TRIAZINE COMPOUNDS AS PI3 KINASE AND MTOR INHIBITORS

FIELD OF THE INVENTION

This invention relates to 2,4,6-substituted [1,3,5]triazine compounds in which one substituent is an optionally substituted morpholino, tetrahydropyranyl or dihydropyranyl group, which inhibit PI3 kinase and mTOR, to processes for preparing them, to methods of treatment using them and to pharmaceutical compositions containing them..

BACKGROUND OF THE INVENTION

Phosphatidylinositol (hereinafter abbreviated as "PI") is one of the phospholipids in cell membranes. In recent years it has become clear that PI plays an important role also in intracellular signal transduction. It is well recognized in the art that PI (4,5) bisphosphate (PI(4,5)P2 or PIP2) is degraded into diacylglycerol and inositol (1,4,5) triphosphate by phospholipase C to induce activation of protein kinase C and intracellular calcium mobilization, respectively [M. J. Berridge et al., Nature, 312, 315 (1984); Y. Nishizuka, Science, 225, 1365 (1984)].

Phosphatidylinositol-3 kinase ("PI3K") is an enzyme that phosphorylates the 3-position of the inositol ring of phosphatidylinositol [D. Whitman et al., Nature, 332, 664 (1988)]. Pluralities of PI3K subtypes exist. Three major subtypes of PI3Ks have now been identified on the basis of their in vitro substrate specificity, and these three are designated class I (a & b), class II, and class III [B. Vanhaesebroeck, Trend in Biol. Sci., 22, 267(1997)].

The class Ia PI3K subtype has been most extensively investigated to date. Within the class Ia subtype there are three isoforms (α, β, & δ) that exist as hetero dimers of a catalytic 110-kDa subunit and regulatory subunits of 50-85kDa. The regulatory subunits contain SH2 domains that bind to phosphorylated tyrosine residues within growth factor receptors or adaptor molecules and thereby localize PI3K to the inner cell membrane. At the inner cell membrane PI3K converts PIP2 to PIP3 (phosphatidylinositol-3,4,5-trisphosphate) that serves to localize the downstream effectors PDK1 and Akt to the inner cell membrane where Akt activation occurs. Activated Akt mediates a diverse array of effects including inhibition of apoptosis, cell cycle progression, response to insulin signaling, and cell proliferation. Class Ia PI3K subtypes also contain Ras binding domains (RBD) that allow association with activated Ras providing another mechanism for PI3K membrane localization. Activated, oncogenic forms of growth factor receptors, Ras, and even PI3K kinase have been shown to aberrantly elevate signaling in the PI3K/Akt/mTOR pathway resulting in cell transformation. As a central component of the PI3K/Akt/mTOR signaling pathway PI3K (particularly the class Ia a isoform) has become a major therapeutic target in cancer drug discovery.

Substrates for class I PI3Ks are PI, PI(4)P and PI(4,5)P2, with PI(4,5)P2 being the most favored. Class I PI3Ks are further divided into two groups, class Ia and class Ib, because of

their activation mechanism and associated regulatory subunits. The class Ib PI3K is p110γ that is activated by interaction with G protein-coupled receptors. Interaction between p110γ and G protein-coupled receptors is mediated by regulatory subunits of 110, 87, and 84 kDa.

PI and PI(4)P are the known substrates for class II PI3Ks; PI(4,5)P2 is not a substrate for the enzymes of this class. Class II PI3Ks include PI3K C2α, C2β and C2γ isoforms, which contain C2 domains at the C terminus, implying that their activity is regulated by calcium ions.

The substrate for class III PI3Ks is PI only. A mechanism for activation of the class III PI3Ks has not been clarified. Because each subtype has its own mechanism for regulating activity, it is likely that activation mechanism(s) depend on stimuli specific to each respective class of PI3K.

The compound PI103 (3-(4-(4-morpholinyl)pyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl)phenol) inhibits PI3Ka and PI3Kg as well as the mTOR enzymes with IC_{50} values of 2, 3, and 50-80 nM respectively. I.P. dosing in mice of this compound in human tumor xenograft models of cancer demonstrated activity against a number of human tumor models, including the glioblastoma (PTEN null U87MG), prostate (PC3), breast (MDA-MB-468 and MDA-MB-435) colon carcinoma (HCT 116); and ovarian carcinoma (SKOV3 and IGROV-1); (Raynaud et al, Pharmacologic Characterization of a Potent Inhibitor of Class I Phosphatidylinositide 3-Kinases, Cancer Res. 2007 67: 5840-5850).

The compound ZSTK474 (2-(2-difluoromethylbenzoimidazol-1-yl)-4, 6-dimorpholino-1, 3,5-triazine) inhibits PI3Ka and PI3Kg but not the mTOR enzymes with an IC_{50} values of 16, 4.6 and >10,000 nM respectively (Dexin Kong and Takao Yamori, ZSTK474 is an ATP-competitive inhibitor of class I phosphatidylinositol 3 kinase isoforms, Cancer Science, 2007, 98:10 1638-1642). Chronic oral administration of ZSTK474 in mouse human xenograft cancer models, completely inhibited growth which originated from a non–small-cell lung cancer (A549), a prostate cancer (PC-3), and a colon cancer (WiDr) at a dose of 400 mg/kg. (Yaguchi et al, Antitumor Activity of ZSTK474, a New Phosphatidylinositol 3-Kinase Inhibitor, J. Natl. Cancer Inst. 98: 545-556).

The compound NVP-BEZ-235 (2-methyl-2-(4-(3-methyl-2-oxo-8-(quinolin-3-yl)-2,3-dihydro-1H-imidazo[4,5-c]quinolin-1-yl)phenyl)propanenitrile) inhibits both PI3Ka and PI3Kg as well as the mTOR enzymes with IC_{50} values 4, 5, and "nanomolar". Testing in human tumor xenograft models of cancer demonstrated activity against human tumor models of prostrate (PC-3) and glioblastoma (U-87) cancer. It entered clinical trials in December of 2006 (Verheijen, J.C. and Zask, A., Phosphatidylinositol 3-kinase (PI3K) inhibitors as anticancer drugs, Drugs Fut. 2007, 32(6): 537-547).

The compound SF-1126 (a prodrug form of LY-294002, which is 2-(4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one) is "a pan-PI3K inhibitor". It is active in preclinical mouse cancer models of prostrate, breast, ovarian, lung, multiple myeloma, and brain cancers.

(Verheijen, J.C. and Zask, A., Phosphatidylinositol 3-kinase (PI3K) inhibitors as anticancer drugs, Drugs Fut. 2007, 32(6): 537-547).

Although it seems clear that inhibition of the α isoform is essential for the antitumor activity of PI3K inhibitors, it is not clear whether a more selective inhibitor of a particular PI3K isoform may lead to fewer unwanted biological effects. It has recently been reported that non-PI3Kα class I isoforms (PI3Kβ, δ and γ) have the ability to induce oncogenic transformation of cells, suggesting that nonisoform- specific inhibitors may offer enhanced therapeutic potential over specific inhibitors.

Selectivity versus other related kinases is also an important consideration for the development of PI3K inhibitors. While selective inhibitors may be preferred in order to avoid unwanted side effects, there have been reports that inhibition of multiple targets in the PI3K/Akt pathway (e.g., PI3Kα and mTOR [mammalian target of rapamycin]) may lead to greater efficacy. It is possible that lipid kinase inhibitors may parallel protein kinase inhibitors in that nonselective inhibitors may also be brought forward to the clinic.

Mammalian Target of Rapamycin, mTOR, is a cell-signaling protein that regulates the response of tumor cells to nutrients and growth factors, as well as controlling tumor blood supply through effects on Vascular Endothelial Growth Factor, VEGF. Inhibitors of mTOR starve cancer cells and shrink tumors by inhibiting the effect of mTOR. All mTOR inhibitors bind to the mTOR kinase. This has at least two important effects. First, mTOR is a downstream mediator of the PI3K/Akt pathway. The PI3K/Akt pathway is thought to be over activated in numerous cancers and may account for the widespread response from various cancers to mTOR inhibitors. The over-activation of the upstream pathway would normally cause mTOR kinase to be over activated as well. However, in the presence of mTOR inhibitors, this process is blocked. The blocking effect prevents mTOR from signaling to downstream pathways that control cell growth. Over-activation of the PI3K/Akt kinase pathway is frequently associated with mutations in the PTEN gene, which is common in many cancers and may help predict what tumors will respond to mTOR inhibitors. The second major effect of mTOR inhibition is anti-angiogenesis, via the lowering of VEGF levels.

In lab tests, certain chemotherapy agents were found to be more effective in the presence of mTOR inhibitors. George, J.N., et al., Cancer Research, 61, 1527-1532, 2001. Additional lab results have shown that some rhabdomyosarcoma cells die in the presence of mTOR inhibitors.

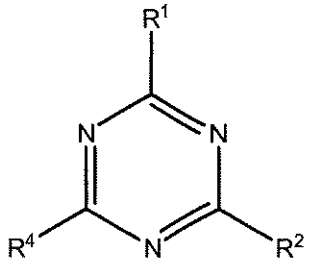
There are three mTOR inhibitors, which have progressed into clinical trials. These compounds are Wyeth's Torisel, also known as 42-(3-hydroxy-2-(hydroxymethyl)-rapamycin 2-methylpropanoate, CCI-779 or Temsirolimus; Novartis' Everolimus, also known as 42-O-(2-hydroxyethyl)-rapamycin, or RAD 001; and Ariad's AP23573 also known as 42-(dimethylphopsinoyl)-rapamycin. The FDA has approved Torisel for the treatment of advanced

renal cell carcinoma. In addition, Torisel is active in a NOS/SCID xenograft mouse model of acute lymphoblastic leukemia [Teachey et al, Blood, 107(3), 1149-1155, 2006]. On March 30, 2009, the U. S. Food and Drug Administration (FDA) approved Everolimus (AFINITOR™) for the treatment of patients with advanced renal cell carcinoma. AP23573 has been given orphan drug and fast-track status by the FDA for treatment of soft-tissue and bone sarcomas.

The three mTOR inhibitors have non-linear, although reproducible pharmacokinetic profiles. Mean area under the curve (AUC) values for these drugs increase at a less than dose related way. The three compounds are all semi-synthetic derivatives of the natural macrolide antibiotic rapamycin. It would be desirable to find fully synthetic compounds, which inhibit mTOR that are more potent and exhibit improved pharmacokinetic behaviors.

SUMMARY OF THE INVENTION

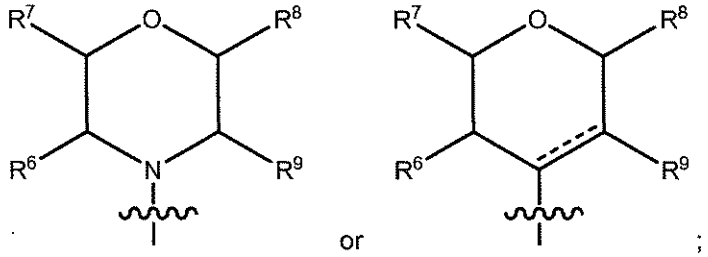
This invention provides compounds of formula I



I

wherein:

R^1 is



or ;

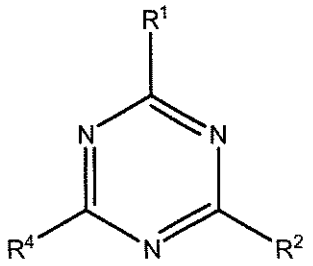
and R^2, R^4, and R^{6-9} are defined below, and pharmaceutically acceptable salts and esters thereof. These compounds are useful as inhibitors of mTOR and PI3 kinases.

This invention further provides compositions containing one or more of the aforementioned compounds, which compositions may contain a pharmaceutically acceptable carrier.

The present invention provides methods for making the compounds of the invention, as described below. Methods of using the invention are also provided, for example: a method for inhibiting mTOR, a method for inhibiting a PI3 kinase, and methods for treating various forms of cancer.

DETAILED DESCRIPTION OF THE INVENTION

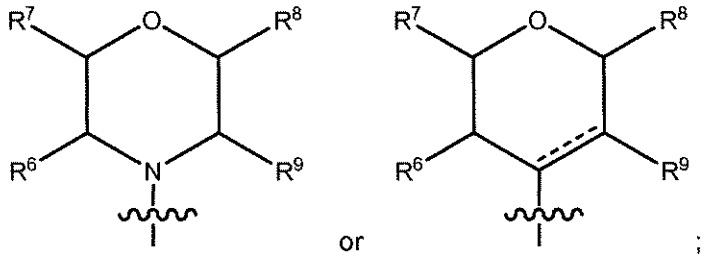
In one aspect, the present invention provides compounds of formula I



I

wherein:

R^1 is



;

wherein:

R^6, R^7, R^8, R^9 are each independently selected from the group consisting of a hydrogen atom, and a C_1-C_6alkyl optionally substituted with C_2-C_6alkenyl, C_4-C_6alkadienyl, C_2-C_6alkynyl or C_4-C_6alkadiynyl;

or one of R^6 and R^7 or R^8 and R^9, together with the carbon atoms to which they are attached form an optionally substituted 5-8 membered saturated or unsaturated ring containing 0, 1 or 2 atoms independently selected from O, NH and S;

the dashed line - - - - - represents an optional second bond;

R^2 is optionally substituted C_6-C_{14}aryl-NH-COR^3, optionally substituted C_1-C_9heteroaryl-NH-COR^3, -CH=CH-C_6-C_{10}aryl-NH-COR^3 or -CH=CH-C_1-C_9heteroaryl-NH-COR^3;

R^3 is OR^5, NR^5R^5 or NHR^5;

R^5 is independently selected from the group consisting of C_1-C_6alkyl, C_3-C_6alkenyl, C_3-C_6alkynyl, optionally substituted C_6-C_{10}aryl, C_1-C_6haloalkyl, optionally substituted C_1-C_9heteroaryl, C_1-C_6hydroxylalkyl-, C_3-C_{10}saturated or unsaturated mono or bicyclic C_3-C_{10}cycloalkyl optionally substituted with OH, $NR^{11}R^{11}$ or 3-7 membered C_1-C_6heterocyclyl, and 3-10 membered saturated or unsaturated mono or bicyclic C_1-C_9heterocyclyl, with the proviso that three-membered cycloalkyl and heterocyclyl rings are saturated;

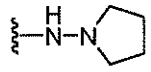
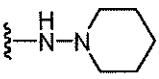
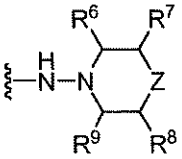
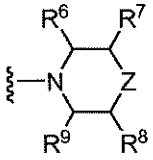
or two R^5 groups taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring system optionally substituted with C_1-C_6alkyl, which ring system is

saturated or unsaturated and has, in addition to said nitrogen atom, 0 to 2 heteroatom ring members selected from O, S, S(O), $S(O)_2$ and NR^{10};

R^{10} is selected from the group consisting of H, C_1-C_6alkyl, -SO_2(C_1-C_6alkyl), -COO(C_1-C_6alkyl), -CONH(C_1-C_6alkyl), -CON(C_1-C_6alkyl)$_2$, -CO(C_1-C_6alkyl), and -SO_2NHR^{11};

R^{11} is selected from the group consisting of H, C_1-C_6alkyl optionally substituted with OH, $NR^{11}R^{11}$ or a 3-7 membered C_1-C_6heterocyclyl, -CO(C_1-C_6alkyl), optionally substituted C_6-C_{10}aryl, and optionally substituted C_1-C_9heteroaryl;

R^4 is selected from the group consisting of: a) C_1-C_6alkyl optionally substituted with: i) 3-10 membered C_1-C_9heterocyclyl optionally substituted with C_1-C_6alkyl-, ii) H_2N-, iii) (C_1-C_6alkyl)NH-, iv) (C_1-C_6alkyl)$_2$N-, v) $NH(CH_2)_aN(C_1$-C_6alkyl)$_2$ wherein a is 2, 3 or 4, and vi) CHO, b) C_3-C_6alkenyl, c) C_3-C_6alkynyl, d) -O-C_1-C_8alkyl optionally substituted with -O-C_1-C_8alkyl, e) -O-C_3-C_8alkenyl, f) -O-C_3-C_8alkynyl, g) saturated or unsaturated mono or bicyclic C_3-C_8cycloalkyl, and h) saturated or unsaturated mono or bicyclic -O-C_3-C_{12}cycloalkyl, all the above optionally substituted with OH, $NR^{11}R^{11}$ or a 3-7 membered C_1-C_6heterocyclyl optionally substituted with C_1-C_6alkyl-, provided that an OH or $NR^{11}R^{11}$ is not directly bonded to a carbon atom that is double- or triple-bonded to another carbon atom; i) -CH=CH-C_6-C_{10}aryl; j) -CH=CH-C_1-C_9heteroaryl; k) optionally substituted C_6-C_{10}aryl; l) optionally substituted 5-10 membered C_1-C_9heteroaryl attached to the triazine moiety via a carbon atom; m) 3-10 membered saturated or unsaturated monocyclic C_1-C_9heterocyclyl attached to the triazine moiety through a carbon or nitrogen atom and optionally substituted with from 1 to 3 substituents independently selected from: OH, $NR^{11}R^{11}$, C_1-C_6alkyl, (C_1-C_6alkyl)amido-, (C_1-C_6alkyl)C(O)-, (C_1-C_6alkoxy)carbonyl-, adamantyl, C_1-C_6hydroxylalkyl-, (C_1-C_6alkyl)amido-; or a 3-7 membered C_1-C_6heterocyclyl, with the proviso that 3 membered heterocyclyl is saturated and attached to the triazine moiety through a nitrogen atom, and 5 membered bicyclic heterocyclyl is saturated; n) optionally substituted -O-C_6-C_{10}aryl; o) optionally substituted -O-C_1-C_9heteroaryl; p) -O-(3-12 membered saturated or unsaturated mono or bicyclic)C_1-C_9heterocyclyl optionally substituted with (C_1-C_6alkoxy)carbonyl-, $H_2NS(O)_2$-, or C_1-C_6alkyl further optionally substituted with OH, $NR^{11}R^{11}$ or a 3-7 membered C_1-C_6heterocyclyl, with the proviso that three membered heterocyclyl is saturated; q) -NHC_6-C_{10}aryl, r) -NHC_1-C_9heteroaryl, s) -$NHNH_2$, t) -NHNHC_1-C_6alkyl, u) -NHN(C_1-C_6alkyl)$_2$, v) -NHOH, w) -COOH, x) -COO-C_1-C_6alkyl, y) -$CONR^{12}R^{13}$, z) -$NR^{12}R^{13}$,

aa)  bb)  cc)  dd) 

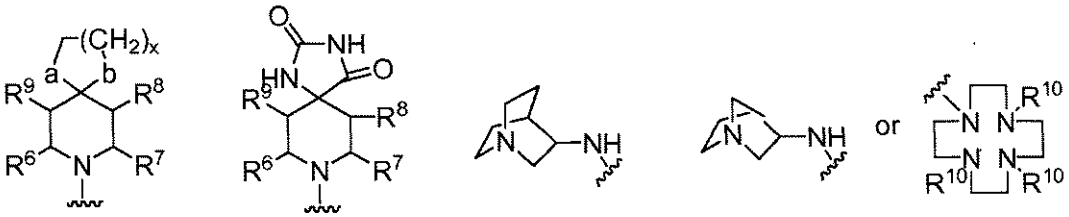
wherein Z is CH_2, O, $S(O)_n$ or NR^{10} and n is 0, 1 or 2;

ee) halogen, ff) C_6-C_{14}aryl-$S(O)_2$-NH-, gg) $R^{11}NHC(O)NH$-O-, and hh) optionally substituted 5-membered monocyclic C_1-C_4heteroaryl attached to the triazine moiety via a nitrogen atom;

R^{12} and R^{13} are each independently selected from H, optionally mono or disubstituted C_1-C_8alkyl, optionally substituted C_3-C_8alkenyl, and optionally substituted C_3-C_8alkynyl, the optional substituents being selected from C_1-C_6alkoxy, OH, $NR^{11}R^{11}$, and 3-7 membered C_1-C_6heterocyclyl, provided that an OH or $NR^{11}R^{11}$ is not directly bonded to a carbon atom that is double- or triple-bonded to another carbon atom;

or R^{12} and R^{13} taken together with the nitrogen atom to which they are attached form a 3 to 8 membered monocyclic ring system optionally substituted with C_1-C_6alkyl, which ring system is saturated or unsaturated and has, in addition to said nitrogen atom, 0 to 2 heteroatom ring members selected from O, $S(O)_n$ and NR^{10};

or R^{12} and R^{13} taken together with the nitrogen atom to which they are attached form



wherein a and b are each independently -CH_2-, O, S, or NR^{10}, and x is 1-3;

C_1-C_9heteroaryl refers to a 5-10 membered aromatic ring system having one or more rings and 1, 2, 3 or 4 ring members independently selected from O, NR^{10}, and $S(O)_n$;

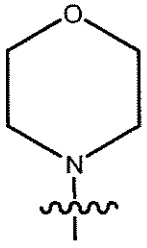
C_1-C_9heterocyclyl refers to a 3-10 membered ring system having one or more rings and 1, 2, 3 or 4 ring members independently selected from O, NR^{10}, and $S(O)_n$; and

optionally substituted aryl and heteroaryl groups are unsubstituted or are substituted with 1 or 2 moieties selected from the group consisting of: a) C_1-C_6alkyl optionally substituted with OH, NH_2, $NH(C_1$-C_6alkyl), $N(C_1$-C_6alkyl$)_2$, -$NH(CH_2)_wN(C_1$-C_6alkyl$)_2$ wherein w is 2, 3 or 4, or 3-10 membered C_1-C_9heterocyclyl optionally substituted with from 1 to 3 independently selected C_1-C_6alkyl- substituents; b) halogen; c) hydroxy; d) NH_2; e) NO_2; f) SO_2NH_2; g) COOH; h) $COO(C_1$-C_6alkyl); i) $NHCOO(C_1$-C_6alkyl); j) $NH(C_1$-C_6alkyl); k) $N(C_1$-C_6alkyl$)_2$; l) $C(O)NR^aR^b$, wherein R^a is H or C_1-C_6alkyl, and R^b is H, C_1-C_6alkyl, (C_6-C_{14}aryl)alkyl-, or (C_1-C_9heteroaryl)alkyl-; m) -Y-Q, wherein Y is: i) O, ii) NH, iii) $N(C_1$-C_6alkyl), iv) $NHSO_2$, v) SO_2NH, vi) NHCONH, vii) $NHCON(C_1$-C_6alkyl), viii) $S(O)_q$, q is 0, 1 or 2, ix) -C(O)NH-, x) –NHC(O)- xi) -$C(O)N(CH_3)$-, xii) C(O), or xiii) absent, and Q is selected from: i) C_6-C_{10}aryl, optionally substituted with from 1 to 3 substituents independently selected from: A) C_1-C_6alkoxy- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, 3) di(C_1-C_6alkyl)amino-, 4) C_1-C_9heterocyclyl-

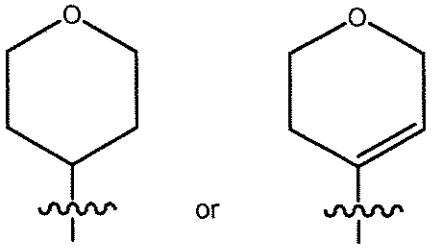
optionally substituted by C_1-C_6alkyl-, or 5) hydroxyl, B) (C_1-C_6alkoxy)carbonyl-, C) (C_1-C_6alkoxy)C(O)NH-, D) C_1-C_6alkyl- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, E) (C_1-C_6alkyl)amino-, F) di(C_1-C_6alkyl)amino-, G) (C_1-C_6alkyl)amido- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, H) (C_1-C_6alkyl)carboxyamido-, I) C_1-C_9heterocyclyl- optionally substituted by C_1-C_6alkyl- or C_1-C_6hydroxylalkyl-, J) heterocyclyl(C_1-C_6alkyl)- optionally substituted by C_1-C_6alkyl-, K) halogen, L) hydroxyl, M) C_1-C_6hydroxylalkyl-, N) perfluoro(C_1-C_6)alkyl-, O) H_2N-, P) O_2N-, Q) H_2NSO_2-, R) HO_2C-, and S) NC-, ii) 5-10 membered C_1-C_9heteroaryl, optionally substituted with from 1 to 3 substituents independently selected from: A) C_1-C_6alkoxy- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, 3) di(C_1-C_6alkyl)amino-, 4) C_1-C_9heterocyclyl- optionally substituted by C_1-C_6alkyl-, or 5) hydroxyl, B) (C_1-C_6alkoxy)carbonyl-, C) (C_1-C_6alkoxy)C(O)NH-, D) C_1-C_6alkyl- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, E) (C_1-C_6alkyl)amino-, F) di(C_1-C_6alkyl)amino-, G) (C_1-C_6alkyl)amido- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, H) (C_1-C_6alkyl)carboxyamido-, I) C_1-C_9heterocyclyl- optionally substituted by C_1-C_6alkyl- or C_1-C_6hydroxylalkyl-, J) heterocyclyl(C_1-C_6alkyl)- optionally substituted by C_1-C_6alkyl-, K) halogen, L) hydroxyl, M) C_1-C_6hydroxylalkyl-, N) perfluoro(C_1-C_6)alkyl-, O) H_2N-, P) O_2N-, Q) H_2NSO_2-, R) HO_2C-, and S) NC-, iii) 3-10 membered C_1-C_9heterocyclyl, optionally substituted with from 1 to 3 substituents independently selected from: A) C_1-C_6alkyl-, B) heterocyclyl(C_1-C_6alkyl)-, C) (C_6-C_{14}aryl)alkyl-, D) C_1-C_8acyl-, E) (C_1-C_6alkoxy)carbonyl-, F) (C_1-C_6alkyl)carboxyl- , G) halogen, H) C_1-C_6haloalkyl-, I) hydroxyl, J) C_1-C_6hydroxyalkyl-, K) H_2N-, L) (C_1-C_6alkyl)amino-, M) di(C_1-C_6alkyl)amino-, N) HO_2C-, O) (C_1-C_6alkoxy)carbonyl-, P) (C_1-C_6alkyl)carboxyl-, Q) (C_1-C_6alkyl)amido-, R) $H_2NC(O)$-, S) (C_1-C_6alkyl)carboxyamido-, T) 5-10 membered C_1-C_9heteroaryl, U) C_6-C_{14}ary, V) C_3-C_8cycloalkyl W) 3-10 membered C_1-C_9heterocyclyl, X) NC-; and Y) $-NO_2$; iv) C_3-C_{10}cycloalkyl, v) C_1-C_6alkyl, vi) C_2-C_6alkenyl, vii) C_2-C_6alkynyl, viii) C_1-C_6hydroxyalkyl-, ix) $(CH_2)_vO(C_1$-C_6alkyl), x) $(CH_2)_vNH_2$, xi) $(CH_2)_vNH(C_1$-C_6alkyl), xii) $(CH_2)_vN(C_1$-C_6alkyl)$_2$, xiii) $O(CH_2)_vN(C_1$-C_6alkyl)$_2$, xiv) $(CH_2)_vC_6$-C_{10}aryl, xv) –CN, xvi) $(CH_2)_v$ 5-10 membered C_1-C_9heteroaryl, xvii) $(CH_2)_v$ 3-10 membered C_1-C_9heterocyclyl, optionally substituted by C_1-C_6alkyl-, wherein v is 1, 2, 3 or 4, and xviii) C_1-C_6perfluoroalkyl- ; and n) $C(O)R^c$ wherein R^c is: i) H, ii) C_1-C_6alkyl, or iii) C_3-C_6cycloalkyl,

and pharmaceutically acceptable salts and esters thereof.

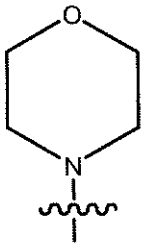
In some embodiments of the invention, R^1 and/or R^4 is



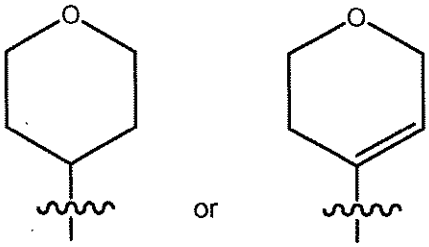
In some embodiments, R^1 and/or R^4 is



In some embodiments, one of R^1 or R^4 is



and the other is



In some embodiments, R^2 is optionally substituted C_6-C_{14}aryl-NH-COR^3; in others R^2 is optionally substituted phenyl-NH-COR^3.

In some embodiments, R^3 is NHR^5 or OR^5. In some embodiments, R^5 is optionally substituted C_6-C_{10}aryl, such as optionally substituted phenyl or C_1-C_9heteroaryl. In some embodiments, the optionally substituted C_6-C_{10}aryl or phenyl is substituted with –Y-Q, $C(O)NR^aR^b$ or $C(O)R^c$.

In some embodiments, R^5 is phenyl substituted with –Y-Q.

The following compounds exemplify illustrative compounds of Formula I:

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-3-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-phenylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-thiophen-2-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-methylphenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-fluorophenyl)urea;

1-(2,4-dimethoxyphenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-urea;

1-(4-chlorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-methoxyphenyl)urea;

(4-chlorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

(2,4-difluorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-ethylurea;

tert-butyl 3-{[4-(4-{[(4-fluorophenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(phenylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-3-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate;

tert-butyl 3-{[4-(4-{[(4-methylphenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-fluorophenyl)urea;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-methylphenyl)urea;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(2-hydroxyethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-hydroxyphenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(trifluoromethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-hydroxyphenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5-(trifluoromethyl)pyridin-2-yl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea;

methyl 4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-[4-(hydroxymethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-(2-methylpyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-[2-(methylamino)ethyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-(3-acetylphenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(dimethylamino)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

4-[3-{4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl}ureido]benzoic acid;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide HCl salt;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-morpholinopiperidine-1-carbonyl)phenyl)urea;

4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(quinuclidin-3-yl)benzamide;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(pyrrolidin-1-yl)piperidine-1-carbonyl)phenyl)urea;

1-(4-(1,4'-bipiperidine-1'-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyridin-2-yl)acetyl)phenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(trifluoromethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5-(trifluoromethyl)pyridin-2-yl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-[4-(2-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-[4-(2-hydroxymethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(2-methylpyridin-4-yl)urea;

1-[4-(1-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}-amino)benzoate;

1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(1-methylpiperidin-4-yl)urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(1-methylpiperidin-4-yl)urea;

1-{4-[4-(3,6-Dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea;

1-{4-[4-Morpholin-4-yl-6-(tetrahydro-pyran-4-yl)-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea;

3-({4-Morpholin-4-yl-6-[4-(3-pyridin-4-yl-ureido)-phenyl]-[1,3,5]triazin-2-ylamino}-methyl)-azetidine-1-carboxylic acid tert-butyl ester;

1-(4-{4-[(azetidin-3-ylmethyl)-amino]-6-morpholin-4-yl-[1,3,5]triazin-2-yl}-phenyl)-3-pyridin-4-yl-urea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-[4-(dimethylamino)phenyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-cyanophenyl)-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(2-methylpyridin-4-yl)urea;

1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(4-morpholin-4-yl-6-quinolin-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(morpholin-4-ylcarbonyl)phenyl]urea;

1-[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl] phenyl}urea;

4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-({4-[2-(dimethylamino) ethyl]piperazin-1-yl}carbonyl)phenyl]-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid; N-[2-(dimethylamino)ethyl]-4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2yl)phenyl] carbamoyl} amino) benzoic acid; mp 204 °C;

1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; mp 170 °C;

4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-{4-[4-(1-ethoxyvinyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-[4-(4-acetyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-[({4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-{4-[4-(1-hydroxyethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-(4-{4-morpholin-4-yl-6-[2-(pyridin-4-ylamino)ethyl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]benzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methyl-N-[2-(methylamino)ethyl]benzamide;

1-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[4-(4-methylpiperazin-1-yl)phenyl]benzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]urea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[4-(4-methylpiperazin-1-yl)phenyl]benzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}urea;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-formylphenyl)urea;

4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(pyridin-2-ylmethyl)benzamide;

1-(4-{4-[2-(1,3-dioxan-2-yl)ethyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-(4-{4-[2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-{4-[2-(dimethylamino)ethoxy]phenyl}benzamide;

1-{4-[(4-benzylpiperidin-1-yl)carbonyl]phenyl}-3-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

1-(4-{4-[3-(dimethylamino)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-[4-(4-{3-[(1-methylethyl)amino]propyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-pyrrolidin-1-ylpropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-(4-{4-[3-(4-methylpiperazin-1-yl)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-{4-[4-(3-{[2-(dimethylamino)ethyl]amino}propyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(3-hydroxypropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-oxopropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]benzamide;

1-[4-(4-methylpiperazin-1-yl)phenyl]-3-[4-(4-morpholin-4-yl-6-propyl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylazetidin-3-yl)benzamide;

methyl 4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate

N-[2-(dimethylamino)ethyl]-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-(1-methylazetidin-3-yl)-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-pyridin-4-ylbenzamide;

4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-pyridin-3-ylbenzamide;

N-cyclobutyl-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-phenylpiperidin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(pyridin-4-ylmethyl)benzamide;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

methyl 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-yl)phenyl)urea;

1-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((S)-3-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((R)-3-methylpiperazin-1-yl)phenyl)urea;

1-(4-((3R,5S)-3,5-dimethylpiperazin-1-yl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-(dimethylamino)ethoxy)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-ethylpiperazin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-isopropylpiperazin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

(R)-1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N,N-dimethylbenzamide;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea;

4-({[4-(4-{4-[(methylcarbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-{4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

3-({[4-(4-{4-[(methylcarbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-3-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)phenyl]urea;

1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)phenyl]urea;

3-[({4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-[({4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-methylurea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridazin-4-ylurea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(oxetan-3-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-isopropyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-pyrimidin-5-ylphenyl)urea;

1-(4-{4-[(2,2-dimethoxyethyl)amino]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea;

1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-pyridin-4-ylphenyl)urea;

1-(4-iodophenyl)-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-{4-[2-(dimethylamino)pyrimidin-5-yl]phenyl}-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]azetidine-1-carboxylate;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-nitrophenyl)urea;

1-(4-aminophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-methylpiperazine-1-carboxamide;

4-(dimethylamino)-N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]piperidine-1-carboxamide;

1-[2-(dimethylamino)ethyl]-3-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-1-methylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[(2-piperidin-1-ylethyl)carbamoyl]amino}phenyl)urea;

N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-methyl-1,4-diazepane-1-carboxamide;

N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-ethylpiperazine-1-carboxamide;

1-{4-[(dimethylcarbamoyl)amino]phenyl}-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide;

4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-piperidin-1-ylethyl)benzamide;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-piperidin-1-ylethyl)benzamide;

4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-[({4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

methyl 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

methyl 4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(dimethylamino)ethyl]benzamide;

1-{4-[(4-isopropylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

N-(2-methoxyethyl)-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-(2-methoxyethyl)-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea;

N-[3-(dimethylamino)propyl]-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperidin-1-ylcarbonyl)phenyl]urea;

N-[3-(dimethylamino)propyl]-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea;

methyl 4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea;

4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

N-[3-(dimethylamino)propyl]-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

methyl 3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-(3-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

methyl 3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

methyl 3-({[4-(4-morpholin-4-yl-6-thiophen-2-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

N-[2-(dimethylamino)ethyl]-3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

methyl 3-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{3-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

3-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

methyl 4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

methyl 4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

1-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

N-[3-(dimethylamino)propyl]-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

N-(2-methoxyethyl)-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

methyl 4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

N-[3-(dimethylamino)propyl]-4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(dipropylamino)piperidin-1-yl]carbonyl}phenyl)urea;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea;

4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea;

methyl 4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(2-methylpropyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylpropyl)piperazin-1-yl]carbonyl}phenyl)urea;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(4-methylpiperazin-1-yl)ethyl]benzamide;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-propylpiperidin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(piperidin-1-ylcarbonyl)phenyl]urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-propylpiperazin-1-yl)carbonyl]phenyl}urea;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-methoxyethyl)benzamide;

1-{4-[4-morpholin-4-yl-6-(4-tricyclo[3.3.1.13,7]dec-1-ylpiperazin-1-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-{[(4-{4-[4-(dimethylcarbamoyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

N,N-dimethyl-4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperazine-1-carboxamide;

N,N-dimethyl-4-(4-{4-[({4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)piperazine-1-carboxamide;

N,N-dimethyl-4-{4-morpholin-4-yl-6-[4-({[4-(pyridazin-4-ylcarbamoyl)phenyl]carbamoyl}amino)phenyl]-1,3,5-triazin-2-yl}piperazine-1-carboxamide;

N,N-dimethyl-4-(4-morpholin-4-yl-6-{4-[({4-[(4-propylpiperidin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperazine-1-carboxamide;

4-{[(4-{4-[4-(dimethylcarbamoyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

4-(4-{4-[({4-[(2-methoxyethyl)carbamoyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-dimethylpiperazine-1-carboxamide;

4-[4-(4-{[(4-{[2-(dimethylamino)ethyl](methyl)carbamoyl}phenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]-N,N-dimethylpiperazine-1-carboxamide;

4-(4-{4-[({4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-dimethylpiperazine-1-carboxamide;

1-(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

methyl 4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

N-[3-(dimethylamino)propyl]-4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

methyl 4-{[(4-{4-[4-(acetylamino)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[1-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperidin-4-yl]acetamide;

4-{[(4-{4-[4-(acetylamino)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-{1-[(4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}phenyl)carbonyl]piperidin-4-yl}acetamide;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3S)-3-methylmorpholin-4-yl]carbonyl}phenyl)urea;

1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[(4-methylpiperazin-1-yl)amino]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-phenylurea;

1-(4-{4-[(1-methylpiperidin-4-yl)oxy]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(piperidin-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

ethyl 4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxylate;

N-ethyl-4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxamide;

tert-butyl 4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxylate;

4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-sulfonamide;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-[4-(dimethylamino)phenyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-cyanophenyl)-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(2-methylpyridin-4-yl)urea;

1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(4-morpholin-4-yl-6-quinolin-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-{4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-[({4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-(4-{4-morpholin-4-yl-6-[2-(pyridin-4-ylamino)ethyl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methyl-N-[2-(methylamino)ethyl]benzamide;

1-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide;

1-(4-{4-[2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-(4-{4-[2-(1,3-dioxan-2-yl)ethyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-(4-{4-[3-(dimethylamino)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-[4-(4-{3-[(1-methylethyl)amino]propyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-pyrrolidin-1-ylpropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-(4-{4-[3-(4-methylpiperazin-1-yl)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-{4-[4-(3-{[2-(dimethylamino)ethyl]amino}propyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(3-hydroxypropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-oxopropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

N-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)benzenesulfonamide;

N-{4-[4-({[4-(4-methylpiperazin-1-yl)phenyl]carbamoyl}amino)phenyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}benzenesulfonamide;

N-(4-{4-[({4-[2-(dimethylamino)ethoxy]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)benzenesulfonamide;

N-(4-{4-[({4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)benzenesulfonamide;

N-{4-morpholin-4-yl-6-[4-({[4-(piperazin-1-ylcarbonyl)phenyl]carbamoyl}amino)phenyl]-1,3,5-triazin-2-yl}benzenesulfonamide;

N-[4-(4-{[(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]benzenesulfonamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

methyl 4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(6-morpholin-4-yl-4-oxo-4,5-dihydro-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(quinuclidin-4-yl)phenyl)urea;

1-(4-(4-cyclopropylpiperazin-1-yl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(cyclopropylmethyl)piperazin-1-yl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(quinuclidin-4-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-cyclopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(cyclopropylmethyl)piperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(methylamino)ethyl)-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-methyl-N-(2-(methylamino)ethyl)-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-((R)-3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea ;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

4-(3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-chlorophenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-fluorophenyl)urea;

methyl4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2yl)phenyl)ureido) benzoate;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoic acid;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)benzamide;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)urea;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea; ;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea ;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-chlorophenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-fluorophenyl)urea;

Methyl-4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoate;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoic acid;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)benzamide;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)urea;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

tert-butyl 4-(4-(4-(3-(4-(methoxycarbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxylate;

methyl4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl) ureido)benzoate;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-chlorophenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-fluorophenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

N-methyl-4-(4-morpholino-6-(4-(3-phenylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide (M+H) 532.2;

4-(4-(4-(3-(4-chlorophenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-fluorophenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(2-(dimethylamino)ethylcarbamoyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-((2-(dimethylamino)ethyl)(methyl)carbamoyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-carbamoylphenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

N-methyl-4-(4-morpholino-6-(4-(3-(4-(piperazine-1-carbonyl)phenyl)ureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-methyl-4-(4-(4-(3-(4-(4-methylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-isopropyl-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-(4-(3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-isopropyl-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-(4-(3-(4-(4-methylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-(4-(piperazine-1-carbonyl)phenyl)ureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyridazin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyrimidin-5-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyridin-3-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-acetylphenyl)-3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)acetyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-morpholinoacetyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxyacetyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(methoxymethyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-methoxyethyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(1-hydroxyethyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxypropan-2-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxypropyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxy-2-methylpropyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-cyanophenyl)urea;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N,N-dimethylbenzamide;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)urea;

(R)-1-(4-((dimethylamino)methyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

(R)-1-(4-acetylphenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-(dimethylamino)acetyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-morpholinoacetyl)phenyl)urea;

(R)-1-(4-(2-hydroxyacetyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(methoxymethyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-methoxyethyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(1-hydroxyethyl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-hydroxypropan-2-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2-hydroxypropyl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-hydroxy-2-methylpropyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-cyanophenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-N-methyl-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

(R)-N,N-dimethyl-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

(R)-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

methyl 4-(3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoate;

4-(3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoic acid;

4-(3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(azetidin-3-yloxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

N-(1-methylethyl)-3-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]azetidine-1-carboxamide;

N-{1-[(4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}phenyl)carbonyl]piperidin-4-yl}acetamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)-1,4-diazepan-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(3-oxa-8-azabicyclo[3.2.1]oct-8-ylcarbonyl)phenyl]urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-cyanopiperidin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(2-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(3,3,4-trimethylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3R)-3-methylpiperazin-1-yl]carbonyl}phenyl)urea;

1-(4-{[(3R)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]carbonyl}phenyl)urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3S)-3-methylpiperazin-1-yl]carbonyl}phenyl)urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

N-[3-(dimethylamino)propyl]-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

1-[4-(morpholin-4-ylcarbonyl)phenyl]-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

N-(2-methoxyethyl)-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

1-[4-(1,4-diazepan-1-ylcarbonyl)phenyl]-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(propan-2-yl)-1,4-diazepan-1-yl]carbonyl}phenyl)urea;

1-(4-{[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3S)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(3,3,4-trimethylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[(3S)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3S)-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea; and

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea.

The invention also includes pharmaceutical compositions comprising a compound of formula I and a pharmaceutically acceptable carrier. The invention includes a compound of formula I when provided as a pharmaceutically acceptable prodrug, hydrated salt, such as pharmaceutically acceptable salt, or mixtures thereof.

In other aspects, the invention provides that the pharmaceutically acceptable carrier suitable for oral administration and the composition comprises an oral dosage form.

In other aspects, the invention provides a composition comprising a compound of Formula I, a second compound selected from the group consisting of a topoisomerase I inhibitor, a MEK 1/2 inhibitor, a HSP90 inhibitor, procarbazine, dacarbazine, gemcitabine, capecitabine, methotrexate, taxol, taxotere, mercaptopurine, thioguanine, hydroxyurea, cytarabine, cyclophosphamide, ifosfamide, nitrosoureas, cisplatin, carboplatin, mitomycin, dacarbazine, procarbizine, etoposide, teniposide, campathecins, bleomycin, doxorubicin, idarubicin, daunorubicin, dactinomycin, plicamycin, mitoxantrone, L-asparaginase, doxorubicin, epirubicin, 5-fluorouracil, docetaxel, paclitaxel, leucovorin, levamisole, irinotecan, estramustine, etoposide, nitrogen mustards, BCNU, carmustine, lomustine, vinblastine, vincristine, vinorelbine, cisplatin, carboplatin, oxaliplatin, imatinib mesylate, Avastin (bevacizumab), hexamethylmelamine, topotecan, tyrosine kinase inhibitors, tyrphostins, herbimycin A, genistein, erbstatin, hydroxyzine, glatiramer acetate, interferon beta-1a, interferon beta-1b, natalizumab and lavendustin A; and a pharmaceutically acceptable carrier.

In other aspects, the second compound is Avastin.

In other aspects, the invention provides a method of treating a PI3K-related disorder, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat a PI3K-related disorder.

In other aspects, the PI3K-related disorder is selected from restenosis, atherosclerosis, bone disorders, arthritis, diabetic retinopathy, psoriasis, benign prostatic hypertrophy, atherosclerosis, inflammation, angiogenesis, immunological disorders, pancreatitis, kidney disease, and cancer.

In other aspects, the PI3K-related disorder is cancer.

In other aspects, the cancer is selected from the group consisting of leukemia, skin cancer, bladder cancer, breast cancer, uterus cancer, ovary cancer, prostate cancer, lung cancer, colon cancer, pancreas cancer, renal cancer, gastric cancer, and brain cancer.

In other aspects, the invention provides a method of treating an mTOR-related disorder, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat an mTOR-related disorder.

In other aspects, the mTOR-related disorder is selected from restenosis, atherosclerosis, bone disorders, arthritis, diabetic retinopathy, psoriasis, benign prostatic hypertrophy, atherosclerosis, inflammation, angiogenesis, immunological disorders, pancreatitis, kidney disease, and cancer.

In other aspects, the mTOR-related disorder is cancer.

In other aspects, the cancer is selected from the group consisting of leukemia, skin cancer, bladder cancer, breast cancer, uterus cancer, ovary cancer, prostate cancer, lung cancer, colon cancer, pancreas cancer, renal cancer, gastric cancer, and brain cancer.

In other aspects, the invention provides a method of treating a hSMG-1-related disorder, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat a hSMG-1-related disorder.

In other aspects, the hSMG-1-related disorder is selected from restenosis, atherosclerosis, bone disorders, arthritis, diabetic retinopathy, psoriasis, benign prostatic hypertrophy, atherosclerosis, inflammation, angiogenesis, immunological disorders, pancreatitis, kidney disease, and cancer.

In other aspects, the hSMG-1-related disorder is cancer.

In other aspects, the cancer is selected from the group consisting of leukemia, skin cancer, bladder cancer, breast cancer, uterus cancer, ovary cancer, prostate cancer, lung cancer, colon cancer, pancreas cancer, renal cancer, gastric cancer, and brain cancer.

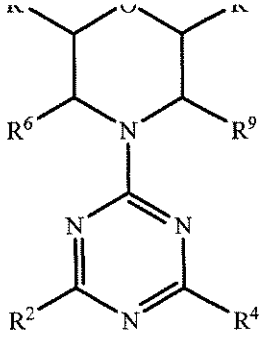
In other aspects, the invention provides a method of treating advanced renal cell carcinoma, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat advanced renal cell carcinoma.

In other aspects, the invention provides a method of treating acute lymphoblastic leukemia, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat acute lymphoblastic leukemia.

In other aspects, the invention provides a method of treating acute malignant melanoma, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat malignant melanoma.

In other aspects, the invention provides a method of treating soft-tissue or bone sarcoma, comprising administering to a mammal in need thereof a compound of Formula I in an amount effective to treat soft-tissue or bone sarcoma.

In other aspects, the invention provides a method of treating a cancer selected from the group consisting of leukemia, skin cancer, bladder cancer, breast cancer, uterus cancer, ovary cancer, prostate cancer, lung cancer, colon cancer, pancreas cancer, renal cancer, gastric cancer, and brain cancer comprising administering to a mammal in need thereof a composition comprising a compound of Formula I; a second compound selected from the group consisting of a topoisomerase I inhibitor, a MEK 1/2 inhibitor, a HSP90 inhibitor, procarbazine, dacarbazine,



gemcitabine, capecitabine, methotrexate, taxol, taxotere, mercaptopurine, thioguanine, hydroxyurea, cytarabine, cyclophosphamide, ifosfamide, nitrosoureas, cisplatin, carboplatin, mitomycin, dacarbazine, procarbizine, etoposide, teniposide, campathecins, bleomycin, doxorubicin, idarubicin, daunorubicin, dactinomycin, plicamycin, mitoxantrone, L-asparaginase, doxorubicin, epirubicin, 5-fluorouracil, docetaxel, paclitaxel, leucovorin, levamisole, irinotecan, estramustine, etoposide, nitrogen mustards, BCNU, carmustine, lomustine, vinblastine, vincristine, vinorelbine, cisplatin, carboplatin, oxaliplatin, imatinib mesylate, Avastin (bevacizumab), hexamethylmelamine, topotecan, tyrosine kinase inhibitors, tyrphostins, herbimycin A, genistein, erbstatin, and lavendustin A; and a pharmaceutically acceptable carrier. in an amount effective to treat the cancer.

In other aspects, the invention provides a method of inhibiting mTOR in a subject, comprising administering to a subject in need thereof a compound of Formula I in an amount effective to inhibit mTOR.

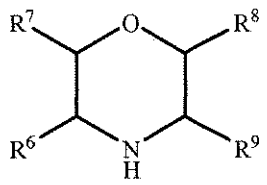
In other aspects, the invention provides a method of inhibiting PI3K in a subject, comprising administering to a subject in need thereof a compound of Formula I in an amount effective to inhibit PI3K.

In other aspects, the invention provides a method of inhibiting hSMG-1 in a subject, comprising administering to a subject in need thereof a compound of Formula I in an amount effective to inhibit hSMG-1.

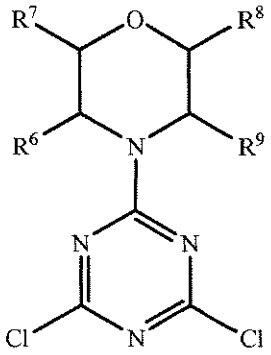
In other aspects, the invention provides a method of inhibiting mTOR, PI3K, and hSMG-1 together in a subject, comprising administering to a subject in need thereof a compound of Formula I in an amount effective to inhibit mTOR, PI3K, and hSMG-1.

In another aspect, the invention provides a method of synthesizing compounds of the Formula I, which are:

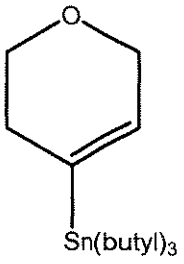
said method comprising reacting 2,4,6-trichloro[1,3,5]triazine with



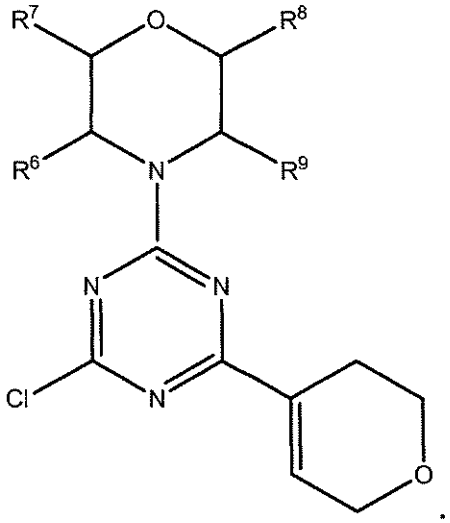
to form the intermediate dichlorotriazine compound



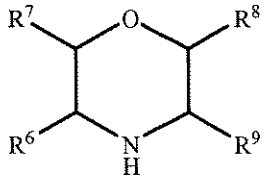
The method of synthesizing compounds of the Formula I further comprising reacting the intermediate dichlorotriazine compound with



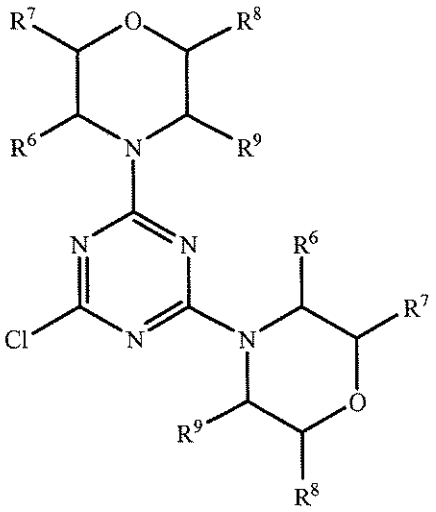
to form the intermediate compound



The method of synthesizing compounds of the Formula I further comprising reacting the intermediate dichlorotriazine compound with



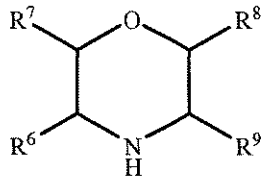
to form the intermediate compound



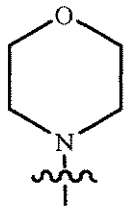
,

wherein each R^6, R^7, R^8 and R^9 is independently selected and defined according to formula I.

The method of synthesizing compounds of the Formula I wherein the reacting moiety

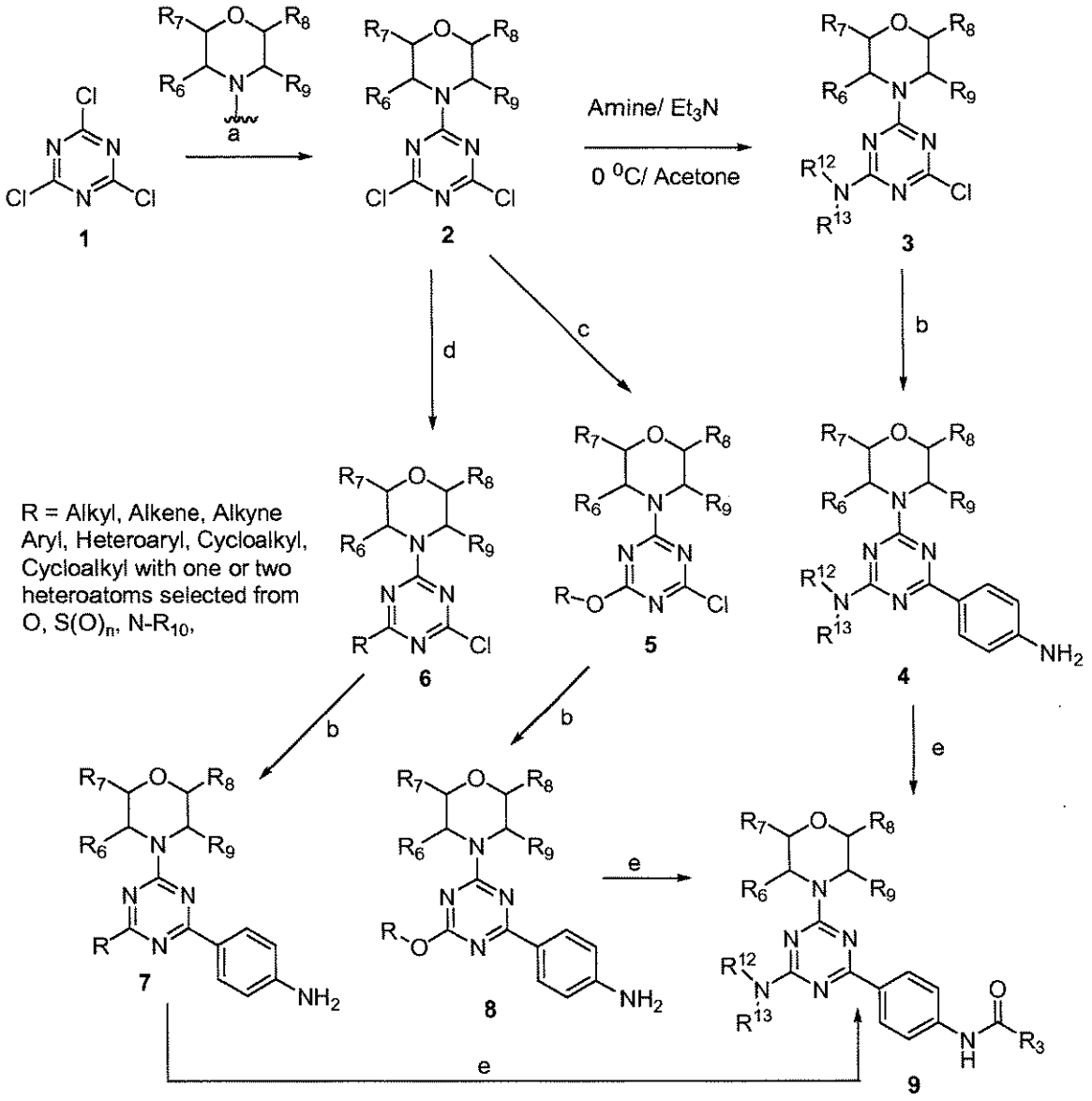


is



Procedures used to synthesize the compounds of the present invention are described in Schemes 1-12 and are illustrated in the examples. Reasonable variations of the described procedures are intended to be within the scope of the present invention:

Scheme 1



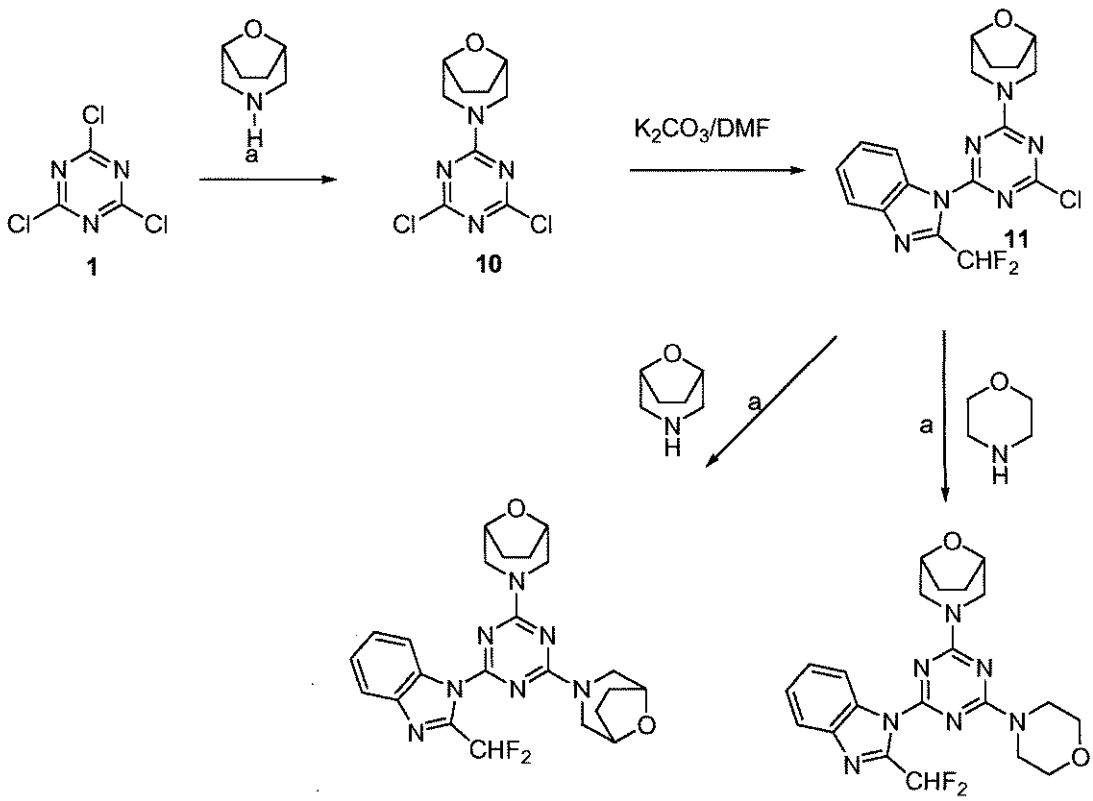
(a) Acetone/ H_2O/ Et_3N/ -10 °C; (b) 4-aminophenyl boronic acid/ $(Ph_3)_4P(Pd)$/ Na_2CO_3/ DME/ Reflux or m Wave
(c) Corresponding alcohol/ n-BuLi or NaH/ THF/ RT or Reflux; (d) When R = alky RMgBr/ Pd (0)/ THF;
when R = Alkene or cycloalkyl or cycloalkyl with one or two heteroatoms the transfomation is via vinyl stanane/ Pd(0)/ Organic solvent/ Reflux (Stille coupling); When R = aryl or heteroaryl the transformation is via Aryl bornate/ $(Ph_3)_4P(Pd)$/ Na_2CO_3/ DME/ Reflux or m Wave (Suzuki coupling); (e) When R_3 is $-OR_5$, DCM/ $ClCOOR_5$/ Et_3N/ 0 °C-RT; When R_5 is NHR_5, DMAP/ DCM/ R_5NCO or $(COCl_2)_3$/ Et_3N/R_5NH_2

Compounds of the present inventions were prepared by a multi-step sequence as depicted in Scheme 1. One chlorine atom at a time was selectively replaced at different temperatures. The commercially available cyanuric acid chloride 1 was reacted with morpholine or substituted morpholine derivatives at –10 °C to give the mono morpholine derivative 2. This pivotal intermediate 2 can be reacted with different nucleophiles. In this present invention, intermediates 2 were reacted with different amines and alcohols to give 3 and 5 respectively.

The third chlorine atom in intermediates 3 and 5 was replaced with 4-aminoaryl and aminoheteroaryl boronic acid in the presence of $(Ph_3)_4P(Pd)$/ Na_2CO_3/ DME/ Reflux or microwave condition to yield 4 and 8 respectively. The amino group was converted to the urea derivatives by different two procedures depending upon the availability of the starting material. Some of the examples reported here were transformed into the urea derivative by reacting 4 or 8 with an appropriately substituted isocyanate derivative. Many of the urea derivatives reported here were prepared by reacting intermediates 4 or 8 with triphosgene/ Et_3N and an appropriately substituted primary amine derivative. The corresponding carbamate derivatives were prepared by reacting intermediates 4 or 8 with an appropriately substituted chloroformate reagents. The intermediates 2 were also used to prepare derivatives of 6, where in R is a alkyl, alkene, alkyne, aryl or heteroaryl. Reacting 6 with the appropriately substituted alkyl introduced alkyl or cycloalkyl groups in intermediate 6 or cycloalkyl magnesium bromide or the corresponding appropriately substituted organo- zinc reagent. Alkenes can be introduced in compound 6 by a Pd catalyzed appropriately substituted vinyl tin derivatives. Similarly, aryl or heteroaryl substituents can be introduced either by reacting 6 with the corresponding boronic acid (Suzuki coupling) or aryl or heteroaryl magnesium bromide. Alkynes can be introduced by reacting compound 6 with an appropriately substitute alkyne and Pd(0). The alkyne and the alkene introduced can also be functionally converted into other derivatives such as alkyl, alcohol and amine moieties. Detailed procedures are described in the experimental section for each derivative prepared.

Scheme 2

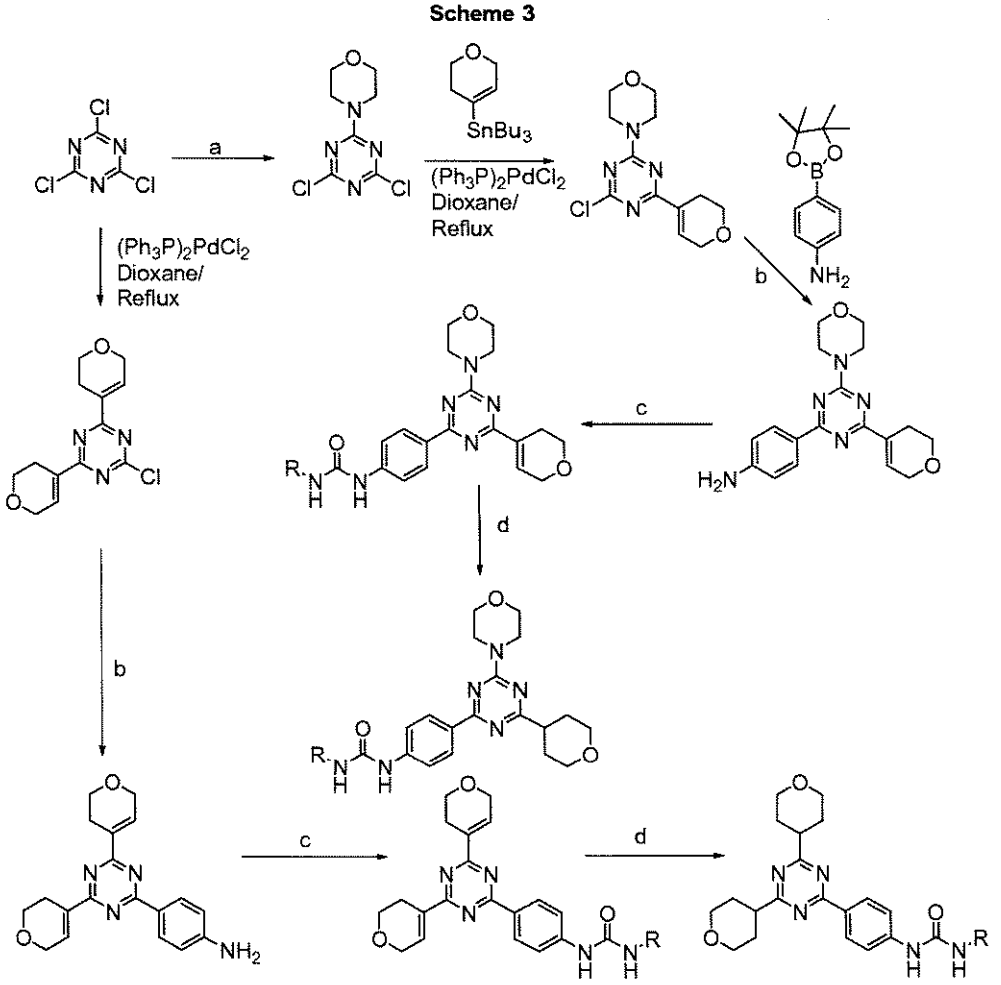
Scheme 2



(a) Acetone/ H_2O/ Et_3N/ -10 °C to Room temperature

Certain compounds of the invention were prepared by the methods outlined in Scheme 2.

Scheme 3

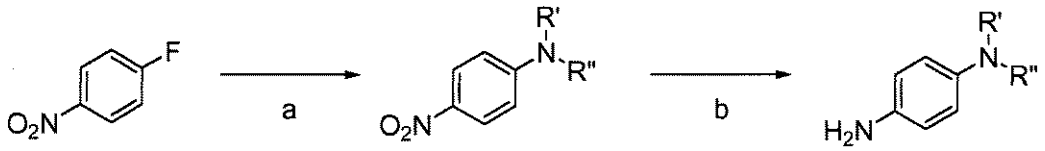


(a) 1 Eq. of morpholine/ Et_3N/ Acetone/ Water/ -20 ^{0}C; (b) $(Ph_3P)_4Pd$, DME, Na_2CO_3, Reflux; (c) RNCO, CH_2Cl_2, RT or $(COCl_2)_3$, RNH_2, Et_3N, $CHCl_3$; (d) H_2/ Pd (0)

Compounds of the invention were also prepared according to the method illustrated in Scheme 3.

Scheme 4

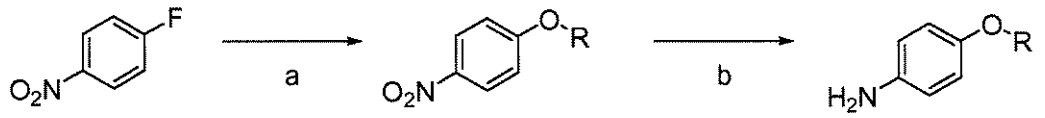
The benzene-1,4-diamine intermediates were prepared from 4-fluoronitrobenzene and



(a) NHR'R"/ toluene; (b) H_2/palladium on carbon, ethyl acetate, methanol.
NOTE: If either R' or R" = H or contain a nucleophilic amine, that amine was converted to its Boc derivative. Deprotection was accomplished following the final step of urea formation.

the appropriate amine as shown in Scheme 4.

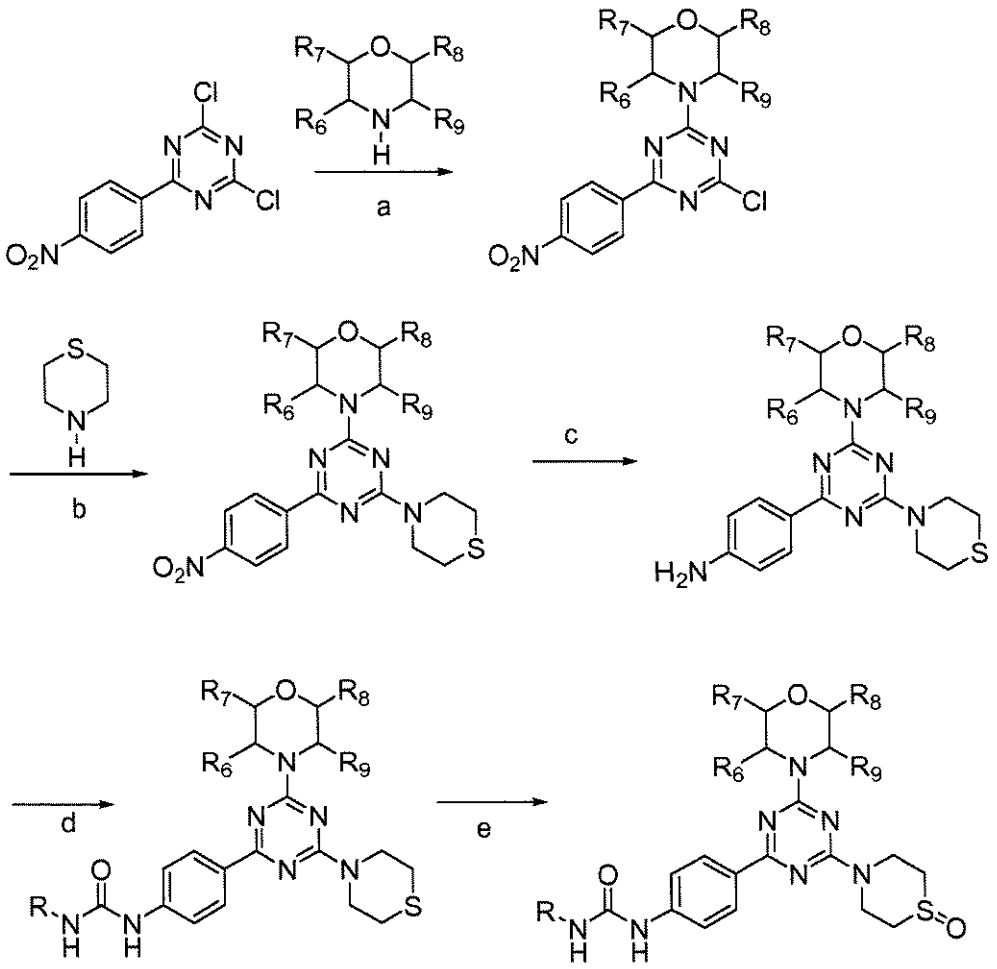
Scheme 5



(a) ROH/ NaH/ toluene; (b) H_2/palladium on carbon, ethyl acetate, methanol.
NOTE: If R contains a nucleophilic amine, that amine was converted to its Boc derivative. Deprotection was accomplished following the final step of urea formation.

The 4-(alkoxy)aniline intermediates were prepared from 4-fluoronitrobenzene and the appropriate alcohol as shown in Scheme 5.

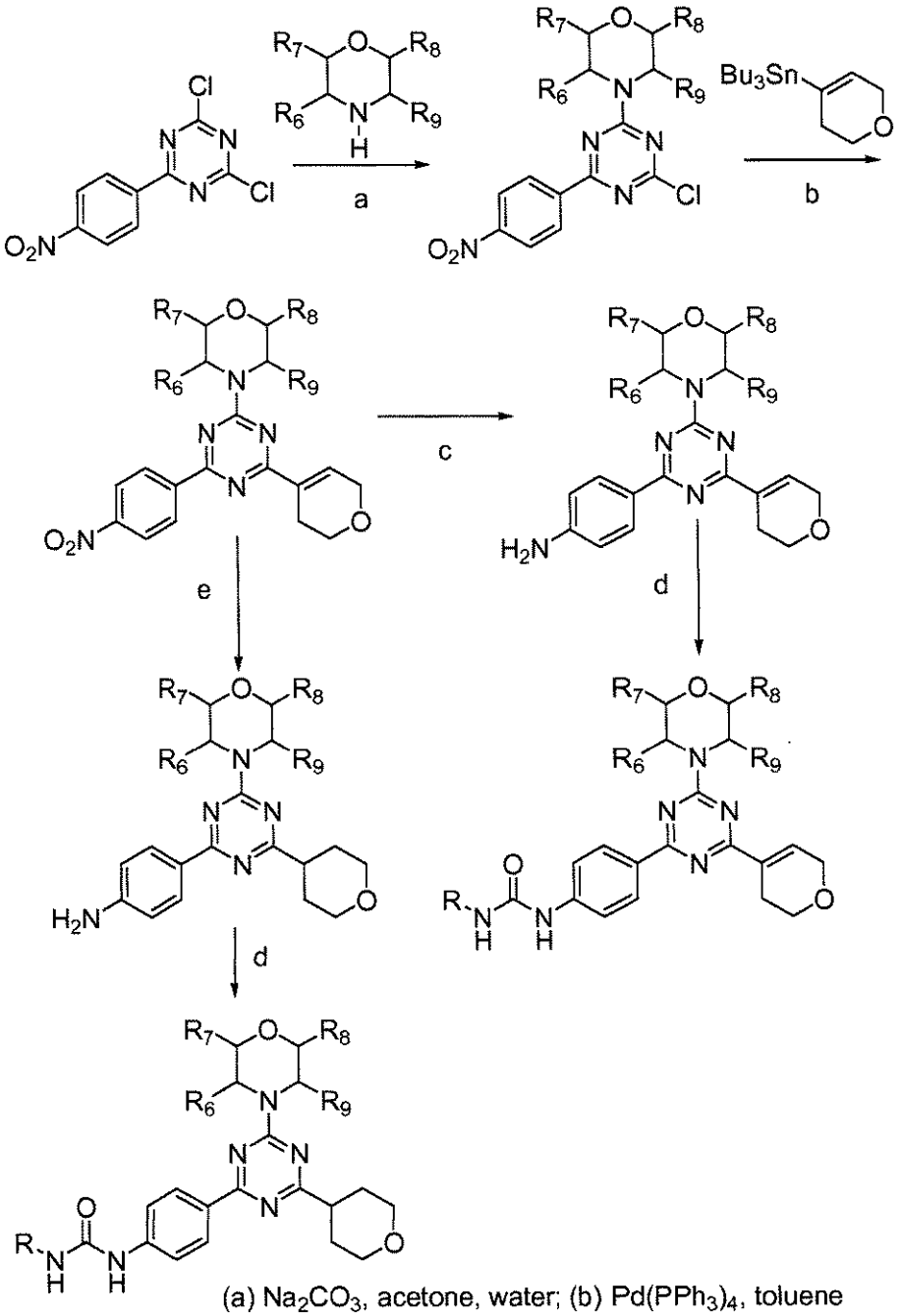
Scheme 6



(a) Na_2CO_3, acetone, water; (b) $NaHCO_3$, acetone, water
(c) $SnCl_2$, pyridine, DMF; (d) triphosgene, Et_3N, CH_2Cl_2, then RNH_2
(e) oxone, acetonitrile, water.

The thiomorpholine and bis morpholine compounds were prepared from 2,4-dichloro-6-(4-nitrophenyl)-1,3,5-triazine and the appropriate morpholine and thiomorpholine reagents as shown in Scheme 6.

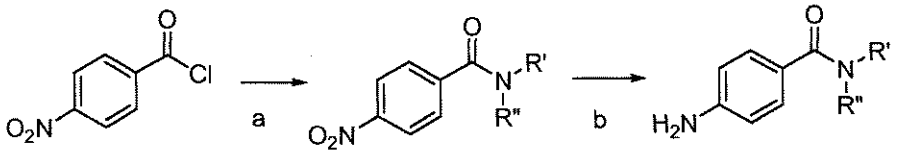
Scheme 7



(a) Na_2CO_3, acetone, water; (b) $Pd(PPh_3)_4$, toluene
(c) Fe, acetic acid, ethyl acetate, water
(d) triphosgene, Et_3N, CH_2Cl_2, then RNH_2
(e) H_2/Pd-C, ethyl acetate, methylene chloride, methanol.

The dihydropyran and tetrahydropyran compounds were prepared from 2,4-dichloro-6-(4-nitrophenyl)-1,3,5-triazine, tributyl(3,6-dihydro-2H-pyran-4-yl)stannane, and the appropriate morpholine as shown in Scheme 7.

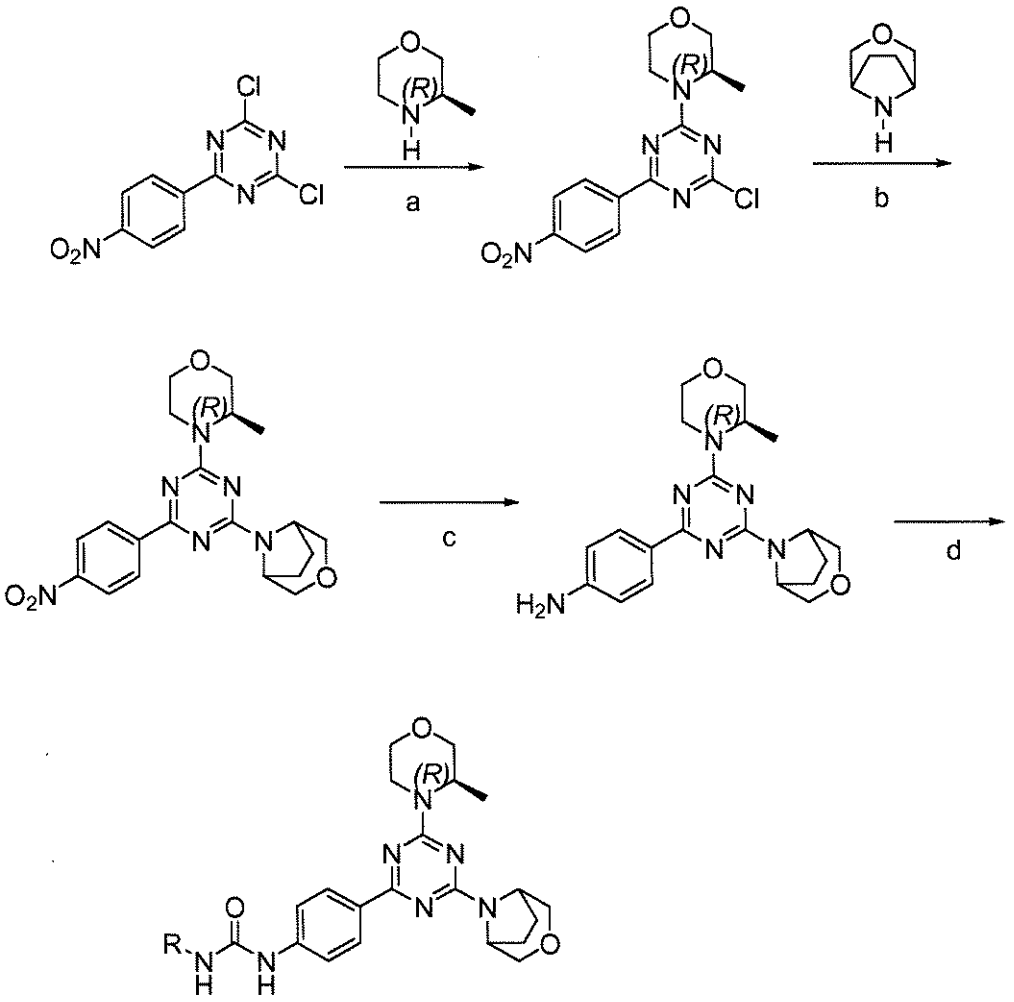
Scheme 8



(a) NHR'R", Et_3N, CH_2Cl_2
(b) H_2,/palladium on carbon, ethyl acetate, methanol.
NOTE: If R_1 or R_2 contain a nucleophilic amine, that amine was converted to its Boc derivative. Deprotection was accomplished following the final step of urea formation.

The (4-aminophenyl)(piperazin-1-yl)methanone intermediates were prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

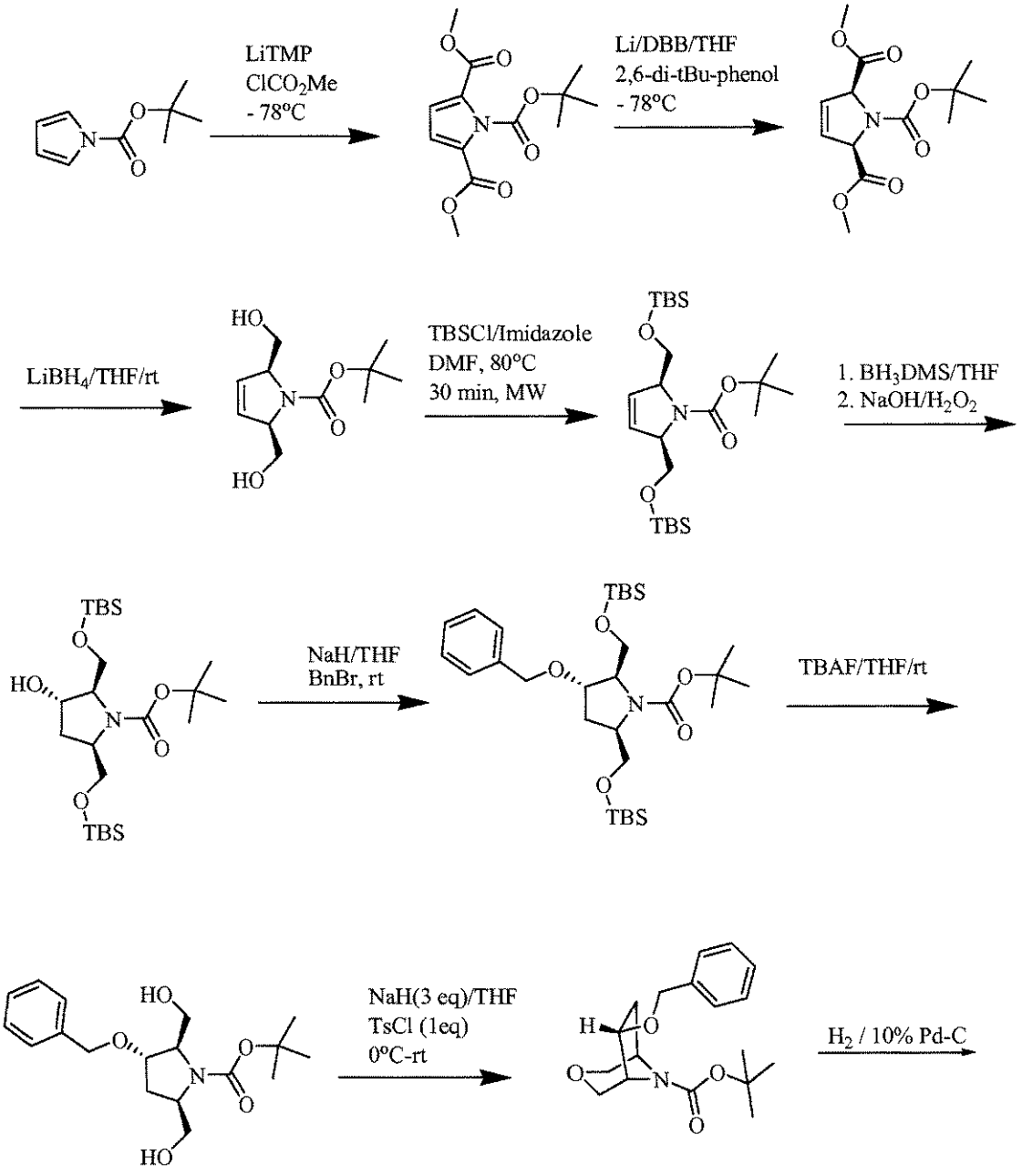
Scheme 9

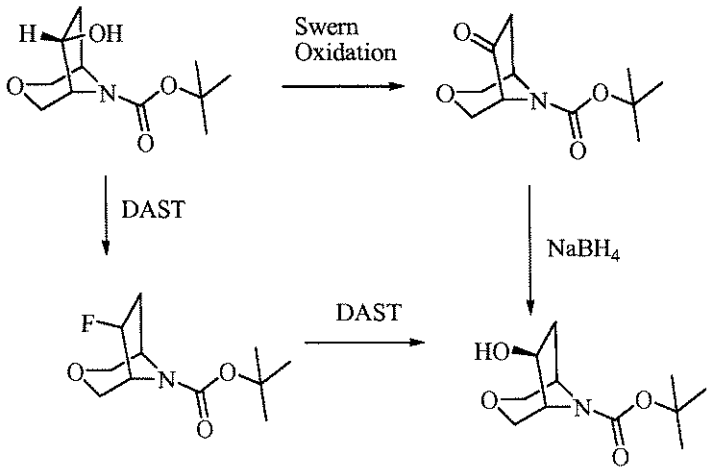


(a) Na_2CO_3, acetone, water; (b) $NaHCO_3$, acetone, water
(c) H_2-Pd-C, ethyl acetate, methylene chloride, methanol
(d) triphosgene, Et_3N, CH_2Cl_2, then RNH_2.

The 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-urea compounds were prepared from 2,4-dichloro-6-(4-nitrophenyl)-1,3,5-triazine, (R)-3-methylmorpholine, 3-oxa-8-azabicyclo[3.2.1]octane-hydrochloride, and the appropriate amine as shown in Scheme 9.

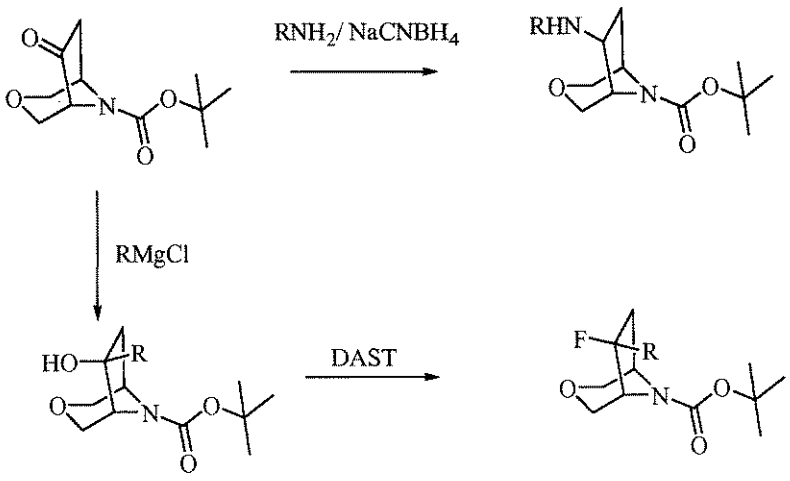
Scheme 10


LiTMP
ClCO2Me
- 78°C
Li/DBB/THF
2,6-di-tBu-phenol
- 78°C
LiBH4/THF/rt
TBSCl/Imidazole
DMF, 80°C
30 min, MW
1. BH3DMS/THF
2. NaOH/H2O2
NaH/THF
BnBr, rt
TBAF/THF/rt
NaH(3 eq)/THF
TsCl (1eq)
0°C-rt
H2 / 10% Pd-C



The preparation of both the (6S') and (6R') isomers of tert-butyl 6-hydroxy-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate from tert-butyl 1H-pyrrole-1-carboxylate is shown in Scheme 10.

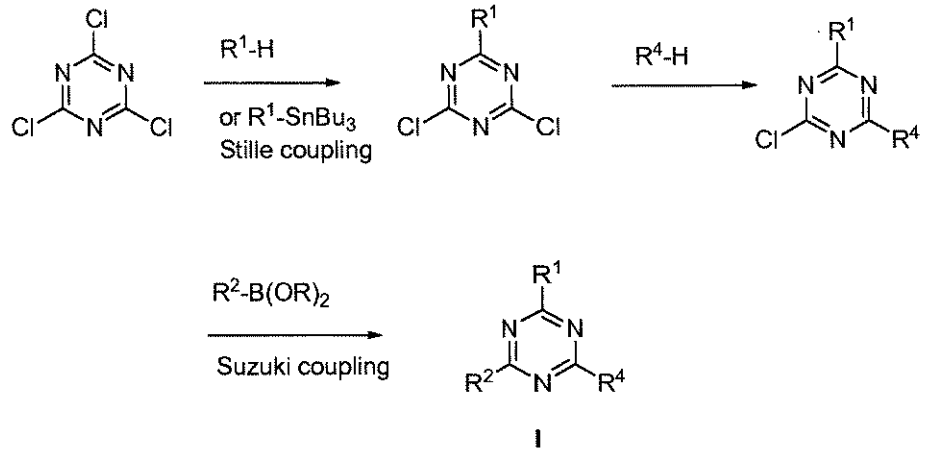
Scheme 11



R = Alkyl, aryl or heteroaryl

The (6S')-tert-butyl 6-amino-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate and (6R')-tert-butyl 6-fluoro-6-(alkyl, aryl, or heteroaryl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate compounds could be prepared from tert-butyl 6-oxo-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (Scheme 10) and the appropriate amine or Grignard reagent as shown in Scheme 11.

Scheme 12



I

Compounds of formula I can be prepared from cyanuric chloride as shown in Scheme 12.

DEFINITIONS

The following definitions are used in connection with the compounds of the present invention unless the context indicates otherwise. In general, the number of carbon atoms present in a given group is designated "C_x-C_y", where x and y are the lower and upper limits, respectively. For example, a group designated as "C_1-C_6" contains from 1 to 6 carbon atoms. The carbon number as used in the definitions herein refers to carbon backbone and carbon branching, but does not include carbon atoms of the substituents, such as alkoxy substitutions and the like. Unless indicated otherwise, the nomenclature of substituents that are not explicitly defined herein are arrived at by naming from left to right the terminal portion of the functionality followed by the adjacent functionality toward the point of attachment. For example, the substituent "arylalkyloxycabonyl" refers to the group (C_6-C_{14}aryl)-(C_1-C_6alkyl)-O-C(O)-. Terms not defined herein have the meaning commonly attributed to them by those skilled in the art.

"Acyl-" refers to a group having a straight, branched, or cyclic configuration or a combination thereof, attached to the parent structure through a carbonyl functionality. Such groups may be saturated or unsaturated, aliphatic or aromatic, and carbocyclic or heterocyclic. Examples of a C_1-C_8acyl- group include acetyl-, benzoyl-, nicotinoyl-, propionyl-, isobutyryl-, oxalyl-, and the like. Lower-acyl refers to acyl groups containing one to four carbons. An acyl group can be unsubstituted or substituted with one or more of the following groups: halogen, H_2N-, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, H_2NC(O)-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, -CN, hydroxyl, C_1-C_6alkoxy-, C_1-C_6alkyl-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, or C_3-C_8cycloalkyl-.

"Alkyl" refers to a hydrocarbon chain that may be a straight chain or branched chain, containing the indicated number of carbon atoms, for example, a C_1-C_{12}alkyl group may have from 1 to 12 (inclusive) carbon atoms in it. Examples of C_1-C_6alkyl groups include, but are not limited to, methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, and isohexyl. Examples of C_1-C_8alkyl groups include, but are not limited to, methyl, propyl, pentyl, hexyl, heptyl, 3-methylhex-1-yl, 2,3-dimethylpent-2-yl, 3-ethylpent-1-yl, octyl, 2-methylhept-2-yl, 2,3-dimethylhex-1-yl, and 2,3,3-trimethylpent-1-yl. An alkyl group can be unsubstituted or substituted with one or more groups, including: halogen, $-NH_2$, (C_1-C_6alkyl)NH, (C_1-C_6alkyl)(C_1-C_6alkyl)N-, -N(C_1-C_3alkyl)C(O)(C_1-C_6alkyl), -NHC(O)(C_1-C_6alkyl), -NHC(O)H, $-C(O)NH_2$, -C(O)NH(C_1-C_6alkyl), -C(O)N(C_1-C_6alkyl)(C_1-C_6alkyl), -CN, hydroxyl, C_1-C_6alkoxy, C_1-C_6alkyl, -C(O)OH, -C(O)O(C_1-C_6alkyl), -C(O)(C_1-C_6alkyl), C_6-C_{14}aryl, C_1-C_9heteroaryl, C_3-C_8cycloalkyl, C_1-C_6haloalkyl-, C_1-C_6aminoalkyl-, -OC(O)(C_1-C_6alkyl), C_1-C_6carboxyamidoalkyl-, and $-NO_2$.

"Alkadienyl" refer to a straight or branched chain unsaturated hydrocarbon containing at least two double bonds, and either may exist in the E or Z conformation. Examples of a C_4-

C_6alkadienyl group include, but are not limited to, buta-1,3-dienyl, buta-2,3-dienyl, isoprenyl, penta-1,3-dienyl, and penta-2,4-dien-2-yl.

"Alkadiynyl" refer to a straight or branched chain unsaturated hydrocarbon containing at least two triple bonds. Examples of a C_4-C_6alkadiynyl group include, but are not limited to, buta-1,3-diynyl, buta-2,3-diynyl, penta-1,3-diynyl, and penta-2,4-diynyl.

"Alkenyl" refer to a straight or branched chain unsaturated hydrocarbon containing at least one double bond, and may exist in the E or Z conformation. Examples of a C_2-C_8alkenyl group include, but are not limited to, ethylene, propylene, 1-butylene, 2-butylene, isobutylene, sec-butylene, 1-pentene, 2-pentene, isopentene, 1-hexene, 2-hexene, 3-hexene, isohexene, 1-heptene, 2-heptene, 3-heptene, 1-octene, 2-octene, 3-octene, and 4-octene. Examples of a C_2-C_6alkenyl group include, but are not limited to, ethylene, propylene, 1-butylene, 2-butylene, isobutylene, sec-butylene, 1-pentene, 2-pentene, isopentene, 1-hexene, 2-hexene, 3-hexene, and isohexene. Examples of a C_3-C_8alkenyl group include, but are not limited to, propylene, 1-butylene, 2-butylene, isobutylene, sec-butylene, 1-pentene, 2-pentene, isopentene, 1-hexene, 2-hexene, 3-hexene, isohexene, 1-heptene, 2-heptene, 3-heptene, 1-octene, 2-octene, 3-octene, and 4-octene. Examples of a C_3-C_6alkenyl group include, but are not limited to, prop-2-enyl, but-3-enyl, but-2-enyl, 2-methyallyl, pent-4-enyl, and hex-5-enyl. An alkenyl group can be unsubstituted or substituted with one or more groups, including: halogen, -NH_2, (C_1-C_6alkyl)NH-, (C_1-C_6alkyl)(C_1-C_6alkyl)N-, -N(C_1-C_3alkyl)C(O)(C_1-C_6alkyl), -NHC(O)(C_1-C_6alkyl), -NHC(O)H, -C(O)NH2, -C(O)NH(C_1-C_6alkyl), -C(O)N(C_1-C_6alkyl)(C_1-C_6alkyl), -CN, hydroxyl, C_1-C_6alkoxy, C_1-C_6alkyl, -C(O)OH, -C(O)O(C_1-C_6alkyl), -C(O)(C_1-C_6alkyl), C_6-C_{14}aryl, C_1-C_9heteroaryl, and C_3-C_8cycloalkyl.

"Alkynyl" refers to a straight or branched chain unsaturated hydrocarbon containing at least one triple bond. Examples of a C_2-C_6alkynyl group include, but are not limited to, acetylene, propyne, 1-butyne, 2-butyne, isobutyne, sec-butyne, 1-pentyne, 2-pentyne, isopentyne, 1-hexyne, 2-hexyne, 3-hexyne, and isohexyne. Examples of a C_3-C_6alkynyl group include, but are not limited to, prop-2-ynyl, but-3-ynyl, but-2-ynyl, pent-4-ynyl, and hex-5-ynyl. Examples of a C_3-C_8alkynyl group include, but are not limited to, prop-2-ynyl, but-3-ynyl, but-2-ynyl, pent-4-ynyl, hex-5-ynyl, hept-3-ynyl, 2-methylhex-3-ynyl, oct-4-ynyl, and 2-methylhept-3-ynyl. An alkynyl group can be unsubstituted or substituted with one or more groups, including: halogen, -NH_2, (C_1-C_6alkyl)NH, (C_1-C_6alkyl)(C_1-C_6alkyl)N-, -N(C_1-C_3alkyl)C(O)(C_1-C_6alkyl), -NHC(O)(C_1-C_6alkyl), -NHC(O)H, -C(O)NH2, -C(O)NH(C_1-C_6alkyl), -C(O)N(C_1-C_6alkyl)(C_1-C_6alkyl), -CN, hydroxyl, C_1-C_6alkoxy, C_1-C_6alkyl, -C(O)OH, -C(O)O(C_1-C_6alkyl), -C(O)(C_1-C_6alkyl), C_6-C_{14}aryl, C_1-C_9heteroaryl, and C_3-C_8cycloalkyl.

"Alkoxy-" refers to the group R-O- where R is an alkyl group, as defined above. Exemplary C_1-C_6alkoxy- groups include but are not limited to methoxy, ethoxy, n-propoxy, 1-propoxy, n-butoxy and t-butoxy. An alkoxy group can be unsubstituted or substituted with one or

more of the following groups: halogen, hydroxyl, C_1-C_6alkoxy-, H_2N-, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, $H_2NC(O)$-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, NC-, C_1-C_6alkoxy-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, C_3-C_8cycloalkyl-, C_1-C_6haloalkyl-, amino(C_1-C_6alkyl)-, (C_1-C_6alkyl)carboxyl-, C_1-C_6carboxyamidoalkyl-, or O_2N-.

"(Alkoxy)carbonyl-" refers to the group alkyl-O-C(O)-. Exemplary (C_1-C_6alkoxy)carbonyl- groups include but are not limited to methoxy, ethoxy, n-propoxy, 1-propoxy, n-butoxy and t-butoxy. An (alkoxy)carbonyl group can be unsubstituted or substituted with one or more of the following groups: halogen, hydroxyl, H_2N-, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, $H_2NC(O)$-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, NC-, C_1-C_6alkoxy-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, C_3-C_8cycloalkyl-, C_1-C_6haloalkyl-, amino(C_1-C_6alkyl)-, (C_1-C_6alkyl)carboxyl-, C_1-C_6carboxyamidoalkyl-, or O_2N-.

"(Alkyl)amido-" refers to a -C(O)NH- group in which the nitrogen atom of said group is attached to a C_1-C_6alkyl group, as defined above. Representative examples of a (C_1-C_6alkyl)amido- group include, but are not limited to, $-C(O)NHCH_3$, $-C(O)NHCH_2CH_3$, $-C(O)NHCH_2CH_2CH_3$, $-C(O)NHCH_2CH_2CH_2CH_3$, $-C(O)NHCH_2CH_2CH_2CH_2CH_3$, $-C(O)NHCH(CH_3)_2$, $-C(O)NHCH_2CH(CH_3)_2$, $-C(O)NHCH(CH_3)CH_2CH_3$, $-C(O)NH-C(CH_3)_3$ and $-C(O)NHCH_2C(CH_3)_3$.

"(Alkyl)amino-" refers to an -NH group, the nitrogen atom of said group being attached to a alkyl group, as defined above. Representative examples of an (C_1-C_6alkyl)amino- group include, but are not limited to CH_3NH-, CH_3CH_2NH-, $CH_3CH_2CH_2NH$-, $CH_3CH_2CH_2CH_2NH$-, $(CH_3)_2CHNH$-, $(CH_3)_2CHCH_2NH$-, $CH_3CH_2CH(CH_3)NH$- and $(CH_3)_3CNH$-. An (alkyl)amino group can be unsubstituted or substituted with one or more of the following groups: halogen, H_2N-, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, $H_2NC(O)$-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, NC-, hydroxyl, C_1-C_6alkoxy-, C_1-C_6alkyl-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, C_3-C_8cycloalkyl-, C_1-C_6haloalkyl-, amino(C_1-C_6alkyl)-, (C_1-C_6alkyl)carboxyl-, C_1-C_6carboxyamidoalkyl-, or O_2N-.

"Aminoalkyl-" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with $-NH_2$; one or both H of the NH_2 may be replaced by a substituent.

"Alkylcarboxyl-" refers to an alkyl group, defined above that is attached to the parent structure through the oxygen atom of a carboxyl (C(O)-O-) functionality. Examples of (C_1-C_6alkyl)carboxyl- include acetoxy, propionoxy, propylcarboxyl, and isopentylcarboxyl.

"(Alkyl)carboxyamido-" refers to a -NHC(O)- group in which the carbonyl carbon atom of said group is attached to a C_1-C_6alkyl group, as defined above. Representative examples of a

(C_1-C_6alkyl)carboxyamido- group include, but are not limited to, -NHC(O)CH_3, -NHC(O)CH_2CH_3, -NHC(O)$CH_2CH_2CH_3$, -NHC(O)$CH_2CH_2CH_2CH_3$, -NHC(O)$CH_2CH_2CH_2CH_2CH_3$, -NHC(O)$CH(CH_3)_2$, -NHC(O)$CH_2CH(CH_3)_2$, -NHC(O)$CH(CH_3)CH_2CH_3$, -NHC(O)-$C(CH_3)_3$ and -NHC(O)$CH_2C(CH_3)_3$.

"Alkylene", "alkenylene", and "alkynylene" refers to alkyl, alkenyl and alkynyl groups, as defined above, having two points of attachment within a chemical structure. Examples of C_1-C_6alkylene include ethylene, propylene, and dimethylpropylene. Likewise, examples of C_2-C_6alkenylene include ethenylene and propenylene. Examples of C_2-C_6alkynylene include ethynylene and propynylene.

Aryl refers to an aromatic hydrocarbon group. Examples of a C_6-C_{14}aryl group include, but are not limited to, phenyl, α-naphthyl, β-naphthyl, biphenyl, anthryl, tetrahydronaphthyl, fluorenyl, indanyl, biphenylenyl, and acenanaphthyl. Examples of a C_6-C_{10}aryl group include, but are not limited to, phenyl, α-naphthyl, β-naphthyl, biphenyl, and tetrahydronaphthyl. An aryl group can be unsubstituted or substituted with one or more groups, including: C_1-C_6alkyl, halo, haloalkyl-, hydroxyl, hydroxyl(C_1-C_6alkyl)-, -NH_2, aminoalkyl-, dialkylamino-, -COOH, -C(O)O-(C_1-C_6alkyl), -OC(O)(C_1-C_6alkyl), N-alkylamido-, -C(O)NH_2, (C_1-C_6alkyl)amido-, or -NO_2.

"(Aryl)alkyl" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with an aryl group as defined above. (C_6-C_{14}Aryl)alkyl- moieties include benzyl, benzhydryl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 2-phenylpropyl, 1-naphthylmethyl, 2-naphthylmethyl and the like. An (aryl)alkyl group can be unsubstituted or substituted with one or more of the following groups: halogen, H_2N-, hydroxyl, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, $H_2NC(O)$-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, NC-, hydroxyl, C_1-C_6alkoxy-, C_1-C_6alkyl-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, C_3-C_8cycloalkyl-, C_1-C_6haloalkyl-, amino(C_1-C_6alkyl)-, (C_1-C_6alkyl)carboxyl-, C_1-C_6carboxyamidoalkyl-, or O_2N-.

"(Aryl)amino" refers to a radical of formula (aryl)-NH-, wherein aryl is as defined above. "(Aryl)oxy" refers to the group Ar-O- where Ar is an aryl group, as defined above.

"Cycloalkyl" refers to a non-aromatic, saturated, monocyclic, bicyclic or polycyclic hydrocarbon ring system. Representative examples of a C_3-C_{12}cycloalkyl include, but are not limited to, cyclopropyl, cyclopentyl, cycloheptyl, cyclooctyl, decahydronaphthalen-1-yl, octahydro-1H-inden-2-yl, decahydro-1H-benzo[7]annulen-2-yl, and dodecahydros-indacen-4-yl. Representative examples of a C_3-C_{10}cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, decahydronaphthalen-1-yl, and octahydro-1H-inden-2-yl. Representative examples of a C_3-C_8cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, and octahydropentalen-2-yl. A cycloalkyl can be unsubstituted or substituted with one or more

groups, including: halogen, -NH_2, (C_1-C_6alkyl)NH, (C_1-C_6alkyl)(C_1-C_6alkyl)N-, -N(C_1-C_3alkyl)C(O)(C_1-C_6alkyl), -NHC(O)(C_1-C_6alkyl), -NHC(O)H, -C(O)NH_2, -C(O)NH(C_1-C_6alkyl), -C(O)N(C_1-C_6alkyl)(C_1-C_6alkyl), -CN, hydroxyl, C_1-C_6alkoxy, C_1-C_6alkyl, -C(O)OH, -C(O)O(C_1-C_6alkyl), -C(O)(C_1-C_6alkyl), C_6-C_{14}aryl, C_1-C_9heteroaryl, C_3-C_8cycloalkyl, C_1-C_6haloalkyl-, C_1-C_6aminoalkyl-, -OC(O)(C_1-C_6alkyl), C_1-C_6carboxyamidoalkyl-, and -NO_2. Additionally, each of any two hydrogen atoms on the same carbon atom of the carbocyclic ring can be replaced by an oxygen atom to form an oxo (=O) substituent.

"Cycloalkenyl" refers to a non-aromatic, unsaturated, monocyclic, bicyclic or polycyclic hydrocarbon ring system containing at least one double bond connecting two ring carbon atoms. Representative examples of a C_5-C_8cycloalkenyl include, but are not limited to, cyclopentenyl, cyclohexenyl, 4,4a-octalin-3-yl, and cyclooctenyl. A cycloalkenyl can be unsubstituted or substituted with one or more groups, including: halogen, -NH_2, (C_1-C_6alkyl)NH, (C_1-C_6alkyl)(C_1-C_6alkyl)N-, -N(C_1-C_3alkyl)C(O)(C_1-C_6alkyl), -NHC(O)(C_1-C_6alkyl), -NHC(O)H, -C(O)NH_2, -C(O)NH(C_1-C_6alkyl), -C(O)N(C_1-C_6alkyl)(C_1-C_6alkyl), -CN, hydroxyl, C_1-C_6alkoxy, C_1-C_6alkyl, -C(O)OH, -C(O)O(C_1-C_6alkyl), -C(O)(C_1-C_6alkyl), C_6-C_{14}aryl, C_1-C_9heteroaryl, and C_3-C_8cycloalkyl. Additionally, each of any two hydrogen atoms on the same carbon atom of the carbocyclic ring can be replaced by an oxygen atom to form an oxo (=O) substituent.

"Di(alkyl)amino-" refers to a nitrogen atom attached to two alkyl groups, as defined above. Each alkyl group can be independently selected. Representative examples of an di(C_1-C_6alkyl)amino- group include, but are not limited to, -$N(CH_3)_2$, -$N(CH_2CH_3)(CH_3)$, -$N(CH_2CH_3)_2$, -$N(CH_2CH_2CH_3)_2$, -$N(CH_2CH_2CH_2CH_3)_2$, -$N(CH(CH_3)_2)_2$, -$N(CH(CH_3)_2)(CH_3)$, -$N(CH_2CH(CH_3)_2)_2$, -$NH(CH(CH_3)CH_2CH_3)_2$, -$N(C(CH_3)_3)_2$, -$N(C(CH_3)_3)(CH_3)$, and -$N(CH_3)(CH_2CH_3)$. The two alkyl groups on the nitrogen atom, when taken together with the nitrogen to which they are attached, can form a 3- to 7- membered nitrogen containing heterocycle wherein up to two of the carbon atoms of the heterocycle can be replaced with -N(H)-, -N(C_1-C_6alkyl)-, -N(C_3-C_8cycloalkyl)-, -N(C_6-C_{14}aryl)-, -N(C_1-C_9heteroaryl)-, -N(amino(C_1-C_6alkyl))-, -N(C_6-C_{14}arylamino)-, -O-, -S-, -S(O)-, or -$S(O)_2$-.

"Halo" or "halogen" refers to -F, -Cl, -Br and -I.

"C_1-C_6Haloalkyl-" refers to a C_1-C_6alkyl group, as defined above, wherein one or more of the C_1-C_6alkyl group's hydrogen atoms has been replaced with -F, -Cl, -Br, or -I. Each substitution can be independently selected from -F, -Cl, -Br, or -I. Representative examples of an C_1-C_6haloalkyl- group include, but are not limited to, -CH_2F, -CCl_3, -CF_3, CH_2CF_3, -CH_2Cl, -CH_2CH_2Br, -CH_2CH_2I, -$CH_2CH_2CH_2F$, -$CH_2CH_2CH_2Cl$, -$CH_2CH_2CH_2CH_2Br$, -CH_2CH_2 CH_2CH_2 I, -$CH_2CH_2CH_2CH_2CH_2Br$, -$CH_2CH_2CH_2CH_2CH_2I$, -$CH_2CH(Br)CH_3$, -CH_2 $CH(Cl)CH_2CH_3$, -$CH(F)CH_2CH_3$ and -$C(CH_3)_2(CH_2Cl)$.

"Heteroaryl" refers to a monocyclic, bicyclic, or polycyclic aromatic ring system containing at least one ring atom selected from the heteroatoms oxygen, sulfur and nitrogen.

Examples of C_1-C_9heteroaryl groups include furan, thiophene, indole, azaindole, oxazole, thiazole, isoxazole, isothiazole, imidazole, N-methylimidazole, pyridine, pyrimidine, pyrazine, pyrrole, N-methylpyrrole, pyrazole, N-methylpyrazole, 1,3,4-oxadiazole, 1,2,4-triazole, 1-methyl-1,2,4-triazole, 1H-tetrazole, 1-methyltetrazole, benzoxazole, benzothiazole, benzofuran, benzisoxazole, benzimidazole, N-methylbenzimidazole, azabenzimidazole, indazole, quinazoline, quinoline, and isoquinoline. Bicyclic C_1-C_9hetroaryl groups include those where a phenyl, pyridine, pyrimidine or pyridazine ring is fused to a 5 or 6-membered monocyclic heteroaryl ring having one or two nitrogen atoms in the ring, one nitrogen atom together with either one oxygen or one sulfur atom in the ring, or one O or S ring atom. Examples of monocyclic C_1-C_4heteroaryl groups include 2H-tetrazole, 3H-1,2,4-triazole, furan, thiophene, oxazole, thiazole, isoxazole, isothiazole, imidazole, and pyrrole. A heteroaryl group can be unsubstituted or substituted with one or more groups, including: C_1-C_6alkyl, halo, haloalkyl-, hydroxyl, hydroxyl(C_1-C_6alkyl)-, $-NH_2$, aminoalkyl-, dialkylamino-, -COOH, -C(O)O-(C_1-C_6alkyl), -OC(O)(C_1-C_6alkyl), N-alkylamido-, $-C(O)NH_2$, (C_1-C_6alkyl)amido-, or $-NO_2$.

"(Heteroaryl)alkyl-" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with a heteroaryl- group as defined above. Examples of (C_1-C_9heteroaryl)alkyl- moieties include 2-pyridylmethyl, 2-thiophenylethyl, 3-pyridylpropyl, 2-quinolinylmethyl, 2-indolylmethyl, and the like. A (heteroaryl)alkyl group can be unsubstituted or substituted with one or more of the following groups: halogen, H_2N-, hydroxyl, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, $H_2NC(O)$-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, NC-, hydroxyl, C_1-C_6alkoxy-, C_1-C_6alkyl-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, C_3-C_8cycloalkyl-, C_1-C_6haloalkyl-, amino(C_1-C_6alkyl)-, (C_1-C_6alkyl)carboxyl-, C_1-C_6carboxyamidoalkyl-, or O_2N-.

The term "heteroatom" refers to a sulfur, nitrogen, or oxygen atom.

"Heterocycle" or "heterocyclyl" refers to monocyclic, bicyclic and polycyclic groups in which at least one ring atom is a heteroatom. A heterocycle may be saturated or partially saturated. Exemplary C_1-C_9heterocyclyl- groups include but are not limited to aziridine, oxirane, oxirene, thiirane, pyrroline, pyrrolidine, dihydrofuran, tetrahydrofuran, dihydrothiophene, tetrahydrothiophene, dithiolane, piperidine, 1,2,3,6-tetrahydropyridine-1-yl, tetrahydropyran, pyran, thiane, thiine, piperazine, oxazine, 5,6-dihydro-4H-1,3-oxazin-2-yl, 2,5-diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.2]octane, 3,6-diazabicyclo[3.1.1]heptane, 3,8-diazabicyclo[3.2.1]octane, 6-oxa-3,8-diazabicyclo[3.2.1]octane, 7-oxa-2,5-diazabicyclo[2.2.2]octane, 2,7-dioxa-5-azabicyclo[2.2.2]octane, 2-oxa-5-azabicyclo[2.2.1]heptane-5-yl, 2-oxa-5-azabicyclo[2.2.2]octane, 3,6-dioxa-8-azabicyclo[3.2.1]octane, 3-oxa-6-azabicyclo[3.1.1]heptane, 3-oxa-8-azabicyclo[3.2.1]octan-8-yl, 5,7-dioxa-2-azabicyclo[2.2.2]octane, 6,8-dioxa-3-azabicyclo[3.2.1]octane, 6-oxa-3-

azabicyclo[3.1.1]heptane, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, 2-methyl-2,5-diazabicyclo[2.2.1]heptane-5-yl, 1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl, 3-hydroxy-8-azabicyclo[3.2.1]octan-8-yl-, 7-methyl-3-oxa-7,9-diazabicyclo[3.3.1]nonan-9-yl, 9-oxa-3-azabicyclo[3.3.1]nonan-3-yl, 3-oxa-9-azabicyclo[3.3.1]nonan-9-yl, 3,7-dioxa-9-azabicyclo[3.3.1]nonan-9-yl, 4-methyl-3,4-dihydro-2H-1,4-benzoxazin-7-yl, thiazine, dithiane, and dioxane. The contemplated heterocycle rings or ring systems have a minimum of 3 members. Therefore, for example, C_1heterocyclyl- radicals would include but are not limited to oxaziranyl, diaziridinyl, and diazirinyl, C_2heterocyclyl- radicals include but are not limited to aziridinyl, oxiranyl, and diazetidinyl, C_9heterocyclyl- radicals include but are not limited to azecanyl, tetrahydroquinolinyl, and perhydroisoquinolinyl. A heterocyclyl group can be unsubstituted or substituted with one or more groups, including: C_1-C_6alkyl, halo, haloalkyl-, hydroxyl, hydroxyl(C_1-C_6alkyl)-, -NH_2, aminoalkyl-, dialkylamino-, -COOH, -C(O)O-(C_1-C_6alkyl), -OC(O)(C_1-C_6alkyl), N-alkylamido-, -C(O)NH_2, (C_1-C_6alkyl)amido-, or -NO_2.

"Heterocyclyl(alkyl)-" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with a heterocycle group as defined above. Heterocyclyl(C_1-C_6alkyl)- moieties include 2-pyridylmethyl, 1-piperazinylethyl, 4-morpholinylpropyl, 6-piperazinylhexyl, and the like. A heterocyclyl(alkyl) group can be unsubstituted or substituted with one or more of the following groups: halogen, H_2N-, (C_1-C_6alkyl)amino-, di(C_1-C_6alkyl)amino-, (C_1-C_6alkyl)C(O)N(C_1-C_3alkyl)-, (C_1-C_6alkyl)carboxyamido-, HC(O)NH-, H_2NC(O)-, (C_1-C_6alkyl)NHC(O)-, di(C_1-C_6alkyl)NC(O)-, NC-, hydroxyl, C_1-C_6alkoxy-, C_1-C_6alkyl-, HO_2C-, (C_1-C_6alkoxy)carbonyl-, (C_1-C_6alkyl)C(O)-, 4- to 7-membered monocyclic heterocycle, C_6-C_{14}aryl-, C_1-C_9heteroaryl-, or C_3-C_8cycloalkyl-.

"Hydroxylalkyl-" refers to a alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with hydroxyl groups. Examples of C_1-C_6hydroxylalkyl- moieties include, for example, -CH_2OH, -CH_2CH_2OH, -$CH_2CH_2CH_2OH$, -$CH_2CH(OH)CH_2OH$, -$CH_2CH(OH)CH_3$, -$CH(CH_3)CH_2OH$ and higher homologs.

"Monocyclic heterocyclyl" refers to monocyclic groups in which at least one ring atom is a heteroatom. A heterocycle may be saturated or partially saturated. Exemplary monocyclic C_1-C_9heterocyclyl- groups include but are not limited to aziridine, oxirane, oxirene, thiirane, pyrroline, pyrrolidine, dihydrofuran, tetrahydrofuran, dihydrothiophene, tetrahydrothiophene, dithiolane, piperidine, 1,2,3,6-tetrahydropyridine-1-yl, tetrahydropyran, pyran, thiane, thiine, piperazine, oxazine, 5,6-dihydro-4H-1,3-oxazin-2-yl, 4-methyl-3,4-dihydro-2H-1,4-benzoxazin-7-yl, thiazine, dithiane, and dioxane. The contemplated heterocycle ring systems have a minimum of 3 members. Therefore, for example, C_1heterocyclyl- radicals would include but are not limited to oxaziranyl, diaziridinyl, and diazirinyl, C_2heterocyclyl- radicals include but are not limited to aziridinyl, oxiranyl, and diazetidinyl, C_9heterocyclyl- radicals include but are not limited to azecanyl. A heterocyclyl group can be unsubstituted or substituted with one or more groups,

including: C_1-C_6alkyl, halo, haloalkyl-, hydroxyl, hydroxyl(C_1-C_6alkyl)-, -NH_2, aminoalkyl-, dialkylamino-, -COOH, -C(O)O-(C_1-C_6alkyl), -OC(O)(C_1-C_6alkyl), N-alkylamido-, -C(O)NH_2, (C_1-C_6alkyl)amido-, or -NO_2.

"Perfluoroalkyl-" refers to alkyl group, defined above, having two or more fluorine atoms. Examples of a C_1-C_6perfluoroalkyl- group include CF_3, CH_2CF_3, CF_2CF_3 and $CH(CF_3)_2$.

A "subject" is a mammal, e.g., a human, mouse, rat, guinea pig, dog, cat, horse, cow, pig, or non-human primate, such as a monkey, chimpanzee, baboon or gorilla.

The term "optionally substituted" as used herein means that at least one hydrogen atom of the optionally substituted group has been substituted with halogen, -NH_2, -NH(C_1-C_6alkyl), -N(C_1-C_6alkyl)(C_1-C_6alkyl), -N(C_1-C_3alkyl)C(O)(C_1-C_6alkyl), -NHC(O)(C_1-C_6alkyl), -NHC(O)H, -C(O)NH_2, -C(O)NH(C_1-C_6alkyl), -C(O)N(C_1-C_6alkyl)(C_1-C_6alkyl), -CN, hydroxyl, C_1-C_6alkoxy, C_1-C_6alkyl, -C(O)OH, -C(O)O(C_1-C_6alkyl), -C(O)(C_1-C_6alkyl), C_6-C_{14}aryl, C_1-C_9heteroaryl, or C_3-C_8cycloalkyl.

Representative "pharmaceutically acceptable salts" include but are not limited to, *e.g.*, water-soluble and water-insoluble salts, such as the acetate, aluminum, amsonate (4,4-diaminostilbene-2,2-disulfonate), benzathine (N,N'-dibenzylethylenediamine), benzenesulfonate, benzoate, bicarbonate, bismuth, bisulfate, bitartrate, borate, bromide, butyrate, calcium, calcium edetate, camsylate (camphorsulfonate), carbonate, chloride, choline, citrate, clavulariate, diethanolamine, dihydrochloride, diphosphate, edetate, edisylate (camphorsulfonate), esylate (ethanesulfonate), ethylenediamine, fumarate, gluceptate (glucoheptonate), gluconate, glucuronate, glutamate, hexafluorophosphate, hexylresorcinate, hydrabamine (N,N'-bis(dehydroabietyl)ethylenediamine), hydrobromide, hydrochloride, hydroxynaphthoate, 1-hydroxy-2-naphthoate, 3-hydroxy-2-naphthoate, iodide, isothionate (2-hydroxyethanesulfonate), lactate, lactobionate, laurate, lauryl sulfate, lithium, magnesium, malate, maleate, mandelate, meglumine (1-deoxy-1-(methylamino)-D-glucitol), mesylate, methyl bromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, N-methylglucamine ammonium salt, oleate, oxalate, palmitate, pamoate (4,4'-methylenebis-3-hydroxy-2-naphthoate, or embonate), pantothenate, phosphate, picrate, polygalacturonate, potassium, propionate, p-toluenesulfonate, salicylate, sodium, stearate, subacetate, succinate, sulfate, sulfosaliculate, suramate, tannate, tartrate, teoclate (8-chloro-3,7-dihydro-1,3-dimethyl-1H-purine-2,6-dione), triethiodide, tromethamine (2-amino-2-(hydroxymethyl)-1,3-propanediol), valerate, and zinc salts.

An "effective amount" when used in connection with a compound of this invention is an amount effective for inhibiting mTOR or PI3K in a subject.

Some compounds within the present invention possess one or more chiral centers, and the present invention includes each separate enantiomer of such compounds as well as mixtures of the enantiomers. Where multiple chiral centers exist in compounds of the present invention, the invention includes each combination as well as mixtures thereof. All chiral,

diastereomeric, and racemic forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials.

The compounds of the present invention exhibit an mTOR inhibitory activity and therefore, can be utilized in order to inhibit abnormal cell growth in which mTOR plays a role. Thus, the compounds of the present invention are effective in the treatment of disorders with which abnormal cell growth actions of mTOR are associated, such as restenosis, atherosclerosis, bone disorders, arthritis, diabetic retinopathy, psoriasis, benign prostatic hypertrophy, atherosclerosis, inflammation, angiogenesis, immunological disorders, pancreatitis, kidney disease, cancer, *etc.* In particular, the compounds of the present invention possess excellent cancer cell growth inhibiting effects and are effective in treating cancers, preferably all types of solid cancers and malignant lymphomas, and especially, leukemia, skin cancer, bladder cancer, breast cancer, uterus cancer, ovary cancer, prostate cancer, lung cancer, colon cancer, pancreas cancer, renal cancer, gastric cancer, brain tumor, advanced renal cell carcinoma, acute lymphoblastic leukemia, malignant melanoma, soft-tissue or bone sarcoma, *etc.*

The compounds of the present invention exhibit a PI3 kinase inhibitory activity and, therefore, can be utilized in order to inhibit abnormal cell growth in which PI3 kinases play a role. Thus, the compounds of the present invention are effective in the treatment of disorders with which abnormal cell growth actions of PI3 kinases are associated, such as restenosis, atherosclerosis, bone disorders, arthritis, diabetic retinopathy, psoriasis, benign prostatic hypertrophy, atherosclerosis, inflammation, angiogenesis, immunological disorders, pancreatitis, kidney disease, cancer, *etc.* In particular, the compounds of the present invention possess excellent cancer cell growth inhibiting effects and are effective in treating cancers, preferably all types of solid cancers and malignant lymphomas, and especially, leukemia, skin cancer, bladder cancer, breast cancer, uterus cancer, ovary cancer, prostate cancer, lung cancer, colon cancer, pancreas cancer, renal cancer, gastric cancer, brain tumor, advanced renal cell carcinoma, acute lymphoblastic leukemia, malignant melanoma, soft-tissue or bone sarcoma, *etc.*

For therapeutic use, the pharmacologically active compounds of Formula I will normally be administered as a pharmaceutical composition comprising as the (or an) essential active ingredient at least one such compound in association with a solid or liquid pharmaceutically acceptable carrier and, optionally, with pharmaceutically acceptable adjutants and excipients employing standard and conventional techniques.

The pharmaceutical compositions of this invention include suitable dosage forms for oral, parenteral (including subcutaneous, intramuscular, intradermal and intravenous) bronchial or nasal administration. Thus, if a solid carrier is used, the preparation may be tableted, placed in a hard gelatin capsule in powder or pellet form, or in the form of a troche or lozenge. The

solid carrier may contain conventional excipients such as binding agents, fillers, tableting lubricants, disintegrants, wetting agents and the like. The tablet may, if desired, be film coated by conventional techniques. If a liquid carrier is employed, the preparation may be in the form of a syrup, emulsion, soft gelatin capsule, sterile vehicle for injection, an aqueous or non-aqueous liquid suspension, or may be a dry product for reconstitution with water or other suitable vehicle before use. Liquid preparations may contain conventional additives such as suspending agents, emulsifying agents, wetting agents, non-aqueous vehicle (including edible oils), preservatives, as well as flavoring and/or coloring agents. For parenteral administration, a vehicle normally will comprise sterile water, at least in large part, although saline solutions, glucose solutions and like may be utilized. Injectable suspensions also may be used, in which case conventional suspending agents may be employed. Conventional preservatives, buffering agents and the like also may be added to the parenteral dosage forms. Particularly useful is the administration of a compound of Formula I directly in parenteral formulations. The pharmaceutical compositions are prepared by conventional techniques appropriate to the desired preparation containing appropriate amounts of the active ingredient, that is, the compound of Formula I according to the invention. See, for example, *Remington: The Science and Practice of Pharmacy*, 20th Edition. Baltimore, MD: Lippincott Williams & Wilkins, 2000.

The dosage of the compounds of Formula I to achieve a therapeutic effect will depend not only on such factors as the age, weight and sex of the patient and mode of administration, but also on the degree of potassium channel activating activity desired and the potency of the particular compound being utilized for the particular disorder of disease concerned. It is also contemplated that the treatment and dosage of the particular compound may be administered in unit dosage form and that one skilled in the art would adjust the unit dosage form accordingly to reflect the relative level of activity. The decision as to the particular dosage to be employed (and the number of times to be administered per day is within the discretion of the physician, and may be varied by titration of the dosage to the particular circumstances of this invention to produce the desired therapeutic effect.

A suitable dose of a compound of Formula I or pharmaceutical composition thereof for a mammal, including man, suffering from, or likely to suffer from any condition as described herein is an amount of active ingredient from about 0.01 mg/kg to 10 mg/kg body weight. For parenteral administration, the dose may be in the range of 0.1 mg/kg to 1 mg/kg body weight for intravenous administration. For oral administration, the dose may be in the range about 0.1 mg/kg to 5 mg/kg body weight. The active ingredient will preferably be administered in equal doses from one to four times a day. However, usually a small dosage is administered, and the dosage is gradually increased until the optimal dosage for the host under treatment is determined.

However, it will be understood that the amount of the compound actually administered will be determined by a physician, in the light of the relevant circumstances including the condition to be treated, the choice of compound of be administered, the chosen route of administration, the age, weight, and response of the individual patient, and the severity of the patient's symptoms.

The amount of the compound of the present invention or a pharmaceutically acceptable salt thereof that is effective for inhibiting mTOR or PI3K in a subject. In addition, *in vitro* or *in vivo* assays can optionally be employed to help identify optimal dosage ranges. The precise dose to be employed can also depend on the route of administration, the condition, the seriousness of the condition being treated, as well as various physical factors related to the individual being treated, and can be decided according to the judgment of a health-care practitioner. Equivalent dosages may be administered over various time periods including, but not limited to, about every 2 hours, about every 6 hours, about every 8 hours, about every 12 hours, about every 24 hours, about every 36 hours, about every 48 hours, about every 72 hours, about every week, about every two weeks, about every three weeks, about every month, and about every two months. The number and frequency of dosages corresponding to a completed course of therapy will be determined according to the judgment of a health-care practitioner. The effective dosage amounts described herein refer to total amounts administered; that is, if more than one compound of the present invention or a pharmaceutically acceptable salt thereof is administered, the effective dosage amounts correspond to the total amount administered.

In one embodiment, the compound of the present invention or a pharmaceutically acceptable salt thereof is administered concurrently with another therapeutic agent.

In one embodiment, a composition comprising an effective amount of a compound of the present invention or a pharmaceutically acceptable salt thereof and an effective amount of another therapeutic agent within the same composition can be administered.

Effective amounts of the other therapeutic agents are well known to those skilled in the art. However, it is well within the skilled artisan's purview to determine the other therapeutic agent's optimal effective amount range. The compound of the present invention or a pharmaceutically acceptable salt thereof and the other therapeutic agent can act additively or, in one embodiment, synergistically. In one embodiment, of the invention, where another therapeutic agent is administered to an animal, the effective amount of the compound of the present invention or a pharmaceutically acceptable salt thereof is less than its effective amount would be where the other therapeutic agent is not administered. In this case, without being bound by theory, it is believed that the compound of the present invention or a pharmaceutically acceptable salt thereof and the other therapeutic agent act synergistically.

Methods useful for making the compounds of Formula I are set forth in the Examples below and generalized in Schemes 1-3:

Scheme 1:

One of skill in the art will recognize that Schemes 1-3 can be adapted to produce the other compounds of Formula I and pharmaceutically acceptable salts of compounds of Formula I according to the present invention.

The following abbreviations are used herein and have the indicated definitions: ACN is acetonitrile, AcOH is acetic acid, ATP is adenosine triphosphate, CHAPS is 3[(3-cholamidopropyl)dimethylammonio]-propanesulfonic acid, DEAD is diethyl azodicarboxylate, DIAD is diisopropyl azodicarboxylate, DMAP is dimethyl aminopyridine, DMF is N,N-dimethylformamide, DMF-DMA is dimethylformamide dimethyl acetal, DMSO is dimethylsulfoxide. Dowtherm™ is a eutectic mixture of biphenyl ($C_{12}H_{10}$) and diphenyl oxide ($C_{12}H_{10}O$). Dowtherm™ is a registered trademark of Dow Corning Corporation. DPBS is Dulbecco's Phosphate Buffered Saline Formulation, EDTA is ethylenediaminetetraacetic acid, ESI stands for Electrospray Ionization, EtOAc is ethyl acetate, EtOH is ethanol, HEPES is 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid, GMF is Glass, Hunig's Base is diisopropylethylamine, HPLC is high pressure liquid chromatography, LPS is lipopolysaccharide, MeCN is acetonitrile, MeOH is methanol, MS is mass spectrometry, NEt_3 is triethylamine, NMR is nuclear magnetic resonance, PBS is phosphate-buffered saline (pH 7.4), RPMI 1640 is a buffer (Sigma-Aldrich Corp., St. Louis, MO, USA), SDS is dodecyl sulfate (sodium salt), SRB is Sulforhodamine B, TBSCl is tert-butyldimethylsilyl chloride, TCA is tricholoroacetic acid, TFA is trifluoroacetic acid, THF is tetrahydrofuran, TLC is thin-layer chromatography, and TRIS is tris(hydroxymethyl)aminomethane.

METHODS

The following methods outline the synthesis of the compounds of Formula I. The following examples are presented to illustrate certain embodiments of the present invention, but should not be construed as limiting the scope of this invention.

Example 1: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea

Step 1: Preparation of 2-chloro-4,6-di-morpholin-4-yl-[1,3,5]triazine:

To a stirred solution of cyanuric chloride (18.4 g, 10 mmol) in acetone (100 ml) and crushed ice (500 g), a mixture of triethylamine (30.0 g, excess) and morpholine (17.4 g, 20 mmol) was added at –10 °C. After the addition, reaction mixture was stirred at room temperature and for 1 hour and diluted with 50 ml water. Separated white solid was filtered and washed with water. The white solid was dried and filtered. The crude product was found to be pure and taken to next step without purification. Yield: 25 g, 87%; (M+H) 286.7

Step 2: Preparation of 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline

A mixture of 2-chloro-4,6-di-morpholin-4-yl-[1,3,5]triazine (1.4 g , 4.9 mmoles), a catalytic amount of tetrakis(triphenylphosphine)palladium(0) (70 mg , 0.061 mmoles), sodium carbonate solution 2 M (3 mL), 4-aminophenylboronic acid pinacol ester (1.6 g, 7.3 mmoles) and DME (100 mL) was refluxed for 24 hours. The solvent was evaporated, and the residue was dissolved in methylene chloride and filtered through Celite™. The filtrate was washed with water (200 mL) and the organic layer was dried with magnesium sulfate. This was filtered and the solvent was evaporated. The residue was purified by Silica gel column chromatography and eluted with Ethyl acetate/hexanes (1:1) to give 1.40 g, (83% yield) of 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline as an amorphous solid. (M+H) 343.

Step 3: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea

To a mixture of 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.20 g 0.40 mmoles) in methylene chloride (80mL) at 0 °C was added triphosgene (0.25 mg, 0.84 mmoles) and triethylamine (3 mL). The mixture was stirred for 20 minutes at 0 °C and 4-amino pyridine (0.10 g 0.83 mmoles) was added to the reaction mixture and stirred for another 2 hours at room temperature. The solvent was evaporated and the residue was submitted to the HPLC using acetonitrile/TFA as mobile phase to give 98.2 mg (36 % yield) of 1-[4-(4,6-dimophorlin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea. (M+H) = 463.3.

Procedure A for preparation of ureas using aryl isocyanates:

To a stirred mixture of 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (140 mg, 0.40 mmoles) and a catalytic amount of dimethylaminopyridine (DMAP) in methylene chloride 100 (mL), was added a small excess of aryl isocyanate (0.61 mmoles). The mixture was stirred at room temperature for 48 hours. The reaction mixture was concentrated to half of its original volume and the separated precipitate was collected by filtration and washed with methanol (15 ml) and then with diethyl ether. In some cases the crude product obtained was purified by Silica gel column chromatography by eluting it with appropriate solvents, depending upon the polarity of the products.

The following compounds were prepared according to Procedure A:

Example 2: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-3-ylurea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.08 g 0.23 mmoles) and 3-pyridyl isocyanate (30 mg, 0.25 mmoles) the title compound was isolated as a white solid. The product was purified by Silica gel column chromatography by eluting it with 10% MeOH: ethyl acetate. Yield; 60 mg (56 %); (M+H)= 463.5.

Example 3: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-phenylurea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (140 mg, 0.40 mmoles) and phenyl isocyanate (72 mg, 0.61 mmoles), the title compound was isolated as a white solid. The product was purified by Silica gel column chromatography by eluting it with ethyl acetate. Yield: 0.128 g (68%) (M+H) = 462.3

Example 4: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-thiophen-2-ylurea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (60 mg, 0.17 mmoles) and 2-thienyl isocyanate (18 mg, 0.14 mmoles), the title compound was isolated as a grey solid after Silica gel column chromatography by eluting with 5% ethyl acetate: methanol. Yield: 12 mg (14%); (M+H) = 470.

Example 5: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-methylphenyl)urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140 g 0.40 mmoles) and 4-methylphenyl isocyanate (74 mg, 0.56 mmoles), the title compound was isolated as a white solid. Yield; 65 mg (33 %) (M+H)= 476.4

Example 6: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-fluorophenyl)urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140 g 0.40 mmoles) and 4-fluorophenyl isocyanate (83 mg, 0.61 mmole), 65 mg (33% yield) of the title product was isolated as white solid. (M+H) = 480.3

Example 7: Preparation of 1-(2,4-dimethoxyphenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140 g 0.40 mmoles) and 2,4-dimethoxyphenyl isocyanate (131 mg, 0.73 mmoles), the title compound was isolated as a white solid. Yield; 76 mg (36 %); (M+H)= 522.4

Example 8: Preparation of 1-(4-chlorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140 g 0.40 mmoles) and 4-chlorophenyl isocyanate (94 mg, 0.61 mmoles), the title compound was isolated as a white solid. Yield; 60 mg (30 %); (M+H)= 496.3

Example 9: Preparation 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-methoxyphenyl)urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140 g 0.40 mmoles) and 4-methoxyphenyl isocyanate (91 mg, 0.63 mmoles) the title compound was isolated as a white solid. Yield; 48 mg (24 %); (M+H)= 492.3

Example 10: Preparation of (4-chlorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140 g 0.40 mmoles) and 4-chlorophenyl isocyanate (94 mg, 0.61 mmoles) the title compound was isolated as a white solid. Yield; 60 mg (30 %); (M+H)= 496.3

Example 11: Preparation of (2,4-difluorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.105 g 0.30 mmoles) and 2,4-difluorophenyl isocyanate (71 mg, 0.45 mmoles) the title compound was isolated as a white solid. Yield; 40 mg (27 %); (M+H)= 498.6

Example 12: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-ethylurea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.130 g 0.38 mmoles) and ethyl isocyanate (260 mg, 10 fold excess) the title compound was isolated as a white solid. Yield; 38 mg (25 %); (M+H)= 414.4

Example 13: Preparation of tert-butyl 3-{[4-(4-{[(4-fluorophenyl)carbamoyl]-amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate

Step 1: Preparation of 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine:

To a stirred solution of cyanuric chloride (18.4 g, 10 mmol) in acetone (100 ml) and crushed ice (500 g), a mixture of triethylamine (30.0 g, excess) and morpholine (8.7 g, 10 mmol) was added at –10 °C. After the addition, reaction mixture was stirred at room temperature and for 1 hour and diluted with 50 ml water. Separated white solid was filtered and washed with water. The white solid was dried and filtered. The crude product was found to be pure and taken to next step with out purification. Yield: 18 g, 76%; (M+H) 236.4

Step 2: Preparation of tert-butyl 3-(4-chloro-6-morpholine-1,3,5-triazin-2-2-ylamino)azetidine-1-carboxylate

To a stirred solution of 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine (2.35 g, 10 mmol) in acetone (50 ml) and crushed ice, a mixture of triethylamine and 1-boc-3-(amino)azetidine (1.72 g) was added slowly. The reaction mixture was stirred at room temperature for 6 hours and the separated solid was filtered. The product was dried and taken to next step with out purification. Yield: 3.0 g (81%); (M+H) 373

Step 3: Preparation of tert-butyl-3-4-(4-(4-aminophenyl)-6-morpholine-1,3,5-triazin-2-ylamino)azetidine-1-carboxylate.

A mixture of tert-butyl 3-(4-chloro-6-morpholine-1,3,5-triazin-2-2-ylamino)azetidine-1-carboxylate (1.1 g , 3.0 mmoles), tetrakis(triphenylphosphine)palladium (0) in catalytic amount (70 mg , 0061 mmoles), sodium carbonate solution 2 M (3 mL), 4-aminophenylboronic acid pinacol ester (0.97 g, 4.5 mmoles), DME (100 mL) was refluxed for 24 hours. The solvent was evaporated and the residue was dissolved in methylene chloride and filtered though Celite™. The organic layer was washed with water (200 mL) and dried over magnesium sulfate. It was filtered and the solvent was evaporated. The residue was chromatographed on silica gel column using Ethyl acetate/hexanes (1:1) as an eluent, to give 0.86 g, (68% yield) of tert-butyl-3-4-(4-(4-aminophenyl)-6-morpholine-1,3,5-triazin-2-ylamino)azetidine-1-carboxylate. (M+H) 428

Step 4: Preparation of tert-butyl 3-{[4-(4-{[(4-fluorophenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl- 1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate

A mixture of tert-butyl 3-{[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate (100 mg, 0.23 mmol), 4-fluorophenylisocyanate (63 mg, 0.46 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; Yield 40 mg (30%); (M+H) 565.6

Example 14: Preparation of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(phenylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

The titled compound was prepared by starting from tert-butyl 3-{[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate (140 mg, 0.32 mmol) phenylisocyanate (58 mg, 0.49 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; Yield 40 mg (31%); (M+H) 547.6

Example 15: Preparation of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-3-ylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

The titled compound was prepared by starting from tert-butyl 3-{[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate (140 mg, 0.32 mmol) 3-pyridylisocyanate (70 mg, 0.58 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; Yield 40 mg (23%); (M+H) 548.7.

Example 16: Preparation of tert-butyl 3-{[4-(4-{[(4-methylphenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl- 1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate

The titled compound was prepared by starting from tert-butyl 3-{[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate (130 mg, 0.27 mmol) 4-tolyl isocyanate (40 mg, 0.30 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; Yield 85 mg (47%); (M+H) 561.6.

Example 17: Preparation of 1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3- phenylurea

To a stirred solution of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(phenylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

30 mg (0.055 mmoles) in DCM, (20 ml) TFA (1.5 ml) was added at room temperature and stirred for 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. Yield: 20 (83%); (M+H) 447.

Example 18: Preparation of 1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea

To a stirred solution of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridin-3-ylcarbamoyl)amino]phenyl}- 1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate

30 mg (0.055 mmoles) in DCM, (20 ml) TFA (1.5 ml) was added at room temperature and stirred for 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. Yield: 21 (83%); (M+H) 448.5.

Example 19: Preparation of 1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-fluorophenyl)urea

To a stirred solution of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(4-fluoro-phenylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

30 mg (0.053 mmoles) in DCM, (20 ml) TFA (1.5 ml) was added at room temperature and stirred for 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. Yield: 20 (83%); (M+H) 465.5.

Example 20: Preparation of 1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-methylphenyl)urea

To a stirred solution of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(4-methyl-phenylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

130 mg (0.23 mmoles) in DCM, (20 ml) TFA (1.5 ml) was added at room temperature and stirred for 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. Yield: 40 (37%); (M+H) 461.5.

Example 21: Preparation of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-4-ylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

To a stirred solution of tert-butyl 3-{[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate (200 mg, 0.47 mmol) in DCM (100 ml) at 0 oC, triphosgene (300 mg) and triethylamine (3 ml) was added slowly. The reaction mixture was stirred for 15 minutes and 4-aminopyridine (200 mg. 2.1 mmol) was added. The reaction mixture was stirred at room temperature for 24 hours and concentrated. It was quenched with cold water and the separated solid was filtered and washed with water. It was dried and purified by Gilson HPLC. Yield 100 mg (40%); (M+H) 548.6

Example 22: Preparation of 1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

To a stirred solution of tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-4-ylcarbamoyl)amino]phenyl}-1,3,5- triazin-2-yl)amino]azetidine-1-carboxylate

40 mg (0.073 mmoles) in DCM, (20 ml) TFA (1.5 ml) was added at room temperature and stirred for 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. Yield: 26 (81%); (M+H) 448.5.

Example 23: Preparation of 1-{4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea

Step 1: Preparation of 3-(4-chloro-6-morpholin-4-yl-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane

To a stirred acetone/crushed ice suspension of 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine (1.5 g, 6.5 mmol), 8-oxa-3-azabicyclo[3.2.1]octane (980 mg, 6.5 mmol) and triethylamine (3 ml) was added and stirred at room temperature for 6 hours. At the end, the separated solid was filtered and washed with water. The crude product was found to be pure enough for further transformations. Yield: 2.0 g (99%); mp. 118; (M+H) 313.1

Step 2: Preparation of 4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]aniline

A mixture of 3-(4-chloro-6-morpholin-4-yl-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane (2.0 g, 6.4 mmol), tetrakis(triphenylphosphine)palladium (0) in catalytic amount (100 mg), sodium carbonate solution 2 M (5 mL), 4-aminophenylboronic acid pinacol ester (1.5 g, 6.43 mmoles), DME (200 mL) was refluxed for 24 hours. The solvent was evaporated and the residue was dissolved in methylene chloride and filtered though Celite™. The organic layer was washed with

water (200 mL) and dried over magnesium sulfate. It was filtered and the solvent was evaporated. The residue was chromatographed on silica gel column using Ethyl acetate/hexanes (1:1) as an eluent, to give 1.4 g, (59% yield) of the titled product. mp. 154; (M+H) 369.4.

Step 3: Preparation of 1-{4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea

The titled compound was prepared by starting from 4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]aniline (120 mg, 0.32 mmol) phenylisocyanate (80 mg, 0.67 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; mp: 242; Yield 35 mg (28%); (M+H) 488.56

Example 24: Preparation of 1-(4-fluorophenyl)-3-{4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea

The titled compound was prepared by starting from 4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]aniline (100 mg, 0.27 mmol)4-fluoro phenylisocyanate (50 mg, 0.36 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; mp: 248; Yield 86 mg (86%); (M+H) 506.4

Example 25: Preparation of 1-(4-methylphenyl)-3-{4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea

The titled compound was prepared by starting from 4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]aniline (100 mg, 0.27 mmol)4-tolylisocyanate (60 mg, 0.45 mmol) and DMAP (5 mg) was stirred at room temperature for a period of 24 hours. At the end, reaction mixture was concentrated and purified by Gilson HPLC, using ACN/water and TFA. White solid; mp: 228; Yield 80 mg (80%); (M+H) 502.4

Following the procedure as outlined in **example 25**, compounds described in **examples 26** to **32** were prepared.

Example 26: 1-[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]-3-methylurea (M+H) 452.53

Example 27: 2-hydroxyethyl [4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]carbamate (M+H) 483.54

Example 28: 1-[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea (M+H) 612.8

Example 29: 1-[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]-3-ethylurea (M+H) 466.56

Example 30: 1-cyclopropyl-3-[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]urea (M+H) 478.55

Example 31: 1-[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea (M+H) 515

Example 32: 1-[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea (M+H) 544.6

Example 33: Preparation of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline

Step 1: Synthesis of 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine

To a solution of cyanuric chloride (2.5 g, 13.5 mmol) in CH_2Cl_2 (150 mL) was added dropwise morpholine (1.14 g, 13.5 mmol) at –78 oC, followed by addition of Et3N (3.0 mL, 21.5 mmol). The resulting reaction mixture was stirred at -78 oC for 20 min, and then diluted with CH_2Cl_2. The organic phase was washed with water and brine, and dried over $MgSO_4$. The solvent was removed in vacuum to give the title compound as white crystalline solid (3.027 g, 95% yield). MS(ESI) m/z 235.1.

Step 2: Synthesis of 8-(4-chloro-6-morpholino-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3,2,1]octane

To a solution of 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (2.34 g, 10 mmol) in CH_2Cl_2 (100 mL) were added 3-oxa-8-azabicyclo[3,2,1]octane hydrochloride (1.645 g, 11 mmol) and Et3N (4.2 mL, 30 mmol). The mixture was stirred at room temperature over night. The reaction mixture was washed with water and brine, and dried over $MgSO_4$. The solvent was removed in vacuum to give the title compound as white solid (3.0 g, 96% yield). MS(ESI) m/z 312.1.

Step 3: Synthesis of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline

To a 10 mL vial were added 8-(4-chloro-6-morpholino-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3,2,1]octane (311 mg, 1.0 mmol), 4-aminophenylboronic acid pinacol ester (328 mg, 1.5 mmol), Pd(PPh3)4 (58 mg, 5 mol%), 1,2-dimethoxyethane (DME, 2.5 mL) and 2M Na2CO3 aqueous solution (1.5 mL). The resulting mixture was heated at 130 oC for 30 min in microwave oven. The reaction mixture was cooled to room temperature. The aqueous phase was extracted with EtOAc, and the combined organic phases were dried over ($MgSO_4$). The solvent was removed under reduced pressure and the residue was subjected to HPLC separation to give the title compound as off-white solid (280 mg, 76% yield). MS(ESI) m/z 369.2.

Example 34: Preparation of 1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

To a solution of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) in CHCl3 (1 mL) were added Et3N (25 mL, 0.18 mmol) and triphosgene (18 mg, 0.06 mmol). The mixture was stirred at room temperature for 15 min and 4-aminopyridine (17 mg, 0.18 mmol) was added. The mixture was stirred at room temperature overnight. The solvent was removed, and the residue was subjected to HPLC separation to give the title compound as off-white solid (1TFA salt, 8.8 mg, 24% yield). MS(ESI) m/z 489.2.

Example 35: Preparation of 4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 4-aminobenzamide (25 mg, 0.18 mmol) gave the title compound as off-white solid (10.6 mg, 33% yield). MS(ESI) m/z 531.2.

Example 36: Preparation of 1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 3-aminopyridine (17 mg, 0.18 mmol) gave the title compound as off-white solid (1TFA salt, 14.8 mg, 41% yield). MS(ESI) m/z 489.5.

Example 37: Preparation of 1-(4-fluorophenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 4-fluoroaniline (20 mg, 0.18 mmol) gave the title compound as off-white solid (14.8 mg, 49% yield). MS(ESI) m/z 506.5.

Example 38: Preparation of 1-[4-(hydroxymethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 4-aminobenzyl alcohol (22 mg, 0.18 mmol) gave the title compound as off-white solid (9.6 mg, 31% yield). MS(ESI) m/z 518.5.

Example 39: Preparation of 1-[4-(2-hydroxyethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 4-aminophenethyl alcohol (24 mg, 0.18 mmol) gave the title compound as off-white solid (10.6 mg, 33% yield). MS(ESI) m/z 532.5.

Example 40: Preparation of 2-(diethylamino)ethyl 4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and procaine hydrochloride (50 mg, 0.18 mmol) gave the title compound as off-white solid (1TFA salt, 14.6 mg, 33% yield). MS(ESI) m/z 613.6.

Example 41: Preparation of 1-(4-methylphenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol,

triphosgene (18 mg, 0.06 mmol) and p-toluidine (20 mg, 0.18 mmol) gave the title compound as off-white solid (9.2 mg, 31% yield). MS(ESI) m/z 502.5.

Example 42: Preparation of 1-(4-cyanophenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 4-aminobezonitrile (21 mg, 0.18 mmol) gave the title compound as off-white solid (14.3 mg, 46% yield). MS(ESI) m/z 513.5.

Example 43: Preparation of 1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and 4-(4-methylpiperazin-1-yl)aniline (54 mg, 0.18 mmol) gave the title compound as off-white solid (2TFA salt, 3.2 mg, 7% yield). MS(ESI) m/z 586.6.

Example 44: Preparation of 1-isopropyl-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and isopropylamine (11 mg, 0.18 mmol) gave the title compound as off-white solid (13.6 mg, 50% yield). MS(ESI) m/z 454.5.

Example 45: Preparation of 1-(2-hydroxyethyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

Following the procedure described in **example 34**, reaction of 4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline (22 mg, 0.06 mmol) (22 mg, 0.06 mmol, triphosgene (18 mg, 0.06 mmol) and ethanolamine (11 mg, 0.18 mmol) gave the title compound as off-white solid (14.4 mg, 53% yield). MS(ESI) m/z 456.5.

Example 46: Preparation of 1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea, MS (ES+) 513.62 (M+H)+

Example 47: Preparation of 1-{4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea, MS (ESI) m/z 489.3.

Example 48: Preparation of 1-{4-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea, mp 258 °C; MS (ESI) m/z 489.3.

Following the procedure as outlined in **example 1**, step 3 the following compounds were prepared.

Example 49: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea MS (ESI) m/z 477.3.

Example 50: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(2-hydroxyethyl)phenyl]urea MS (ESI) m/z 506.4.

Example 51: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea.

Example 52: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea MS (ESI) m/z 506.4.

Example 53: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(trifluoromethyl)phenyl]urea MS (ESI) m/z 530.2.

Example 54: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-hydroxyphenyl)urea MS (ESI) m/z 478.2.

Example 55: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5-(trifluoromethyl)pyridin-2-yl]urea MS (ESI) m/z 530.5.

Example 56: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea MS (ESI) m/z 621.54.

Example 57: 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea MS (ESI) m/z 506.3.

Example 58: methyl 4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate MS (ESI) m/z 520.3.

Example 59: Preparation of 1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

Step 1: To a stirred solution of NaH (50% 460 mg) in dry THF tetrahydro-2H-pyran-4-ol (1.02 g, 10 mmol) was slowly added at room temperature. The reaction mixture was stirred at room temperature for 30 min and 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine (2.35 g, 10 mmol) in THF (50 ml) was slowly added. The reaction mixture was stirred at room temperature for 48 hours and slowly quenched with ice-cold water. It was extracted with $CHCl_3$; washed well with water and dried over anhydrous $MgSO_4$. It was filtered and concentrated and 2-chloro-4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazine was purified by silica gel column chromatography by eluting it with 40% ethyl acetate:hexane. Yield: 1.5 g, 50%; White solid; mp 91 °C; MS (ESI) m/z 301.52

Step 2: 4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]aniline was prepared by the procedure as described in **example 1**, step 2. Starting from 2-chloro-4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazine (1.5 g, 4.9 mmol) 980 mg (56% yield) of the product was isolated after purification using Silica gel column chromatography by eluting it with ethyl acetate. Mp. 188 oC; MS (ESI) m/z 358.2.

Step 3: 1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea was prepared by the procedure as described in **example 1**, step 3. Starting from 4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]aniline (212 mg. 0.59 mmol) 190 mg (Yield, 67%) of the final product was isolated as a white solid. mp 238 °C; MS (ESI) m/z 478.3.

Example 60: Preparation of 1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea was prepared by reacting the 4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]aniline and the corresponding phenylisocyanate. Product was purified by Gilson, HPLC. MS (ESI) m/z 476.5.

Example 61: Preparation of 1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea was prepared by reacting the 4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-

triazin-2-yl]aniline and the corresponding 3-pyridylisocyanate. Product was purified by Gilson, HPLC. MS (ESI) m/z 477.53.

Example 62: Preparation of 1-[4-(hydroxymethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea

1-[4-(hydroxymethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea was prepared by the triphosgene procedure as described in **example 1**, step 3. Product was purified by Gilson, HPLC. MS (ESI) m/z 506.6.

Example 63: Preparation of 1-(2-methylpyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea

1-(2-methylpyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea was prepared by the triphosgene procedure as described in **example 1**, step 3. Product was purified by Gilson, HPLC. MS (ESI) m/z 491.5.

Example 64: Preparation of 1-[2-(methylamino)ethyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea

1-[2-(methylamino)ethyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea was prepared by the triphosgene procedure as described in **example 1**, step 3. Product was purified by Gilson, HPLC. MS (ESI) m/z 457.54.

Example 65: Preparation of 1-(3-acetylphenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea

1-(3-acetylphenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea was prepared by reacting the 4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]aniline and the corresponding 3-acetylisocyanate. Product was purified by Gilson, HPLC. MS (ESI) m/z 518.58.

Example 66: Preparation of 1-[4-(dimethylamino)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea

1-[4-(dimethylamino)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea was prepared by reacting the 4-[4-morpholin-4-yl-6-(tetrahydro-2H-

pyran-4-yloxy)-1,3,5-triazin-2-yl]aniline and the corresponding 4-(N,N-dimethyl amino)phenylisocyanate. Product was purified by Gilson, HPLC. MS (ESI) m/z 519.61.

Example 67: Preparation of 4-[3-{4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl}ureido]benzoic acid

To a stirred mixture of methyl 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoate (1.4 g, 2.69 mmol), THF (10 mL), MeOH (5 mL) and H2O (2.5 mL) was added LiOH.H2O (339 mg, 8.07 mmol) then heated under reflux for 8 hrs. Concentrated and added H2O (5 mL) then acidified with 2N HCl. The solid was filtered washed with H2O and dried to give the product as a tan solid (1.3 g, 96% yield); MS (ESI) m/z = 506.3

Example 68: Preparation of N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide

To a stirred solution of 4-[3-{4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl}ureido]benzoic acid (150 mg; 0.297 mmol), Hunig's base (303 µL, 1.782 mmol), HBTU (563 mg, 1.485 mmol) in 2 mL of NMP was stirred for 1 hr. at room temperature and added N',N'-dimethylethane-1,2-diamine (130 µL, 1.188 mmol) then stirred overnight. Added CH_2Cl_2 (40 mL) and washed with sat. NaHCO3 and H2O. Concentrated and purified by silica gel chromatography CH_2Cl_2:MeOH:7N NH3 in MeOH (10:1:0.22) to give the product as a white solid (98 mg, 57% yield); MS (ESI) m/z = 576.4.

Example 68: Preparation N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide as an HCl salt

To the N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide (72 mg, 0.125 mmol) and MeOH (1 mL) was added 4N HCl in dioxane (1 mL) and stirred for 3 hrs. The solid was filtered and washed with ether to give the product as a white solid (73 mg, yield= 95%); MS (ESI) m/z = 576.4.

Example 69: Preparation of 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea hydrochloride

To a stirred solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (150 mg; 0.297 mmol), Hunig's base (303 µL, 1.782 mmol), HBTU (563 mg, 1.485 mmol) in 2 mL of NMP was reacted according to **example 68** with 1-methylpiperazine (132 µL, 1.188

mmol) to give 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea as a white solid (95 mg, 54% yield); MS (ESI) m/z = 588.4.

To a 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea (70 mg, 0.119 mmol) and MeOH (1 mL) was added 4N HCl in Dioxane (1 mL), stirred for 3 hrs. The solid was filtered and washed with ether to give the product as a white solid (74 mg, yield= 100%).

Example 70: Preparation of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide

To the stirred solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (150 mg; 0.297 mmol), Hunig's base (303 µL, 1.782 mmol), HBTU (563 mg, 1.485 mmol) in 2 mL of NMP was reacted according to **example 68** with methylamine (594 µL, 2M solution. in THF) to give the product as a white solid (118 mg, 77% yield); MS (ESI) m/z = 519.3.

Example 71: Preparation of N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide hydrochloride

To the stirred solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (150 mg; 0.297 mmol), Hunig's base (303 µL, 1.782 mmol), HBTU (563 mg, 1.485 mmol) in 2 mL of NMP was reacted according to **example 68** with N1,N1,N2-trimethylethane-1,2-diamine (154 µL, 1.188 mmol) to give N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide as a white solid (88mg, 50% yield); MS (ESI) m/z = 590.2.

To the N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide (55 mg, 0.127 mmol) and MeOH (1 mL) was added 4N HCl in Dioxane (1 mL) and stirred for 3 hrs. The solid was filtered and washed with ether to give the product as a white solid (70 mg, yield= 88%).

Example 72: Preparation of 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-morpholinopiperidine-1-carbonyl)phenyl)urea

To the stirred solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 µL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 1 mL of NMP was reacted according to **example 68** with 4-(piperidin-4-yl)morpholine (67 mg, 0.396

mmol). Evaporated the solvent and purified by HPLC to give the product (40.1 mg, 62% yield); MS (ESI) m/z = 658.7

Example 73: Preparation of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(quinuclidin-3-yl)benzamide

To the solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 μL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 2 mL of NMP was reacted according to according to **example 68** with quinuclidin-3-amine (79 mg, 0.396 mmol). Evaporated the solvent and purified by HPLC to give the product (24.3 mg, 40% yield); MS (ESI) m/z = 614.7

Example 74: Preparation of 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(pyrrolidin-1-yl)piperidine-1-carbonyl)phenyl)urea

To the solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 μL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 2 mL of NMP was reacted according to **example 68** with 4-[1-pyrrolidinyl]piperidine (61 mg, 0.396 mmol). Evaporated the solvent and purified by HPLC to give the product as a white solid (37 mg, 58% yield); MS (ESI) m/z = 642.7

Example 75: Preparation of 1-(4-(1,4'-bipiperidine-1'-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea

To the solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 μL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 2 mL of NMP was reacted according to **example 68** with 1,4'-bipiperidine (67 mg, 0.396 mmol). Evaporated the solvent and purified by HPLC to give the product as a white solid (39 mg, 60% yield); MS (ESI) m/z = 656.8.

Example 76: Preparation of 1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea

To the solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 μL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 2 mL of NMP was reacted according to **example 68** with N,N-dimethylpiperidin-4-amine (51 mg, 0.396 mmol). Evaporated the solvent and purified by HPLC to give the product (30.6 mg, 52% yield); MS (ESI) m/z = 616.7

Example 77: Preparation of 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea

To the solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 μL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 2 mL of NMP was reacted according to **example 68** with piperazine (34 mg, 0.396 mmol). Evaporated the solvent and purified by HPLC to give the product (17.2 mg, 30% yield); MS (ESI) m/z = 573.6

Example 78: Preparation of 1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyridin-2-yl)acetyl)phenyl)urea

To the solution of 4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl)ureido)benzoic acid (50 mg; 0.099 mmol), Hunig's base (103 μL, 0.594 mmol), HBTU (188 mg, 0.495 mmol) in 2 mL of NMP was reacted according to **example 68** with pyridin-2-ylmethanamine (43 mg, 0.396 mmol). Evaporated the solvent and purified by HPLC to give the product (9 mg, 15% yield); MS (ESI) m/z = 596.6.

Preparation of 3-(4,6-dichloro-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane

To a solution of cyanuric chloride (2.00 g, 10.85 mmoles) in acetone (20 mL) and water (10 mL) at 0 °C was added a solution of 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (1.46 g, 9.76 mmoles) in saturated aqueous NaHCO3 (25 mL) and acetone (25 mL) via addition funnel over 15 minutes. The reaction was stirred at 0 °C for 2 hours, then filtered to collect a white precipitate. The precipitate was washed with water (25 mL) and dried. The crude product was purified by column chromatography (30:70 ethyl acetate in hexanes) to provide 3-(4,6-dichloro-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane (1.55 g) as a white solid.

Procedure to prepare 3-(4-chloro-6-(substituted amino)-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane:

To a solution of 3-(4,6-dichloro-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane (0.085 g, 0.33 mmoles) and Na2CO3 (0.041 g, 0.39 mmoles) in acetone (1 mL) and water (1 mL) was added the desired amine (0.36 mmoles). The solution was heated to 55 °C and stirred for 2 hours then concentrated to provide crude amino-triazine, which was used directly without purification. Following this procedure, the following compounds were prepared.

3-(4-chloro-6-(piperidin-1-yl)-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane:

(310.3, M+H)

3-(4-chloro-6-(pyrrolidin-1-yl)-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane

(296.3, M+H)

t-butyl 2-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-ylamino)ethylcarbamate

(385.3, M+H)

2-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-ylamino)ethanol

(286.3, M+H)

4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-N-phenyl-1,3,5-triazin-2-amine

(318.3, M+H)

4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-N-cyclohexyl-1,3,5-triazin-2-amine

(324.3, M+H)

t-butyl 3-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-ylamino)azetidine-1-carboxylate

(397.3, M+H)

Method to prepare 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(substituted amino)-1,3,5-triazin-2-yl)aniline

A suspension of bis-amino triazine chloride (0.33 mmoles) in toluene (2 mL), ethanol (2 mL), and 2M aqueous Na2CO3 (0.700 mL) in a microwave vial was sparged with N2 for 5 minutes. Pd(PPh3)4 (0.021 mgs, 0.018 mmoles) and 4-aminophenylboronic acid pinacol ester (0.094 mgs, 0.43 mmoles) were added and the vial was sealed and heated to 110 °C for 1 hour. The mixture was cooled and filtered through Celite™. The filter cake was washed with ethyl acetate and the filtrate was washed with brine, dried, and concentrated. The crude material was purified by HPLC (Waters system, 5-70 % CH3CN in H2O w/ 0.05% NH4OH) to provide the aryl-

substituted triazine compounds. Following this procedure, the following compounds were prepared.

4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperidin-1-yl)-1,3,5-triazin-2-yl)aniline

(367.4, M+H)

4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline

(353.3, M+H)

2-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-1,3,5-triazin-2-ylamino)ethanol; (343.3, M+H)

4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-N-phenyl-1,3,5-triazin-2-amine; (375.3, M+H)

4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-N-cyclohexyl-1,3,5-triazin-2-amine; (381.4, M+H)

t-butyl 3-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-1,3,5-triazin-2-ylamino)azetidine-1-carboxylate; (454.4, M+H).

Procedure to prepare 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(substituted amino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea:

A solution of triphosgene (0.034 mgs, 0.114 mmoles) in CH_2Cl_2 (1 mL) was prepared. A solution of the desired triazine aniline derivative (0.23 mmoles) in CH_2Cl_2 (1 mL) and triethylamine (0.095 mL, 0.68 mmoles) was added and the reaction was allowed to stir at room temperature for 15 minutes. A solution of 4-aminopyridine (0.043 mgs, 0.46 mmoles) in THF (1 mL) was then added and the solution was stirred at room temperature for 3 hours, then concentrated and purified by HPLC (Waters system, 5-70 % CH3CN in H2O w/ 0.05% NH4OH) to provide the 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(substituted amino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea derivatives. The following compounds were prepared by this procedure:

Example 79: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea; 487.2, M+H.

Example 80: Preparation of1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(pyrrolidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea; 474.2, M+H.

Example 81: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea

To a stirred mixture of 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140, 0.40 mmoles) in methylene chloride at 0 oC was added triphosgene (0.25, 0.84 mmoles) and Et3N (3 mL). The reaction mixture was stirred for 20 minutes at 0 oC. Then 1-(4-aminophenyl)ethanol (0.10 g, 0.73 mmoles) was added to the mixture. The reaction mixture was stirred for about 16 hours at room temperature. The solvent was removed. The residue was dissolved in DMSO and place at HPLC using acetonitrile buffer TFA to give 48 mg (24 %) of [4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea. M+H 506.4.

Example 82: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140, 0.40 mmoles) and 2-methyl-4-aminopyridine (80 mg, 0.73 mmol) and following the procedure as outlined in

Example 81, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea was isolated by HPLC purification. Yield: 60 mg, 27%; MS (ESI) m/z = 477.3.

Example 83: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140, 0.40 mmoles) and 4-aminophenylmethanol (100 mg, 0.81 mmol) and following the procedure described in

example 81, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4- (hydroxymethyl)-phenyl]urea was isolated by HPLC purification. Yield: 58 mg, 26%; MS (ESI) m/z = 492.3.

Example 84: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-hydroxyphenyl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140, 0.40 mmoles) and 4-aminophenol (89 mg, 0.81 mmol) and following the procedure as outlined in

example 81, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4- hydroxyphenyl]urea was isolated by HPLC purification. Yield: 62 mg, 16%; MS (ESI) m/z = 478.2.

Example 85: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(trifluoromethyl)phenyl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140, 0.40 mmoles) and 4-trifluoromethylaniline (100 mg, 0.62 mmol) and following the procedure as outlined in **example 81**, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4- (trifluoromethyl)phenyl]urea was isolated by HPLC purification. Yield: 25 mg, 13%; MS (ESI) m/z = 430.2.

Example 86: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1- hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.140, 0.40 mmoles) and 4-trifluoromethylaniline (140 mg, 0.40 mmol) and following the procedure as outlined in **example 81**, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1- hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea was isolated by HPLC purification. Yield: 40 mg, 16%; MS (ESI) m/z = 628.3.

Example 87: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5-(trifluoromethyl)pyridin-2-yl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.160, 0.47 mmoles) and 2-amino-5-trifluorophenylpyridine (100 mg, 0.61 mmol) and following the procedure as outlined in **example 81**, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5- (trifluoromethyl)pyridin-2-yl]urea was isolated by HPLC purification. Yield: 10 mg, 4.1%; MS (ESI) m/z = 531.3.

Example 88: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (0.160, 0.47 mmoles) and 1-(3-aminophenyl)ethanol (100 mg, 0.73 mmoles)and following the procedure as outlined in **example 81**, 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea was isolated by HPLC purification. Yield: 10 mg, 4.1%; MS (ESI) m/z = 531.3.

Example 89: Preparation of 1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

Step 1: Preparation of 2-chloro-4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazine:

To a stirred solution of dichoromonomorpholino derivative of 1,3,5-triazine (2.0 g , 8.5 mmoles) in methylene chloride 200 mL, was added 3S-3-methylmorpholine (0.85 g , 8.5 mmoles) combined with two equivalents of triethylamine 1.7 mL dropwise manner. After the addition reaction mixture was stirred at room temperature for 3 hours and quenched with water. The aqueous layer was washed well with water; dried over anhydrous $MgSO_4$ and filtered. The solvent was evaporated and the residue obtained was triturated with diethyl ether/ hexane (1:1) and filtered. The solid was used without further purification. (1.0 g, 40% yield). M+H 357.3.

Step2 : Preparation of 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline:

A mixture of 2-chloro-4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazine

(1.26, 4.2 mmol), sodium carbonate solution (2M, 2 mL), tetrakis palladium triphenylphosphine 70 mg (catalytic amount) and 4-aminophenyl boronic pinacol ester (1.37 g, 6.3 mmoles) in DME (100 mL) was heated to reflux for 24 hours. The solvent was evaporated, the residue was re-dissolved in methylene chloride and filtered through Celite™. The solvent was evaporated and the residue was chromatographed on silica gel eluting with first 26/4 hexanes/ethyl acetate then increased to 1/1 hexanes ethyl acetate to give 1.0 of 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (71% yield); M+H 357.2.

Step 3: Preparation of 1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea:

Starting from 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (0.160, 0.44 mmoles) and 4-aminopyridine (100 mg, 1.06 mmoles)and following the procedure as outlined in **example 81**, 1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea was isolated by HPLC purification. Yield: 125 mg, 60%; MS (ESI) m/z 477.3.

Example 90: Preparation of 1-[4-(2-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin- 4-yl-1,3,5-triazin-2-yl}phenyl)urea

Starting from 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (0.160, 0.44 mmoles) and 4-(1-hydroxyethyl)aniline (137 mg, 1 mmole)and following the procedure described in **example 81**, 1-[4-(2-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin- 4-yl-1,3,5-triazin-2-yl}phenyl)urea was isolated by HPLC purification. Yield: 125 mg, 60%; MS (ESI) m/z 519.6

Example 91: Preparation of 1-[4-(2-hydroxymethyll)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin- 4-yl-1,3,5-triazin-2-yl}phenyl)urea

Starting from 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (0.160, 0.44 mmoles) and 4-aminophenylmethanol (0.10 g , 0.81 mmoles) and following the procedure as outlined in **example 81**, 1-[4-(2-hydroxymethyll)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin- 4-yl-1,3,5-triazin-2-yl}phenyl)urea was isolated by HPLC purification. Yield: 55 mg, 16%; MS (ESI) m/z 506.3.

Example 92: Preparation of 1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(2-methylpyridin-4-yl)urea

Starting from 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (0.160, 0.44 mmoles) and 2-methyl-4-aminopyridine (0.10 g , 0.92 mmoles) and following the procedure as outlined in **example 81**, 1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(2-methylpyridin-4-yl)urea was isolated by HPLC purification. Yield: 75 mg, 36%; MS (ESI) m/z 491.3.

Example 93: Preparation of 1-[4-(1-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea

Starting from 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (0.160, 0.44 mmoles) and 1-(4-aminophenyl)ethanol (126 mg , 0.92 mmoles) and following the procedure as outlined in **example 81**, 1-[4-(1-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea was isolated by HPLC purification. MS (ESI) m/z 519.6.

Example 94: Preparation of 1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea

Step 1: To a stirred solution of isopropanol (250 mg, 4.1 mmol) in dry THF (50 ml) at –78 oC, n-butyllithium (2.6 ml, 1.6 mol solution) was slowly added. The reaction mixture was stirred for 30

minutes and a solution of 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine (1.00 g, 4.25 mmol) in THF was added to the solution. The reaction mixture was stirred at room temperature for 24 hours and quenched with water and extracted with DCM. The crude product obtained was taken to next step without purification.

Step 2: A mixture of (crude) 4-(chloro-6-isopropoxyl-1,2,3-triazin-2yl)morpholine of (2.91 g, 11.27 mmol) 4-amino-phenylboronic acid pinacol ester (3.59 g, 16.4 mmoles) , tetrakis palladium triphenylphosphine (120 mg catalytic amount) and sodium carbonate solution (2M, 2 mL) was refluxed in DME (100 mL) for 24 hours. The solvent was removed and the residue was re-dissolved in methylene chloride and filtered through Celite™. The solvent was evaporated and the residue was chromatographed on silica gel eluting with first 26:4 hexane:ethyl acetate then increased to 1/1 hexanes ethyl acetate to give 0.65 g (yield 18%) of 4-(4-isopropoxy-6-morpholino-1,3,5-triazin-2-yl)aniline. M+H 316.3.

Step 3: Starting from 4-(4-isopropoxy-6-morpholino-1,3,5-triazin-2-yl)aniline (0.140, 0.44 mmoles) and 4-aminopyridine (100 mg , 1.06 mmoles) and following the procedure as outlined in **example 81**, 1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea was isolated by HPLC purification. Yield: 15 mg, 7.8%; MS (ESI) m/z = 436.3.

Example 95: Preparation of methyl 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate

A mixture of 4-(4-isopropoxy-6-morpholino-1,3,5-triazin-2-yl)aniline (1.3 g, 4.1 mmol), triethylamine (2 ml) and 4-carbomethoxy-phenylisocyanate (1451 mg, 8.2 mmol) was stirred for 48 hours and quenched with water and washed well. The organic layer was dried and filtered. It was concentrated and purified by column chromatography by eluting it initially with 10% ethyl acetate: hexane and latter with 40% ethyl acetate:hexane. White solid; 600 mg, 30%; MS (ESI) m/z 492.5.

Example 96: Preparation of 1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea

Starting from methyl 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl] carbamoyl}amino)benzoic acid (160 mg, 0.33 mmol) and 4-methylpiperazine following the procedure as outlined in Experimental 71, 80 mg (44% Yield) of the titled compound was isolated as white solid. MS (ESI) m/z 281.2.

Example 97: Preparation of 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide

Starting from methyl 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl] carbamoyl}amino)benzoic acid (200 mg, 0.42 mmol) and 4-amino-1-methylpiperidine following the procedure as outlined in Experimental 71, 65 mg (27% Yield) of the titled compound was isolated as white solid. MS (ESI) m/z 574.68.

Example 98: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(1-methylpiperidin-4-yl)urea

Starting from 4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)aniline (140 mg 0.40 mmoles) and 4-amino-1-methylpiperidine (70 mg, 0.62 mmol) and following the procedure as outlined in **example 1**, step 3, 20 mg (10 % Yield) of the final compound was isolated as a solid. MS (ESI) m/z = 483.4

Example 99: Preparation of 1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(1-methylpiperidin-4-yl)urea

Starting from 4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}aniline (0.140, 0.39 mmoles) and 4-amino-1-methylpiperidine (70 mg, 0.62 mmol) and following the procedure as outlined in **example 81**, the titled product was prepared and purified by HPLC. Yield: 120 mg, 40%; 497.4.

Example 100: Preparation of 1-{4-[4-(3,6-Dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea

Step 1: Preparation of 2-Chloro-4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazine:

In a three necked flask under nitrogen equipped was dissolved 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine (610 mg, 2.6 mmol), tributyldihydropyranylstanane (1.45 g, 3.89 mmol, 1.5 eq), and $(Ph_3P)_2PdCl_2$ (150 mg, 0.21 mmol, 0.1eq) in anhydrous dioxan (5 ml). The reaction mixture was heated under stirring to 90 oC for 16 hrs. For purification silica gel (10 g) was added to the mixture and the solvent was removed to let the product adsorbed on the silica gel. The silica gel plug was placed on a column and the mixture was flash chromatographed with hexane:ethyl acetate (10:1) to give after removal solvent the product as off white solid (345 mg = 47% yield); MS (ESI) m/z 281.

Step 2: Preparation of 4-[4-(3,6-Dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenylamine:

To a microwave processing tube was added dimethoxyethane (4 mL), aqueous Na_2CO_3 (2 molar)(1 mL, 2 mmol, 2 eq), $(Ph_3P)_4Pd$ (101 mg, 0.088 mmol), 4-anilinoboronic acid or ester (581 mg, 2.65 mmol, 1.5 eq) and the 2-chloro-4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazine (500 mg, 1.76 mmol) and the vessel was sealed. The mixture was heated to 140 °C for 60 minutes. The solvents were distilled and the crude compound was purified by silica gel chromatography using CH_2Cl_2/ethyl acetate (10:1) and later CH_2Cl_2/MeOH/NH3 (20:1:0.1) to give the product as a off-white solid (520 mg, 87 % yield); MS (ESI) m/z 340.2

Step 3: Preparation of 1-{4-[4-(3,6-Dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea:

To a stirred solution of triphosgene (140 mg, 0.47 mmol) in CH_2Cl_2 (6 mL) was added 4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenylamine (200 mg, 0.59 mmol) at 25 oC. The reaction mixture was stirred for 15 min and 4-aminopyridine (166 mg, 1.77 mmol) and NEt_3 (814 μL, 5.89 mmol) were added and the reaction mixture was stirred for additional 1hr. The solvents were distilled and the crude mixture was purified by semi-prep-HPLC (TFA-method) to give 1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea (75 mg, 22 % yield); MS (ESI) m/z 460

Example 101: Preparation of 1-{4-[4-Morpholin-4-yl-6-(tetrahydro-pyran-4-yl)-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea (130 mg, 0.28 mmol) and Pd-C (10%, wet) (113 mg) were suspended in methanol/THF/CH_2Cl_2 (4:1:1) (30mL) and hydrogenated (at 1 atm pressure) for 3h. After completion, the catalyst was removed by filtration over Celite™ and the solvents were removed *in vacuo* to obtain the crude product, which was purified by semi-prep-HPLC (TFA-method), to give (32mg=20%yield) of 1-{4-[4-Morpholin-4-yl-6-(tetrahydro-pyran-4-yl)-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea; MS (ESI) m/z 462.

Example 102: Preparation of 1-{4-[4-(8-methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea

Step 1: Preparation of 3-(4-Chloro-6-morpholin-4-yl-[1,3,5]triazin-2-yloxy)-8-methyl-8-aza-bicyclo[3.2.1]octane:

In a three neck flask equipped with stirring bar under N_2 atmosphere tropine (1g, 4.24 mmol) was suspended in (anhydrous) THF (15 mL). The mixture was cooled to –78 °C and BuLi (2M in THF) (5.53 ml, 1.2 eq) was added dropwise and the mixture was allowed to warm to 25 °C over 30 minutes. To the reaction mixture 2,4,-dichloro-6-morpholin-4-yl-[1,3,5]triazine (996 mg, 4,24, mmole) was added and allowed to stir overnight. For work up, ether(100 mL) was added. The organic layer was washed with water (20 mL) and brine (20 mL) and dried over $MgSO_4$. filtered and the solvents were removed to obtain a colorless oil. Further purification by flash-chromatography using CH_2Cl_2/MeOH/NH3 (15:1:0.1) gave the product as white solid (600mg, 42% yield); MS (ESI) m/z 340

Step 2: Preparation of 4-[4-(8-Methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenylamine:

To a microwave processing tube was added dimethoxyethane (4 mL), aqueous Na2CO3 (2 molar)(1 mL, 2 mmol, 2 eq), (Ph3P)4Pd (85 mg, 0.074 mmol), 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (482 mg, 2.21 mmol, 1.5 eq) and the 3-(4-chloro-6-morpholin-4-yl-[1,3,5]triazin-2-yloxy)-8-methyl-8-aza-bicyclo[3.2.1]octane (500 mg, 1.47 mmol) and the vessel was sealed. The mixture was heated to 140 oC for 60 minutes. The solvents were distilled and the crude compound was purified by silica gel chromatography using CH_2Cl_2/ethyl acetate (10:1) and later with CH_2Cl_2/MeOH/NH3 (10:1:0.1) to give the product as an off-white solid (300mg, 51 % yield); MS (ESI) m/z 369.

Step 3: Preparation of 1-{4-[4-(8-methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea:

To a stirred solution of triphosgene (60 mg, 0.20 mmol) in CH_2Cl_2 (3 mL) was added 4-[4-(8-Methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenylamine (100 mg, 0.25 mmol) at 25 oC. The reaction mixture was stirred for 15 min and 4-aminopyridine (70 mg, 0.75 mmol) and NEt_3 (346 μL, 2.5 mmol) were added and the reaction mixture was stirred for additional 1hr. The solvents were removed and the crude mixture was purified by semi-prep-HPLC (NH3-method) to give 1-{4-[4-(8-methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea (28 mg, 22 % yield); MS (ESI)m/z 517.

Example 103: Preparation of 4-(3-{4-[4-(8-Methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-ureido)-benzamide

To a stirred solution of triphosgene (120 mg, 0.40 mmol) in CH_2Cl_2 (3 mL) was added 4-[4-(8-Methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenylamine (200

mg, 0.5 mmol) at 25 oC. The reaction mixture was stirred for 15 min and 4-aminobenzamide (204 mg, 1.5 mmol) and NEt_3 (692 μL, 5 mmol) were added and the reaction mixture was stirred for additional 1hr. The solvents were removed and the crude mixture was purified by semi-prep-HPLC (NH3-method) to give 4-(3-{4-[4-(8-Methyl-8-aza-bicyclo[3.2.1]oct-3-yloxy)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-ureido)-benzamide (42 mg, 15 % yield)MS (ESI) m/z 559.

Example 104: Preparation of 3-({4-Morpholin-4-yl-6-[4-(3-pyridin-4-yl-ureido)-phenyl]-[1,3,5]triazin-2-ylamino}-methyl)-azetidine-1-carboxylic acid tert-butyl ester

Step1: Preparation of 3-[(4-Chloro-6-morpholin-4-yl-[1,3,5]triazin-2-ylamino)-methyl]-azetidine-1-carboxylic acid tert-butyl ester:

To a solution of the 3-aminomethyl-azetidine-1-carboxylic acid tert-butyl ester HCl salt (945mg, 4.24 mmol) and NEt_3 (856 mg, 8.48 mmol) in THF (10 mL) at 0 oC was added a suspension of 2,4-dichloro-6-morpholin-4-yl-[1,3,5]triazine (996 mg, 4.24 mmol) at 0 oC. The reaction mixture was stirred for another 1 hr at 0 oC and allowed to warm to 20 oC and stirred for 1-4 hrs to drive the reaction to completion. Silica gel (20 g) was added to the reaction mixture and the solvent was removed so that product was adsorbed on the silica gel. The silica gel plug was placed on top of a column to purify by flash chromatography using CH_2Cl_2/MeOH/NH3 (20:1:01) eluent. After unifying the product fraction, and evaporation of solvent, (750 mg, 46%yield) product was obtained as yellow solid; MS (ESI) m/z 385

Step 2: Preparation of 3-{[4-(4-Amino-phenyl)-6-morpholin-4-yl-[1,3,5]triazin-2-ylamino]-methyl}-azetidine-1-carboxylic acid tert-butyl ester:

To a microwave processing tube was added dimethoxyethane (15 mL), aqueous Na2CO3 (2 molar)(4 mL, 8 mmol, 2 eq), (Ph3P)4Pd (317 mg, 0.55 mmol), 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (1.81 g, 8.30 mmol, 1.5 eq) and 3-[(4-Chloro-6-morpholin-4-yl-[1,3,5]triazin-2-ylamino)-methyl]-azetidine-1-carboxylic acid tert-butyl ester (1.3 g, 5.53 mmol) and the vessel was sealed. The mixture was heated to 140 oC for 60 minutes. The solvents were removed and the crude compound was purified by silica gel chromatography using CH_2Cl_2/Ethyl acetate (10:1) and later CH_2Cl_2/MeOH/NH3 (15:1:0.1) to give the product as a off-white solid (1.3 g, 53 % yield).

MS (ESI) m/z = 442

Step 3: Preparation of 3-({4-Morpholin-4-yl-6-[4-(3-pyridin-4-yl-ureido)-phenyl]-[1,3,5]triazin-2-ylamino}-methyl)-azetidine-1-carboxylic acid tert-butyl ester

To a stirred solution of triphosgene (269 mg, 0.90 mmol) in CH_2Cl_2 (5 mL) was added 3-{[4-(4-Amino-phenyl)-6-morpholin-4-yl-[1,3,5]triazin-2-ylamino]-methyl}-azetidine-1-carboxylic acid tert-butyl ester (500 mg, 1.13 mmol) at 25 oC. The reaction mixture was stirred for 15 min and 4-aminopyridine (319 mg, 3.39 mmol) and NEt_3 (1.56 mL, 11.3 mmol) were added and the reaction mixture was stirred for additional 1hr. The solvents were removed on a rotary evaporator and the crude mixture was purified by semi-prep-HPLC (TFA-method) to give 3-({4-Morpholin-4-yl-6-[4-(3-pyridin-4-yl-ureido)-phenyl]-[1,3,5]triazin-2-ylamino}-methyl)-azetidine-1-carboxylic acid tert-butyl ester (150 mg, 16 % yield); MS (ESI) m/z 562.

Example 105: Preparation of 1-(4-{4-[(azetidin-3-ylmethyl)-amino]-6-morpholin-4-yl-[1,3,5]triazin-2-yl}-phenyl)-3-pyridin-4-yl-urea

3-({4-Morpholin-4-yl-6-[4-(3-pyridin-4-yl-ureido)-phenyl]-[1,3,5]triazin-2-ylamino}-methyl)-azetidine-1-carboxylic acid tert-butyl ester (100mg, 0.18 mmol) was dissolved CH_2Cl_2 (1 mL) and TFA (1 mL) was added. It was stirred for 16 hrs at 25 oC and then the solvents were removed under reduced pressure and the residue was treated with acetonitrile/MeOH (1:1) (2 mL) to obtain a white solid, which was collected by filtration to obtain the product as bis-TFA salt (59 mg, 46% yield). MS(ESI) m/z 462.

Example 106: Preparation of Tert-butyl 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperazine-1-carboxylate

Tert-butyl 4-(4,6-dichloro-1,3,5-triazin-2-yl)piperazine-1-carboxylate was prepared according to Löwik, D.W.P.M. and Lowe, C.R. Eur. J. Org. Chem. 2001, 2825-2839.

Step1: Preparation of tert-butyl 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-yl)piperazine-1-carboxylate:

To a solution of 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (0.49 g, 3.3 mmol) in water (18 mL) was added a suspension of tert-butyl 4-(4,6-dichloro-1,3,5-triazin-2-yl)piperazine-1-carboxylate (1.0 g, 3.0 mmol) in acetone (about 10 mL). The suspension was stirred magnetically while solid sodium carbonate (0.70 g, 6.6 mmol) was added in a single portion. The mixture was stirred for two hours while heating in a 70 - 75 °C in an oil bath. After allowing the mixture to cool to room temperature, the title compound was removed by filtration, washed with water, and dried under vacuum.

MS (ES+) 411.0, 412.3 (M+H) +

Step 2: Preparation of tert-butyl 4-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-1,3,5-triazin-2-yl)piperazine-1-carboxylate:

A suspension of tert-butyl 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-yl)piperazine-1-carboxylate (1.0 g, 2.4 mmol), 4-aminophenylboronic acid, pinacol ester (0.69 g, 3.2 mmol), and tetrakis(triphenylphosphine) palladium (0.28 g, 0.24 mmol) in aqueous 2 M sodium carbonate solution (3 mL) and 1:1 ethanol/toluene (12 mL) was irradiated in the microwave at 120 °C for 1 hour. After cooling, the biphasic mixture was extracted thrice with ethyl acetate. The extracts were washed with saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated to dryness under reduced pressure to give the title compound.

MS (ES+) 468.1 (M+H) +

Step 3: Preparation of tert-butyl 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperazine-1-carboxylate:

Crude tert-butyl 4-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-1,3,5-triazin-2-yl)piperazine-1-carboxylate (approx. 1.4 mmol) was dissolved in tetrahydrofuran (20 mL) and then treated sequentially with triphosgene (0.30 g, 1.0 mmol) and triethylamine (2 mL). After 5 minutes, the mixture was treated with a solution of 4-aminopyridine (0.53 g, 5.6 mmol) in tetrahydrofuran. The mixture was concentrated under reduced pressure to give crude tert-butyl 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperazine-1-carboxylate, a sample of which was purified by reversed phase HPLC to give a pure title compound.

MS (ES+) 588.2 (M+H) +

Example 107: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Crude tert-butyl 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperazine-1-carboxylate (approx 1.4 mmol) was taken up in dichloromethane (20 mL) and treated with trifluoroacetic acid (5 mL). The mixture was concentrated under reduced the pressure. To the residue was added diethyl ether to give the title compound as a solid di-TFA salt, which was collected by filtration and dried under house vacuum; MS (ES+) 488.1 (M+H) +

Example 108: Preparation of 1-{4-[4-(4-methylpiperazin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5- triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (115 mg) in 1:1 98 % formic acid and 37 % formalin (4 mL) was heated at 75 °C for 90 minutes, then concentrated to dryness and purified on HPLC to give the title compound as its di-TFA salt; MS (ES+) 502.3 (M+H) +

Example 109: Preparation of 1-{4-[4-(4-benzylpiperazin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5- triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (130 mg) in dichloromethane (4 mL) and triethylamine (0.10 mL) was treated with benzaldehyde (0.10 mL), followed by sodium triacetoxyborohydride (80 mg). The mixture was concentrated to dryness and purified on HPLC to give the title compound as its di-TFA salt; MS (ES+) 578.3 (M+H) +.

Example 110: Preparation of 1-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[4-(pyridin-3-ylmethyl)piperazin- 1-yl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (150 mg) in dichloromethane (4 mL) and triethylamine (0.12 mL) was treated with 3-pyridinecarboxaldehyde (0.1 mL), followed by sodium triacetoxyborohydride (80 mg). The mixture was concentrated to dryness and purified on HPLC to give the title compound as its tri-TFA salt; MS (ES+) 579.3 (M+H) +

Example 111: Preparation of 1-{4-[4-(4-acetylpiperazin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5- triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (230 mg) in dichloromethane (4 mL) and triethylamine (1 mL) was treated with acetyl chloride. The mixture was concentrated to dryness and purified on HPLC to give the title compound as its TFA salt; MS (ES+) 530.3 (M+H) +.

Example 112: Preparation of 1-(4-{4-[4-(N,N-dimethylglycyl)piperazin-1-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (64 mg) in dichloromethane (4 mL) and triethylamine (1 mL) was treated with dimethylaminoacetyl chloride hydrochloride (100 mg). The mixture was heated with a heat gun, then concentrated to dryness and purified on HPLC to give the title compound as its di-TFA salt; MS (ES+) 573.3 (M+H) +.

Example 113: Preparation of 1-{4-[4-(4-isonicotinoylpiperazin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- 1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (100 mg) in dichloromethane (4 mL) and triethylamine (1 mL) was treated with isonicotinoyl chloride (100 mg). The mixture was concentrated to dryness and purified on HPLC to give the title compound as its di-TFA salt; MS (ES+) 593.1 (M+H) +

Example 114: Preparation of Methyl 4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]piperazine-1-carboxylate

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(piperazin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·2TFA (75 mg) in dichloromethane (2 mL), tetrahydrofuran (2 mL), and triethylamine (1 mL) was treated with methyl chloroformate (0.10 mL). The mixture was concentrated to dryness and purified on RP-HPLC to give the title compound as its TFA salt. MS (ES+) 546.3 (M+H) +

Example 115: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Step 1: Preparation of 1-(4,6-dichloro-1,3,5-triazin-2-yl)piperidin-4-one:

To magnetically stirred ice-water (72 mL) was added a solution of cyanuric chloride (2.2 g, 12 mmol) in acetone (48 mL), followed by piperidone monohydrate hydrochloride (1.8 g, 12 mmol) as a suspension in acetone (20 mL) and water (10 mL). To the mixture was added a suspension of sodium hydrogen carbonate (2.2 g, 24 mmol) in water (25 mL). The mixture was stirred at 0 °C for two hours. The title compound was collected by filtration, washed with water, and dried under vacuum.

MS (ES+) 248.8 (M+H)+

Step 2: Preparation of 1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-yl)piperidin-4-one:

To an aqueous solution of 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (66 mL) was added 1-(4,6-dichloro-1,3,5-triazin-2-yl)piperidin-4-one (2.7 g, 11 mmol) as a suspension in acetone (40 mL). To the mixture was added solid sodium carbonate (2.5 g, 24 mmol). The suspension was stirred at 80 °C for two hours and then allowed to cool to room temperature. The title compound was collected by filtration, washed with water, and dried under vacuum; MS (ES+) 324.4 (M+H)+

Step 3: Preparation of 1-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-1,3,5-triazin-2-yl)piperidin-4-one:

A suspension of 1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-yl)piperidin-4-one (1.0 g, 3.1 mmol), 4-aminophenylboronic acid, pinacol ester (1.0 g, 4.7 mmol), and tetrakis(triphenylphosphine) palladium (0.20 g, 0.17 mmol) in aqueous 2 M sodium carbonate solution (3 mL) and 1:1 ethanol/toluene (12 mL) was irradiated in the microwave at 120 °C for 1 hour. After cooling, the biphasic mixture was extracted thrice with ethyl acetate. The extracts were washed with saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated to dryness under reduced pressure to give the title compound as a golden yellow foam.

MS (ES+) = 381.6 (M+H)+

Step 4: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea:

A mixture of crude 1-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-1,3,5-triazin-2-yl)piperidin-4-one (approx. 3.1 mmol) and triethylamine (4 mL) in dichloromethane (30 mL) was treated with triphosgene (0.71 g, 2.4 mmol). The mixture was then treated with a solution of 4-aminopyridine (1.8 g, 19 mmol) in tetrahydrofuran (20 mL). The mixture was concentrated to dryness under reduced pressure and the residue purified by HPLC to give the title compound as its TFA salt. MS (ES+) 501.2 (M+H)+

Example 116: Preparation of 1-{4-[4-(4-hydroxypiperidin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5- triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (56 mg) was taken up in methanol/tetrahydrofuran (1:1, 6 mL), and the mixture at 0 °C was treated with sodium borohydride (10 mg). After warming to room temperature, the mixture was concentrated to a residue which then was purified by HPLC to give the title compound as its TFA salt.; MS (ES+) 503.0 (M+H)+

Example 117: Preparation of 1-(4-{4-[4-(benzylamino)piperidin-1-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- 1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (85 mg) in dichloromethane (3 mL) and tetrahydrofuran (3 mL) was treated with benzylamine (0.030 mL), followed by glacial acetic acid (0.016 mL) and sodium triacetoxyborohydride (89 mg). After completion of the reaction, methanol was added and mixture was concentrated to dryness. The residue was purified by HPLC to give the title compound as its di-TFA salt.

MS (ES+) 592.3 (M+H)+

Example 118: Preparation of 1-(4-{4-[4-(methylamino)piperidin-1-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- 1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) in tetrahydrofuran (5 mL) was treated with methylamine (2.0 M solution in tetrahydrofuran, 0.16 mL), followed by glacial acetic acid (0.009 mL) and sodium triacetoxyborohydride (51 mg). After completion of the reaction, methanol was added and mixture was concentrated to dryness. The residue was purified by HPLC to give the title compound as its di-TFA salt; MS (ES+) 516.3 (M+H)+

Example 119: Preparation of 1-(4-{4-[4-(ethylamino)piperidin-1-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- 1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) in tetrahydrofuran (5 mL) was treated with ethylamine (2.0 M solution in tetrahydrofuran, 0.16 mL), followed by glacial acetic acid (0.009 mL) and sodium triacetoxyborohydride (51 mg). After completion of the reaction, methanol was added and mixture was concentrated to dryness. The residue was purified by HPLC to give the title compound as its di-TFA salt; MS (ES+) 530.3 (M+H)+

Example 120: Preparation of 1-{4-[4-(4-{[2-(dimethylamino)ethyl]amino}piperidin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

The titled compound was prepared by the procedure as outlined in **example 118**, by reacting 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) with N,N-dimethylethylenediamine (0.026 mL) and purified by HPLC and isolated as its tri-TFA salt; MS (ES+) 573.7 (M+H)+.

Example 121: Preparation of 1-{4-[4-(4-morpholin-4-ylpiperidin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- 1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

By reacting 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) with 1-(2-aminoethyl)pyrrolidine (0.030 mL) and following the procedure as mentioned in Experimental 118, the title product was isolated as its tri-TFA salt; MS (ES+) 599.8 (M+H)+.

Example 122: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(4-methylpiperazin-1-yl)piperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

By reacting1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (40 mg) and 1-methylpiperazine (0.050 mL) and following the procedure as outlined in **example 118**, the titled compound was isolated after HPLC purification as its tri-TFA salt; MS (ES+) 585.9 (M+H)+

Example 123: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(2-hydroxyethylamino)piperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Starting from 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) and ethanolamine (0.020 mL) and following the procedure as outlined in **example 118**, the title compound was isolated as its di-TFA salt after HPLC purification. MS (ES+) 546.7 (M+H)+

Example 124: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(2-morpholinoethylamino)piperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Starting from1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg)and 1-(2-aminoethyl)morpholine (0.031 mL) and

following the procedure as outlined in **example 118**, the titled compound was isolated as its tri-TFA salt after HPLC purification; MS (ES+) 615.9 (M+H)+

Example 125: Preparation of Methyl 2-(1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperidin-4-ylamino)acetate

Starting from 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) and glycine methyl ester hydrochloride (20 mg) and triethylamine (10 drops) and following the procedure as outlined in **example 118** the title compound was isolated as its di-TFA salt after HPLC purification; MS (ES+) 574.8 (M+H)+.

Example 126: Preparation of 2-(1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperidin-4-ylamino)acetamide

Starting from1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (50 mg) and glycinamide hydrochloride (18 mg) and triethylamine (10 drops) and following the procedure as outlined in **example 118** the title compound was isolated as its di-TFA salt after HPLC purification; MS (ES+) 559.8 (M+H)+

Example 127: Preparation of Tert-butyl 2-(1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperidin-4-ylamino)acetate

Starting from 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-oxopiperidin-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea·TFA (60 mg) and glycine tert-butyl ester hydrochloride (33 mg) and triethylamine (10 drops) and following the procedure as outlined in **example 118**, the title compound was isolated as its di-TFA salt after HPLC purification; MS (ES+) 616.9 (M+H)+.

Example 128: Preparation of 2-(1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperidin-4-ylamino)acetic acid

Tert-butyl 2-(1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)piperidin-4-ylamino)acetate (28 mg) in dichloromethane (3 mL) was treated with trifluoroacetic acid (1 mL) and then concentrated to dryness to give the title compound as its TFA salt.

MS (ES+) 560.2 (M+H)+.

Example 129: Preparation of 4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]aniline; MS (ES+) 399.47 (M+H)+.

Example 130: Preparation of 1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ES+) 519.58 (M+H)+.

Example 131: Preparation of 1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ES+) 519.58 (M+H)+.

Example 132: Preparation of 1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea; MS (ES+) 518.59 (M+H)+.

Example 133: Preparation of 1-[4-(dimethylamino)phenyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ES+) 561.66 (M+H)+.

Example 134: Preparation of 1-(4-cyanophenyl)-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ES+) 543.60 (M+H)+.

Example 135: Preparation of 1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(2-methylpyridin-4-yl)urea; MS (ES+) 533.61 (M+H)+

Example 136: Preparation of 1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ES+) 513.62 (M+H)+

Example 137: Preparation of 1-[4-(4-morpholin-4-yl-6-quinolin-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea

HRMS: calcd for C28H24N8O2 + H+, 505.20950; found (ESI, [M+H]+ Obs'd), 505.2098;

HRMS: calcd for C28H24N8O2 + H+, 505.20950; found (ESI, [M+H]+ Calc'd), 505.2095;

Example 138: Preparation of 2-(difluoromethyl)-1-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)-1H-benzimidazole

A solution of cyanuric chloride (922 mg, 5 mmol) in acetone (5 mL) was added to ice. A solution of 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (750 mg, 5 mmol) and triethylamine (2.1 mL, 15 mmol) in aqueous acetone was then added. After 20 min the precipitate was collected to give 1.0 g of a white powder which was a 7:3 mixture of 3-(4,6-dichloro-1,3,5-triazine-2,4-diyl)-8-oxa-

3-azabicyclo[3.2.1]octane and 3,3'-(6-chloro-1,3,5-triazine-2,4-diyl)bis(8-oxa-3-azabicyclo[3.2.1]octane). Treatment of the mixture (400 mg) with 2-(difluoromethyl)-1H-benzo[d]imidazole (146 mg, 0.87 mmol) and K2CO3 (967 mg, 7 mmol) in DMF (2.5 mL) for 18 hours, followed by addition of 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (150 mg) gave, after 1h, 3,3'-(6-(2-(difluoromethyl)-1H-benzo[d]imidazol-1-yl)-1,3,5-triazine-2,4-diyl)bis(8-oxa-3-azabicyclo[3.2.1]octane) after purification by HPLC. (M+H) 475.

Example 139: Preparation of 2-(difluoromethyl)-1-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]-1H-benzimidazole

To a stirred solution of 3-(4,6-dichloro-1,3,5-triazine-2,4-diyl)(8-oxa-3-azabicyclo[3.2.1]octane) (2.61 g, 10 mmol) in acetone/ice, morpholine (900 mg, 12 mmol) and triethylamine (5 ml) was added. The reaction mixture was stirred at room temperature for 3 hours. Separated white solid was filtered and washed with water. The crude product obtained was pure enough and taken to next step without purification. Treatment of the mixture (270 mg. 0.87 mmol) with 2-(difluoromethyl)-1H-benzo[d]imidazole (146 mg, 0.87 mmol) and K2CO3 (967 mg, 7 mmol) in DMF (2.5 mL) for 18 hours gave 2-(difluoromethyl)-1-[4-morpholin-4-yl-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]-1H-benzimidazole after purification by HPLC. (M+H) 445.

Example 140: Preparation of 1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; mp 212 °C; MS (ESI) m/z 433.3.

Example 141: Preparation of methyl 4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate; mp 212 °C; MS (ESI) m/z 490.2.

Example 142: Preparation of 1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; MS (ESI) m/z 561.6.

Example 143: Preparation of 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide

MS (ESI) m/z 575.6

Example 144: Preparation of 1-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(2-piperidin-1-ylethoxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 531.5

Example 145: Preparation of methyl(4-{4-[4-({[4-(4-methylpiperazin-1-yl)phenyl]carbamoyl}amino)phenyl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)carbamate; MS (ESI) m/z 650.7

Example 146: Preparation of 1-cyclopropyl-3-(4-{4-[4-({[4-(4-methylpiperazin-1-yl)phenyl]carbamoyl}amino)phenyl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 675.8

Example 147: Preparation of N',N'''-{[6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazine-2,4-diyl]di-4,1-phenylene}bis{1-[4-(4-methylpiperazin-1-yl)phenyl]urea}; MS (ESI) m/z 809.9

Example 148: Preparation of 1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-{4-[(pyridin-4ylcarbamoyl)amino] phenyl}-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 712.8

Example 149: Preparation of 1-(4-{4-[(2-aminoethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea

HRMS: calcd for C23H27N9O2 + H+, 462.23605; found (ESI, [M+H]+ Obs'd), 462.2358.

Example 150: Preparation of 1-{4-[4-anilino-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea

HRMS: calcd for C27H26N8O2 + H+, 495.22515; found (ESI, [M+H]+ Obs'd), 495.2249.

Example 151: Preparation of 4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide

MS (ESI) m/2 308.6; HRMS: calcd for C32H41N9O4 + H+, 616.33543; found (ESI, [M+H]+ Obs'd), 616.3347; HRMS: calcd for C32H41N9O4 + H+, 616.33543; found (ESI, [M+H]+ Calc'd), 616.3354;

Example 152: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(morpholin-4-ylcarbonyl)phenyl]urea

MS (ESI) m/z 575.3; HRMS: calcd for C29H34N8O5 + H+, 575.27249; found (ESI, [M+H]+ Obs'd), 575.2722; HRMS: calcd for C29H34N8O5 + H+, 575.27249; found (ESI, [M+H]+ Calc'd), 575.2725.

Example 153: Preparation of 1-(4-{4-[(2-hydroxyethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 463.5.

Example 154: Preparation of 1-{4-[4-(azetidin-3-ylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 474.5

Example 155: Preparation of 1-(4-{4-[(2-morpholin-4-ylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 532.6.

Example 156: Preparation of 1-(4-{4-[(3-aminopropyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 476.5.

Example 157: Preparation of 1-(4-{4-[(4-cyclopentylpiperazin-1-yl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 571.7

Example 158: 1-{4-[4-isopropoxy-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 462.53

Example 159: Preparation of 1-{4-[4-isopropoxy-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea

Example 160: Preparation of 1-{4-[4-chloro-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 438.8

Example 161: Preparation of 1-[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; MS (ESI) m/z 391.5

Example 162: Preparation of methyl 4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate; MS (ESI) m/z 449.2.

Example 163: Preparation of 1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl] phenyl}urea; MS (ESI) m/z 584.7

Example 164: Preparation of 4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide; MS (ESI) m/z 530.63.

Example 165: Preparation of N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide; MS (ESI) m/z 518.6

Example 166: Preparation of 1-[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; MS (ESI) m/z 516.6.

Example 167: Preparation of 1-(4-{[3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea

HRMS: calcd for C31H39N9O4 + H+, 602.31978; found (ESI, [M+H]+ Obs'd), 602.3192;

Example 168: Preparation of 1-[4-({4-[2-(dimethylamino) ethyl]piperazin-1-yl}carbonyl)phenyl]-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; HRMS: calcd for C33H44N10O4 + H+, 645.36198; found (ESI, [M+H]+ Obs'd), 645.3615;

Example 169: Preparation of 1-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(piperidin-4-ylmethyl)amino]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 515.6

Example 170: Preparation of 1-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(2-piperidin-4-ylethyl)amino]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 529.65.

Example 171: Preparation of 1-{4-[4-(3-methylimidazolidin-1-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 487.5

Example 172: Preparation of 1-{4-[4-(3-methyltetrahydropyrimidin-1(2H)-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 501.6

Example 173: Preparation of 1-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(2-piperidin-1-ylethoxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 530.6

Example 174: Preparation of 1-(4-{4-[2-methoxy-1-(methoxymethyl)ethoxy]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea; MS (ESI) m/z 521.58

Example 175: Preparation of 1-(4-{4-[2-methoxy-1-(methoxymethyl)ethoxy]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-[4-(4-methylpiperazin-1-yl)phenyl]urea; MS (ESI) m/z 618.7.

Example 176: Preparation of 2-hydroxyethyl (4-{4-[2-methoxy-1-(methoxymethyl)ethoxy]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)carbamate; MS (ESI) m/z 489.53.

Example 177: Preparation of 1-(4-{4-[2-methoxy-1-(methoxymethyl)ethoxy]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-methylurea; MS (ESI) m/z 458.52.

Example 178: Preparation of 1-cyclopropyl-3-(4-{4-[2-methoxy-1-(methoxymethyl)ethoxy]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 484.56.

Example 179: Preparation of 1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea

MS (ESI) m/z 642.4; HRMS: calcd for C34H43N9O4 + H+, 642.35108; found (ESI-FTMS, [M+H]1+), 642.3491;

Example 180: Preparation of 1-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(piperidin-3-ylmethoxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 516.61

Examples 181: Preparation of 1-{4-[4-(4-aminobutoxy)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 490.57

Examples 182: Preparation of 1-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(2-piperidin-4-ylethoxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 530.63

Example 183: Preparation of 1-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(piperidin-4-ylmethoxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 516.61

Example 184: Preparation 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid; MS (ESI) m/z 476.53

Example 185: Preparation of N-[2-(dimethylamino)ethyl]-4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide; MS (ESI) m/z 562.6

Example 186: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; MS (ESI) m/z 433.5

Example 187: Preparation of N-[2-(dimethylamino)ethyl]-4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide; MS (ESI) m/z 548.67

Example 188: Preparation of methyl 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate; MS (ESI) m/z 490.56.

Example 189: Preparation of 1-(4-{4-morpholin-4-yl-6-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

HRMS: calcd for C24H26N8O3 + H+, 475.22006; found (ESI, [M+H]+ Obs'd), 475.2201.

Example 190: Preparation of 1-{4-[4-(methylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 432.49.

Example 191: Preparation of 1-{4-[4-(ethylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 446.52

Example 192: Preparation of 1-{4-[4-(dimethylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 446.52.

Example 193: Preparation of 1-{4-[4-(isopropylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 460.54

Example 194: Preparation of 1-{4-[4-(diethylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 474.57.

Example 195: Preparation of 4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2yl)phenyl] carbamoyl} amino) benzoic acid; mp 204 °C; MS (ESI) m/z 476.2;

Example 196: Preparation of 1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; mp 170 °C; MS (ESI) m/z 558.2.

Example 197: Preparation of 4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide

MS (ESI) m/z 280.7;

Example 198: Preparation of 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide

Example 199: Preparation of 1-{4-[4-(1-ethoxyvinyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 447.499.

Example 200: Preparation of 1-{4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

HRMS: calcd for C22H25N7O4 + H+, 452.20408; found (ESI, [M+H]+ Obs'd), 452.2047;

Example 201: Preparation of 1-(diethylcarbamoyl)-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]pyridinium

HRMS: calcd for C30H38N9O4 + H+, 589.31195; found (ESI, [M+H]+), 589.3035;

Example 202: Preparation of 1-(4-{4-[ethyl(methyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 460.54.

Example 203: Preparation of 1-{4-[4-(sec-butylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 474.57.

Example 204: Preparation of 1-{4-[4-{[2-hydroxy-1-(hydroxymethyl)ethyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 492.54.

Example 205: Preparation of 1-(4-{4-[bis(2-hydroxyethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 506.57

Example 206: Preparation of 1-(4-{4-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 499.58.

Example 207: Preparation of 1-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 592.71.

Example 208: Preparation of 1-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 578.68.

Example 209: Preparation of 1-[4-(4-acetyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; MS (ESI) m/z 419.406

Example 210: Preparation of 1-(4-{4-morpholin-4-yl-6-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea; MS (ESI) m/z 654.3; HRMS: calcd for C35H43N9O4 + H+, 654.35108; found (ESI-FTMS, [M+H]1+), 654.35129;

Example 211: Preparation of methyl 4-[({4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate

HRMS: calcd for C25H28N6O6 + H+, 509.21431; found (ESI, [M+H]+ Obs'd), 509.214.

Example 212: Preparation of 1-methyl-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 397.48.

Example 213: Preparation of 1-cyclopropyl-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 423.52.

Example 214: Preparation of 1-(2-hydroxyethyl)-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 427.51.

Example 215: Preparation of 1-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea; MS (ESI) m/z 460.54.

Example 216: Preparation of 1-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]urea; MS (ESI) m/z 460.54.

Example 217: Preparation of 1-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-[4-(4-methylpiperazin-1-yl)phenyl]urea; MS (ESI) m/z 557.70.

Example 218: Preparation of 1-{4-[(2,2-dimethylhydrazino)carbonyl]phenyl}-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 545.65.

Example 219: Preparation of 4-{[(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-pyrrolidin-1-ylbenzamide; MS (ESI) m/z 571.69.

Example 220: Preparation of 1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 546.68.

Example 221: Preparation of 1-[4-(hydroxymethyl)phenyl]-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 489.58

Example 222: Preparation of 1-[4-(2-hydroxyethyl)phenyl]-3-(4-{4-[(1-methylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 503.61.

Example 223: Preparation of 1-{4-[4-(1-hydroxyethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 421.46.

Example 224: Preparation of 1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; MS (ESI) m/z 514.59.

Example 225: Preparation of methyl 4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate; MS (ESI) m/z 462.51

Example 226: Preparation of methyl 4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate; MS (ESI) m/z 516.55.

Example 227: Preparation of 4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid; MS (ESI) m/z 502.53

Example 228: Preparation of 1-(4-{4-morpholin-4-yl-6-[2-(pyridin-4-ylamino)ethyl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

HRMS: calcd for C26H27N9O2 + H+, 498.23605; found (ESI, [M+H]+ Obs'd), 498.2383;

Example 229: Preparation of 1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

HRMS: calcd for C31H39N9O3 + H+, 586.32486; found (ESI, [M+H]+ Obs'd), 586.3245;

Example 230: Preparation of 1-(4-acetylphenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

HRMS: calcd for C28H31N7O4 + H+, 530.25103; found (ESI, [M+H]+ Obs'd), 530.2508;

Example 231: Preparation of 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]benzamide; MS (ESI) m/z 546.676.

Example 232: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea

MS (ESI) m/z 559.4.

Example 233: Preparation of 4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid; MS (ESI) m/z 448.483

Example 234: Preparation of 1-methyl-3-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-1,3,5-triazin-2-yl]phenyl}urea

HRMS: calcd for C23H30N8O3 + H+, 467.25136; found (ESI, [M+H]+ Obs'd), 467.2525.

Example 235: Preparation of 1-{4-[4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea

HRMS: calcd for C27H31N9O3 + H+, 530.26226; found (ESI, [M+H]+ Obs'd), 530.2638;

Example 236: Preparation of 1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; MS (ESI) m/z 531.1.

Example 237: Preparation of N-[2-(dimethylamino)ethyl]-4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide

Example 238: Preparation of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 558.711

Example 239: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea; MS (ESI) m/z 462.554.

Example 240: Preparation of 4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide; MS (ESI) m/z 586.721.

Example 241: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea; MS (ESI) m/z 586.741.

Example 242: Preparation of N-[2-(dimethylamino)ethyl]-4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide; MS (ESI) m/z 532.649.

Example 243: Preparation of N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide; MS (ESI) m/z 534.62.

Example 244: Preparation of N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide; MS (ESI) m/z 520.60.

Example 245: Preparation of 4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methyl-N-[2-(methylamino)ethyl]benzamide; MS (ESI) m/z 520.60.

Example 246: Preparation of 1-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; MS (ESI) m/z 532.61.

Example 247: Preparation of 1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 546.63.

Example 248: Preparation of 4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide; MS (ESI) m/z 560.66.

Example 249: Preparation of 1-(4-ethenylphenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 514.3;

HRMS: calcd for C28H31N7O3 + H+, 514.25611; found (ESI, [M+H]+ Obs'd), 514.2561.

Example 250: Preparation of 1-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea;

HRMS: calcd for C32H41N9O3 + H+, 600.34051; found (ESI, [M+H]+ Obs'd), 600.3405.

Example 251: Preparation of 4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[4-(4-methylpiperazin-1-yl)phenyl]benzamide; MS (ESI) m/z 621.77.

Example 252: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]urea; MS (ESI) m/z 532.71.

Example 253: Preparation of 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[4-(4-methylpiperazin-1-yl)phenyl]benzamide; MS (ESI) m/z 649.82.

Example 254: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}urea; MS (ESI) m/z 544.728.

Example 255: Preparation of 1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-formylphenyl)urea; MS (ESI) m/z 461.2.

Example 256: Preparation of tert-butyl(1R,4R)-5-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)-2,5-diazabicyclo[2.2.1]heptane-2-carboxylate; mp 192 °C; MS (ESI) m/z 574.3.

Example 257: Preparation of tert-butyl (1R,4R)-5-[4-(4-{[(4-acetylphenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]-2,5-diazabicyclo[2.2.1]heptane-2-carboxylate; mp 202 °C; MS (ESI) m/z 615.3;

Example 258: Preparation of 1-(4-{4-[(2-methoxyethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 476.54

Example 259: Preparation of 1-{4-[4-{[(1S)-2-hydroxy-1-methylethyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 476.54.

Example 260: Preparation of 1-{4-[4-{[(1R)-2-hydroxy-1-methylethyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 476.54.

Example 261: Preparation of 1-(4-{4-[(2-hydroxy-1,1-dimethylethyl)amino]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea; MS (ESI) m/z 490.57.

Example 262: Preparation of 1-{4-[4-(tert-butylamino)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea; MS (ESI) m/z 474.57.

Example 263: Preparation of 4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(pyridin-2-ylmethyl)benzamide;

mp 296-298 °C; MS (ESI) m/z 298.6;

HRMS: calcd for C31H33N9O4 + H+, 596.27283; found (ESI, [M+H]+ Obs'd), 596.2724;

HRMS: calcd for C31H33N9O4 + H+, 596.27283; found (ESI, [M+H]+ Calc'd), 596.2728.

Example 264: Preparation of 1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-piperazin-1-ylphenyl)urea;

HRMS: calcd for C32H39N9O3 + H+, 598.32486; found (ESI, [M+H]+ Obs'd), 598.3247;

HRMS: calcd for C32H39N9O3 + H+, 598.32486; found (ESI, [M+H]+ Calc'd), 598.3249;

Example 265: Preparation of 1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

HRMS: calcd for C33H41N9O3 + H+, 612.34051; found (ESI, [M+H]+ Obs'd), 612.3402;

Example 266: Preparation of 1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

HRMS: calcd for C30H38N8O4 + H+, 575.30888; found (ESI, [M+H]+ Obs'd), 575.3088;

HRMS: calcd for C30H38N8O4 + H+, 575.30888; found (ESI, [M+H]+ Calc'd), 575.3089.

Example 267: Preparation of 1-(4-{4-[2-(1,3-dioxan-2-yl)ethyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

HRMS: calcd for C25H29N7O4 + H+, 492.23538; found (ESI, [M+H]+ Obs'd), 492.2364.

Example 268: Preparation of 1-(4-{4-[2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

HRMS: calcd for C25H30N8O4 + H+, 507.24628; found (ESI, [M+H]+ Obs'd), 507.2471.

Example 269: Preparation of 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-{4-[2-(dimethylamino)ethoxy]phenyl}benzamide; MS (ESI) m/z 638.773.

Example 270: Preparation of 1-{4-[(4-benzylpiperidin-1-yl)carbonyl]phenyl}-3-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 633.821.

Example 271: Preparation of 4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide; MS (ESI) m/z 545.3.

Example 272: Preparation of 4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide; MS (ESI) m/z 573.4.

Example 273: Preparation of 1-{4-[4-(6-hydroxy-3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 504.551.

Example 274: Preparation of 1-(4-{4-[3-(dimethylamino)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea; MS (ESI) m/z 462.56.

Example 275: Preparation of 1-[4-(4-{3-[(1-methylethyl)amino]propyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; MS (ESI) m/z 476.59.

Example 276: Preparation of 1-{4-[4-morpholin-4-yl-6-(3-pyrrolidin-1-ylpropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 488.60.

Example 277: Preparation of 1-(4-{4-[3-(4-methylpiperazin-1-yl)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea; MS (ESI) m/z 517.64.

Example 278: Preparation of 1-{4-[4-(3-{[2-(dimethylamino)ethyl]amino}propyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 505.63.

Example 279: Preparation of 1-{4-[4-(3-hydroxypropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 435.49.

Example 280: Preparation of 1-{4-[4-morpholin-4-yl-6-(3-oxopropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 433.47.

Example 281: Preparation of tert-butyl-7-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)-9-oxa-3,7-diazabicyclo[3.3.1]nonane-3-carboxylate

HRMS: calcd for C30H37N9O5 + H+, 604.29904; found (ESI, [M+H]+ Obs'd), 604.2993.

Example 282: Preparation of 1-{4-[4-(6,8-dioxa-3-azabicyclo[3.2.1]oct-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

HRMS: calcd for C24H26N8O4 + H+, 491.21498; found (ESI, [M+H]+ Obs'd), 491.2155.

Example 283: Preparation of 1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea; MS (ESI) m/z 612.759.

Example 284: Preparation of 4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]benzamide; MS (ESI) m/z 572.694.

Example 285: Preparation of 1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}urea; MS (ESI) m/z 625.78

Example 286: Preparation of N-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]piperazine-1-carboxamide; MS (ESI) m/z 506.61

Example 287: Preparation of 1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea; MS (ESI) m/z 543.63.

Example 288: Preparation of 1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(methylamino)methyl]phenyl}urea; MS (ESI) m/z 556.67.

Example 289: Preparation of 1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 600.73.

Example 290: Preparation of 1-{4-[4-morpholin-4-yl-6-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 503.57.

Example 291: Preparation of 1-{4-[4-(7-methyl-9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 517.60.

Example 292: Preparation of 1-{4-[4-(7-acetyl-9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea; MS (ESI) m/z 545.61.

Example 293: Preparation of 1-(4-{4-[7-(methylsulfonyl)-9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea; MS (ESI) m/z 581.66.

Example 294: Preparation of 1-[4-(4-methylpiperazin-1-yl)phenyl]-3-[4-(4-morpholin-4-yl-6-propyl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 517.4.

Example 295: Preparation of 1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 492.2.

Example 296: Preparation of 1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea; MS (ESI) m/z 503.

Example 297: Preparation of 1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 530.701.

Example 298: Preparation of 1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 544.684.

Example 299: Preparation of 4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylazetidin-3-yl)benzamide

MS (ESI) m/z 517.3;

MS (ESI) m/z 259.2;

Example 300: Preparation of methyl 4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate

mp 218 °C;

MS (ESI) m/z 477.3.

Example 301: Preparation of 4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid

MS (ESI) m/z 463.3.

Example 302: Preparation of tert-butyl-(1R,4R)-5-{4-[4-({[4-(1-hydroxyethyl)phenyl]carbamoyl}amino)phenyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}-2,5-diazabicyclo[2.2.1]heptane-2-carboxylate

MS (ESI) m/z 617.4.

Example 303: Preparation of 1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea

HRMS: calcd for C33H41N9O3 + H+, 612.34051; found (ESI, [M+H]+ Obs'd), 612.3402;

HRMS: calcd for C33H41N9O3 + H+, 612.34051; found (ESI, [M+H]+ Calc'd), 612.3405.

Example 304: Preparation of 1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; MS (ESI) m/z 544.66.

Example 305: Preparation of N-[2-(dimethylamino)ethyl]-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 532.65.

Example 306: Preparation of N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 546.68.

Example 307: Preparation of N-(1-methylazetidin-3-yl)-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 530.63.

Example 308: Preparation of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 572.72.

Example 309: Preparation of 4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-pyridin-4-ylbenzamide; MS (ESI) m/z 538.61.

Example 310: Preparation of 4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-pyridin-3-ylbenzamide; MS (ESI) m/z 538.61.

Example 311: Preparation of N-cyclobutyl-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 515.62.

Example 312: Preparation of 1-{4-[4,6-di-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea; MS (ESI) m/z 583.70.

Example 313: Preparation of 1-{4-[4,6-di-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-piperazin-1-ylphenyl)urea; MS (ESI) m/z 569.67.

Example 314: Preparation of 1-{4-[4,6-di-(1R,4R)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea; MS (ESI) m/z 583.70.

Example 315: Preparation of 1-(2-fluoroethyl)-3-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 561.6.

Example 316: Preparation of 1-cyclopropyl-3-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 555.71.

Example 317: Preparation of 1-methyl-3-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 529.67.

Example 318: Preparation of 4-[({4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 634.745.

Example 319: 1-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea; MS (ESI) m/z 591.72.

Example 320: Preparation of 1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-phenylpiperidin-1-yl)carbonyl]phenyl}urea

MS m/z 08-301429LMS.

Example 321: Preparation of 4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(pyridin-4-ylmethyl)benzamide

MS (ESI) m/z 539.4;

MS (ESI) m/z 270.2.

Example 322: Preparation of 1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 558.711.

Example 323: Preparation of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 586.765.

Example 324: Preparation of N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 560.727.

Example 325: Preparation of 1-methyl-3-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 515.62.

Example 326: Preparation of 1-cyclopropyl-3-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 541.66.

Example 327: Preparation of 1-(2-fluoroethyl)-3-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 547.64.

Example 328: Preparation of 1-(2-hydroxyethyl)-3-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)urea; MS (ESI) m/z 545.65.

Example 329: Preparation of 4-{[(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide; MS (ESI) m/z 620.72.

Example 330: Preparation of 1-(4-{4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-6-[(4-piperazin-1-ylphenyl)amino]-1,3,5-triazin-2-yl}phenyl)-3-phenylurea; MS (ESI) m/z 577.69.

Example 331: Preparation of 1-methyl-3-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 529.67.

Example 332: Preparation of 1-cyclopropyl-3-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 555.71.

Example 333:Preparation of 1-(2-fluoroethyl)-3-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 561.69.

Example 334:Preparation of 4-[({4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-yl]phenyl}carbamoyl) amino] benzamide; MS (ESI) m/z 634.745.

Example 335:Preparation of 1-{4-[4-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea; MS (ESI) m/z 591.72;

Example 336:Preparation of 1-(2,3'-bipyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea

MS (ESI) m/z 566.4; HRMS: calcd for C30H31N9O3 + H+, 566.26226; found (ESI, [M+H]+ Calc'd), 566.2623.

Example 337:Preparation of 1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea

MS (ESI) m/z 593.5.

Example 338:Preparation of N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide; MS (ESI) m/z 595.5.

Example 339:Preparation of 1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea

MS (ESI) m/z 593.4.

Example 340:Preparation of 1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea. MS (ESI) m/z 468.3.

Example 341:Preparation of 1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 531.4.

Example 342:Preparation of 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid, MS (ESI) m/z 511.4.

Example 343:Preparation of 1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea; MS (ESI) m/z 565.4.

Example 344:Preparation of methyl 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate; MS (ESI) m/z 525.4.

Example 345:Preparation of 1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 578.745

Example 346:Preparation of 1-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea; MS (ESI) m/z 454.1.

Preparation of (2S,5R)-pyrrolidine-2,5-diyldimethanol hydrochloride

((2S,5R)-1-benzylpyrrolidine-2,5-diyl)dimethanol (2.2 g, 10 mmol) was dissolved in ethanol/tetrahydrofuran (200 mL, 1:1), and the mixture was treated with 10 % palladium on carbon (250 mg). The suspension was shaken under 50 psi of hydrogen until the consumption of hydrogen had ceased. The mixture was filtered through a pad of Celite™ diatomaceous earth, eluting with ethanol. The filtrate was concentrated to dryness to provide the title compound as a golden oil that solidified upon prolonged storage. MS (ES^+) = 132.2 $(M+H)^+$

Preparation of ((2S,5R)-1-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol

A suspension of 2,4-dichloro-6-(4-nitrophenyl)-1,3,5-triazine (2.2 g, 8.0 mmol) in acetone (40 mL) was added to magnetically stirred ice water (60 mL). The mixture was treated with a solution of (2S,5R)-pyrrolidine-2,5-diyldimethanol hydrochloride (1.0 g, 6.0 mmol) in acetone/water (20 mL, 3:1), followed by a suspension of sodium hydrogen carbonate (1.0 g, 12 mmol) in water (12 mL). After 30 minutes of stirring at 0 °C, the mixture was treated with an additional quantity of (2S,5R)-pyrrolidine-2,5-diyldimethanol hydrochloride (0.26 g, 1.6 mmol) in water (3 mL), followed by sodium hydrogen carbonate (0.35 g) in water (5 mL). The suspension was allowed to stir overnight while regaining room temperature. The title compound was isolated by Büchner filtration, washed with water, and dried under house vacuum. Compound identification by mass spectrometry was achieved via the analysis of the product reaction product of ((2S,5R)-1-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol with excess morpholine in ethanol. MS (ES^+) = 417.2 (M + morpholine - Cl)$^+$

Preparation of ((2S,5R)-1-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol

A suspension of ((2S,5R)-1-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol (0.91 g, 2.5 mmol), 3-oxa-8-azabicyclo[3.2.1]octane hydrochloride (0.37 g, 2.5 mmol) in ethanol (13 mL) was treated with triethylamine (1 mL) and heated in a microwave reactor for 20 minutes at 130 °C. The reaction mixture was purified by automated flash chromatography (methanol/chloroform) to provide the title compound as a hard peach colored foam. MS (ES^+) = 443.2 $(M+H)^+$

Preparation of 8-(4-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane

A solution of ((2S,5R)-1-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol (approximately 2.7 mmol) in dichloromethane (15 mL) was treated successively with tert-butyl dimethyl chlorosilane (1.0 g, 6.8 mmol) and imidazole (0.55 g, 8.1 mmol). The resulting suspension was stirred overnight at room temperature and then quenched with water. The aqueous phase was extracted three times with dichloromethane. The combined extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated to dryness under reduced pressure. The crude residue was purified by automated flash chromatography (hexanes/ethyl acetate) to provide the title material. MS (ES^+) = 671.4 $(M+H)^+$

Preparation of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline

A suspension of palladium on charcoal (10 %, 50 mg) and 8-(4-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.55 g, 1.2 mmol) in tetrahydrofuran (20 mL) was stirred under a balloon of hydrogen overnight. The mixture was filtered through a pad of Celite™ diatomaceous earth and concentrated under reduced pressure to provide the title compound as a tan foam (0.42 g, 80 %). MS (ES^+) = 642.4 $(M+H)^+$

Example 347: Preparation of 1-(4-{4-[(2R,5S)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

A solution of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline (0.16 mmol) in dichloromethane (4 mL) was treated successively with triethylamine (1.6 mmol, 210 µL) and a triphosgene (24 mg, 0.08 mmol) solution in dichloromethane (500 µL). After 5 minutes, the mixture was treated with a solution of 4-aminopyridine (45 mg, 0.48 mmol) in warm tetrahydrofuran. After 1 hour, the reaction mixture was quenched with methanol and concentrated to dryness. The crude residue was treated with a saturated solution of hydrogen chloride in methanol. Upon complete desilylation, the mixture was concentrated to dryness and the residue purified by reverse-phase high performance liquid chromatography using a Phenomenex Prodigy column running a gradient elution of 5 % acetonitrile/95 % of 0.1 % aqueous trifluoroacetic acid to 50 % acetonitrile over 25 minutes. After concentration, the title compound was obtained as it trifluoroacetic acid salt (132 mg). MS (ES^+) = 533.3 $(M+H)^+$

Example 348: Preparation of 1-(4-{4-[(2R,5S)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl}phenyl)-3-[4-(4-methylpiperazin-1-yl)phenyl]urea

A solution of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline (0.16 mmol) in dichloromethane (4 mL) was treated successively with triethylamine (1.6 mmol, 210 μL) and a triphosgene (24 mg, 0.08 mmol) solution in dichloromethane (500 μL). After 5 minutes, the mixture was treated with 4-(4-methylpiperazin-1-yl)aniline (61 mg, 0.32 mmol). After 1 hour, the reaction mixture was quenched with methanol and concentrated to dryness. The crude residue was treated with a saturated solution of hydrogen chloride in methanol. Upon complete desilylation, the mixture was concentrated to dryness and the residue purified by reverse-phase high performance liquid chromatography using a Phenomenex Prodigy column running a gradient elution of 5 % acetonitrile/95 % of 0.1 % aqueous trifluoroacetic acid to 50 % acetonitrile over 25 minutes. After concentration, the title compound was obtained as it trifluoroacetic acid salt (100 mg). MS (ES^+) = 630.4 $(M+H)^+$

Example 349: Preparation of 1-(6-chloropyridin-3-yl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea. HRMS: calcd for C25H27ClN8O3 + H+, 523.19674; found (ESI, [M+H]+ Obs'd), 523.1975.

Example 350: Preparation of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea; MS (ESI) m/z 614.8

Example 351: Preparation of 1-(4-aminophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea; MS (ESI) m/z 477.1.

Example 352: Preparation of N-[4-({[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-N2,N2-dimethylglycinamide

The 4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)aniline (50 mg, 0.127 mmol) was dissolved in dichloromethane (1.5 mL) and triethylamine (0.120 mL) and added to a solution of triphosgene (17 mg) in dichloromethane (0.5 mL). Stir for 5 minutes then added N-(4-aminophenyl)-N2,N2-dimethylglycinamide (27 mg, 0.14 mmol). Purified by Gilson HPLC to provide the title compound as the TFA salt: 31.8 mg (35%) (M+H) m/z 614.3.

Example 353: Preparation of N-[4-({[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-2-pyrrolidin-1-ylacetamide

The 4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)aniline (50 mg, 0.127 mmol) was dissolved in dichloromethane (1.5 mL) and triethylamine (0.120 mL) and added to a solution of triphosgene (17 mg) in dichloromethane (0.5 mL). Stir for 5 minutes then added N-(4-aminophenyl)-2-pyrrolidin-1-ylacetamide (30 mg, 0.14 mmol) Purified by Gilson HPLC to provide the title compound as the TFA salt: 63.1 mg (66%) (M+H) m/z 640.3.

Example 354: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(piperazin-1-yl)phenylamino)-1,3,5-triazin-2-yl)phenyl)-3-methylurea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using methylamine, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 516.3.

Example 355: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(piperazin-1-yl)phenylamino)-1,3,5-triazin-2-yl)phenyl)-3-cyclopropylurea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using cyclopropylamine, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 542.3.

Example 356: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(piperazin-1-yl)phenylamino)-1,3,5-triazin-2-yl)phenyl)-3-(2-fluoroethyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using 2-fluoroethylamine, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 548.3.

Example 357: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(piperazin-1-yl)phenylamino)-1,3,5-triazin-2-yl)phenyl)-3-(2-hydroxyethyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using 2-aminoethanol, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 546.3.

Example 358: Preparation of 4-(3-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(piperazin-1-yl)phenylamino)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using 4-aminobenzamide, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 621.3.

Example 359: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-(piperazin-1-yl)phenylamino)-1,3,5-triazin-2-yl)phenyl)-3-phenylurea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using aniline, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 578.3.

Example 360: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(piperidin-4-ylamino)-1,3,5-triazin-2-yl)phenyl)-3-ethylurea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-aminopiperidine-1-carboxylate in the second nucleophilic aromatic substitution step. Following urea formation using ethylamine, the Boc-piperidine intermediate was treated with TFA to provide the title compound. (M+H) 453.6.

Example 361: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(piperidin-4-ylamino)-1,3,5-triazin-2-yl)phenyl)-3-ethylurea

Prepared as shown in Scheme 1, using N1-(2-(dimethylamino)ethyl)-N1-methylbenzene-1,4-diamine in the urea formation step. (M+H) 614.3.

The required benzene-1,4-diamine intermediates for the following compounds were prepared as outlined in Scheme 4.

Example 362: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(piperidin-4-ylamino)-1,3,5-triazin-2-yl)phenyl)-3-ethylurea

Prepared as shown in Scheme 1, using 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine in the urea formation step. (M+H) 640.4.

Preparation of 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 363: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(piperidin-4-ylamino)-1,3,5-triazin-2-yl)phenyl)-3-ethylurea

Prepared as shown in Scheme 1, using N1-(2-methoxyethyl)benzene-1,4-diamine in the urea formation step. (M+H) 587.3.

Preparation of N1-(2-methoxyethyl)benzene-1,4-diamine:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 364: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(piperidin-4-ylamino)-1,3,5-triazin-2-yl)phenyl)-3-ethylurea

Prepared as shown in Scheme 1, using 2-(4-aminophenylamino)ethanol in the urea formation step. (M+H) 573.3.

Preparation of 2-(4-aminophenylamino)ethanol:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 365: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(piperidin-4-ylamino)-1,3,5-triazin-2-yl)phenyl)-3-ethylurea

Prepared as shown in Scheme 1, using N1-(1-methylpiperidin-4-yl)benzene-1,4-diamine in the urea formation step. (M+H) 626.3.

Preparation of N1-(1-methylpiperidin-4-yl)benzene-1,4-diamine:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 366: Preparation of 1-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-ylmethyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminobenzyl)piperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-piperidine intermediate was treated with TFA to provide the title compound. (M+H) 612.3.

Example 367: Preparation of 1-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. (M+H) 571.3.

Example 368: Preparation of 1-(4-(aminomethyl)phenyl)-3-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-aminobenzylcarbamate in the urea formation step. Following urea formation, the Boc-amine intermediate was treated with TFA to provide the title compound. (M+H) 543.3.

Example 369: Preparation of 1-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-(pyrrolidin-1-ylmethyl)aniline in the urea formation step. (M+H) 597.3.

Example 370: Preparation of 1-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(4-methylpiperazin-1-yl)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(4-methylpiperazin-1-yl)ethoxy)aniline in the urea formation step. (M+H) 656.4.

The required 4-(alkoxy)aniline intermediates for the following compounds were prepared as outlined in Scheme 5.

Example 371: Preparation of 1-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(pyrrolidin-1-yl)ethoxy)aniline in the urea formation step. (M+H) 627.3.

Preparation of 4-(2-(pyrrolidin-1-yl)ethoxy)aniline:

Prepared from 4-fluoronitrobenzene and the appropriate alcohol as shown in Scheme 5.

Example 372: Preparation of 1-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxyethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 2-(4-aminophenoxy)ethanol in the urea formation step. (M+H) 574.3.

Preparation of 2-(4-aminophenoxy)ethanol:

Prepared from 4-fluoronitrobenzene and the appropriate alcohol as shown in Scheme 5.

Example 373: Preparation of N-(4-(3-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)ureido)phenyl)-2-(dimethylamino)acetamide

Prepared as shown in Scheme 1, using commercially available N-(4-aminophenyl)-2-(dimethylamino)acetamide in the urea formation step. (M+H) 614.3.

Example 374: Preparation of N-(4-(3-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)ureido)phenyl)-2-(4-methylpiperazin-1-yl)acetamide

Prepared as shown in Scheme 1, using commercially available N-(4-aminophenyl)-2-(4-methylpiperazin-1-yl)acetamide in the urea formation step. (M+H) 669.4.

Example 375: Preparation of N-(4-(3-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)ureido)phenyl)-2-(pyrrolidin-1-yl)acetamide

Prepared as shown in Scheme 1, using commercially available N-(4-aminophenyl)-2-(pyrrolidin-1-yl)acetamide in the urea formation step. (M+H) 640.3.

Example 376: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea

Prepared as shown in Scheme 1, using commercially available pyridin-3-amine in the urea formation step. (M+H) 461.2.

Example 377: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Prepared as shown in Scheme 1, using commercially available pyridin-4-amine in the urea formation step. (M+H) 461.2.

Example 378: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. (M+H) 558.3.

Example 379: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((4-methylpiperazin-1-yl)methyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-((4-methylpiperazin-1-yl)methyl)aniline in the urea formation step. (M+H) 572.3.

Example 380: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-ylmethyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminobenzyl)piperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-piperazine intermediate was treated with TFA to provide the title compound. (M+H) 558.3.

Example 381: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. (M+H) 517.3.

Example 382: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(aminomethyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-aminobenzylcarbamate in the urea formation step. Following urea formation, the Boc-amine intermediate was treated with TFA to provide the title compound. (M+H) 489.3.

Example 383: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-(pyrrolidin-1-ylmethyl)aniline in the urea formation step. (M+H) 543.3.

Example 384: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(pyrrolidin-1-yl)ethoxy)aniline in the urea formation step. (M+H) 573.3.

Example 385: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. (M+H) 547.3.

Preparation of 4-(2-(dimethylamino)ethoxy)aniline:

Prepared from 4-fluoronitrobenzene and the appropriate alcohol as shown in Scheme 5.

Example 386: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea

Prepared as shown in Scheme 1, using commercially available 5-(4-methylpiperazin-1-yl)pyridin-2-amine in the urea formation step. (M+H) 559.3.

Example 387: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-yl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-amine intermediate was treated with TFA to provide the title compound. (M+H) 544.3.

Example 388: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropylamino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea

Prepared as shown in Scheme 1, using 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine in the urea formation step. (M+H) 586.4.

Example 389: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropyl(methyl)amino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. (M+H) 572.3.

Example 390: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropyl(methyl)amino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. (M+H) 531.3.

Example 391: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(isopropyl(methyl)amino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. (M+H) 561.3.

Example 392: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea (Scheme 6).

Step 1: Preparation of 8-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane:

A solution of 2,4-dichloro-6-(4-nitrophenyl)-1,3,5-triazine (1.25 g, 4.61 mmol) in acetone (20 mL) and ice water (20 mL) was prepared. To this was added dropwise over 10 minutes a suspension of 3-oxa-8-azabicyclo[3.2.1]octane-hydrochloride (0.655 g, 4.38 mmol) and sodium bicarbonate (0.775 g, 9.22 mmol) in acetone (15 mL) and water (15 mL). The resulting tan solution was allowed to stir at 0 ^{o}C for 2 hours, then gradually allowed to warm to room temperature over 18 hours. The light brown suspension was filtered and washed with water. The crude product was purified by silica gel column chromatography, eluting with 0-1.5% methanol in methylene chloride to provide 8-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.89 g, 56%) as an off-white solid. (M+H) 348.1.

Step 2: Preparation of 8-(4-(4-nitrophenyl)-6-thiomorpholino-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane:

A solution of 8-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.450 g, 1.29 mmol) in acetone (5 mL) and water (10 mL) was prepared. To this was added sodium carbonate (0.274 g, 2.59 mmoles), followed by thiomorpholine (0.134 ml, 1.42 mmol). The resulting light tan suspension was allowed to stir at 60 ^{o}C for 2.5 hours. The suspension was filtered and the solid was washed with water and dried in vacuo to provide 8-(4-(4-nitrophenyl)-6-thiomorpholino-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.455 g, 85%) as a white solid. HRMS 415.1546 (M+H, calc.), 415.1526 (M+H, obs.).

Step 3: Preparation of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)aniline:

A suspension of 8-(4-(4-nitrophenyl)-6-thiomorpholino-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.418 g, 1.01 mmol) in pyridine (3 ml) and DMF (6 ml) was prepared. Tin(II) chloride dihydrate (0.569 g, 2.52 mmol) was then added and the off-white suspension was allowed to stir at room temperature for 16 hours, at which time the suspension was light yellow. The suspension was filtered, washing with methanol, and concentrated. LCMS indicated reaction had not gone to completion. The crude product was dissolved in DMF (6 ml) and pyridine (3 ml) and additional tin(II) chloride dihydrate (0.569 g, 2.52 mmol) was added. The solution was allowed to stir at room temperature for 18 hours, then filtered. The precipitate was washed with methanol and the filtrate was concentrated to provide 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)aniline (0.195 g, 50%) as a yellow solid. (M+H) 385.1.

Step 4: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea:

The method of urea formation using triphosgene and triethylamine in methylene chloride, described in Scheme 1, was utilized using commercially available pyridin-3-amine as the amine component. Purification by HPLC (5-95% acetonitrile in water over 20 minutes, 0.05% TFA buffer, Waters Atlantis column) provided 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea (0.032 g, 63%) as an off-white solid. (M+H) 505.2.

Example 393: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Prepared as shown in Scheme 6, using commercially available pyridin-4-amine in the urea formation step. Yield; 28 mg (54%); (M+H) 505.2.

Example 394: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea

Prepared as shown in Scheme 6, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. Yield; 44 mg (73%); (M+H) 602.3.

Example 395: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea

Prepared as shown in Scheme 6, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. Yield; 19 mg (34%); (M+H) 561.3.

Example 365: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea

Prepared as shown in Scheme 6, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. Yield; 35 mg (59%); (M+H) 591.3.

Example 397: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea

Prepared as shown in Scheme 1, using commercially available pyridin-4-amine in the urea formation step. Yield; 44 mg (75%); (M+H) 491.2.

Example 398: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea

Prepared as shown in Scheme 1, using commercially available pyridin-3-amine in the urea formation step. Yield; 46 mg (79%); (M+H) 491.2.

Example 399: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. Yield; 57 mg (81%); (M+H) 588.3.

Example 400: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea

Prepared as shown in Scheme 1, using commercially available 5-(4-methylpiperazin-1-yl)pyridin-2-amine in the urea formation step. Yield; 56 mg (79%); (M+H) 589.3.

Example 401: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea

Prepared as shown in Scheme 1, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. Yield; 28 mg (43%); (M+H) 547.3.

Example 402: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. Yield; 50 mg (72%); (M+H) 577.3.

Example 403: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)urea

Prepared as shown in Scheme 1, using 4-(2-(pyrrolidin-1-yl)ethoxy)aniline in the urea formation step. Yield; 41 mg (57%); (M+H) 603.3.

Example 404: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(3,6-dihydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea (Scheme 7)

Step 1: Preparation of 8-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane: Prepared as shown in Scheme 6, described in **Example 392**, Step 1.

Step 2: Preparation of 8-(4-(3,6-dihydro-2H-pyran-4-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane:

A microwave vial was charged with 8-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.440 g,1.27 mmoles). Toluene (6 mL) was then added and the solution was sparged with nitrogen for 10 minutes. Tetrakis(triphenylphosphine)palladium(0) (0.088 g, 0.076 mmol) and tributyl(3,6-dihydro-2H-pyran-4-yl)stannane (0.567 g, 1.52 mmol) were added. The vial was sealed and heated to 100 °C for 40 minutes via microwave. Additional tributyl(3,6-dihydro-2H-pyran-4-yl)stannane (0.283 g, 0.76 mmoles) and tetrakis(triphenylphosphine)palladium(0) (0.022 g, 0.019 mmol) were added and the suspension was heated to 110 °C by microwave for additional 90 minutes. The suspension was then cooled

to room temperature and filtered through Celite™. The filter cake was washed with ethyl acetate and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography, eluting with 0-2% methanol in methylene chloride, to provide 8-(4-(3,6-dihydro-2H-pyran-4-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.430 g, 86 %) as a light yellow solid. HRMS 396.1666 (M+H, calc.), 396.1668 (M+H, obs.).

Step 3: Preparation of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(3,6-dihydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)aniline:

A mixture of iron powder (0.071 g, 1.27 mmoles) in acetic acid (2 ml) was heated to 55 °C for 15 minutes. Water (2 ml) was then added and oil bath was turned off. A solution of 8-(4-(3,6-dihydro-2H-pyran-4-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.100 g, 0.253 mmol) in ethyl acetate (2 ml) was then added to this warm solution over 5 minutes. The mixture was cooled to RT and allowed to stir for 16 hours. The mixture was extracted with ethyl acetate by decantation (4X) into a sep. funnel containing saturated aqueous sodium carbonate. The combined organic extracts were washed with water, brine, dried, and concentrated to provide 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(3,6-dihydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)aniline (0.068 g, 74%), which was used in the next step without purification. (M+H) 366.4.

Step 4: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(3,6-dihydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea :

The method of urea formation using triphosgene and triethylamine in methylene chloride, described in Scheme 1, was utilized using commercially available pyridin-4-amine as the amine component. Purification by HPLC (5-95% acetonitrile in water over 20 minutes, 0.05% TFA buffer, Waters Atlantis column) provided 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(3,6-dihydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea (0.034 g, 75%) as a light yellow solid. (M+H) 486.2.

Example 405: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(3,6-dihydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step.. Yield; 44 mg (82%); (M+H) 583.3.

Example 406: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea :

Prepared as shown in Scheme 7; representative synthesis described below.

Preparation of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)aniline:

A solution of 8-(4-(3,6-dihydro-2H-pyran-4-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (prepared as described in Example DJR-51, Step 2) (0.260 g, 0.658 mmol) in ethyl acetate (5 ml), methanol (5 ml), and methylene chloride (2 ml - added due to poor solubility of SM in EA/methanol) was prepared and 10% palladium on carbon (0.078 g, 30% by weight) was added. The flask was purged with hydrogen gas (balloon) and allowed to stir under positive pressure of hydrogen for 16 hours. Additional palladium on carbon (0.039 g) was added and the suspension was purged with hydrogen gas (balloon) and stirred for an additional 3 hours. The flask was purged with hydrogen gas and stirred for an additional 1 hour. The suspension was filtered through Celite™, the filter cake was washed with ethyl acetate, and the filtrate was concentrated to provide 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)aniline (0.220 g, 91%) as an off-white solid. HRMS 368.2080 (M+H, calc.), 368.2085 (M+H, obs.).

Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea :

The method of urea formation using triphosgene and triethylamine in methylene chloride, described in Scheme 1, was utilized using commercially available pyridin-4-amine as the amine component. Purification by HPLC (5-95% acetonitrile in water over 20 minutes, 0.05% TFA buffer, Waters Atlantis column) provided 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea (0.0461 g, 82%) as an off-white solid. (M+H) 488.2.

Example 407: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. Yield; 54 mg (79%); (M+H) 585.3.

Example 408: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea :

Prepared as shown in Scheme 7, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. Yield; 49 mg (73%); (M+H) 572.3.

Example 409: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available 4-((dimethylamino)methyl)aniline in the urea formation step. Yield; 21 mg (33%); (M+H) 544.3.

Example 410: Preparation of 1-(4-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea :

Prepared as shown in Scheme 1, using commercially available pyridin-4-amine in the urea formation step. Yield; 45 mg (70%); (M+H) 489.2.

Example 411: Preparation of 1-(4-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea :

Prepared as shown in Scheme 1, using commercially available pyridin-3-amine in the urea formation step. Yield; 60 mg (95%); (M+H) 489.2.

Example 412: Preparation of 1-(4-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. Yield; 69 mg (90%); (M+H) 586.3.

Example 413: Preparation of 1-(4-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((4-methylpiperazin-1-yl)methyl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-((4-methylpiperazin-1-yl)methyl)aniline in the urea formation step. Yield; 73 mg (94%); (M+H) 600.3.

Example 414: Preparation of 1-(4-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-(pyrrolidin-1-ylmethyl)aniline in the urea formation step. Yield; 56 mg (75%); (M+H) 571.3.

Example 415: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea :

Prepared as shown in Scheme 1, using commercially available pyridin-3-amine in the urea formation step. Yield; 44 mg (66%); (M+H) 503.2.

Example 416: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea :

Prepared as shown in Scheme 1, using commercially available pyridin-4-amine in the urea formation step. Yield; 35 mg (53%); (M+H) 503.2.

Example 417: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. Yield; 58 mg (62%); (M+H) 600.3.

Example 418: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-(pyrrolidin-1-ylmethyl)aniline in the urea formation step. Yield; 41 mg (45%); (M+H) 585.5.

Example 419: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea :

Prepared as shown in Scheme 1, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. Yield; 43 mg (47%); (M+H) 589.3.

Example 420: Preparation of (R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea :

Prepared as shown in Scheme 7, using commercially available pyridin-3-amine in the urea formation step. Yield; 45 mg (77%); (M+H) 476.2.

Example 421: Preparation of (R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available 4-(4-methylpiperazin-1-yl)aniline in the urea formation step. Yield; 53 mg (75%); (M+H) 573.3.

Example 422: Preparation of (R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-piperazine intermediate was treated with TFA to provide the title compound. Yield; 63 mg (90%); (M+H) 559.3.

Example 423: Preparation of 1-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((S)-3-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using (S)-tert-butyl 4-(4-aminophenyl)-3-methylpiperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-piperazine intermediate was treated with TFA to provide the title compound. Yield; 60 mg (71%); (M+H) 573.3.

Preparation of (S)-tert-butyl 4-(4-aminophenyl)-3-methylpiperazine-1-carboxylate:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 424: Preparation of 1-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((R)-3-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using (R)-tert-butyl 4-(4-aminophenyl)-3-methylpiperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-piperazine intermediate was treated with TFA to provide the title compound. Yield; 68 mg (90%); (M+H) 573.3.

Preparation of (R)-tert-butyl 4-(4-aminophenyl)-3-methylpiperazine-1-carboxylate:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 425: Preparation of 1-(4-((3R,5S)-3,5-dimethylpiperazin-1-yl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 7, using (3,5-cis)-tert-butyl 4-(4-aminophenyl)-3,5-dimethylpiperazine-1-carboxylate in the urea formation step. Following urea formation, the Boc-piperazine intermediate was treated with TFA to provide the title compound. Yield; 67 mg (77%); (M+H) 587.3.

Preparation of (3,5-cis)-tert-butyl 4-(4-aminophenyl)-3,5-dimethylpiperazine-1-carboxylate:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 426: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-sulfoxymorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 6. A solution of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-thiomorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea (0.020 g, 0.033 mmol) in acetonitrile (1.5 ml) and water (0.5 ml) was prepared and oxone (0.020 g, 0.033 mmol) was added. The solution was stirred at room temperature for 16 hours. The suspension was diluted with ethyl acetate and washed with saturated sodium bicarbonate. The organic phase was washed with brine, dried, and concentrated, then purified by HPLC (5-95% acetonitrile in water over 20 minutes, 0.05% TFA buffer, Waters Atlantis column) to provide the TFA salt of the sulfoxide of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-sulfoxymorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea (0.0029 g, 14%) as a white solid. (M+H) 618.4.

Example 427: Preparation of (R)-1-(4-(2-(dimethylamino)ethoxy)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 7, using 4-(2-(dimethylamino)ethoxy)aniline in the urea formation step. Yield; 34 mg (51%); (M+H) 562.3.

Example 428: Preparation of (R)-1-(4-(4-ethylpiperazin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available 4-(4-ethylpiperazin-1-yl)aniline in the urea formation step. Yield; 66 mg (93%); (M+H) 587.3.

Example 429: Preparation of (R)-1-(4-(4-isopropylpiperazin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 7, using 4-(4-isopropylpiperazin-1-yl)aniline in the urea formation step. Yield; 66 mg (91%); (M+H) 601.4.

Preparation of 4-(4-isopropylpiperazin-1-yl)aniline:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 430: Preparation of (R)-1-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 7, using 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine in the urea formation step. Yield; 69 mg (95%); (M+H) 601.4.

Example 431: Preparation of (R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 7, using (4-aminophenyl)(4-methylpiperazin-1-yl)methanone in the urea formation step. Yield; 38 mg (52%); (M+H) 601.3.

The (4-aminophenyl)(piperazin-1-yl)methanone intermediates prepared as shown in Scheme 8 were used to make the following compounds.

Example 432: Preparation of (R)-1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 7, using (4-aminophenyl)(4-isopropylpiperazin-1-yl)methanone in the urea formation step. Yield; 68 mg (89%); (M+H) 629.3.

Preparation of (4-aminophenyl)(4-isopropylpiperazin-1-yl)methanone:

Prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

Example 433: Preparation of (R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea :

Prepared as shown in Scheme 7, using commercially available 6-(4-methylpiperazin-1-yl)pyridin-3-amine in the urea formation step. Yield; 69 mg (99%); (M+H) 574.3.

Example 434: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using commercially available 4-(4-ethylpiperazin-1-yl)aniline in the urea formation step. Yield; 32 mg (43%); (M+H) 599.3.

Example 435: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using 4-(4-isopropylpiperazin-1-yl)aniline in the urea formation step. Yield; 51 mg (66%); (M+H) 613.4.

Example 436: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-cyclopropylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using 4-(4-cyclopropylpiperazin-1-yl)aniline in the urea formation step. Yield; 11 mg (14%); (M+H) 611.3.

Preparation of 4-(4-cyclopropylpiperazin-1-yl)aniline:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 437: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea :

Prepared as shown in Scheme 7, using 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine in the urea formation step. Yield; 28 mg (36%); (M+H) 613.4.

Example 438: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 7, using (4-aminophenyl)(4-methylpiperazin-1-yl)methanone in the urea formation step. Yield; 36 mg (46%); (M+H) 613.3.

Example 439: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 7, using (4-aminophenyl)(4-isopropylpiperazin-1-yl)methanone in the urea formation step. Yield; 41 mg (50%); (M+H) 641.3.

The following 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-urea compounds were prepared as shown in Scheme 9.

Example 440: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea :

Step 1: Preparation of (R)-4-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-methylmorpholine:

A solution of 2,4-dichloro-6-(4-nitrophenyl)-1,3,5-triazine (1.25 g, 4.61 mmol) and sodium bicarbonate (0.775 g, 9.22 mmol) in acetone (20 mL) and ice water (20 mL) was prepared. To this was added dropwise over 5 minutes (R)-3-methylmorpholine (0.466 g, 4.61 mmol). The resulting tan solution was allowed to stir at 0 ^{o}C for 2 hours, then gradually allowed to warm to room temperature over 18 hours. The light brown suspension was filtered and washed with water to provide (R)-4-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-methylmorpholine (1.40 g, 90%) as a light brown solid. HRMS 336.0857 (M+H, calc.), 336.0845 (M+H, obs.).

Step 2: Preparation of 8-(4-((R)-3-methylmorpholino)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane:

A solution of (R)-4-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-methylmorpholine (0.94 g, 2.80 mmol) in acetone (10 mL) and ice water (10 mL) was prepared. To this was added dropwise over 10 minutes a suspension of 3-oxa-8-azabicyclo[3.2.1]octane-hydrochloride (0.419 g, 2.80 mmol) and sodium bicarbonate (0.470 g, 5.60 mmol) in acetone (10 mL) and water (10 mL). The resulting tan solution was allowed to stir at 0 ^{o}C for 2 hours, then gradually allowed to warm to room temperature over 3 hours. The light brown suspension was filtered and washed with water to provide 8-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.964 g, 83%) as a brown solid. HRMS 413.1931 (M+H, calc.), 413.1936 (M+H, obs.).

Step 3: Preparation of 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)aniline:

A solution of 8-(4-((R)-3-methylmorpholino)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-3-oxa-8-azabicyclo[3.2.1]octane (0.915 g, 2.22 mmol) in ethyl acetate (10 ml), methanol (10 ml), and methylene chloride (5 ml - added due to poor solubility of SM in EA/methanol) was prepared

and 10% palladium on carbon (0.270 g, 30% by weight) was added. The flask was purged with hydrogen gas (balloon) and allowed to stir under positive pressure of hydrogen for 16 hours. The suspension was filtered through Celite™, the filter cake was washed with ethyl acetate, and the filtrate was concentrated to provide 4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)aniline (0.587 g, 69%) as an off-white solid. (M+H) 383.3.

Step 4: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea :

The method of urea formation using triphosgene and triethylamine in methylene chloride, described in Scheme 1, was utilized using commercially available 4-(4-ethylpiperazin-1-yl)aniline as the amine component. Purification by HPLC (5-95% acetonitrile in water over 20 minutes, 0.05% TFA buffer, Waters Atlantis column) provided 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea (0.0761 g, 95%) as a light yellow solid. (M+H) 614.3.

Example 441 : Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 9, using 4-(4-isopropylpiperazin-1-yl)aniline in the urea formation step. Yield; 82 mg (100%); (M+H) 628.4.

Example 442: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-cyclopropylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 9, using 4-(4-cyclopropylpiperazin-1-yl)aniline in the urea formation step. Yield; 32 mg (39%); (M+H) 626.3.

Example 443: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea :

Prepared as shown in Scheme 9, using 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine in the urea formation step. Yield; 77 mg (93%); (M+H) 628.4.

Example 444: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 9, using (4-aminophenyl)(4-methylpiperazin-1-yl)methanone in the urea formation step. Yield; 43 mg (52%); (M+H)628.3.

Example 445: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 9, using (4-aminophenyl)(4-isopropylpiperazin-1-yl)methanone in the urea formation step. Yield; 72 mg (84%); (M+H) 656.4.

Example 446: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea :

Prepared as shown in Scheme 9, using commercially available 6-(4-methylpiperazin-1-yl)pyridin-3-amine in the urea formation step. Yield; 74 mg (94%); (M+H) 601.3.

Example 447: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-(4-ethylpiperazin-1-yl)aniline in the urea formation step. Yield; 80 mg (99%); (M+H) 602.3.

Example 448: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea :

Prepared as shown in Scheme 1, using 4-(4-isopropylpiperazin-1-yl)aniline in the urea formation step. Yield; 74 mg (88%); (M+H) 616.4.

Example 449: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea :

Prepared as shown in Scheme 1, using 1-(4-aminophenyl)-N,N-dimethylpiperidin-4-amine in the urea formation step. Yield; 80 mg (96%); (M+H) 616.4.

Example 450: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 1, using (4-aminophenyl)(4-methylpiperazin-1-yl)methanone in the urea formation step. Yield; 79 mg (95%); (M+H) 616.3.

Example 451: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 1, using (4-aminophenyl)(4-isopropylpiperazin-1-yl)methanone in the urea formation step. Yield; 18 mg (20%); (M+H) 644.4.

Example 452: Preparation of 4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N,N-dimethylbenzamide :

Prepared as shown in Scheme 1, using commercially available 4-amino-N,N-dimethylbenzamide in the urea formation step. Yield; 43 mg (57%); (M+H) 561.3.

Example 453: Preparation of 1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea :

Prepared as shown in Scheme 1, using commercially available 4-(pyrrolidin-1-ylmethyl)aniline in the urea formation step. Yield; 61 mg (79%); (M+H) 573.3.

Example 454: Preparation of 4-(3-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide :

Prepared as shown in Scheme 7, using commercially available 4-aminobenzamide in the urea formation step. Yield; 22 mg (21%); (M+H) 530.2.

Example 455: Preparation of 4-(3-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)-N,N-dimethylbenzamide :

Prepared as shown in Scheme 7, using commercially available 4-amino-N,N-dimethylbenzamide in the urea formation step. Yield; 22 mg (21%); (M+H) 558.3.

Example 456: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)urea :

Prepared as shown in Scheme 7, using (4-aminophenyl)(pyrrolidin-1-yl)methanone in the urea formation step. Yield; 41 mg (36%); (M+H) 584.3.

Preparation of (4-aminophenyl)(pyrrolidin-1-yl)methanone:

Prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

Example 457: Preparation of 4-(3-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)benzamide :

Prepared as shown in Scheme 7, using 4-amino-N-(2-(dimethylamino)ethyl)benzamide in the urea formation step. Yield; 36 mg (32%); (M+H) 601.3.

Preparation of 4-amino-N-(2-(dimethylamino)ethyl)benzamide:

Prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

Example 458: Preparation of 4-(3-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(methylamino)ethyl)benzamide :

Prepared as shown in Scheme 7, using tert-butyl 2-(4-aminobenzamido)ethyl(methyl)carbamate in the urea formation step. Following urea formation, the Boc-amine intermediate was treated with TFA to provide the title compound. Yield; 25 mg (22%); (M+H) 587.3.

Preparation of tert-butyl 2-(4-aminobenzamido)ethyl(methyl)carbamate:

Prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

Example 459: Preparation of 4-(3-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide :

Prepared as shown in Scheme 7, using 4-amino-N-(2-(dimethylamino)ethyl)-N-methylbenzamide in the urea formation step. Yield; 10 mg (9%); (M+H) 615.3.

Preparation of 4-amino-N-(2-(dimethylamino)ethyl)-N-methylbenzamide:

Prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

Example 460: Preparation of 1-(4-(4-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(morpholine-4-carbonyl)phenyl)urea :

Prepared as shown in Scheme 7, using (4-aminophenyl)(morpholino)methanone in the urea formation step. Yield; 25 mg (21%); (M+H) 600.3.

Preparation of (4-aminophenyl)(morpholino)methanone:

Prepared from 4-nitrobenzoyl chloride and the appropriate amine as shown in Scheme 8.

Example 461: Preparation of 1-(4-(2-aminoethylamino)phenyl)-3-(4-(4,6-di(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-1,3,5-triazin-2-yl)phenyl)urea :

Prepared as shown in Scheme 1, using di-Boc protected N1-(2-aminoethyl)benzene-1,4-diamine in the urea formation step. Following urea formation, the di-Boc-amine intermediate was treated with TFA to provide the title compound. Yield; x mg (x%); HRMS 572.3092 (M+H, calc.), 572.3098 (M+H, obs.).

Preparation of di-Boc protected N1-(2-aminoethyl)benzene-1,4-diamine:

Prepared from 4-fluoronitrobenzene and the appropriate amine as shown in Scheme 4.

Example 462: Preparation of 4-({[4-(4-{4-[(methylcarbamoyl) amino] phenyl}-6-morpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl] carbamoyl} amino) benzamide

Step 1: Preparation of phenyl 4-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxaborolan-2-yl)phenylcarbamate

To a solution of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (25.0g, 114 mmol) and pyridine (4mL, 57 mmol)in dry dichloromethane (250 mL) phenyl chloroformate (12mL, 114 mmol) was added drop wise at -10 °C. The reaction mixture was stirred at -10 °C for 30 min and then at room temperature for 30 minutes. The reaction mixture was diluted with dichloromethane (100 mL) and washed with water (2 x 70 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to get the crude product. Then the crude product was dissolved in diethyl ether (15 mL) and sonicated for 10 min and then pentane (30 mL) was added. the resulting solid was filtered and washed with pentane to give phenyl 4-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxaborolan-2-yl) phenylcarbamate (26g, 88% yield).

^{1}HNMR (300 MHz, $CDCl_3$): δ 7.8 (d, 2H) 7.5 (d, 2H), 7.4(m, 2H), 7.2(m, 3H), 7.0(s, 1H), 1.3(s, 12H).

Step 2: Preparation of 1-methyl-3-(4-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxaborolan-2-yl) phenyl) urea

A mixture of phenyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenylcarbamate (26g, 76.6mmol)), 2.0M Methylamine/THF (265 mL, 530 mmol) in 150 mL of THF was stirred at room temperature for 6 hours, then excess solvent was distilled off from the reaction mixture; residue was dissolved into water, extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by silica gel column chromatography by using 5-60% ethyl acetate in pet-ether as an eluent. to give 1-methyl-3- [4-(4,4,5,5-tetramethyl- [1,3,2] dioxaborolan-2-yl)-phenyl]-urea.(20g, 88%yield) as white solid.

^{1}HNMR (300 MHz, $CDCl_3$): δ 7.7(d, 2H), 7.2 (d, 2H), 6.7(s, 1H), 5.0(s, 1H), 2.8(s, 3H), 1.2(s, 12H).

Step 3: Preparation of 4-(4, 6-dichloro-1, 3, 5-triazin-2-yl) morpholine

Morpholine (9.5mL, 108 mmol)) was added to a solution of cyanuric chloride (20g, 108 mmol) in chloroform (10 mL) and stirred at -5 °C for 1 hour. Reaction mixture was diluted with water, extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 5% ethyl acetate in pet-ether as an eluent to give 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (10g, 39% yield).

Step 4: Preparation of 1-(4-(4-chloro-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea

A mixture of compound 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (10g, 42.7 mmol), Pd $(PPh_3)_4$ (2.46g, 2.1mmol), 1-methyl-3- [4-(4,4,5,5-tetramethyl- [1,3,2] dioxaborolan-2-yl)-phenyl]-urea.(11.7g, 42.4 mmol) and 1N Na_2CO_3 (168mL, 168 mmol)in degassed 1,2-dimethoxyethane (400mL) was heated to 65 °C for 8 hours under N_2 atmosphere. The reaction mixture filtered, diluted with water, extracted with ethyl acetate and washed with water, brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 20-60% ethyl acetate in pet-ether as an eluent. To

give 1-(4-(4-chloro-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea (5.0g, 34% yield).

^{1}HNMR (300 MHz, DMSO-d6): δ 9.4 (br, 1H), 8.2(d, 2H), 7.6(d, 2H), 6.6 (br, 1H), 4.0 (m, 2H), 3.8(m, 6H), 2.8 (s, 3H).

Step 5: Preparation of 1-(4-(4-(4-aminophenyl)-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea

The title compound was prepared by following the procedure of **Example 462** step 4 using 1-(4-(4-chloro-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-methylurea and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline. Yield 2g, 45% yield.

Step 6: Preparation of phenyl 4-carbamoylphenylcarbamate

To a solution of 4-aminobenzamide (5.0g, 36.7 mmol) and pyridine (2.9g, 36.7mmol)) in dry CH_2Cl_2 (100 mL) at -10 °C, phenyl chloroformate (6.9g, 44.1mmol) was added dropwise, stirred at -10 °C for 30 min and then at room temperature for 30 minutes The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with water (2 x 70 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to get the crude product. The crude product was dissolved in diethyl ether (15 mL) and sonicated for 10 minutes and then pentane (30 mL) was added, the resulting solid was filtered and washed with pentane to give phenyl 4-carbamoylphenylcarbamate (7.2g, 77% yield).

Step 7: Preparation of 4-({[4-(4-{4-[(methylcarbamoyl) amino] phenyl}-6-morpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl] carbamoyl} amino) benzamide

To a solution of 1-(4-(4-(4-aminophenyl)-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea (0.6g, 1.5 mmol) and triethylamine (4-5 mL) in dry DMF (10 mL), phenyl 4-carbamoylphenylcarbamate (1.15g, 4.5mmol).) was added at room temperature and mixture was heated to 90 °C for 10 hours under nitrogen atmosphere. After cooling to room temperature reaction mixture was quenched with ice water and resulting solid was filtered to get crude product. Crude product was purified by Preparative HPLC to give 4-({[4-(4-{4-[(methylcarbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide (45mg, 5.3% yield).

Example 463: Preparation of 1-{4-[4-(3, 5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl] phenyl}-3-pyridin-3-ylurea

Step 1: Preparation of 4-(4, 6-dichloro-1, 3, 5-triazin-2-yl)-3, 5-dimethylmorpholine

The title compound was prepared by following the procedure of **Example 462** step 3 using cyanuric chloride and 3, 5-dimethylmorpholine. Yield 5g, 35% yield.

^{1}HNMR (300 MHz, $CDCl_3$): δ 4.6 (m, 2H), 3.6 (m, 2H), 2.8(m, 2H), 1.2(d, 6H).

Step 2: Preparation of 1-(4-(4-chloro-6-(3, 5-dimethylmorpholino)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea

The title compound was prepared by following the procedure of example 462 step 4 using 4-(4,6-dichloro-1,3,5-triazin-2-yl)-3,5-dimethylmorpholine and 1-methyl-3- [4-(4,4,5,5-tetramethyl-[1,3,2] dioxaborolan-2-yl)-phenyl]-urea.. Yield 1.15g, 16% yield.

Step 3: Preparation of 1-(4-(4-(4-aminophenyl)-6-(3, 5-dimethyl morpholino)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea

The title compound was prepared by following the procedure of example 462 step 4 using 1-(4-(4-chloro-6-(3,5-dimethylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-methylurea and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline. Yield 2g, 86% yield.

Step 4: Preparation of phenyl pyridin-3-ylcarbamate

The title compound was prepared by following the procedure of example 462 step 6 using 3-aminopyridine and phenyl chloroformate. Yield 7g, 62% yield.

Step 5: Preparation of 1-{4-[4-(3, 5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl] phenyl}-3-pyridin-3-ylurea

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(3, 5-dimethylmorpholino)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl pyridin-3-ylcarbamate. Yield 77mg, 6% yield.

EXAMPLE 464: Preparation of 4-[({4-[4-{4-[(methylcarbamoyl)amino]phenyl}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

Step 1: Preparation of 3-(4, 6-dichloro-1, 3, 5-triazin-2-yl)-8-oxa-3-azabicyclo [3.2.1]octane

The title compound was prepared by following the procedure of example 462 step 3 using cyanuric chloride and 8-oxa-3-azabicyclo [3.2.1] octane. Yield 10g, 47% yield.

Step 2: Preparation of 1-(4-(4-(8-oxa-3-azabicyclo [3.2.1]octan-3-yl)-6-chloro-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea

The title compound was prepared by following the procedure of example 462 step 4 using 3-(4,6-dichloro-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane and 1-methyl-3- [4-(4,4,5,5-tetramethyl- [1,3,2] dioxaborolan-2-yl)-phenyl]-urea.. Yield 5g, 29% yield.

Step 3: Preparation of 1-(4-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo [3.2.1]octan-3-yl)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea

The title compound was prepared by following the procedure of example 462 step 4 using 1-(4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-chloro-1,3,5-triazin-2-yl)phenyl)-3-methylurea and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline. Yield 2.8g, 49% yield.

Step 4: Preparation of 4-[({4-[4-{4-[(methylcarbamoyl) amino]phenyl}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo [3.2.1] octan-3-yl)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl 4-carbamoylphenylcarbamate. Yield 90mg, 13% yield.

EXAMPLE 465 Preparation of 3-[({4-[4-{4-[(methylcarbamoyl)amino]phenyl}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

Step 1: Preparation of phenyl 3-carbacarbamoylphenylcarbamate

The title compound was prepared by following the procedure of example 462 step 6 using 3-aminobenzamide and phenyl chloroformate. Yield 7g, 74% yield.

Step 2: Preparation of 3-[({4-[4-{4-[(methylcarbamoyl) amino]phenyl}-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo [3.2.1] octan-3-yl)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl 3-carbamoylphenylcarbamate. Yield 90mg, 13% yield.

EXAMPLE: 466: Preparation of 3-({[4-(4-{4-[(methylcarbamoyl) amino] phenyl}-6-morpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl] carbamoyl} amino) benzamide

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl 3-carbamoylphenylcarbamate. Yield 51mg, 4% yield.

EXAMPLE 467: Preparation of 1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-3-ylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl) phenyl] urea

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl pyridin-3-ylcarbamate. Yield 77mg, 6% yield.

Example 468: Preparation of 1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl) phenyl] urea

Step 1: Preparation of phenyl pyridin-4-ylcarbamate

The title compound was prepared by following the procedure of example 462 step 6 using 4-aminopyridine and phenyl chloroformate. Yield 6g, 534% yield.

Step 2: Preparation of 1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl) phenyl] urea

The title compound was prepared by following the procedure of example 462 step7 using 1-(4-(4-(4-aminophenyl)-6-morpholino-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl pyridin-4-ylcarbamate. Yield 75mg, 3.9% yield.

Example 469: Preparation of 3-[({4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(3, 5-dimethylmorpholino)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl 3-carbamoylphenylcarbamate. Yield 56mg, 4.1% yield.

Example 470: Preparation of 4-[({4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(3, 5-dimethylmorpholino)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl 4-carbamoylphenylcarbamate. Yield 70mg, 12.8% yield.

Example 471: Preparation of 1-methyl-3-{4-[4-(8-oxa-3-azabicyclo [3.2.1]oct-3-yl)-6-{4-[(pyridin-4-ylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl] phenyl} urea

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(8-oxa-3-azabicyclo [3.2.1] octan-3-yl)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl pyridin-4-ylcarbamate. Yield 51mg, 4% yield.

Example 472: Preparation of 1-{4-[4-(3, 5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl) amino] phenyl}-1, 3, 5-triazin-2-yl] phenyl}-3-pyridin-4-ylurea

The title compound was prepared by following the procedure of example 462 step 7 using 1-(4-(4-(4-aminophenyl)-6-(3, 5-dimethylmorpholino)-1, 3, 5-triazin-2-yl) phenyl)-3-methylurea and phenyl pyridin-4-ylcarbamate. Yield 15mg, 0.8% yield.

Example 473: Preparation of N-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-2, 2-difluoroacetamide

Step 1: Preparation of 4, 4'-(6-chloro-1, 3, 5-triazine-2, 4-diyl)dimorpholine

A solution of morpholine (8.71g, 100mmol) in 100 mL of methylene was added dropwise to a mixture of cyanuric chloride (9.22 g, 50.0 mmol) and triethylamine (10.1g, 100mmol) in 200 mL of methylene chloride at 0 °C. Then the reaction mixture was stirred at 0 °C for 1hr and slowly warmed up to room temperature. After stirring at room temperature for 1hr, the reaction mixture was filtered to remove the triethylamine hydrochloride salt. The filtrate was concentrated to give 4, 4'-(6-chloro-1, 3, 5-triazine-2, 4-diyl) dimorpholine (14.2g, 100 yield) as a white solid. HPLC: Rt = 2.43min; MS 286, 288 [M+H].

Step 2:Preparation of 4-(4, 6-dimorpholino-1, 3, 5-triazin-2-yl)aniline

A mixture of 4,4'-(6-chloro-1,3,5-triazine-2,4-diyl)dimorpholine (1.40g, 4.90 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (2.62g, 11.9mmol) and tetrakis (triphenylphosphine) palladium (0) (282 mg, 0.240 mmol) in 2M sodium carbonate aqueous solution (10 mL, 20 mmol) and 40 mL of DME was stirred at 80 °C for 2hr. The reaction mixture was diluted with 300 mL of ethyl acetate and washed with water. The organic layer was concentrated and purified by

flash chromatography (ISCO, 120g silica gel column, eluting with 0-100% EtOAc/Hexane) to give 4-(4,6-dimorpholino-1,3,5-triazin-2-yl)aniline (0.68g, 40%yield). HPLC: Rt = 2.09min; MS 343 [M+H].

Step 3: Preparation of N-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-2, 2-difluoroacetamide

To a mixture of 2, 2-difluoroacetic acid (20 mg, 0.21 mmol), HBTU (76mg, 0.2 mmol), and DIEA (52 mg, 0.40 mmol) in 2 mL of DMF was added 4-(4, 6-dimorpholino-1, 3, 5-triazin-2-yl) aniline (40 mg, 0.12 mmol). The reaction was stirred at 60 °C 16hr. Then the reaction mixture was cooled to room temperature and purified by reverse phase chromatography to give N-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-2, 2-difluoroacetamide (23mg, 46% yield). HPLC: Rt = 2.19min; MS 421 [M+H].

Example 474: Preparation of N-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-4, 5-dihydro-1H-imidazol-2- amine

A mixture of 4-(4,6-dimorpholino-1,3,5-triazin-2-yl)aniline (40 mg, 0.12 mmol), imidazolidine-2-thione (15mg, 0.15 mmol0 and mercury(II) chloride (40mg, 0.15 mmol) in 2 mL of DMF was stirred at 140 °C 16hr. Then the reaction mixture was cooled to room temperature and filtered through Celite™. The filtration was concentrated and purified by reverse phase chromatography to give N-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-4, 5-dihydro-1H-imidazol-2- amine (9.0mg, 22% yield). HPLC: Rt = 1.74min; MS 411 [M+H].

Example 475: Preparation of 2, 4-dimorpholin-4-yl-6-[4-(2H-tetrazol-5-yl) phenyl]-1, 3, 5-triazine

Step 1:Preparation of 4-(4, 6-dimorpholino-1, 3, 5-triazin-2-yl)benzonitrile

The title compound was prepared by following the procedure of example 473 step 2 using 4, 4'-(6-chloro-1, 3, 5-triazine-2, 4-diyl) dimorpholine and 4-cyanophenyl-boronic acid. Yield 86 mg, 50% yield; HPLC: Rt = 2.60min; MS 353 [M+H].

Step 2:Preparation of 2, 4-dimorpholin-4-yl-6-[4-(2H-tetrazol-5-yl) phenyl]-1, 3, 5-triazine

A mixture of 4-(4,6-dimorpholino-1,3,5-triazin-2-yl)benzonitrile (11mg, 0.031mmol), sodium azide (5.5mg, 0.085 mmol) and triethylamine hydrochloride (6.0mg, 0.043mmol) in 2 mL of DMF was stirred at 120 °C for 6hr. Then the reaction mixture was cooled to room temperature and

purified by reverse phase chromatography to give 2,4-dimorpholin-4-yl-6-[4-(2H-tetrazol-5-yl)phenyl]-1,3,5-triazine. Yield 12mg, 97% yield; HPLC: Rt = 2.09min; MS 394 [M-H].

Example 476: Preparation of 1-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-3-methylurea

Step 1:Preparation of 1-Methyl-3- [4-(4, 4, 5, 5-tetramethyl- [1, 3, 2] dioxaborolan-2-yl)-phenyl]-urea

A mixture of 2-(4-isocyanatophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (750mg, 3.06 mmol), 2.0M Methylamine/THF (2.3 mL, 4.60 mmol) in 50 mL of THF was stirred at room temperature for 6 hr. Then the traction mixture was concentrated to give 1-methyl-3- [4-(4, 4, 5, 5-tetramethyl- [1, 3, 2] dioxaborolan-2-yl)-phenyl]-urea. (760 mg, 90%yield). Rt = 2.21min; 277 [M+H].

Step 2:Preparation of 1-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-3-methylurea

The title compound was prepared by following the procedure of example 473 step 2 using 4,4'-(6-chloro-1,3,5-triazine-2,4-diyl)dimorpholine and 1-Methyl-3- [4-(4,4,5,5-tetramethyl- [1,3,2] dioxaborolan-2-yl)-phenyl]-urea. Yield 13mg, 11% yield; HPLC: Rt = 1.98min; MS 400 [M+H].

Example 477: Preparation of 2-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-N-pyridin-3-ylacetamide

Step 1: Preparation of 2-(4-(4, 6-dimorpholino-1, 3, 5-triazin-2-yl) phenyl)acetic acid

A mixture of 4,4'-(6-chloro-1,3,5-triazine-2,4-diyl)dimorpholine (285mg, 1.0mmol), 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetic acid. (315mg, 1.2mmol) and tetrakis (triphenylphosphine) palladium (0) (58 mg, 0.05 mmol) in 2M sodium carbonate aqueous solution (3 mL, 8 mmol) and 20 mL of DME was stirred at 80 °C for 2hr. Then the reaction mixture was diluted with 50 mL of ethyl acetate and extracted with 1N NaOH (50mL, three times)). The combined aqueous layers were neutralized to pH=6. Then the aqueous solution was extracted with ethyl acetate (50 mL, three times). The combined organic layers were washed with saturated sodium carbonate and brine. Then the organic layer was dried over anhydrous sodium sulfate and concentrated to give 2-(4-(4, 6-dimorpholino-1, 3, 5-triazin-2-yl) phenyl) acetic acid (68mg, 18%yield). HPLC: Rt = 2.04min; MS 386 [M+H].

Step 2: Preparation of 2-[4-(4, 6-dimorpholin-4-yl-1, 3, 5-triazin-2-yl) phenyl]-N-pyridin-3-ylacetamide

The title compound was prepared by following the procedure of example 473 step 3 using 2-(4-(4, 6-dimorpholino-1, 3, 5-triazin-2-yl) phenyl) acetic acid and 3-aminopyridine. Yield 21 mg, 44% yield; HPLC: Rt = 1.91min; MS 462 [M+H].

Preparation of ((2S,5R)-1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol

A suspension of ((2S,5R)-1-(4-chloro-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol (1.3 g, 2.7 mmol), 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (0.51 g, 3.4 mmol) in ethanol (15 mL) was treated with triethylamine (1.35 mL, 10 mmol) and heated with a heat gun briefly to reflux. The reaction mixture was purified by automated flash chromatography (methanol/chloroform) to provide the title compound as a hard peach colored foam. MS (ES^+) = 443.2 $(M+H)^+$

Preparation of 3-(4-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane

A solution of ((2S,5R)-1-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)pyrrolidine-2,5-diyl)dimethanol (1.5 g, 3.4 mmol) in dichloromethane (15 mL) was treated successively with tert-butyl dimethyl chlorosilane (1.3 g, 8.5 mmol) and imidazole (0.69 g, 10 mmol). The resulting suspension was stirred overnight at room temperature and then quenched with water. The aqueous phase was extracted three times with dichloromethane. The combined extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated to dryness under reduced pressure. The crude residue (a peach-colored solid) was carried on to the following step without further purification. MS (ES^+) = 671.4 $(M+H)^+$

Preparation of 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline

A suspension of palladium on charcoal (10 %, 100 mg) and crude 3-(4-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-6-(4-nitrophenyl)-1,3,5-triazin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane (3.4 mmol maximum) in tetrahydrofuran (30 mL) was shaken for 8 hours under 50 psi of hydrogen. The mixture was filtered through a pad of Celite™ diatomaceous earth and concentrated under reduced pressure to provide the title compound as an orange foam. MS (ES^+) = 642.4 $(M+H)^+$

Example 667: Preparation of 1-(4-{4-[(2R,5S)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea

A solution of 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline (0.24 g, 0.37 mmol) in dichloromethane (5 mL) was treated successively with triethylamine (500 μL) and a triphosgene (56 mg) solution in dichloromethane (1 mL). After 5 minutes, the mixture was treated with a solution of 4-aminopyridine (70 mg) in warm tetrahydrofuran. After 1 hour, the reaction mixture was quenched with methanol and concentrated to dryness. Half of the crude residue was treated with a saturated solution of hydrogen chloride in methanol. Upon complete desilylation, the mixture was concentrated to dryness and the residue purified by reverse-phase high performance liquid chromatography using a Phenomenex Prodigy column running a gradient elution of 5 % acetonitrile/95 % of 0.1 % aqueous trifluoroacetic acid to 50 % acetonitrile over 25 minutes. After concentration, the title compound was obtained as it trifluoroacetic acid salt (75 mg). MS (ES^+) = 533.3 $(M+H)^+$

Example 668: Preparation of 1-(4-{4-[(2R,5S)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-[4-(4-methylpiperazin-1-yl)phenyl]urea

A solution of 4-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6-((2S,5R)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidin-1-yl)-1,3,5-triazin-2-yl)aniline (0.25 g, 0.39 mmol) in dichloromethane (5 mL) was treated successively with triethylamine (500 μL) and a triphosgene (59 mg, 0.08 mmol) solution in dichloromethane (1 mL). After 5 minutes, the mixture was treated with 4-(4-methylpiperazin-1-yl)aniline (150 mg). After 1 hour, the reaction mixture was quenched with methanol and concentrated to dryness. The crude residue was treated with a saturated solution of hydrogen chloride in methanol. Upon complete desilylation, the mixture was concentrated to dryness and the residue purified by reverse-phase high performance liquid chromatography using a Phenomenex Gemini column running a gradient elution of 5 % acetonitrile/55 % of 0.1 % aqueous trifluoroacetic acid to 50 % acetonitrile over 15 minutes. After concentration, the title compound was obtained as it trifluoroacetic acid salt (130 mg). MS (ES^+) = 630.4 $(M+H)^+$

Example 823 Preparation of 1-[4-(4,6-di-3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea

To a solution of cyanuric chloride (0.368 g, 2 mmol) in CH_2Cl_2 (20 mL) was added 3,7-dioxa-9-azabicyclo[3.3.1]nonane. HCO_2H (0.718 g, 4.1 mmol), followed by addition of Et_3N (0.98 mL, 7 mmol). The resulting reaction mixture was stirred for 24h, and then diluted with CH_2Cl_2. The

organic phase was washed with aqueous 1N HCl (3X) and dried over $MgSO_4$. The solvent was removed in vacuum to give 9,9'-(6-chloro-1,3,5-triazine-2,4-diyl)bis(3,7-dioxa-9-azabicyclo[3.3.1]nonane) as white solid (0.15 g, 95% yield).

To a 10 mL vial were added 9,9'-(6-chloro-1,3,5-triazine-2,4-diyl)bis(3,7-dioxa-9-azabicyclo[3.3.1]nonane) (150 mg, 0.406 mmol), 4-aminophenylboronic acid pinacol ester (133 mg, 0.61 mmol), $Pd(PPh_3)_4$ (10 mg), toluene (1 mL), EtOH (1 mL) and 2M Na_2CO_3 aqueous solution (0.305 mL). The resulting mixture was heated at 120 °C for 20 minutes in microwave oven. The reaction mixture was cooled to room temperature. The aqueous phase was extracted with EtOAc, and the combined organic phases were dried over ($MgSO_4$). The solvent was removed under reduced pressure and the residue was subjected to HPLC separation to give 4-(4,6-di(3,7-dioxa-9-azabicyclo[3.3.1]nonan-9-yl)-1,3,5-triazin-2-yl)aniline as a white solid (120 mg).

To a solution of 4-(4,6-di(3,7-dioxa-9-azabicyclo[3.3.1]nonan-9-yl)-1,3,5-triazin-2-yl)aniline (120 mg, 0.281 mmol) in CH_2Cl_2 was added Et_3N (0.237 mL, 1.69 mmol) and triphosgene (42 mg, 0.14 mmol). The mixture was stirred at room temperature for 15 minutes and 4-(4-methylpiperazin-1-yl)aniline (107 mg, 0.56 mmol) was added. The mixture was stirred at room temperature overnight. The solvent was removed, and the residue was subjected to HPLC separation to give the title compound (1TFA salt) MS(ESI) m/z 644.3306.

Preparation of (6S)-tert-butyl 6-hydroxy-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (Scheme 10)

Step 1: (2R',5S')-1-tert-butyl 2,5-dimethyl 1H-pyrrole-1,2,5(2H,5H)-tricarboxylate (cis-diester) was synthesized by following the procedure described in literature: *Organic Letters* 2004, *6(18),* 3055-8.

Step 2: Reduction of cis-diester to (2R',5S')-tert-butyl 2,5-bis(hydroxymethyl)-2,5-dihydro-1H-pyrrole-1-carboxylate (cis-diol)

To a solution of (2R',5S')-1-tert-butyl 2,5-dimethyl 1H-pyrrole-1,2,5(2H,5H)-tricarboxylate (6.6 g, 23.1 mmol) in THF (100 mL) was added slowly of $LiBH_4$ solution (2M in THF, 34.7 mL, 69.4 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 3 hours, then cooled to 0 °C again. HCl solution (1M, 30 mL) was added to the reaction mixture, and stirred for 10 minutes before diluted with EtOAc. The organic layer was separated, and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with water and brine, and dried ($MgSO_4$). The organic solvent was removed *in vacuo* to give the crude product, which

was purified by flash chromatography in silica gel with EtOAc:Hex:MeOH(50:50:10) to give the cis-diol (3.8 g, 72%).

Step 3: Preparation of (2R',5S')-tert-butyl 2,5-bis((tert-butyldimethylsilyloxy)methyl)-2,5-dihydro-1H-pyrrole-1-carboxylate

To a solution of the cis-diol (3.57 g, 15.6 mmol) in DMF (15 mL) were added TBSCl (5.16 g, 34.3 mmol) and imidazole (3.18 g, 46.7 mmol). The mixture was heated at 80 °C for 30 minutes in microwave oven (150 watt). Cooled to room temperature, the mixture was taken up in water (50 mL) and EtOAc (50 mL). The organic layer was separated, and the aqueous phase was extracted with EtOAc. Combined organic phases were washed with water and brine, and dried ($MgSO_4$). The organic solvent was removed *in vacuo* to give the crude product, which was purified by flash chromatography in silica gel with EtOAc:Hex (10:90) to give the title compound (7.12 g, 98%).

Step 4: Synthesis of (2R',3S',5R')-tert-butyl 2,5-bis((tert-butyldimethylsilyloxy)methyl)-3-hydroxypyrrolidine-1-carboxylate (trans-alcohol)

To a solution of (2R',5S')-tert-butyl 2,5-bis((tert-butyldimethylsilyloxy)methyl)-2,5-dihydro-1H-pyrrole-1-carboxylate (4.8 g, 10.5 mmol) in THF (50 mL) was added slowly of BH_3 DMS solution (2M in THF, 6.97 mL, 13.9 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 3 hours, then cooled to 0 °C again. NaOH solution (5M, 12.6 mL, 63.2 mmol) was added to the reaction mixture, followed by addition of H_2O_2 (30%, 6.33 mL, 62.0 mmol). The resulting mixture was stirred for 5 hours before diluted with EtOAc. The organic layer was separated, and the aqueous phase was extracted with EtOAc. Combined organic phases were washed with water and brine, and dried ($MgSO_4$). The organic solvent was removed *in vacuo* to give the crude product, which was purified by flash chromatography in silica gel with EtOAc:Hex (30:70) to give the title compound (3.8 g, 77%).

Step 5: Benzyl protection of the trans alcohol

To a solution of (2R',3S',5R')-tert-butyl 2,5-bis((tert-butyldimethylsilyloxy)methyl)-3-hydroxypyrrolidine-1-carboxylate (2.515 g, 5.3 mmol) in THF (50 mL) were added NaH (60%, 0.423 g, 10.6 mmol). The mixture was stirred at room temperature for 30 minutes, and benzyl bromide (1.085 g, 6.3 mmol) and TBAI (0.195 g, 0.5 mmol) were added. The mixture was stirred at room temperature for 12 hours, and quenched by addition of sat.NH_4Cl solution (20 mL). Concentrated *in vacuo*, and the residue was taken up in water and EtOAc. The organic layer was separated, and the aqueous phase was extracted with EtOAc. Combined organic phases

were washed with water and brine, and dried ($MgSO_4$). The organic solvent was removed in vacuo to give the crude product, which was purified by flash chromatography in silica gel with EtOAc:Hex (10:90) to give (2R',3S',5R')-tert-butyl 3-(benzyloxy)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidine-1-carboxylate (3.0 g, 100%) as colorless oil.

Step 6: Synthesis of (2R',3S',5R')-tert-butyl 3-(benzyloxy)-2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (benzyloxy diol)

To a solution of (2R',3S',5R')-tert-butyl 3-(benzyloxy)-2,5-bis((tert-butyldimethylsilyloxy)methyl)pyrrolidine-1-carboxylate (3.0 g, 5.3 mmol) in THF (50 mL) was added slowly of TBAF solution (1M in THF, 21.8 mL, 21.8 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 6, and quenched by addition of sat.NH_4Cl solution (10 mL). Concentrated *in vacuo*, and the residue was treated with water and EtOAc. The organic layer was separated, and the aqueous phase was extracted with EtOAc. Combined organic phases were washed with water and brine, and dried ($MgSO_4$). The organic solvent was removed in vacuo to give the crude product, which was purified by flash chromatography in silica gel with EtOAc:Hex:MeOH (50:50:5) to give the title compound (1.15 g, 62.5%).

Step 7: Synthesis of (6S')-tert-butyl 6-(benzyloxy)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate by cyclization

To a solution of (2R',3S',5R')-tert-butyl 3-(benzyloxy)-2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (1.15 g, 3.4 mmol) in THF (50 mL) was added NaH (60%, 0.409 g, 10.2 mmol). The mixture was stirred at room temperature for 30 minutes , and cooled down to 0 °C. A solution of p-TsCl (0.65 g, 3.4 mmol) in THF (5 mL) was slowly added to the mixture. The reaction mixture was then stirred at room temperature for 12 hours, and quenched by addition of sat.NH_4Cl solution (20 mL). Concentrated *in vacuo*, and the residue was taken up in water and EtOAc. The organic layer was separated, and the aqueous phase was extracted with EtOAc. Combined organic phases were washed with water and brine, and dried ($MgSO_4$). The organic solvent was removed *in vacuo* to give the crude product, which was purified by flash chromatography in silica gel with EtOAc:Hex (20:80) to give the title compound (716 mg, 66%) as off-white solid.

The compounds in Table I were made by the proceeding methods.

Table I

Example	Name	MS (ESI) m/z

Example	Name	MS (ESI) m/z
478	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	615.5
479	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)urea	589.6
480	1-{4-[4-(5-hydroxy-3-oxa-7-azabicyclo[4.1.1]oct-7-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	505.3 253.2 273.8
481	1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridazin-4-ylurea	464.2 253.1
482	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(oxetan-3-yloxy)-1,3,5-triazin-2-yl]phenyl}urea	575.5
483	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridazin-4-ylurea	490.6
484	1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	602.5
485	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	602.6
486	1-[4-(4-isopropyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	545.1 293.5 273
487	1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-pyrimidin-5-ylphenyl)urea	497.3
488	1-(4-{4-[(2,2-dimethoxyethyl)amino]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea	481.2 241.1 261.6
489	1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-pyridin-4-ylphenyl)urea	496.3 248.6 269.1
490	1-(4-iodophenyl)-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	545.1
491	1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea	573.4 287.2
492	1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea	586.6
493	1-{4-[2-(dimethylamino)pyrimidin-5-yl]phenyl}-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	540.5
494	tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]azetidine-1-carboxylate	549.6

Example	Name	MS (ESI) m/z
495	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	616.4 308.7
496	1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-nitrophenyl)urea	507.1
497	1-(4-aminophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	477.1 259.6
498	N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-methylpiperazine-1-carboxamide	603.2 302.1 322.6
499	4-(dimethylamino)-N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]piperidine-1-carboxamide	631.3
500	1-[2-(dimethylamino)ethyl]-3-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-1-methylurea	605.3
501	1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[(2-piperidin-1-ylethyl)carbamoyl]amino}phenyl)urea	631.3
502	N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-methyl-1,4-diazepane-1-carboxamide	617.3
503	N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-ethylpiperazine-1-carboxamide	617.3
504	1-{4-[(dimethylcarbamoyl)amino]phenyl}-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	548.3
505	1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea	613.4
506	4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide	587.4
507	1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	585.3
508	4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]benzamide	573.3
509	N-[4-({[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-2-(4-methylpiperazin-1-yl)acetamide	668.4
510	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	615.5

Example	Name	MS (ESI) m/z
511	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	587.3
512	N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	575.3
513	4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide	601.3
514	4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-piperidin-1-ylethyl)benzamide	615.3
515	1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea	616.3 308.6 329.2
516	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	627.7
517	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-	449.4
518	4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	616.4
519	N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	616.4
520	4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-piperidin-1-ylethyl)benzamide	616.4
521	4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide	616.4
522	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)urea	616.4
523	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	616.4
524	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	616.4

Example	Name	MS (ESI) m/z
525	4-[({4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	477.3
526	1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea	565.4
527	4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	511.4
528	methyl 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	525.4
529	1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	531.4
530	1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	468.3
531	1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	593.4
532	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	595.5
533	1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	593.5
534	1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}urea	594.5
535	1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea	579.5
536	1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	531.1
537	1-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea	454.1
538	methyl 4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate	511
539	N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	581.2
540	methyl 4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	548
541	4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid	497

Example	Name	MS (ESI) m/z
542	N-[2-(dimethylamino)ethyl]-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	581.3
543	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea	579.2
544	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea	661.5
545	N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	567.2
546	4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(dimethylamino)ethyl]benzamide	604.4
547	1-{4-[(4-isopropylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	621.5
548	4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide	607.5
549	4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	534.5
550	N-(2-methoxyethyl)-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	568.2
551	N-(2-methoxyethyl)-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	554.2
552	4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-pyrrolidin-1-ylethyl)benzamide	593.5
553	1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea	567.6
554	N-[3-(dimethylamino)propyl]-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	595.4
555	1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperidin-1-ylcarbonyl)phenyl]urea	578.1
556	N-[3-(dimethylamino)propyl]-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	581.4 291.2
557	1-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	460.2 230.6

Example	Name	MS (ESI) m/z
558	4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	503.4
559	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea	585.5
560	methyl 4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	517.2
561	N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	560.3
562	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	587.3 294.1
563	N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	573.1
564	4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(dimethylamino)ethyl]-N-methylbenzamide	618.4 309.7
565	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	616.4 329.2 308.7
566	1-{4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	477.2
567	methyl 4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	534.4
568	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea	613.4 307.2
569	4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	520.3
570	N-[3-(dimethylamino)propyl]-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	587.3 294.2
571	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea	587.5
572	N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	590.3 295.6
573	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	602.3 322.2 301.7
574	N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	577.2

Example	Name	MS (ESI) m/z
575	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea	599.3 300.2 320.7
576	1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	593.3 317.7 521.3
577	3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	511.2
578	methyl 3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	525.2
579	1-(3-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	521.3
580	N-[2-(dimethylamino)ethyl]-N-methyl-3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	595.3 298.2
581	methyl 3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate	463.5
582	methyl 3-({[4-(4-morpholin-4-yl-6-thiophen-2-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate	517.2
583	N-[2-(dimethylamino)ethyl]-3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	581.3 291.1
584	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	604.4 302.7
585	3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid	449.4
586	methyl 3-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate	511.4
587	1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{3-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}urea	594.6
588	N-[2-(dimethylamino)ethyl]-3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide	533.3 267.1
589	1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	531.3 266.1 286.7
590	3-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid	497.3
591	methyl 4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate	518.3

Example	Name	MS (ESI) m/z
592	1-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea	461.3
593	4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid	504..3
594	methyl 4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate	504.5
595	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	604.5
596	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	600.5
597	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	586.5
598	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	614.5
599	4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid	490.5
600	1-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea	447.5
601	N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	474.6
602	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	600.4 300.7
603	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	600.4 300.7
604	N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	574.6
605	N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	588.3 294.6
606	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	586.3 293.7 286.7
607	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea	572.3

Example	Name	MS (ESI) m/z
608	N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	560.1 280.6
609	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	491.2 266.6 246.1
610	N-[3-(dimethylamino)propyl]-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	588.3 294.6
611	N-(2-methoxyethyl)-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	561.4 281.2
612	1-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea	543.3
613	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}urea	630.6
614	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea	644.7
615	methyl 4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	534.3
616	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea	644.6
617	1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	602.3 322.2 301.7
618	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea	630.4315.7
619	4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	520.2
620	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea	616.4 308.7 329.2
621	N-[3-(dimethylamino)propyl]-4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	604.6
622	4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide	616.5

Example	Name	MS (ESI) m/z
623	1-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	616.4 308.7 329.2
624	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(dipropylamino)piperidin-1-yl]carbonyl}phenyl)urea	700.6 350.8
625	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea	630.5 315.7
626	4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	534.3
627	1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea	658.6
628	methyl 4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	548.2
629	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}urea	658.5 329.7
630	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea	644.5
631	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(2-methylpropyl)piperazin-1-yl]carbonyl}phenyl)urea	658.5
632	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylpropyl)piperazin-1-yl]carbonyl}phenyl)urea	658.6
633	4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(4-methylpiperazin-1-yl)ethyl]benzamide	659.6
634	N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	604.5
635	4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide	626.5
636	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-propylpiperidin-1-yl)carbonyl]phenyl}urea	643.4 322.2

Example	Name	MS (ESI) m/z
637	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(piperidin-1-ylcarbonyl)phenyl]urea	601.5
638	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-propylpiperazin-1-yl)carbonyl]phenyl}urea	643.5
639	4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-methoxyethyl)benzamide	591.6
640	1-{4-[4-morpholin-4-yl-6-(4-tricyclo[3.3.1.13,7]dec-1-ylpiperazin-1-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	596.7
641	methyl 4-{[(4-{4-[4-(dimethylcarbamoyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	590.5
642	N,N-dimethyl-4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperazine-1-carboxamide	533.6
643	N,N-dimethyl-4-(4-{4-[({4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)piperazine-1-carboxamide	658.3 329.7
644	N,N-dimethyl-4-{4-morpholin-4-yl-6-[4-({[4-(pyridazin-4-ylcarbamoyl)phenyl]carbamoyl}amino)phenyl]-1,3,5-triazin-2-yl}piperazine-1-carboxamide	653.3
645	N,N-dimethyl-4-(4-morpholin-4-yl-6-{4-[({4-[(4-propylpiperidin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperazine-1-carboxamide	685.6
646	4-{[(4-{4-[4-(dimethylcarbamoyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	576.2
647	4-(4-{4-[({4-[(2-methoxyethyl)carbamoyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-dimethylpiperazine-1-carboxamide	633.3 317.1
648	4-[4-(4-{[(4-{[2-(dimethylamino)ethyl](methyl)carbamoyl}phenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]-N,N-dimethylpiperazine-1-carboxamide	660.3 330.7
649	4-(4-{4-[({4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-dimethylpiperazine-1-carboxamide	672.6
650	1-(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	554.2

Example	Name	MS (ESI) m/z
651	methyl 4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	611.2
652	4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	597.7
653	N-[3-(dimethylamino)propyl]-4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	681.2 341.1
654	N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	667.3 334.2
655	4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	561.5
656	methyl 4-{[(4-{4-[4-(acetylamino)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	575.4
657	1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	643.6
658	N-[1-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperidin-4-yl]acetamide	518.5
659	4-{[(4-{4-[4-(acetylamino)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	561.5
660	N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	631.5
661	N-{1-[(4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}phenyl)carbonyl]piperidin-4-yl}acetamide	685.6
662	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea	657.4 329.2 219.8
663	1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea	671.4 336.2 224.5
664	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3S)-3-methylmorpholin-4-yl]carbonyl}phenyl)urea	617.5

Example	Name	MS (ESI) m/z
665	1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea	685.6
666	N-[4-({[4-(4,6-di-8-oxa-3-azabicyclo[3.2.1]oct-3-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-2-(4-methylpiperazin-1-yl)acetamide	
667	1-(4-{4-[(2R,5S)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-(8-oxa-3- azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	533.3
668	1-(4-{4-[(2R,5S)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-(8-oxa-3- azabicyclo[3.2.1]oct-3-yl)-1,3,5-triazin-2-yl}phenyl)-3-[4-(4-methylpiperazin-1-yl)phenyl]urea	630.4
669	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	489.3
670	4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	531.2
671	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea	489.5
672	1-(4-fluorophenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	506.5
673	1-[4-(hydroxymethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	518.5
674	1-[4-(2-hydroxyethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	532.5
675	2-(diethylamino)ethyl 4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	631.6
676	1-(4-methylphenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	502.5
677	1-(4-cyanophenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	513.5
678	1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	586.6
679	1-isopropyl-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	454.5
680	1-(2-hydroxyethyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	456.5

Example	Name	MS (ESI) m/z
681	4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]aniline	369.2
682	{3-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}methanol	384.4
683	3-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenol	370.4
684	5-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]-1H-benzimidazol-2-amine	409.4
685	1-{4-[4-(3-hydroxy-8-azabicyclo[3.2.1]oct-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea	502.5
686	1-(4-{4-[(4-methylpiperazin-1-yl)amino]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-phenylurea	490.5
687	1-(4-{4-[(1-methylpiperidin-4-yl)oxy]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	491.5
688	1-{4-[4-morpholin-4-yl-6-(piperidin-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	477.5
689	ethyl 4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxylate	549.5
690	N-ethyl-4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxamide	548.5
691	tert-butyl 4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxylate	577.3
692	4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-sulfonamide	556.5
693	methyl 4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	546.3
694	N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	602.4
695	N,N-dimethyl-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	559.2
696	N-methyl-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	545.2

Example	Name	MS (ESI) m/z
697	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	614.3
698	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	616.4
699	N-(2-hydroxyethyl)-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	575.4
700	N-[3-(dimethylamino)propyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	616.4
701	N-methyl-N-[2-(methylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	602.4
702	N-(2-morpholin-4-ylethyl)-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	644.4
703	1-{4-[(3,5-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	628.4
704	4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]aniline	399.3
705	1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	519.7
706	1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea	519.2
707	1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea	518.2
708	1-[4-(dimethylamino)phenyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	561.3
709	1-(4-cyanophenyl)-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	543.2
710	1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(2-methylpyridin-4-yl)urea	533.7
711	1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	513.7

Example	Name	MS (ESI) m/z
712	1-[4-(4-morpholin-4-yl-6-quinolin-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea	505.7
713	1-(diethylcarbamoyl)-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]pyridinium	588.3
714	1-{4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	452.6
715	methyl 4-[({4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	509.4
716	4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)aniline	395.3
717	1-[4-(4,6-di-3-oxa-8-azabicyclo[3.2.1]oct-8-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea	515.8
718	1-(4-{4-morpholin-4-yl-6-[2-(pyridin-4-ylamino)ethyl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	498.6
719	1-(4-acetylphenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	530.4
720	N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide	535.5
721	N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide	521.5
722	4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methyl-N-[2-(methylamino)ethyl]benzamide	521.5
723	1-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	533.5
724	1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	547.5
725	4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide	561.5
726	1-(4-ethenylphenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	514.3
727	1-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	601.1

Example	Name	MS (ESI) m/z
728	1-(4-{4-[2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	508
729	1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	575.5
730	1-(4-{4-[2-(1,3-dioxan-2-yl)ethyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	492.9
731	1-(4-{4-[3-(dimethylamino)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	463.4
732	1-[4-(4-{3-[(1-methylethyl)amino]propyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea	477.4
733	1-{4-[4-morpholin-4-yl-6-(3-pyrrolidin-1-ylpropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	489.4
734	1-(4-{4-[3-(4-methylpiperazin-1-yl)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	518.4
735	1-{4-[4-(3-{[2-(dimethylamino)ethyl]amino}propyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	506.5
736	1-{4-[4-(3-hydroxypropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	436.3
737	1-{4-[4-morpholin-4-yl-6-(3-oxopropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	434.3
738	4-[4-(6,8-dioxa-3-azabicyclo[3.2.1]oct-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]aniline	371.3
739	tert-butyl 7-[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]-9-oxa-3,7-diazabicyclo[3.3.1]nonane-3-carboxylate	484.4
740	1-{4-[4-(6,8-dioxa-3-azabicyclo[3.2.1]oct-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	491.3
741	tert-butyl 7-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)-9-oxa-3,7-diazabicyclo[3.3.1]nonane-3-carboxylate	604.4
742	1-{4-[4-morpholin-4-yl-6-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	504.4
743	1-{4-[4-(7-methyl-9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	518.4

Example	Name	MS (ESI) m/z
744	1-{4-[4-(7-acetyl-9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	546.4
745	1-(4-{4-[7-(methylsulfonyl)-9-oxa-3,7-diazabicyclo[3.3.1]non-3-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	582.5
746	1-(2-chloropyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	523.3
747	1-(2,3'-bipyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	566.4
748	tert-butyl N-[4-morpholin-4-yl-6-(4-nitrophenyl)-1,3,5-triazin-2-yl]glycinate	417.2
749	1-(6-chloropyridin-3-yl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	523.3
750	N-[4-morpholin-4-yl-6-(4-nitrophenyl)-1,3,5-triazin-2-yl]glycine	361.3
751	1,3-bis{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	763.5
752	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	642.4
753	N-[2-(4-methylpiperazin-1-yl)ethyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	657.4
754	1-{4-[(4-isopropylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	642.4
755	1-{4-[(4-cyclopentylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	668.4
756	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea	600.4
757	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-morpholin-4-ylpiperidin-1-yl)carbonyl]phenyl}urea	684.4
758	4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide	628.4

Example	Name	MS (ESI) m/z
759	4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-piperidin-1-ylethyl)benzamide	642.4
760	1-[4-(1,4'-bipiperidin-1'-ylcarbonyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	682.5
761	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea	668.5
762	1-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}-3-[4-(thiomorpholin-4-ylcarbonyl)phenyl]urea	617.3
763	1-[4-(morpholin-4-ylcarbonyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	601.4
764	4-[({4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	532.3
765	1-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	505.3
766	1-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	587.4
767	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	658.4
768	N-[2-(dimethylamino)ethyl]-4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-methylbenzamide	632.4
769	1-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	630.4
770	methyl 4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate	562.3
771	4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid	548.3
772	1-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea	616.3
773	1-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-isopropylpiperazin-1-yl)carbonyl]phenyl}urea	658.3

Example	Name	MS (ESI) m/z
774	4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide	644.3
775	4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-piperidin-1-ylethyl)benzamide	658.4
776	1-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea	684.4
777	1-[4-(1,4'-bipiperidin-1'-ylcarbonyl)phenyl]-3-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea	698.4
778	4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyridin-2-ylethyl)benzamide	652.4
779	4-[({4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyridin-4-ylethyl)benzamide	652.4
780	N-[4-(4-aminophenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]benzenesulfonamide	413.2
781	N-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)benzenesulfonamide	533.4
782	N-{4-[4-({[4-(4-methylpiperazin-1-yl)phenyl]carbamoyl}amino)phenyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}benzenesulfonamide	630.3
783	N-(4-{4-[({4-[2-(dimethylamino)ethoxy]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)benzenesulfonamide	619.3
784	N-(4-{4-[({4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)benzenesulfonamide	658.3
785	N-{4-morpholin-4-yl-6-[4-({[4-(piperazin-1-ylcarbonyl)phenyl]carbamoyl}amino)phenyl]-1,3,5-triazin-2-yl}benzenesulfonamide	644.4
786	N-[4-(4-{[(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]benzenesulfonamide	686.4
787	N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	660.4
788	N-[2-(dimethylamino)ethyl]-4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	646.4

Example	Name	MS (ESI) m/z
789	methyl 4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate	590.3
790	4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid	576.2
791	1-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	503.2
792	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}urea	628.5
793	1-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea	614.5
794	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}urea	656.5
795	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	630.4
796	N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	616.4
797	N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	603.4
798	4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide	642.4
799	4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-piperidin-1-ylethyl)benzamide	656.4
800	1-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea	682.5
801	N-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	656.6
802	N-methyl-N-[2-(methylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	616.5

Example	Name	MS (ESI) m/z
803	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	628.3
804	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}urea	642.5
805	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)-1,3,5-triazin-2-yl]phenyl}urea	656.3
806	1-{4-[4-(3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}urea	644.5
807	1-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	489.2
808	1-(1,3-dimethyl-1H-pyrazol-5-yl)-3-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}urea	506.2
809	1-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}-3-(1H-pyrazol-3-yl)urea	478.2
810	1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}urea	642.2
811	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}urea	642.5
812	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}urea	628.2
813	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}urea	614.2
814	1-{4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea	600.3
815	N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	602.5
816	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(2-oxa-5-azabicyclo[2.2.2]oct-5-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	616.3
817	2-tert-butoxy-4-morpholin-4-yl-6-(4-nitrophenyl)-1,3,5-triazine	360.1

Example	Name	MS (ESI) m/z
818	1-(4-{4-[(6S)-6-hydroxy-3-oxa-8-azabicyclo[3.2.1]oct-8-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	505.2
819	1-(4-{4-[6-(benzyloxy)-3-oxa-8-azabicyclo[3.2.1]oct-8-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	595.2
820	1-(4-{4-[(6R)-6-hydroxy-3-oxa-8-azabicyclo[3.2.1]oct-8-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	505.2
821	1-(4-{4-[(6R)-6-(benzyloxy)-3-oxa-8-azabicyclo[3.2.1]oct-8-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea	595.2
822	1-{4-[(1,1-dioxidothiomorpholin-4-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	649.1
823	1-[4-(4,6-di-3,7-dioxa-9-azabicyclo[3.3.1]non-9-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea	644.3306
824	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	628.5, 314.8, 356.8
825	1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)-1,3,5-triazin-2-yl]phenyl}urea	628.5, 314.8, 356.8
826	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(6-morpholin-4-yl-4-oxo-4,5-dihydro-1,3,5-triazin-2-yl)phenyl]urea	519.1, 280.5, 260
827	1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea	
828	1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea	671.4;336.2; 224.5;
829	1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea	657.4;329.2; 219.8;
830	1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	587.6;314.8; 294.3;
831	1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	
832	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea	

Example	Name	MS (ESI) m/z
833	1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	615.5;308.3; 328.8;
834	N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide	589.5;295.3;
835	1-{4-[4-(azetidin-3-yloxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea	449.1;225.1;
836	N-(1-methylethyl)-3-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]azetidine-1-carboxamide	534.4;267.7;
837	N-{1-[(4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}phenyl)carbonyl]piperidin-4-yl}acetamide	658.5;329.8;
838	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)-1,4-diazepan-1-yl]carbonyl}phenyl)urea	658.8;329.8;
839	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(3-oxa-8-azabicyclo[3.2.1]oct-8-ylcarbonyl)phenyl]urea	629.7;315.3;
840	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-cyanopiperidin-1-yl)carbonyl]phenyl}urea	
841	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)urea	
842	1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)urea	
843	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea	657.6;329.3; 233.6;
844	1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea	657.5;329.3;
845	1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(2-methylpiperazin-1-yl)carbonyl]phenyl}urea	
846	1-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea	
847	1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea	

Example	Name	MS (ESI) m/z
848	1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(3,3,4-trimethylpiperazin-1-yl)carbonyl]phenyl}urea	616.3;638.3; 654.3;
849	1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3R)-3-methylpiperazin-1-yl]carbonyl}phenyl)urea	
850	1-(4-{[(3R)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
851	1-(4-{[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
852	1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]carbonyl}phenyl)urea	
853	1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3S)-3-methylpiperazin-1-yl]carbonyl}phenyl)urea	
854	N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	
855	1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea	
856	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea	
857	N-[3-(dimethylamino)propyl]-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	
858	N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	
859	1-[4-(morpholin-4-ylcarbonyl)phenyl]-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea	
860	N-(2-methoxyethyl)-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide	
861	1-[4-(1,4-diazepan-1-ylcarbonyl)phenyl]-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea	643.4;
862	1-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(propan-2-yl)-1,4-diazepan-1-yl]carbonyl}phenyl)urea	

Example	Name	MS (ESI) m/z
863	1-(4-{[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
864	1-(4-{[(3S)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
865	1-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(3,3,4-trimethylpiperazin-1-yl)carbonyl]phenyl}urea	
866	1-(4-{[(3S)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
867	1-(4-{[(3S)-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
868	1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	
869	1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea	

BIOLOGICAL EVALUATION

mTOR kinase assay methods

Human mTOR assays (*See* Toral-Barza, *et al. Biochem Biophys. Res. Commun.* 2005 June 24;332(1):304-10) with purified enzyme are performed in 96-well plates by DELFIA format as follows. Enzymes are first diluted in kinase assay buffer (10 mM HEPES (pH 7.4), 50 mM NaCl, 50 mM β-glycerophosphate, 10 mM $MnCl_2$, 0.5 mM DTT, 0.25 mM microcystin LR, and 100 mg/mL BSA). To each well, 12 µL of the diluted enzyme is mixed briefly with 0.5 µL test inhibitor or control vehicle dimethylsulfoxide (DMSO). The kinase reaction is initiated by adding 12.5 µL kinase assay buffer containing ATP and His6-S6K to give a final reaction volume of 25 µL containing 800 ng/mL FLAG-TOR, 100 mM ATP and 1.25 mM His6-S6K. The reaction plate is incubated for 2 hours (linear at 1-6 hours) at room temperature with gentle shaking and then terminated by adding 25 µL Stop buffer (20 mM HEPES (pH 7.4), 20 mM EDTA, 20 mM EGTA). The DELFIA detection of the phosphorylated (Thr-389) His6-S6K is performed at room temperature using a monoclonal anti-P(T389)-p70S6K antibody (1A5, Cell Signaling) labeled with Europium-N1-ITC (Eu) (10.4 Eu per antibody, PerkinElmer). The DELFIA Assay buffer and Enhancement solution can be purchased from PerkinElmer. 45 µL of the terminated kinase reaction mixture is transferred to a MaxiSorp plate (Nunc) containing 55 µL PBS. The His6-S6K

is allowed to attach for 2 hours after which the wells are aspirated and washed once with PBS. 100 µL of DELFIA Assay buffer with 40 ng/mL Eu-P(T389)-S6K antibody is added. The antibody binding is continued for 1 hour with gentle agitation. The wells are then aspirated and washed 4 times with PBS containing 0.05% Tween-20 (PBST). 100 µL of DELFIA Enhancement solution is added to each well and the plates are read in a PerkinElmer Victor model plate reader. Data obtained is used to calculate enzymatic activity and enzyme inhibition by potential inhibitors.

PI3K-alpha and PI3K-gamma Fluorescence Polarization Assay Protocols

The reaction buffer was 20 mM HEPES, pH 7.5, 2 mM $MgCl_2$, 0.05% CHAPS; and 0.01% βME (added fresh). The Stop/Detection Buffer was 100 mM HEPES, pH 7.5, 4 mM EDTA, 0.05% CHAPS; ATP 20 mM in water; PIP2 (diC8, Echelon, Salt Lake City Utah cat # P-4508) 1 mM in water (MW=856.5). The GST-GRP was 1.75 mg/mL or 1.4 mg/mL in 10% glycerol. The Red detector (TAMRA) was 2.5 µM. Nunc 384-well black polypropylene fluorescent plates were used for PI3K assays.

The assay is run by placing 5 µL of diluted enzyme per well, then 5 µL of diluted compound (or 9.5 µL enzyme then 0.5 µL compound in DMSO) is added and mixed. Then, 10 µL substrate is added to start the reaction. The samples are incubated 30-60 minutes, then the reaction is stopped by adding 20 µL stop/detector mix. PI3K is diluted with reaction buffer (*e.g.*, 5 µL or 7.5 µL PI3K into 620 µL reaction buffer), and 5 µL of diluted enzyme is used per well. A 5 µL portion of reaction buffer or of drug diluted in buffer (*e.g.*, 4 µL/100 so final DMSO is 1% in reaction) is added to each. Pipetting up and down mixes the samples. Alternatively, the enzyme can be diluted to 1215 µL. In this case 9.8 µL is added per well and 0.2 µL compound is added in DMSO.

To prepare 1 mL of substrate solution, 955 µL reaction buffer, 40 µL PIP2, and 2.5 µL ATP are mixed. 10 µL of substrate is added to each well to start the reaction. This results in 20 µM PIP2, and 25 µM ATP per reaction. The stop/detector mix is prepared by mixing 4 µL Red detector and 1.6 µL or 2.0 µL GST-GRP with 1 mL stop buffer, which results in 10 nM probe and 70 nM GST-GRP. 20 µL of the stop/detector mix is added to each well to stop the reaction. The plates are read after 30-90 minutes keeping the red probe solutions dark. For the zero time point, stop/detector mix is added to the enzyme just before adding substrate. For an extra control, stop/detector mix is added to buffer (no enzyme) and substrate or to just buffer (no substrate). Pooled PI3K preparations had a protein concentration of 0.25 mg/mL. The recommended reaction has 0.06 µL per 20 µL (0.015 µg/20 µL) or 0.01125 µg/15 µL or 0.75 µg/mL.

Plates are read on machines with filters for TAMRA. The units are mP with no enzyme controls reading app 190-220 mP units. Fully active enzyme reduces fluorescence polarization down to 70-100 mP after 30 minutes. An active compound raises the mP values halfway to control or to 120-150 mP units.

In vitro cell culture growth assay methods

Cell Lines used are human breast MDA-MB-361, human prostate PC3-mm2, and human prostate LNCap tumor cell lines. Cells are plated in 96-well culture plates at approximately 3000 cells per well. One day following plating, various concentrations of PI3K inhibitors in DMSO are added to cells (final DMSO concentration in cell assays is 0.25%). Three days after drug treatment, viable cell densities are determined by cell mediated metabolic conversion of the dye MTS, a well-established indicator of cell proliferation *in vitro*. Cell growth assays are performed using kits purchased from Promega Corporation (Madison, WI), following the protocol provided by the vendor. Measuring absorbance at 490 nm generates MTS assay results. Compound effect on cell proliferation is assessed relative to untreated control cell growth. The drug concentration that conferred 50% inhibition of growth is determined as IC_{50} (μM).

hSMG-1 kinase assay

The human SMG-1 (hSMG-1) kinase assay employs the recombinant hSMG-1 protein prepared from transiently transfected HEK293 cells and a GST-p53 (aa 1-70) fusion substrate protein derived from cellular tumor suppressor gene p53. The routine assay is performed in a 96-well plate format as follows. Enzymes were first diluted in kinase assay buffer (10 mM HEPES, pH 7.4, 50 mM NaCl, 0.2 mM DTT, 50 mM β-glycerophosphate, 0.5 μM microcystin LR, 10 mM $MnCl_2$). To each well, 12 μL of the diluted enzyme were mixed briefly with 0.5 μL test inhibitor or control vehicle dimethylsulfoxide (DMSO). The kinase reaction was initiated by adding 12.5 μL kinase assay buffer containing ATP and GST-p53 to give a final reaction volume of 25 μL containing 400-800 ng/mL FLAG-hSMG-1, 0.5 μg GST-p53, 10 μM ATP. The reaction was carried out at room temperature for 1.0 hour before terminated by addition of 25 μl stop solution. The assay mixture was then transferred to FluoroNunc Plates with MaxiSorp Surface (Nunc #439454). The plates were incubated at room temperature for 2 hr (4 °C for overnight) to achieve efficient binding of substrate protein to the plate. The plates were aspirated, washed with PBS. Phospho-substrate proteins were detected by incubating for 1 hour with 125 ng of europium-labeled anti-mouse secondary antibody (PerkinElmer AD2027) and the primary phospho(S15)-p53 monoclonal antibody (Cell Signal #9286) in 100 μL DELFIA assay buffer (PerkinElmer #1244-111). Plates were then washed and incubated for 0.5 hour with 100 μl of DELFIA enhancement solution (PerkinElmer #1244-105). DELFIA assay results are recorded in a Victor Plate Reader (PerkinElmer). Data obtained were used to calculate enzymatic activity and enzyme inhibition by potential inhibitors.

Table 2 shows the results of the described PI3K-α, PI3K-γ, and mTOR kinase assays.

Table 2

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
1	3	29	0.0013
2	2	35	0.001
3	3	27	0.00385
4	2	23	0.0017
5	17	438	0.0063
6	6	53	0.006
7	>10000	>100000	>4,0000
8	20	220	0.008
9	10	65	0.004
10	75	289	0.068
11	61	528	0.00925
12	248	815	0.011
13	51	879	0.0115
14	25	154	0.00845
15	23	177	0.0025
16	>10,000	>100000	0.01205
17	8	90	0.01395
18	9	71	0.036
19	23	206	0.039
20	41	258	0.0305
21	22	92	0.00175
22	12	142	0.00475
23	18	51	0.00205
24	22	99	0.0027
25	58	105	0.00405
26	680	10,000	0.0025
27	1230	>10,000	0.00415
28	54	5550	0.00095
29	2690	>10,000	0.0028
30	2120	>10,000	0.00265
31	142	3520	0.00049
32	45	2540	0.00029
33	NA	NA	0.091
34	9	95	0.00049
35	6	54	0.00021
36	17	150	0.00051
37	39	155	0.00195
38	7	91	0.00028
39	14	75	0.00032
40	21	136	0.00066
41	69	122	0.0013
42	86	290	0.00335
43	28	35	0.00165
44	NA	NA	0.0135

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
45	NA	NA	0.0036
46	208	4920	0.024
47	13	52	0.0016
48	6	40	0.0018
49	3	21	0.01
50	1	21	0.002
51	1	15	0.0019
52	2	38	0.001
53	45	403	0.024
54	10	88	0.00475
55	205	1580	0.05
56	122	444	0.015
57	8	74	0.0165
58	13	85	0.0025
59	3	30	0.00105
60	5	36	0.0018
61	9	32	0.00076
62	2	24	0.00068
63	5	36	0.00195
64	1457	1190	1.5
65	15	83	0.00505
66	7	30	0.00165
67	6	48	0.00145
68	0.3	7	0.00057
69	0.4	8	0.00085
70	2	20	0.0007
71	0.4	8	0.00067
72	2	19	0.00085
73	0.3	7	0.00077
74	0.4	8	0.00063
75	0.6	10	0.00075
76	0.4	8	0.00067
77	0.3	4	0.00068
78	3	23	0.00085
79	773	193	0.0051
80	851	2120	0.00715
81	2	38	0.001
82	3	21	0.0089
83	1	15	0.0019
84	10	88	0.00475
85	45	403	0.018
86	122	444	0.01
87	205	1580	0.05
88	8	74	0.0165
89	10	31	0.0016
90	8	42	0.00083

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
91	6	73	0.00071
92	11	92	0.00235
93	12	133	0.00855
94	5	56	0.001
95	48	101	0.00275
96	NA	NA	0.0012
97	NA	NA	0.0011
98	1350	9000	2.1
99	1520	7500	0.46
100	5	38	0.0035
101	6	33	0.00044
102	6	84	0.0061
103	3	73	0.0053
104	19	234	0.015
105	14	112	0.0305
106	393	1840	0.00755
107	115	1490	0.019
108	586	4150	0.019
109	1460	2960	0.0735
110	884	3510	0.029
111	116	1830	0.0023
112	488	777	0.012
113	NA	NA	0.0037
114	106	1180	0.00315
115	109	2000	0.0032
116	1740	2310	0.0027
117	177	3000	0.083
118	379	297	0.195
119	1240	7530	0.14
120	262	1550	0.079
121	1850	4000	0.0435
122	1160	9500	0.0745
123	760	6350	0.115
124	1650	9650	0.155
125	840	8750	0.016
126	510	5510	0.0195
127	1390	4730	0.0515
128	1330	10,000	0.031
129	7217	10,000	2.35
130	14	132	0.008
131	25	336	0.0145
132	14	234	0.026
133	39	8890	0.043
134	20	183	0.0245
135	15	143	0.034
136	208	4920	0.024

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
137	9	117	0.00855
138	123.5	459	0.0435
139	24	43	0.074
140	27	100	0.027
141	241	3380	0.026
142	3	50	0.0011
143	2	22	0.0012
144	NA	NA	NA
145	574	1000	0.009
146	>10000	>100000	0.003
147	1930	6830	0.006
148	300	620	0.008
149	889	1400	0.08
150	832	>10,000	0.005
151	0.6	8117	0.007
152	2	5	0.002
153	868	10,000	0.015
154	275	3820	0.064
155	2300	4940	0.016
156	746	10,000	0.053
157	1451	7090	0.17
158	300	1290	0.007
159	133	3920	0.002
160	358	9070	0.007
161	39	155	0.03
162	10	495	0.023
163	2	9	0.0039
164	378	1380	4
165	9	101	0.028
166	4	33	0.06
167	0.8	7	0.00068
168	1	3	0.0036
169	408	7960	0.0083
170	384	9500	0.004
171	300	9500	0.0012
172	435	10,000	0.008
173	1210	10,000	0.084
174	861	727	0.0021
175	549	453	0.0048
176	1120	3730	0.022
177	5840	4120	0.0016
178	>10,000	>10,000	0.014
179	1	13	0.001
180	531	8000	0.0016

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
181	426	6730	0.011
182	308	5000	0.003
183	526	11000	0.014
184	30	143	0.004
185	1	18	0.0029
186	28	221	0.006
187	3	24	0.0035
188	7540	2380	0.011
189	19	203	0.028
190	780	1320	0.0063
191	435	4630	0.016
192	1120	453	0.043
193	401	3133	0.0008
194	NA	NA	0.027
195	115	498	0.021
196	6	55	0.013
197	2	36	0.024
198	2	33	0.002
199	44	144	0.001
200	14	128	0.0065
201	28	606	0.0009
202	NA	NA	0.0055
203	NA	NA	0.001
204	NA	NA	0.0035
205	NA	NA	0.002
206	NA	NA	0.056
207	NA	NA	0.00084
208	Na	NA	0.0005
209	24	99	0.009
210	6	31	NA
211	80	108	0.006
212	902	8770	0.0064
213	5280	10,000	0.0095
214	2670	10,000	0.0029
215	187	3160	0.0012
216	521	7030	0.003
217	253	3230	0.0032
218	279	2780	0.0026
219	561	8280	0.0059
220	275	2830	0.0035
221	214	4280	0.0027
222	152	572	0.0005
223	2	200	NA

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
224	444	5870	0.0004
225	109	388	0.047
226	75	294	0.062
227	23	81	0.0073
228	46	280	0.051
229	19	70	0.00077
230	22	119	0.0012
231	4	63	0.0025
232	6	37	0.083
233	55	121	0.0079
234	4534	9534	NA
235	3206	4110	NA
236	3	15	0.011
237	2	23	0.003
238	1	10	0.0036
239	11	38	0.0032
240	1	6	0.0016
241	6	23	0.009
242	2	24	0.007
243	1	9	0.0077
244	1	9	0.0051
245	1	13	0.01
246	1	12	0.015
247	2	5	0.019
248	2	18	0.0064
249	25	216	0.002
250	21	190	0.0009
251	2	21	0.006
252	22	184	0.018
253	8	267	0.009
254	63	253	0.017
255	48	85	0.016
256	68	182	0.032
257	90	323	0.085
258	403	6170	0.0023
259	408	5410	0.0024
260	417	4730	0.0009
261	158	2530	0.00031
262	105	954	0.00029
263	3	20	0.001
264	947	5440	NA
265	1079	10,000	0.0015
266	16	93	0.0017

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
267	17	58	0.0035
268	12	41	0.00039
269	6	140	0.08
270	68	318	0.16
271	2	23	0.013
272	5	54	0.03
273	4	33	0.0008
274	34	616	0.059
275	46	711	0.07
276	34	597	0.06
277	30	276	0.06
278	26	344	0.25
279	10	70	0.035
280	5	29	0.004
281	2188	4981	2.8
282	10	32	0.0047
283	1	11	0.0031
284	0.7	12	0.0009
285	1127	3433	0.001
286	4195	10,000	120
287	253	3304	0.00016
288	226	2784	0.00097
289	955	3880	0.0015
290	97	166	0.15
291	368	711	0.19
292	1501	3693	0.07
293	764	533	0.5
294	9	26	0.018
295	19	81	0.029
296	13	35	0.021
297	38	70	0.01
298	2	24	0.021
299	3	34	0.08
300	39	106	0.0053
301	21	58	0.0008
302	35	263	0.036
303	NA	NA	0.017
304	2	18	0.0025
305	1	18	0.0006
306	1	19	0.0021
307	3	30	0.0028
308	3	14	0.0029
309	12	95	0.0035

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
310	14	82	0.0059
311	40	125	0.012
312	3440	10,000	0.037
313	1730	7490	0.037
314	1820	10,000	0.08
315	1100	7900	0.005
316	1410	2690	0.071
317	216	6830	0.084
318	15.5	679	0.855
319	80	1446	0.0044
320	3.3	25	0.0129
321	25	116	0.0165
322	2.4	30	0.006
323	2.9	32	0.007
324	1	22	0.0052
325	74	6244	0.0046
326	830	6189	0.0122
327	394	5899	0.0063
328	261	14,000	0.0046
329	9.5	385	0.00068
330	42	827	0.0033
331	NA	NA	0.0035
332	NA	NA	0.011
333	NA	NA	0.0058
334	16	680	0.0009
335	81	144	0.004
336	40	44	0.0036
337	7	98	0.07
338	3	77	0.022
339	71	485	0.09
340	92	706	0.046
341	10	48	0.012
342	20	127	0.0066
343	97	6700	0.04
344	1610	4140	1.5
345	43	112	0.08
346	43	89	0.023
347	796	8440	NA
348	1030	10,000	NA
349	59	163	NA
350	1	7	NA
351	3	16	0.0042
352	13.5	732	0.00024

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
353	8.5	501	0.00022
354	69	6224	0.0046
355	830	6189	0.012
356	394	5899	0.0063
357	261	14000	0.0046
358	9	363	0.00068
359	42	827	0.0034
360	6672	>10000	0.082
361	6028	>10000	0.0013
362	3090	>10000	0.00074
363	1097	7142	0.00077
364	1465	8038	0.0035
365	6340	>10000	0.0012
366	585	2996	0.0011
367	499	4076	0.001
368	109	1936	0.00068
369	362	2560	0.0013
370	483	3502	0.00085
371	389	2256	0.00084
372	961	7245	0.00025
373	70	2962	0.00016
374	64	3915	0.00014
375	44	2589	0.00015
376	2602	>10000	0.0023
377	2614	4718	0.0039
378	2506	5375	0.0054
379	4749	5255	0.0073
380	3344	3559	0.0051
381	2955	5395	0.0059
382	522	4306	0.0045
383	2978	3609	0.0061
384	4220	5381	0.0064
385	3397	4692	0.0057
386	5122	4476	0.0042
387	3416	2858	0.0032
388	3450	4285	0.0048
389	4766	5663	0.0065
390	2467	2354	0.012
391	2398	4000	0.0096
392	1178	2781	0.0055
393	444	1539	0.0036
394	592	3226	0.0088
395	584	2221	0.014

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
396	586	2432	0.01
397	173	2073	0.00016
398	644	3909	0.00021
399	330	1691	0.0011
400	846	4099	0.0017
401	413	3247	0.002
402	543	3643	0.0018
403	314	2383	0.00075
404	63	433	0.00069
405	50	193	0.00064
406	478	1881	0.00038
407	766	2255	0.00052
408	876	3342	0.00072
409	856	4487	0.0015
410	826	5684	0.0023
411	1896	>10000	0.0036
412	1230	7483	0.0073
413	1518	>10000	0.0092
414	969	5453	0.0069
415	787	3263	0.00038
416	446	2505	0.00055
417	656	4299	0.0011
418	520	3476	0.0015
419	610	4272	0.0017
420	593	4363	0.00063
421	414	1571	0.00072
422	269	1221	0.00079
423	610	1854	0.0011
424	576	1871	0.0014
425	309	2383	0.0012
426	1224	8477	0.053
427	580	1419	0.0013
428	450	840	0.0014
429	483	1005	0.0019
430	402	484	0.0017
431	43	340	0.001
432	90	480	0.00069
433	220	1510	0.0023
434	571	4740	0.00056
435	643	4603	0.00075
436	749	3119	0.00062
437	381	1612	0.00056
438	77	663	0.00081

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
439	182	1283	0.00042
440	1006	>10000	0.0012
441	970	>10000	0.0012
442	1756	>10000	0.0015
443	427	1883	0.00089
444	60	1099	0.00057
445	100	1002	0.00041
446	835	4013	0.00082
447	390	2802	0.0019
448	519	>10000	0.0023
449	287	1640	0.0019
450	76	888	0.0017
451	85	702	0.0014
452	41	502	0.00055
453	659	4273	0.0033
454	278	1490	0.0002
455	113	1390	0.0003
456	150	1547	0.0007
457	63	839	0.0002
458	33	512	0.0002
459	26	483	0.0003
460	143	1083	0.0004
461	482	4415	0.0011
462			< 0.001
463			0.017
464			0.001
465			0.001
466			0.001
467			< 0.001
468			< 0.001
469			0.023
470			0.007
471			0.000
472			0.035
473			0.035
474			0.048
475			18.500
476			0.005
477			14.000
478	1.1	6.0	0.00089
479	<2.1	14.0	0.0017
480	13.0	53.0	0.0029
481	11.0	65.0	0.0023

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
482	0.6	10.0	0.00305
483	28.5	150.0	0.00155
484	1.0	8.0	0.00063
485	1.4	10.0	0.00125
486	1.1	7.0	0.0045
487	32.3	27.0	0.0018
488	42.0	180.0	0.0034
489	3671.7	9045.0	0.0022
490	586.0	1077.0	0.0116
491	3.5	17.0	0.0011
492	6.5	35.0	0.018
493	2924.0	1078.0	0.0325
494	16.5	104.0	0.0042
495	<1.00	6.0	0.00195
496	NA	NA	NA
497	3.0	19.0	0.0046
498	<1.70	2.5	0.00235
499	<1.90	4.5	0.0022
500	0.4	10.0	0.00109
501	<1.75	6.5	0.00069
502	0.5	6.0	0.001
503	0.5	1.8	
504	1.8	10.0	0.00135
505	0.6	5.0	NA
506	0.3	7.0	NA
507	1.6	8.7	0.0032
508	<1.9	12.5	0.00097
509	11.5	662.5	0.00045
510	1.1	6.3	0.00089
511	2.3	10.3	0.00052
512	<1.9	10.0	0.00012
513	<2.4	12.0	0.00012
514	1.6	15.0	0.00017
515	0.4	7.6	0.00155
516	2.1	17.0	NA
517	3.4	18.5	0.00106
518	0.9	6.5	0.0011
519	<1.1	4.8	0.00071
520	1.4	8.0	0.00038
521	1.4	6.0	0.0003
522	1.4	7.5	0.00106
523	3.2	9.5	0.00043
524	0.8	10.0	0.00026

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
525	NA	NA	NA
526	96.5	6701.5	0.0475
527	20.5	127.0	0.0093
528	1612.0	4140.0	1.6
529	10.5	48.5	0.0155
530	92.0	705.5	0.0495
531	71.5	484.5	0.08
532	3.0	76.5	0.019
533	7.0	98.5	0.0705
534	2.1	11.1	0.0534
535	43.5	112.0	0.0815
536	1.5	13.0	0.0094
537	43.5	89.0	0.000022
538	333.0	197.0	0.000125
539	1.1	16.0	0.0000085
540	54.0	121.0	0.0000034
541	28.000	57.000	0.017
542	8.000	67.000	0.0215
543	3.500	15.500	0.042
544	3.500	20.500	0.017
545	4.000	17.000	0.0109
546	3.500	73.500	0.000225
547	11.000	70.000	0.00775
548	40.000	387.000	0.00975
549	724.000	4541	0.0265
550	47.000	374.000	0.0124
551	24.000	117.500	0.01
552	11.500	127.000	0.00355
553	12.500	72.000	0.0195
554	15.000	156.500	0.0119
555	87.500	378.500	0.405
556	8.500	54.000	0.0044
557	18.000	64.000	0.00855
558	17.000	41.000	0.0061
559	2.000	13.500	0.01005
560	269.000	504.500	0.1
561	11.5	59.0	0.006
562	1.0	10.5	0.004
563	2.5	33.5	0.003
564	0.6	16.5	0.001
565	4.1	38.0	0.001
566	2.6	18.0	0.002
567	14.5	90.0	0.002

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
568	3.5	18.0	0.010
569	74.5	375.0	0.008
570	5.5	48.0	0.013
571	21.0	108.0	0.000
572	0.9	15.0	0.000
573	6.5	64.0	0.004
574	1.0	12.5	0.006
575	3.0	19.0	0.015
576	761.0	2081.0	0.140
577	63.0	104.0	0.030
578	2406.0	2511.0	2.100
579	462.0	658.0	0.120
580	465.0	1315.0	0.100
581	113.5	461.0	0.037
582	513.0	1094.0	0.230
583	123.0	718.0	0.048
584			
585	65.0	131.0	0.012
586	947.0	1246.0	0.365
587	350.0	675.0	0.100
588	524.5	2249.0	0.054
589	718.0	1615.0	0.057
590	343.0	403.5	0.049
591	250.0	726.0	0.033
592	25.5	122.0	0.009
593	40.0	143.0	0.012
594	349.5	744.0	0.022
595	6.5	58.5	0.010
596	5.0	40.5	0.013
597	5.0	58.0	0.011
598	5.5	40.0	0.010
599	64.5	190.0	0.013
600	45.5	161.5	0.008
601	3.5	57.5	0.003
602	7.0	46.5	0.011
603	8.5	50.5	0.017
604	3.5	55.5	0.010
605	2.2	46.0	0.003
606	12.0	87.0	0.026
607	12.0	94.0	0.019
608	9.0	107.0	0.005
609	11.5	93.5	0.003
610	3.5	50.5	0.005

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
611	18.5	151.5	0.013
612	5.5	67.0	0.061
613	3.8	53.5	0.001
614	2.7	32.5	0.001
615	26.5	115.5	0.001
616	4.0	58.5	0.001
617	2.5	27.0	0.001
618	2.0	18.5	0.001
619	33.0	137.0	0.001
620	4.0	32.5	0.003
621	3.5	43.5	0.001
622	3.0	50.5	0.000
623	12.5	104.0	0.001
624	17.5	58.5	0.001
625	16.5	102.5	0.003
626	59.0	207.5	0.001
627	18.5	101.5	0.002
628			
629	26.0	95.0	0.004
630	13.5	84.5	0.001
631	28.0	133.0	0.004
632	15.0	74.5	0.001
633	11.5	175.0	0.001
634	6.0	121.5	0.000
635	22.0	377.5	0.000
636	231.0	468.5	0.027
637	21.5	190.5	0.004
638	16.0	113.5	0.002
639	14.5	123.0	0.001
640	345.0	795.0	2.800
641	88.5	275.5	0.007
642	69.0	254.5	0.001
643	6.2	42.5	0.007
644	7.8	59.5	0.001
645	105.0	230.5	0.120
646	23.0	85.5	0.006
647	24.3	107.0	0.003
648	2.0	27.0	0.003
649	6.4	38.0	0.006
650	23.5	103.5	0.022
651	71.0	247.5	0.014
652	36.0	84.5	0.004
653	4.1	34.0	0.007

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
654	6.0	70.0	0.008
655	91.5	745.5	0.625
656	73.0	651.0	0.019
657	11.5	127.5	0.385
658	41.5	265.0	0.020
659	3621.0	10000.0	0.720
660	7.5	168.5	0.305
661	56.5	461.5	0.580
662	34.3	197.0	0.770
663	47.3	296.0	0.590
664	NA	NA	NA
665	71.0	283.5	0.445
666	11.5	662.5	0.000
667	102	1081	0.000405
668	122	625.000	0.00056
669	8.0	89.0	0.00048
670	5.0	53.0	0.000212
671	17.5	150.5	0.000505
672	39.5	154.5	0.00195
673	7.0	98.7	0.00043
674	14.0	74.5	0.000325
675	21.0	135.5	0.00066
676	69.5	122.0	0.0013
677	86.5	290.0	0.00335
678	21.3	45.3	0.001168
679	1575.0	9500.0	0.0135
680	504.0	2083.0	0.0036
681	2547	>10,000	0.091
682	84.3	1282.5	0.0885
683	121.3	1329.0	0.025
684	154.3	2345.0	0.0235
685	7.0	26.5	0.000825
686	77.0	540.0	0.026
687	4.0	39.5	0.00485
688	3.0	35.5	0.008
689	217.4	2482	0.03902
690	5.0	83.5	0.000525
691	6.0	199.0	0.00135
692	3.2	29.0	0.00375
693	69.0	289.0	0.00135
694	2.0	40.0	0.000245
695	4.0	70.5	0.00028
696	4.5	73.5	0.000275

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
697	2.7	42.7	0.000459
698	2.7	44.7	0.000302
699	5.0	62.5	0.0003
700	2.5	41.5	0.00053
701	2.0	25.0	0.00036
702	6.5	125.5	0.000555
703	1.5	23.5	0.00051
704	7217	>10,000	2.35
705	13.5	132.0	0.0124
706	25.5	336.0	0.0145
707	14.0	234.5	0.034
708	39.5	8890.5	0.043
709	20.0	182.5	0.0245
710	15.5	143.5	0.034
711	207.5	4919.5	0.02
712	9.5	117.0	0.00855
713	36.0	444.0	0.0009
714	15.5	69.0	0.00645
715	59.5	146.5	0.006
716	NA	NA	NA
717	444.0	5874.0	0.000395
718	40.5	210.5	0.055
719	17.5	96.0	0.00015
720	0.4	7.0	0.0077
721	0.6	10.5	0.00565
722	0.8	9.5	0.0145
723	1.3	13.5	0.0225
724	1.5	4.0	0.0185
725	2.0	20.5	0.0082
726	25.0	216.5	0.0025
727	21.0	189.5	0.000805
728	10.5	47.0	0.00038
729	14.5	100.0	0.00185
730	15.5	64.5	0.0043
731	33.0	413.0	0.059
732	44.0	478.0	0.069
733	31.5	412.0	0.0755
734	25.5	210.0	0.0595
735	26.5	289.5	0.1225
736	9.5	53.5	0.0036
737	7.0	30.0	0.00445
738	NA	NA	NA
739	NA	NA	NA

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
740	11.5	34.5	0.00405
741	2188	4981	2.80
742	97.0	166.0	0.145
743	368.0	711.0	0.19
744	1501.0	3693.0	0.068
745	764.0	533.0	0.47
746	23.5	99.0	0.001265
747	40.0	44.0	0.00345
748	NA	NA	NA
749	59.0	163.5	0.002
750	NA	NA	NA
751	143.0	403.5	0.003
752	1.2	18.5	0.00029
753	2.0	31.0	0.000315
754	3.0	28.0	0.000327
755	2.0	26.5	0.00057
756	0.5	7.0	0.0002
757	5.5	37.5	0.00028
758	2.0	16.0	0.00017
759	2.0	38.0	0.00016
760	4.3	28.3	0.00021
761	2.0	19.0	0.00012
762	2.7	19.7	0.000428
763	3.0	24.0	0.000445
764	8.5	67.5	0.00021
765	8.5	78.5	0.000195
766	24.0	85.5	0.001315
767	2.1	17.0	0.0002
768	1.2	18.5	0.000115
769	2.1	17.5	0.00023
770	30.5	99.0	0.00027
771	19.5	66.0	0.000215
772	0.8	9.5	0.00029
773	3.0	36.5	0.000305
774	2.0	41.5	0.00023
775	2.5	46.5	0.00023
776	3.0	29.5	0.000345
777	4.0	39.0	0.000265
778	11.5	126.0	0.00028
779	4.2	49.7	0.00023
780	NA	NA	NA
781	136.0	374.5	0.0305
782	124.5	251.5	0.11

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
783	346.0	736.0	0.295
784	40.5	174.0	0.088
785	6.0	45.5	0.0555
786	30.5	129.0	0.089
787	10.5	145.5	0.0585
788	13.0	160.0	0.026
789	870.0	1163.0	0.059
790	244.0	593.0	0.065
791	12.5	64.5	0.00068
792	3.3	35.5	0.00081
793	1.0	15.0	0.00042
794	4.1	26.0	0.00063
795	2.7	26.5	0.000425
796	2.6	31.5	0.00039
797	11.5	76.0	0.0013
798	4.1	43.5	0.000445
799	5.0	71.5	0.0005
800	5.5	35.5	0.00072
801	5.0	38.0	0.000455
802	3.5	23.0	0.000675
803	3.0	29.0	0.00019
804	6.0	59.5	0.000425
805	6.5	64.0	0.000415
806	4.5	47.0	0.00024
807	Na	NA	NA
808	381.0	1261.0	0.26
809	395.0	2189.0	0.067
810	2.8	30.5	0.00205
811	3.2	33.5	0.0015
812	2.8	30.5	0.002
813	3.1	30.0	0.0019
814	0.8	10.0	0.00105
815	1.9	24.0	0.000765
816	2.4	26.0	0.001065
817	NA	NA	NA
818	37.7	185.0	0.002
819	44.0	357.5	0.017
820	6.1	67.0	0.000515
821	9.3	58.3	0.0034
822	3.0	31.5	0.000335
823	661.0	2788.0	0.0000015
824	2	17	NA
825	2	13	NA

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
826	15	96	1.200
827	71.000	283.500	445.000
828	47.333	296.000	590.000
829	34.333	197.000	770.000
830	2.125	10.800	0.393
831	0.950	7.500	0.635
832	1.350	10.500	1.250
833	2.575	8.250	0.430
834	0.750	10.000	0.255
835	4.150	18.500	8.550
836	5.000	17.500	4.050
837	11.900	75.000	1.450
838	4.950	24.500	0.965
839	6.650	29.000	2.500
840	5.150	15.000	1.700
841	6.500	107.500	0.990
842	3.550	54.500	0.325
843	28.500	291.000	1500.000
844	21.000	237.500	345.000
845	0.250	2.750	1.300
846	3.500	22.500	485.000
847	10.500	87.500	165.000
848	1.050	6.000	2.200
849	0.300	3.167	0.865
850	0.650	6.100	1.200
851	0.850	5.600	1.010
852	0.400	5.550	1.250
853	0.300	5.050	1.400
854	8.840	164.000	260.000
855	54.000	864.000	305.000
856	28.500	532.000	11.000
857	10.000	145.500	660.000
858	5.000	134.500	290.000
859	17.850	239.500	830.000
860	57.000	434.500	150.000
861	4.000	56.000	425.000
862	23.500	154.000	835.000
863	2.100	8.000	3.600
864	1.000	7.500	5.250
865	2.450	12.000	1.350
866	1.600	16.500	0.980
867	0.400	7.000	0.610
868	0.650	4.500	

Example	IC_{50} PI3Kα nM	IC_{50} PI3Kγ nM	IC_{50} mTOR M
869	0.600	6.500	

Table 3 shows the results of the described hSMG-1 kinase assay.

Table 3

Example	hSMG-1 IC_{50} (μM)
462	0.001
463	0.510
464	0.003
465	0.005
466	0.000
467	0.000
468	<0.000
469	0.130
470	0.195
471	0.005
472	0.200
473	3.650
474	5.650
475	>20
476	0.019
477	9.250

Table 4 shows the results of the described MDA-MB-361, PC3-mm2, and LNCap assays.

Table 4

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
1	45.0	43.0	
2	45.0	43.0	
3	45.0	43.0	
4	45.0	43.0	
5	45.0	43.0	
6	45.0	43.0	
7	ND	ND	
8	407.0	293.0	
9	102.0	161.0	
10	2709.0	1782.0	
11	794.0	5630.5	
12	ND	ND	
13	603.0	845.0	
14	376.0	590.0	
15	255.0	328.0	
16	ND	ND	
17	501.0	994.0	
18	2656.0	7102.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
19	1031.0	1596.0	
20	> 10000	> 10000	
21	129.0	246.0	
22	1424.0	2445.0	
23	104.0	147.0	
24	122.0	142.0	
25	264.0	258.0	
26	ND	ND	190.0
27	ND	ND	350.0
28	ND	ND	2.4
29	ND	ND	180.0
30	ND	ND	90.0
31	ND	ND	45.0
32	ND	ND	0.7
33	ND	ND	
34	28.0	41.0	
35	22.5	27.5	
36	73.0	98.0	
37	98.0	176.0	
38	15.0	28.0	
39	22.0	30.0	
40	< 30	62.0	
41	167.0	301.0	
42	345.0	3600.0	
43	35.8	40.0	
44	ND	ND	
45	ND	ND	
46	ND	ND	
47	116.0	95.0	
48	38.0	48.0	
49	84.0	79.0	
50	36.0	39.0	
51	< 30	< 30	
52	< 30	49.0	
53	662.0	987.0	
54	133.0	214.0	
55	ND	ND	
56	ND	ND	
57	119.0	187.0	
58	115.0	45.0	
59	14.0	16.0	
60	83.0	92.0	
61	48.0	23.0	
62	27.0	34.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
63	69.0	62.0	
64	ND	ND	
65	151.0	267.0	
66	59.0	66.0	
67	816.0	28.0	
68	< 3	11.0	
69	10.0	13.0	
70	19.0	24.0	
71	< 9.8	18.3	
72	1.0	13.0	
73	30.0	107.0	
74	< 3	8.3	
75	< 3	7.0	
76	4.0	13.1	
77	< 30	< 30	
78	68.0	31.0	
79	ND	320.0	
80	ND	320.0	
81	ND	ND	
82	ND	ND	
83	ND	ND	
84	ND	ND	
85	ND	ND	
86	ND	ND	
87	ND	ND	
88	ND	ND	
89	30.0	47.0	
90	19.0	19.0	
91	25.0	1567.0	
92	140.0	87.0	
93	42.0	60.0	
94	54.0	82.0	
95	333.0	364.0	
96	5.0	33.0	
97	< 30	52.0	
98	ND	ND	
99	ND	ND	
100	56.0	56.0	
101	32.7	37.3	3.0
102	592.0	854.0	
103	2917.0	4453.0	
104	412.0	684.0	
105	3710.0	> 10000	
106	ND	ND	370.0

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
107	ND	ND	1000.0
108	ND	ND	320.0
109	ND	ND	1900.0
110	ND	ND	220.0
111	ND	ND	58.0
112	ND	ND	300.0
113	ND	ND	120.0
114	ND	ND	38.0
115	ND	ND	200.0
116	ND	ND	70.0
117	ND	ND	700.0
118	ND	ND	3000.0
119	ND	ND	2800.0
120	ND	ND	1200.0
121	ND	ND	1000.0
122	ND	ND	900.0
123	ND	ND	4100.0
124	ND	ND	1950.0
125	ND	ND	1000.0
126	ND	ND	1300.0
127	ND	ND	1350.0
128	ND	ND	30000.0
129	ND	ND	
130	191.0	416.0	
131	696.0	839.0	
132	586.0	1012.0	
133	795.0	1950.0	
134	805.0	857.0	
135	533.0	509.0	
136	ND	ND	
137	582.0	551.0	
138	ND	ND	680.0
139	ND	ND	180.0
140	225	279	
141	ND	ND	
142	5	33	
143	ND	52	
144	ND	ND	1500
145	ND	ND	120
146	ND	ND	5
147	ND	ND	1000
148	ND	ND	680
149	ND	ND	32000
150	ND	ND	290

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
151	ND	14	
152	9	14	
153	ND	ND	4200
154	ND	ND	22000
155	ND	ND	400
156	ND	ND	22000
157	ND	ND	2700
158	ND	ND	49
159	ND	ND	1.2
160	ND	ND	220
161	328	675	
162	ND	ND	
163	10.7	28.3	
164	ND	ND	
165	210	333	
166	134	249	
167	ND	10	
168	ND	ND	
169	ND	ND	5000
170	ND	ND	4500
171	ND	ND	5200
172	ND	ND	9500
173	ND	ND	2500
174	ND	ND	4.25
175	ND	ND	9.5
176	ND	ND	1000
177	ND	ND	600
178	ND	ND	850
179	ND	8.333	
180	ND	ND	5800
181	ND	ND	3400
182	ND	ND	3500
183	ND	ND	8500
184	1246	2094	
185	5	13	
186	473	703	
187	11	41	
188	ND	ND	
189	84	99	
190	ND	ND	950
191	ND	ND	220
192	ND	ND	620
193	ND	ND	105
194	ND	ND	600

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
195	ND	ND	
196	50	82	
197	17	49	
198	ND	43	
199	96	93	
200	162	248	
201	29	44	
202	ND	ND	700
203	ND	ND	78
204	ND	ND	6000
205	ND	ND	400
206	ND	ND	5100
207	ND	ND	33.333
208	ND	ND	50
209	174	278	
210	ND	ND	
211	254	389	
212	ND	ND	420
213	ND	ND	420
214	ND	ND	700
215	ND	ND	30
216	0	ND	50
217	ND	ND	13
218	ND	ND	12
219	ND	ND	40
220	ND	ND	40
221	ND	ND	120
222	ND	ND	10
223	187	229	
224	ND	ND	
225	ND	ND	
226	ND	ND	
227	1495	4026	
228	3924	7174	
229	35.75	40	
230	ND	ND	
231	20	121	
232	38	177	
233	1214	3337	
234	ND	ND	10000
235	ND	ND	7900
236	22.333	67	
237	28	69	
238	23	61	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
239	184	317	
240	ND	12	
241	24	135	
242	11	49	
243	15	34	
244	ND	71	
245	110	374	
246	35	91	
247	30	111	
248	ND	69	
249	92	142	
250	14	31	
251	ND	65	
252	219	747	
253	12	574	
254	ND	ND	
255	174	328	
256	ND	ND	
257	ND	ND	
258	ND	ND	60
259	ND	ND	580
260	ND	ND	380
261	ND	ND	30
262	ND	ND	22
263	68	31	
264	ND	ND	
265	ND	ND	1.7
266	ND	ND	
267	94	200	
268	59	107	38
269	ND	144	
270	397	953	
271	68	129	
272	70	340	
273	32	80	
274	1000	1491	
275	3100	4309	
276	1347	1654	
277	530	572	
278	2297	3701	
279	176	247	
280	176	404	
281	ND	ND	
282	83	84	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
283	12.333	33.333	
284	12	36.333	
285	ND	ND	4
286	ND	ND	32000
287	ND	ND	
288	ND	ND	3
289	ND	ND	3
290	ND	ND	
291	ND	ND	
292	ND	ND	
293	ND	ND	
294	69	154	
295	133	189	
296	83	133	
297	115	290	
298	38	165	
299	73	219	
300	297	340	
301	430	759	
302	299	539	
303	ND	ND	0.8
304	7	39.333	
305	4	46	
306	7	30	
307	ND	362	
308	4	53	
309	64	109	
310	44	117	
311	126	366	
312	ND	ND	80
313	ND	ND	100
314	ND	ND	550
315	ND	ND	300
316	ND	ND	320
317	ND	ND	120
318	ND	ND	1000
319	ND	ND	220
320	32.333	73.667	
321	106	325	
322	13	86	
323	ND	77	
324	4	35	
325	ND	ND	310
326	ND	ND	580

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
327	ND	ND	400
328	ND	ND	1500
329	ND	ND	5900
330	ND	ND	260
331	0	0	0
332	0	0	0
333	0	0	0
334	0	0	0
335	0	0	0
336	56	45	0
337	142	373	
338	122	266	
339	ND	ND	
340	ND	ND	
341	150	237	
342	1256	2429	
343	ND	ND	
344	ND	ND	
345	554	395	
346	ND	ND	
347	ND	ND	9
348	ND	ND	
349	87	81	
350	ND	8.5	
351	50	66	
352	ND	ND	< 0.8
353	ND	ND	< 0.8
354	ND	ND	310
355	ND	ND	580
356	ND	ND	400
357	ND	ND	1500
358	ND	ND	5900
359	ND	ND	260
360	ND	ND	10000
361	ND	ND	2.2
362	ND	ND	1
363	ND	ND	1.2
364	ND	ND	70
365	ND	ND	3
366	ND	ND	2.8
367	ND	ND	5
368	ND	ND	0.7
369	ND	ND	3
370	ND	ND	0.8

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
371	ND	ND	0.8
372	ND	ND	0.8
373	ND	ND	1
374	ND	ND	< 0.8
375	ND	ND	< 0.8
376	ND	ND	50
377	ND	ND	90
378	ND	ND	50
379	ND	ND	140
380	ND	ND	300
381	ND	ND	140
382	ND	ND	48
383	ND	ND	150
384	ND	ND	50
385	ND	ND	70
386	ND	ND	140
387	ND	ND	70
388	ND	ND	110
389	ND	ND	240
390	ND	ND	650
391	ND	ND	300
392	ND	ND	480
393	ND	ND	580
394	ND	ND	800
395	ND	ND	590
396	ND	ND	280
397	ND	ND	7
398	ND	ND	12
399	ND	ND	3
400	ND	ND	12
401	ND	ND	21
402	ND	ND	7
403	ND	ND	8
404	ND	ND	60
405	ND	ND	25
406	ND	ND	2.4
407	ND	ND	0.8
408	ND	ND	9
409	ND	ND	50
410	ND	ND	110
411	ND	ND	250
412	ND	ND	25
413	ND	ND	150
414	ND	ND	120

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
415	ND	ND	29
416	ND	ND	12
417	ND	ND	6
418	ND	ND	40
419	ND	ND	12
420	ND	ND	2
421	ND	ND	1
422	ND	ND	2
423	ND	ND	2.8
424	ND	ND	1
425	ND	ND	2.8
426	ND	ND	700
427	ND	ND	7
428	ND	ND	1
429	ND	ND	9
430	ND	ND	16
431	ND	ND	< 0.8
432	ND	ND	< 0.8
433	ND	ND	40
434	ND	ND	< 0.8
435	ND	ND	4
436	ND	ND	10
437	ND	ND	1
438	ND	ND	< 0.8
439	ND	ND	1
440	ND	ND	1
441	ND	ND	6
442	ND	ND	13
443	ND	ND	8
444	ND	ND	< 0.8
445	ND	ND	< 0.8
446	ND	ND	15
447	ND	ND	8
448	ND	ND	18
449	ND	ND	40
450	ND	ND	< 0.8
451	ND	ND	< 0.8
452	ND	ND	< 0.8
453	ND	ND	30
454	ND	ND	< 0.8
455	ND	ND	< 0.8
456	ND	ND	< 0.8
457	ND	ND	< 0.8
458	ND	ND	8

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
459	ND	ND	< 0.8
460	ND	ND	< 0.8
461	ND	ND	68
462	ND	ND	ND
463	ND	ND	ND
464	ND	ND	ND
465	ND	ND	ND
466	ND	ND	420
467	ND	ND	170
468	ND	ND	50
469	ND	ND	2800
470	ND	ND	1000
471	ND	ND	130
472	ND	ND	3800
473	ND	ND	ND
474	ND	ND	ND
475	ND	ND	ND
476	ND	ND	ND
477	ND	ND	ND
478	< 3.080	8.5	
479	6	21	
480	ND	ND	
481	ND	ND	
482	ND	ND	
483	ND	ND	
484	ND	ND	
485	ND	ND	
486	7.0	39.3	
487	175.0	339.0	
488	ND	ND	
489	ND	ND	4300
490	ND	ND	
491	8.0	35.0	
492	26.0	57.0	
493	ND	ND	
494	115.0	276.0	
495	4.0	13.1	
496	ND	ND	
497	50.0	66.0	
498	4.0	16.5	
499	21.0	31.0	
500	1.0	6.5	
501	< 31	41	
502	4.0	11.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
503	7.5	12.5	
504	22.5	25.5	
505	12.3	33.3	
506	< 21.7	12	
507	10.7	28.3	
508	12.0	36.3	
509	ND	ND	< 0.8
510	ND	ND	
511	2.0	10.0	
512	1.0	8.0	
513	2.0	13.0	
514	< 3.2	12	
515	3	12	
516	ND	ND	
517	18.0	7.0	
518	4.0	24.0	
519	3.0	9.0	
520	5.0	18.0	
521	8.0	27.0	
522	3.0	11.0	
523	ND	ND	
524	ND	ND	
525	ND	ND	
526	ND	ND	
527	1256.0	2429.0	
528	ND	ND	
529	150.0	237.0	
530	ND	ND	
531	ND	ND	
532	122.0	266.0	
533	142.0	373.0	
534	32.3	73.7	
535	554.0	395.0	
536	22.3	67.0	
537	< 31	< 31	
538	ND	ND	
539	9.0	161.0	
540	165.0	309.0	
541	964.0	1764.0	
542	281.0	569.0	
543	< 31	262.0	
544	58.0	253.0	
545	30.0	219.0	
546	7.0	25.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
547	68.0	197.0	
548	524.0	869.0	
549	ND	ND	
550	315.0	711.0	
551	106.0	270.0	
552	105.0	243.0	
553	113.0	522.0	
554	521.0	>1000	
555	ND	ND	
556	128.0	379.0	
557	34.0	31.0	
558	751.0	939.0	
559	8.0	149.0	
560	ND	ND	
561	66.0	218.0	
562	3.0	93.0	
563	10.0	171.0	
564	1.0	7.0	
565	9.0	27.0	
566	28.0	55.0	
567	106.0	130.0	
568	18.0	107.0	
569	ND	ND	
570	28.0	344.0	
571	90.0	168.0	
572	13.0	56.0	
573	99.0	206.0	
574	6.0	25.0	
575	15.0	242.0	
576	ND	ND	
577	ND	ND	
578	ND	ND	
579	ND	ND	
580	ND	ND	
581	ND	ND	
582	ND	ND	
583	ND	ND	
584	ND	ND	
585	ND	ND	
586	ND	ND	
587	ND	ND	
588	ND	ND	
589	ND	ND	
590	ND	ND	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
591	ND	ND	
592	239.0	718.0	
593	>1000	>1000	
594	ND	ND	
595	43.0	193.0	
596	26.0	155.0	
597	45.0	229.0	
598	22.0	214.0	
599	ND	ND	
600	ND	ND	
601	22.0	155.0	
602	17.0	122.0	
603	17.0	137.0	
604	4.0	73.0	
605	7.0	92.0	
606	28.0	173.0	
607	24.0	213.0	
608	52.0	298.0	
609	24.0	26.0	
610	28.0	297.0	
611	194.0	581.0	
612	38.0	227.0	
613	6.0	21.0	
614	4.0	15.0	
615	88.0	123.0	
616	4.0	21.0	
617	4.0	17.0	
618	2.0	13.0	
619	ND	ND	
620	4.0	16.0	
621	8.0	35.0	
622	5.0	25.0	
623	6.0	32.0	
624	4.0	19.0	
625	12.0	43.0	
626	ND	ND	
627	16.0	55.0	
628	ND	ND	
629	28.0	133.0	
630	5.0	23.0	
631	28.0	120.0	
632	9.0	38.0	
633	15.0	64.0	
634	5.0	16.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
635	26.0	106.0	
636	ND	ND	
637	26.0	62.0	
638	9.0	44.0	
639	16.0	27.0	
640	ND	ND	
641	ND	ND	
642	ND	ND	
643	19.0	59.0	
644	51.0	185.0	
645	ND	ND	
646	32.0	223.0	
647	46.0	136.0	
648	12.0	34.0	
649	9.0	37.0	
650	ND	ND	
651	ND	ND	
652	ND	ND	
653	ND	ND	
654	ND	ND	
655	ND	ND	
656	ND	ND	
657	ND	ND	
658	ND	ND	
659	ND	ND	
660	ND	ND	
661	ND	ND	
662	ND	ND	
663	ND	ND	
664	ND	ND	
665	ND	ND	
666	ND	ND	
667	ND	ND	60.0
668	ND	ND	0.8
669	28.0	41.0	
670	22.5	27.5	
671	73.0	98.0	
672	98.0	176.0	
673	15.0	28.0	
674	22.0	30.0	
675	< 30	62.0	
676	167.0	301.0	
677	345.0	3600.0	
678	35.8	40.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
679	ND	ND	
680	ND	ND	
681	ND	ND	
682	1044.0	766.0	
683	673.0	584.0	
684	806.0	1015.0	
685	>10000	>10000	
686	569.0	1105.0	
687	355.0	389.0	
688	1412.0	1950.0	
689	53.0	85.0	
690	112.0	405.0	
691	52.0	131.0	
692	97.0	326.0	
693	ND	ND	
694	< 3	11.0	
695	6.0	7.0	
696	13.0	13.0	
697	< 30	< 30	
698	< 3	6.0	
699	36.0	40.0	
700	5.0	20.0	
701	< 30	< 30	
702	4.0	14.0	
703	< 3	13.0	
704	ND	ND	
705	191.0	416.0	
706	696.0	839.0	
707	586.0	1012.0	
708	795.0	1950.0	
709	805.0	857.0	
710	533.0	509.0	
711	ND	ND	
712	582.0	551.0	
713	29.0	44.0	
714	162.0	248.0	
715	254.0	389.0	
716	ND	ND	
717	ND	ND	< 0.8
718	3924.0	7174.0	
719	< 31	< 31	
720	15.0	34.0	
721	< 31	71.0	
722	110.0	374.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
723	35.0	91.0	
724	30.0	111.0	
725	< 31	69.0	
726	92.0	142.0	
727	14.0	31.0	
728	59.0	107.0	38.000
729	< 31	< 31	
730	94.0	200.0	
731	1000.0	1491.0	
732	3100.0	4309.0	
733	1347.0	1654.0	
734	530.0	572.0	
735	2297.0	3701.0	
736	176.0	247.0	
737	176.0	404.0	
738	ND	ND	
739	ND	ND	
740	83.0	84.0	
741	ND	ND	
742	ND	ND	
743	ND	ND	
744	ND	ND	
745	ND	ND	
746	93.0	118.0	
747	56.0	45.0	
748	ND	ND	
749	87.0	81.0	
750	ND	ND	
751	144.0	238.0	
752	< 3	6.0	
753	4.0	14.0	
754	31.3	70.8	
755	3.0	13.0	
756	< 3	12.000	
757	< 3	6.000	
758	3.0	14.0	
759	1.0	10.0	
760	0.0	4.0	
761	< 3	4.0	
762	8.0	7.0	
763	4.0	7.0	
764	628.0	678.0	
765	21.0	27.0	
766	26.0	50.0	

Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
767	5.0	13.0	
768	7.0	8.0	
769	6.0	14.0	
770	40.0	25.0	
771	>1000	>1000	
772	5.0	15.0	
773	4.0	6.0	
774	14.0	19.0	
775	5.0	7.0	
776	< 3.2	6.0	
777	2.0	4.0	
778	17.0	29.0	
779	13.0	23.0	
780	ND	ND	
781	ND	ND	
782	ND	ND	
783	ND	ND	
784	>1000	>1000	
785	>1000	>1000	
786	>1000	>1000	
787	>1000	>1000	
788	>1000	>1000	
789	ND	ND	
790	ND	ND	
791	11.0	42.0	
792	2.0	16.0	
793	2.0	26.0	
794	2.0	20.0	
795	< 3.2	10.0	
796	2.0	18.0	
797	11.0	29.0	
798	3.0	24.0	
799	< 3.2	24.0	
800	1.0	11.0	
801	3.0	32.0	
802	3.0	50.0	
803	1.0	6.0	
804	3.0	11.0	
805	3.0	13.0	
806	< 3.2	9.0	
807	35.000	37.000	
808	ND	ND	
809	ND	ND	
810	2.0	26.0	

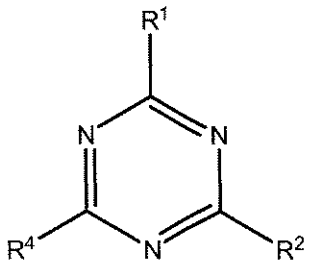
Example	IC_{50} MDA-MB-361 (nM)	IC_{50} PC3-mm2 (nM)	IC_{50} LNCap (nM)
811	2.0	19.0	
812	3.0	23.0	
813	< 3.2	24.0	
814	4.0	37.0	
815	3.0	24.0	
816	2.0	11.0	
817	ND	ND	
818	129.0	237.0	
819	442.0	768.0	
820	ND	ND	
821	ND	ND	
822	ND	ND	
823	ND	ND	55.0
823	ND	ND	
825	ND	ND	
826	>1000	>1000	

While particular aspects of the present invention have been illustrated and described, it would be obvious to those skilled in the art that various other changes and modifications can be made without departing from the spirit and scope of the invention. It is therefore intended to cover in the appended claims all such changes and modifications that are within the scope of this invention.

Throughout this application, various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described and claimed herein.

WHAT IS CLAIMED IS:

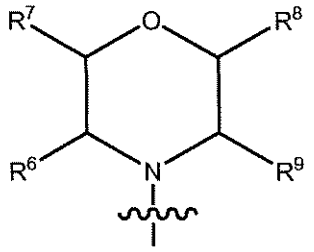
1. A compound of the Formula I:



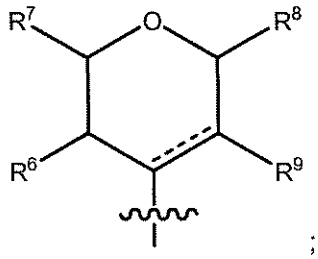
I

wherein:

R^1 is



or



;

wherein:

R^6, R^7, R^8, R^9 are each independently selected from the group consisting of a hydrogen atom, and a C_1-C_6alkyl optionally substituted with C_2-C_6alkenyl, C_4-C_6alkadienyl, C_2-C_6alkynyl or C_4-C_6alkadiynyl;

or one of R^6 and R^7 or R^8 and R^9, together with the carbon atoms to which they are attached form an optionally substituted 5-8 membered saturated or unsaturated ring containing 0, 1 or 2 atoms independently selected from O, NH and S;

the dashed line - - - - - represents an optional second bond;

R^2 is optionally substituted C_6-C_{14}aryl-NH-COR^3, optionally substituted C_1-C_9heteroaryl-NH-COR^3, -CH=CH-C_6-C_{10}aryl-NH-COR^3 or -CH=CH-C_1-C_9heteroaryl-NH-COR^3;

R^3 is OR^5, NR^5R^5 or NHR^5;

R^5 is independently selected from the group consisting of C_1-C_6alkyl, C_3-C_6alkenyl, C_3-C_6alkynyl, optionally substituted C_6-C_{10}aryl, C_1-C_6haloalkyl, optionally substituted C_1-C_9heteroaryl, C_1-C_6hydroxylalkyl-, C_3-C_{10}saturated or unsaturated mono or bicyclic C_3-C_{10}cycloalkyl optionally substituted with OH, $NR^{11}R^{11}$ or 3-7 membered C_1-C_6heterocyclyl, and 3-10 membered saturated or unsaturated mono or bicyclic C_1-C_9heterocyclyl, with the proviso that three-membered cycloalkyl and heterocyclyl rings are saturated;

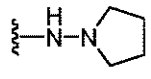
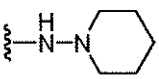
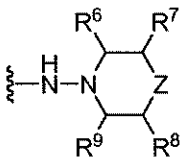
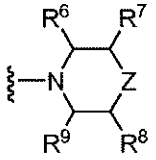
or two R^5 groups taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring system optionally substituted with C_1-C_6alkyl, which ring system is

saturated or unsaturated and has, in addition to said nitrogen atom, 0 to 2 heteroatom ring members selected from O, S, S(O), $S(O)_2$ and NR^{10};

R^{10} is selected from the group consisting of H, C_1-C_6alkyl, -SO_2(C_1-C_6alkyl), -COO(C_1-C_6alkyl), -CONH(C_1-C_6alkyl), -CON(C_1-C_6alkyl)$_2$, -CO(C_1-C_6alkyl), and -SO_2NHR^{11};

R^{11} is selected from the group consisting of H, C_1-C_6alkyl optionally substituted with OH, $NR^{11}R^{11}$ or a 3-7 membered C_1-C_6heterocyclyl, -CO(C_1-C_6alkyl), optionally substituted C_6-C_{10}aryl, and optionally substituted C_1-C_9heteroaryl;

R^4 is selected from the group consisting of: a) C_1-C_6alkyl optionally substituted with: i) 3-10 membered C_1-C_9heterocyclyl optionally substituted with C_1-C_6alkyl-, ii) H_2N-, iii) (C_1-C_6alkyl)NH-, iv) (C_1-C_6alkyl)$_2$N-, v) $NH(CH_2)_aN(C_1$-C_6alkyl)$_2$ wherein a is 2, 3 or 4, and vi) CHO, b) C_3-C_6alkenyl, c) C_3-C_6alkynyl, d) -O-C_1-C_8alkyl optionally substituted with -O-C_1-C_8alkyl, e) -O-C_3-C_8alkenyl, f) -O-C_3-C_8alkynyl, g) saturated or unsaturated mono or bicyclic C_3-C_8cycloalkyl, and h) saturated or unsaturated mono or bicyclic -O-C_3-C_{12}cycloalkyl, all the above optionally substituted with OH, $NR^{11}R^{11}$ or a 3-7 membered C_1-C_6heterocyclyl optionally substituted with C_1-C_6alkyl-, provided that an OH or $NR^{11}R^{11}$ is not directly bonded to a carbon atom that is double- or triple-bonded to another carbon atom; i) -CH=CH-C_6-C_{10}aryl; j) -CH=CH-C_1-C_9heteroaryl; k) optionally substituted C_6-C_{10}aryl; l) optionally substituted 5-10 membered C_1-C_9heteroaryl attached to the triazine moiety via a carbon atom; m) 3-10 membered saturated or unsaturated monocyclic C_1-C_9heterocyclyl attached to the triazine moiety through a carbon or nitrogen atom and optionally substituted with from 1 to 3 substituents independently selected from: OH, $NR^{11}R^{11}$, C_1-C_6alkyl, (C_1-C_6alkyl)amido-, (C_1-C_6alkyl)C(O)-, (C_1-C_6alkoxy)carbonyl-, adamantyl, C_1-C_6hydroxylalkyl-, (C_1-C_6alkyl)amido-; or a 3-7 membered C_1-C_6heterocyclyl, with the proviso that 3 membered heterocyclyl is saturated and attached to the triazine moiety through a nitrogen atom, and 5 membered bicyclic heterocyclyl is saturated; n) optionally substituted -O-C_6-C_{10}aryl; o) optionally substituted -O-C_1-C_9heteroaryl; p) -O-(3-12 membered saturated or unsaturated mono or bicyclic)C_1-C_9heterocyclyl optionally substituted with (C_1-C_6alkoxy)carbonyl-, $H_2NS(O)_2$-, or C_1-C_6alkyl further optionally substituted with OH, $NR^{11}R^{11}$ or a 3-7 membered C_1-C_6heterocyclyl, with the proviso that three membered heterocyclyl is saturated; q) -NHC_6-C_{10}aryl, r) -NHC_1-C_9heteroaryl, s) -$NHNH_2$, t) -NHNHC_1-C_6alkyl, u) -NHN(C_1-C_6alkyl)$_2$, v) -NHOH, w) -COOH, x) -COO-C_1-C_6alkyl, y) -$CONR^{12}R^{13}$, z) -$NR^{12}R^{13}$,

aa)  bb)  cc)  dd) 

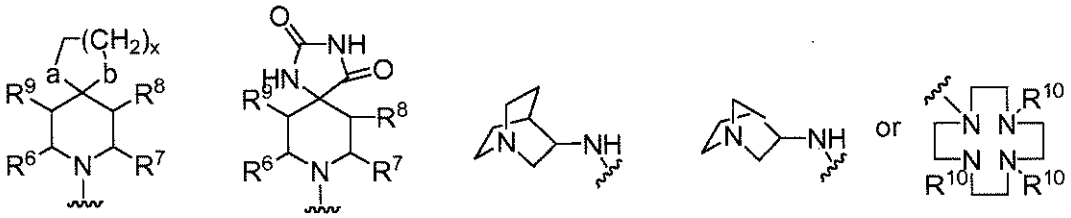
wherein Z is CH_2, O, $S(O)_n$ or NR^{10} and n is 0, 1 or 2;

ee) halogen, ff) C_6-C_{14}aryl-$S(O)_2$-NH-, gg) $R^{11}NHC(O)NH$-O-, and hh) optionally substituted 5-membered monocyclic C_1-C_4heteroaryl attached to the triazine moiety via a nitrogen atom;

R^{12} and R^{13} are each independently selected from H, optionally mono or disubstituted C_1-C_8alkyl, optionally substituted C_3-C_8alkenyl, and optionally substituted C_3-C_8alkynyl, the optional substituents being selected from C_1-C_6alkoxy, OH, $NR^{11}R^{11}$, and 3-7 membered C_1-C_6heterocyclyl, provided that an OH or $NR^{11}R^{11}$ is not directly bonded to a carbon atom that is double- or triple-bonded to another carbon atom;

or R^{12} and R^{13} taken together with the nitrogen atom to which they are attached form a 3 to 8 membered monocyclic ring system optionally substituted with C_1-C_6alkyl, which ring system is saturated or unsaturated and has, in addition to said nitrogen atom, 0 to 2 heteroatom ring members selected from O, $S(O)_n$ and NR^{10};

or R^{12} and R^{13} taken together with the nitrogen atom to which they are attached form



wherein a and b are each independently -CH_2-, O, S, or NR^{10}, and x is 1-3;

C_1-C_9heteroaryl refers to a 5-10 membered aromatic ring system having one or more rings and 1, 2, 3 or 4 ring members independently selected from O, NR^{10}, and $S(O)_n$;

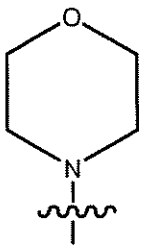
C_1-C_9heterocyclyl refers to a 3-10 membered ring system having one or more rings and 1, 2, 3 or 4 ring members independently selected from O, NR^{10}, and $S(O)_n$; and

optionally substituted aryl and heteroaryl groups are unsubstituted or are substituted with 1 or 2 moieties selected from the group consisting of: a) C_1-C_6alkyl optionally substituted with OH, NH_2, $NH(C_1$-C_6alkyl), $N(C_1$-C_6alkyl)$_2$, -$NH(CH_2)_wN(C_1$-C_6alkyl)$_2$ wherein w is 2, 3 or 4, or 3-10 membered C_1-C_9heterocyclyl optionally substituted with from 1 to 3 independently selected C_1-C_6alkyl- substituents; b) halogen; c) hydroxy; d) NH_2; e) NO_2; f) SO_2NH_2; g) COOH; h) $COO(C_1$-C_6alkyl); i) $NHCOO(C_1$-C_6alkyl); j) $NH(C_1$-C_6alkyl); k) $N(C_1$-C_6alkyl)$_2$; l) $C(O)NR^aR^b$, wherein R^a is H or C_1-C_6alkyl, and R^b is H, C_1-C_6alkyl, (C_6-C_{14}aryl)alkyl-, or (C_1-C_9heteroaryl)alkyl-; m) -Y-Q, wherein Y is: i) O, ii) NH, iii) $N(C_1$-C_6alkyl), iv) $NHSO_2$, v) SO_2NH, vi) NHCONH, vii) $NHCON(C_1$-C_6alkyl), viii) $S(O)_q$, q is 0, 1 or 2, ix) -C(O)NH-, x) –NHC(O)- xi) -$C(O)N(CH_3)$-, xii) C(O), or xiii) absent, and Q is selected from: i) C_6-C_{10}aryl, optionally substituted with from 1 to 3 substituents independently selected from: A) C_1-C_6alkoxy- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, 3) di(C_1-C_6alkyl)amino-, 4) C_1-C_9heterocyclyl-

optionally substituted by C_1-C_6alkyl-, or 5) hydroxyl, B) (C_1-C_6alkoxy)carbonyl-, C) (C_1-C_6alkoxy)C(O)NH-, D) C_1-C_6alkyl- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, E) (C_1-C_6alkyl)amino-, F) di(C_1-C_6alkyl)amino-, G) (C_1-C_6alkyl)amido- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, H) (C_1-C_6alkyl)carboxyamido-, I) C_1-C_9heterocyclyl- optionally substituted by C_1-C_6alkyl- or C_1-C_6hydroxylalkyl-, J) heterocyclyl(C_1-C_6alkyl)- optionally substituted by C_1-C_6alkyl-, K) halogen, L) hydroxyl, M) C_1-C_6hydroxylalkyl-, N) perfluoro(C_1-C_6)alkyl-, O) H_2N-, P) O_2N-, Q) H_2NSO_2-, R) HO_2C-, and S) NC-, ii) 5-10 membered C_1-C_9heteroaryl, optionally substituted with from 1 to 3 substituents independently selected from: A) C_1-C_6alkoxy- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, 3) di(C_1-C_6alkyl)amino-, 4) C_1-C_9heterocyclyl- optionally substituted by C_1-C_6alkyl-, or 5) hydroxyl, B) (C_1-C_6alkoxy)carbonyl-, C) (C_1-C_6alkoxy)C(O)NH-, D) C_1-C_6alkyl- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, E) (C_1-C_6alkyl)amino-, F) di(C_1-C_6alkyl)amino-, G) (C_1-C_6alkyl)amido- optionally substituted with 1) H_2N-, 2) (C_1-C_6alkyl)amino-, or 3) di(C_1-C_6alkyl)amino-, H) (C_1-C_6alkyl)carboxyamido-, I) C_1-C_9heterocyclyl- optionally substituted by C_1-C_6alkyl- or C_1-C_6hydroxylalkyl-, J) heterocyclyl(C_1-C_6alkyl)- optionally substituted by C_1-C_6alkyl-, K) halogen, L) hydroxyl, M) C_1-C_6hydroxylalkyl-, N) perfluoro(C_1-C_6)alkyl-, O) H_2N-, P) O_2N-, Q) H_2NSO_2-, R) HO_2C-, and S) NC-, iii) 3-10 membered C_1-C_9heterocyclyl, optionally substituted with from 1 to 3 substituents independently selected from: A) C_1-C_6alkyl-, B) heterocyclyl(C_1-C_6alkyl)-, C) (C_6-C_{14}aryl)alkyl-, D) C_1-C_8acyl-, E) (C_1-C_6alkoxy)carbonyl-, F) (C_1-C_6alkyl)carboxyl- , G) halogen, H) C_1-C_6haloalkyl-, I) hydroxyl, J) C_1-C_6hydroxyalkyl-, K) H_2N-, L) (C_1-C_6alkyl)amino-, M) di(C_1-C_6alkyl)amino-, N) HO_2C-, O) (C_1-C_6alkoxy)carbonyl-, P) (C_1-C_6alkyl)carboxyl-, Q) (C_1-C_6alkyl)amido-, R) $H_2NC(O)$-, S) (C_1-C_6alkyl)carboxyamido-, T) 5-10 membered C_1-C_9heteroaryl, U) C_6-C_{14}ary, V) C_3-C_8cycloalkyl W) 3-10 membered C_1-C_9heterocyclyl, X) NC-; and Y) -NO_2; iv) C_3-C_{10}cycloalkyl, v) C_1-C_6alkyl, vi) C_2-C_6alkenyl, vii) C_2-C_6alkynyl, viii) C_1-C_6hydroxyalkyl-, ix) $(CH_2)_vO(C_1$-C_6alkyl), x) $(CH_2)_vNH_2$, xi) $(CH_2)_vNH(C_1$-C_6alkyl), xii) $(CH_2)_vN(C_1$-C_6alkyl)$_2$, xiii) $O(CH_2)_vN(C_1$-C_6alkyl)$_2$, xiv) $(CH_2)_vC_6$-C_{10}aryl, xv) –CN, xvi) $(CH_2)_v$ 5-10 membered C_1-C_9heteroaryl, xvii) $(CH_2)_v$ 3-10 membered C_1-C_9heterocyclyl, optionally substituted by C_1-C_6alkyl-, wherein v is 1, 2, 3 or 4, and xviii) C_1-C_6perfluoroalkyl- ; and n) $C(O)R^c$ wherein R^c is: i) H, ii) C_1-C_6alkyl, or iii) C_3-C_6cycloalkyl,

and pharmaceutically acceptable salts thereof.

2. The compound of claim 1 wherein R^1 is



3. The compound of claim 1 or claim 2 wherein R^2 is optionally substituted C_6-C_{14}aryl-NH-COR^3.

4. The compound of claim 3 wherein R^2 is optionally substituted phenyl-NH-COR^3.

5. The compound of claim 4 wherein R^3 is NHR^5.

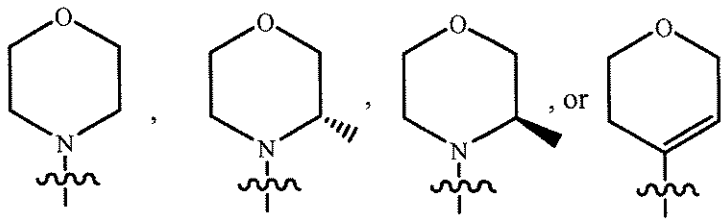
6. The compound of claim 5 wherein R^5 is optionally substituted phenyl or C_1-C_9heteroaryl.

7. The compound of claim 6 wherein R^5 is phenyl substituted with –Y-Q.

8. The compound of claim 7 wherein –Y- is C(O).

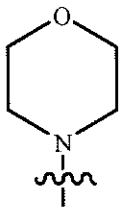
9. The compound of claim 8 wherein Q is 3-10 membered C_1-C_9heterocyclyl, substituted with di(C_1-C_6alkyl)amino-.

10. The compound of any of claims 1-9 wherein R^4 is



and pharmaceutically acceptable salts thereof.

11. The compound of claim 10 wherein R^4 is



and pharmaceutically acceptable salts thereof.

12. The compound selected from the group consisting of:

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-3-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-phenylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-thiophen-2-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-methylphenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-fluorophenyl)urea;

1-(2,4-dimethoxyphenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-urea;

1-(4-chlorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-methoxyphenyl)urea;

(4-chlorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

(2,4-difluorophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-ethylurea;

tert-butyl 3-{[4-(4-{[(4-fluorophenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(phenylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-3-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate;

tert-butyl 3-{[4-(4-{[(4-methylphenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]amino}azetidine-1-carboxylate;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-fluorophenyl)urea;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-methylphenyl)urea;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridine-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)amino]azetidine-1-carboxylate;

1-{4-[4-(azetidin-3-ylamino)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea

1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(2-hydroxyethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-hydroxyphenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(trifluoromethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-hydroxyphenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5-(trifluoromethyl)pyridin-2-yl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea;

methyl 4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-[4-(hydroxymethyl)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-(2-methylpyridin-4-yl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-[2-(methylamino)ethyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-(3-acetylphenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(dimethylamino)phenyl]-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

4-[3-{4-(4,6-dimorpholino-1,3,5-triazin-2yl)phenyl}ureido]benzoic acid;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide HCl salt;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-morpholinopiperidine-1-carbonyl)phenyl)urea;

4-(3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(quinuclidin-3-yl)benzamide;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(pyrrolidin-1-yl)piperidine-1-carbonyl)phenyl)urea;

1-(4-(1,4'-bipiperidine-1'-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyridin-2-yl)acetyl)phenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(1-hydroxyethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(2-methylpyridin-4-yl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(trifluoromethyl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl}urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[5-(trifluoromethyl)pyridin-2-yl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[3-(1-hydroxyethyl)phenyl]urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-[4-(2-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-[4-(2-hydroxymethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(2-methylpyridin-4-yl)urea;

1-[4-(1-hydroxyethyl)phenyl]-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}-amino)benzoate;

1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(1-methylpiperidin-4-yl)urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(1-methylpiperidin-4-yl)urea;

1-{4-[4-(3,6-Dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea;

1-{4-[4-Morpholin-4-yl-6-(tetrahydro-pyran-4-yl)-[1,3,5]triazin-2-yl]-phenyl}-3-pyridin-4-yl-urea;

3-({4-Morpholin-4-yl-6-[4-(3-pyridin-4-yl-ureido)-phenyl]-[1,3,5]triazin-2-ylamino}-methyl)-azetidine-1-carboxylic acid tert-butyl ester;

1-(4-{4-[(azetidin-3-ylmethyl)-amino]-6-morpholin-4-yl-[1,3,5]triazin-2-yl}-phenyl)-3-pyridin-4-yl-urea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-[4-(dimethylamino)phenyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-cyanophenyl)-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(2-methylpyridin-4-yl)urea;

1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(4-morpholin-4-yl-6-quinolin-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(morpholin-4-ylcarbonyl)phenyl]urea;

1-[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl] phenyl}urea;

4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-[4-(4-methyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-({4-[2-(dimethylamino) ethyl]piperazin-1-yl}carbonyl)phenyl]-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-pyrrolidin-1-ylpiperidin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid; N-[2-(dimethylamino)ethyl]-4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-isopropoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2yl)phenyl] carbamoyl} amino) benzoic acid; mp 204 °C;

1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea; mp 170 °C;

4-({[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-{4-[4-(1-ethoxyvinyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-[4-(4-acetyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-[({4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-{4-[4-(1-hydroxyethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-(4-{4-morpholin-4-yl-6-[2-(pyridin-4-ylamino)ethyl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[2-(dimethylamino)ethyl]benzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(hydroxymethyl)phenyl]urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methyl-N-[2-(methylamino)ethyl]benzamide;

1-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[4-(4-methylpiperazin-1-yl)phenyl]benzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]urea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-[4-(4-methylpiperazin-1-yl)phenyl]benzamide;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}urea;

1-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-formylphenyl)urea;

4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(pyridin-2-ylmethyl)benzamide;

1-(4-{4-[2-(1,3-dioxan-2-yl)ethyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-(4-{4-[2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-{4-[2-(dimethylamino)ethoxy]phenyl}benzamide;

1-{4-[(4-benzylpiperidin-1-yl)carbonyl]phenyl}-3-[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

4-({[4-(4-butyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylpiperidin-4-yl)benzamide;

1-(4-{4-[3-(dimethylamino)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-[4-(4-{3-[(1-methylethyl)amino]propyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-pyrrolidin-1-ylpropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-(4-{4-[3-(4-methylpiperazin-1-yl)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-{4-[4-(3-{[2-(dimethylamino)ethyl]amino}propyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(3-hydroxypropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-oxopropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]benzamide;

1-[4-(4-methylpiperazin-1-yl)phenyl]-3-[4-(4-morpholin-4-yl-6-propyl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[2-(dimethylamino)ethoxy]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

1-[4-(4-methylpiperazin-1-yl)phenyl]-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(1-methylazetidin-3-yl)benzamide;

methyl 4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate

N-[2-(dimethylamino)ethyl]-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-(1-methylazetidin-3-yl)-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-pyridin-4-ylbenzamide;

4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-pyridin-3-ylbenzamide;

N-cyclobutyl-4-[({4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-phenylpiperidin-1-yl)carbonyl]phenyl}urea;

4-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(pyridin-4-ylmethyl)benzamide;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

methyl 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-((dimethylamino)methyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)ethoxy)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-yl)phenyl)urea;

1-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((S)-3-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-((R)-3-methylpiperazin-1-yl)phenyl)urea;

1-(4-((3R,5S)-3,5-dimethylpiperazin-1-yl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-(dimethylamino)ethoxy)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-ethylpiperazin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-isopropylpiperazin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

(R)-1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N,N-dimethylbenzamide;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(pyrrolidin-1-ylmethyl)phenyl)urea;

4-({[4-(4-{4-[(methylcarbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-{4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

3-({[4-(4-{4-[(methylcarbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-3-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)phenyl]urea;

1-methyl-3-[4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)phenyl]urea;

3-[({4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-[({4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(3,5-dimethylmorpholin-4-yl)-6-{4-[(methylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-methylurea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridazin-4-ylurea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(oxetan-3-yloxy)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-isopropyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-pyrimidin-5-ylphenyl)urea;

1-(4-{4-[(2,2-dimethoxyethyl)amino]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-3-ylurea;

1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-pyridin-4-ylphenyl)urea;

1-(4-iodophenyl)-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-[4-(4-azetidin-1-yl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-{4-[2-(dimethylamino)pyrimidin-5-yl]phenyl}-3-{4-[4-(1-methylethyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

tert-butyl 3-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]azetidine-1-carboxylate;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-nitrophenyl)urea;

1-(4-aminophenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-methylpiperazine-1-carboxamide;

4-(dimethylamino)-N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]piperidine-1-carboxamide;

1-[2-(dimethylamino)ethyl]-3-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-1-methylurea;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[(2-piperidin-1-ylethyl)carbamoyl]amino}phenyl)urea;

N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-methyl-1,4-diazepane-1-carboxamide;

N-[4-({[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)phenyl]-4-ethylpiperazine-1-carboxamide;

1-{4-[(dimethylcarbamoyl)amino]phenyl}-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-{4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

4-[({4-[4-(3,6-dihydro-2H-pyran-4-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-[2-(dimethylamino)ethyl]benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide;

4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-piperidin-1-ylethyl)benzamide;

1-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-piperidin-1-ylethyl)benzamide;

4-{[(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-morpholin-4-yl-6-[(3S)-tetrahydrofuran-3-yloxy]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-[({4-[4-(2-methylpropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(4-methylpiperazin-1-yl)phenyl]urea;

4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

methyl 4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4-(dimethylamino)piperidin-1-yl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

methyl 4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

methyl 4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(dimethylamino)ethyl]benzamide;

1-{4-[(4-isopropylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]-N-(2-pyrrolidin-1-ylethyl)benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

N-(2-methoxyethyl)-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-(2-methoxyethyl)-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea;

N-[3-(dimethylamino)propyl]-4-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-[4-(piperidin-1-ylcarbonyl)phenyl]urea;

N-[3-(dimethylamino)propyl]-4-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea;

methyl 4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea;

4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

N-[3-(dimethylamino)propyl]-4-[({4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-(2-methoxyethyl)-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(2-thienyl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoic acid;

methyl 3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-(3-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-{4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

methyl 3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

methyl 3-({[4-(4-morpholin-4-yl-6-thiophen-2-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

N-[2-(dimethylamino)ethyl]-3-[({4-[4-(4-methylphenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(1,4-oxazepan-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

methyl 3-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{3-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-3-({[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

1-[4-(4-ethyl-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

3-({[4-(4-morpholin-4-yl-6-phenyl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

methyl 4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

methyl 4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoate;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzoic acid;

1-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]urea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

N-[3-(dimethylamino)propyl]-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

N-(2-methoxyethyl)-4-({[4-(4-morpholin-4-yl-6-piperidin-1-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

1-[4-(4-morpholin-4-yl-6-pyrrolidin-1-yl-1,3,5-triazin-2-yl)phenyl]-3-[4-(pyrrolidin-1-ylcarbonyl)phenyl]urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

methyl 4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)urea;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

N-[3-(dimethylamino)propyl]-4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(dipropylamino)piperidin-1-yl]carbonyl}phenyl)urea;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea;

4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea;

methyl 4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(2-methylpropyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylpropyl)piperazin-1-yl]carbonyl}phenyl)urea;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-[2-(4-methylpiperazin-1-yl)ethyl]benzamide;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[(3R)-3-methylmorpholin-4-yl]-6-[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-pyrrolidin-1-ylethyl)benzamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-propylpiperidin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(piperidin-1-ylcarbonyl)phenyl]urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-propylpiperazin-1-yl)carbonyl]phenyl}urea;

4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}-N-(2-methoxyethyl)benzamide;

1-{4-[4-morpholin-4-yl-6-(4-tricyclo[3.3.1.13,7]dec-1-ylpiperazin-1-yl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-{[(4-{4-[4-(dimethylcarbamoyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

N,N-dimethyl-4-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperazine-1-carboxamide;

N,N-dimethyl-4-(4-{4-[({4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)piperazine-1-carboxamide;

N,N-dimethyl-4-{4-morpholin-4-yl-6-[4-({[4-(pyridazin-4-ylcarbamoyl)phenyl]carbamoyl}amino)phenyl]-1,3,5-triazin-2-yl}piperazine-1-carboxamide;

N,N-dimethyl-4-(4-morpholin-4-yl-6-{4-[({4-[(4-propylpiperidin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperazine-1-carboxamide;

4-{[(4-{4-[4-(dimethylcarbamoyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

4-(4-{4-[({4-[(2-methoxyethyl)carbamoyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-dimethylpiperazine-1-carboxamide;

4-[4-(4-{[(4-{[2-(dimethylamino)ethyl](methyl)carbamoyl}phenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]-N,N-dimethylpiperazine-1-carboxamide;

4-(4-{4-[({4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-dimethylpiperazine-1-carboxamide;

1-(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

methyl 4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

N-[3-(dimethylamino)propyl]-4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[4-(ethylsulfonyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

methyl 4-{[(4-{4-[4-(acetylamino)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

N-[1-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)piperidin-4-yl]acetamide;

4-{[(4-{4-[4-(acetylamino)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-{1-[(4-{[(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}phenyl)carbonyl]piperidin-4-yl}acetamide;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3S)-3-methylmorpholin-4-yl]carbonyl}phenyl)urea;

1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[(4-methylpiperazin-1-yl)amino]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-phenylurea;

1-(4-{4-[(1-methylpiperidin-4-yl)oxy]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(piperidin-4-yloxy)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

ethyl 4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxylate;

N-ethyl-4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxamide;

tert-butyl 4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-carboxylate;

4-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]piperidine-1-sulfonamide;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-3-ylurea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-phenylurea;

1-[4-(dimethylamino)phenyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-cyanophenyl)-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-(2-methylpyridin-4-yl)urea;

1-[2-(dimethylamino)ethyl]-3-{4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}urea;

1-[4-(4-morpholin-4-yl-6-quinolin-3-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-{4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

methyl 4-[({4-[4-(2-methoxyethoxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzoate;

1-(4-{4-morpholin-4-yl-6-[2-(pyridin-4-ylamino)ethyl]-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methylbenzamide;

N-[2-(dimethylamino)ethyl]-4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)benzamide;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-methyl-N-[2-(methylamino)ethyl]benzamide;

1-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[(3,3-dimethylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

4-({[4-(4-methoxy-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]carbamoyl}amino)-N-(2-piperidin-1-ylethyl)benzamide;

1-(4-{4-[2,5-bis(hydroxymethyl)pyrrolidin-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-(4-{4-[2-(1,3-dioxan-2-yl)ethyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-(4-{4-[3-(dimethylamino)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-[4-(4-{3-[(1-methylethyl)amino]propyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)phenyl]-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-pyrrolidin-1-ylpropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-(4-{4-[3-(4-methylpiperazin-1-yl)propyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-pyridin-4-ylurea;

1-{4-[4-(3-{[2-(dimethylamino)ethyl]amino}propyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-(3-hydroxypropyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

1-{4-[4-morpholin-4-yl-6-(3-oxopropyl)-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

N-(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)benzenesulfonamide;

N-{4-[4-({[4-(4-methylpiperazin-1-yl)phenyl]carbamoyl}amino)phenyl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}benzenesulfonamide;

N-(4-{4-[({4-[2-(dimethylamino)ethoxy]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)benzenesulfonamide;

N-(4-{4-[({4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}carbamoyl)amino]phenyl}-6-morpholin-4-yl-1,3,5-triazin-2-yl)benzenesulfonamide;

N-{4-morpholin-4-yl-6-[4-({[4-(piperazin-1-ylcarbonyl)phenyl]carbamoyl}amino)phenyl]-1,3,5-triazin-2-yl}benzenesulfonamide;

N-[4-(4-{[(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)carbamoyl]amino}phenyl)-6-morpholin-4-yl-1,3,5-triazin-2-yl]benzenesulfonamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-[2-(dimethylamino)ethyl]-4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

methyl 4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoate;

4-{[(4-{4-morpholin-4-yl-6-[(phenylsulfonyl)amino]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzoic acid;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-[4-(6-morpholin-4-yl-4-oxo-4,5-dihydro-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4,6-dimorpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-2-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-isopropyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3,4-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-cyclobutyl-3-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3,3-dimethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3,3,4-trimethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-cyclobutylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(2-methylmorpholino)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(quinuclidin-4-yl)phenyl)urea;

1-(4-(4-cyclopropylpiperazin-1-yl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(cyclopropylmethyl)piperazin-1-yl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)-3-(4-(4-((2R,5S)-2,5-dimethylpyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(quinuclidin-4-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-cyclopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(cyclopropylmethyl)piperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazin-1-yl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((2S,5R)-2,5-bis(hydroxymethyl)pyrrolidin-1-yl)-6-((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(methylamino)ethyl)-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-methyl-N-(2-(methylamino)ethyl)-4-(3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-((R)-3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-methylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-morpholino-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea ;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

4-(3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-((S)-3-methylmorpholino)-6-(tetrahydrofuran-3-yloxy)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-chlorophenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-fluorophenyl)urea;

methyl4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2yl)phenyl)ureido) benzoate;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoic acid;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)benzamide;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)urea;

4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-methyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-ethyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

N-(2-(dimethylamino)ethyl)-4-(3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

N-(2-(dimethylamino)ethyl)-N-methyl-4-(3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-propyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-isopropyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea; ;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea ;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-chlorophenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-fluorophenyl)urea;

Methyl-4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoate;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoic acid;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)benzamide;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)urea;

4-(3-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-n-propylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-acetyl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(4-isobutyryl-1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

tert-butyl 4-(4-(4-(3-(4-(methoxycarbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxylate;

methyl4-(3-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl) ureido)benzoate;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-chlorophenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-fluorophenyl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(1,4-diazepan-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

N-methyl-4-(4-morpholino-6-(4-(3-phenylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide (M+H) 532.2;

4-(4-(4-(3-(4-chlorophenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-fluorophenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(2-(dimethylamino)ethylcarbamoyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-((2-(dimethylamino)ethyl)(methyl)carbamoyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-carbamoylphenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

N-methyl-4-(4-morpholino-6-(4-(3-(4-(piperazine-1-carbonyl)phenyl)ureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-methyl-4-(4-(4-(3-(4-(4-methylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-methyl-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-isopropyl-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-(4-(3-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

4-(4-(4-(3-(4-(4-ethylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-N-isopropyl-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-(4-(3-(4-(4-methylpiperazine-1-carbonyl)phenyl)ureido)phenyl)-6-morpholino-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-(4-(piperazine-1-carbonyl)phenyl)ureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyridin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyridazin-4-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyrimidin-5-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

N-isopropyl-4-(4-morpholino-6-(4-(3-pyridin-3-ylureido)phenyl)-1,3,5-triazin-2-yl)-1,4-diazepane-1-carboxamide;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-morpholino-6-(1H-pyrazol-1-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(2-methyl-1H-imidazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-acetylphenyl)-3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazin-1-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-(dimethylamino)acetyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-morpholinoacetyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxyacetyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(methoxymethyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-methoxyethyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(1-hydroxyethyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxypropan-2-yl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxypropyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-hydroxy-2-methylpropyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)urea;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(4-cyanophenyl)urea;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N-methylbenzamide;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)-N,N-dimethylbenzamide;

4-(3-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(4,6-bis((R)-3-methylmorpholino)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)urea;

(R)-1-(4-((dimethylamino)methyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

(R)-1-(4-acetylphenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-(dimethylamino)acetyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(4-(2-morpholinoacetyl)phenyl)urea;

(R)-1-(4-(2-hydroxyacetyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(methoxymethyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-methoxyethyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(1-hydroxyethyl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-hydroxypropan-2-yl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(2-hydroxypropyl)phenyl)-3-(4-(4-((R)-3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(2-hydroxy-2-methylpropyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-1-(4-cyanophenyl)-3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)urea;

(R)-N-methyl-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

(R)-N,N-dimethyl-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

(R)-4-(3-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

(R)-1-(4-(4-(3-methylmorpholino)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl)phenyl)-3-(6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyrimidin-5-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-3-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridin-4-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(pyridazin-4-yl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-phenylurea;

1-(4-chlorophenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-fluorophenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

methyl 4-(3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoate;

4-(3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzoic acid;

4-(3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)ureido)benzamide;

1-(4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(piperazine-1-carbonyl)phenyl)urea;

1-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)-3-(4-(4-methylpiperazine-1-carbonyl)phenyl)urea;

1-(4-(4-ethylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-isopropylpiperazine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-(4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)-3-(4-(4-(3-methyl-1H-pyrazol-1-yl)-6-morpholino-1,3,5-triazin-2-yl)phenyl)urea;

1-{4-[(4-butylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)urea;

1-{4-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-3-(4-{4-[4-(1-methylethyl)-1,4-diazepan-1-yl]-6-morpholin-4-yl-1,3,5-triazin-2-yl}phenyl)urea;

1-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

1-(4-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-[({4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}carbamoyl)amino]benzamide;

1-{4-[4-(azetidin-3-yloxy)-6-morpholin-4-yl-1,3,5-triazin-2-yl]phenyl}-3-pyridin-4-ylurea;

N-(1-methylethyl)-3-[(4-morpholin-4-yl-6-{4-[(pyridin-4-ylcarbamoyl)amino]phenyl}-1,3,5-triazin-2-yl)oxy]azetidine-1-carboxamide;

N-{1-[(4-{[(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}phenyl)carbonyl]piperidin-4-yl}acetamide;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(1-methylethyl)-1,4-diazepan-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(3-oxa-8-azabicyclo[3.2.1]oct-8-ylcarbonyl)phenyl]urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-cyanopiperidin-1-yl)carbonyl]phenyl}urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)urea;

1-(4-{4,6-bis[(3S)-3-methylmorpholin-4-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(2-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-[4-(piperazin-1-ylcarbonyl)phenyl]urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(3,3,4-trimethylpiperazin-1-yl)carbonyl]phenyl}urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3R)-3-methylpiperazin-1-yl]carbonyl}phenyl)urea;

1-(4-{[(3R)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]carbonyl}phenyl)urea;

1-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-(4-{[(3S)-3-methylpiperazin-1-yl]carbonyl}phenyl)urea;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

1-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-{4-[(4-methylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-(4-{4-[(3S)-3-methylmorpholin-4-yl]-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

N-[3-(dimethylamino)propyl]-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

N-[2-(dimethylamino)ethyl]-N-methyl-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

1-[4-(morpholin-4-ylcarbonyl)phenyl]-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

N-(2-methoxyethyl)-4-{[(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)carbamoyl]amino}benzamide;

1-[4-(1,4-diazepan-1-ylcarbonyl)phenyl]-3-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)urea;

1-(4-{4-(morpholin-4-yl)-6-[4-(propan-2-yl)-1,4-diazepan-1-yl]-1,3,5-triazin-2-yl}phenyl)-3-(4-{[4-(propan-2-yl)-1,4-diazepan-1-yl]carbonyl}phenyl)urea;

1-(4-{[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3S)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4,6-di(morpholin-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}-3-{4-[(3,3,4-trimethylpiperazin-1-yl)carbonyl]phenyl}urea;

1-(4-{[(3S)-3,4-dimethylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3S)-3-methylpiperazin-1-yl]carbonyl}phenyl)-3-{4-[4-(morpholin-4-yl)-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea;

1-(4-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea; and

1-(4-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}phenyl)-3-{4-[4-morpholin-4-yl-6-(tetrahydro-2H-pyran-4-yl)-1,3,5-triazin-2-yl]phenyl}urea.

13. The compound of claim 12, which is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea.

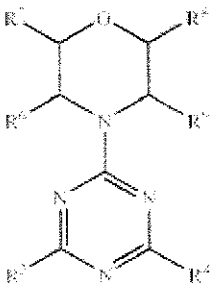
14. A composition comprising a compound of any one of claims 1-13 and a pharmaceutically acceptable carrier.

15. The composition of claim 14, wherein the pharmaceutically acceptable carrier suitable for oral administration and the composition comprises an oral dosage form.

16. A composition comprising a compound of any one of claims 1-13; a second compound selected from the group consisting of a topoisomerase I inhibitor, a MEK 1/2 inhibitor, a HSP90 inhibitor, procarbazine, dacarbazine, gemcitabine, capecitabine, methotrexate, taxol, taxotere, mercaptopurine, thioguanine, hydroxyurea, cytarabine, cyclophosphamide, ifosfamide, nitrosoureas, cisplatin, carboplatin, mitomycin, dacarbazine, procarbizine, etoposide, teniposide, campathecins, bleomycin, doxorubicin, idarubicin, daunorubicin, dactinomycin, plicamycin, mitoxantrone, L-asparaginase, doxorubicin, epirubicin, 5-fluorouracil, docetaxel, paclitaxel, leucovorin, levamisole, irinotecan, estramustine, etoposide, nitrogen mustards, BCNU, carmustine, lomustine, vinblastine, vincristine, vinorelbine, cisplatin, carboplatin, oxaliplatin, imatinib mesylate, Avastin (bevacizumab), hexamethylmelamine, topotecan, tyrosine kinase inhibitors, tyrphostins, herbimycin A, genistein, erbstatin, hydroxyzine, glatiramer acetate, interferon beta-1 a, interferon beta-1 b, natalizumab and lavendustin A; and a pharmaceutically acceptable carrier.

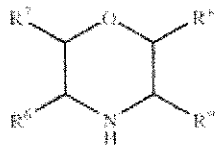
17. The composition of claim 16, wherein the second compound is Avastin.

18. A method of making a compound of claim 1 having the formula

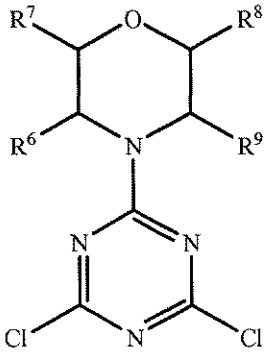


said method comprising:

a) reacting 2,4,6-trichloro[1 ,3,5]triazine with

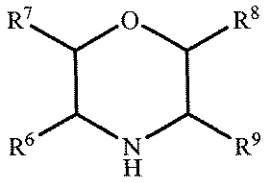


to form the intermediate dichlorotriazine compound

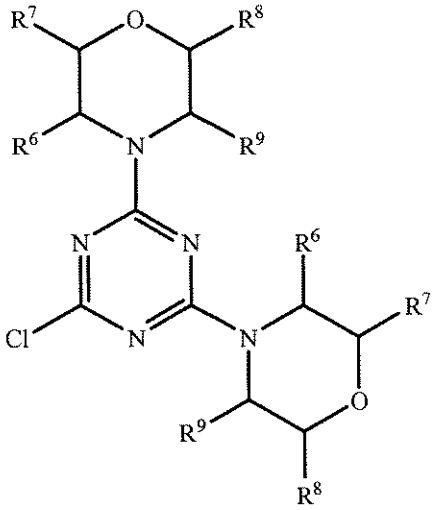


,

b) reacting the intermediate dichlorotriazine compound from step a) with



to form the intermediate compound



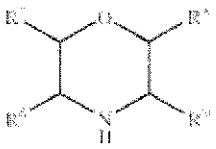
,

c) reacting the intermediate from step b) with:

i) a compound of formula R^2-$B(OH)_2$ or ester thereof wherein R^2 is as defined in claim 1 to give a compound of formula 1, or

ii) an aminoaryl or aminoheteroaryl boronic acid or ester thereof and converting the amino group to a urea of formula I.

19. The method of claim 18 wherein the reacting moiety



is

