CO_3 in dioxane/H_2O followed by *t*Bu 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 **1e** 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 **1f** 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 **1g** 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 **1h** 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 **1i** 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 **1j** 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 **1k** 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 **1l** 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 **1m** 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 **1n** 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)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 **1o** and **2c** using general method E, replacing the TFA *t*Bu ester deprotection by a methyl ester saponification using LiOH in THF/H_2O.

Example **39**: compound n°39: (S)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid was synthesized from intermediates **1p** and **2c** using general method E, replacing the TFA *t*Bu ester deprotection by a methyl ester saponification using LiOH in THF/H_2O.

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 **1j** 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 **1i** 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 **1r** 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 **1s** 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-1H-inden-1-yl)-4-oxobutanoic acid may be synthesized from intermediates **1t** and **2c** using general method E. **1t** 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 **1b** 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 **1b** 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-((1H-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 **1v** and **2a**

using general method E.

Example **62**: compound n°62: (S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(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-yl)(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-ylcarbamoyl)-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-((1H-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 **1w** and **2c** using general method E. Intermediate **1w** was synthesized by hydrogenation of intermediate **1b** using PtO_2 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-*tert*-butoxy-2-oxoethyl)-4-methylpentanoic acid using general method E. (R)-2-(2-*tert*-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 **1b** 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 *t*Bu ester using *t*Bu-TCA. Treatment of this *t*Bu ester with LiHMDS followed by the addition of *t*-butyl bromoacetate provided 1-*tert*-butyl 4-methyl 2-phenylsuccinate. *t*Bu 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 **1y** 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 **1b** 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 **1b** 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-*tert*-butoxy-2-(4-methoxybenzyl)-4-oxobutanoic acid and intermediate **2c** using general method E. 4-*tert*-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 **1b** and commercially available 4-(2,5-dimethylthiophen-3-yl)thiazol-2-amine using

general method E.

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 PtO_2 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 **1z** 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 **1b** 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 **1b** 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-([1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid was synthesized from intermediate **1b** and 4-([1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine using general method E. 4-([1,1'-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 **1b** 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 **1a1** (4-(*tert*-butoxy)-2-(cyclopropylmethyl)-4-oxobutanoic acid) and **2c** using general method E. **1a1** 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 **1b1** (4-(*tert*-butoxy)-4-oxo-2-(thiazol-4-ylmethyl)butanoic

acid) and **2c** using general method E. **1b1** 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 **2l** using the methodology shown in **Scheme 15**.

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

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

Example **121**: compound n°121: (R)-4-((2-amino-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)(3-methoxy-3-oxopropyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** 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 **1c1** (2-(bicyclo[2.2.1]heptan-2-ylmethyl)-4-(tert-butoxy)-4-oxobutanoic acid) and **2c** using general method E. **1c1** 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 **2l** 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 **2l** 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 **2a1** using general method E.

Example **131**: compound n°131: (R)-1-(5-(2-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)phenyl)pyridin-2-yl)pyrrolidin-1-ium 2,2,2-trifluoroacetate was synthesized from intermediates **1b** and **2b1** (N-methyl-4-(2-(6-(pyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate **2b1** was synthesized from 2-(pyrrolidin-1-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine and **2l** 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 **2c1** (N-methyl-4-(4'-morpholino-[1,1'-biphenyl]-2-yl)thiazol-2-amine) using general method E. Intermediate **2c1** 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 **2d1** (N-methyl-4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate **2d1** 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 **2e1** (4-(3'-chloro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2e1** was synthesized from (3-chlorophenyl)boronic acid and **2l** using the methodology 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 **2f1** (4-(2-(furan-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate **2f1** 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 **2g1** (4-(2-(6-(2-methoxyethoxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate **2g1** 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 **2h1** (4-(4'-isopropyl-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2h1** was synthesized from (4-isopropylphenyl)boronic acid and **2l** 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 was synthesized from (R)-4-*tert*-butoxy-2-(cyclopentylmethyl)-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 **2i1** (4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate **2i1** 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 **2j1** (N-methyl-4-(2-(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)phenyl)thiazol-2-amine) using general method E. Intermediate **2j1** was synthesized from 5-bromo-2-((tetrahydro-2H-pyran-4-yl)oxy)pyridine and **2l** 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)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid was synthesized from intermediates **1d1** (4-(*tert*-butoxy)-2-(furan-2-ylmethyl)-4-oxobutanoic acid) and **2c** using general method E. **1d1** 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 **1b** and **2k1** (4-(2-cyclopropylphenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2k1** was synthesized from cyclopropylboronic acid and **2l** using the methodology described in **Scheme 15**.

Example **145**: compound n°145: (R)-3-benzyl-4-((4-(4'-(dimethylamino)-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2l1** (4-(4'-(dimethylamino)-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E. Intermediate **2l1** 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-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2m1** (4-(3'-fluoro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2m1** 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-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2n1** (4-(3',5'-difluoro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E. Intermediate **2n1** was synthesized from (3,5-difluorophenyl)boronic acid and **2l** 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 **1b** and commercially available **2o1** (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 **1b** and **2p1** (4-(4'-chloro-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2p1** was synthesized from (4-chlorophenyl)boronic acid and **2l** by Suzuki coupling with the conditions described in **Scheme 15**.

Example **150**: compound n°150: (R)-3-benzyl-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2q1** (1-(5-(2-(2-(methylamino)thiazol-4-yl)phenyl)pyridin-2-yl)pyrrolidin-2-one) using general method E. Intermediate **2q1** was synthesized from 1-(5-bromopyridin-2-yl)pyrrolidin-2-one and **2l** 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 **1b** and **2r1** (4-(4-chloro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate **2r1** 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 **1b** and **2s1** (4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate **2s1** 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 **2t1** (4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2t1** 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 **1e1** 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 **2u1** using general method E followed by debenzylation with $FeCl_3$ 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 **2v1** using general method E followed by debenzylation with $FeCl_3$ 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 **2w1** (4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E. Intermediate **2w1** was synthesized from 5-bromo-3-chloro-2-methoxypyridine and **2l** 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 **2x1** (4-(2-(6-(benzyloxy)pyridin-3-yl)phenyl)-N-methylthiazol-2-amine) using general method E and preparative HPLC purification. Intermediate **2x1** was synthesized from (6-benzyloxypyridin-3-

yl)boronic acid and **2l** 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 **1f1** and **2a1** 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 **1g1** 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 **1b** and **2y1** 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 **1b** and **2z1** 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 **1b** 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 **1b** 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 **1f1** 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 **1f1** 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 **1g1** 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 **1g1** and **2a1** 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 **1f1** 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 **1b** and **2d2** (N-(2-(benzyloxy)ethyl)-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-amine) using general method E followed by debenzylation with $FeCl_3$ 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 **1f1** and **2d1** 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 **1f1** and **2d3** using general method E followed by

debenzylation with $FeCl_3$ in DCM.

Example **173**: compound n°173: (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid was synthesized from intermediates **1g1** and **2c** using general method E.

Example **174**: compound n°174: (R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2e2** using general method E.

Example **175**: compound n°175: (R)-3-benzyl-4-(methyl(4-(2,3,5-trichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2f2** using general method E.

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

Example **177**: compound n°177: (R)-3-benzyl-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2h2** (4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)-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)-N-methylthiazol-2-amine by Suzuki coupling with the conditions described in **Scheme 15**. 4-(5-bromo-2-chlorophenyl)-N-methylthiazol-2-amine was synthesized using general method C.

Example **178**: compound n°178: (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** 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 **1g1** 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 **1b** 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 **1f1** 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 **1b** 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 **2l** using the methodology described in **Scheme 17**.

Example **183**: compound n°183: (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2k2** (1-(5-(2-(2-(cyclopropylamino)thiazol-4-yl)phenyl)pyridin-2-yl)pyrrolidin-2-one) using general method E. Intermediate **2k2** was synthesized from 1-(5-bromopyridin-2-yl)pyrrolidin-2-one and 4-(2-bromo-4-chlorophenyl)-N-cyclopropylthiazol-2-amine using the methodology described in **Scheme 17**. 1-(5-bromopyridin-2-

yl)pyrrolidin-2-one was synthesized by reacting 5-bromopyridin-2-amine with Na_2HPO_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 **1g1** 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 **1b** and **2l2** 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 **1b** 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 **1f1** 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 **1b** 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 **1b** 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 **1g1** 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 **1b** 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 **1b** 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 **1g1** and **2o2** using general method E.

Example **194**: compound n°194: (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 was synthesized from intermediates **1f1** and **2p2** (N-cyclopropyl-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. Intermediate **2p2** was synthesized from commercially available 7-bromo-4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazine and **2l** 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 **1h1** 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 **1b** 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 **1j1** ((R)-4-(*tert*-butoxy)-2-(cyclopentylamino)-4-oxobutanoic acid) and **2c** using general method E. **1j1** was made from (R)-2-amino-4-(*tert*-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 **2u1** 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-

(trifluoromethyl)phenyl)-1H-pyrazol-5-amine) using general method E.

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 from intermediates **1k1** (4-(*tert*-butoxy)-2-(4-(methoxymethoxy)benzyl)-4-oxobutanoic acid) and **2c** using general method E, the MOM group was deprotected with TFA in DCM. **1k1** was synthesized from 4-(methoxymethoxy)benzaldehyde using the HWE methodology (**Scheme 13**).

Example **206**: compound n°206: (R)-3-benzyl-4-((4-(4'-cyano-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2x2** (2'-(2-(methylamino)thiazol-4-yl)-[1,1'-biphenyl]-4-carbonitrile) using general method E. Intermediate **2x2** was synthesized from (4-cyanophenyl)boronic acid and **2l** 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-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2z2** (4-(3'-methoxy-[1,1'-biphenyl]-2-yl)-N-methylthiazol-2-amine) using general method E. Intermediate **2z2** was synthesized from (3-methoxyphenyl)boronic acid and **2l** 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 **1l1** (4-(*tert*-butoxy)-2-((2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid) and **2c** using general method E. **1l1** 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 **1m1** (4-(*tert*-butoxy)-2-((5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid) and **2c** using general method E. **1m1** 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 **2l** 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 **2l** 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 **1n1** (4-(*tert*-butoxy)-2-(oxazol-4-ylmethyl)-4-oxobutanoic acid) and **2c** using general method E. **1n1** 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 **1o1** 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-(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 **2l** 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 $RuCl_2$-[(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 **1b** (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 **1b** 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 **2l** 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 **1f1** 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 **1f1** 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 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 **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 **1f1** 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 **1f1** and **2l3** (4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)-N-cyclopropylthiazol-2-amine) using general method E. **2l3** 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 **1f1** 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 **1p1** ((S)-2-benzyl-4-(*tert*-butoxy)-4-oxobutanoic acid) and **2a** using general method E. **1p1** 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-([1,1'-biphenyl]-4-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1q1** (2-([1,1'-biphenyl]-4-ylmethyl)-4-(tert-butoxy)-4-oxobutanoic acid) and **2c** using general method E. **1q1** was synthesized from [1,1'-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 **1b** 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 **1b** 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 **1b** 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 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and **2l** 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 **1b** 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 **2l** 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 **1b** 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 **1b** 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-(2-oxopyrrolidin-1-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2r3** (1-(2-(2-(methylamino)thiazol-4-yl)phenyl)pyrrolidin-2-one) using general method E. **2r3** was synthesized as described in **Scheme 16**.

Example **238**: compound n°238: (S)-2-((1-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)oxy)acetic acid was synthesized as described in **Scheme 22**.

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

Example **240**: compound n°240: (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 was synthesized from intermediates **1b** and **2s3** (1-(2-methoxyethyl)-5-(2-(2-(methylamino)thiazol-4-yl)phenyl)pyridin-2(1H)-one) using general method E. **2s3** was synthesized from 5-bromo-1-(2-methoxyethyl)pyridin-2(1H)-one and **2l** using the methodology described in **Scheme 17**.

Example **241**: compound n°241: (R)-3-benzyl-4-(methyl(4-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2t3** (1-methyl-5-(2-(2-(methylamino)thiazol-4-yl)phenyl)pyridin-2(1H)-one) using general method E. **2t3** was synthesized from 5-bromo-1-methylpyridin-2(1H)-one and **2l** 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 **1r1** (*tert*-butyl 4-amino-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoate) and **2c** using general method E. **1r1** 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 **1s1** (4-(*tert*-butoxy)-2-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid) and **2c** using general method E. **1s1** 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 $FeCl_3$ 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 **1b** and **2v3** 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 **1b** 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 **2a1** 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 **2z1** 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 **1t1** and **2m** using general method E.

Example **254**: compound n°254: (S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid was synthesized from intermediates **1u1** and **2c** using general method E.

Example **255**: compound n°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 **1b** 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 **Scheme 15**. 4-(2-bromo-5-chlorophenyl)-N-cyclopropylthiazol-2-amine was synthesized using general method C.

Example **256**: compound n°256: (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2k2** using general method E.

Example **257**: compound n°257: (R)-3-benzyl-4-((4-(2,3-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2z3** using general method E.

Example **258**: compound n°258: (R)-3-benzyl-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid was synthesized from intermediates **1b** and **2a4** using general method E.

Example **259**: compound n°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 **1g1** and **2n2** using

general method E.

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 **1t1** and **2c** 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 **1g1** and **2a4** 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 **1b** and **2b4** 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 **1g1** and **2b4** 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 *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-1 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, [^{35}S]GTPγS, was used to demonstrate enhance binding of [^{35}S]GTPγS to membranes expressing receptors. The assay uses the ability of GPCR to stimulate [^{35}S]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 $MgCl_2$, 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 $MgCl_2$, 0.3 mM EDTA,

1mM EGTA, 250 mM 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 [^{35}S]GTPγS assay was incubated in 20 mM HEPES pH7.4, 100 mM NaCl, 10 µg/ml saponin, 30 mM of $MgCl_2$, 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% (EC_{50}) 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 EC_{50} ranging from 13 nM to 2910 nM.

Table 3: Compounds EC_{50} values in GTPγ^{35}S assay.

Compound n°	**EC_{50} (nM)**
1	109
2	273
3	653
4	759
5	292
8	563
9	60
10	405
11	680
12	424
13	875

14	109
15	426
16	389
17	643
18	104
19	322
20	96
21	260
22	365
23	327
83	98
89	37
90	88
91	354
92	249
93	493
60	95
94	200
95	628
96	249
97	32
98	113
99	567
100	142
101	67
102	442
103	137
105	76
106	216
107	361
108	305
109	457
110	452
111	393

112	538
113	226
114	539
115	72
116	175
119	421
121	766
123	134
126	183
129	858
131	96
132	276
133	241
135	796
139	38
141	996
142	14
143	77
144	897
149	225
150	353
154	832
155	94
156	867
158	49
160	244
164	161
165	30
166	13
168	43
169	19
171	50
172	355
175	57

177	127
178	30
182	92
183	57
191	37
194	30
195	2169
196	1832
197	1910
199	1383
201	1362
202	1509
203	1783
206	2317
207	2910
209	2466
210	2678
216	341
217	126
218	32
220	27
222	102
223	87
224	27
246	628

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 Gα16. 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 (100µl/well) and the plate is incubated overnight at 37°C with 5% CO_2. On day 2, the medium is removed and the compounds of the invention, at increasing concentrations, are added (24µl/well) and the plate is incubated for 30 min. at 37°C in a humidified atmosphere of 95% air with 5% CO_2. The IP1 concentrations are then estimated using the IP1-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 (10µg/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 à 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. 25µl (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-(^{3}H)-2 deoxyglucose (0.2 µCi/well) and D-2-deoxyglucose (0.1mM) 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 1M at 55°C for 60 minutes. NaOH is neutralized with HCl 1M. 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° 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., (Mol. 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 (~1µM) 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-1) secretion.

<u>GLP-1 release.</u>

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-1 amount is assessed using a GLP-1 specific ELISA assay kit according the manufacturer's recommendations (ALPCON).

When tested in the GLP-1 release assay described above and by way of illustration the compound n° 169 significantly increases the GLP-1 secretion from NCI-H716 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 cm^3) 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.

<u>Glucose uptake assay in isolated adipocytes.</u>

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, 200nM 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, 10µM and 1µM) in the presence or absence of insulin (10nM) for 30 min. 2-deoxyglucose and 2-deoxy-D-[1-^{3}H]-glucose (^{3}H-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., (Mol. 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 l/ g). Additional blood samples are taken at 1, 5, 10, 20, 50, and 75 min after injection. Following immediate centrifugation at 4C, plasma is separated and stored at -20C 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.

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.

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

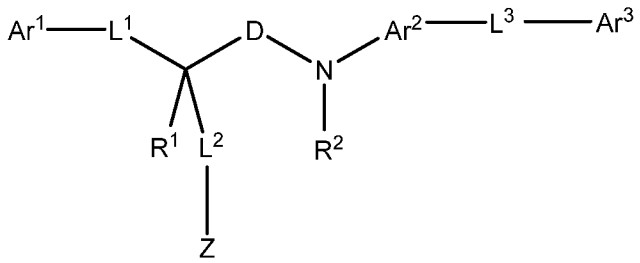
Male C57BL/6N wild-type are housed one per cage in a room maintained on a 12h light/dark cycle under constant temperature (22-25°C) with *ad libitum* access to food and water. The anti-lipolytic effects of the compounds of the invention are studied in awake mice. Animals are fasted overnight before experimental 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 tri-potassium EDTA added sodium fluoride (200 µl blood, K_3-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 n° 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 n° 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 ant 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^1 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_3-C_6 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, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkoxyalkoxy, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, 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, alkylamino, alkylcarbonyl, alkylheteroaryl, alkylsulfonyl, aralkyl, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl;

L^1 is a single bond, C_1-C_2 alkylene, C_1-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; or L^1 is $-N(R^N)-$, wherein R^N is H or C_1-C_2 alkyl; or **L^1** and **R^1** together are =CH-;

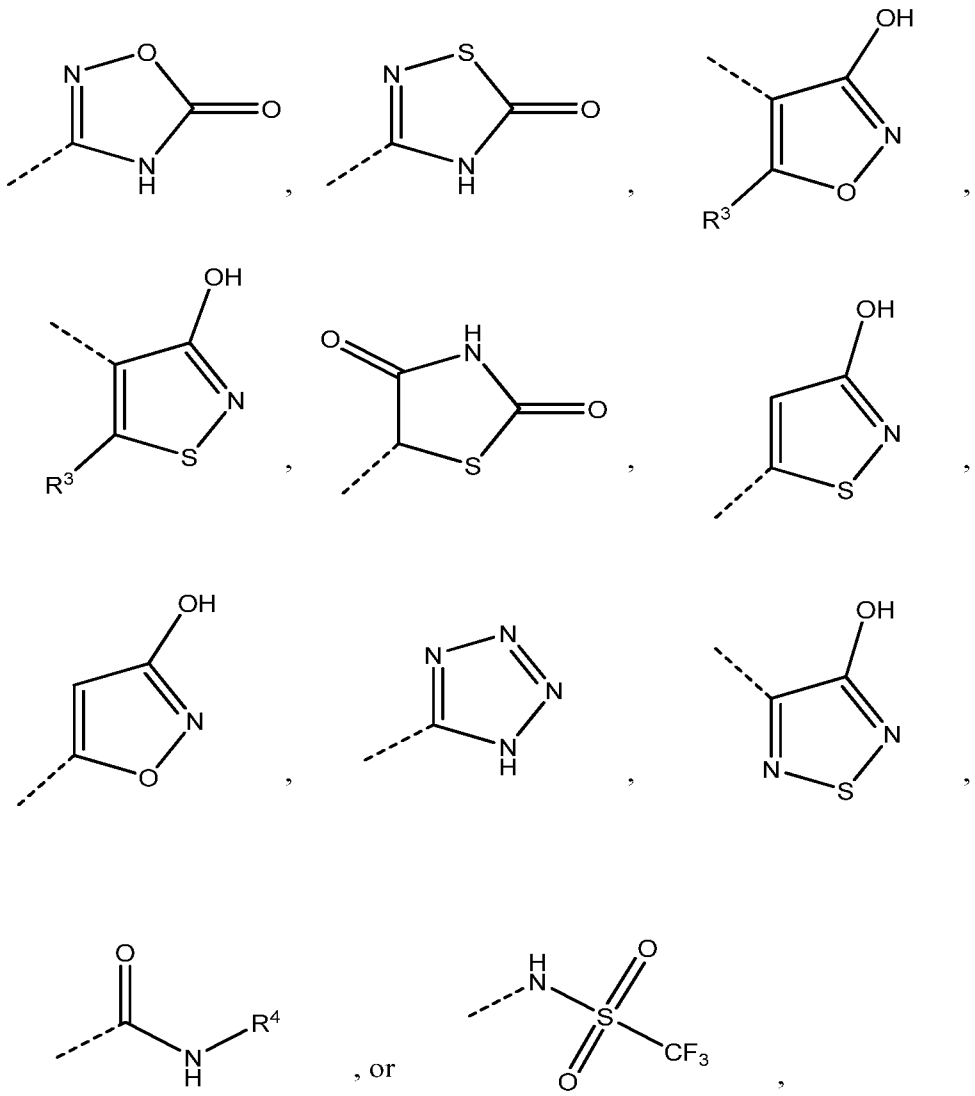
R^1 is H, halo, allyl, or a C_1-C_4 alkyl group, which may optionally be substituted by one or more groups selected from halo or C_1-C_4 alkyl;

L^2 is a C_1-C_3 alkylene, C_2-C_4 alkenylene, C_3-C_6 cylcloalkylene, each of which being optionally substituted by one or more groups selected from halo, alkyl, alkoxy, or haloalkyl; or **L^2** is -O-CH_2-

R^1 and **L^2** together are =CH-, under the condition that **$-L^1$-Ar^1** is H; or

R^1 and **L^2** together are a 5- to 6-membered saturated or unsaturated carbocyclic or heterocyclic group, preferably a cyclohexenyl group, under the condition that **$-L^1$-Ar^1** is H;

Z is selected from the group consisting of -COOR,



wherein **R** is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene, $\mathbf{R^3}$ is H, methyl or ethyl, and $\mathbf{R^4}$ is hydroxyl $-SO_2CH_3$, $-SO_2$cyclopropyl or $-SO_2CF_3$;

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, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group,

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, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group,

L^3 is a single bond, C_1-C_3 alkylene, C_1-C_3 cycloalkylene C_1-C_3 alkenylene or carbonylamino;

Ar^3 is an aryl, heteroaryl, or C_1-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, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, 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, alkylaminoalkyl, alkylaminocarbonyl, alkylcarbonyl, cycloalkylcarbonylamino, alkylheterocyclyl, alkylheteroaryl, alkylsulfonyl, alkylsulfonylamino, aralkyl, aralkyloxy, aryl, arylamino, aryloxy, cyano, haloalkoxy, haloalkyl, heteroaryl, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, heterocyclyloxy, hydroxyl, oxo, or sulfonyl, or $\mathbf{L^3}$-$\mathbf{Ar^3}$ form an aryl, preferably phenyl, or heteroaryl group fused to $\mathbf{Ar^2}$, wherein each of said aryl or heteroaryl groups fused to $\mathbf{Ar^2}$ are optionally substituted by one or more halo, preferably chloro and fluoro;

with the following provisos:

$\mathbf{Ar^2}$-$\mathbf{L^3}$-$\mathbf{Ar^3}$ 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-isobutylphenyl)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-butyl)phenyl)-5-methylthiazol-2-yl, 4-(4-isopropylphenyl)-5-methylthiazol-2-yl, 4-(4-isobutylphenyl)-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-isobutyl-3-methylphenyl)-5-methylthiazol-2-yl, 4-(4-(tert-butyl)-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-yl]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-dimethylpheny1)-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-yl]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]-cyclohexanecarboxybic 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-l-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-carboxybic 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-2yl]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-[[(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]-cyclohexanecarboxybic 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]-cyclohexanecarboxybic 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)carbony1]-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,

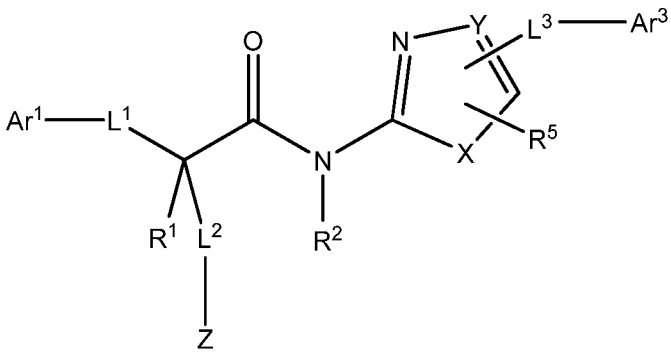
2-[[(5-acetyl-4-methyl-2-thiazolyl)amino]carbonyl]-cyclohexanecarboxylic acid,

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[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:

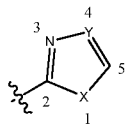


Ib

wherein **Z**, **Ar^1**, **Ar^3**, **L^1**, **L^2**, **L^3**, and **R^2** and as defined in claim 1;

X is S or O;

Y is CH or N;

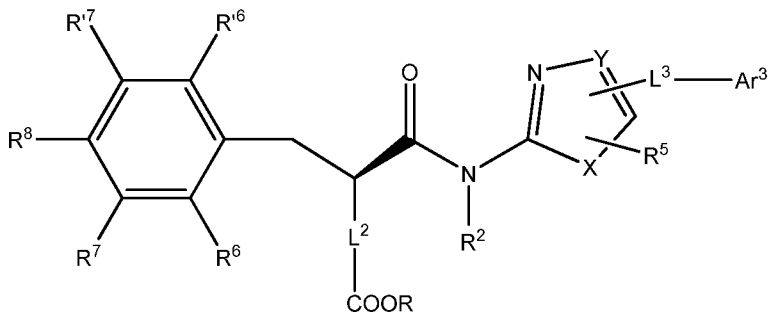
L^3 is attached to the heterocyclic group  either in position 4 or 5, preferably in position 4; and

if **Y** is CH, **R^5** is H, halo, cyano, hydroxyl, linear or branched C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, preferably methyl and 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 pharmaceutically acceptable salts, and solvates thereof.

3. The compound according to claim 2 having the formula Ib-1a:



Ib-1a

wherein **X**, **Y**, **Ar^3**, **L^2**, **L^3**, **R^2** and **R^5**and as defined in claim 1;

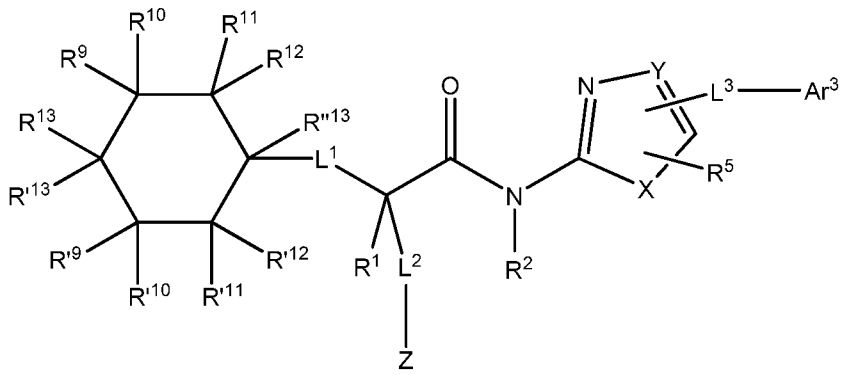
R is H or linear or branched alkyl, aryl, acyloxyalkyl, dioxolene;

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, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, heterocyclyloxy, aryloxy, amino, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or R^6 and R^7 or R^7 and R^8 or R'^{6} and R'^{7} or R'^{7} and R^8

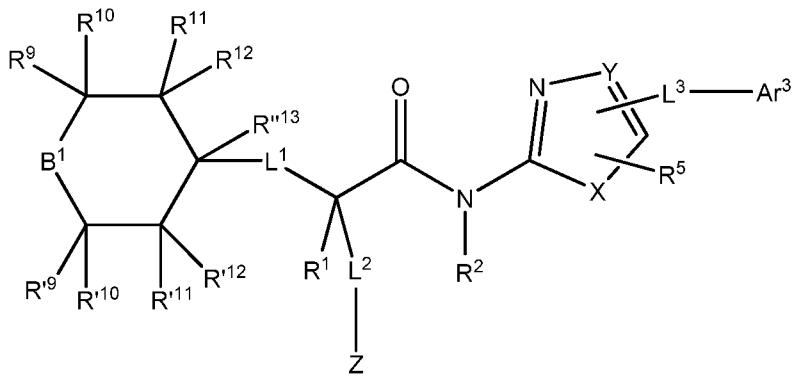
together form an alkylenedioxy group or a haloalkylenedioxy group, or R^6 and R^7 or R^7 and R^8 or R'^6 and R'^7 or R'^7 and R^8 together form a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the phenyl group they are attached to, each of said substituents being optionally substituted 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.

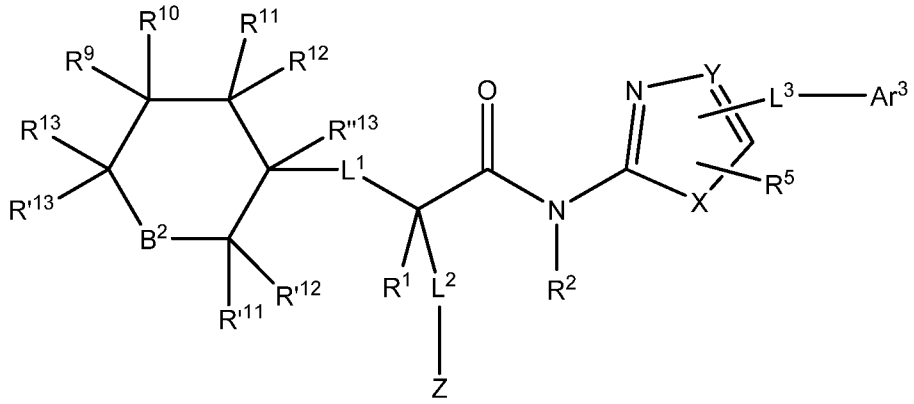
4. The compound according to claim 2 selected form the group consisting of formulae Ib-2a, Ib-2b, Ib-2c, Ib-2d, Ib-2e and Ib-2f:



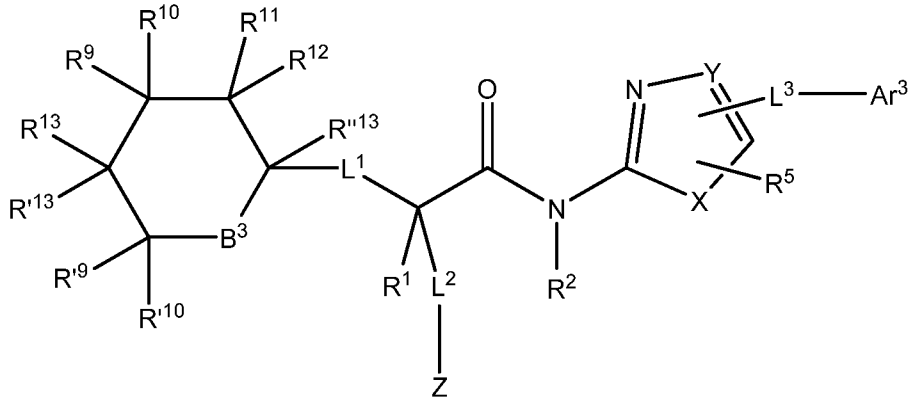
Ib-2a



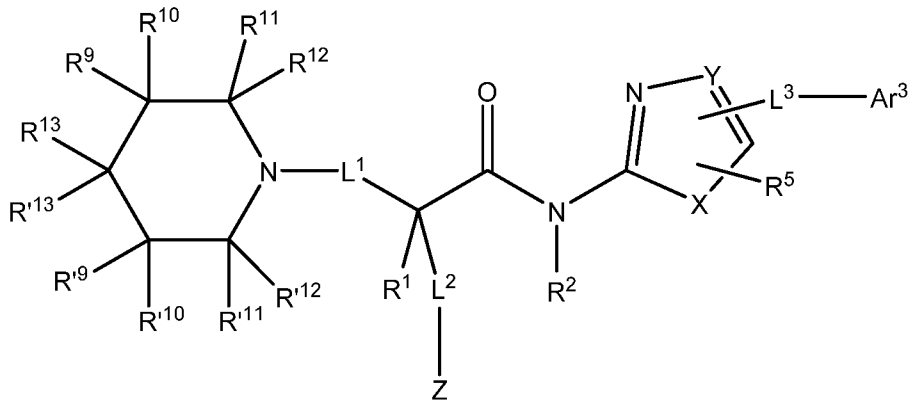
Ib-2b



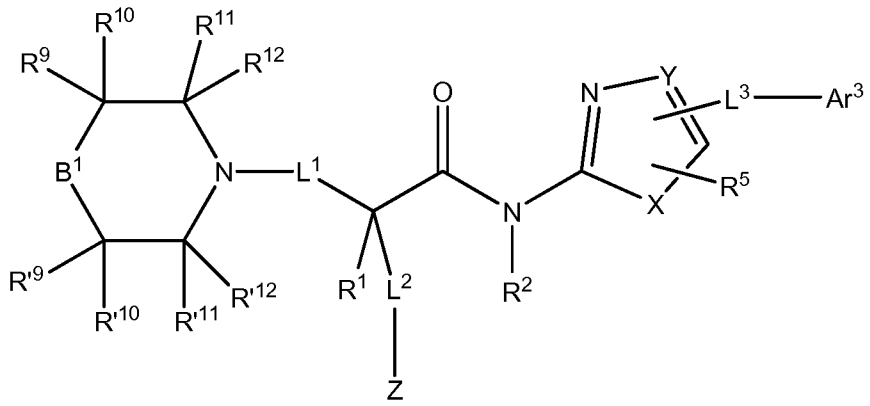
Ib-2c



Ib-2d



Ib-2e



Ib-2f

wherein **X**, **Y**, **Z**, **Ar^3**, **L^2**, **L^3**, **R^1**, **R^2**, and **R^5** are as defined in claim 2;

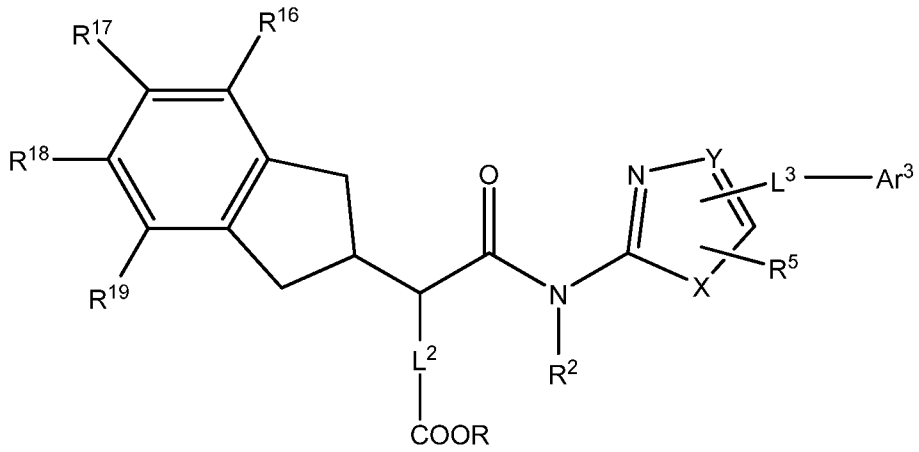
B^1, **B^2** and **B^3** are independently CF_2, O, NR^a, CO, or SO_2, wherein **R^a** is H or alkyl, preferably linear or branched C_1-C_4 alkyl; C_1-C_4 alkylcarbonyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylaminocarbonyl, aryl, arylcarbonyl, arylsulfonyl or arylaminocarbonyl; and

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 H, 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, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl,

heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, 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^{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 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}, 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, alkylsulfonyl, aralkyl, aryl, arylamino, 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:



Ib-3,

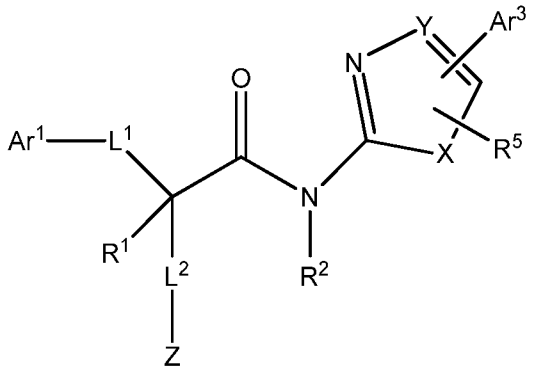
wherein L^2, L^3, Ar^3, X, Y, R, R^1, R^2 and R^5 are as defined in claim 2;

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, alkylamino, aminoalkyl, carboxy, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, or 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, heteroarylalkyl, heteroarylcarbonyl, heterocyclyl, hydroxyl, oxo, or sulfonyl;

and pharmaceutically acceptable salts, and solvates thereof.

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



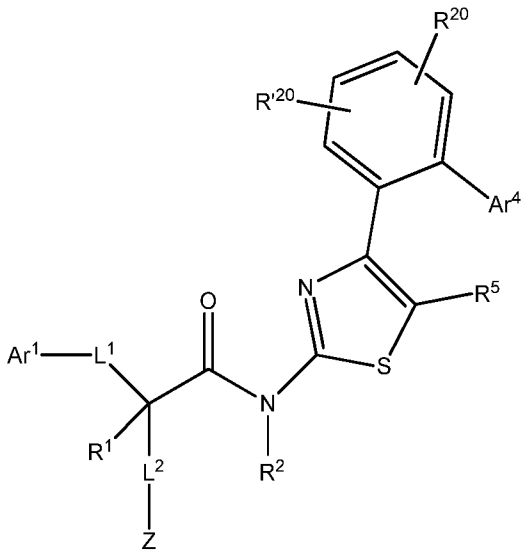
Ib-4,

wherein

Ar^1, **Ar^3**, **L^1**, **L^2**, **R^1**, **R^2**, **R^5**, **X**, **Y** and **Z** are as defined in claim 2;

and pharmaceutically acceptable salts, and solvates thereof.

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



Ib-4b

wherein

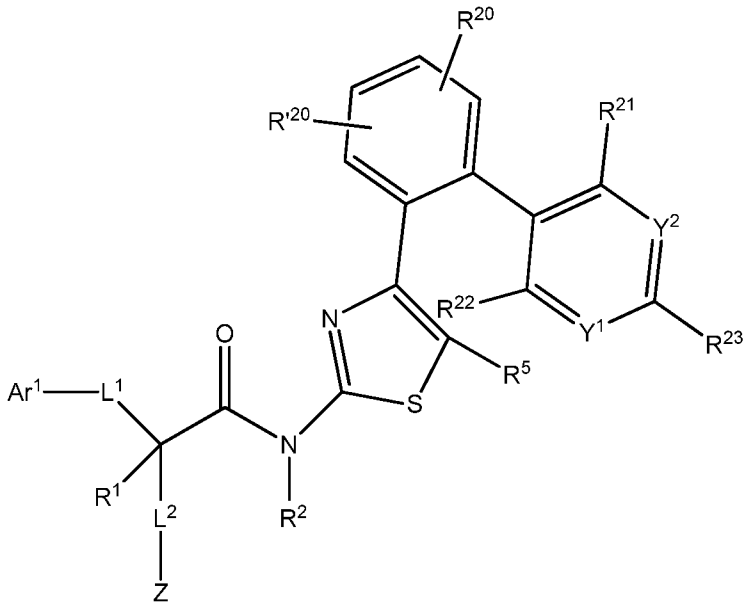
Ar^1, L^1, L^2, R^1, R^2, R^5, and **Z** are as defined in claim 2;

R^{20} and R'^{20} are independently selected from halo, cyano, C_1-C_3 alkyl, cyclopropyl, haloalkyl, alkoxy, haloalkoxy, alkoxycarbonylamino, or the two substituents form an alkylenedioxy group or a haloalkylenedioxy group;

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 substituents selected from halo, cyano, hydroxyl, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxyalkoxy, alkylaminoalkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, alkylamino, alkylaminoalkyl, cycloalkylamino, arylamino, aralkylamino, alkylaminocarbonyl, heteroarylcarbonyl, alkylcarbonylamino, cycloalkylcarbonylamino, alkylsulfonyl, haloalkylsulfonyl, alkylsulfonylamino, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, 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:



Ib-4c

wherein

Ar^{1}, **L**^{1}, **L**^{2}, **R**^{1}, **R**^{2}, **R**^{5}, and **Z** are as defined in claim 2,

R^{20} and **R'**^{20}, are as defined in claim 7,

R^{21} and **R**^{22} are independently selected from H, halo, alkoxy;

R^{23} 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, each of said cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyloxy, cycloalkylalkyloxy, heterocyclyloxy, aryloxy, aralkyloxy, heteroarylcarbonyl, cycloalkylamino, arylamino, aralkylamino, cycloalkylcarbonylamino being optionally substituted by one or more further substituents selected from halo, oxo or alkyl;

Y^{1} is N or C-**R**^{24} where **R**^{24} is H, halo, alkoxy, alkyl, heterocyclyl, or

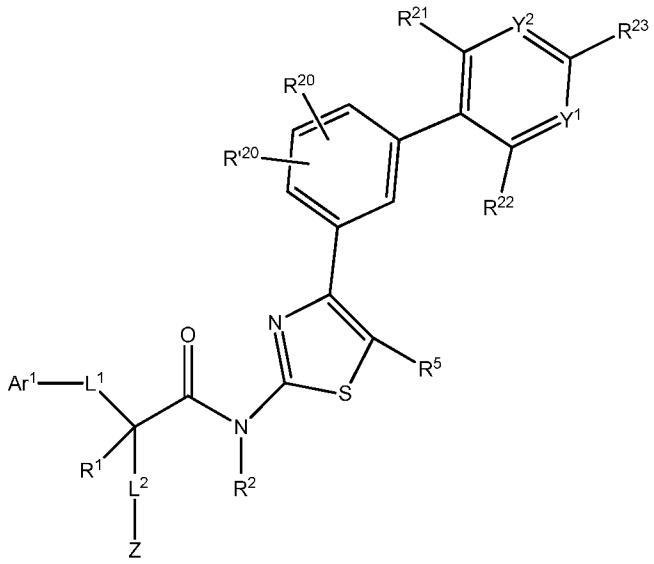
Y^1 is C-R^{24} and R^{24} and R^{23} together form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, thus forming a fused ring system, the latter fused ring system being optionally substituted by one or more group selected from oxo, alkyl or halo; and

Y^2 is N or C-R^{25} where R^{25} is H, halo, alkoxy, alkyl, heterocyclyl, or

Y^2 is C-R^{25} and R^{25} and R^{23} 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 R^{24} and R^{23} together do not form a 5 or 6 membered cycloalkyl, aryl, heterocyclyl or heteroaryl moiety;

and pharmaceutically acceptable salts, and solvates thereof.

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



Ib-4i,

wherein

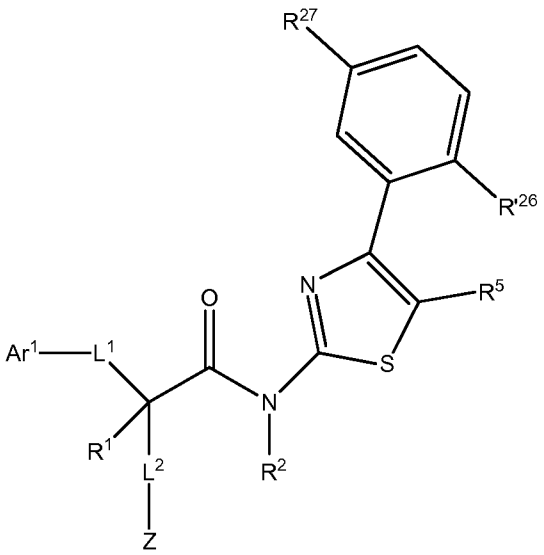
Ar^1, L^1, L^2, R^1, R^2, R^5, and **Z** are as defined in respect claim 2;

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:



Ib-4m

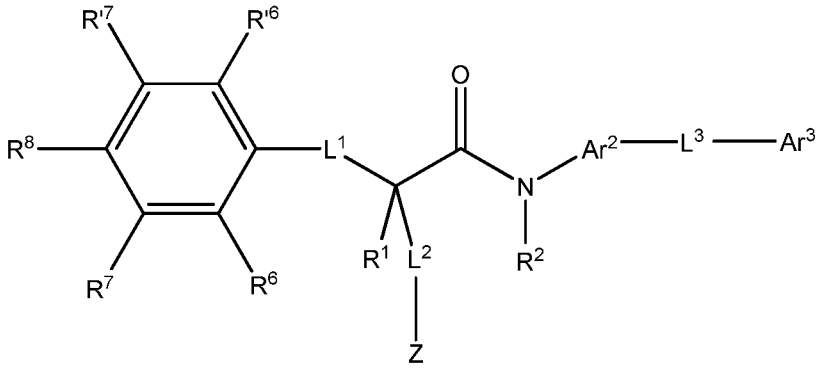
wherein

Ar^{1}, **L**^{1}, **L**^{2}, **R**^{1}, **R**^{2}, **R**^{5}, and **Z** are as defined in respect claim 2; and

R'^{26} and **R**^{27} are independently selected from H, halo, cyano, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, hydroxyl, alkoxy, haloalkoxy, cycloalkyloxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, acylamino, carbamoyl, alkoxycarbamoyl, cycloalkylcarbamoyl, alkylcarbamoylamino, cycloalkylaminocarbamoyl, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, 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:



Ic

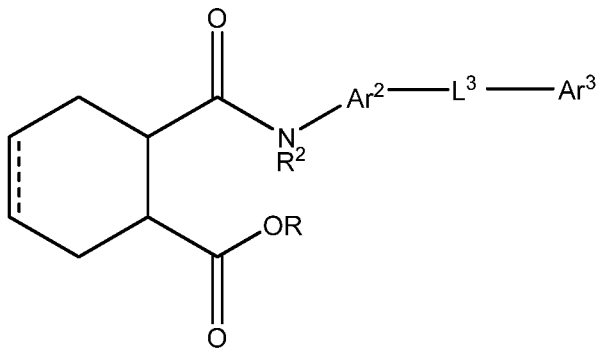
wherein **Ar²**, **Ar³**, **R¹**, **R²**, **L¹**, **L²**, **L³** and **Z** are as defined in claim 1;

R⁶, **R⁷**, **R'⁶**, **R'⁷** and **R⁸** 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, alkoxycarbonyl, cycloalkyloxycarbonyl, heterocyclyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbonyloxy, cycloalkylcarbonyloxy, heterocyclylcarbonyloxy, arylcarbonyloxy, heteroarylcarbonyloxy, arylalkyloxy, alkylcarbonylamino, haloalkylcarbonylamino, cycloalkylcarbonylamino, heterocyclylcarbonylamino arylcarbonylamino, heteroarylcarbonylamino, alkylcarbonylaminoalkyl, acylamino, carbamoyl, hydroxycarbamoyl, alkylcarbamoyl, arylcarbamoyl, heteroarylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, cycloalkylsulfonyl, heterocyclylsulfonyl, arylsulfonyl, heteroarylsulfonyl sulfamoyl, alkylsulfamoyl, arylsulfamoyl, heteroarylsulfamoyl, alkylsulfonylamino, cycloalkylsulfonylamino, heterocyclylsulfonylamino,

arylsulfonylamino, heteroarylsulfonylamino, haloalkylsulfonylamino, 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 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.

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



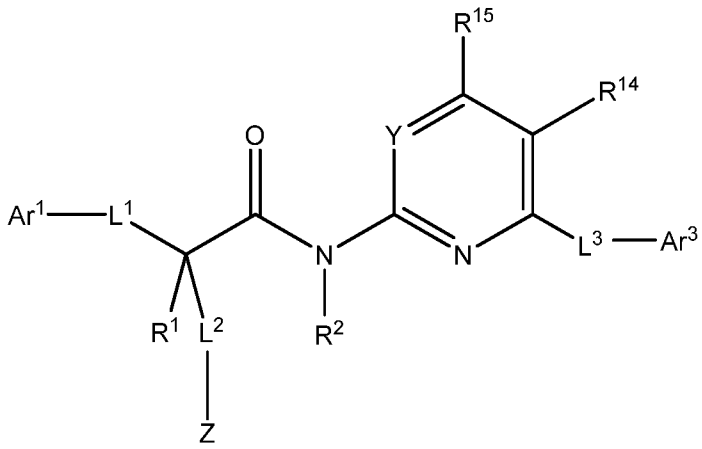
Id

wherein the dotted line is present or absent;

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

pharmaceutically acceptable salts, and solvates thereof.

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



Ie

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-enecarboxylic 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

5	(R)-3-benzyl-4-((4-(3,4-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
8	(R)-3-benzyl-4-((4-(4-cyanophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
9	(S)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-phenylbutanoic acid
10	(Z)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobut-2-enoic acid
11	(R)-3-benzyl-4-oxo-4-((3-phenyl-1,2,4-thiadiazol-5-yl)amino)butanoic acid
12	(R)-3-benzyl-4-((4-(3-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
13	(R)-3-benzyl-4-oxo-4-((4-(3-(trifluoromethyl)phenyl)thiazol-2-yl)amino)butanoic acid
14	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
15	(R)-3-benzyl-4-((5-(2-chlorophenyl)pyridin-2-yl)amino)-4-oxobutanoic acid
16	(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)heptanoic acid
17	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(4-fluorobenzyl)-4-oxobutanoic acid
18	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid
19	(R)-3-((4-(2-chlorophenyl)thiazol-2-yl)carbamoyl)-5-methylhexanoic acid
20	(R)-3-benzyl-4-((4-(2-chlorophenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid
21	(R)-3-benzyl-4-((5-chloro-4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
22	(R)-4-(allyl(4-(2-chlorophenyl)thiazol-2-yl)amino)-3-benzyl-4-oxobutanoic acid
23	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)(2-methoxy-2-oxoethyl)amino)-4-oxobutanoic acid

24 (R)-methyl-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoate

26 (R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid

27 (S)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-5-phenylpentanoic acid

28 (R)-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-4-oxo-3-(4-(trifluoromethyl)benzyl)butanoic acid

29 (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)amino)-4-oxo-3-(3-(trifluoromethyl)benzyl)butanoic acid

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

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

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

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

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

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

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

37 (R)-3-benzyl-4-oxo-4-(4-(2,4,6-trichlorophenyl)thiazol-2-ylamino)butanoic acid

38 (R)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid

39 (S)-4-benzyl-5-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-5-oxopentanoic acid

40 (R)-methyl 4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate

41 (S)-methyl 4-benzyl-5-(4-(2-chlorophenyl)thiazol-2-ylamino)-5-oxopentanoate

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

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

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

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

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

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

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

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

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

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

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

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

54 (3S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(2,3-dihydro-1H-inden-1-yl)-4-oxobutanoic acid

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

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

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

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

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

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

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

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

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

64 (3R)-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)-4-phenylpentanoic acid

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

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

68 (3R)-3-benzyl-4-(4-(2-chlorophenyl)thiazol-2-ylamino)-2-methyl-4-oxobutanoic acid

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

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

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

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

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

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

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

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

80 (R)-3-benzyl-3-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)hex-5-enoic acid

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

82 (3S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid

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

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

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

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

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

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

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

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

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

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

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

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

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

98 cis-6-(4-(2-chlorophenyl)thiazol-2-ylcarbamoyl)cyclohex-3-enecarboxylic acid

99	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methoxybenzyl)-4-oxobutanoic acid
100	cis-6-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohex-3-enecarboxylic acid
101	cis-2-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)cyclohexanecarboxylic acid
102	(R)-3-benzyl-4-(4-(2,5-dimethylthiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid
103	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclohexylmethyl)-4-oxobutanoic acid
105	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid
106	(3S,4R)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid
107	(R)-3-benzyl-4-(methyl(4-(2-(thiophen-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
108	(R)-3-benzyl-4-((4-(2-(6-chloropyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
109	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(phenylamino)butanoic acid
110	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-methylbenzyl)-4-oxobutanoic acid
111	(R)-4-((4-([1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-3-benzyl-4-oxobutanoic acid
112	(R)-3-benzyl-4-(4-(2,5-dichlorothiophen-3-yl)thiazol-2-ylamino)-4-oxobutanoic acid
113	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopropylmethyl)-4-oxobutanoic acid
114	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiazol-4-ylmethyl)butanoic acid
115	(R)-3-benzyl-4-((4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

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

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

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

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

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

122 (R)-3-benzyl-4-oxo-4-((4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)butanoic acid

123 (R)-3-benzyl-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

124 (R)-3-benzyl-4-((4-(3-chloro-4-fluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

125 (R)-3-benzyl-4-((4-(3-chloro-4-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

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

127 3-(bicyclo[2.2.1]heptan-2-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

129 (R)-3-benzyl-4-((4-(4'-methoxy-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

130 (R)-3-benzyl-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

131 (R)-1-(5-(2-(2-(2-benzyl-3-carboxy-N-methylpropanamido)thiazol-4-yl)phenyl)pyridin-2-yl)pyrrolidin-1-ium 2,2,2-trifluoroacetate

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

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

134 (R)-3-benzyl-4-((4-(3'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

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

138 (R)-3-benzyl-4-((4-(4'-isopropyl-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

139 (R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

140 (R)-3-benzyl-4-((4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

142 (R)-3-benzyl-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

143 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

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

145 (R)-3-benzyl-4-((4-(4'-(dimethylamino)-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

146 (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-[1,1'-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-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

150 (R)-3-benzyl-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-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

162 (R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

163 (R)-3-benzyl-4-((4-(3,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

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

166 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

167 (R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

168 (R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

169 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

170 (R)-3-benzyl-4-((2-hydroxyethyl)(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

171 (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

172 (R)-3-(cyclopentylmethyl)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(2-hydroxyethyl)amino)-4-oxobutanoic acid

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

174 (R)-3-benzyl-4-((4-(5-chloro-2-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

175 (R)-3-benzyl-4-(methyl(4-(2,3,5-trichlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

176 (R)-3-benzyl-4-((4-(4-chloro-[1,1'-biphenyl]-3-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

177 (R)-3-benzyl-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

178 (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

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

180 (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

181 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-morpholinopyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

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

183 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

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

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

186 (R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

187 (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

188 (R)-3-benzyl-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

189 (R)-3-benzyl-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

190 (R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

191 (R)-3-benzyl-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

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

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

194 (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

195 (3R,4S)-3-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)carbamoyl)-4-phenylpentanoic acid

196 (R)-2-(2-benzyl-3-carboxypropanamido)-5-(2-chlorophenyl)pyridine 1-oxide

197 (R)-3-benzyl-4-((5-(2-chlorophenyl)pyrazin-2-yl)amino)-4-oxobutanoic acid

198 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(morpholinomethyl)-4-oxobutanoic acid

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

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

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

202 (R)-3-benzyl-4-((4-(5-methylfuran-2-yl)thiazol-2-yl)amino)-4-oxobutanoic acid

203 (R)-3-benzyl-4-oxo-4-((3-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)amino)butanoic acid

204 (R)-3-benzyl-4-((4-(5-chloro-2-methoxyphenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

205 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(4-hydroxybenzyl)-4-oxobutanoic acid

206 (R)-3-benzyl-4-((4-(4'-cyano-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

207 (3R)-3-benzyl-4-((3-carbamoyl-4-(2,4-dichlorophenyl)-5-methylthiophen-2-yl)amino)-4-oxobutanoic acid

208 (R)-3-benzyl-4-((4-(3'-methoxy-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

209 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2-methylthiazol-4-yl)methyl)-4-oxobutanoic acid

210 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylisoxazol-3-yl)methyl)-4-oxobutanoic acid

211 (R)-3-benzyl-4-((4-(2'-chloro-[1,1'-biphenyl]-2-yl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

212 (R)-3-benzyl-4-((4-(2-(2-methoxypyrimidin-5-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

213 (R)-3-benzyl-4-((4-(2,5-difluorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

214 4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(oxazol-4-ylmethyl)-4-oxobutanoic acid

215 (3R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydrofuran-3-yl)methyl)butanoic acid

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

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

218 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(dimethylamino)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

219 (R)-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

220 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

221 (R)-3-benzyl-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

222 (R)-3-benzyl-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

223 (R)-4-((4-(5-chloro-2-(5-chloro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

224 (R)-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

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

227 (R)-3-benzyl-4-((4-benzylthiazol-2-yl)amino)-4-oxobutanoic acid

229 (R)-3-benzyl-4-oxo-4-((5-phenyl-4H-1,2,4-triazol-3-yl)amino)butanoic acid

230 3-([1,1'-biphenyl]-4-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

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

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

234 (3R)-3-benzyl-4-((4-(2-(3,5-dimethylisoxazol-4-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

236 (R)-3-benzyl-4-((6-(2-chlorophenyl)pyridazin-3-yl)amino)-4-oxobutanoic acid

237 (R)-3-benzyl-4-(methyl(4-(2-(2-oxopyrrolidin-1-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

238	(S)-2-((1-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)oxy)acetic acid
239	(R)-3-benzyl-4-((1-methyl-5-phenyl-1H-imidazol-2-yl)amino)-4-oxobutanoic acid
240	(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
241	(R)-3-benzyl-4-(methyl(4-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
242	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((2,5-dimethyloxazol-4-yl)methyl)-4-oxobutanoic acid
243	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((1-methyl-1H-pyrazol-5-yl)methyl)-4-oxobutanoic acid
244	(R)-3-benzyl-4-((4-(2-(6-hydroxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
245	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((S)-2-hydroxypropyl)amino)-4-oxobutanoic acid
246	(R)-3-benzyl-4-((4-(2-chlorophenyl)thiazol-2-yl)((R)-2-hydroxypropyl)amino)-4-oxobutanoic acid
247	(R)-3-(cyclohexylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid
248	(R)-3-benzyl-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
250	(R)-3-benzyl-4-((4-(4,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
251	(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid
252	(R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid
253	(R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

254 (S)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(thiophen-2-ylmethyl)butanoic acid

255 (R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

256 (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

257 (R)-3-benzyl-4-((4-(2,3-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

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

259 (R)-4-(cyclopropyl(4-(3-(difluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

260 (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

261 (R)-4-(methyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

262 (R)-3-benzyl-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

263 (R)-4-(cyclopropyl(4-(3-(trifluoromethoxy)phenyl)thiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

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

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

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

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

268 (R)-3-benzyl-4-(methyl(4-(2-(6-(N-methylcyclopropanecarboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

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

270 (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

271 (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

272 (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

273 (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

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

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

276 (R)-3-benzyl-4-(methyl(4-(2-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

277 (R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

278 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(3-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

279 (R)-3-benzyl-4-((4-(2-(5-chloro-6-methoxypyridin-3-yl)-3-fluorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

280 (R)-3-benzyl-4-((4-(3-fluoro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

281 (R)-3-benzyl-4-((4-(5-chloro-2-(5-fluoro-6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

282 (R)-3-benzyl-4-((4-(3,5-difluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

283 (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(((S)-tetrahydrofuran-2-yl)methyl)butanoic acid

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

285 (R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

286 (R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

287 (R)-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

288 (R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

289 (R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

290 (R)-4-((4-(2-chloro-5-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

291 (R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethyl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

292 (R)-3-(furan-2-ylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

293 (R)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

294 (R)-4-(cyclopropyl(4-(2,5-dichlorophenyl)thiazol-2-yl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

295 (R)-4-((4-(2-chloro-5-fluorophenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

296 (R)-4-((4-(2-chloro-5-(trifluoromethyl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

297 (R)-4-((4-(2-chloro-5-(trifluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid

298	(R)-4-((4-(2-chloro-5-(difluoromethoxy)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(furan-2-ylmethyl)-4-oxobutanoic acid
299	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((5-methylfuran-2-yl)methyl)-4-oxobutanoic acid
300	4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-3-((4,5-dimethylfuran-2-yl)methyl)-4-oxobutanoic acid
301	3-(benzofuran-2-ylmethyl)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid
302	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyridin-2-ylmethyl)butanoic acid
303	(R)-4-((4-(2-chlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-(pyrimidin-2-ylmethyl)butanoic acid
304	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-2-yl)methyl)butanoic acid
305	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-3-yl)methyl)butanoic acid
306	(R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R,3R)-2-methyltetrahydro-2H-pyran-3-yl)methyl)-4-oxobutanoic acid
307	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((2R)-2-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid
308	(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
309	(3R)-4-((4-(2,5-dichlorophenyl)thiazol-2-yl)(methyl)amino)-3-(((3S)-3-methyltetrahydro-2H-pyran-4-yl)methyl)-4-oxobutanoic acid
310	(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
311	(R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(4-hydroxy-1,2,5-thiadiazol-3-yl)-N-methylpropanamide

312 (R)-2-benzyl-N-(4-(2-chlorophenyl)thiazol-2-yl)-3-(3-hydroxy-5-methylisoxazol-4-yl)-N-methylpropanamide

313 (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

314 (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

315 (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

316 (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

317 (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

318 (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

319 (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

320 (R)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

321 (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

322 (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

323 (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

324 (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

325 (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

326 (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

327 (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

328 (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

329 (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

330 (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

331 (R)-4-(cyclopropyl(5-fluoro-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

332 (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

333 (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

334 (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

335 (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

336 (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

337 (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

338 (R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

339 (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

340 (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

341 (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

342 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

343 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

344 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

345 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

346 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

347 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

348 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

349 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

350 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

351 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

352 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

353 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

354 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

355 (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

356 (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

357 (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

358 (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

359 (R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

360 (R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(cyclopropyl)amino)-4-oxobutanoic acid

361 (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

362 (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

363 (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

364 (R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

365 (R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

366 (R)-3-benzyl-4-(cyclopropyl(4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)amino)-4-oxobutanoic acid

367 (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

368 (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

369 (R)-3-benzyl-4-(cyclopropyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

370 (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

371 (R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

372 (R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

373 (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

374 (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

375 (R)-3-benzyl-4-(cyclopropyl(4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

376 (R)-3-benzyl-4-(cyclopropyl(5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

377 (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

378 (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

379 (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

380 (R)-4-((4-(5-chloro-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

381 (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

382 (R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

383 (R)-4-((4-(5-chloro-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

384 (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

385 (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

386 (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

387 (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

388 (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

389 (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

390 (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

391 (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

392 (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

393 (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

394 (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

395 (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

396 (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

397 (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

398	(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
399	(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
400	(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
401	(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
402	(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
403	(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
404	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid
405	(R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid
406	(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
407	(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

408 (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

409 (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

410 (R)-3-(cyclopentylmethyl)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

411 (R)-3-(cyclopentylmethyl)-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

412 (R)-3-(cyclopentylmethyl)-4-((4-(5-(difluoromethoxy)-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

413 (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

414 (R)-3-(cyclopentylmethyl)-4-(methyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

415 (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

416 (R)-3-(cyclopentylmethyl)-4-((4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

417 (R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

418 (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

419 (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

420 (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

421 (R)-3-(cyclopentylmethyl)-4-((4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

422 (R)-3-(cyclopentylmethyl)-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

423 (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

424 (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

425 (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

426 (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

427 (R)-3-benzyl-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

428 (R)-3-benzyl-4-((4-(5-chloro-2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

429 (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

430 (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

431 (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

432 (R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

433 (R)-3-benzyl-4-((4-(5-(difluoromethoxy)-2-(6-methoxypyridin-3-yl)phenyl)-5-fluorothiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

434 (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

435 (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

436 (R)-3-benzyl-4-(methyl(4-(2-(6-(2-oxopiperidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

437 (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

438 (R)-3-benzyl-4-((5-fluoro-4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

439 (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

440 (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

441 (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

442 (R)-3-benzyl-4-((5-fluoro-4-(5-fluoro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(methyl)amino)-4-oxobutanoic acid

443 (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

444 (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

445 (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

446 (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

447 (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

448 (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

449 (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

450 (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

451 (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

452 (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

453 (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

454 (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

455 (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

456 (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)amino)-4-oxobutanoic acid

457 (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

458 (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

459 (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

460 (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

461 (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

462 (R)-3-benzyl-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

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

464 (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

465 (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

466 (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

467 (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

468 (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

469 (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

470 (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

471 (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

472 (R)-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-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

473 (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

474 (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

475 (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

476 (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

477 (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

478 (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

479 (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

480 (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

481 (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

482 (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

483 (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

484 (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

485 (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

486 (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

487 (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

488 (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

489 (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

490 (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

491 (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

492 (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

493 (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

494 (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

495 (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

496 (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

497 (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)(methyl)amino)-4-oxobutanoic acid

498 (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

499 (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

500 (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

501 (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

502 (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

503 (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

504 (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

505 (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

506 (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

507 (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

508 (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

509 (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

510 (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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

536 (R)-3-(cyclopentylmethyl)-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

537 (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

538 (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

539 (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

540 (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

541 (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

542 (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

543 (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

544 (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

545 (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

546 (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

547 (R)-3-benzyl-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

548 (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

549 (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

550 (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

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

552 (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)(methyl)amino)-4-oxobutanoic acid

553 (R)-3-benzyl-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

554 (R)-3-(cyclopentylmethyl)-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

555 (R)-3-(cyclopentylmethyl)-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

556 (R)-4-((5-fluoro-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

557 (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

558 (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

559 (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

560 (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

561 (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

562 (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

563 (R)-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-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

564 (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

565 (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

566 (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

577 (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

578 (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

579 (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

580 (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

581 (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)butanoic acid

582 (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

583 (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

584 (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-(cyclopentylmethyl)-4-oxobutanoic acid

585 (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-(cyclopentylmethyl)-4-oxobutanoic acid

586 (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

587 (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

588 (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

589 (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

590 (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

591 (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

592 (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)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

593 (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)-4-oxo-3-((tetrahydro-2H-pyran-4-yl)methyl)butanoic acid

594 (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

595 (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

596 (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)(methyl)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

607 (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

608 (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

609 (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

610 (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

611 (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

612 (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

613 (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

614 (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

615 (R)-3-(cyclopentylmethyl)-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)amino)-4-oxobutanoic acid

616 (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

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

618 (R)-3-benzyl-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

619 (R)-3-benzyl-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)amino)-4-oxobutanoic acid

620 (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

621 (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

622 (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

623 (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

624 (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

625 (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

626 (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

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

628 (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

629 (R)-4-(cyclopropyl(5-fluoro-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

630 (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

631 (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

632 (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

633 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-6-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

634 (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

635 (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

636 (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

637 (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

638 (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

639 (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

640 (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

641 (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

642 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(1-methyl-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-7-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

643 (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

644 (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

645 (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

646 (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

647 (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

648 (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

649 (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

650 (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

651 (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

652 (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

653 (R)-4-((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

654 (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

655 (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

656 (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

657 (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

658 (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

659 (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

660 (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

661 (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

662 (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

663 (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

664 (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

665 (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

666 (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

667 (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

668 (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

669 (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

670 (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

671 (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

672 (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

673 (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

674 (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

675 (R)-4-(cyclopropyl(4-(2,5-dimethyl-4-(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

676 (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

677 (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

678 (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

679 (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

680 (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

681 (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

682 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-2-oxopiperidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

683 (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

684 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(N-methylacetamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

685 (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

686 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(5-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

687 (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

688 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(pyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

689 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

690 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1-methyl-5-oxopyrrolidin-2-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

691 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(4-methyl-3-oxopiperazin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

692 (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

693 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(dimethylcarbamoyl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

694 (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

695 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-isopropoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

696 (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

697 (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

698 (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

699 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxotetrahydropyrimidin-1(2H)-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

700 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(1,3-dimethyl-2-oxoimidazolidin-4-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

701 (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

702 (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

703 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(N-methylcyclopropanecarboxamido)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

704 (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

705 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(cyclopropylmethoxy)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

706 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

707 (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

708 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(methoxymethyl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

709 (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

710 (3R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(5-oxopyrrolidin-2-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

711 (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

712 (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

713 (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

714 (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

715 (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

716 (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

717 (R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(pyrimidin-2-ylmethyl)butanoic acid

718 (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

719 (R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxo-3-(((S)-tetrahydrofuran-2-yl)methyl)butanoic acid

720 (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

721 (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

722 (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-3-yl)methyl)butanoic acid

723 (3R)-4-(cyclopropyl(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

724 (R)-4-(cyclopropyl(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

725 (3R)-4-(cyclopropyl(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

726 (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

727 (R)-3-(benzofuran-2-ylmethyl)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

728 (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

729 (R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((5-methylfuran-2-yl)methyl)-4-oxobutanoic acid

730 (3R)-4-(cyclopropyl(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

731 (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

732 (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

733 (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

734 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

735 (R)-4-((4-(5-chloro-2-(6-methoxypyridin-3-yl)phenyl)thiazol-2-yl)(cyclopropyl)amino)-3-(cyclopentylmethyl)-4-oxobutanoic acid

736 (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

737 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

738 (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

739 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

740 (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

741 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

742 (R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-methyloxetan-3-yl)methyl)-4-oxobutanoic acid

743 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

744 (R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-methyloxetan-3-yl)methyl)-4-oxobutanoic acid

745 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

746 (R)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-methyloxetan-3-yl)methyl)-4-oxobutanoic acid

747 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

748 (S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-fluorooxetan-3-yl)methyl)-4-oxobutanoic acid

749 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(oxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

750 (S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-fluorooxetan-3-yl)methyl)-4-oxobutanoic acid

751 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-methyloxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-4-oxobutanoic acid

752 (S)-4-(cyclopropyl(4-(2-(6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-3-((3-fluorooxetan-3-yl)methyl)-4-oxobutanoic acid

753 (R)-3-(cyclopentylmethyl)-4-(cyclopropyl(4-(2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)phenyl)thiazol-2-yl)amino)-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

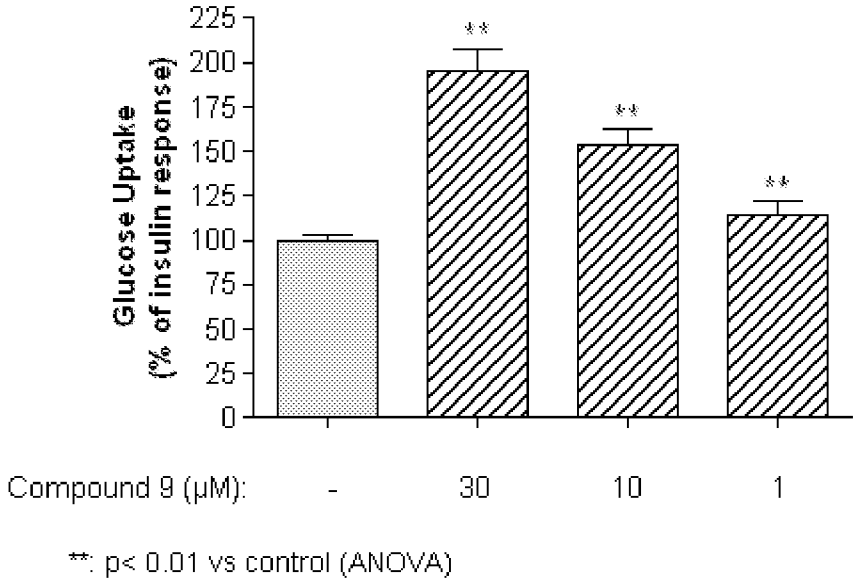
and/or adjuvant.

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).

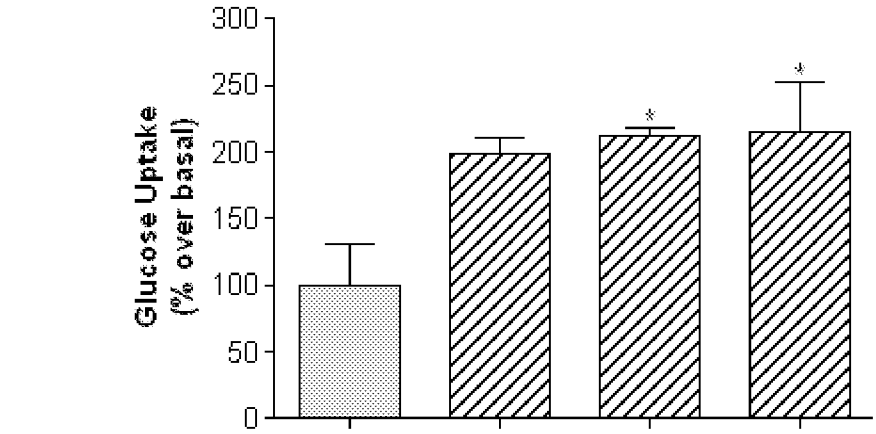
18. Use of a compound according to any of Claims **1** to **14** or a pharmaceutically acceptable salt or solvate thereof as a modulator of GPR43 receptor activity.

19. Use according to Claim **18,** wherein the compound is an agonist or partial agonist of GPR43 receptor activity.



**: p< 0.01 vs control (ANOVA)

Figure 1



*: p< 0.05 vs control (ANOVA)

Figure 2

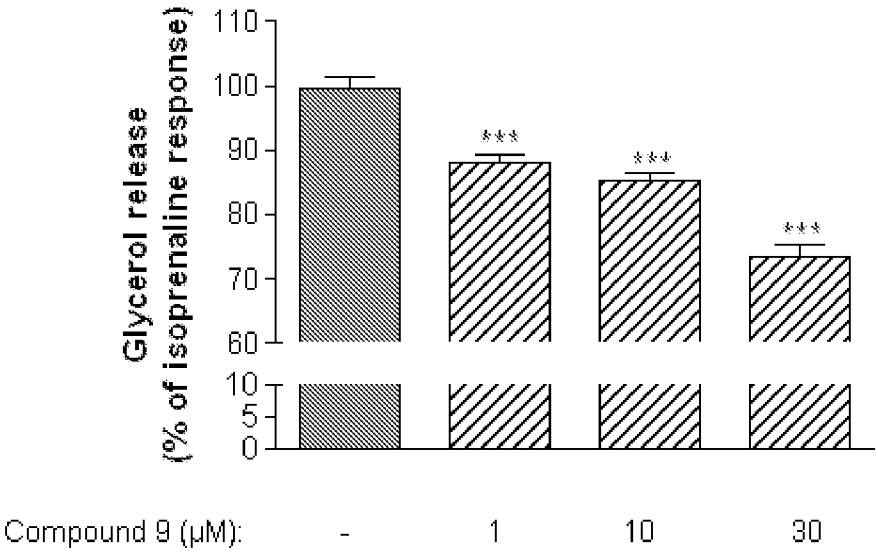
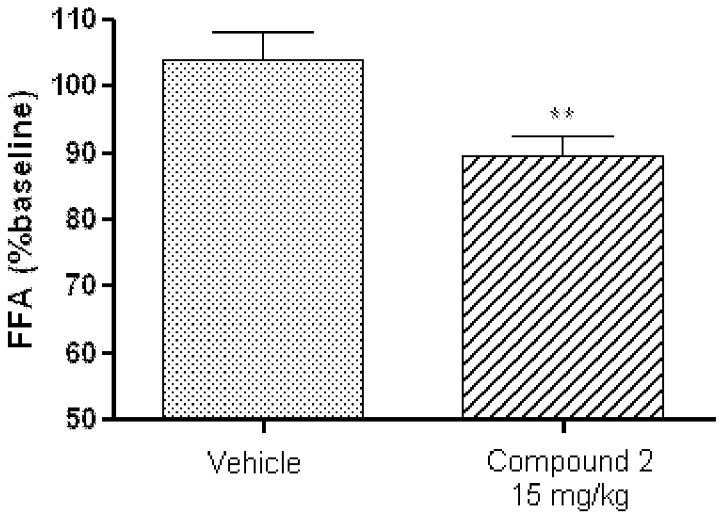
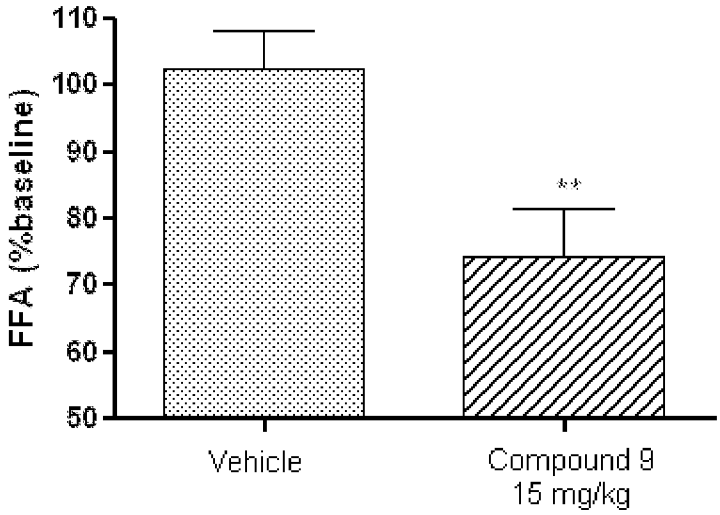


Figure 3



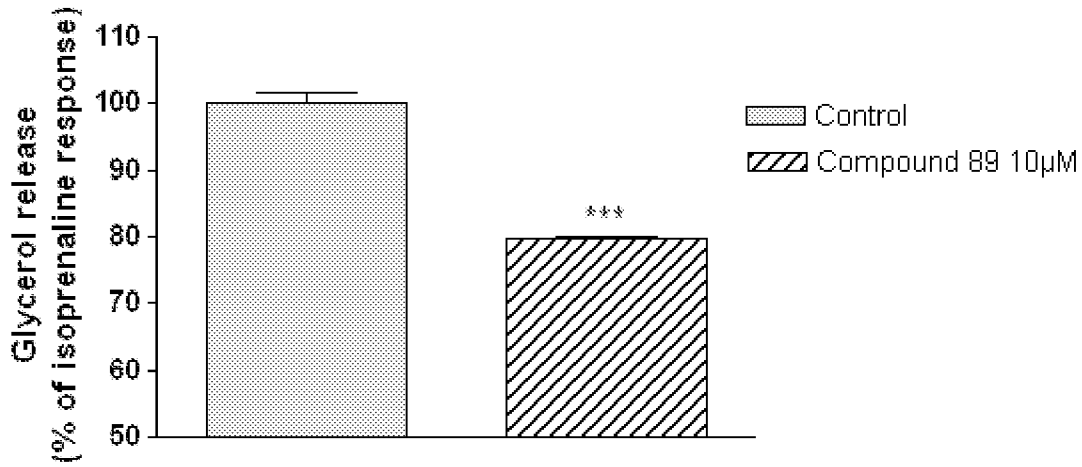
Statistics: One-way ANOVA followed by Dunnett post-hoc
***p<0.01 for treatment vs vehicle. N= 10 mice/group*

Figure 4



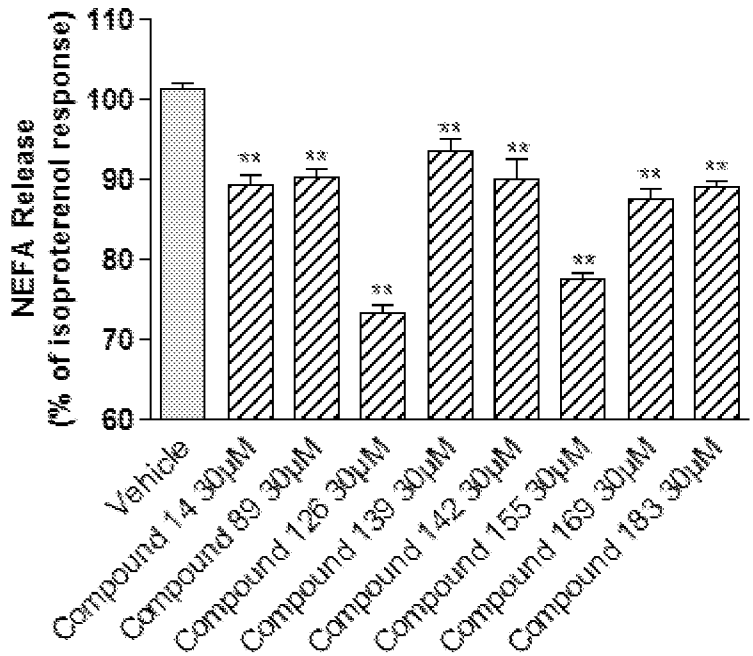
Statistics: One-way ANOVA followed by Dunnett post-hoc
***p<0.01 for treatment vs vehicle. N= 5 mice/group*

Figure 5



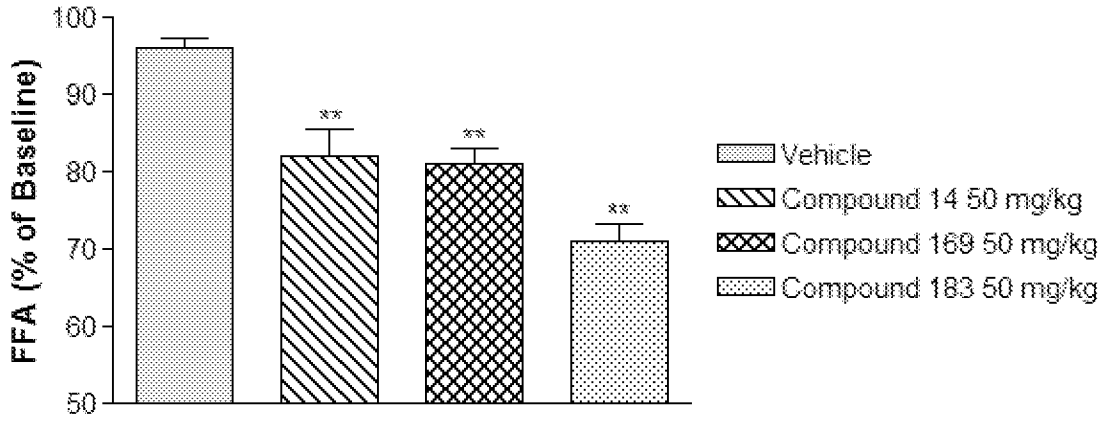
**** p< 0.001 for treatment vs control*
(Student t test).

Figure 6



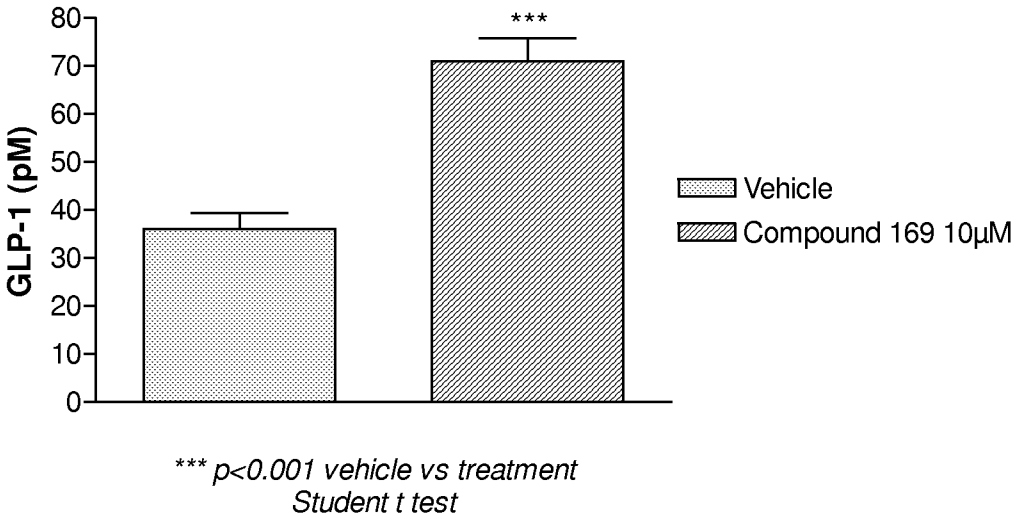
*** p<0.01treatment vs control.*
One-way ANOVA and Dunnett's post-hoc

Figure 7



***p<0.01 vehicle vs treatment*
One-way ANOVA and Dunnett's post-hoc

Figure 8



*** 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

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/078942 A (HARVARD COLLEGE [US]; WAGNER GERHARD [US]; CHOREV MICHAEL [US]; MOERKE) 27 July 2006 (2006-07-27) compounds o and p -page 91; page 29, line 8 - page 34, line 15; claims; figures	1-3, 6-11, 14-19
X	KANNO H ET AL: "Synthesis and evaluation of 2-(biphenylmethyl)glutaric acid amide derivatives as neutral endopeptidase inhibitors" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 6, no. 13, 9 July 1996 (1996-07-09), pages 1487-1490, XP004175738 ISSN: 0960-894X	1,3,6-11
A	table 1	14-19

-/--

[X] Further documents are listed in the continuation of Box C.

[X] 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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 April 2010	04/05/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Gavriliu, Daniela

2

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CHEMCATS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; AKG-3483-0211(ON); 18 July 2008 (2008-07-18), XP002528050 retrieved from STN Database accession no. 2056955583	1-3,6-11
A	abstract & "AKOS SCREENING LIBRARY" 18 July 2008 (2008-07-18), AKOS-CONSULTING AND SOLUTIONS GMBH, AUSTR. 26, STEINEN, D-78585, GERMANY	14-19
Y	DATABASE CAPLUS, [Online] 1 January 2008 (2008-01-01), LEE TAEWEON ET AL: "Identification and functional characterization of allosteric agonists for the G protein-coupled receptor FFA2" XP002528051 retrieved from CAPLUS Database accession no. 2008:1457592 abstract compounds with rn: 1103523-24-5 and 1103523-25-6 & MOLECULAR PHARMACOLOGY, vol. 74, no. 6, 25 September 2008 (2008-09-25), pages 1599-1609, ISSN: 0026-895X	1-3, 6-11, 14-19
Y	WO 2007/131620 A1 (SANOFI AVENTIS [FR]; DEFOSSA ELISABETH [DE]; GOERLITZER JOCHEN [DE]; K) 22 November 2007 (2007-11-22) claims; examples	1-3, 6-11, 14-19
Y	WO 2004/072066 A1 (OSI PHARM INC [US]; FYFE MATTHEW COLIN THOR [GB]; GARDNER LISA SARAH [) 26 August 2004 (2004-08-26) claims; examples 19, 22-24, 30, 34	1-3, 6-11, 14-19
Y	WO 2005/103021 A1 (PROSIDION LTD [GB]; FYFE MATTHEW [GB]) 3 November 2005 (2005-11-03)	1-3,6,7, 9-11, 14-19
A	claims; examples 3,6,9,12,15	8
A	WO 2004/002480 A1 (NOVO NORDISK AS [DK]) 8 January 2004 (2004-01-08) page 189, line 5 - page 192, line 23; claims; examples 6,13, 20,255, 286, 307, 318, , 329, 363, 380, 397,	1,2,8, 14-19

2

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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-1a 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

International application No
PCT/EP2009/066536

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006078942 A	27-07-2006	AU 2006206286 A1	27-07-2006
		CA 2619153 A1	27-07-2006
		EP 1868604 A2	26-12-2007
		JP 2008528502 T	31-07-2008
WO 2007131620 A1	22-11-2007	AR 060992 A1	30-07-2008
		AU 2007250211 A1	22-11-2007
		CA 2651657 A1	22-11-2007
		CN 101421251 A	29-04-2009
		DE 102006021874 A1	22-11-2007
		EP 2024340 A1	18-02-2009
		JP 2009536627 T	15-10-2009
		KR 20090006845 A	15-01-2009
		US 2009149487 A1	11-06-2009
		UY 30339 A1	02-01-2008
WO 2004072066 A1	26-08-2004	EP 1594863 A1	16-11-2005
WO 2005103021 A1	03-11-2005	AU 2005235798 A1	03-11-2005
		BR PI0510163 A	02-10-2007
		CA 2563192 A1	03-11-2005
		EA 200601747 A1	27-04-2007
		EP 1740560 A1	10-01-2007
		JP 2007533722 T	22-11-2007
		KR 20060134179 A	27-12-2006
		US 2008242869 A1	02-10-2008
WO 2004002480 A1	08-01-2004	AU 2003233780 A1	19-01-2004
		EP 1519723 A1	06-04-2005
		JP 2006500325 T	05-01-2006