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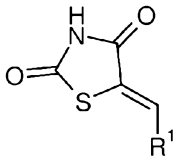


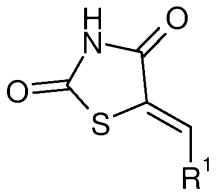
(I)

(57) Abstract: The invention relates to chemical compounds of formula (I), and salts thereof. In some embodiments, the invention relates to inhibitors or modulators of PIM-1 and/or PIM-2, and/or PIM-3 protein kinase activity or enzyme function. In still further embodiments, the invention relates to pharmaceutical compositions comprising compounds disclosed herein, and their use in the prevention and treatment of PIM kinase related conditions and diseases, preferably cancer.

CHEMICAL COMPOUNDS 251

FIELD OF INVENTION

The invention relates to chemical compounds of formula I,



formula I

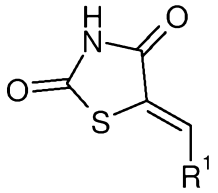
and salts thereof. In some embodiments, the invention relates to inhibitors or modulators of PIM-1 and/or PIM-2, and/or PIM-3 protein kinase activity or enzyme function. In still further embodiments, the invention relates to pharmaceutical compositions comprising compounds disclosed herein, and their use in the prevention and treatment of PIM kinase related conditions and diseases, preferably cancer.

BACKGROUND

PIM-1 gene was first identified as a proviral insertion site in Moloney murine leukemia virus-induced T-cell lymphoma. PIM-1 gene translates a Ser/Thr protein kinase. The known PIM kinase family also includes PIM-2 and PIM-3. Mice studies suggest that physiologically the PIM kinases are involved in growth factor and cytokine signaling. Deregulated PIM kinase expression occurs a in large number of hematopoietic tumors, such as myeloid and lymphoblastic leukemias and lyphomas. PIM kinases are also expressed in solid tumors, such as prostate cancer and pancreatic cancer, and transgenic mice which express PIM-1 develop T-cell lymphoma. Dhanasekaran et al., (2001). Nature 412: 822–826 and Li et al., (2006) Cancer Res 66: 6741–6747. Accordingly, it is believed that PIM Kinase inhibitors will be useful in the treatment and/or prevention of cancer. Thus, there is a need to identify inhibitors of PIM kinases.

SUMMARY OF INVENTION

The invention relates to chemical compounds of formula I,



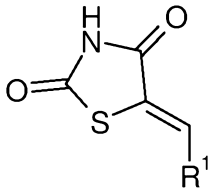
formula I

and salts thereof. In some embodiments, the invention relates to inhibitors or modulators of PIM-1 and/or PIM-2, and/or PIM-3 protein kinase activity or enzyme function. In still further embodiments, the invention relates to pharmaceutical compositions comprising compounds disclosed herein, and their use in the prevention and treatment of PIM kinase related conditions and diseases, preferably cancer.

DETAILED DESCRIPTION

The invention relates to a method of treating or preventing cancer comprising,

a) providing a pharmaceutical composition comprising a compound of formula I,



formula I,

or pharmaceutically acceptable salts thereof, functioning to inhibit a PIM kinase, wherein

R^1 is selected from a carbocyclyl, aryl, and heterocyclyl, wherein R^1 is optionally substituted with one or more, the same or different, R^2;

R^2 is selected from C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfamoyl, arylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^2 is optionally substituted with one or more, the same or different, R^3;

R^3 is selected from C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^3 is optionally substituted with one or more, the same or different, R^4;

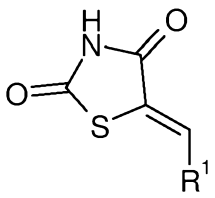
R^4 is selected from C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more, the same or different, R^5; and

R^5 is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, *N*-methyl-*N*-ethylsulfamoyl, carbocyclyl, aryl, and heterocyclyl; and

b) administering said pharmaceutical composition to a subject diagnosed with, exhibiting symptoms of, or at risk for cancer with the proviso that said compound of formula I is not 5-[[2-[(2,6-dichloro-3-methylphenyl)amino]phenyl]methylene]-2,4-thiazolidinedione.

In some embodiments, the invention relates to a method of treating or preventing cancer comprising,

a) providing a pharmaceutical composition comprising a compound of formula I,



formula I,

or salts thereof, functioning to inhibit a PIM kinase, wherein

R^1 is selected from a carbocyclyl, aryl, and heterocyclyl, wherein R^1 is optionally substituted with one or more, the same or different, R^2;

R^2 is selected from halogen, C_{1-6}alkyl, halogenated C_{1-6}alkyl, amino, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, and heterocyclyl, wherein R^2 is optionally substituted with one or more, the same or different, R^3;

R^3 is selected from C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^3 is optionally substituted with one or more, the same or different, R^4;

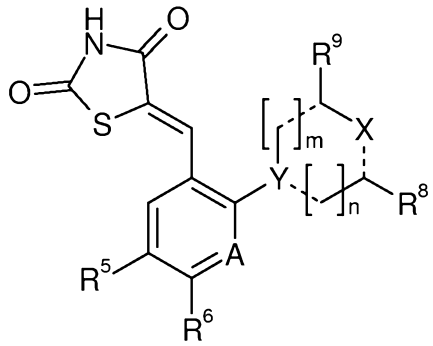
R^4 is selected from C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more, the same or different, R^5; and

R^5 is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, *N*-methyl-*N*-ethylsulfamoyl, carbocyclyl, aryl, and heterocyclyl; and

b) administering said pharmaceutical composition to a subject diagnosed with, exhibiting symptoms of, or at risk for cancer under conditions such that cancer is reduced or prevented.

In further embodiments, the invention relates to a method of treating cancer comprising administering to a subject in need thereof a pharmaceutical composition comprising a compound of the formula disclosed herein, wherein said cancer is selected from a leukemia, lymphoma, prostate cancer, pancreatic cancer or other solid tumors.

In further embodiments, the invention relates to a compound of formula IA,



formula IA,

or salts thereof, wherein,

--- is individually at each occurrence selected from a single and double bond;

n is selected from 0, 1, or 2;

m is selected from 0, 1, or 2;

A is selected from N and CR^7;

X is selected from O, S, CHR^{10} and NR^{11};

Y is selected from N, CH, and C;

R^5, R^6, and R^7 are each individually and independently from hydrogen, C_{1-6}alkyl, halogen, cyano, nitro, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, carbocyclyl, aryl, and heterocyclyl, wherein R^5, R^6, and R^7 are each optionally substituted with one or more, the same or different, R^{12};

R^8 and R^9 are each individually and independently selected from hydrogen, amino, hydroxyl, mercapto, C_{1-6}alkyl, C_{1-6}alkylamino, carbocyclyl, aryl, and heterocyclyl wherein R^8 and R^9 are each optionally substituted with one or more, the same or different, R^{15};

R^{10} is selected from hydrogen, C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfamoyl, arylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{10} is optionally substituted with one or more, the same or different, R^{12};

R^{11} is selected from hydrogen, formyl, C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, C_{1-6}alkoxycarbonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{11} is optionally substituted with one or more, the same or different, R^{12};

R^{12} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, *N*-methyl-*N*-ethylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{12} is optionally substituted with one or more, the same or different, R^{16};

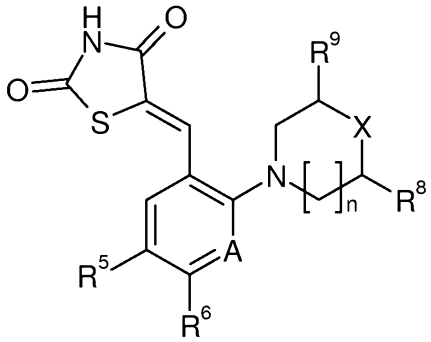
R^{15} is selected from C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, and C_{1-6}alkoxycarbonyl wherein R^{15} is optionally substituted with one or more, the same or different, R^{12};

R^{16} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, aminomethyl, aminoethyl, aminopropyl, aminobutyl, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, and *N*-methyl-*N*-ethylsulfamoyl; and

provided that R^5, R^6, and R^7 are not all hydrogen and

provided the compound is not 5-((5-nitro-2-(1-piperidinyl)phenyl)methylene)-2,4-thiazolidinedione or 5-((2-(4-morpholinyl)-5-nitrophenyl)methylene)-2,4-thiazolidinedione.

In some embodiments, the invention relates to a compound of formula ID,



formula ID,

or salts thereof, wherein,

n is selected from 0, 1, or 2;

A is selected from N and CR^7;

X is selected from O, S, CHR^{10} and NR^{11};

R^5, R^6, and R^7 are each individually and independently from hydrogen, C_{1-6}alkyl, halogen, cyano, nitro, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, carbocyclyl, aryl, and heterocyclyl, wherein R^5, R^6, and R^7 are each optionally substituted with one or more, the same or different, R^{12};

R^8 and R^9 are each individually and independently selected from hydrogen, amino, hydroxyl, mercapto, C_{1-6}alkyl, C_{1-6}alkylamino, carbocyclyl, aryl, and heterocyclyl wherein R^8 and R^9 are each optionally substituted with one or more, the same or different, R^{15};

R^{10} is selected from hydrogen, C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfamoyl, arylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{10} is optionally substituted with one or more, the same or different, R^{12};

R^{11} is selected from hydrogen, formyl, C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, C_{1-6}alkoxycarbonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{11} is optionally substituted with one or more, the same or different, R^{12};

R^{12} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino,

diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, *N*-methyl-*N*-ethylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{12} is optionally substituted with one or more, the same or different, R^{16};

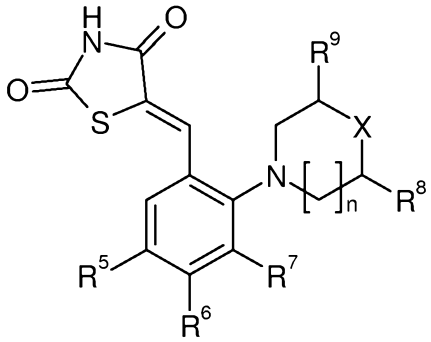
R^{15} is selected from C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, and C_{1-6}alkoxycarbonyl wherein R^{15} is optionally substituted with one or more, the same or different, R^{12};

R^{16} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, aminomethyl, aminoethyl, aminopropyl, aminobutyl, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, and *N*-methyl-*N*-ethylsulfamoyl.

In some embodiments with regard to any of the compound formula provided herein, R^5, R^6, and R^7 are not all hydrogen.

In some embodiments with regard to any of the compound formula provided herein, R^5, R^6, and R^7 are not 5-((5-nitro-2-(1-piperidinyl)phenyl)methylene)-2,4-thiazolidinedione or 5-((2-(4-morpholinyl)-5-nitrophenyl)methylene)-2,4-thiazolidinedione.

In some embodiments, the invention relates to a compound of formula IB,



formula IB,

or salts thereof, wherein,

n is selected from 0, 1, or 2;

X is selected from O, CHR^{10} and NR^{11};

R^5, R^6, and R^7 are each individually and independently from hydrogen, halogen, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, and *N*-methyl-*N*-ethylsulfamoyl;

R^8 and R^9 are each individually and independently selected from hydrogen, amino, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkylamino, wherein R^8 and R^9 are each optionally substituted with one or more, the same or different, R^{15};

R^{10} is selected from hydrogen, $C_{1\text{-}6}$alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkylthio, $C_{1\text{-}6}$alkylamino, $(C_{1\text{-}6}alkyl)_2$amino, $C_{1\text{-}6}$alkylsulfamoyl, arylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{10} is optionally substituted with one or more, the same or different, R^{12};

R^{11} is selected from hydrogen, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkanoyl, $C_{1\text{-}6}$alkylsulfinyl, $C_{1\text{-}6}$alkylsulfonyl, arylsulfonyl, $C_{1\text{-}6}$alkoxycarbonyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{11} is optionally substituted with one or more, the same or different, R^{12};

R^{12} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl,

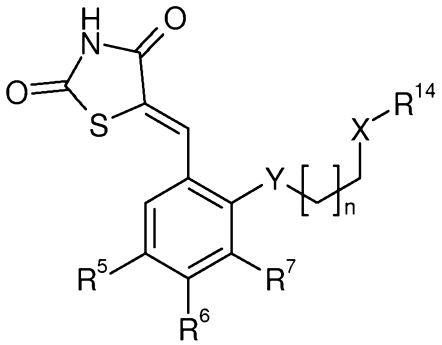
methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, *N*-methyl-*N*-ethylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{12} is optionally substituted with one or more, the same or different, R^{16};

R^{15} is selected from C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, and C_{1-6}alkoxycarbonyl wherein R^{15} is optionally substituted with one or more, the same or different, R^{12};

R^{16} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, and *N*-methyl-*N*-ethylsulfamoyl.

In some embodiments, with regard to any of the compound formula provided herein, said compound is not, 5-[[2-(4-methyl-1-piperazinyl)phenyl]methylene]-2,4-thiazolidinedione or 5-[[2-[(2,6-dichloro-3-methylphenyl)amino]phenyl]methylene]-2,4-thiazolidinedione.

In further embodiments, the invention relates to a compound of formula IC,



formula IC,

or salts thereof, wherein,

n is selected from 0, 1, 2, 3, 4, 5, 6, 7 or 8;

X is selected from O, S, CHR^{10} and NR^{11};

Y is selected from O, S, and NR^{13};

R^5, R^6, and R^7 are each individually and independently from C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, C_{1-6}dialkylamino, carbocyclyl, aryl, and heterocyclyl, wherein R^5, R^6, and R^7 are each optionally substituted with one or more, the same or different, R^{12};

R^{10} is selected from hydrogen, C_{1-6}alkyl, halogen, nitro, cyano, hydroxy, amino, mercapto, formyl, carboxy, carbamoyl, C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkylsulfamoyl, arylsulfamoyl, carbocyclyl, aryl, and heterocyclyl, wherein R^{10} is optionally substituted with one or more, the same or different, R^{12};

R^{11}, R^{13}, and R^{14} are each individually and independently selected from hydrogen, C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulfinyl, C_{1-6}alkylsulfonyl, arylsulfonyl, and C_{1-6}alkoxycarbonyl wherein R^{11} is optionally substituted with one or more, the same or different, R^{12};

or R^{11} and R^{14}, taken together with the atoms to which they are attached form a five, six, or seven membered heterocyclic ring optionally substituted with one or more, the same or different, R^{12};

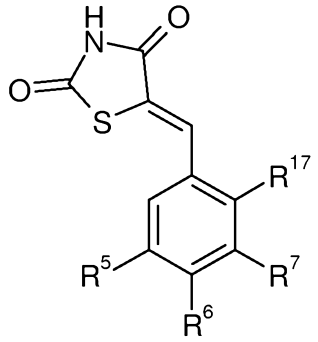
R^{12} is selected from halogen, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, formyl, carboxy, carbamoyl, mercapto, sulfamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulfinyl, ethylsulfinyl, mesyl, ethylsulfonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulfamoyl, *N*-ethylsulfamoyl, *N,N*-dimethylsulfamoyl, *N,N*-diethylsulfamoyl, *N*-methyl-*N*-ethylsulfamoyl, carbocyclyl, aryl, and heterocyclyl.

In some embodiments with regard to any of the compound formula provided herein, Y is NR^{13}, wherein R^{13} is a C_{1-6}alkyl.

In some embodiments with regard to any of the compound formula provided herein, R^5 is a halogenated C_{1-6}alkyl.

In some embodiments with regard to any of the compound formula provided herein, R^7 is a halogen.

In some embodiments, the invention relates to a compound of formula IX,



formula IX,

or salts thereof, wherein

R^5 is selected from hydrogen, C_{1-6}alkoxy, carbamoyl, and halogenated C_{1-6}alkyl;

R^6 is selected from hydrogen, halogen, C_{1-6}alkoxy, and 2-(1-piperidyl)ethoxy;

R^7 is selected from hydrogen, halogen, and C_{1-6}alkoxy;

R^{17} is a heterocarbocylcyl, wherein R^{17} is optionally substituted with one or more, the same or different, R^{18};

R^{18} is selected from halogen, formyl, amino, C_{1-6}alkyl, C_{1-6}alkylamino, $(C_{1-6}alkyl)_2$amino, carbocyclyl, aryl, heterocyclyl, wherein R^{18} is optionally substituted with one or more, the same or different, R^{19};

R^{19} is selected from amino, C_{1-6}alkyl, hydroxy, carbocyclyl, and heterocyclyl wherein R^{19} is optionally substituted with one or more, the same or different, R^{20}; and

R^{20} is selected from amino, C_{1-6}alkyl, and halogen.

In further embodiments, R^{17} is selected from (3R)-3-aminopyrrolidin-1-yl, (3R)-3-dimethylaminopyrrolidin-1-yl, (3S)-3-(3-aminopropylamino)pyrrolidin-1-yl, (3S)-3-(5-aminopentanoylamino)pyrrolidin-1-yl, (3S)-3-amino-1-piperidyl, (3S)-3-aminopyrrolidin-1-yl, (3S)-3-dimethylaminopyrrolidin-1-yl, (3S,5R)-3,5-

dimethylpiperazin-1-yl, 1,4-diazepan-1-yl, 2-(1-piperidyl)ethoxy, 2-diethylaminoethoxy, 2-dimethylaminoethyl-methyl-amino, 2-hydroxyethoxy, 2-morpholinoethoxy, 3-(2-aminoethylamino)pyrrolidin-1-yl, 3-(2-hydroxyethylamino)pyrrolidin-1-yl, 3-(2-methylaminoethylamino)pyrrolidin-1-yl, 3-(3-aminopropanoylamino)pyrrolidin-1-yl, 3-(3-aminopropylamino)pyrrolidin-1-yl, 3-(3-methyl-1,2,4-oxadiazol-5-yl)-1-piperidyl, 3-(aminomethyl)-1-piperidyl, 3-(aminomethyl)pyrrolidin-1-yl, 3-acetamidopyrrolidin-1-yl, 3-aminopyrrolidin-1-yl, 3-dimethylaminopropoxy, 3-dimethylaminopropyl-methyl-amino, 3-dimethylaminopyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 3-pyridyl, 4-(1-methyl-4-piperidyl)piperazin-1-yl, 4-(1-piperidyl)-1-piperidyl, 4-(2-aminoethyl)piperazin-1-yl, 4-(2-hydroxyethyl)-1,4-diazepan-1-yl, 4-(2-hydroxyethyl)-1-piperidyl, 4-(2-hydroxyethyl)piperazin-1-yl, 4-(2-methylaminoethyl)piperazin-1-yl, 4-(2-morpholinoethyl)piperazin-1-yl, 4-(3-aminopropanoyl)-1,4-diazepan-1-yl, 4-(3-aminopropanoyl)piperazin-1-yl, 4-(3-aminopropyl)piperazin-1-yl, 4-(3-hydroxypropyl)piperazin-1-yl, 4-(3-methyl-1,2,4-oxadiazol-5-yl)-1-piperidyl, 4-(4-aminobutanoyl)-1,4-diazepan-1-yl, 4-(4-aminobutanoyl)piperazin-1-yl, 4-(4-chloro-2-fluoro-phenyl)piperazin-1-yl, 4-(4-fluorophenyl)piperazin-1-yl, 4-(4-pyridylmethyl)piperazin-1-yl, 4-(5-aminopentanoyl)-1,4-diazepan-1-yl, 4-(5-aminopentanoyl)piperazin-1-yl, 4-(azetidine-3-carbonyl)piperazin-1-yl, 4-(benzo[1,3]dioxol-5-ylmethyl)piperazin-1-yl, 4-(cyclopropylmethyl)piperazin-1-yl, 4-(hydroxymethyl)-1-piperidyl, 4-(piperidine-3-carbonyl)-1,4-diazepan-1-yl, 4-(piperidine-3-carbonyl)piperazin-1-yl, 4-(piperidine-4-carbonyl)piperazin-1-yl, 4-[(2-chlorophenyl)methyl]piperazin-1-yl, 4-[3-(aminomethyl)benzoyl]piperazin-1-yl, 4-[4-(piperazin-1-ylmethyl)benzoyl]piperazin-1-yl, 4-acetylpiperazin-1-yl, 4-amino-1-piperidyl, 4-butyl-1,4-diazepan-1-yl, 4-cyclopentylpiperazin-1-yl, 4-dimethylamino-1-piperidyl, 4-hydroxy-1-piperidyl, 4-isobutylpiperazin-1-yl, 4-isopropylpiperazin-1-yl, 4-methylpiperazin-1-yl, 4-morpholino-1-piperidyl, 4-pyridyl, 4-pyrrolidin-1-yl-1-piperidyl, 4-tert-butoxycarbonylpiperazin-1-yl, 4-tert-butylpiperazin-1-yl, morpholino, piperazin-1-yl, and pyrrolidin-1-yl.

In further embodiments, the invention relates to a compound selected from:

5-({2-[(3S)-3-aminopiperidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3R)-3-aminopiperidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[2-(4-aminopiperidin-1-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({2-[3-(aminomethyl)piperidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(1,4-diazepan-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-cyclopentylpiperazin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(4-fluorophenyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(3-methyl-1,2,4-oxadiazol-5-yl)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-pyrrolidin-1-ylpiperidin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(1-methylethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-methylpropyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-hydroxyethyl)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(4-chloro-2-fluorophenyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[3-(3-methyl-1,2,4-oxadiazol-5-yl)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(pyridin-4-ylmethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-chlorobenzyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(1-methylpiperidin-4-yl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-morpholin-4-ylethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(cyclopropylmethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-morpholin-4-ylpiperidin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(3-hydroxypropyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(dimethylamino)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-{[3-(dimethylamino)propyl](methyl)amino}-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-hydroxyethyl)-1,4-diazepan-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[2-(4-butyl-1,4-diazepan-1-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-hydroxyethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-morpholin-4-yl-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[2-(4-tert-butylpiperazin-1-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[2-(1,4'-bipiperidin-1'-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-methylpiperazin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-bromo-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione; and

5-({2-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione,

(5Z)-5-({3-[3-(4-methylpiperazin-1-yl)propoxy]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

2-{3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenoxy}acetamide;

(5Z)-5-{[3-(3-piperidin-1-ylpropoxy)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-[(4-methylpiperazin-1-yl)methyl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

N-[2-(dimethylamino)ethyl]-2'-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-N-methylbiphenyl-4-sulfonamide;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-methoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({5-chloro-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-4-methylphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-methylphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({5-bromo-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-3-fluorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-chloro-6-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-(aminomethyl)pyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-(aminomethyl)pyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-methoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-bromophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-bromophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-ethoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(2-methylpropoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclohexylmethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclohexyloxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R,4R)-3-amino-4-hydroxypiperidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-{[3-chloro-2-(1,4-diazepan-1-yl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(1-methylethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-(1-methylethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-ethoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-{[4-(aminomethyl)benzyl]amino}piperidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-chloro-2-[(3R)-3-{[2-(methylamino)ethyl]amino}piperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S,4S)-3-amino-4-hydroxypyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-chloro-2-[4-methyl-3-(methylamino)piperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-{[2-(3-amino-4-methylpiperidin-1-yl)-3-chlorophenyl]methylidene}-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(2,2,2-trifluoroethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-(2,2,2-trifluoroethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(2-methoxyethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-(2-methoxyethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclopentyloxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclobutyloxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

4-[(3R)-3-aminopiperidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzamide;

4-[(3S)-3-aminopiperidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzamide;

4-[(3R)-3-aminopiperidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzoic acid;

4-[(3S)-3-aminopyrrolidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzoic acid;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]biphenyl-3-yl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[2-(3-aminopropoxy)-5-methoxyphenyl]methylidene}-1,3-thiazolidine-2,4-dione;

N-{4-[3-(dimethylamino)pyrrolidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}acetamide;

(5Z)-5-[(3-chloro-2-{(3R)-3-[(2-hydroxyethyl)amino]piperidin-1-yl}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

(5Z)-5-[(3-chloro-2-{(3R)-3-[(3-hydroxypropyl)amino]piperidin-1-yl}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-1-methyl-1H-imidazole-2-carboxamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-methoxyacetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-1-methyl-1H-pyrazole-3-carboxamide;

N^2-carbamoyl-N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]glycinamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-pyridin-3-ylacetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-pyridin-4-ylacetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-1-methyl-1H-pyrazole-4-carboxamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-(1-oxidothiomorpholin-4-yl)acetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-4-sulfamoylbutanamide;

N'-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-N,N-dimethylbutanediamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-N~2~,N~2~-dimethylglycinamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-cyanoacetamide;

N^2-acetyl-N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]glycinamide;

(5Z)-5-({3-chloro-2-[(3R)-3-(dipropylamino)piperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-[(3-chloro-2-{(3R)-3-[(3,3,3-trifluoropropyl)amino]piperidin-1-yl}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

5-[(5-methoxy-2-{3-[(1-methylethyl)amino]propoxy}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

(5Z)-5-({5-amino-2-[3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione; and

5-[(2-amino-4,5-dimethoxyphenyl)methylidene]-1,3-thiazolidine-2,4-dione,

or salts thereof.

In some embodiments, the invention relates to any of the compounds disclosed herein that are in the (Z) isomer.

In some embodiments, the invention relates to any of the compounds disclosed herein that are in the (E) isomer.

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In some embodiments, the invention relates to compositions comprising a mixture of the (Z) and (E) isomers.

The invention further provides use of a compound selected from the list above in the manufacture of a medicament for producing an anti-cancer effect in a subject.

Also provided is a method for producing an anti-cancer effect in a subject in need thereof comprising administering to said subject a compound selected from the list above.

In some embodiments, the invention relates to a pharmaceutical composition comprising a substituted 5-(3-halo-2-[piperidin-1-yl]phenylmethylidene)-1,3-thiazolidine-2,4-dione functioning to inhibit a PIM kinase.

In further embodiments, the invention relates to a pharmaceutical composition comprising a compound of formula I, IA, IB, IC, ID, or IX or a pharmaceutically acceptable salt thereof.

In further embodiments, the invention relates to a method of inhibiting a PIM kinase comprising, providing a compound of formula I, IA, IB, IC, ID, or IX, as defined herein, and mixing a PIM kinase and said compound under conditions such that PIM kinase phosphorylation is inhibited.

In further embodiments, said method is an in vitro method.

In further embodiments, said method is an in vivo method.

In further embodiments, the invention relates to a method of inhibiting a PIM kinase in a subject comprising administering to the subject a therapeutically effective amount of a compound of any of the formula disclosed herein or a pharmaceutically acceptable salt thereof.

In further embodiments, said PIM kinase is selected from PIM-1, PIM-2, and PIM-3.

In further embodiments, the invention relates to the use of a compound of the formula I, IA, IB, IC, ID, or IX, or a pharmaceutically acceptable salt thereof, as defined herein, for the manufacture of a medicament for the production of a PIM kinase inhibitory effect in a subject.

In further embodiments, the invention relates to the use of a compound of the formula I, IA, IB, IC, ID, or IX, or a pharmaceutically acceptable salt thereof, as disclosed

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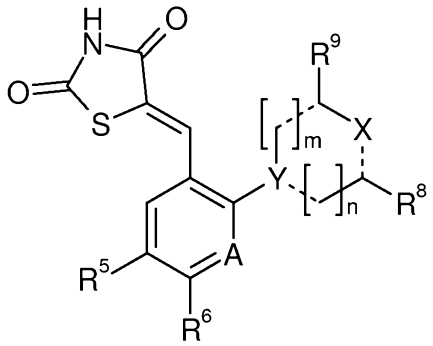
herein, for the manufacture of a medicament for the production of an anti-cancer effect in a subject.

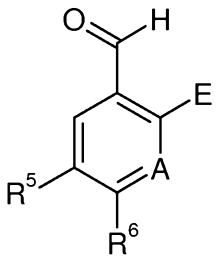
In some embodiments, the invention relates to a method of making a compound of formula IA as defined herein,



formula IA,

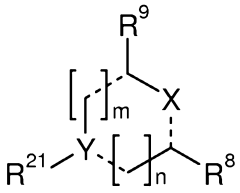
or salt thereof, comprising

a) mixing a compound of formula XI,



formula XI,

or salt thereof, wherein E is a halogen, and R^5, R^6, and A are defined herein, with a compound of formula XII,



formula XII,

or salt thereof, wherein

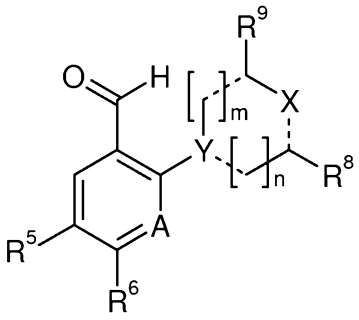
---, R^8, R^9, n, m, Y and X are defined herein,

if Y is N, then R^{21} is hydrogen,

if Y is C, then R^{21} is selected from boronic acid and a boronic ester, and

if Y is CH, then R^{21} is selected from a metal halide,

under conditions such that composition comprising a compound of formula XIII,



formula XIII,

or salt thereof, is formed; and

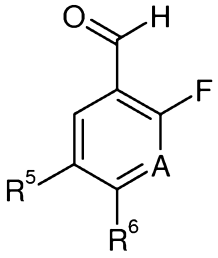
b) mixing the compound of formula XIII and thiazolidine-2,4-dione under conditions such that a compound of formula IA is formed.

In further embodiments, said metal halide is selected from lithium chloride and magnesium bromide.

In further embodiments, said boronic ester is a dialkyl boronic ester, such as diethyl boronic ester, or a cyclic boronic ester, such as the boronic ester of 1,2-alkyldiols, such as 1,3,2-dioxaborolane, or cycloalkyldiols which may be optionally substituted.

In further embodiments, the invention relates to a method of making a compound of formula ID, or salt thereof comprising

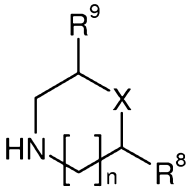
a) mixing a compound of formula II,



formula II,

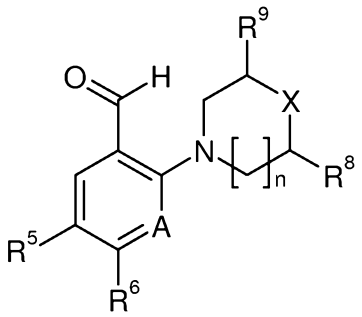
or salt thereof, wherein R^5, R^6, and A are defined herein,

with a compound of formula III,



formula III,

or salt thereof, wherein R^8, R^9, n, and X are defined herein, under conditions such that composition comprising a compound of formula IV,

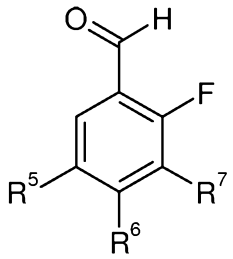


formula IV

or salt thereof, is formed; and

b) mixing the compound of formula IV and thiazolidine-2,4-dione under conditions such that a compound of formula ID is formed.

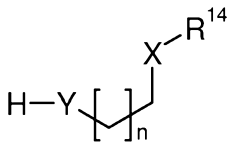
In further embodiments, the invention relates to a method of making a compound of formula IC, or salt thereof comprising a) mixing a compound of formula V,



formula V,

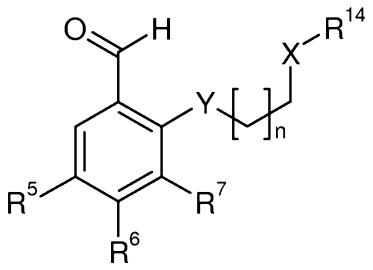
or salt thereof, wherein R^5, R^6, and R^7 are defined herein,

with a compound of formula VI,



formula VII,

or salt thereof, wherein R^{14}, n, X and Y are defined herein, under conditions such that a composition comprising a compound of formula VIII,



formula VIII

or salt thereof, is formed; and

b) mixing the compound of formula VIII and thiazolidine-2,4-dione under conditions such that a compound of formula IC is formed.

In some embodiments, the invention relates to compounds of formula I, IA, IB, IC, ID, or IX provided that they are not selected from 5-((2-dipropylamino-5-nitrophenyl)methylene)-2,4-thiazolidinedione;

5-((5-nitro-2-(1-piperidinyl)phenyl)methylene)-2,4-thiazolidinedione;

5-((2-(4-morpholinyl)-5-nitrophenyl)methylene)-2,4-thiazolidinedione;

5-[[2-(4-methyl-1-piperazinyl)phenyl]methylene]-2,4-thiazolidinedione;

5-[[2-[(2,6-dichloro-3-methylphenyl)amino]phenyl]methylene]-2,4-thiazolidinedione;

[2S-[2α(Z),4α]]-1-([1,1'-biphenyl]-4-ylsulfonyl)-N-[2-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenyl]-4-(methylthio)-2-pyrrolidinemethanamine;

1,1-dimethylethyl ester [[2S-[2α(Z),4α]]-3-[[[1-([1,1'-biphenyl]-4-ylsulfonyl)-4-(methylthio)-2-pyrrolidinyl]methyl]amino]-4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenyl] carbamic acid; and

[2S-[2α(Z),4α]]-N-[5-amino-2-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenyl]-1-([1,1'-biphenyl]-4-ylsulfonyl)-4-(methylthio)-2-pyrrolidinemethanamine.

It is the Applicants understanding that WO 2001002377 discloses 5-((2-dipropylamino-5-nitrophenyl)methylene)-2,4-thiazolidinedione,

5-((5-nitro-2-(1-piperidinyl)phenyl)methylene)-2,4-thiazolidinedione, and 5-((2-(4-morpholinyl)-5-nitrophenyl)methylene)-2,4-thiazolidinedione.

It is the Applicants understanding that WO 9814433 discloses 5-[[2-(4-methyl-1-piperazinyl)phenyl]methylene]-2,4-thiazolidinedione.

It is the Applicants understanding that US Patent No. 6,211,209 discloses, 5-[[2-[(2,6-dichloro-3-methylphenyl)amino]phenyl]methylene]-2,4-thiazolidinedione.

It is the Applicants understanding that WO 9705135 discloses, [2S-[2α(Z),4α]]-1-([1,1'-biphenyl]-4-ylsulfonyl)-N-[2-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenyl]-4-(methylthio)-2-pyrrolidinemethanamine, 1,1-dimethylethyl ester [[2S-[2α(Z),4α]]-3-[[[1-([1,1'-biphenyl]-4-ylsulfonyl)-4-(methylthio)-2-pyrrolidinyl]methyl]amino]-4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenyl]-carbamic acid, and [2S-[2α(Z),4α]]-N-[5-amino-2-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenyl]-1-([1,1'-biphenyl]-4-ylsulfonyl)-4-(methylthio)-2-pyrrolidinemethanamine.

The preceding understandings are not intended to be admissions.

In some embodiments, compounds disclosed herein could be used in the clinic either as a single agent by itself or in combination with other clinically relevant agents. This compound could also prevent the potential cancer resistance mechanisms that may arise due to mutations in a set of genes.

The anti-cancer treatment defined herein may be applied as a sole therapy or may involve, in addition to the compound of the invention, conventional surgery or radiotherapy or chemotherapy. Such chemotherapy may include one or more of the following categories of anti-tumour agents:

(i) antiproliferative/antineoplastic drugs and combinations thereof, as used in medical oncology, such as alkylating agents (for example cis-platin, carboplatin, cyclophosphamide, nitrogen mustard, melphalan, chlorambucil, busulfan and nitrosoureas); antimetabolites (for example antifolates such as fluoropyrimidines like 5-fluorouracil and tegafur, raltitrexed, methotrexate, cytosine arabinoside and hydroxyurea); antitumour antibiotics (for example anthracyclines like adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin and mithramycin); antimitotic agents (for example vinca alkaloids like vincristine, vinblastine, vindesine and vinorelbine and taxoids like taxol and taxotere); and topoisomerase inhibitors (for example epipodophyllotoxins like etoposide and teniposide, amsacrine, topotecan and camptothecin); and proteosome inhibitors (for example bortezomib [Velcade®]); and the agent anegrilide [Agrylin®]; and the agent alpha-interferon

(ii) cytostatic agents such as antioestrogens (for example tamoxifen, toremifene, raloxifene, droloxifene and iodoxyfene), oestrogen receptor down regulators (for example fulvestrant), antiandrogens (for example bicalutamide, flutamide, nilutamide and cyproterone acetate), LHRH antagonists or LHRH agonists (for example goserelin, leuprorelin and buserelin), progestogens (for example megestrol acetate), aromatase inhibitors (for example as anastrozole, letrozole, vorazole and exemestane) and inhibitors of 5α-reductase such as finasteride;

(iii) agents which inhibit cancer cell invasion (for example metalloproteinase inhibitors like marimastat and inhibitors of urokinase plasminogen activator receptor function);

(iv) inhibitors of growth factor function, for example such inhibitors include growth factor antibodies, growth factor receptor antibodies (for example the anti-erbb2 antibody trastuzumab [Herceptin™] and the anti-erbb1 antibody cetuximab [C225]) , farnesyl transferase inhibitors, tyrosine kinase inhibitors and serine/threonine kinase inhibitors, for example inhibitors of the epidermal growth factor family (for example EGFR family tyrosine kinase inhibitors such as:

N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (gefitinib, AZD1839),

N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine (erlotinib, OSI-774), and

6-acrylamido-N-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)quinazolin-4-amine (CI 1033),

for example inhibitors of the platelet-derived growth factor family and for example inhibitors of the hepatocyte growth factor family, for example inhibitors or phosphotidylinositol 3-kinase (PI3K) and for example inhibitors of mitogen activated protein kinase kinase (MEK1/2) and for example inhibitors of protein kinase B (PKB/Akt), for example inhibitors of Src tyrosine kinase family and/or Abelson (Abl) tyrosine kinase family such as AZD0530 and dasatinib (BMS-354825) and imatinib mesylate (Gleevec™); and any agents that modify STAT signaling.

(v) antiangiogenic agents such as those which inhibit the effects of vascular endothelial growth factor, (for example the anti-vascular endothelial cell growth factor

antibody bevacizumab [Avastin™], compounds such as those disclosed in International Patent Applications WO 97/22596, WO 97/30035, WO 97/32856 and WO 98/13354) and compounds that work by other mechanisms (for example linomide, inhibitors of integrin αvβ3 function and angiostatin);

(vi) vascular damaging agents such as Combretastatin A4 and compounds disclosed in International Patent Applications WO 99/02166, WO 00/40529, WO 00/41669, WO 01/92224, WO 02/04434 and WO 02/08213;

(vii) antisense therapies, for example those which are directed to the targets listed above, such as ISIS 2503, an anti-ras antisense;

(viii) gene therapy approaches, including for example approaches to replace aberrant genes such as aberrant p53 or aberrant BRCA1 or BRCA2, GDEPT (gene-directed enzyme pro-drug therapy) approaches such as those using cytosine deaminase, thymidine kinase or a bacterial nitroreductase enzyme and approaches to increase patient tolerance to chemotherapy or radiotherapy such as multi-drug resistance gene therapy; and

(ix) immunotherapy approaches, including for example ex-vivo and in-vivo approaches to increase the immunogenicity of patient tumour cells, such as transfection with cytokines such as interleukin 2, interleukin 4 or granulocyte-macrophage colony stimulating factor, approaches to decrease T-cell anergy, approaches using transfected immune cells such as cytokine-transfected dendritic cells, approaches using cytokine-transfected tumour cell lines and approaches using anti-idiotypic antibodies, and approaches using the immunomodulatory drugs thalidomide and lenalidomide [Revlimid®].

Such conjoint treatment may be achieved by way of the simultaneous, sequential or separate dosing of the individual components of the treatment. Such combination products employ the compounds of this invention, or pharmaceutically acceptable salts thereof, within the dosage range described hereinbefore and the other pharmaceutically-active agent within its approved dosage range.

The invention relates to phosphorylation inhibitors of PIM kinases. In still further embodiments, the invention relates to pharmaceutical composition comprising compounds disclosed herein and their use in the prevention and treatment of cancer.

It is understood the compositions disclosed herein may exist in solid and solution form tautomers. For example, imidazole and imidazole containing heterocycles may be drawn in a formula such that one or the other of the nitrogens contain a hydrogen atom. However, as provided herein, embodiments of such a formula are considered to encompass alternative tautomeric forms.

As used herein, "alkyl" means a noncyclic straight chain or branched, unsaturated or saturated hydrocarbon such as those containing from 1 to 10 carbon atoms, while the term "lower alkyl" or "C_{1-6}alkyl" has the same meaning as alkyl but contains from 1 to 6 carbon atoms. The term "higher alkyl" has the same meaning as alkyl but contains from 7 to 10 carbon atoms. Representative saturated straight chain alkyls include methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl, n-septyl, n-octyl, n-nonyl, and the like; while saturated branched alkyls include isopropyl, sec-butyl, isobutyl, tert-butyl, isopentyl, and the like. Unsaturated alkyls contain at least one double or triple bond between adjacent carbon atoms (referred to as an "alkenyl" or "alkynyl", respectively). Representative straight chain and branched alkenyls include ethylenyl, propylenyl, 1-butenyl, 2-butenyl, isobutylenyl, 1-pentenyl, 2-pentenyl, 3-methyl-1-butenyl, 2-methyl-2-butenyl, 2,3-dimethyl-2-butenyl, and the like; while representative straight chain and branched alkynyls include acetylenyl, propynyl, 1-butynyl, 2-butynyl, 1-pentynyl, 2-pentynyl, 3-methyl-1-butynyl, and the like.

A "halogenated alkyl" refers to an alkyl group where one or more or all of the hydrogen(s) are substituted with halogen(s). A representative halogenated alkyl includes trifluoromethyl (i.e., $-CF_3$).

Non-aromatic mono or polycyclic alkyls are referred to herein as "carbocycles" or "carbocyclyl" groups. Representative saturated carbocycles include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like; while unsaturated carbocycles include cyclopentenyl and cyclohexenyl, aryls and the like.

"Heterocarbocycles" or heterocarbocyclyl" groups are carbocycles which contain from 1 to 4 heteroatoms independently selected from nitrogen, oxygen and sulfur which may be saturated or unsaturated (but not aromatic), monocyclic or polycyclic, and wherein the nitrogen and sulfur heteroatoms may be optionally oxidized, and the nitrogen heteroatom may be optionally quaternized. Heterocarbocycles include morpholinyl,

pyrrolidinonyl, pyrrolidinyl, piperidinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyridinyl, tetrahydroprimidinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, tetrahydropyrimidinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, and the like.

"Aryl" means an aromatic carbocyclic monocyclic or polycyclic ring such as phenyl or naphthyl.

As used herein, "heteroaryl" refers an aromatic heterocarbocycle having 1 to 4 heteroatoms selected from nitrogen, oxygen and sulfur, and containing at least 1 carbon atom, including both mono- and polycyclic ring systems. Polycyclic ring systems may, but are not required to, contain one or more non-aromatic rings, as long as one of the rings is aromatic. Representative heteroaryls are furyl, benzofuranyl, thiophenyl, benzothiophenyl, pyrrolyl, indolyl, isoindolyl, azaindolyl, pyridyl, quinolinyl, isoquinolinyl, oxazolyl, isooxazolyl, benzoxazolyl, pyrazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, and quinazolinyl. It is contemplated that the use of the term "heteroaryl" includes N-alkylated derivatives such as a 1-methylimidazol-5-yl substituent.

As used herein, "heterocycle" or "heterocyclyl" refers to mono- and polycyclic ring systems having 1 to 4 heteroatoms selected from nitrogen, oxygen and sulfur, and containing at least 1 carbon atom. The mono- and polycyclic ring systems may be aromatic, non-aromatic or mixtures of aromatic and non-aromatic rings. Heterocycle includes heterocarbocycles, heteroaryls, and the like.

"Alkylthio" refers to an alkyl group as defined above with the indicated number of carbon atoms attached through a sulfur bridge. An example of an alkylthio is methylthio, (i.e., -S-CH_3).

"Alkoxy" refers to an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. Preferred alkoxy groups are methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy.

"Alkylamino" refers an alkyl group as defined above with the indicated number of carbon atoms attached through an amino bridge. An example of an alkylamino is methylamino, (i.e., -NH-CH_3).

"Alkanoyl" refers to an alkyl as defined above with the indicated number of carbon atoms attached through a carbonyl bride (i.e., -(C=O)alkyl).

"Alkylsulfonyl" refers to an alkyl as defined above with the indicated number of carbon atoms attached through a sulfonyl bridge (i.e., -$S(=O)_2$alkyl) such as mesyl and the like, and "Arylsulfonyl" refers to an aryl attached through a sulfonyl bridge (i.e., -$S(=O)_2$aryl).

"Alkylsulfamoyl" refers to an alkyl as defined above with the indicated number of carbon atoms attached through a sulfamoyl bridge (i.e., -$NHS(=O)_2$alkyl), and an "Arylsulfamoyl" refers to an alkyl attached through a sulfamoyl bridge (i.e., (i.e., -$NHS(=O)_2$aryl).

"Alkylsulfinyl" refers to an alkyl as defined above with the indicated number of carbon atoms attached through a sulfinyl bridge (i.e. -S(=O)alkyl).

The term "substituted" refers to a molecule wherein at least one hydrogen atom is replaced with a substituent. When substituted, one or more of the groups are "substituents." The molecule may be multiply substituted. In the case of an oxo substituent ("=O"), two hydrogen atoms are replaced. Example substituents within this context may include halogen, hydroxy, alkyl, alkoxy, nitro, cyano, oxo, carbocyclyl, carbocycloalkyl, heterocarbocyclyl, heterocarbocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, -NR_aR_b, -$NR_aC(=O)R_b$, -$NR_aC(=O)NR_aNR_b$, -$NR_aC(=O)OR_b$, -$NR_aSO_2R_b$, -$C(=O)R_a$, -$C(=O)OR_a$, -$C(=O)NR_aR_b$, -$OC(=O)NR_aR_b$, -OR_a, -SR_a, -SOR_a, -$S(=O)_2R_a$, -$OS(=O)_2R_a$ and -$S(=O)_2OR_a$. R_a and R_b in this context may be the same or different and independently hydrogen, halogen hydroxyl, alkyl, alkoxy, alkyl, amino, alkylamino, dialkylamino, carbocyclyl, carbocycloalkyl, heterocarbocyclyl, heterocarbocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl.

The term "optionally substituted," as used herein, means that substitution is optional and therefore it is possible for the designated atom to be unsubstituted.

As used herein, the terms "prevent" and "preventing" include the prevention of the recurrence, spread or onset. It is not intended that the present invention be limited to

complete prevention. In some embodiments, the onset is delayed, or the severity of the disease is reduced.

As used herein, the terms "treat" and "treating" are not limited to the case where the subject (e.g. patient) is cured and the disease is eradicated. Rather, embodiments, of the present invention also contemplate treatment that merely reduces symptoms, and/or delays disease progression.

As used herein, "salts" refer to derivatives of the disclosed compounds where the parent compound is modified making acid or base salts thereof. Examples of salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines, alkylamines, or dialkylamines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. In preferred embodiment the salts are conventional non-toxic pharmaceutically acceptable salts including the quaternary ammonium salts of the parent compound formed, and non-toxic inorganic or organic acids. Preferred salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound that contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

“Subject” means any animal, preferably a human patient, livestock, or domestic pet.

"Cancer" refers any of various cellular diseases with malignant neoplasms characterized by the proliferation of cells. It is not intended that the diseased cells must actually invade surrounding tissue and metastasize to new body sites. Cancer can involve any tissue of the body and have many different forms in each body area. Within the context of certain embodiments, whether "cancer is reduced" may be identified by a variety of diagnostic manners known to one skill in the art including, but not limited to, observation the reduction in size or number of tumor masses or if an increase of apoptosis of cancer cells observed, e.g., if more than a 5 % increase in apoptosis of cancer cells is observed for a sample compound compared to a control without the compound. It may also be identified by a change in relevant biomarker or gene expression profile, such as PSA for prostate cancer, her2 for breast cancer, or others.

The present pharmaceutical compositions can take the form of solutions, suspensions, emulsion, tablets, pills, pellets, capsules, capsules containing liquids, powders, sustained-release formulations, suppositories, emulsions, aerosols, sprays, suspensions, or any other form suitable for use.

Administration may be topical, i.e., substance is applied directly where its action is desired, enteral or oral, i.e., substance is given via the digestive tract, parenteral, i.e., substance is given by other routes than the digestive tract such as by injection.

In a preferred embodiment, the active compound and optionally another therapeutic or prophylactic agent are formulated in accordance with routine procedures as pharmaceutical compositions adapted for intravenous administration to human beings. Typically, the active compound for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the compositions can also include a solubilizing agent. Compositions for intravenous administration can optionally include a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule. Where the active compound is to be administered by infusion, it can be dispensed, for example, with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the active compound is administered by

injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients can be mixed prior to administration.

Compositions for oral delivery can be in the form of tablets, lozenges, aqueous or oily suspensions, granules, powders, emulsions, capsules, syrups, or elixirs, for example. Orally administered compositions can contain one or more optional agents, for example, sweetening agents such as fructose, aspartame or saccharin; flavoring agents such as peppermint, oil of wintergreen, or cherry; coloring agents; and preserving agents, to provide a pharmaceutically palatable preparation. A time delay material such as glycerol monostearate or glycerol stearate can also be used. Oral compositions can include standard vehicles such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like. Such vehicles are preferably of pharmaceutical grade.

Compositions for use in accordance with the present invention can be formulated in conventional manner using one or more physiologically acceptable carriers or excipients. Thus, the compound and optionally another therapeutic or prophylactic agent and their physiologically acceptable salts and solvates can be formulated into pharmaceutical compositions for administration by inhalation or insufflation (either through the mouth or the nose) or oral, parenteral or mucosol (such as buccal, vaginal, rectal, sublingual) administration. In one embodiment, local or systemic parenteral administration is used.

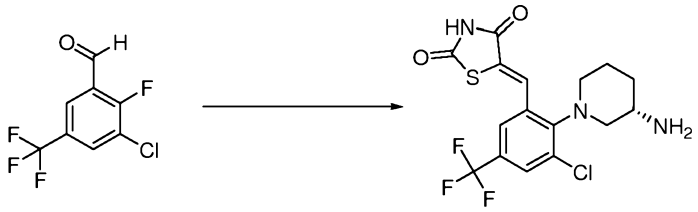
For oral administration, the compositions can take the form of, for example, tablets or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (e.g., pregelatinised maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (e.g., lactose, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (e.g., potato starch or sodium starch glycolate); or wetting agents (e.g., sodium lauryl sulfate). The tablets can be coated by methods well known in the art. Liquid preparations for oral administration can take the form of, for example, solutions, syrups or suspensions, or they can be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations can be prepared by conventional means with pharmaceutically acceptable additives such as suspending

agents (e.g., sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters, ethyl alcohol or fractionated vegetable oils); and preservatives (e.g., methyl or propyl-p-hydroxybenzoates or sorbic acid). The preparations can also contain buffer salts, flavoring, coloring and sweetening agents as appropriate.

EXPERIMENTAL

The following is intended to provide examples on methods of making and using embodiments of the invention. It is not intended to limit the scope.

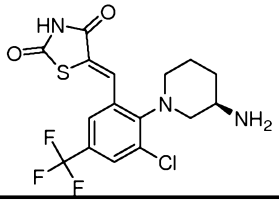
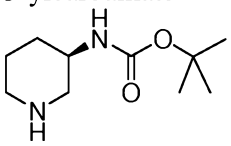
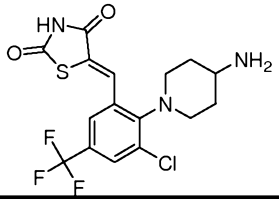
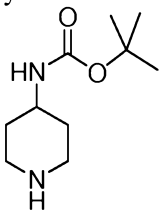
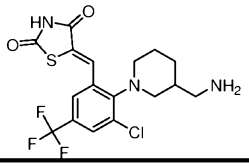
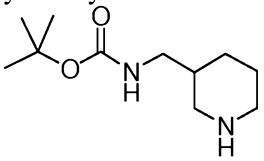
Example 1:

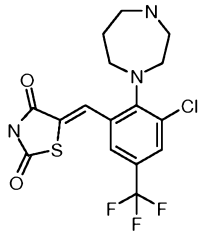
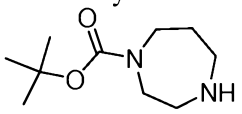
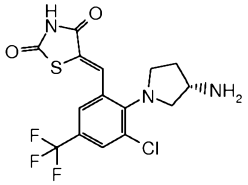
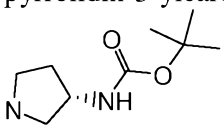


(*S,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione trifluoroacetate:

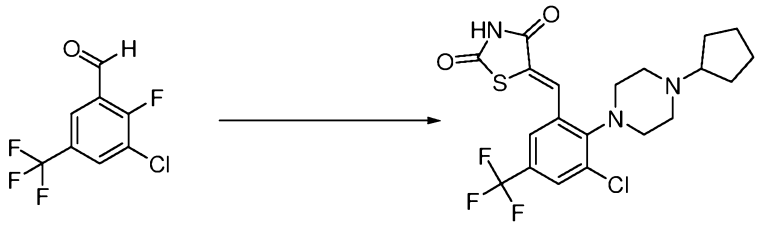
A 40 mL vial was charged with a magentic stir bar, 3-chloro-2-fluoro-5-(trifluoromethyl)benzaldehyde (0.134 ml, 1.10 mmol), acetonitrile (2.76 ml), (*S*)-*tert*-butyl piperidin-3-ylcarbamate (0.221 g, 1.10 mmol), and K_2CO_3 (0.229 g, 1.66 mmol). The vial was heated to 70 °C with stirring for 2 h. The vessel was cooled to rt and the mixture was diluted with DCM and filtered. The filtrate was conc. *in vacuo* to afford the substituted aldehyde which was dissolved in EtOH (2.76 ml). Thiazolidine-2,4-dione (0.155 g, 1.32 mmol) and piperidine (9.40 mg, 0.11 mmol) were then added. The mixture was heated to reflux for 4 h before being allowed to cool to rt and the mixture was conc. *in vacuo*. The product was dissolved DCM (2 mL) and TFA (1 mL) and stirred at rt for 1 h before being conc. *in vacuo*. The residue was dissolved in DMSO (~ 2 mL) and purified via reverse phase HPLC to afford (*S,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione trifluoroacetate (0.214 g, 37.3 %). ^{1}H NMR (300 MHz, DMSO-D6) δ ppm 12.78 (s, 1 H) 7.95 (m, 3 H) 7.79 (s, 1 H) 7.62 (s, 1 H) 3.40-3.20 (s, 5 H) 2.12-2.06 (m, 1H) 1.79-1.70 (m 1H) 1.65-1.60 (m, 1 H) 1.52-1.41 (m, 1 H); *m/z* 406.

The following examples were prepared by the procedure of Example 1, using the appropriate starting materials. The following parent compounds obtained after chromatography may be converted to their corresponding hydrochloride salts using the procedure in Example 6, or a similar procedure.

Ex.	Compound	^{1}H NMR (300 MHz)	m/z	SM
2	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione trifluoroacetate 	12.79 (s, 1 H) 7.98 (s, 2 H) 7.95 (s, 1 H) 7.79 (s, 1 H) 7.62 (s, 1 H) 3.31-3.20 (m, 5 H) 2.12-2.09 (m, 1 H) 1.85 - 1.77 (m, 1 H) 1.66-1.63 (m, 1 H) 1.45-1.40 (m, 1 H)	406	(*R*)-*tert*-butyl piperidin-3-ylcarbamate 
3	(*Z*)-5-(2-(4-aminopiperidin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione trifluoroacetate 	12.76 (s, 1 H) 7.99 (s, 1 H) 7.91 (s, 2 H) 7.78 (s, 1 H) 7.60 (s, 1 H) 3.33-3.18 (m, 5 H) 1.94 (d, 2 H) 1.71-1.60 (m, 2 H)	406	*tert*-butyl piperidin-4-ylcarbamate 
4	(*Z*)-5-(2-(3-(aminomethyl)piperidin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione trifluoroacetate 	12.78 (s, 1 H) 7.93 (s, 1 H) 7.84 (s, 1 H) 7.75 (s, 1 H) 7.61 (s, 1 H) 3.31-3.05 (m, 6 H) 2.79-2.71 (m, 1 H) 1.95-1.89 (m, 2 H) 1.72-1.55 (m, 2 H) 1.29-1.10 (m, 1 H)	421	*tert*-butyl piperidin-3-ylmethylcarbamate 

5A	(Z)-5-(3-chloro-2-(1,4-diazepan-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.83 (brs, 1 H) 9.20 (brs, 2 H) 8.05 (d, 1 H) 7.90 (s, 1 H) 7.66 (d,1 H) 3.51 (brs, 2 H) 3.35 (d, 2 H) 3.26 - 3.03 (m, 4 H) 2.27 – 1.99 (m, 2 H)	405	*tert*-butyl 1,4-diazepane-1-carboxylate 
5B	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 	12.73 (brs, 1 H) 8.29 (brs, 3 H) 7.93 (s, 1 H) 7.83 (s, 1 H) 7.66 (s, 1 H) 3.88 (brs, 1 H) 3.66 (dd, 1 H), 3.52 - 3.27 (m, 3 H) 2.42-2.19 (m, 1 H) 2.12-1.88 (m, 1 H)	392	*tert*-butyl (3*S*)-pyrrolidin-3-ylcarbamate 

Example 6:

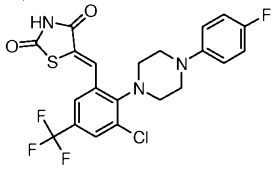
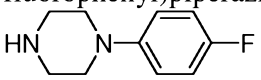
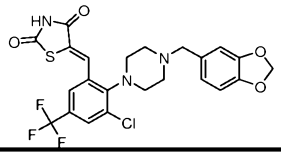
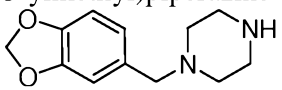
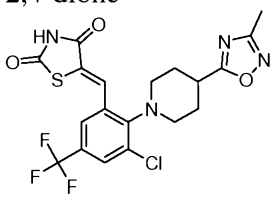
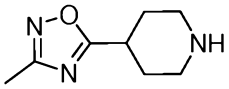


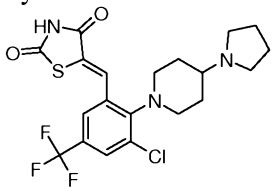
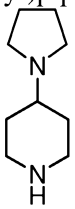
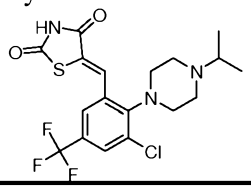
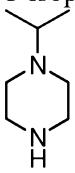
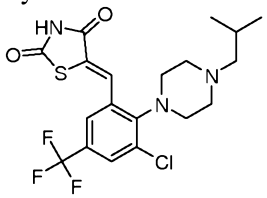
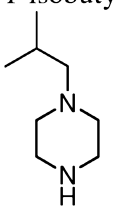
(Z)-5-(3-chloro-2-(4-cyclopentylpiperazin-1-yl)-5 (trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride:

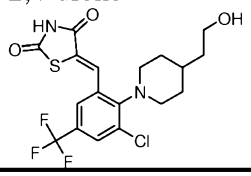
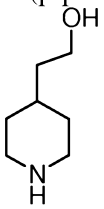
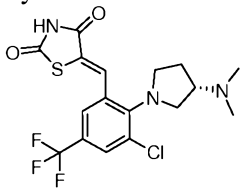
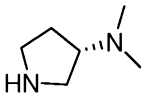
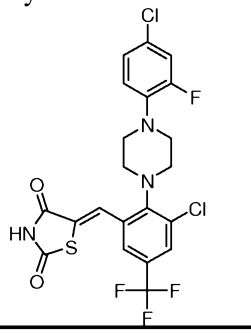
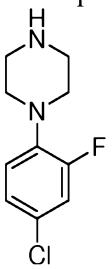
A 40 mL vial was charged with a magnetic stir bar, 3-chloro-2-fluoro-5-(trifluoromethyl)benzaldehyde (0.134 ml, 1.10 mmol), acetonitrile (2.76 ml), 1-cyclopentylpiperazine (0.213 g, 1.38 mmol), and K_2CO_3 (0.229 g, 1.66 mmol). The vial was heated to 70 °C with stirring for 2 h. The vessel was then cooled to rt and the

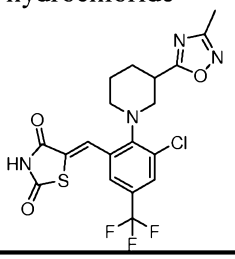
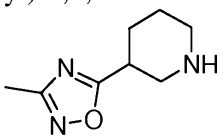
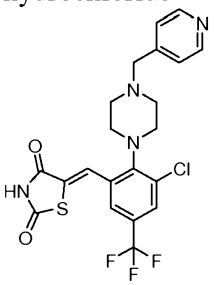
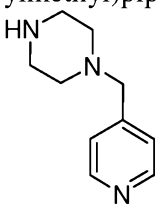
mixture was diluted with DCM and filtered. The filtrate was conc. *in vacuo* to afford the substituted aldehyde which was dissolved in EtOH (2.76 ml). Thiazolidine-2,4-dione (0.155 g, 1.32 mmol) and piperidine (9.40 mg, 0.11 mmol) were then added and the mixture was heated to reflux for 4 h before being allowed to cool to rt. The mixture was then conc. *in vacuo* to afford the product which was dissolved in DMSO (~ 2 mL) and purified via reverse phase HPLC to afford fractions that were conc. *in vacuo*, suspended in methanol (~5 mL) and 1N HCl in diethyl ether (~2 mL). This mixture was conc. *in vacuo* to afford (*Z*)-5-(3-chloro-2-(4-cyclopentylpiperazin-1-yl)-5-(trifluoromethyl) benzylidene)thiazolidine-2,4-dione hydrochloride (0.215 g, 39.3 %). ^{1}H NMR (300 MHz, DMSO-D6) δ ppm 12.78 (s, 1 H) 7.96 (s, 1 H) 7.83 (s, 1 H) 7.63 (s, 1 H) 3.77-3.50 (m, 5 H) 3.30-3.22 (m, 2 H) 3.08-2.99 (m, 2 H) 2.03-1.99 (m, 2 H) 1.84-1.61 (m, 4 H) 1.60-1.50 (m, 2 H); *m/z* 461.

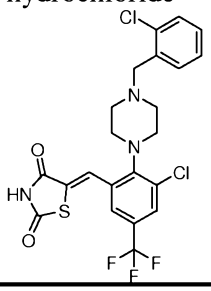
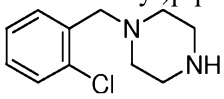
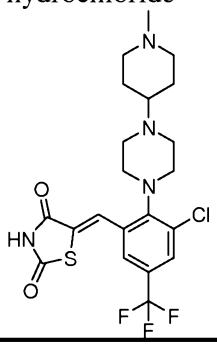
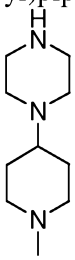
The following examples were prepared by the procedure of Example 6, using the appropriate starting materials. The following parent compounds obtained after chromatography may be converted to their corresponding hydrochloride salt in a manner similar as described in example 6.

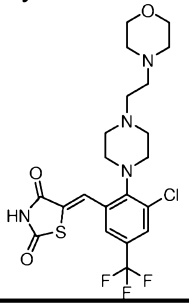
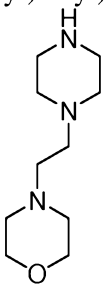
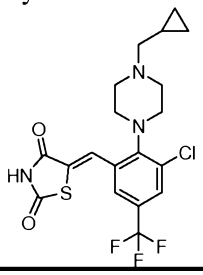
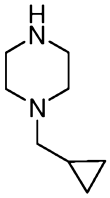
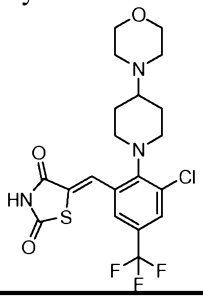
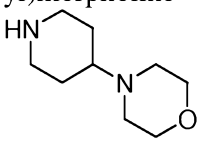
Ex.	Compound	^{1}H NMR	m/z	SM
7	(Z)-5-(3-chloro-2-(4-(4-fluorophenyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 	12.74 (s, 1 H) 7.89 - 8.01 (m, 2 H) 7.62 (s, 1 H) 6.99 - 7.13 (m, 4 H) 3.34-3.23 (m, 8 H)	486	1-(4-fluorophenyl)piperazine 
8	(Z)-5-(2-(4-(benzo[d][1,3]dioxol-5-ylmethyl)piperazin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione trifluoroacetate 	12.77 (s, 1 H) 7.97 (d, 1 H) 7.97 (s, 1 H) 7.77 (s, 1 H) 7.63 (s, 1 H) 7.10 (s, 1 H) 7.02 (s, 2 H) 6.08 (s, 2 H) 4.34 (s, 2 H) 3.58-3.11 (m, 8 H)	526	1-(benzo[d][1,3]dioxol-5-ylmethyl)piperazine 
9	(Z)-5-(3-chloro-2-(4-(3-methyl-1,2,4-oxadiazol-5-yl)piperidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 	12.72 (s, 1 H) 7.91 (s, 1 H) 7.84 (s, 1 H) 7.61 (s, 1 H) 3.33-3.18 (m, 4 H) 2.79-2.71 (m, 1 H) 2.33 (s, 3 H) 2.06 (d, 2 H) 1.98-1.80 (m, 2 H)	473	3-methyl-5-(piperidin-4-yl)-1,2,4-oxadiazole 

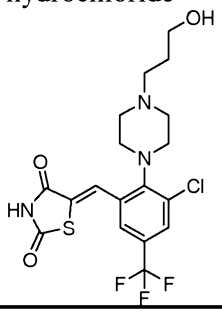
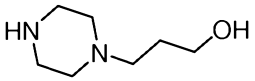
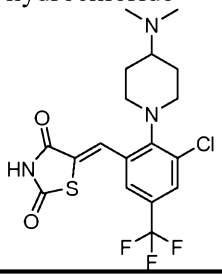
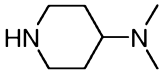
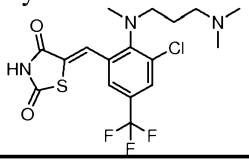
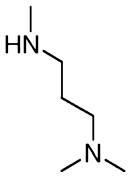
10	(Z)-5-(3-chloro-2-(4-(pyrrolidin-1-yl)piperidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.78 (s, 1 H) 7.92 (s, 1 H) 7.79 (s, 1 H) 7.60 (s, 1 H) 3.33 - 3.20 (m, 5 H) 3.12 - 3.03 (m, 4 H) 2.09 (d, 2 H) 1.97 - 1.78 (m, 6 H)	461	4-(pyrrolidin-1-yl)piperidine 
11	(Z)-5-(3-chloro-2-(4-isopropylpiperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.80 (s, 1 H) 7.96 (s, 1 H) 7.82 (s, 1 H) 7.62 (s, 1 H) 3.85 (t, 2 H) 3.55-3.52 (m, 1 H) 3.41 (d, 2 H) 3.26 (d, 2 H) 3.10 - 3.06 (m, 2 H) 1.32 (d, 6 H)	434	1-isopropylpiperazine 
12	(Z)-5-(3-chloro-2-(4-isobutylpiperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.80 (s, 1 H) 7.96 (d, 1 H) 7.80 (s, 1 H) 7.63 (s, 1 H) 3.87 (brs, 2 H) 3.52 (d, 2 H) 3.27 (brs, 2 H) 3.11 - 3.00 (m, 4 H) 2.10 (qq, 1 H) 1.00 (d, 6 H)	450	1-isobutylpiperazine 

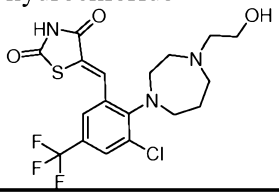
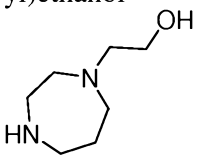
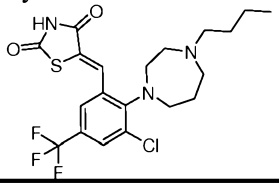
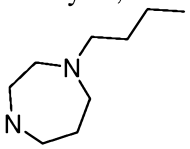
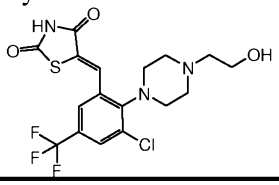
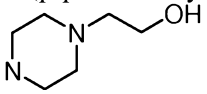
13	(*Z*)-5-(3-chloro-2-(4-(2-hydroxyethyl)piperidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 	12.73 (s, 1 H) 7.87 (s, 1 H) 7.83 (s, 1 H) 7.59 (s, 1 H) 3.46 (t, 2 H) 3.23 (t, 2 H) 3.07 (brs, 2 H) 1.70 (d, 2 H) 1.61 - 1.52 (m, 1 H) 1.42 (q, 2 H) 1.33 - 1.20 (m, 2 H)	437	2-(piperidin-4-yl)ethanol 
14	(*S,Z*)-5-(3-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.65 (s, 1 H) 7.82 (s, 1 H) 7.72 (s, 1 H) 7.53 (s, 1 H) 3.59 - 3.50 (m, 1 H) 3.38 - 3.30 (m, 4 H) 2.56 (s, 6 H) 2.31 - 2.28 (m, 1 H) 2.09 - 2.01 (m, 1 H)	421	(*S*)-*N,N*-dimethylpyrrolidin-3-amine 
15	(*Z*)-5-(3-chloro-2-(4-(4-chloro-2-fluorophenyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.75 (brs, 1 H) 8.06 – 7.90 (m, 2 H) 7.64 (d, 1 H) 7.38 (dd, 1 H) 7.23 (dd, 1 H) 7.11 (t, 1 H) 3.42 (m, 4 H) 3.15 (d, 4 H)	520	1-(4-chloro-2-fluorophenyl)piperazine 

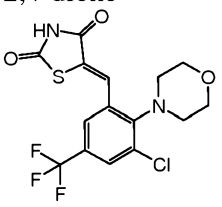
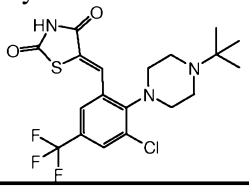
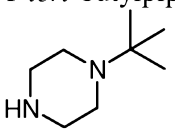
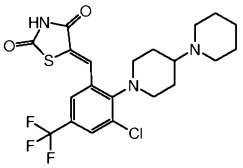
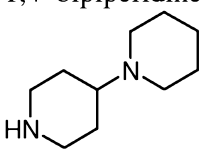
16	(Z)-5-(3-chloro-2-(3-(3-methyl-1,2,4-oxadiazol-5-yl)piperidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 		471	3-methyl-5-(piperidin-3-yl)-1,2,4-oxadiazole 
17	(Z)-5-(3-chloro-2-(4-(pyridin-4-ylmethyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.75 (brs, 1H) 8.78 (d, 2 H) 7.98 (s, 1 H) 7.74 (brs, 1 H) 7.71 (s, 1 H) 7.64 (s, 1 H) 4.44 (brs, 2 H) 3.44 (brs, 4 H) 3.17 (s, 4 H)	483	1-(pyridin-4-ylmethyl)piperazine 

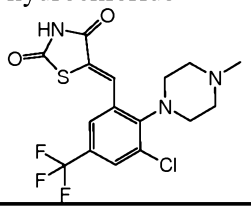
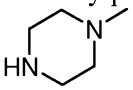
18	(Z)-5-(3-chloro-2-(4-(2-chlorobenzyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	7.98 (d, 1 H) 7.73 (dd, 1 H) 7.68 - 7.59 (m, 2 H) 7.58 - 7.42 (m, 3 H) 4.53 (brs, 2 H) 3.75-3.30 (m, 8 H)	517	1-(2-chlorobenzyl)piperazine 
19	(Z)-5-(3-chloro-2-(4-(1-methylpiperidin-4-yl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	10.68 (brs, 1 H) 7.92 (d, 1 H) 7.78 (brs, 1 H) 7.58 (s, 1 H) 3.73 - 3.63 (m, 1 H) 3.61-3.41 (m, 6 H) 3.10 (brs, 3 H) 2.93 (brs, 3 H) 2.67 (s, 3 H) 2.39 - 2.18 (m, 2 H) 2.07 (brs, 2 H)	489	1-(1-methylpiperidin-4-yl)piperazine 

20	(Z)-5-(3-chloro-2-(4-(2-morpholinoethyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	11.12 (brs, 1 H) 7.91 (d, 1 H) 7.79 (brs, 1 H) 7.59 (s, 1 H) 3.80-2.81 (m, 20 H)	505	4-(2-(piperazin-1-yl)ethyl)morpholine 
21	(Z)-5-(3-chloro-2-(4-(cyclopropylmethyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.59 (brs, 1 H) 7.76 (d, 1 H) 7.61 (brs, 1 H) 7.43 (s, 1 H) 3.62 (brs, 2 H) 3.44 - 3.24 (m, 2 H) 3.10 (brs, 2 H) 2.87 (d, 4 H) 0.94 (brs, 1 H) 0.54 - 0.31 (m, 2 H) 0.32 - 0.08 (m, 2 H)	447	1-(cyclopropylmethyl)piperazine 
22	(Z)-5-(3-chloro-2-(4-morpholinopiperidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.92 (brs, 1 H) 8.08 (d, 1 H) 7.95 (brs, 1 H) 7.76 (s, 1 H) 4.14 (brs, 3 H) 3.98 (brs, 2 H) 3.58 (brs, 3 H) 3.53 - 3.34 (m, 3 H) 3.28 (brs, 2 H) 2.32 (brs, 2 H) 1.92 (d, 2 H)	476	4-(piperidin-4-yl)morpholine 

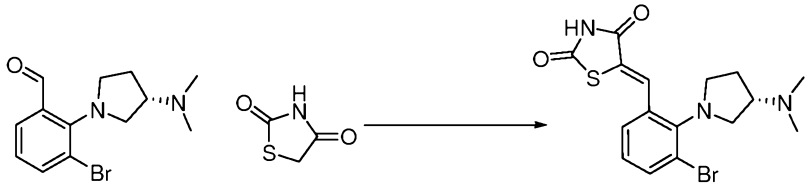
23	(Z)-5-(3-chloro-2-(4-(3-hydroxypropyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.90 (brs, 1 H) 10.52 (brs, 1 H) 7.98 (d, 1 H) 7.84 (brs, 1 H) 7.65 (s, 1 H) 3.90 - 3.65 (m, 2 H) 3.57 - 3.41 (m, 5 H) 3.30 - 3.06 (m, 5 H) 1.96 - 1.73 (m, 2 H)	450	3-(piperazin-1-yl)propan-1-ol 
24	(Z)-5-(3-chloro-2-(4-(dimethylamino)piperidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.79 (brs, 1 H) 7.94 (d, 1 H) 7.82 (s, 1 H) 7.61 (s, 1 H) 3.84 (brs, 1 H) 3.46 - 3.18 (m, 4 H) 2.75 (d, 6 H) 2.10 (d, 2 H) 1.74 (dd, 2 H)	434	*N,N*-dimethylpiperidin-4-amine 
25	(Z)-5-(3-chloro-2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.81 (brs, 1 H) 7.98 (d, 1 H) 7.81 (s, 1 H) 7.65 (d, 1 H) 3.15 (t, 2 H) 3.02 (brs, 2 H) 2.89 (s, 3 H) 2.72 (d, 6 H) 1.99 - 1.74 (m, 2 H)	422	*N1,N1,N3*-trimethylpropane-1,3-diamine 

26	(Z)-5-(3-chloro-2-(4-(2-hydroxyethyl)-1,4-diazepan-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	8.04 (brs, 1 H) 7.79 (d, 1 H) 7.63 (s, 1 H) 3.83 (t, 3 H) 3.71 (m, 2 H) 3.56 (m, 3 H) 3.33 (m, 6 H) 2.21 (m, 2 H)	451	2-(1,4-diazepan-1-yl)ethanol 
27	(Z)-5-(2-(4-butyl-1,4-diazepan-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	10.76 (brs, 1 H) 8.06 (d, 1 H) 7.91 (brs, 1 H) 7.66 (d,1 H) 3.69 (m, 3 H) 3.57 (brs, 1 H) 3.46 (m, 3 H) 3.14 (m, 3 H) 2.34 (brs, 1 H) 2.16 (brs, 1 H) 1.73 (d, 2 H) 1.32 (m, 2 H) 0.93 (t, 3 H)	463	1-butyl-1,4-diazepane 
28	(Z)-5-(3-chloro-2-(4-(2-hydroxyethyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	7.98 (d, 1 H) 7.82 (brs, 1 H) 7.64 (d,1 H) 5.40 (brs, 1 H) 3.74 (m, 4 H) 3.56 (m, 3 H) 3.27 (m, 3 H) 3.18 (brs, 1 H) 3.11 (brs, 1 H)	436	2-(piperazin-1-yl)ethanol 

29	(*Z*)-5-(3-chloro-2-morpholino-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 	12.76 (brs, 1 H) 7.94 (m, 2 H) 7.63 (d, 1 H) 3.71 (t, 4 H) 3.20 (brs, 4 H)	394	morpholine 
30	(*Z*)-5-(2-(4-*tert*-butylpiperazin-1-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.80 (brs, 1 H) 8.00 (d, 1 H) 7.85 (brs, 1 H) 7.65 (d, 1 H) 3.82 (m, 2 H) 3.56 (d, 2 H) 3.29 (dd, 2 H) 3.04 (m, 2 H) 1.39 (s, 9 H)	449	1-*tert*-butylpiperazine 
31	(*Z*)-5-(2-(1,4'-bipiperidin-1'-yl)-3-chloro-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	9.75 (brs, 1 H) 7.94 (d, 1 H) 7.81 (brs, 1 H) 7.62 (s, 1 H) 3.29 (m, 7 H) 2.96 (m, 2 H) 2.14 (d, 2 H) 1.78 (m, 7 H) 1.44 (brs, 1 H)	474	1,4'-bipiperidine 

32	(*Z*)-5-(3-chloro-2-(4-methylpiperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	7.94 (brs, 1 H) 7.75 (d, 1 H) 7.63 (s, 1 H) 3.56 - 3.38 (m, 3 H) 3.31 - 3.21 (m, 5 H) 2.92 (s, 3 H)	406	1-methylpiperazine 

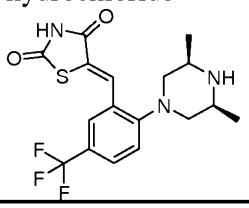
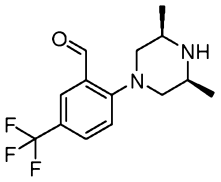
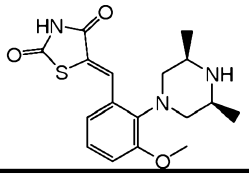
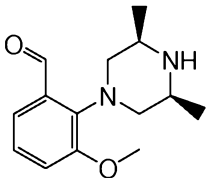
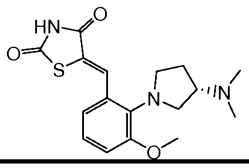
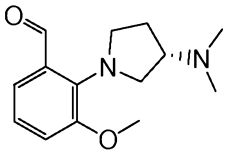
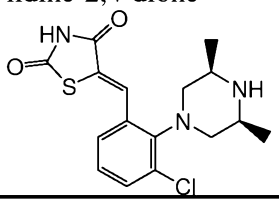
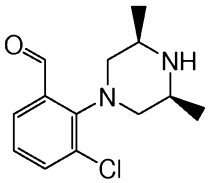
Example 33:

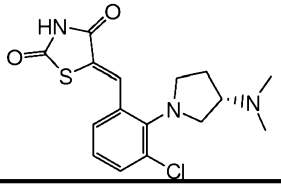
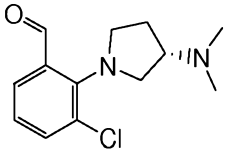
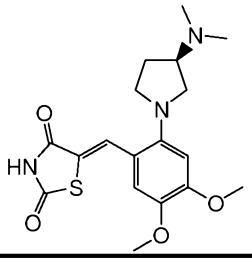
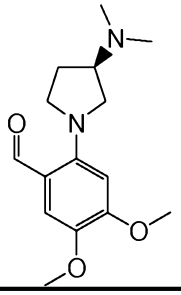
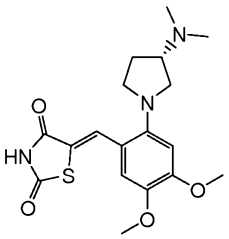
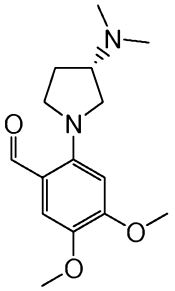


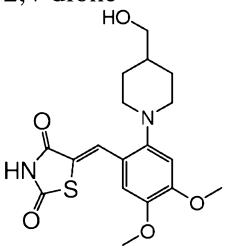
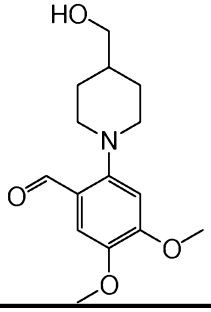
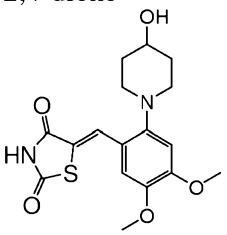
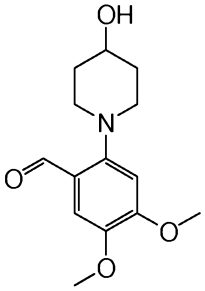
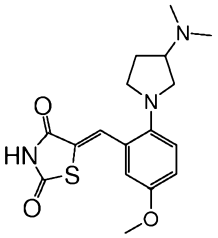
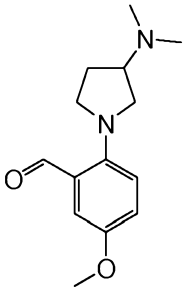
(*S,Z*)-5-(3-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride:

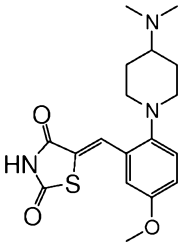
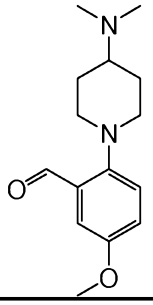
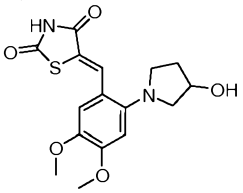
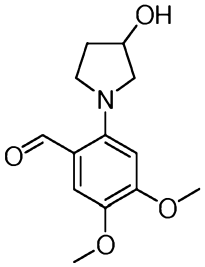
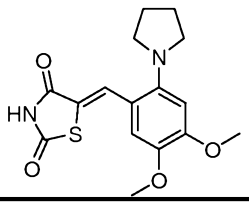
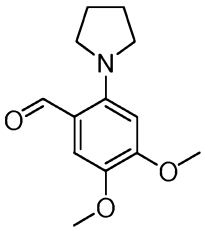
A 100 mL round bottom flask was charged with a magnetic stir bar, (*S*)-3-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde (Method 1) (0.370 g, 1.24 mmol), thiazolidine-2,4-dione (0.146 g, 1.24 mmol), and ethanol (4.15 ml). Piperidine (0.012 ml, 0.12 mmol) was then added and the reaction was heated to reflux for 2 h. Once the reaction was judged to be complete by LCMS, it was allowed to cool to rt and was conc. *in vacuo* to afford the product which was purified on 40 g of silica gel using ethyl acetate / methanol (3:1) as eluent to afford the free base which was suspended in methanol (~ 5 mL) and 1N HCl in diethyl ether (2 mL) and conc. *in vacuo* to afford (*S,Z*)-5-(3-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride (0.141 g, 26.2 %). ^{1}H NMR (300 MHz, DMSO-D6) δ ppm 12.68 (s, 1 H) 7.91 (s, 1 H) 7.77 (d, 1 H) 7.48 (d, 1 H) 7.33 (t, 1 H) 4.10 - 4.02 (m, 1 H) 3.62 (t, 2 H) 3.50 - 3.45 (m, 2 H) 2.81 (s, 6 H) 2.42 - 2.38 (m, 1 H) 2.31 - 2.21 (m, 1 H); *m/z* 398.

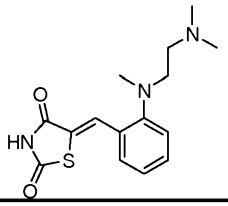
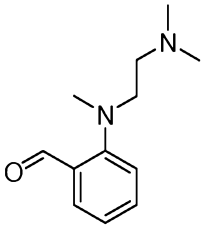
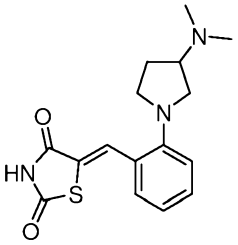
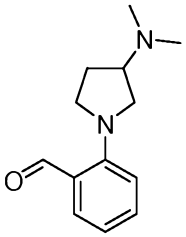
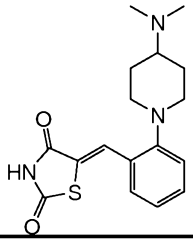
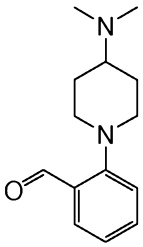
The following examples were prepared by the procedure of Example 33, using the appropriate starting materials. The following parent compounds obtained after chromatography (normal or reverse phase) may be converted to its corresponding hydrochloride salt as described in example 33, or similar procedure.

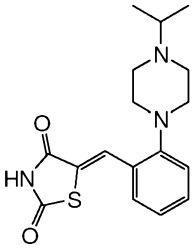
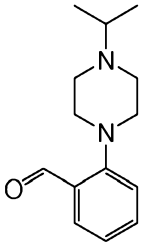
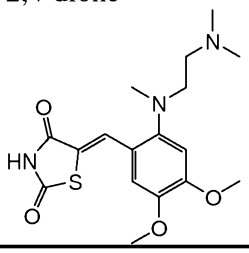
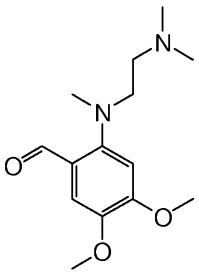
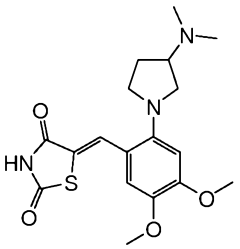
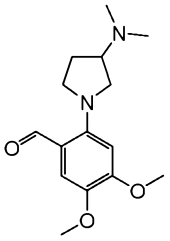
Ex.	Compound	^{1}H NMR	m/z	SM
34	(*Z*)-5-(2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.63 (s, 1 H) 8.99 - 8.94 (m, 1 H) 7.77 (d, 1 H) 7.72 (s, 2 H) 7.40 (d, 1 H) 3.49 - 3.43 (m, 2 H) 3.32 (d, 2 H) 2.92 (t, 2 H) 1.25 (d, 6 H)	387	2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)-5-(trifluoromethyl)benzaldehyde Method 2 
35	(*Z*)-5-(2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)-3-methoxybenzylidene) thiazolidine-2,4-dione 	7.87 (brs, 1 H) 7.24 (t, 1 H) 7.20 - 7.10 (m, 1 H) 7.02 (d, 1 H) 3.81 (s, 3 H) 3.48 - 3.23 (m, 2 H) 3.17 (t, 2 H) 2.89 (d, 2 H) 1.30 - 1.09 (m, 6 H)	348	2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)-3-methoxybenzaldehyde Method 3 
36	(*S,Z*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-3-methoxybenzylidene) thiazolidine-2,4-dione 	7.89 (s, 1 H) 7.26 (m, 1 H) 7.10 (m, 2 H) 3.84 (s, 3 H) 3.41 - 3.29 (m, 7 H) 3.24 - 3.13 (m, 4 H) 2.18 (m, 1 H) 1.99 (m, 1 H)	348	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-3-methoxybenzaldehyde Method 4 
37	(*Z*)-5-(3-chloro-2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)benzylidene)thiazolidine-2,4-dione 	7.80 (s, 1 H) 7.50 (brs, 1 H) 7.38 (d, 1 H) 7.30 (brs, 1 H) 3.34-3.02 (m, 6 H) 1.26 - 1.09 (m, 6 H)	352	3-chloro-2-((3S,5R)-3,5-dimethylpiperazin-1-yl)benzaldehyde Method 5 

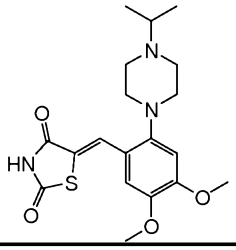
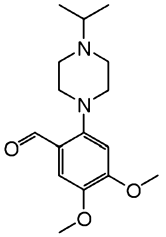
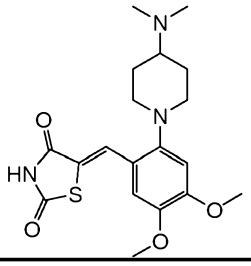
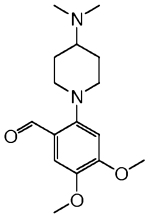
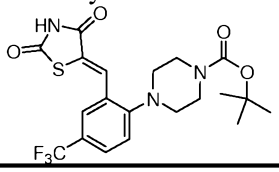
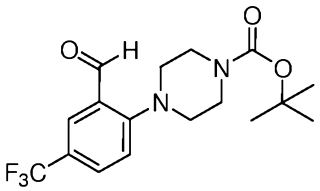
38	(*S,Z*)-5-(3-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione 	7.73 (s, 1 H) 7.52 - 7.47 (m, 2 H) 7.47 (s, 1 H) 7.33 - 7.31 (m, 1 H) 3.58 - 3.52 (m, 1 H) 3.48 (m, 1 H) 3.37 - 3.27 (m, 3 H) 2.56 (s, 6 H) 2.26 - 2.35 (m, 1 H) 2.08 (m, 1 H)	352	(*S*)-3-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde Method 6 
39	(*R,Z*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione 	7.75 (s, 1 H) 6.98 (s, 1 H) 6.68 (s, 1 H) 3.83 (s, 3 H) 3.72 (s, 3 H) 3.24 - 3.06 (m, 4 H) 2.50 (m, 1 H) 2.32 (s, 6 H) 2.12 (m, 1 H) 1.84 (m, 1 H)	378	(*R*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde Method 7 
40	(*S,Z*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione 	7.76 (s, 1 H) 6.98 (s, 1 H) 6.68 (s, 1 H) 3.83 (s, 3 H) 3.72 (s, 3 H) 3.26 – 3.01 (m, 5 H) 2.32 (s, 6 H) 2.15 – 2.09 (m, 1 H) 1.90 – 1.81 (m, 1 H)	378	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde Method 8 

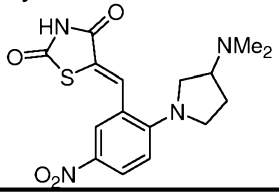
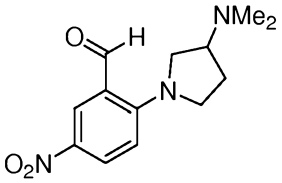
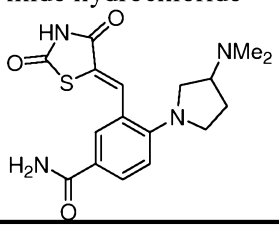
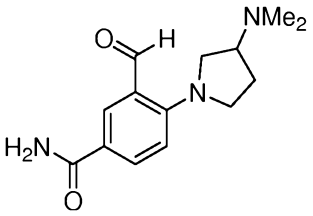
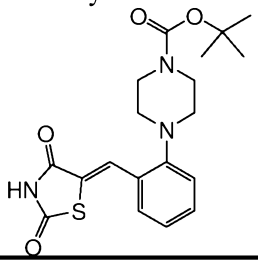
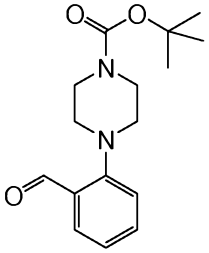
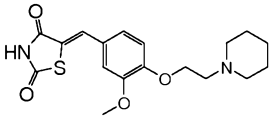
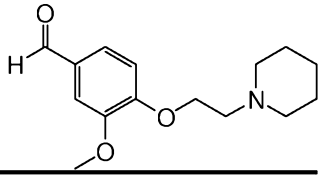
41	(5Z)-5-{2-[4-(hydroxymethyl)piperidin-1-yl]-4,5-dimethoxybenzylidene}-1-,3-thiazolidine-2,4-dione 	12.44 (brs, 1 H) 7.94 (s, 1 H) 7.05 - 6.87 (m, 1 H) 6.80 (s, 1 H) 4.54 (t, 1 H) 3.85 (s, 3 H) 3.76 (s, 3 H) 3.17 (d, 1 H) 3.03 (d, 2 H) 2.71 (t, 2 H) 1.75 (brs, 2 H) 1.56 - 1.26 (m, 3 H)	379	2-(4-(hydroxymethyl)piperidin-1-yl)-4,5-dimethoxybenzaldehyde Method 9 
42	(5Z)-5-[2-(4-hydroxypiperidin-1-yl)-4,5-dimethoxybenzylidene]-1,3-thiazolidine-2,4-dione 	12.50 (brs, 1 H) 8.02 (s, 1 H) 6.99 (s, 1 H) 6.92 - 6.82 (m, 1 H) 4.79 (d, 1 H) 3.90 (s, 3 H) 3.82 (s, 3 H) 3.74 - 3.58 (m, 1 H) 3.13 - 2.96 (m, 2 H) 2.88 - 2.71 (m, 2 H) 2.01 - 1.81 (m, 2 H) 1.78 - 1.58 (m, 2 H)	365	2-(4-hydroxypiperidin-1-yl)-4,5-dimethoxybenzaldehyde Method 10 
43	(5Z)-5-{2-[3-(dimethylamino)pyrrolidin-1-yl]-5-methoxybenzylidene}-1,3-thiazolidine-2,4-dione 	7.51 (s, 1 H) 7.03 (d, 1 H) 6.99 (d, 1 H) 6.84 (dd, 1 H) 3.72 (s, 3 H) 3.09 - 3.21 (m, 1 H) 2.82 - 3.09 (m, 4 H) 2.23 (s, 6 H) 2.06 (d, 1 H) 1.73 - 1.85 (m, 1 H)	348	2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methoxybenzaldehyde Method 11 

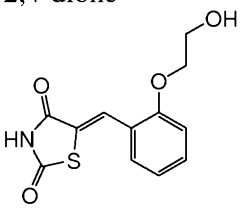
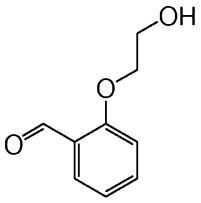
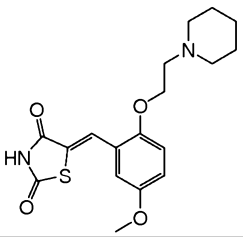
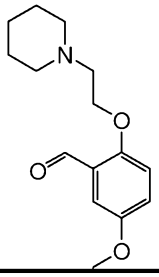
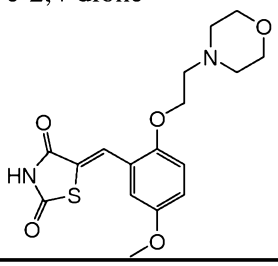
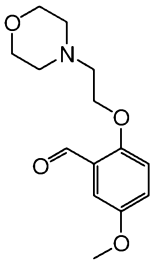
44	(5Z)-5-{2-[4-(dimethylamino)piperidin-1-yl]-5-methoxybenzylidene}-1,3-thiazolidine-2,4-dione 	7.59 (s, 1 H) 7.11 – 6.99 (m, 2 H) 6.85 (dd, 1 H) 3.75 (s, 3 H) 3.03 (m, 2 H) 2.64 - 2.54 (m, 2 H) 2.44 - 2.33 (m, 7 H) 1.91 (s, 2 H) 1.62 (dd, 2 H)	362	2-(4-(dimethylamino)piperidin-1-yl)-5-methoxybenzaldehyde Method 12 
45	(5Z)-5-[2-(3-hydroxypyrrolidin-1-yl)-4,5-dimethoxybenzylidene]-1,3-thiazolidine-2,4-dione 	12.32 (brs, 1 H) 7.88 (s, 1 H) 6.93 (s, 1 H) 6.66 (s, 1 H) 4.34 (brs, 1 H) 3.83 (s, 3 H) 3.72 (s, 3 H) 3.55 - 3.29 (m, 3 H) 3.22 (brs, 1 H) 2.90 (d, 1 H) 2.16 - 1.94 (m, 1 H) 1.84 (d, 1 H)	351	2-(3-hydroxypyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde Method 13 
46	(5Z)-5-(4,5-dimethoxy-2-pyrrolidin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione 	12.21 (brs, 1 H) 7.86 (s, 1 H) 6.94 (s, 1 H) 6.65 (s, 1 H) 3.83 (s, 3 H) 3.72 (s, 3 H) 3.12 (brs, 4 H) 1.90 (brs, 4 H)	335	4,5-dimethoxy-2-(pyrrolidin-1-yl)benzaldehyde Method 14 

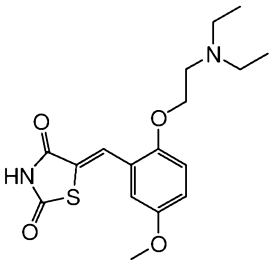
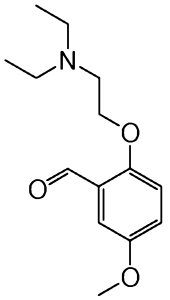
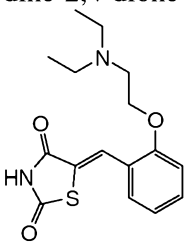
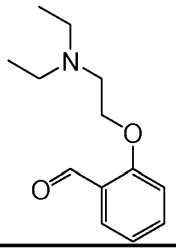
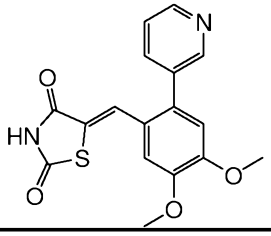
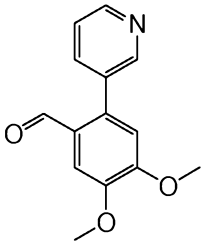
47	(5Z)-5-{2-[[2-(dimethylamino)ethyl](methyl)amino]benzylidene}-1,3-thiazolidine-2,4-dione 	7.62 (s, 1 H) 7.48 (d, 1 H) 7.32 (t, 1 H) 7.17 (d, 1 H) 7.10 (t, 1 H) 3.06 (t, 2 H) 2.86 - 2.62 (m, 5 H) 2.36 (s, 6 H)	306	2-((2-(dimethylamino)ethyl)(methyl)amino)benzaldehyde Method 15 
48	(5Z)-5-{2-[3-(dimethylamino)pyrrolidin-1-yl]benzylidene}-1,3-thiazolidine-2,4-dione 	7.52 (s, 1 H) 7.27 - 7.21 (m, 1 H) 7.14 - 7.05 (m, 1 H) 6.84 (d, 1 H) 6.77 (t, 1 H) 3.17 (s, 1 H) 3.16 - 3.09 (m, 1 H) 3.06 - 2.94 (m, 2 H) 2.86 - 2.77 (m, 1 H) 2.16 - 2.11 (m, 6 H) 2.03 - 1.92 (m, 1 H) 1.66 (dd, 1 H)	318	2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde Method 16 
49	(5Z)-5-{2-[4-(dimethylamino)piperidin-1-yl]benzylidene}-1,3-thiazolidine-2,4-dione 	7.64 (s, 1 H) 7.50 (d, 1 H) 7.35 - 7.27 (m, 1 H) 7.12 (t, 2 H) 3.22 (m, 2 H) 2.88 (m, 1 H) 2.68 (t, 2 H) 2.63 (s, 6 H) 2.04 (s, 2 H) 1.73 (td, 2 H)	332	2-(4-(dimethylamino)piperidin-1-yl)benzaldehyde Method 17 

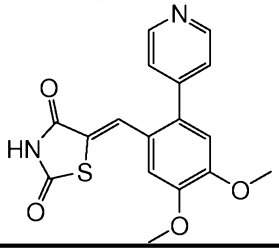
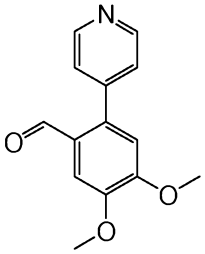
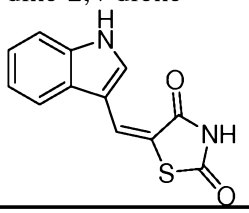
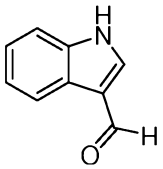
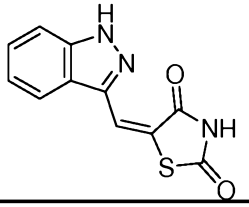
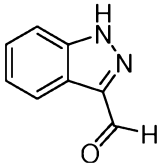
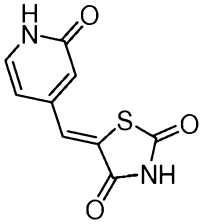
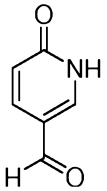
50	(5Z)-5-[2-(4-isopropylpiperazin-1-yl)benzylidene]-1,3-thiazolidine-2,4-dione 	7.80 (s, 1 H) 7.49 - 7.43 (m, 1 H) 7.43 - 7.39 (m, 1 H) 7.22 - 7.13 (m, 2 H) 2.99 - 2.88 (m, 5 H) 2.80 (s, 4 H) 1.13 - 1.04 (m, 6 H)	332	2-(4-isopropylpiperazin-1-yl)benzaldehyde Method 18 
51	(5Z)-5-{2-[[2-(dimethylamino)ethyl](methyl)amino]-4,5-dimethoxybenzylidene}-1,3-thiazolidine-2,4-dione 	7.78 (s, 1 H) 7.02 (s, 1 H) 6.85 (s, 1 H) 3.83 (s, 3 H) 3.76 (s, 3 H) 3.11 - 2.98 (m, 2 H) 2.76 - 2.65 (m, 5 H) 2.37 (s, 6 H)	364	2-((2-(dimethylamino)ethyl)(methyl)amino)-4,5-dimethoxybenzaldehyde Method 19 
52	(5Z)-5-{2-[3-(dimethylamino)pyrrolidin-1-yl]-4,5-dimethoxybenzylidene}-1,3-thiazolidine-2,4-dione 	7.76 (s, 1 H), 6.98 (s, 1 H), 6.68 (s, 1 H), 3.83 (s, 3 H), 3.72 (s, 3 H), 3.25 (m, 1 H), 3.13 (m, 2 H), 3.06 (m, 2 H), 2.32 (s, 6 H), 2.15 – 2.09 (m, 1 H) 1.90 – 1.81 (m, 1 H)	378	2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde Method 20 

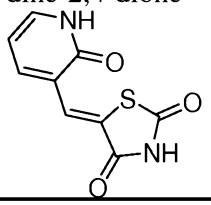
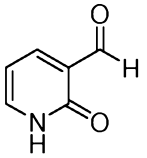
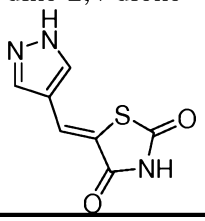
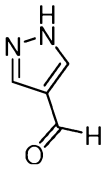
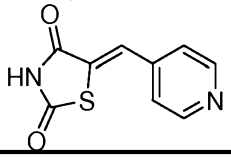
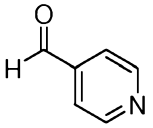
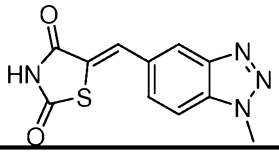
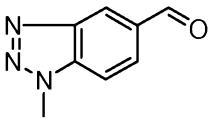
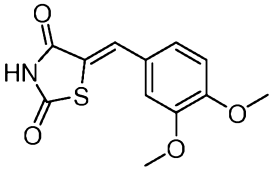
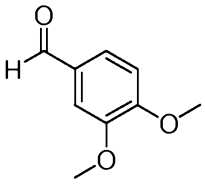
53	(5Z)-5-{2-(4-isopropylpiperazin-1-yl)-4,5-dimethoxybenzylidene}-thiazolidine-2,4-dione 	7.86 (s, 1 H) 6.95 (s, 1 H) 6.77 (s, 1 H) 3.81 (s, 3 H) 3.76 - 3.67 (m, 3 H) 2.91 - 2.79 (m, 5 H) 2.71 (s, 4 H) 1.08 - 1.00 (m, 6 H)	392	2-(4-isopropylpiperazin-1-yl)-4,5-dimethoxybenzaldehyde Method 21 
54	(5Z)-5-{2-(4-(dimethylamino)piperidin-1-yl)-4,5-dimethoxybenzylidene}-thiazolidine-2,4-dione 	7.48 (s, 1 H) 6.82 (s, 1 H) 6.51 (s, 1 H) 3.58 (s, 3 H) 3.51 (s, 3 H) 2.87 (d, 2 H) 2.47 (m, 3 H) 2.35 (s, 6 H) 1.79 (d, 2 H) 1.49 (d, 2 H)	392	2-(4-(dimethylamino)piperidin-1-yl)-4,5-dimethoxybenzaldehyde Method 22 
55	(Z)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazine-1-carboxylate 	12.65 (s, 1 H) 7.82 (s, 1 H) 7.72 (s, 1 H) 7.53 (s, 1 H) 3.59 - 3.50 (m, 1 H) 3.38 - 3.30 (m, 4 H) 2.56 (s, 6 H) 2.31 - 2.28 (m, 1 H) 2.09 - 2.01 (m, 1 H)	458	*tert*-butyl 4-(2-formyl-4-(trifluoromethyl)phenyl)piperazine-1-carboxylate Method 23 

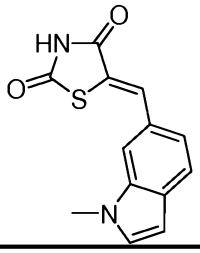
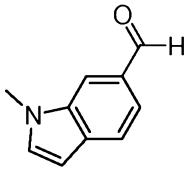
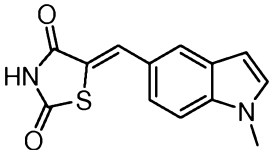
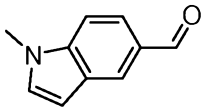
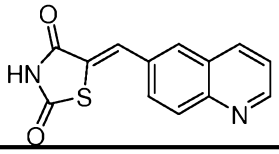
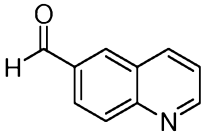
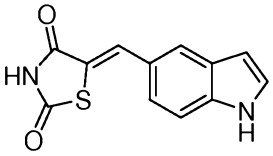
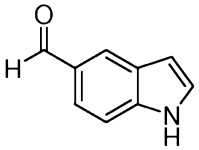
56	(Z)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.64 (s, 1 H) 8.22 (d, 1 H) 8.12 (d, 1 H) 7.95 (d, 1 H) 7.04 (d, 1 H) 3.95 - 3.90 (m, 1 H) 3.70 - 3.65 (m, 2 H) 3.56 - 3.51 (m, 2 H) 2.79 (s, 6 H) 2.41 - 2.35 (m, 1 H) 2.34 - 2.22 (m, 1 H)	363	2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzaldehyde Method 24 
57	(Z)-4-(3-(dimethylamino)pyrrolidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzamide hydrochloride 	12.47 (s, 1 H) 7.92 - 7.84 (m, 4 H) 7.23 (s, 1 H) 7.03 (d, 1 H) 3.98 - 3.91 (m, 1 H) 3.53 - 3.49 (m, 2 H) 3.46 - 3.39 (m, 2 H) 2.79 (s, 6 H) 2.34 - 2.19 (m, 2 H)	361	4-(3-(dimethylamino)pyrrolidin-1-yl)-3-formylbenzamide Method 25 
58	(Z)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carboxylate 	12.55 (s, 1 H) 7.92 (s, 1 H) 7.46 – 7.44 (m, 2 H) 7.21 –7.18 (m, 2 H) 3.48 (brs, 4 H) 2.86 (brs, 4 H) 1.43 (s, 9 H)	389	*tert*-butyl 4-(2-formylphenyl)piperazine-1-carboxylate Method 26 
59	(Z)-5-(3-methoxy-4-(2-(piperidin-1-yl)ethoxy)benzylidene)thiazolidine-2,4-dione 	7.78 (s, 1 H) 7.27 (s, 1 H) 7.21 (s, 2 H) 4.47 (t, 2 H) 3.84 (s, 3 H) 3.49 (t, 4 H) 3.04 (brs, 2 H) 1.80 (d, 4 H) 1.64 (brs, 1 H) 1.43 (brs, 1 H)	363	3-methoxy-4-(2-(piperidin-1-yl)ethoxy)benzaldehyde Commercial 

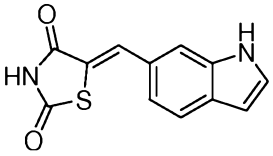
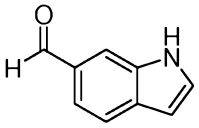
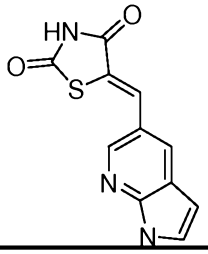
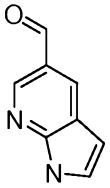
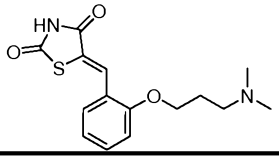
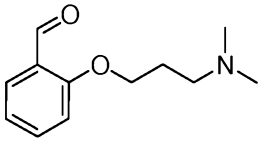
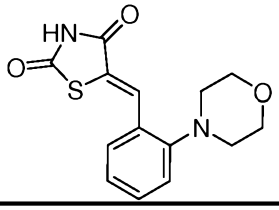
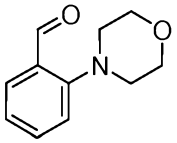
60	(Z)-5-(2-(2-hydroxyethoxy)benzylidene)thiazolidine-2,4-dione 	12.58 (brs, 1 H) 8.06 (s, 1 H) 7.57 - 7.32 (m, 2 H) 7.26 - 7.03 (m, 2 H) 4.95 (brs, 1 H) 4.13 (t, 2 H) 3.77 (brs, 2 H)	266	2-(2-hydroxyethoxy)benzaldehyde Commercial 
61	(Z)-5-(5-methoxy-2-(2-(piperidin-1-yl)ethoxy)benzylidene)thiazolidine-2,4-dione 	7.80 (s, 1 H) 7.10 (d, 1 H) 7.04 – 6.95 (m, 2 H) 4.22 (t, 2 H) 3.75 (s, 3 H) 3.07 (t, 2 H) 2.84 (s, 4 H) 1.62 (dq, 4 H) 1.46 (d, 2 H)	363	5-methoxy-2-(2-(piperidin-1-yl)ethoxy)benzaldehyde Method 27 
62	(Z)-5-(5-methoxy-2-(2-morpholinoethoxy)benzylidene)thiazolidine-2,4-dione 	7.99 (s, 1 H) 7.22 - 7.10 (m, 1 H) 7.09 – 6.97 (m, 1 H) 6.91 (d, 1 H) 4.17 (t, 2 H) 3.76 (s, 3 H) 3.64 - 3.51 (m, 4 H) 2.75 (t, 2 H) 2.51 - 2.62 (m, 4 H)	365	5-methoxy-2-(2-morpholinoethoxy)benzaldehyde Method 28 

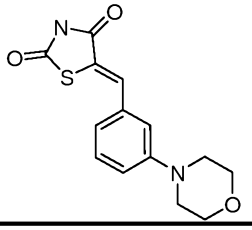
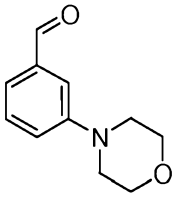
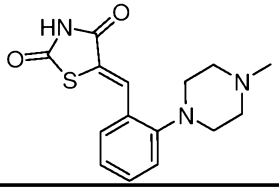
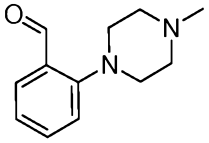
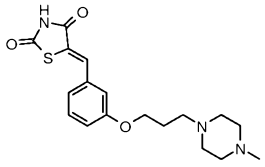
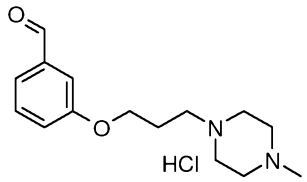
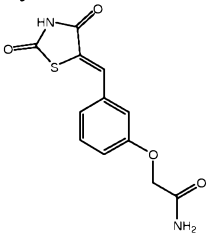
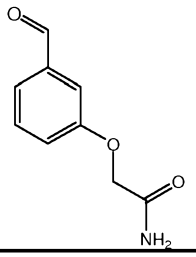
63	(Z)-5-(2-(2-(diethylamino)ethoxy)-5-methoxybenzylidene)thiazolidine-2,4-dione 	7.77 (s, 1 H) 7.08 - 7.05 (m, 1 H) 7.03 – 6.95 (m, 2 H) 4.19 (t, 2 H) 3.75 (s, 3 H) 3.25 - 3.14 (m, 2 H) 2.95 (q, 4 H) 1.17 - 1.08 (m, 6 H)	352	2-(2-(diethylamino)ethoxy)-5-methoxybenzaldehyde Method 29 
64	(Z)-5-(2-(2-(diethylamino)ethoxy)benzylidene)thiazolidine-2,4-dione 	7.84 (s, 1 H) 7.47 (d, 1 H) 7.43 - 7.35 (m, 1 H) 7.14 - 7.04 (m, 2 H) 4.24 (t, 2 H) 3.20 (m, 2 H) 2.90 (q, 4 H) 1.13 (t, 6 H)	321	2-(2-(diethylamino)ethoxy)benzaldehyde Method 30 
65	(Z)-5-(4,5-dimethoxy-2-(pyridin-3-yl)benzylidene)thiazolidine-2,4-dione 	12.55 (brs, 1 H) 8.73 - 8.61 (m, 1 H) 8.58 (brs, 1 H) 7.81 (dd, 1 H) 7.53 (dd, 1 H) 7.46 (s, 1 H) 7.13 (d, 2 H) 3.89 (d, 6 H)	343	4,5-dimethoxy-2-(pyridin-3-yl)benzaldehyde Method 31 

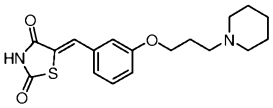
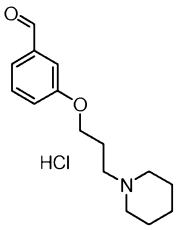
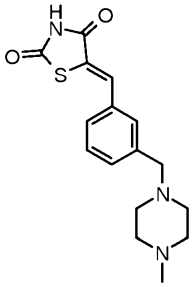
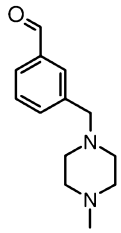
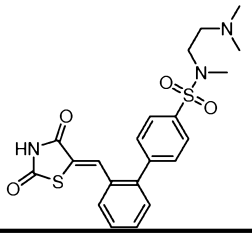
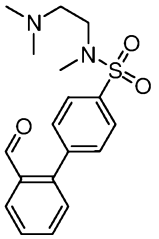
66	(Z)-5-(4,5-dimethoxy-2-(pyridin-4-yl)benzylidene)thiazolidine-2,4-dione 	12.58 (brs, 1 H) 8.67 (d, 2 H) 7.48 (d, 1 H) 7.41 (d, 2 H) 7.12 (d, 2 H) 3.89 (s, 6 H)	343	4,5-dimethoxy-2-(pyridin-4-yl)benzaldehyde Method 32 
67	(Z)-5-((1H-indol-3-yl)methylene)thiazolidine-2,4-dione 	7.21 (dddd, 2 H) 7.50 (d, 1 H) 7.71 (d, 1 H) 7.87 (d, 1 H) 7.99 (s, 1 H) 12.07 (brs, 2 H)	245	1H-indole-3-carbaldehyde Commercial 
68	(Z)-5-((1H-indazol-3-yl)methylene)thiazolidine-2,4-dione 	7.28 (t, 1 H) 7.52 - 7.39 (m, 1 H) 7.64 (d, 1 H) 8.22 - 8.03 (m, 2 H) 12.41 (d, 1 H) 13.96 (s, 1 H)	246	1H-indazole-3-carbaldehyde Commercial 
69	(Z)-5-((6-oxo-1,6-dihydropyridin-3-yl)methylene)thiazolidine-2,4-dione 	11.99 (brs, 1 H) 7.74 (brs, 1 H) 7.69 - 7.58 (m, 1 H) 7.27 (s, 1 H) 6.43 (d, 1 H)	223	6-oxo-1,6-dihydropyridine-3-carbaldehyde Commercial 

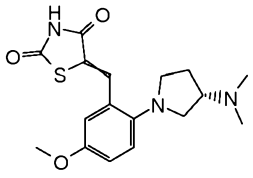
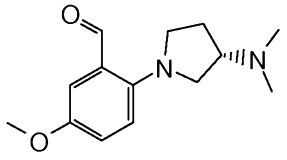
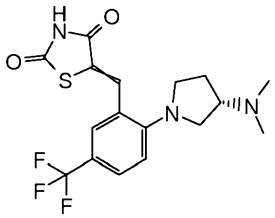
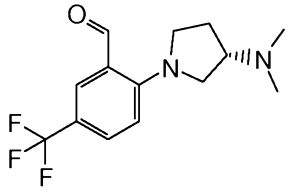
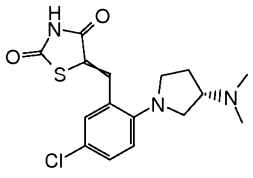
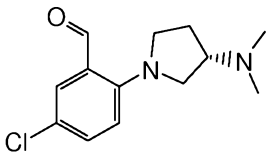
70	(*Z*)-5-((2-oxo-1,2-dihydropyridin-3-yl)methylene)thiazolidine-2,4-dione 	12.43 (brs, 1 H) 12.16 (brs, 1 H) 7.73 (s, 1 H) 7.69 (dd, 1 H) 7.57 (d, 1 H) 6.38 (t, 1 H)	223	2-oxo-1,2-dihydropyridine-3-carbaldehyde Commercial 
71	(*Z*)-5-((1H-pyrazol-4-yl)methylene)thiazolidine-2,4-dione 	13.51 (brs, 1 H) 12.37 (brs, 1 H) 8.20 (s, 1 H) 7.82 (s, 1 H) 7.74 (s, 1 H)	196	1*H*-pyrazole-4-carbaldehyde Commercial 
72	(*Z*)-5-(pyridin-4-ylmethylene)thiazolidine-2,4-dione 	12.61 (brs, 1 H) 8.71 (d, 2 H) 7.74 (s, 1 H) 7.53 (d, 2 H)	207	4-pyridinecarboxaldehyde Commercial 
73	(5*Z*)-5-[(1-methyl-1H-1,2,3-benzotriazol-5-yl)methylene]-1,3-thiazolidine-2,4-dione 	12.65 (brs, 1 H) 8.28 (s, 1 H) 8.00-7.98 (m, 2 H) 7.76 (d, 1 H) 4.33 (s, 3 H)	259	1-methyl-1H-benzo[d][1,2,3]triazole-5-carbaldehyde Commercial 
74	(5*Z*)-5-(3,4-dimethoxybenzylidene)-1,3-thiazolidine-2,4-dione 	12.51 (brs, 1 H) 7.74 (s, 1 H) 7.19 – 7.09 (m, 3 H) 3.82 (s, 3 H) 3.80 (s, 3 H)	266	3,4-dimethoxybenzaldehyde Commercial 

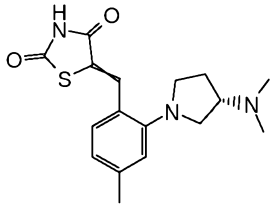
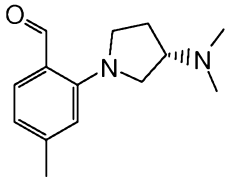
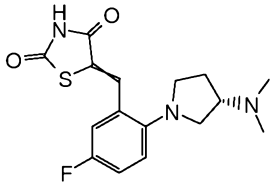
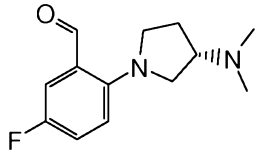
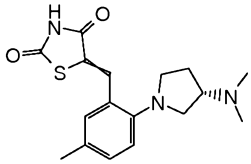
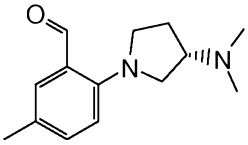
75	(5*Z*)-5-[(1-methyl-1H-indol-6-yl)methylene]-1,3-thiazolidine-2,4-dione 	12.49 (brs, 1 H) 7.92 (s, 1 H) 7.68 (d, 1 H) 7.54 (s 1 H) 7.25 (d, 1 H) 6.50 (s, 1 H) 3.84 (s, 3 H)		1-methyl-1H-indole-6-carbaldehyde Commercial 
76	(5*Z*)-5-[(1-methyl-1H-indol-5-yl)methylene]-1,3-thiazolidine-2,4-dione 	12.45 (brs, 1 H) 7.90 (s, 1 H) 7.84 (d, 1 H) 7.59 (d, 1 H) 7.44 (d, 1 H) 7.38 (d 1 H) 6.57 (d, 1 H) 3.82 (s, 3 H)	259	1-methyl-1H-indole-5-carbaldehyde Commercial 
77	(5*Z*)-5-(quinolin-6-ylmethylene)-1,3-thiazolidine-2,4-dione trifluoroacetate 	12.70 (brs, 1 H) 8.97 (d, 1 H) 8.51 (d, 1 H) 8.24 (s, 1 H) 8.12 (d, 1 H) 7.96 – 7.93 (m, 2 H) 7.64 – 7.61 (m, 1 H)	257	quinoline-6-carbaldehyde Commercial 
78	(5*Z*)-5-(1*H*-indol-5-ylmethylene)-1,3-thiazolidine-2,4-dione 	12.43 (brs, 1 H) 11.44 (brs, 1 H) 7.85 (d, 1 H) 7.53 – 7.51 (m, 2 H) 7.45 – 7.44 (m, 1 H) 7.33 (d, 1 H) 6.56 (s, 1 H)	245	1*H*-indole-5-carbaldehyde Commercial 

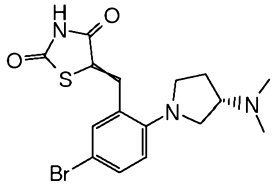
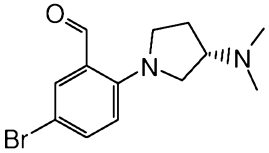
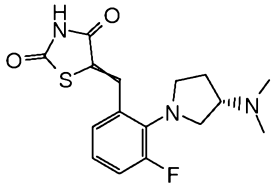
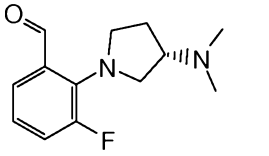
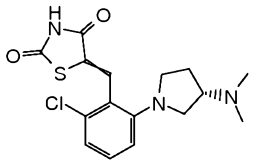
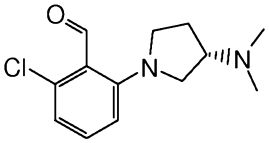
79	(5*Z*)-5-(1*H*-indol-6-ylmethylene)-1,3-thiazolidine-2,4-dione trifluoroacetate 	12.47 (brs, 1 H) 11.48 (brs, 1 H) 7.90 (s, 1 H) 7.69 – 7.66 (m, 2 H) 7.55 – 7.52 (m, 1 H) 7.23 (d, 1 H) 6.51 (s, 1 H)	245	1*H*-indole-6-carbaldehyde Commercial 
80	(5*Z*)-5-(1H-pyrrolo[2,3-b]pyridin-5-ylmethylene)-1,3-thiazolidine-2,4-dione 	12.02 (brs, 1 H) 8.49 (d, 1 H) 8.15 (d, 1 H) 7.92 (s, 1 H) 7.58 (t, 1 H) 6.59 (brs, 1 H)	246	1*H*-pyrrolo[2,3-b]pyridine-5-carbaldehyde Commercial 
81	(5Z)-5-{2-[3-(dimethylamino)propoxy]benzylidene}-1,3-thiazolidine-2,4-dione 	8.16 (s, 1 H) 7.76 (s, 1 H) 7.48 (d, 1 H) 7.34 (s, 1 H) 7.08 (d, 1 H) 4.11 (t, 2 H) 2.86 (t, 2 H) 2.53 (s, 6 H) 2.10 – 1.98 (m, 2 H)	307	2-[3-(dimethylamino)propoxy]benzaldehyde Commercial 
82	(5*Z*)-5-(2-morpholin-4-ylbenzylidene)-1,3-thiazolidine-2,4-dione 	7.89 (s, 1 H) 7.46 (d, 1 H) 7.45 - 7.41 (m, 1 H) 7.22 - 7.14 (m, 2 H) 3.80 - 3.69 (m, 4 H) 2.93 - 2.82 (m, 4 H)	291	2-morpholin-4-ylbenzaldehyde Commercial 

83	(5Z)-5-(3-morpholin-4-ylbenzylidene)-1,3-thiazolidine-2,4-dione trifluoroacetate 	12.58 (brs, 1 H) 7.74 (s, 1 H) 7.37 (t, 1 H) 7.12 (s, 1 H) 7.07 (dd, 1 H) 7.00 (d, 1 H) 3.79 - 3.69 (m, 4 H) 3.20 - 3.09 (m, 4 H)	290	3-morpholin-4-ylbenzaldehyde Commercial 
84A	(5Z)-5-[2-(4-methylpiperazin-1-yl)benzylidene]-1,3-thiazolidine-2,4-dione 	7.78 (s, 1 H) 7.46 (d, 1 H) 7.42 - 7.35 (m, 1 H) 7.19 - 7.11 (m, 2 H) 2.94 (t, 4 H) 2.70 (brs, 4 H) 2.40 (s, 3 H)	304	2-(4-methylpiperazin-1-yl)benzaldehyde Commercial 
84B	(Z)-5-(3-(3-(4-methylpiperazin-1-yl)propoxy)benzylidene)thiazolidine-2,4-dione 	11.37 (brs, 1 H) 7.54 (s, 1 H) 7.38 (t, 1H) 7.12 (m, 2 H), 6.96 (m, 1 H) 4.58 (s, 3 H) 4.05 (t, 2 H) 3.00 - 2.55 (m, 10 H) 1.93 (m, 2 H)	362	3-(3-(4-methylpiperazin-1-yl)propoxy)benzaldehyde hydrochloride 
84C	(Z)-2-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)phenoxy)acetamide 	12.62 (s, 1 H) 7.73 (s, 1 H) 7.60 (s, 1 H) 7.44 (t, 1 H) 7.41 (s, 1 H) 7.19 (d, 1 H) 7.14 (m, 1 H) 7.05 (dd, 1 H) 4.48 (s, 2 H)	279	2-(3-formylphenoxy)acetamide 

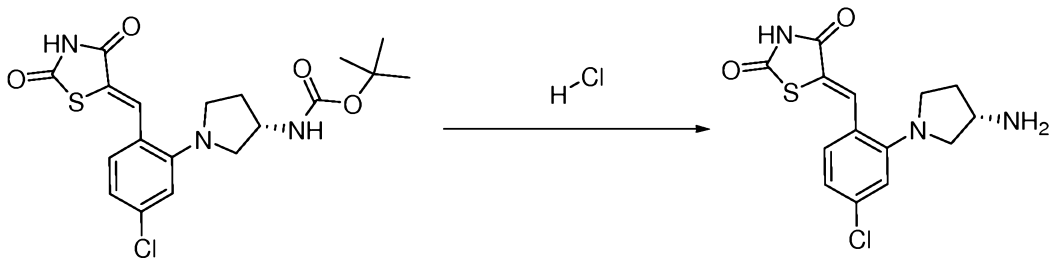
84D	(*Z*)-5-(3-(3-(piperidin-1-yl)propoxy)benzylidene)thiazolidine-2,4-dione 	7.30 (t, 1 H) 7.24 (s, 1 H) 7.08 (m, 2 H) 6.85 (dd, 1 H) 4.01 (t, 2 H) 2.45 (t, 2 H) 2.40 (m, 4 H) 1.88 (m, 2 H) 1.50 (m, 4 H) 1.38 (m, 2 H)	347	3-(3-(piperidin-1-yl)propoxy)benzaldehyde hydrochloride 
84E	(*Z*)-5-(3-((4-methylpiperazin-1-yl)methyl)benzylidene)thiazolidine-2,4-dione 	7.59 (s, 1 H) 7.51 (s, 1 H) 7.46 (m, 2 H) 7.34 (m, 1 H) 3.59 (s, 2 H) 2.96 (m, 4 H) 2.59 (m, 4 H) 2.58 (s, 3 H)	318	3-((4-methylpiperazin-1-yl)methyl)benzaldehyde 
84F	(*Z*)-*N*-(2-(dimethylamino)ethyl)-2'-((2,4-dioxothiazolidin-5-ylidene)methyl)-*N*-methylbiphenyl-4-sulfonamide 	7.90 (d, 2 H) 7.69 (d, 1 H) 7.65-7.49 (m, 4 H) 7.49 - 7.40 (m, 1 H) 7.31 (s, 1 H) 3.24 (t, 2 H) 2.83 (t, 2 H) 2.78 (s, 3 H) 2.48 (s, 6 H)	445	*N*-(2-(dimethylamino)ethyl)-2'-formyl-*N*-methylbiphenyl-4-sulfonamide Method 32B 

84G	(*S*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methoxybenzylidene)thiazolidine-2,4-dione 		348	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methoxybenzaldehyde Method 104 
84H	(*S*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 	12.55 (s, 1 H) 11.25 (brs, 1 H) 7.95 (s, 1 H) 7.78 (s, 1 H) 7.60 (m, 1 H), 7.15 (m, 1 H) 4.00 (m, 1 H) 3.65 (m, 2 H) 3.40 (m, 1 H) 3.32 (m, 1 H) 2.80 (s, 6 H) 2.35 (m, 1 H) 2.20 (m, 1 H)	386	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzaldehyde Method 105 
84I	(*S*)-5-(5-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione 	12.55 (s, 1 H) 7.81 (s, 1H), 7.93 (m, 2H), 7.12 (m, 1H), 3.90(m, 1H), 3.45-3.30 (m, 2H), 3.29 (m, 1H), 3.15 (m, 1H), 2.80 (s, 6H), 2.35 (m, 1H), 2.20 (m, 1H)	352	(*S*)-5-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde Method 106 

84J	(*S*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-4-methylbenzylidene)thiazolidine-2,4-dione 		332	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-4-methylbenzaldehyde Method 107 
84K	(*S*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-fluorobenzylidene)thiazolidine-2,4-dione 	12.55 (s, 1 H) 11.40 (s, 1 H) 7.80 (s, 1 H) 7.30-7.15 (m, 3 H) 3.92 (m, 1 H) 3.45 (m, 1 H) 3.35 (m, 1 H) 3.18 (m, 1 H) 3.15 (m, 1 H) 3.80 (d, 6 H) 2.30 (m, 1 H), 2.20 (m, 1H)	336	(S)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-fluorobenzaldehyde Method 108 
84L	(*S*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methylbenzylidene)thiazolidine-2,4-dione 		332	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methylbenzaldehyde Method 109 

84M	(*S*)-5-(5-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione 		397	(*S*)-5-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde Method 110 
84N	(*S*)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-3-fluorobenzylidene)thiazolidine-2,4-dione 	12.55 (s, 1 H) 10.34 (s, 1 H) 7.87 (d, 1H) 7.33-7.21 (m, 3 H) 3.93 (m, 1 H) 3.40 (m, 2 H) 3.25 (m, 1 H) 3.18 (m, 1 H) 2.79 (s, 6 H) 2.26 (m, 1H) 2.12 (m, 1H)	336	(S)-2-(3-(dimethylamino)pyrrolidin-1-yl)-3-fluorobenzaldehyde Method 111 
84O	(*S*)-5-(2-chloro-6-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione 		352	(*S*)-2-chloro-6-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde Method 112 

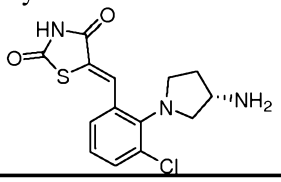
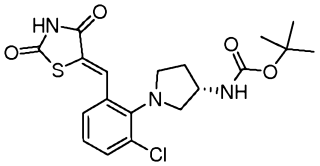
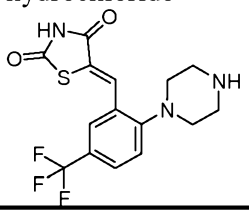
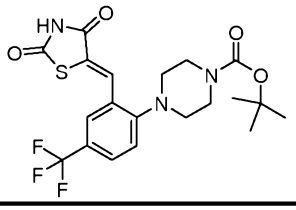
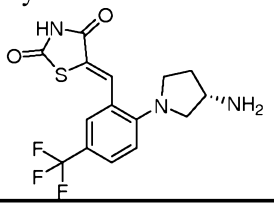
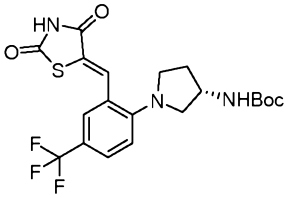
Example 85:

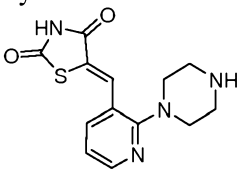
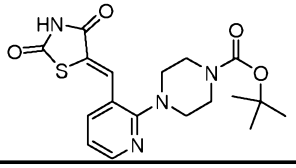
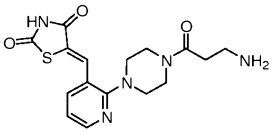
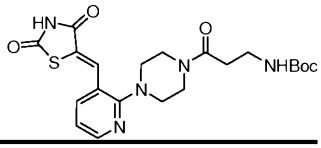
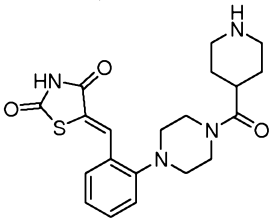
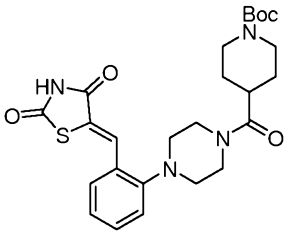


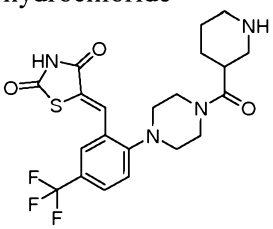
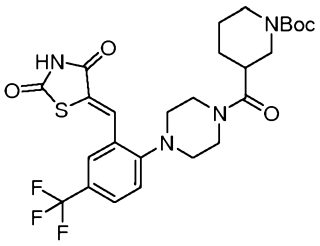
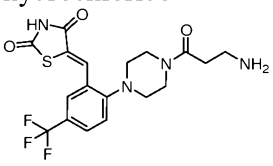
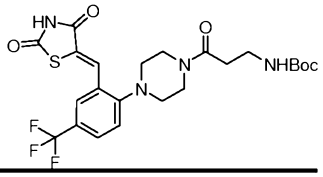
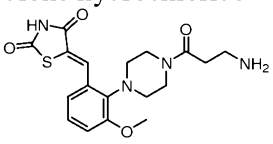
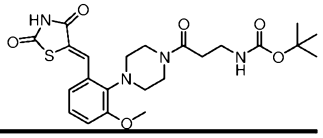
(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride:

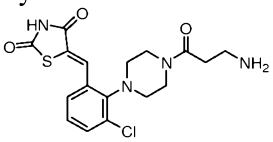
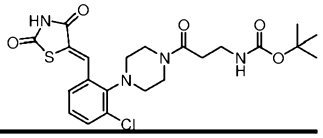
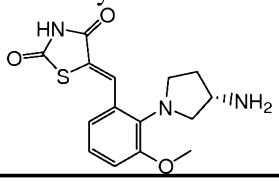
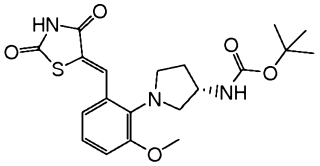
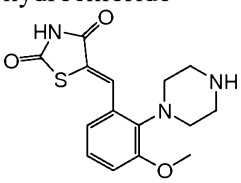
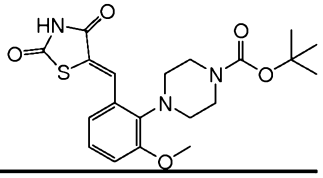
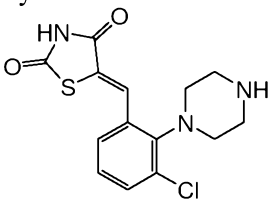
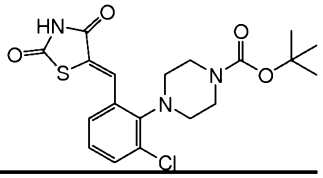
A 100 mL round bottom flask was charged with a magnetic stir bar, (*S,Z*)-*tert*-butyl1-(5-chloro-2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate (Method 33) (1.300 g, 3.07 mmol), MeOH (10.22 ml), and a 1N sol'n of HCl in diethyl ether (2.294 ml, 46.00 mmol). The reaction mixture was allowed to stir overnight at rt before being conc. *in vacuo* to afford the product as its hydrochloride salt. This material was dissolved in DMSO and purified via reverse phase HPLC to afford fractions that were conc. *in vacuo*, suspended in methanol (~ 5 mL) and 1N HCl in diethyl ether (~2 mL). This mixture was conc. *in vacuo* to afford (*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride (0.710 g, 64.3 %). ^{1}H NMR (300 MHz, DMSO-D6) δ ppm 12.51 (s, 1 H) 8.36 (s, 2 H) 7.85 (s, 1 H) 7.35 (d, 1 H) 6.96 (dd, 2 H) 3.90 - 3.75 (m, 1 H) 3.55- 3.47 (m, 1 H) 3.40 (dd, 1 H) 3.31 - 3.21 (m, 1 H) 3.18 - 3.10 (m, 1 H) 2.29 - 2.18 (m, 1 H) 2.10 - 1.96 (m, 1 H); *m/z* 325.

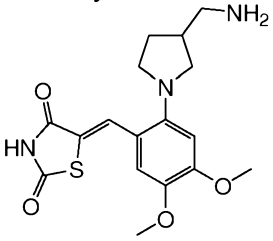
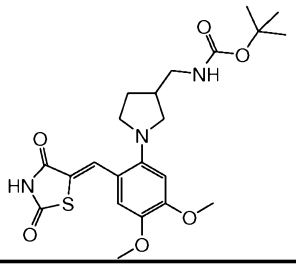
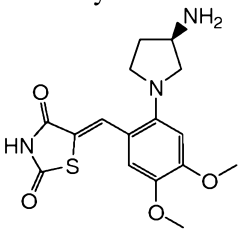
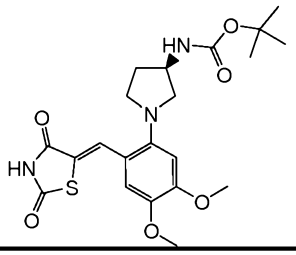
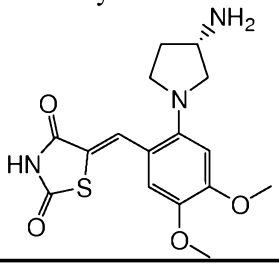
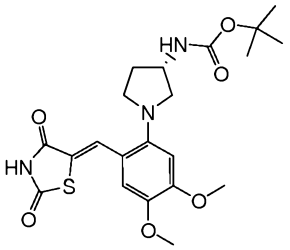
The following examples were prepared by the procedure of Example 85, using the appropriate starting materials. The following parent compounds obtained after chromatography may be converted to their corresponding hydrochloride salt in a manner similar as described in example 85, or similar procedure.

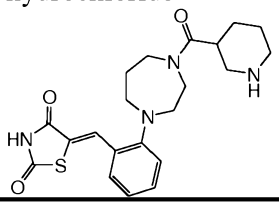
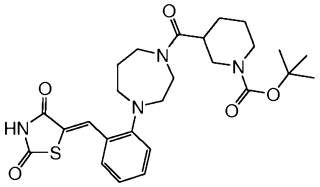
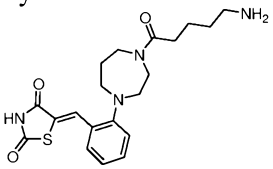
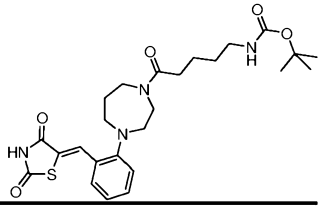
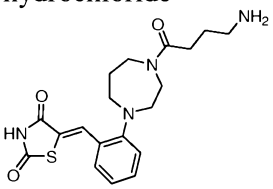
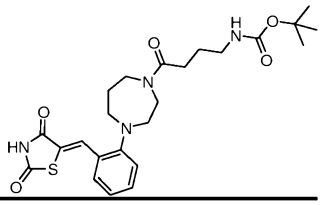
Ex.	Compound	^{1}H NMR	m/z	SM
86	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.69 (s, 1 H) 8.35 (brs, 2 H) 7.94 (s 1 H) 7.57 (d, 1 H) 7.41 - 7.35 (m, 2 H) 3.95 - 3.88 (m, 1 H) 3.53 - 3.26 (m, 4 H) 2.37 - 2.31 (m, 1 H) 2.08 - 2.01 (m, 1 H)	324	(*S,Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate Method 34 
87	(*Z*)-5-(2-(piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.69 (s, 1 H) 9.32 (brs, 2 H) 7.79 (d, 1 H) 7.71 (d, 2 H) 7.37 (d, 1 H) 3.23 (s, 8 H)	358	(*Z*)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazine-1-carboxylate Method 35 
88	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.53 (s, 1 H) 8.17 (brs, 2 H) 7.95 (s, 1 H) 7.65 (s, 1 H) 7.59 (d 1 H) 7.05 (d, 1 H) 3.90 - 3.81 (m, 1 H) 3.56 (q, 1 H) 3.47 - 3.35 (m, 2 H) 3.18 (dd, 1 H) 2.33 - 2.18 (m, 1 H) 2.09 - 1.99 (m, 1 H)	358	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)pyrrolidin-3-ylcarbamate Method 36 

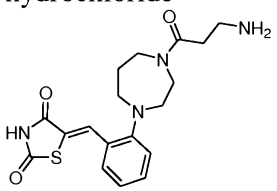
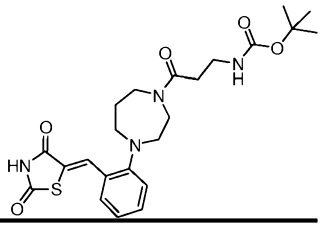
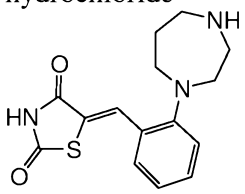
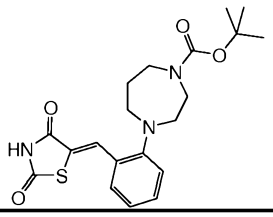
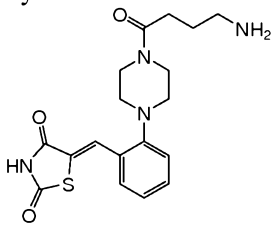
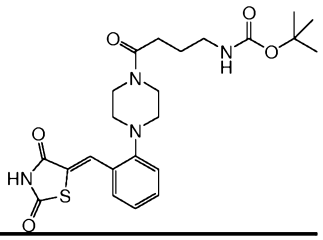
89	(Z)-5-((2-(piperazin-1-yl)pyridin-3-yl)methylene)thiazolidine-2,4-dione hydrochloride 	12.65 (s, 1 H) 8.39 (s, 1 H) 8.33 (d, 1 H) 7.83 (d, 1 H) 7.63 (s, 1 H) 7.15 (dd, 1 H) 3.41 (brs, 4 H) 3.17 (brs, 4 H)	291	(Z)-*tert*-butyl 4-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)pyridin-2-yl)piperazine-1-carboxylate Method 37 
90	(Z)-5-((2-(4-(3-aminopropanoyl)piperazin-1-yl)pyridin-3-yl)methylene)thiazolidine-2,4-dione trifluoroacetate 	12.60 (s, 1 H) 8.32 (d, 1 H) 7.82 (s, 1 H) 7.68 (s, 1 H) 7.63 (brs, 2 H) 7.12 (dd, 1 H) 3.57 (d, 4 H) 3.17 (d, 4 H) 3.00 (q, 2 H) 2.70 (t, 2 H)	362	(Z)-*tert*-butyl 3-(4-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)pyridin-2-yl)piperazin-1-yl)-3-oxopropylcarbamate Method 38 
91	(Z)-5-(2-(4-(piperidine-4-carbonyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione 	9.00 (brs, 1 H) 8.67 (brs, 1 H) 8.18 (s, 1 H) 7.57 - 7.52 (m, 1 H) 7.30 -7.16 (m, 1 H) 3.71 (s, 1 H) 3.63 (s, 1 H) 3.34 (s, 3 H) 3.31 - 3.22 (m, 2 H) 3.13 (s, 3 H) 3.01 -2.87 (m, 5 H) 1.85 - 1.77 (m, 4 H)	401	(Z)-*tert*-butyl 4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)piperidine-1-carboxylate Method 39 

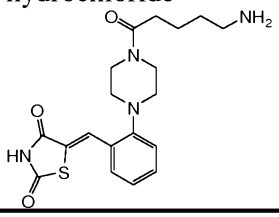
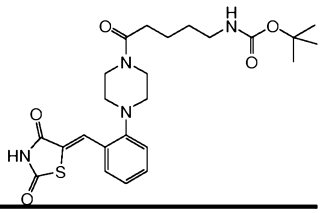
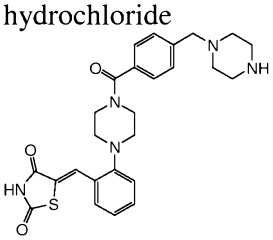
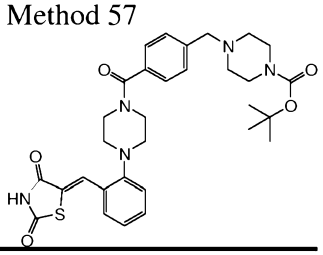
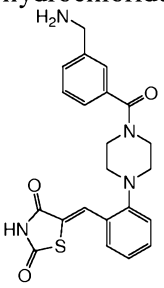
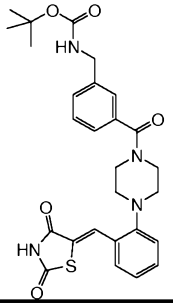
92	(Z)-5-(2-(4-(piperidine-3-carbonyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.68 (s, 1 H) 8.87 (s, 1 H) 7.78 - 7.69 (m, 3 H) 7.32 (d, 1 H) 3.68 - 3.64 (m, 8 H) 3.38 (tt, 1 H) 3.13 - 2.98 (m, 4 H) 1.75 - 1.56 (m, 4 H)	469	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazine-1-carbonyl)piperidine-1-carboxylate Method 40 
93	(Z)-5-(2-(4-(3-aminopropanoyl)piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.67 (s 1 H) 7.93 (brs, 2 H) 7.78 - 7.68 (m, 3 H) 7.32 (d, 1 H) 3.69 - 3.59 (m, 8 H) 3.00 - 2.74 (m, 4 H)	429	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazin-1-yl)-3-oxopropylcarbamate Method 41 
94	(Z)-5-(2-(4-(3-aminopropanoyl)piperazin-1-yl)-3-methoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.53 (brs, 1 H) 8.21 (s, 1 H), 7.58 (brs, 3 H), 7.24 (t, 1 H) 7.11 (d, 1 H) 7.00 (d, 1 H) 3.75 (s, 3 H) 3.35 (brs, 4 H) 3.09 - 2.85 (m, 4 H) 2.65 (brs, 2 H)	391	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)piperazin-1-yl)-3-oxopropylcarbamate Method 42 

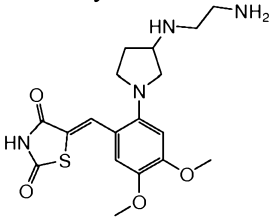
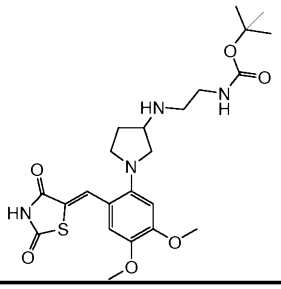
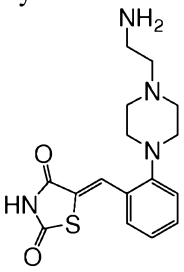
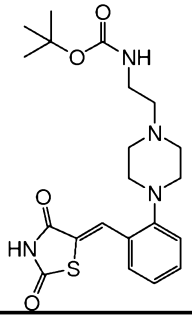
95	(Z)-5-(2-(4-(3-aminopropanoyl)piperazin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.69 (brs, 1 H) 8.12 (s, 1 H) 7.67 (brs, 2 H) 7.55 (dd, 1 H) 7.49 - 7.40 (m, 1 H) 7.35 (t, 1 H) 4.17 (brs, 1 H) 3.75 (brs, 1 H) 3.35 (brs, 3 H) 3.13 - 2.84 (m, 5 H) 2.74 (brs, 2 H)	395	(*Z*)-*tert*-butyl 3-(4-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)-3-oxopropylcarbamate Method 43 
96	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-methoxybenzylidene) thiazolidine-2,4-dione hydrochloride 	12.43 (s, 1 H) 7.94 (s, 1 H) 7.86 (brs, 1 H) 7.16 (t, 1 H) 7.05 (d, 1 H) 6.91 (d, 1 H) 3.71 (s, 3 H) 3.30 (dd, 1 H) 3.17 - 3.08 (m, 1 H) 3.08 - 2.91 (m, 2 H) 2.23 - 2.06 (m, 2 H), 1.80 - 1.75 (m, 1 H)	320	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)pyrrolidin-3-ylcarbamate Method 44 
97	(Z)-5-(3-methoxy-2-(piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.45 (brs, 1 H) 8.59 (brs, 1 H) 7.99 (s, 1 H) 7.15 (t, 1 H) 7.02 (d, 1 H) 6.89 (d, 1 H) 3.67 (s, 3 H) 3.17 - 2.99 (m, 8 H)	320	(*Z*)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)piperazine-1-carboxylate Method 45 
98	(Z)-5-(3-chloro-2-(piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.72 (brs, 1 H) 9.19 (brs, 1 H) 8.01 (s, 1 H) 7.57 (dd, 1 H) 7.50 - 7.40 (m, 1 H) 7.36 (t, 1 H) 3.60 (brs, 2 H), 3.51 - 3.29 (m, 1 H) 3.29 - 3.12 (m, 2 H) 3.06 (brs, 3 H)	324	(*Z*)-*tert*-butyl 4-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carboxylate Method 46 

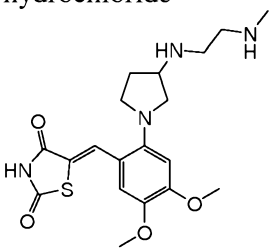
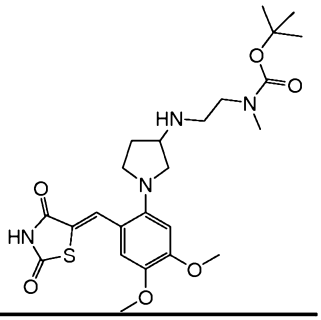
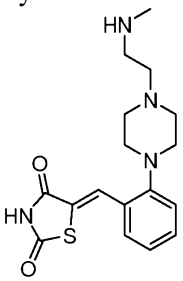
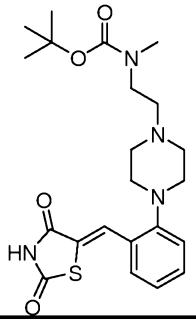
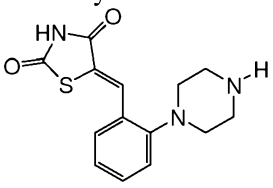
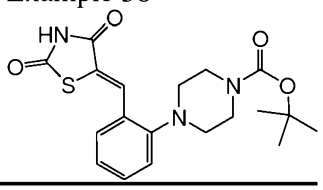
99	(*Z*)-5-(2-(3-(aminomethyl)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.40 (s, 1 H) 9.25 (s, 1 H) 7.88 (s, 1 H) 6.97 (s, 1 H) 6.73 (s, 1 H) 3.85 (s, 3 H) 3.81 (m, 1 H) 3.74 (s, 3 H) 3.40 - 3.31 (m, 2 H) 3.25 - 3.13 (m, 2 H) 2.59 (t, 3 H) 2.31 (dd, 1 H) 2.08 (d, 1 H)	364	(*Z*)-*tert*-butyl (1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)methylcarbamate Method 47 
100	(*R,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.39 (s, 1 H) 8.06 (s, 2 H) 7.89 (s, 1 H) 6.96 (s, 1 H) 6.65 (s, 1 H) 3.84 (s, 4 H) 3.73 (s, 3 H) 3.35 (d, 2 H) 3.20 (s, 1 H) 3.07 (d, 1 H) 2.28 (s, 1 H) 1.97 (s, 1 H)	350	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate Method 48 
101	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.39 (s, 1 H) 8.08 (s, 2 H) 7.89 (s, 1 H) 6.96 (s, 1 H) 6.65 (s, 1 H) 3.84 (s, 4 H) 3.73 (s, 3 H) 3.45 - 3.30 (m, 2 H) 3.24 - 3.14 (m, 1 H) 3.12 - 3.00 (m, 1 H) 2.28 (s, 1 H) 1.98 (s, 1 H)	350	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate Method 49 

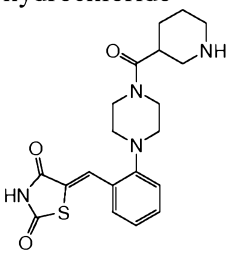
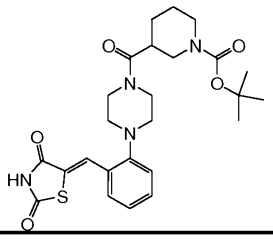
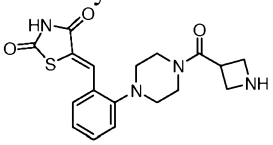
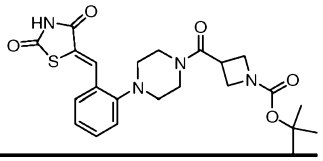
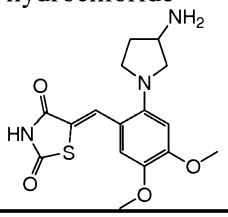
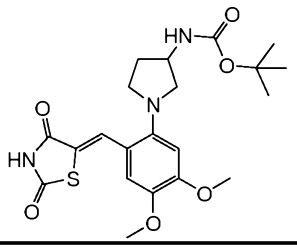
102	(Z)-5-(2-(4-(piperidine-3-carbonyl)-1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.49 (s, 1 H) 8.47 (s, 1 H) 7.82 (d, 1 H) 7.39 - 7.30 (m, 2 H) 7.16 (dd, 1 H) 7.06 (td, 1 H) 3.63 - 3.54 (m, 4 H) 3.29 - 3.06 (m, 9 H) 1.88 - 1.48 (m, 6 H)	415	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepane-1-carbonyl)piperidine-1-carboxylate Method 50 
103	(Z)-5-(2-(4-(5-aminopentanoyl)-1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.57 (s, 1 H) 7.90 (d, 1 H) 7.76 (s, 2 H) 7.47 - 7.36 (m, 2 H) 7.22 (t, 1 H) 7.12 (d, 1 H) 3.63 (d, 4 H) 3.22 (s, 1 H) 3.17 (s, 1 H) 3.05 (s, 2 H) 2.80 (s, 2 H) 2.41 (s, 1 H) 2.34 (s, 1 H) 1.91 (s, 1 H) 1.85 (s, 1 H) 1.57 (d, 4 H)	403	(Z)-*tert*-butyl 5-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepan-1-yl)-5-oxopentylcarbamate Method 51 
104	(Z)-5-(2-(4-(4-aminobutanoyl)-1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.49 (s, 1 H) 7.83 (d, 1 H) 7.65 (s, 2 H) 7.39 - 7.30 (m, 2 H) 7.20 - 7.12 (m, 1 H) 7.09 - 7.01 (m, 1 H) 3.61 - 3.50 (m, 4 H) 3.18 - 3.07 (m, 2 H) 2.98 (d, 2 H) 2.77 (ddd, 2 H) 2.37 (t, 2 H) 1.85 - 1.66 (m, 4 H).	389	(Z)-*tert*-butyl 4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepan-1-yl)-4-oxobutylcarbamate Method 52 

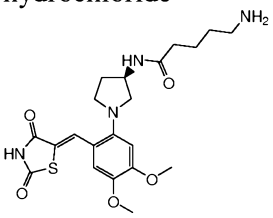
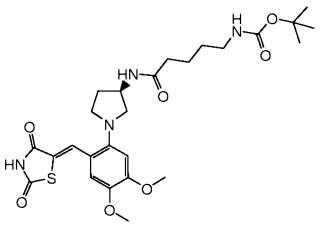
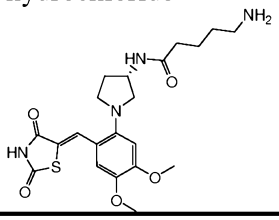
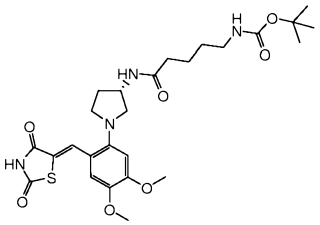
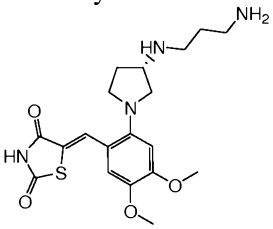
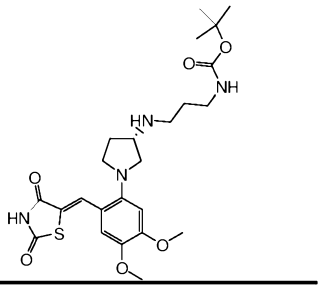
105	(Z)-5-(2-(4-(3-aminopropanoyl)-1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.50 (s, 1 H) 7.83 (s, 1 H) 7.63 (s, 2 H) 7.39 - 7.31 (m, 2 H) 7.16 (dd, 1 H) 7.10 - 7.01 (m, 1 H) 3.64 - 3.52 (m, 4 H) 3.20 - 3.09 (m, 2 H) 2.97 (dt, 4 H) 2.65 (dt, 2 H) 1.87-1.81 (m, 2 H)	375	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepan-1-yl)-3-oxopropylcarbamate Method 53 
106	(Z)-5-(2-(1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.57 (s, 1 H) 9.31 (s, 1 H) 7.91 (s, 1 H) 7.46 - 7.40 (m, 2 H) 7.26 (d, 1 H) 7.18 - 7.09 (m, 1 H) 3.36 (d, 2 H) 3.27 (d, 4 H) 3.19 (dd, 2 H) 2.10 - 2.01 (m, 2 H)	304	(Z)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepane-1-carboxylate Method 54 
107	(Z)-5-(2-(4-(4-aminobutanoyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.60 (s, 1 H) 7.95 (s, 4 H) 7.53 - 7.44 (m, 2 H) 7.26 - 7.17 (m, 2 H) 3.66 - 3.57 (m, 5 H) 2.89 (m, 4 H) 2.85 - 2.76 (m, 3 H) 1.85 - 1.76 (m, 2 H)	375	(Z)-*tert*-butyl 4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)-4-oxobutylcarbamate Method 55 

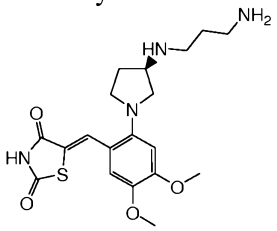
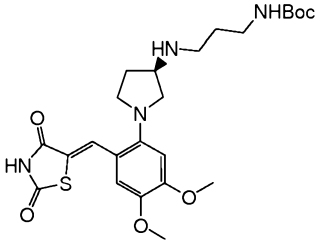
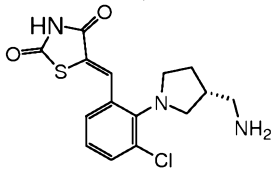
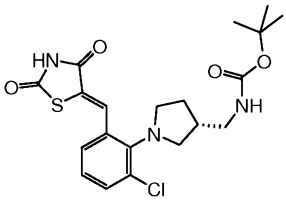
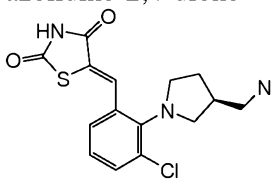
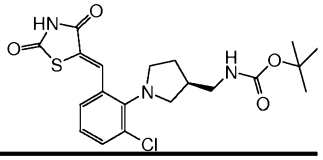
108	(*Z*)-5-(2-(4-(5-aminopentanoyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.66 (s, 1 H) 8.10 (s, 2 H) 7.99 (s, 1 H) 7.52 (s, 1 H) 7.51 - 7.47 (m, 1 H) 7.25 (t, 2 H) 3.67 (s, 4 H) 2.92 - 2.81 (m, 6 H) 2.44 (t, 2 H) 1.62 (s, 4 H)	389	(*Z*)-*tert*-butyl 5-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)-5-oxopentylcarbamate Method 56 
109	(*Z*)-5-(2-(4-(4-(piperazin-1-ylmethyl)benzoyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.57 (brs, 1 H) 9.70 (brs, 1 H) 7.94 (s, 1 H) 7.75 (d, 2 H) 7.52 (m, 2 H) 7.49 - 7.41 (m, 2 H) 7.21 (t, 2 H) 4.45 (brs, 2 H) 3.81 (brs, 2 H) 3.54 - 3.35 (m, 8 H) 3.27 (brs, 2 H) 2.89 (brs, 4 H)	492	(*Z*)-*tert*-butyl 4-(4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)benzyl)piperazine-1-carboxylate Method 57 
110	(*Z*)-5-(2-(4-(3-(aminomethyl)benzoyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.56 (s, 1 H) 8.18 (brs, 2 H) 7.95 (s, 1 H) 7.64 - 7.38 (m, 6 H) 7.36 - 7.11 (m, 2 H) 4.19 - 4.02 (m, 2 H) 3.82 (brs, 2 H) 3.52 (brs, 2 H) 2.92 (brs, 4 H)	423	(*Z*)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)benzylcarbamate Method 58 

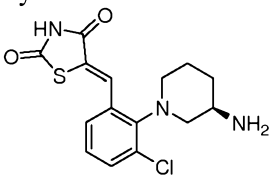
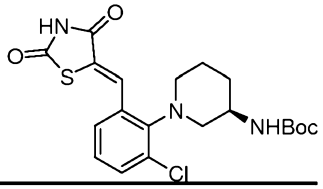
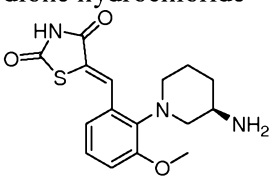
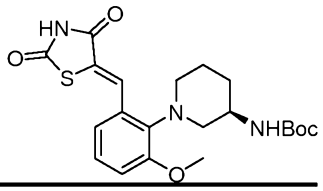
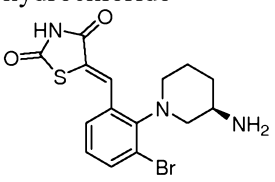
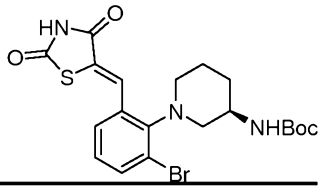
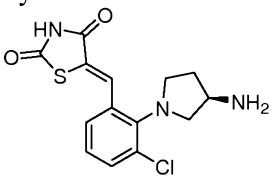
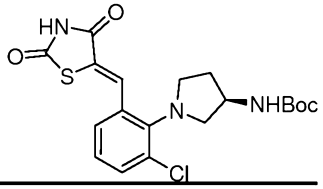
111	(Z)-5-(2-(3-(2-aminoethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.38 (s, 1 H) 9.99 (s, 1 H) 8.44 (s, 2 H) 7.86 (s, 1 H) 6.96 (s, 1 H) 6.76 (s, 1 H) 3.93 (s, 1 H) 3.84 (s, 3 H) 3.73 (s, 3 H) 3.45 - 3.33 (m, 2 H) 3.28 - 3.16 (m, 6 H) 2.32 (s, 1 H) 2.15 (s, 1 H)	393	(Z)-*tert*-butyl 2-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)ethylcarbamate Method 59 
112	(Z)-5-(2-(4-(2-aminoethyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.70 (s, 1 H) 11.43 (s, 1 H) 8.38 (s, 3 H) 7.86 (s, 1 H) 7.49 (m, 2 H) 7.25 (m, 2 H) 3.67 (m, 2 H) 3.42 - 3.30 (m, 8 H)	333	(Z)-*tert*-butyl 2-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)ethylcarbamate Method 60 

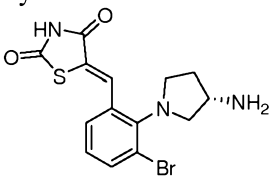
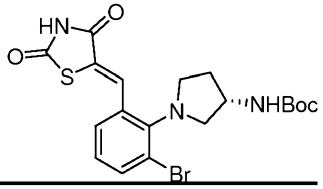
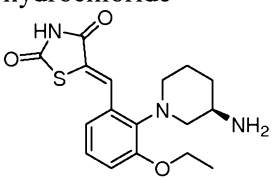
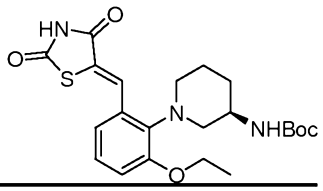
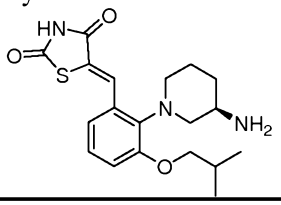
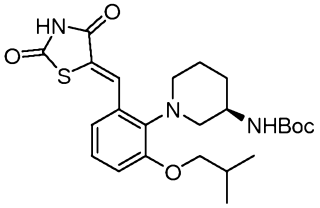
113	(Z)-5-(4,5-dimethoxy-2-(3-(2-(methylamino)ethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.39 (s, 1 H) 9.93 (brs, 1 H) 9.42 (brs, 1 H) 7.87 (s, 1 H) 6.98 (s, 1 H) 6.77 (s, 1 H) 4.00 – 3.91 (m, 1 H) 3.85 (s, 3 H) 3.74 (s, 3 H) 3.44 – 3.16 (m, 8 H) 2.62 (s, 3 H) 2.40 – 2.31 (m, 1 H) 2.20 – 2.14 (m, 1 H)	407	(Z)-*tert*-butyl 2-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)ethyl(methyl)carbamate Method 61 
114	(Z)-5-(2-(4-(2-(methylamino)ethyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.62 (s, 1 H) 11.28 (s, 1 H) 9.28 (s, 1 H) 7.87 (s, 1 H) 7.50 (t, 1 H) 7.26 (t, 1 H) 3.71 (m, 4 H) 3.57 (m, 2 H) 3.45 (m, 2 H) 3.26 (m, 4 H) 2.62 (s, 3 H)	347	(Z)-*tert*-butyl 2-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)ethyl(methyl)carbamate Method 62 
115	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione hydrochloride 	12.61 (s, 1 H) 9.21 (s, 1 H) 7.86 (s, 1 H) 7.49 (t, 2 H) 7.24 (t, 2 H), 3.25 (s, 4 H) 3.12 (s, 4 H)	290	*tert*-butyl-4-{2-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}piperazine-1-carboxylate Example 58 

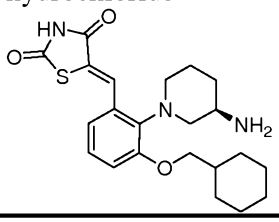
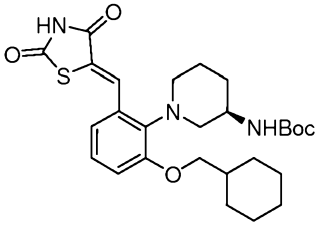
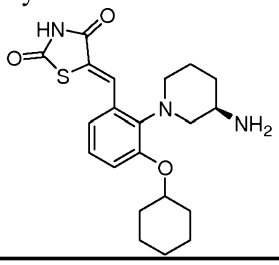
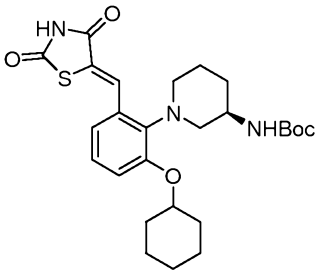
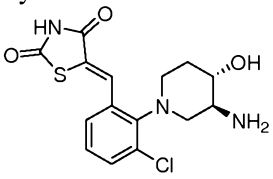
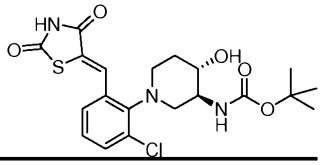
116	5-(2-(4-(piperidine-3-carbonyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.60 (s, 1 H) 9.10 (s, 1 H) 8.90 (s, 1 H) 7.94 (s, 1 H) 7.51 - 7.43 (m, 1 H) 7.21 (t, 2 H) 5.14 (m, 4 H) 3.67 (m, 3 H) 3.17 (m, 2 H) 2.91 - 2.88 (m, 4 H) 1.86 (s, 1 H) 1.81 - 1.71 (m, 2 H) 1.57 (d, 1 H)	401	*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)piperidine-1-carboxylate Method 63 
117	(5*Z*)-5-{2-[4-(azetidin-3-ylcarbonyl)piperazin-1-yl]benzylidene}-1,3-thiazolidine-2,4-dione hydrochloride 	12.59 (s, 1 H) 9.15 (s, 1 H) 8.86 (s, 1 H) 7.93 (s, 1 H) 7.47 (ddd, 2 H) 7.25 - 7.16 (m, 1 H) 4.15 - 4.05 (m, 4 H) 4.01 - 3.91 (m, 1 H) 3.71 (m, 2 H) 3.42 (s, 2 H) 2.89 (d, 4 H)	373	*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)azetidine-1-carboxylate Method 64 
118	(5*Z*)-5-[2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene]-1,3-thiazolidine-2,4-dione hydrochloride 	12.38 (s, 1 H) 8.34 (s, 2 H) 7.90 (s, 1 H) 6.96 (s, 1 H) 6.68 (s, 1 H) 3.89 - 3.80 (m, 4 H) 3.73 (s, 3 H) 3.46 - 3.34 (m, 2 H) 3.23 - 3.13 (m, 1 H) 3.10 (dd, 1 H) 2.28 (dd, 1 H) 2.01 (d, 1 H)	351	*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate Method 65 

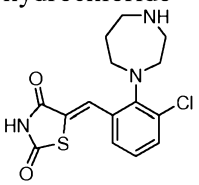
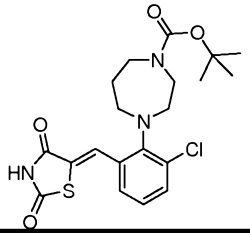
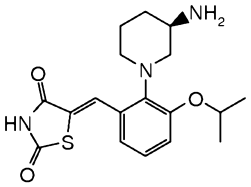
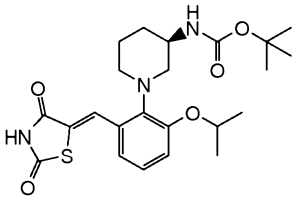
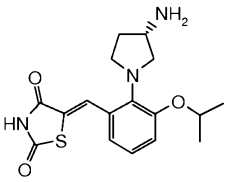
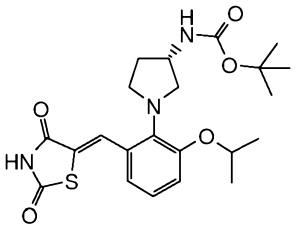
119	(*R,Z*)-5-amino-N-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)pentanamide hydrochloride 	12.24 (s, 1 H) 8.07 (d, 1 H) 7.79 (s, 1 H) 7.60 (brs, 2 H) 6.88 (s, 1 H) 6.55 (s, 1 H) 4.22 (d, 1 H) 3.76 (s, 3 H) 3.65 (s, 3 H) 3.30 - 3.15 (m, 2 H) 3.15 - 2.98 (m, 1 H) 2.86 (dd, 1 H) 2.70 (d, 2 H) 2.17-1.92 (m, 3 H) 1.76 (brs, 1 H) 1.52 - 1.25 (m, 4 H)	449	(*R,Z*)-*tert*-butyl 5-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)-5-oxopentylcarbamate Method 66 
120	(*S,Z*)-5-amino-N-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)pentanamide hydrochloride 	12.24 (s, 1 H) 8.07 (d, 1 H) 7.79 (s, 1 H) 7.60 (brs, 2 H) 6.88 (s, 1 H) 6.55 (s, 1 H) 4.22 (d, 1 H) 3.76 (s, 3 H) 3.65 (s, 3 H) 3.30 - 3.15 (m, 2 H) 3.15 - 2.98 (m, 1 H) 2.86 (dd, 1 H) 2.70 (d, 2 H) 2.17-1.92 (m, 3 H) 1.76 (brs, 1 H) 1.52 - 1.25 (m, 4 H)	449	(*S,Z*)-*tert*-butyl 5-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)-5-oxopentylcarbamate Method 67 
121	(*S,Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.50 (s, 1 H) 9.78 (s, 1 H) 7.92 (s, 1 H) 7.05 (s, 1 H) 6.85 (s, 1 H) 4.21 - 4.11 (m, 1 H) 3.93 (s, 3 H) 3.83 (s, 3 H) 3.42 - 3.25 (m, 8 H) 2.45 (m, 1 H) 2.20 (m, 1 H) 1.32 (m, 2 H)	407	(*S,Z*)-*tert*-butyl 3-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)propylcarbamate Method 68 

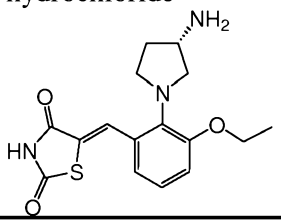
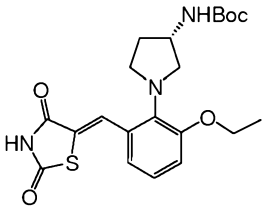
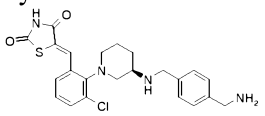
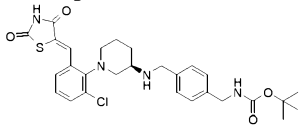
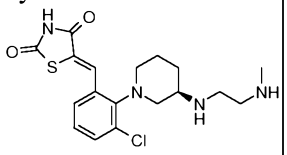
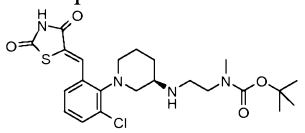
122A	(*R,Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.44 (s, 1 H) 9.78 (s, 1 H) 7.92 (s, 1 H) 7.05 (s, 1 H) 6.85 (s, 1 H) 4.21 - 4.11 (m, 1 H) 3.93 (s, 3 H) 3.83 (s, 3 H) 3.42 - 3.25 (m, 8 H) 2.45 (m, 1 H) 2.20 (m, 1 H) 1.32 (m, 2 H)	407	(*R,Z*)-*tert*-butyl 3-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)propylcarbamate Method 69 
122B	(*R,Z*)-5-(2-(3-(aminomethyl)pyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione 	(400 MHz, MeOD) ppm 8.08 (s, 1 H) 7.49 (dd, 2 H) 7.31 (t, 1 H) 3.56 (t, 1 H) 3.42 – 3.51 (m, 1 H) 3.38 (td, 1 H) 3.09 – 3.15 (m, 2 H) 2.71 – 2.78 (m, 1 H) 2.26 – 2.36 (m, 1 H) 1.86 – 1.96 (m, 1 H) 1.31 (dd, 1 H)	338	(*R,Z*)-*tert*-butyl (1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)methylcarbamate Method 132 
122C	(*S,Z*)-5-(2-(3-(aminomethyl)pyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione 	(400 MHz, MeOD) ppm 8.07 (s, 1 H) 7.49 (dd, 2 H) 7.31 (t, 1 H) 3.56 (t, 1 H) 3.42 – 3.51 (m, 2 H) 3.38 (td, 1 H) 3.07 – 3.16 (m, 2 H) 2.67 – 2.79 (m, 1 H) 2.24 – 2.36 (m, 1 H) 1.90 (dd, 1 H)	338	(*S,Z*)-*tert*-butyl (1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)methylcarbamate Method 133 

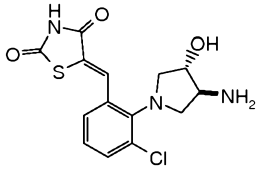
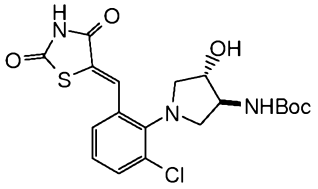
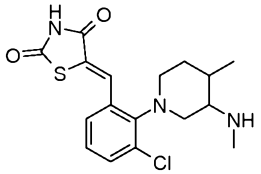
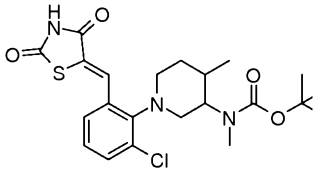
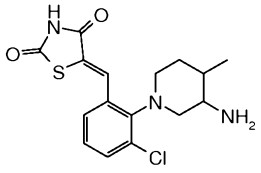
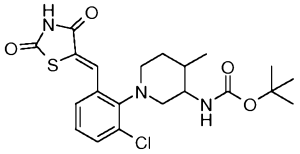
122D	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.70 (s, 1 H) 8.17 (brs, 3 H) 8.01 (s, 1 H) 7.52 (d, 1 H) 7.41-7.31 (m, 2 H) 3.40-3.10 (m, 4 H) 2.84-2.81 (m, 1 H) 2.12-2.10 (m, 1 H) 1.80-1.58 (m, 3 H)	338	(*R,Z*)-tert-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 134 
122E	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-methoxybenzylidene) thiazolidine-2,4-dione hydrochloride 	12.60 (s, 1 H) 8.12 (brs, 4 H) 7.28-7.02 (m, 3 H) 3.82 (s, 3 H) 3.18-2.87 (m, 5 H) 2.10-2.07 (m, 1 H) 1.75-1.38 (m, 3 H)	334	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)piperidin-3-ylcarbamate Method 135 
122F	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-bromobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.70 (s, 1 H) 8.15 (brs, 3 H) 8.01 (s, 1 H) 7.74-7.69 (m, 1 H) 7.46 (d, 1 H) 7.26 (t, 1 H) 3.27-2.99 (m, 4 H) 2.82-2.80 (m, 1 H) 2.12-2.10 (m, 1 H) 1.76-1.40 (m, 3 H)	383	*(R,Z)-tert*-butyl 1-(2-bromo-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 136 
122G	(*R,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.67 (brs, 1 H) 8.30 (brs, 3 H) 7.93 (s, 1 H) 7.55 (d, 1 H) 7.41-7.31 (m, 2 H) 3.87 (brs, 1 H) 3.50-3.27 (m, 4 H) 2.40-2.28 (m, 1 H) 2.08-1.95 (m, 1 H)	324	(*R,Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate Method 137 

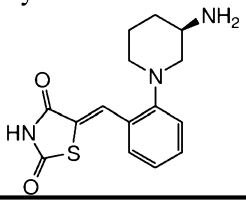
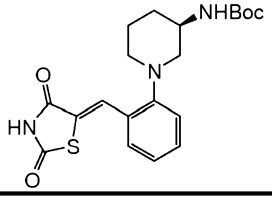
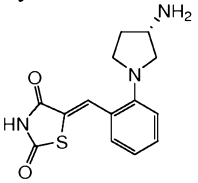
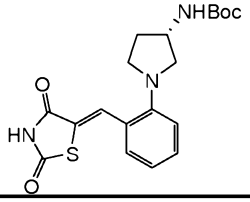
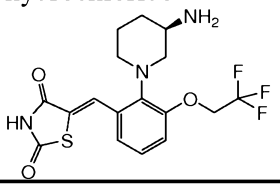
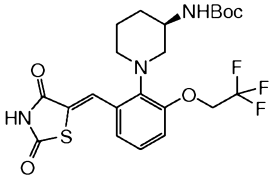
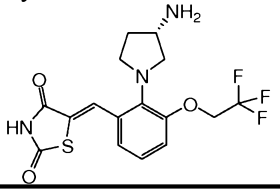
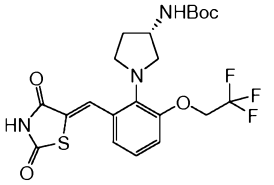
122H	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-bromobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.68 (brs, 1 H) 8.31 (brs, 3 H) 7.90 (s, 1 H) 7.75 (d, 1 H) 7.46 (d, 1 H) 7.29 (t, 1 H) 3.75 (brs, 1 H) 3.55 (t, 1 H) 3.38-3.25 (m, 3 H) 2.40-2.32 (m, 1 H) 2.12-2.02 (m, 1 H)	370	(*S,Z*)-*tert*-butyl 1-(2-bromo-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate Method 138 
122I	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-ethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.58 (s, 1 H) 8.13-8.09 (m, 4 H) 7.26-7.24 (m, 1 H) 7.16-7.14 (m, 1 H) 7.03-7.01 (m, 1 H) 4.07 (q, 2 H) 3.78-3.67 (m, 2 H) 3.22-3.07 (m, 3 H) 2.10-2.07 (m, 1 H) 1.76-1.55 (m, 3 H) 1.38 (t, 3 H)	348	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-ethoxyphenyl)piperidin-3-ylcarbamate Method 139 
122J	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isobutoxyphenyl)piperidin-3-ylcarbamate hydrochloride 	12.60 (s, 1 H) 8.18 (brs, 3 H) 8.15 (s, 1 H) 7.26 (t, 1 H) 7.15 (d, 1 H) 7.02 (d, 1 H) 3.84-3.74 (m, 2 H) 3.20-3.02 (m, 4 H) 2.74 (d, 1 H) 2.14–2.07 (m, 2 H) 1.73-1.21 (m, 3 H) 1.03 (d, 6 H)	376	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isobutoxyphenyl)piperidin-3-ylcarbamate Method 140 

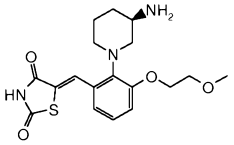
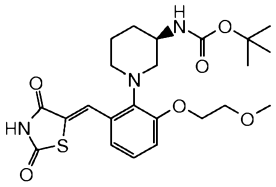
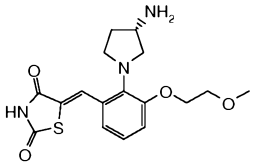
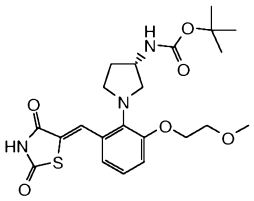
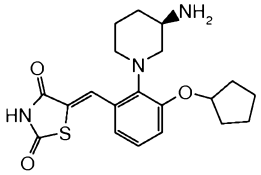
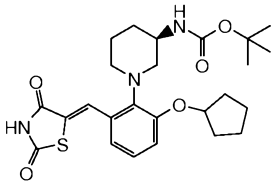
122K	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-(cyclohexylmethoxy) benzylidene)thiazolidine-2,4-dione hydrochloride 	12.60 (s, 1 H) 8.14 (brs, 4 H) 7.25 (t, 1 H) 7.14 (d, 1 H) 7.00 (d, 1 H) 3.82 (brs, 2 H) 3.29-3.00 (m, 4 H) 2.75-2.72 (m, 1 H) 2.12-2.10 (m, 1 H) 1.86-1.50 (m, 8 H) 1.35-1.03 (m, 6 H)	416	(*R*,*Z*)-*tert*-butyl 1-(2-(cyclohexylmethoxy)-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 141 
122L	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-(cyclohexyloxy)benzylidene)thiazolidine-2,4-dione hydrochloride 		402	(*R*,*Z*)-*tert*-butyl 1-(2-(cyclohexyloxy)-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 142 
122M	(±)-(*Z*)-5-(2-3-amino-4-hydroxypiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.68 (s, 1 H) 8.01 (brs, 4 H) 7.53 (d, 1 H) 7.44-7.42 (m, 1 H) 7.35 (t, 1 H) 5.72-5.70 (m, 1 H) 3.32-3.22 (m, 2 H) 3.20-3.11 (m, 3 H) 1.96-1.94 (m, 1 H) 1.40-1.37 (m, 1 H)	354	(±)-*tert*-butyl-1-(2-chloro-6-((*Z*)-(2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-hydroxypiperidin-3-ylcarbamate Method 143 

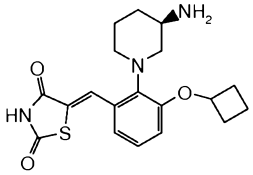
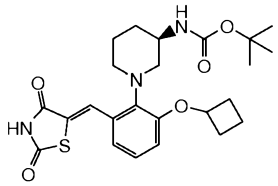
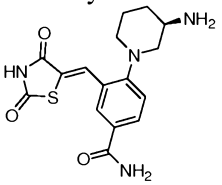
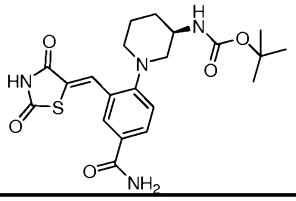
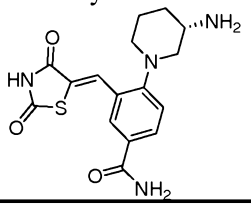
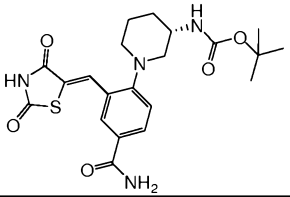
122N	(*Z*)-5-(3-chloro-2-(1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.73 (brs, 1 H), 9.18 (brs, 2 H), 8.04 (s, 1 H), 7.62 (d, 1 H), 7.41 (dt, 2 H), 3.65 (brs, 1 H), 3.34 - 3.30 (m, 5 H), 3.04 (brs, 2 H), 2.14 (brs, 2 H)	338	(*Z*)-*tert*-butyl 4-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepane-1-carboxylate Method 144 
122O	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-isopropoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.61 (brs, 1 H) 8.33 (brs, 3 H) 8.15 (brs, 1 H) 7.34-7.09 (m, 2 H) 6.99 (d, 1 H) 4.67 (ddd 1 H) 3.28 (brs, 1 H) 3.07 (brs, 3 H) 2.70 (brs, 1 H) 2.12 (brs, 1 H) 1.73 (brs, 1 H) 1.57 (brs, 1 H) 1.51 - 1.21 (m, 7 H)	362	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isopropoxyphenyl)piperidin-3-ylcarbamate Method 145 
122P	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-isopropoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.58 (brs, 1 H) 8.52 (brs, 3 H) 8.08 (s, 1 H) 7.39-7.10 (m, 2 H) 6.99 (d, 1 H) 4.70 (d, 1 H) 3.78 (brs, 1 H) 3.52-3.33 (m, 1 H) 3.33 - 3.03 (m, 3 H) 2.28 (brs, 1 H) 2.00 (d, 1 H) 1.32 (d, 6 H)	348	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isopropoxyphenyl)pyrrolidin-3-ylcarbamate Method 146 

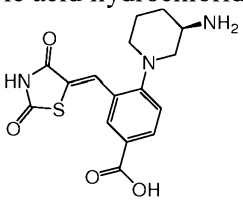
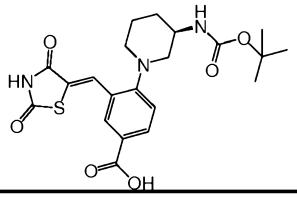
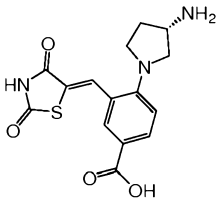
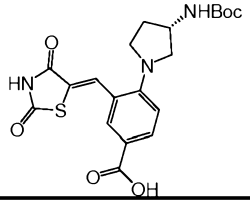
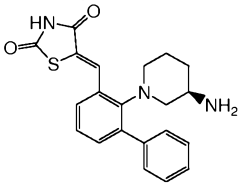
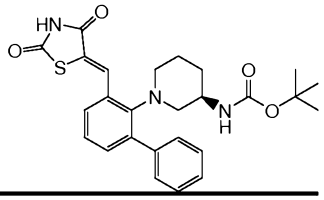
122Q	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-ethoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.58 (brs, 1 H) 8.48 (brs, 3 H) 8.09 (s, 1 H) 7.26 (t, 1 H) 7.16 (d, 1 H) 7.02 (d, 1 H) 4.09 (q, 2 H) 3.80 (d, 1 H) 3.47 (dd, 1 H) 3.28 (m, 1 H) 3.21 (dd, 1 H) 2.29 (d, 1 H) 2.01 (dd, 1 H) 1.40 (t, 3 H)	334	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-ethoxyphenyl)pyrrolidin-3-ylcarbamate Method 147 
122R	(*R,Z*)-5-(2-(3-(4-(aminomethyl)benzylamino)piperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	9.62 (brs, 1 H) 8.46 (brs, 3 H) 7.66-7.49 (m, 5 H) 7.47-7.34 (m, 2 H) 4.26-4.12 (m, 2 H) 4.09-3.94 (m, 2 H) 3.42-3.25 (m, 4 H) 2.83 (brs, 1 H) 2.36 (s, 1 H) 1.85 (m, 1 H) 1.62 (d, 2 H)	457	(*R,Z*)-*tert*-butyl 4-((1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylamino)methyl)benzylcarbamate Example 167 
122S	(*R,Z*)-5-(3-chloro-2-(3-(2-(methylamino)ethylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.68 (brs, 1 H) 9.68 (brs, 2 H) 9.21 (brs, 2 H) 8.05 (s, 1 H) 7.56 (d, 1 H) 7.50-7.42 (m, 1 H) 7.37 (t, 1 H) 3.75-3.65 (m, 5 H) 3.63-3.57 (m, 2 H) 3.16 (d, 1 H) 2.82 (brs, 1 H) 2.60 (brs, 3 H) 2.37-2.28 (m, 1 H) 1.80 (d, 1 H) 1.65 (m, 1H) 1.54 (brs, 1 H)	395	(*R,Z*)-*tert*-butyl 2-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylamino)ethyl(methyl)carbamate Example 168 

122T	(*Z*)-5-(2-((3S,4S)-3-amino-4-hydroxypyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.68 (brs, 1 H) 8.50 (brs, 3 H) 8.10-7.81 (m, 1 H) 7.58 (dd, 1 H) 7.51-7.27 (m, 2 H) 4.56-4.28 (m, 1 H) 3.84 (brs, 1 H) 3.66-3.40 (m, 4 H) 3.39-3.23 (m, 1 H)	339	*tert*-butyl (3*S*,4*S*)-1-(2-chloro-6-((*Z*)-(2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-hydroxypyrrolidin-3-ylcarbamate Method 151 
122U	(*Z*)-5-(3-chloro-2-(4-methyl-3-(methylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.69 (brs, 1 H) 8.63 (brs, 2 H) 8.02 (s, 1 H) 7.57 (d, 1 H) 7.47-7.31 (m, 2 H) 3.58 (m, 1 H) 3.07 (m, 1 H) 2.67 (brs, 1 H) 2.58 (brs, 3 H) 2.40 (m, 1 H) 1.87 (m, 1 H) 1.68 (m, 1 H) 1.29 (m, 1 H) 1.07 (d, 3 H) 0.87 (d, 1 H)	365	(*Z*)-tert-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-methylpiperidin-3-yl(methyl)carbamate Method 152 
122V	(*Z*)-5-(2-(3-amino-4-methylpiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 		351	(*Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-methylpiperidin-3-ylcarbamate Method 153 

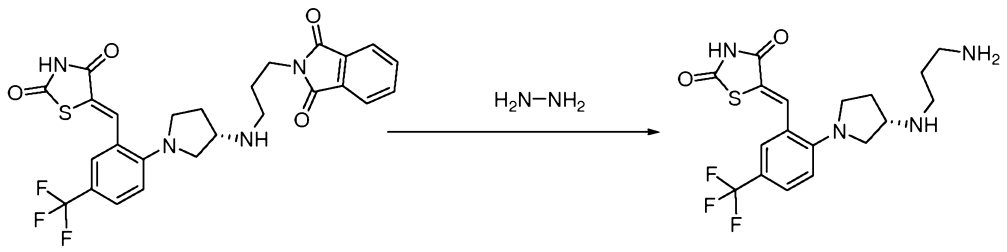
122W	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.58 (s, 1 H), 8.44 (brs, 3 H) 7.89 (s, 1 H) 7.54-7.34 (m, 2 H) 7.27-7.05 (m, 2 H) 3.26 (d, 2 H) 2.94 (d, 1 H), 2.87-2.61 (m, 2 H) 2.05 (brs, 1 H) 1.85 (brs, 1 H) 1.75-1.47 (m, 2 H)	304	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 154 
122X	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.49 (s, 1 H) 8.50 (brs, 3 H) 7.91 (s, 1 H) 7.44-7.22 (m, 2 H) 7.07-6.79 (m, 2 H) 3.83 (d, 1 H) 3.51-3.29 (m, 2 H) 3.28-3.17 (m, 2 H) 2.27 (dd, 1 H), 2.11-1.94 (m, 1 H)	290	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate Method 155 
122Y	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-(2,2,2-trifluoroethoxy)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.57 (brs, 1 H) 8.03 (brs, 1 H) 7.90 (brs, 3 H) 7.36-7.13 (m, 2 H) 7.07 (d, 1 H) 4.85-4.55 (m, 2 H) 2.98 (brs, 4 H) 2.74 (brs, 1 H) 2.02 (d, 1 H) 1.69 (d, 1 H) 1.54 (d, 1 H) 1.30 (brs, 1 H)	402	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2,2,2-trifluoroethoxy)phenyl)piperidin-3-ylcarbamate Method 156 
122Z	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-(2,2,2-trifluoroethoxy)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.52 (brs, 1 H) 8.21-7.91 (m, 4 H) 7.34-7.14 (m, 2 H) 7.07 (d, 1 H) 4.88-4.72 (m, 2 H) 3.74 (d, 1 H) 3.40 (dd, 1 H) 3.22 (td, 1 H) 3.18-3.10 (m, 1 H) 3.06 (dd, 1 H) 2.30-2.10 (m, 1 H) 1.90 (dd, 1 H)	388	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2,2,2-trifluoroethoxy)phenyl)pyrrolidin-3-ylcarbamate Method 157 

122AA	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-(2-methoxyethoxy)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.67 (brs, 1 H) 8.30 (brs, 3 H) 8.20 (brs, 1 H) 7.33 (brs, 1 H) 7.25 (brs, 1 H) 7.10 (d, 1 H) 4.68 (brs, 3 H) 4.22 (t, 2 H) 3.91-3.65 (m, 2 H) 3.42 (s, 3 H) 3.29 (brs, 1 H) 2.80 (brs, 1 H) 2.18 (brs, 1 H) 1.81 (brs, 1 H) 1.68 (brs, 1 H) 1.48 (brs, 1 H)	378	(*R*,*Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2-methoxyethoxy)phenyl)piperidin-3-ylcarbamate Method 158 
122AB	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-(2-methoxyethoxy)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.58 (brs, 1 H) 8.42 (brs, 3 H) 8.10 (s, 1 H) 7.28 (t, 1 H) 7.23-7.11 (m, 1 H) 7.04 (d, 1 H) 4.27-3.97 (m, 2 H) 3.85 (d, 1 H) 3.78-3.63 (m, 2 H) 3.49 (dd, 1 H) 3.34 (s, 3 H) 3.27 (td, 1 H) 3.22-3.06 (m, 2 H) 2.30 (dd, 1 H) 2.02 (dd, 1 H)	364	(*S*,*Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2-methoxyethoxy)phenyl)pyrrolidin-3-ylcarbamate Method 159 
122AC	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-(cyclopentyloxy)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.37 (brs, 1 H) 8.00 (brs, 3H) 7.93 (s, 1 H) 7.02 (d, 1 H) 6.91 (d, 1 H) 6.77 (d, 1 H) 3.02-2.91 (m, 1 H) 2.82 (d, 3 H) 2.48 (brs, 1 H) 1.89-1.40 (m, 12 H) 1.16 (brs, 1 H)	388	(*R*,*Z*)-*ter*t-butyl 1-(2-(cyclopentyloxy)-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 160 

122AD	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-cyclobutoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.60 (brs, 1 H) 8.14 (brs, 4 H) 7.23 (d, 1 H) 7.00 (dd, 2 H), 4.86-4.67 (m, 1 H) 3.25 (m, 1H) 3.05 (m, 2H) 2.74 (brs, 1 H) 2.49-2.35 (m, 2 H) 2.21-1.95 (m, 3 H) 1.93-1.76 (m, 2 H) 1.67 (td, 3 H) 1.42 (brs, 1 H)	374	(*R,Z*)-*tert*-butyl 1-(2-cyclobutoxy-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 161 
122AE	(*R,Z*)-4-(3-aminopiperidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzamide hydrochloride 		347	(*R,Z*)-*tert*-butyl 1-(4-carbamoyl-2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 162 
122AF	(*S,Z*)-4-(3-aminopiperidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzamide hydrochloride 		347	(*S,Z*)-*tert*-butyl 1-(4-carbamoyl-2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate Method 163 

122AG	(*R*,*Z*)-4-(3-aminopiperidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzoic acid hydrochloride 		348	(*R*,*Z*)-4-(3-(*tert*-butoxycarbonylamino)piperidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzoic acid Method 164 
122AH	(*S*,*Z*)-4-(3-aminopyrrolidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzoic acid 		333	(*S*,*Z*)-4-(3-(*tert*-butoxycarbonylamino)pyrrolidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzoic acid Method 165 
122AI	(*R*,*Z*)-5-((2-(3-aminopiperidin-1-yl)biphenyl-3-yl)methylene)thiazolidine-2,4-dione 	12.64 (brs, 1 H) 8.09 (brs, 3 H) 7.92 (s, 1 H) 7.56-7.36 (m, 4 H) 7.36 - 7.16 (m, 4 H) 3.06 (brs, 1 H) 3.00 (brs, 1 H) 2.72 (d, 1 H) 2.35 (brs, 2 H) 2.05 (brs, 1 H) 1.58 (brs, 2 H) 1.32-1.15 (m, 1 H)	380	(*R*,*Z*)-*tert*-butyl 1-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)biphenyl-2-yl)piperidin-3-ylcarbamate Method 166 

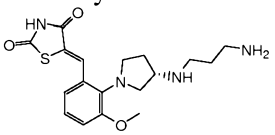
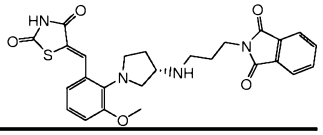
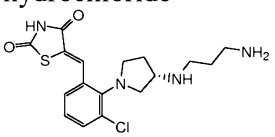
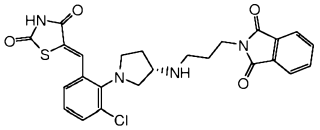
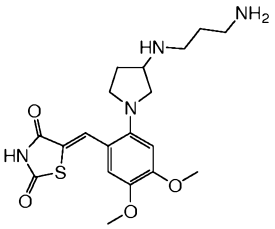
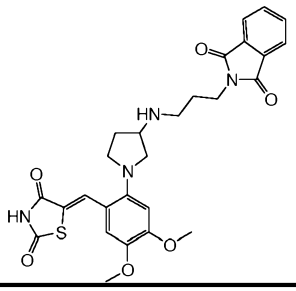
Example 123:

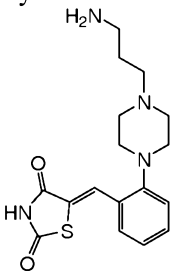
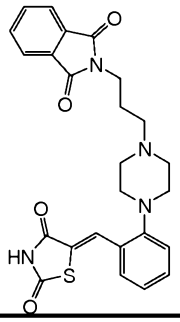
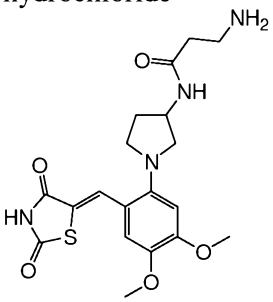
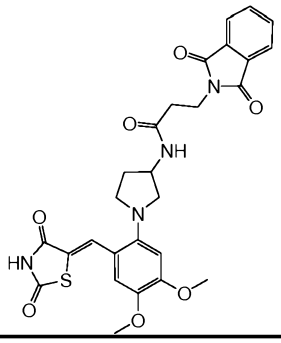


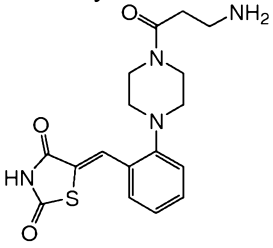
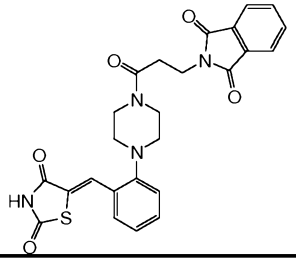
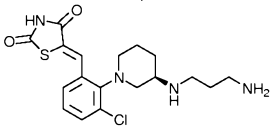
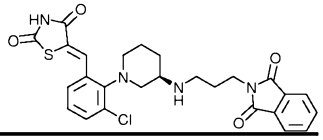
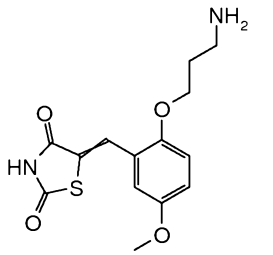
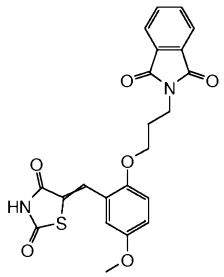
(*S,Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione hydrochloride:

A 25 mL round bottom flask was charged with a magnetic stir bar, (*S,Z*)-5-(2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione (Method 70) (0.271 g, 0.50 mmol), EtOH (2.488 ml), and hydrazine (0.023 ml, 0.75 mmol). The reaction was stirred at rt for 30 min and then filtered through a bed of Celite. The filtrate was conc. *in vacuo* and purified via reverse phase HPLC (MeCN/water) to afford fractions that were conc. *in vacuo*, suspended in methanol (~ 5 mL) and 1N HCl in diethyl ether (~2 mL) and conc. *in vacuo* to afford (*S,Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-5-(trifluoromethyl) benzylidene)thiazolidine-2,4-dione hydrochlride (0.071 g, 29.3 %). ^{1}H NMR (300 MHz, DMSO-D6) δ ppm 12.52 (s, 1 H) 9.49 (s, 1 H) 8.08 (brs, 2 H) 7.93 (s, 1 H) 7.67 (s, 1 H) 7.61 (d, 1 H) 7.08 (d, 1 H) 3.88 - 3.81 (m, 1 H) 3.53 - 3.33 (m, 4 H) 3.08 - 3.05 (m, 2 H) 2.92 - 2.89 (m, 2 H) 2.33 - 2.19 (m, 2 H) 2.04 - 1.96 (m, 2 H); *m/z* 415.

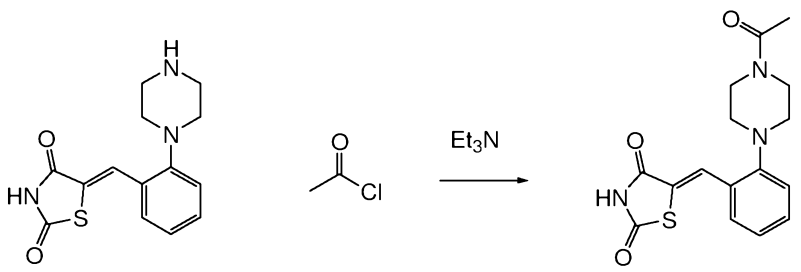
The following examples were prepared by the procedure of Example 123, using the appropriate starting materials. The following parent compounds obtained after chromatography may be converted to their corresponding hydrochloride salt in a manner similar as described in example 123.

Ex.	Compound	^{1}H NMR	m/z	SM
124	(*S,Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-3-methoxybenzylidene)thiazolidine-2,4-dione hydrochloride 	12.59 (brs, 1 H) 9.30 (brs, 1 H) 8.09 (s, 1 H) 8.07 (brs, 1 H) 7.32 (t, 1 H) 7.21 (d, 1 H) 7.08 (d, 1 H) 3.87 (s, 3 H) 3.46 – 3.44 (m, 1 H) 3.39 – 3.25 (m, 2 H) 3.17 – 2.99 (m, 4 H) 2.96 – 2.91 (m 2 H) 2.19 – 2.10 (m, 2 H) 2.08-1.99 (m, 2 H)	377	(*S,Z*)-5-(2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)-3-methoxybenzylidene)thiazolidine-2,4-dione Method 71 
125	(*S,Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride 	12.72 (brs, 1 H) 9.50 (brs, 1 H) 8.10 (brs, 2 H) 7.96 (s, 1 H) 7.60 (d, 1 H) 7.46 – 7.39 (m 2 H) 3.95 – 3.91 (m, 1 H) 3.51 – 3.20 (m, 4 H) 2.99 – 2.92 (m, 2 H) 2.44 – 2.38 (m, 2 H) 2.21 – 2.11 (m, 2 H) 2.08 – 1.99 (m, 2 H)	382	(*S,Z*)-5-(3-chloro-2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione Method 72 
126	(*Z*)-5-(2-(3-(3-aminopropylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione 	12.40 (s, 1 H) 9.78 (s, 1 H) 7.92 (s, 1 H) 7.05 (s, 1 H) 6.85 (s, 1 H) 4.21 - 4.11 (m, 1 H) 3.93 (s, 3 H) 3.83 (s, 3 H) 3.42 - 3.25 (m, 8 H) 2.45 (m, 1 H) 2.20 (m, 1 H) 1.32 (m, 2 H)	407	(*Z*)-5-(2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione Method 73 

127	(Z)-5-(2-(4-(3-aminopropyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione hydrochloride 	12.64 (s, 1 H) 11.50 (s, 1 H) 8.27 (s, 1 H) 7.85 (s, 1 H) 7.49 (t, 2 H) 7.24 (t, 2 H) 3.55 (d, 2 H) 3.32 - 3.16 (m, 8 H) 2.93 (d, 2 H) 2.18 - 2.07 (m, 2 H)	347	(Z)-5-(2-(4-(3-(1,3-dioxoisoindolin-2-yl)propyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione Method 74 
128	(Z)-3-amino-N-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)propanamide hydrochloride 	12.34 (s, 1 H) 8.46 (d, 1 H) 7.86 (s, 3 H) 6.95 (s, 1 H) 6.63 (s, 1 H) 4.36 - 4.26 (m, 1 H) 3.84 (s, 3 H) 3.72 (s, 3 H), 3.32 - 3.21 (m, 3 H) 3.02 - 2.93 (m, 3 H) 2.18 (dd, 2 H) 1.86 (dd, 1 H)	421	(Z)-3-(1,3-dioxoisoindolin-2-yl)-N-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)propanamide Method 75 

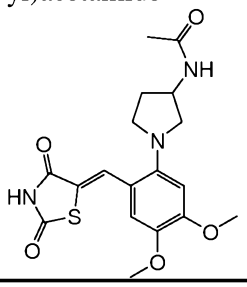
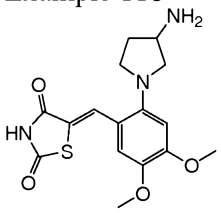
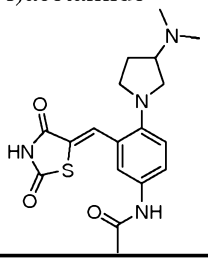
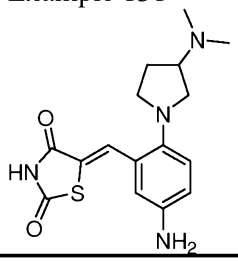
129A	(5*Z*)-5-{2-[4-(3-aminopropanoyl)piperazin-1-yl]benzylidene}-1,3-thiazolidine-2,4-dione hydrochloride 	12.59 (s, 1 H) 7.94 (s, 1 H) 7.82 (s, 2 H) 7.51 - 7.44 (m, 2 H) 7.26 - 7.17 (m, 2 H) 3.66 (m, 2 H) 3.59 (m, 2 H) 3.08 - 2.97 (m, 2 H) 2.96 - 2.86 (m, 4 H) 2.74 (m, 2 H)	361	(5*Z*)-(2-(4-(3-(1,3-dioxoisoindolin-2-yl)propanoyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione Method 76 
129B	(*R,Z*)-5-(2-(3-(3-aminopropylamino)piperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione 	12.69 (brs, 1 H) 9.31 (brs, 1 H) 8.05 (s, 3 H) 7.56 (d, 1 H) 7.49-7.41 (m, 1 H) 7.37 (t, 1 H) 3.76-3.65 (m, 3 H) 3.16 (brs, 1 H) 3.04 (brs, 2 H) 2.94-2.75 (m, 3 H) 2.33 (brs, 1 H) 2.04-1.92 (m, 2 H) 1.78 (d, 1 H) 1.65 (m, 1 H), 1.50 (m, 1 H)	395	(*R,Z*)-5-(3-chloro-2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione Method 171 
129C	5-(2-(3-aminopropoxy)-5-methoxybenzylidene) thiazolidine-2,4-dione 	12.64 (brs, 1 H) 7.94 (brs, 4 H) 7.11 (m, 2 H) 6.93 (s, 1 H) 4.13 (m, 2 H) 3.77 (s, 3 H) 2.97 (m, 2 H) 2.06 (m, 2 H)	309	5-(2-(3-(1,3-dioxoisoindolin-2-yl)propoxy)-5-methoxybenzylidene)thiazolidine-2,4-dione Method 148 

Example 130:

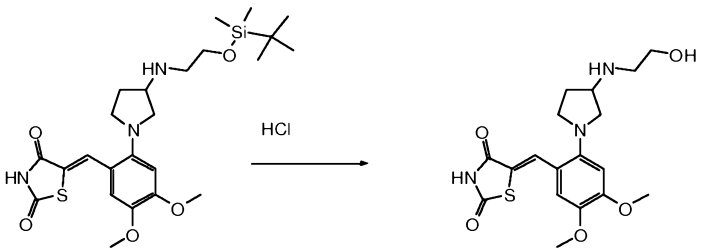


(5Z)-5-[2-(4-acetylpiperazin-1-yl)benzylidene]-1,3-thiazolidine-2,4-dione: To a mixture of (5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione (Example 115) and acetyl chloride (36.1 mg, 0.46 mmol) was added triethylamine (93 mg, 0.92 mmol) at room temperature. The reaction mixture was stirred at room temperature overnight and was then treated with sat'd aqueous $NaHCO_3$ (~ 25 mL). This mixture was allowed to stir at room temperature for 10 min, and was then extracted with DCM (3 X 25 mL). The combined organic extract was dried over anhydrous Na_2SO_4, filtered through a bed of Celite, and the filtrate was conc. *in vacuo* to afford the product which was purified via reverse phase HPLC (acetonitrile:water: 0.1 % TFA = 5 % to 70 %) to afford the title compound as a pale yellow solid (40.0 mg, 35.4 %). ^{1}H NMR (300 MHz, DMSO-D6) δ ppm 12.58 (brs, 1 H) 7.94 (s, 1 H) 7.47 (d, 2 H) 7.30 - 7.07 (m, 2 H) 3.60 (brs, 4 H) 2.90 (brs, 2 H) 2.85 (brs, 2 H) 2.04 (s, 3 H); *m/z* 331.

The following examples were prepared by the procedure of Example 130, using the appropriate starting materials.

Ex.	Compound	^{1}H NMR	m/z	SM
131A	*N*-(1-{2-[(*Z*)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-4,5-dimethoxyphenyl}pyrrolidin-3-yl)acetamide 	12.29 (brs, 1 H) 8.13 (d, 1 H) 7.85 (s, 1 H) 6.94 (s, 1 H) 6.61 (s, 1 H) 4.27 (d, 1 H) 3.83 (s, 3 H) 3.72 (s, 3 H) 3.43 - 3.14 (m, 4 H) 2.94 (dd, 1 H) 2.30 - 2.05 (m, 1 H) 1.82 (s, 3 H)	392	(5*Z*)-5-[2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene]-1,3-thiazolidine-2,4-dione Example 118 
131B	(*Z*)-*N*-(4-(3-(dimethylamino)pyrrolidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)acetamide 	9.86 (s, 1 H) 7.68 (s, 1 H) 7.56 (s, 1 H) 7.49-7.47 (d, 1 H) 6.96-6.94 (d, 1 H) 3.23 (m, 1 H) 3.00 (m, 4 H) 2.51 (s, 6 H) 2.15 (m, 1 H) 2.01 (s, 3 H) 1.55 (m, 1 H)	375	(Z)-5-(5-amino-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione Example 151 

Example 132:

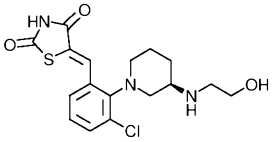
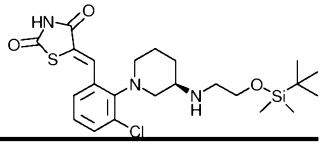
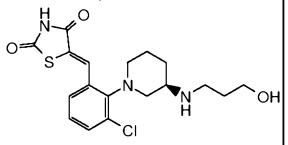
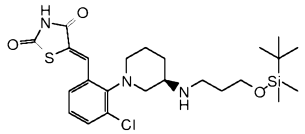


(Z)-5-(2-(3-(2-hydroxyethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione:

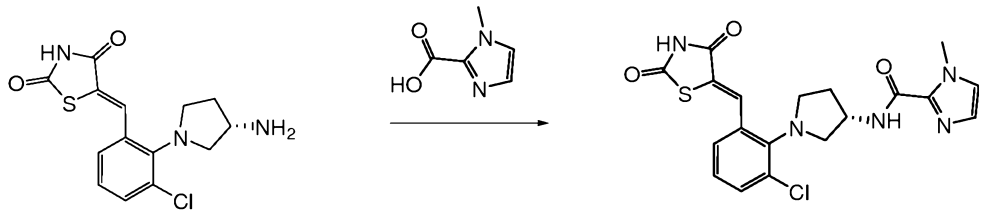
A mixture of (*Z*)-5-(2-(3-(2-(*tert*-butyldimethylsilyloxy)ethylamino)pyrrolidin-1-

yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione (Method 77) (120 mg, 0.24 mmol) in 5 mL of 1.25 M HCl in methanol was stirred at room temperature for 30 min. The mixture was then conc. *in vacuo* to afford the product which was purified via reverse phase HPLC (acetonitrile:water: 0.1 % NH_4OAc = 5 % to 55 %) to yield the title compound as a yellow solid (45.0 mg, 48.4 %). ^1H NMR (300 MHz, DMSO-D6) δ ppm 7.40 (s, 1 H) 7.07 (s, 1 H) 6.57 (s, 1 H) 3.78 (s, 3 H) 3.70 (s, 3 H) 3.45 (m, 2 H) 3.27 - 3.15 (m, 4 H) 2.92 (m, 1 H) 2.59 (m, 2 H) 2.08 (m, 1 H) 1.66 (m, 1 H); *m/z* 394.

The following examples were prepared by the procedure of Example 132 using the appropriate starting materials.

133	(*R,Z*)-5-(3-chloro-2-(3-(2-hydroxyethylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione 	8.81 (brs, 2 H) 7.96 (s, 1 H) 7.48 (d, 1 H) 7.40-7.32 (m, 1 H) 7.31-7.25 (m, 1 H) 3.63-3.55 (m, 2 H) 3.46-3.38 (m, 2 H) 3.08 (brs, 2 H) 2.96 (d, 2 H) 2.75 (brs, 1 H) 2.20 (m, 1H) 1.72 (brs, 1 H) 1.56 (brs, 1 H) 1.44 (brs, 1 H)	382	(*R,Z*)-5-(2-(3-(2-(*tert*-butyldimethylsilyloxy)ethylamino)piperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Method 169 
134	(*R,Z*)-5-(3-chloro-2-(3-(3-hydroxypropylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione 	12.69 (brs, 1 H) 8.84 (brs, 1 H) 8.04 (s, 1 H) 7.56 (d, 1 H) 7.49-7.39 (m, 1 H) 7.36 (t, 1 H) 3.69 (dd, 2 H) 3.17 (brs, 2 H) 3.00 (brs, 2 H) 2.83 (brs, 1 H) 2.26 (brs, 1 H) 1.93-1.72 (m, 4 H) 1.66 (brs, 1 H) 1.50 (brs, 1 H)		(*R,Z*)-5-(2-(3-(3-(*tert*-butyldimethylsilyloxy)propylamino)piperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Method 170 

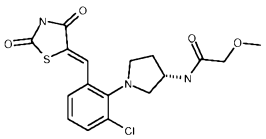
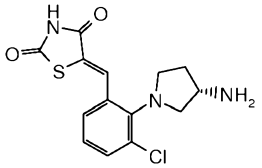
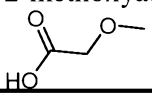
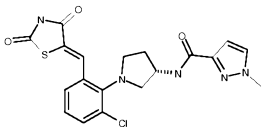
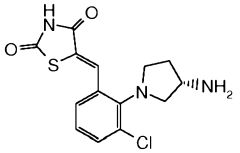
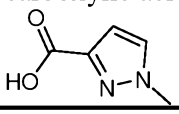
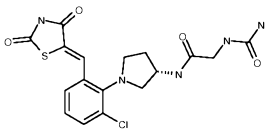
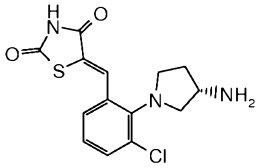
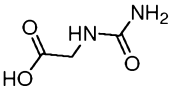
Example 135

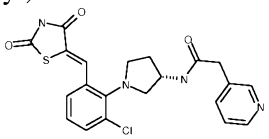
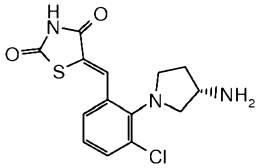
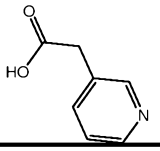
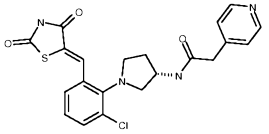
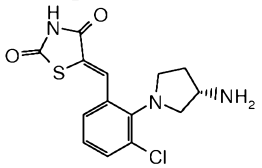
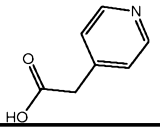


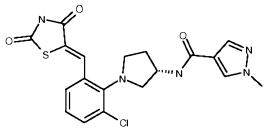
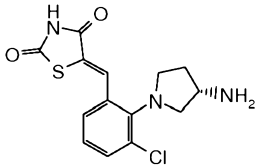
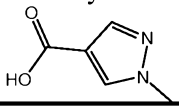
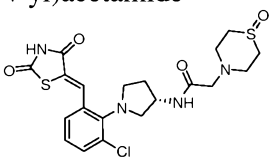
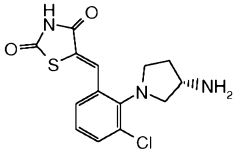
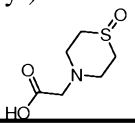
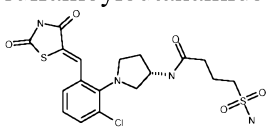
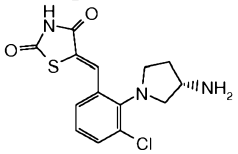
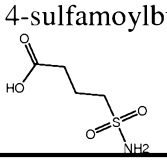
(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-1-methyl-1H-imidazole-2-carboxamide:

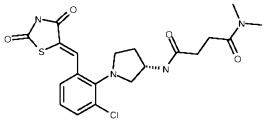
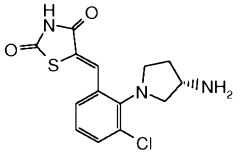
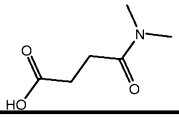
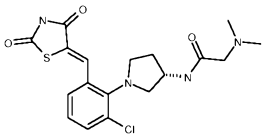
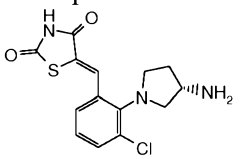
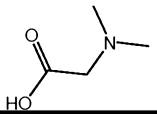
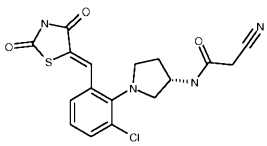
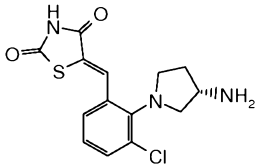
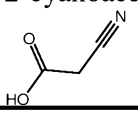
To a 50 mL vial charged with a magnetic stir bar was added (*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione (75 mg, 0.23 mmol) (Example 86), 1-methyl-1H-imidazole-2-carboxylic acid (87 mg, 0.69 mmol), HATU (220 mg, 0.58 mmol) and dichloromethane (5 mL). Hunig's base (0.202 mL, 1.16 mmol) was then added and the mixture was stirred at rt for 4 h. The reaction was then diluted with dichloromethane and washed with water. The mixture was separated with a phase separator tube and the organic phase was evaporated to dryness. The residue was purified by reverse phase chromatography to afford the title compound as a yellow solid (21 mg, 21 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.89 (s, 1 H) 7.51 (dd, 1 H) 7.41 (dd, 1 H) 7.18 – 7.27 (m, 2 H) 7.01 (s, 1 H) 4.67 – 4.77 (m, 1 H) 4.00 (s, 3 H) 3.63 – 3.75 (m, 2 H) 3.47 – 3.54 (m, 1 H) 3.36 – 3.47 (m, 1 H) 2.39 – 2.51 (m, 1 H) 2.14 (dd, 1 H); *m/z* 432.

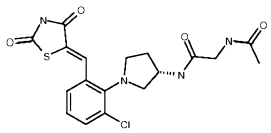
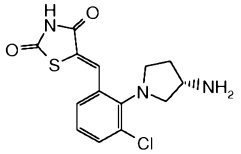
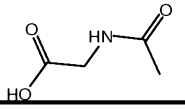
The following examples were prepared by the procedure of 135 using the appropriate starting materials.

136	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-methoxyacetamide 	7.89 (s, 1 H) 7.52 (dd, 1 H) 7.41 (dd, 1 H) 7.25 (t, 1 H) 4.58 – 4.67 (m, 1 H) 3.93 (s, 2 H) 3.65 (dd, 1 H) 3.36 – 3.46 (m, 5 H) 3.13 (dd, 1 H) 2.38 (dd, 1 H) 2.01 – 2.13 (m, 1 H)	396	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-methoxyacetic acid 
137	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-1-methyl-1H-pyrazole-3-carboxamide 	7.93 (s, 1 H) 7.61 (d, 1 H) 7.52 (dd, 1 H) 7.42 (dd, 1 H) 7.25 (t, 1 H) 6.73 (d, 1 H) 4.73 – 4.83 (m, 1 H) 3.92 – 3.99 (m, 3 H) 3.71 (dd, 1 H) 3.38 – 3.50 (m, 2 H) 3.23 (dd, 1 H) 2.38 – 2.50 (m, 1 H) 2.09 – 2.21 (m, 1 H)	432	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 1-methyl-1H-pyrazole-3-carboxylic acid 
138	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-ureidoacetamide 	7.93 (s, 1 H) 7.52 (dd, 1 H) 7.41 (dd, 1 H) 7.25 (t, 1 H) 4.53 (ddd, 1 H) 3.83 – 3.92 (m, 2 H) 3.65 – 3.70 (m, 1 H) 3.42 – 3.49 (m, 1 H) 3.35 – 3.42 (m, 1 H) 3.07 (dd, 1 H) 2.37 (dt, 1 H) 1.98 – 2.10 (m, 1 H)	424	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-ureidoacetic acid 

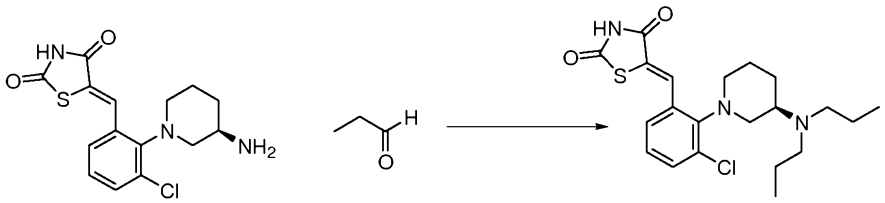
139	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-(pyridin-3-yl)acetamide 	8.44 (br. S., 2 H) 8.02 (s, 1 H) 7.83 (d, 1 H) 7.50 (dd, 1 H) 7.34 – 7.46 (m, 3 H) 7.25 (t, 1 H) 4.51 (t, 1 H) 3.60 – 3.69 (m, 3 H) 3.37 – 3.48 (m, 2 H) 3.08 (dd, 1 H) 2.31 – 2.43 (m, 1 H) 2.03 (dd, 1 H)	443	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-(pyridin-3-yl)acetic acid 
140	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-(pyridin-4-yl)acetamide 	8.47 (br. S., 1 H) 7.98 (s, 1 H) 7.53 (dd, 1 H) 7.41 (dd, 3 H) 7.25 (t, 1 H) 4.53 (t, 1 H) 3.64 – 3.71 (m, 3 H) 3.39 – 3.48 (m, 2 H) 3.07 (dd, 1 H) 2.32 – 2.44 (m, 1 H) 2.03 (dd, 1 H)	443	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-(pyridin-4-yl)acetic acid 

141	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-1-methyl-1H-pyrazole-4-carboxamide 	8.17 (s, 1 H) 8.07 (s, 1 H) 7.94 (s, 1 H) 7.47 (ddd, 2 H) 7.27 (t, 1 H) 4.67 – 4.78 (m, 1 H) 3.89 – 3.97 (m, 3 H) 3.73 (dd, 1 H) 3.44 (t, 2 H) 3.19 (dd, 1 H) 2.42 (dd, 1 H) 2.14 (dd, 1 H)	432	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 1-methyl-1H-pyrazole-4-carboxylic acid 
142	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-(oxidothiomorpholin-4-yl)acetamide 	7.91 (s, 1 H) 7.56 (dd, 1 H) 7.43 (dd, 1 H) 7.27 (t, 1 H) 4.62 (t, 1 H) 3.67 – 3.78 (m, 2 H) 3.41 – 3.48 (m, 2 H) 3.19 – 3.22 (m, 2 H) 3.10 – 3.17 (m, 5 H) 2.92 – 2.98 (m, 2 H) 2.81 – 2.86 (m, 1 H) 2.37 – 2.48 (m, 1 H) 2.02 – 2.13 (m, 1 H)	483	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and (1-oxidothiomorpholin-4-yl)acetic acid 
143	(*S,Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-4-sulfamoylbutanamide 	7.18 (s, 1 H) 6.70 (dd, 1 H) 6.62 (dd, 1 H) 6.45 (t, 1 H) 3.71 (s, 1 H) 2.84 (dd, 1 H) 2.56 – 2.66 (m, 2 H) 2.29 – 2.36 (m, 2 H) 2.26 (dd, 1 H) 1.64 (t, 2 H) 1.57 (d, 1 H) 1.25 – 1.37 (m, 2 H) 1.20 (d, 1 H)	473	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 4-sulfamoylbutanoic acid 

144	(*S*,*Z*)-*N*1-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-*N*4,*N*4-dimethylsuccinamide 	8.01 (s, 1 H) 7.50 (d, 1 H) 7.44 (d, 1 H) 7.26 (t, 1 H) 4.47 – 4.58 (m, 1 H) 3.62 (t, 1 H) 3.42 (t, 2 H) 3.02 – 3.15 (m, 4 H) 2.92 (s, 3 H) 2.67 (d, 2 H) 2.56 (t, 2 H) 2.36 (dd, 1 H) 2.02 (dd, 1 H)	451	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 4-(dimethylamino)-4-oxobutanoic acid 
145	(*S*,*Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-(dimethylamino)acetamide 	7.07 (s, 1 H) 6.69 – 6.74 (m, 1 H) 6.59 (dd, 1 H) 6.43 (t, 1 H) 3.76 (br. S., 1 H) 2.85 – 2.94 (m, 2 H) 2.84 (d, 1 H) 2.36 (br. S., 1 H) 2.29 (dd, 2 H) 1.52 – 1.64 (m, 7 H) 1.18 – 1.28 (m, 1 H)	409	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-(dimethylamino)acetic acid 
146	(*S*,*Z*)-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)-2-cyanoacetamide 	7.95 (s, 1 H) 7.52 (dd, 1 H) 7.42 (dd, 1 H) 7.26 (t, 1 H) 4.50 (ddd, 1 H) 3.68 – 3.78 (m, 1 H) 3.64 (dd, 1 H) 3.44 – 3.50 (m, 1 H) 3.40 (t, 1 H) 3.22 (q, 1 H) 3.09 (dd, 1 H) 2.39 (dt, 1 H) 2.03 (d, 1 H)	391	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-cyanoacetic acid 

147	(*S,Z*)-2-acetamido-*N*-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)acetamide 	7.89 (s, 1 H) 7.54 (dd, 1 H) 7.39 (dd, 1 H) 7.24 (t, 1 H) 4.49 – 4.60 (m, 1 H) 3.86 – 3.98 (m, 1 H) 3.65 (dd, 1 H) 3.36 – 3.48 (m, 2 H) 3.17 – 3.25 (m, 1 H) 3.07 – 3.16 (m, 1 H) 2.31 – 2.43 (m, 1 H) 1.96 – 2.09 (m, 4 H)	423	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione Example 86  and 2-acetamidoacetic acid 

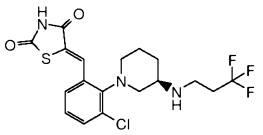
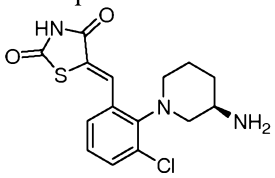
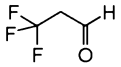
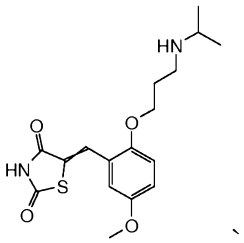
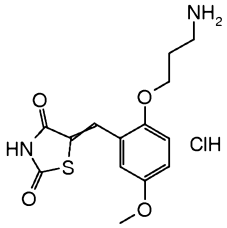
Example 148:



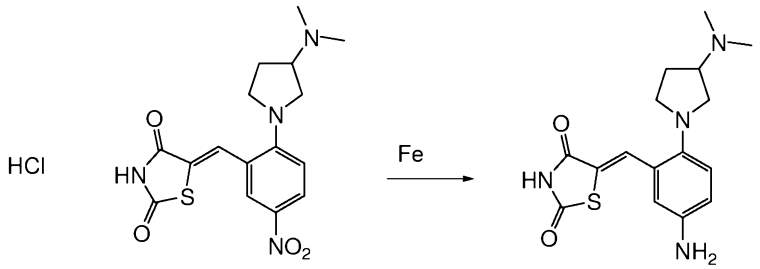
(*R,Z*)-5-(3-chloro-2-(3-(dipropylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione:

A mixture of (*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione (122D) (100 mg, 0.27 mmol) and propionaldehyde (20.17 mg, 0.35 mmol) in CH_2Cl_2 (15 mL) was stirred at 50 °C for 20 min. before sodium triacetoxyborohydride (170 mg, 0.80 mmol) was added. The mixture was then stirred at 50 °C for 4 h. before sat'd aqueous K_2CO_3 (~ 50 mL) was added to the mixture. This solution was poured into a separatory funnel and extracted with $CHCl_3$/isopropanol (5/1) (2 x 50 mL). The combined organic extract was dried over anhydrous Na_2SO_4, filtered, and conc. *in vacuo* affording the product. It was purified with Gilson (0.1% TFA in water:0.1% TFA in CAN=30% to 80%; UV absortion at 322) to yield the title compound as a yellow solid (94 mg, 77 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.96 (s, 1 H) 7.48 (d, 1 H) 7.41-7.34 (m, 1 H) 7.29 (t, 1 H) 3.67-3.58 (m, 2 H) 3.44-3.37 (m, 2 H) 3.03-2.78 (m, 5 H) 2.21 (brs, 1 H), 1.79 (d, 1 H) 1.61 (d, 6 H) 0.84-0.79 (m, 6 H). *m/z* 422.

He following examples were prepared by the procedure of 148, using the appropriate starting materials.

149	(*R,Z*)-5-(3-chloro-2-(3-(3,3,3-trifluoropropylamino) piperidin-1-yl)benzylidene)thiazolidine-2,4-dione 	12.65 (brs, 1 H) 9.35 (brs, 1H) 8.05 (s, 1 H) 7.56 (d, 1 H) 7.44 (brs, 1 H) 7.37 (t, 1 H) 3.75-3.63 (m, 2 H) 3.53-3.45 (m, 2 H) 3.23 (m, 1 H) 2.85-2.65 (m, 4 H) 2.30 (brs, 1 H) 1.85-1.76 (m, 1 H) 1.67 (brs, 1 H) 1.49 (brs, 1 H)	433	(*R,Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride Example 122D  and 3,3,3-trifluoropropanal 
150	5-(2-(3-(isopropylamino)propoxy)-5-methoxybenzylidene) thiazolidine-2,4-dione 	12.65 (s, 1H), 8.91 (s, br, 2H), 7.91 (s, 1H), 7.10 (m, 2H), 7.85 (s, 1H), 4.17 (m, 2H), 3.65 (m, 4H), 3.05 (m, 2H), 2.14 (m, 2H), 1.22 (m, 6H)	351	5-(2-(3-aminopropoxy)-5-methoxybenzylidene)thiazolidine-2,4-dione hydrochloride Example 129C  And Acetone 

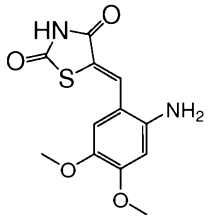
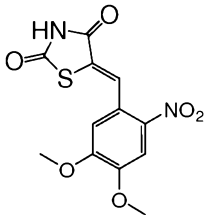
Example 151:



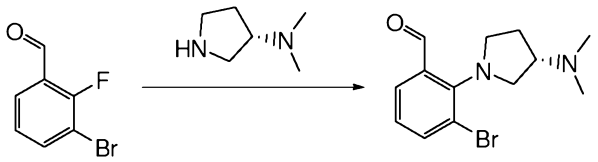
(Z)-5-(5-amino-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione

To a mixture of (Z)-5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzylidene)thiazolidine-2,4-dione (100 mg, 0.28 mmol) (Method 149) and iron (154 mg, 2.76 mmol) chip in MeOH (10 mL) was added 5 drops of conc. HCl and 5 drops of water. The mixture was stirred at 80 °C for 1hr. The mixture was loaded into silica gel, purified with ISCO (100% ethyl acetate to methanol/ethyl acetate=50%) to yield a red solid which was repurified with Gilson (acetonitrile:water:0.1%TFA=0% to 50% fro 7min) to yield a yellow solid as (Z)-5-(5-amino-2-(3-(dimethylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione (51.0 mg, 38.6 %). ^{1}H NMR (400 MHz, DMSO-d6) d ppm 12.55 (brs, 1 H), 11.32 (brs, 1 H), 10.30 (brs, 2 H), 7.80 (s, 1 H), 7.42 (m, 2 H), 7.19 (m, 1 H), 3.95 (m, 1 H), 3.39-3.27 (m, 4 H), 2.78 (s, 6 H), 2.30-2.10 (m, 2 H); *m/z* 333.

The following intermediates were prepared by the procedure of Example 151 using the appropriate starting materials.

Ex	Compound	^{1}H NMR	m/z	SM
152	(*Z*)-5-(2-amino-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione 	12.45 (brs, 1 H) 7.87 (s, 1 H) 6.80 (s, 1 H) 6.79 (s, 1 H) 3.78 (s, 3 H) 3.73 (s, 3 H)	280	(*Z*)-5-(4,5-dimethoxy-2-nitrobenzylidene)thiazolidine-2,4-dione Method 150 

Methods Section:

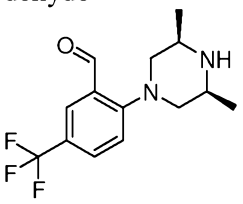
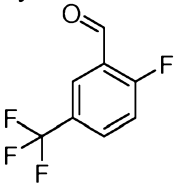
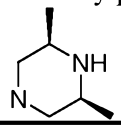
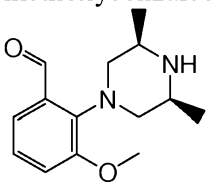
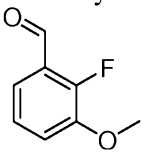
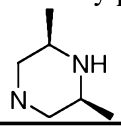
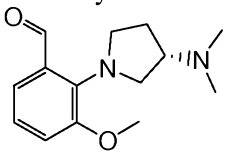
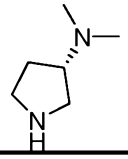


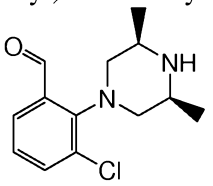
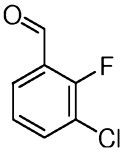
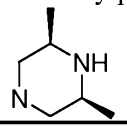
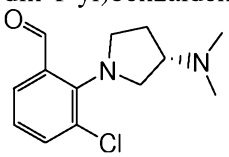
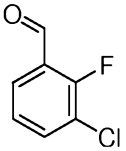
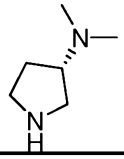
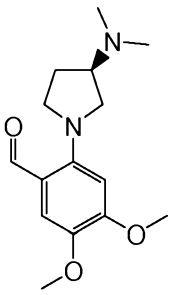
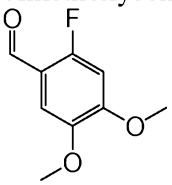
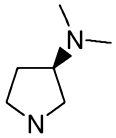
Method 1:

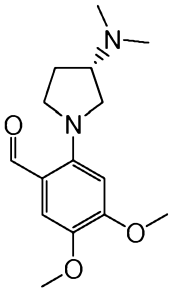
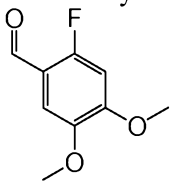
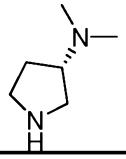
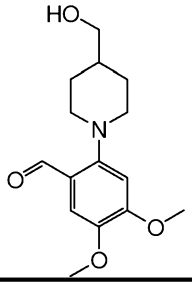
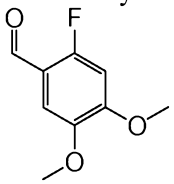
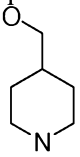
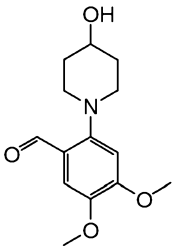
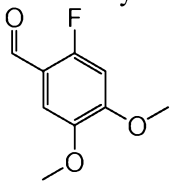
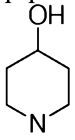
(*S*)-3-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde:

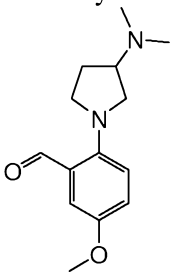
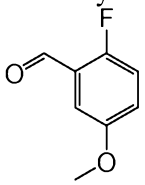
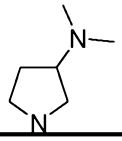
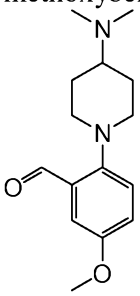
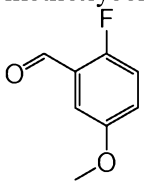
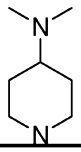
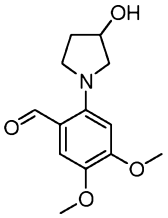
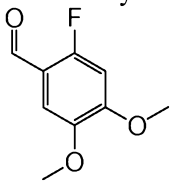
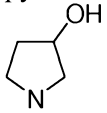
A 50 mL round bottom flask was charged with a magnetic stir bar, 3-bromo-2-fluorobenzaldehyde (0.555 g, 2.73 mmol), (*S*)-*N,N*-dimethylpyrrolidin-3-amine (0.312 g, 2.73 mmol), DMSO (5.47 ml), and potassium carbonate (0.378 g, 2.73 mmol). The mixture was heated to 85 °C overnight with stirring. The reaction was allowed to cool to ambient temperature, was diluted with water, and extracted into methylene chloride. The combined organic extract was dried with $MgSO_4$, filtered, and conc. *in vacuo* to provide the product which was purified via silica gel chromatography (40 g) using ethyl acetate / MeOH (10 : 1) as eluent to afford (*S*)-3-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde (0.369 g, 45.4 %).

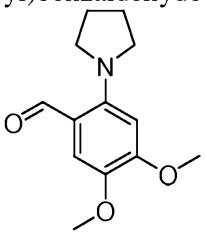
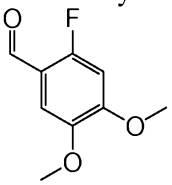
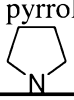
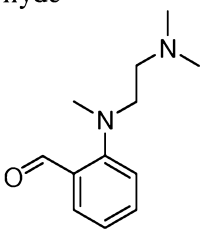
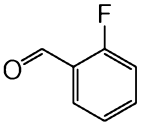
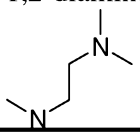
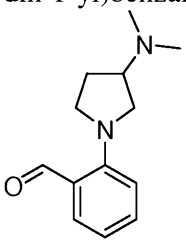
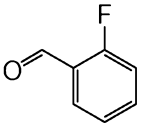
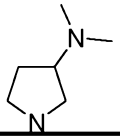
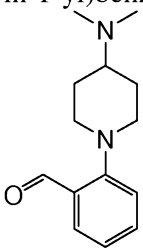
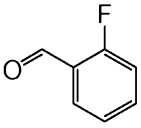
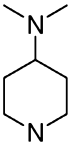
The following intermediates were prepared by the procedure of Method 1, using the appropriate starting materials.

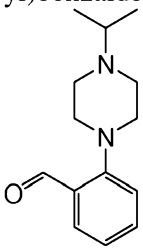
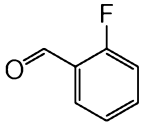
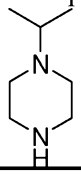
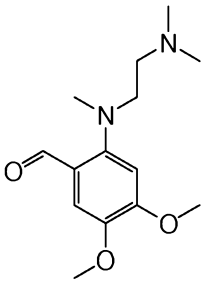
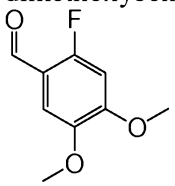
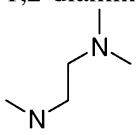
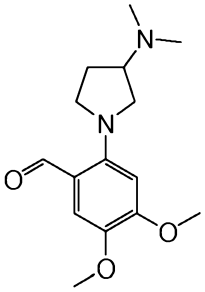
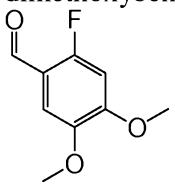
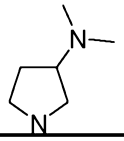
Method	Compound	^{1}H NMR	m/z	SM
2	2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)-5-(trifluoromethyl)benzaldehyde 		287	2-fluoro-5-(trifluoromethyl)benzaldehyde  and (2*R*,6*S*)-2,6-dimethylpiperazine 
3	2-((*3S,5R*)-3,5-dimethylpiperazin-1-yl)-3-methoxybenzaldehyde 		249	2-fluoro-3-methoxybenzaldehyde  and (2*R*,6*S*)-2,6-dimethylpiperazine 
4	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-3-methoxybenzaldehyde 		249	2-fluoro-3-methoxybenzaldehyde  and (*3S*)-*N*,*N*-dimethylpyrrolidin-3-amine 

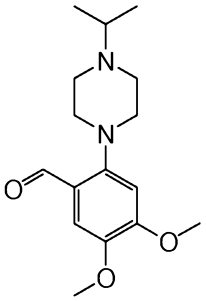
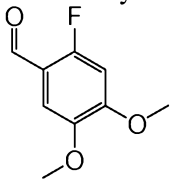
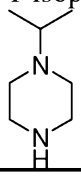
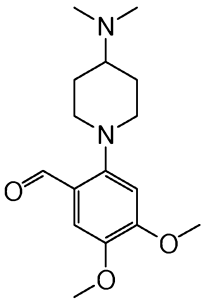
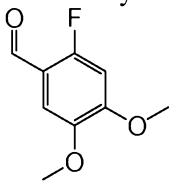
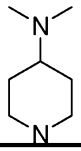
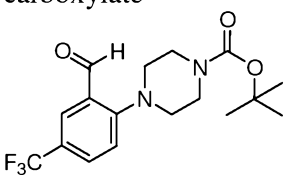
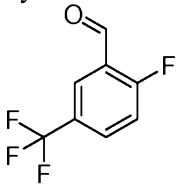
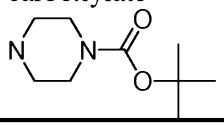
5	3-chloro-2-((3*S*,5*R*)-3,5-dimethylpiperazin-1-yl)benzaldehyde 		254	3-chloro-2-fluorobenzaldehyde  and (2*R*,6*S*)-2,6-dimethylpiperazine 
6	(*S*)-3-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde 		253	3-chloro-2-fluorobenzaldehyde  and (*3S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
7	(*R*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde 		279	2-fluoro-4,5-dimethoxybenzaldehyde  and (3*R*)-*N*,*N*-dimethylpyrrolidin-3-amine 

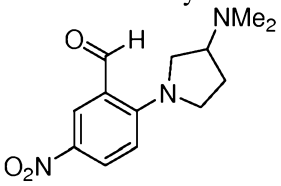
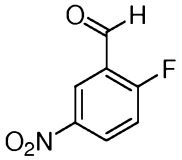
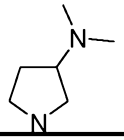
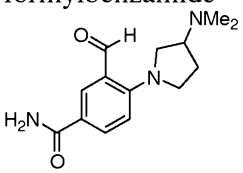
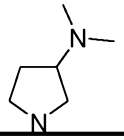
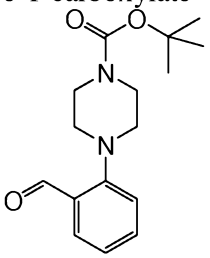
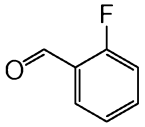
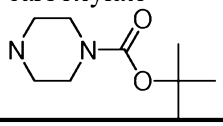
8	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde 		279	2-fluoro-4,5-dimethoxybenzaldehyde  and (*3S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
9	2-(4-(hydroxymethyl)piperidin-1-yl)-4,5-dimethoxybenzaldehyde 		280	2-fluoro-4,5-dimethoxybenzaldehyde  and piperidin-4-ylmethanol 
10	2-(4-hydroxypiperidin-1-yl)-4,5-dimethoxybenzaldehyde 		266	2-fluoro-4,5-dimethoxybenzaldehyde  and piperidin-4-ol 

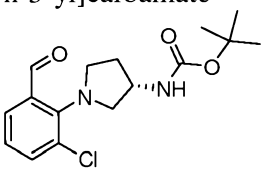
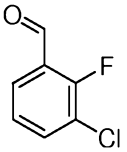
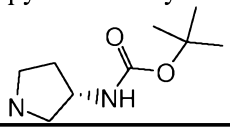
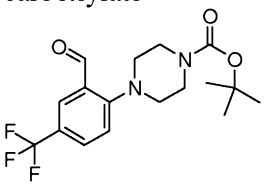
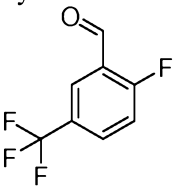
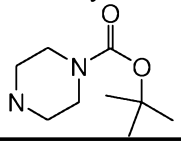
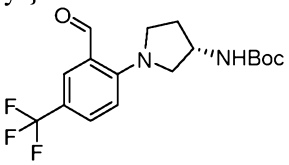
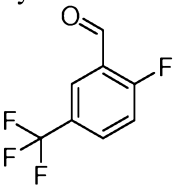
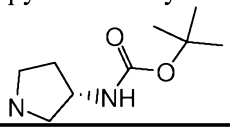
11	2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methoxybenzaldehyde 		249	2-fluoro-5-methoxybenzaldehyde  and *N,N*-dimethylpyrrolidin-3-amine 
12	2-(4-(dimethylamino)piperidin-1-yl)-5-methoxybenzaldehyde 		263	2-fluoro-5-methoxybenzaldehyde  and *N,N*-dimethylpiperidin-4-amine 
13	2-(3-hydroxypyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde 		253	2-fluoro-4,5-dimethoxybenzaldehyde  and pyrrolidin-3-ol 

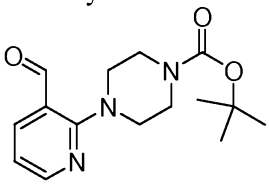
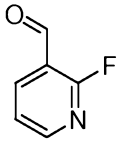
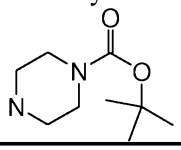
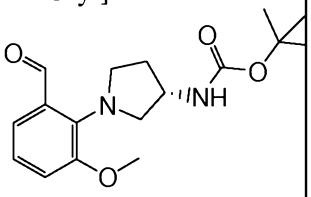
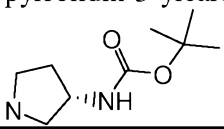
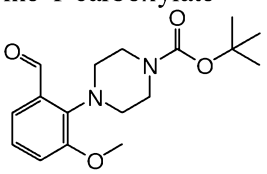
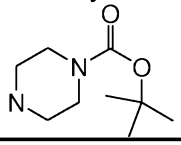
14	4,5-dimethoxy-2-(pyrrolidin-1-yl)benzaldehyde 		236	2-fluoro-4,5-dimethoxybenzaldehyde  and pyrrolidine 
15	2-((2-(dimethylamino)ethyl)(methyl)amino)benzaldehyde 		207	2-fluorobenzaldehyde  and *N,N,N'*-trimethylethane-1,2-diamine 
16	2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde 		219	2-fluorobenzaldehyde  and *N,N*-dimethylpyrrolidin-3-amine 
17	2-(4-(dimethylamino)piperidin-1-yl)benzaldehyde 		233	2-fluorobenzaldehyde  and *N,N*-dimethylpiperidin-4-amine 

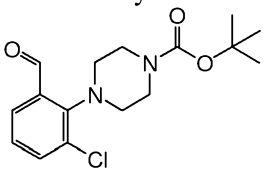
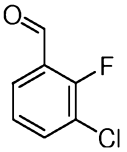
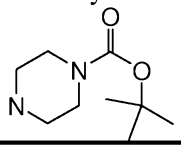
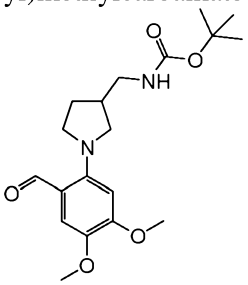
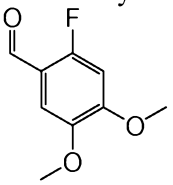
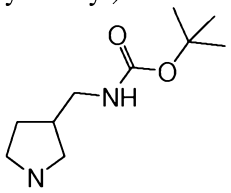
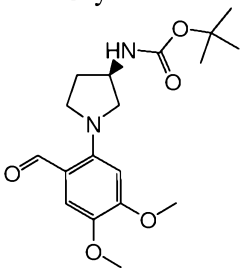
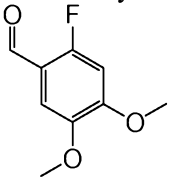
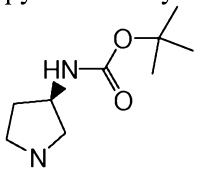
18	2-(4-isopropylpiperazin-1-yl)benzaldehyde 		233	2-fluorobenzaldehyde  and 1-isopropylpiperazine 
19	2-((2-(dimethylamino)ethyl)(methyl)amino)-4,5-dimethoxybenzaldehyde 		267	2-fluoro-4,5-dimethoxybenzaldehyde  and *N,N,N'*-trimethylethane-1,2-diamine 
20	2-(3-(dimethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzaldehyde 		279	2-fluoro-4,5-dimethoxybenzaldehyde  and *N,N*-dimethylpyrrolidin-3-amine 

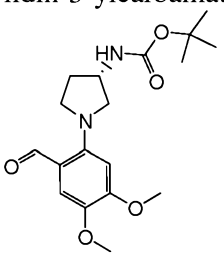
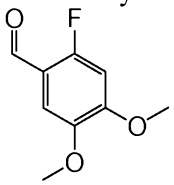
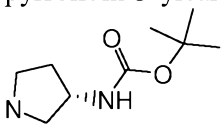
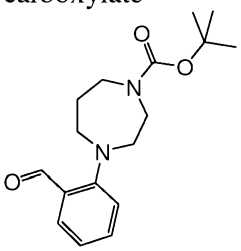
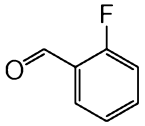
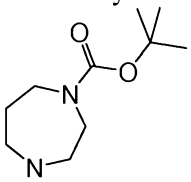
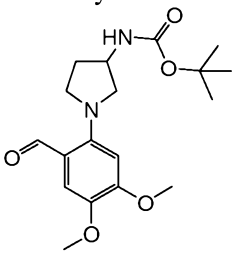
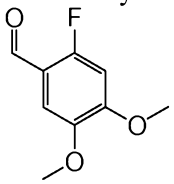
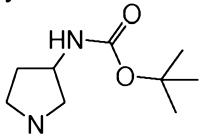
21	2-(4-isopropylpiperazin-1-yl)-4,5-dimethoxybenzaldehyde 		293	2-fluoro-4,5-dimethoxybenzaldehyde  and 1-isopropylpiperazine 
22	2-(4-(dimethylamino)piperidin-1-yl)-4,5-dimethoxybenzaldehyde 		293	2-fluoro-4,5-dimethoxybenzaldehyde  and *N,N*-dimethylpiperidin-4-amine 
23	*tert*-butyl 4-(2-formyl-4-(trifluoromethyl)phenyl)piperazine-1-carboxylate 		359	2-fluoro-5-(trifluoromethyl)benzaldehyde  and *tert*-butyl piperazine-1-carboxylate 

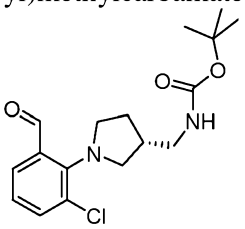
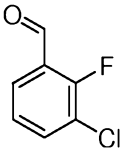
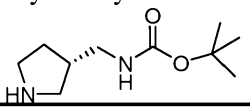
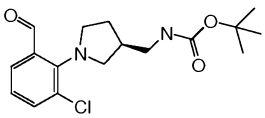
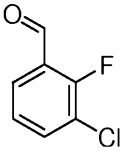
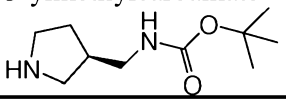
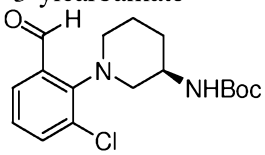
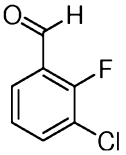
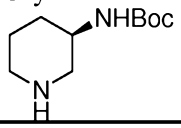
24	2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzaldehyde 		264	2-fluoro-5-nitrobenzaldehyde  and *N,N*-dimethylpyrrolidin-3-amine 
25	4-(3-(dimethylamino)pyrrolidin-1-yl)-3-formylbenzamide 		262	4-fluoro-3-formylbenzamide  and *N,N*-dimethylpyrrolidin-3-amine 
26	*tert*-butyl 4-(2-formylphenyl)piperazine-1-carboxylate 		291	2-fluorobenzaldehyde  and *tert*-butyl piperazine-1-carboxylate 

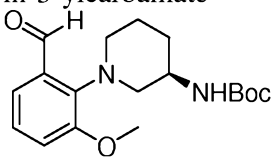
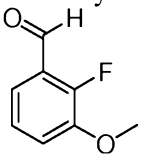
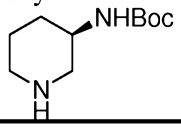
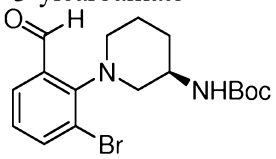
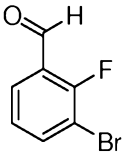
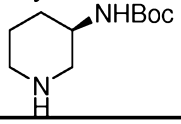
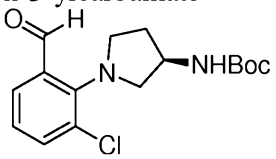
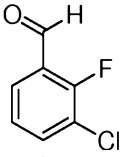
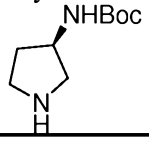
79	*tert*-butyl [(3*S*)-1-(2-chloro-6-formylphenyl)pyrrolidin-3-yl]carbamate 		326	3-chloro-2-fluorobenzaldehyde  and *tert*-butyl (3*S*)-pyrrolidin-3-ylcarbamate 
80	*tert*-butyl4-[2-formyl-4-(trifluoromethyl)phenyl]piperazine-1-carboxylate 		359	2-fluoro-5-(trifluoromethyl)benzaldehyde  and *tert*-butyl piperazine-1-carboxylate 
81	*tert*-butyl{(3*S*)-1-[2-formyl-4-(trifluoromethyl)phenyl]pyrrolidin-3-yl}carbamate 		359	2-fluoro-5-(trifluoromethyl)benzaldehyde  and *tert*-butyl (3*S*)-pyrrolidin-3-ylcarbamate 

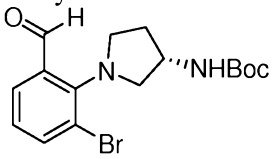
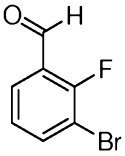
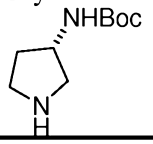
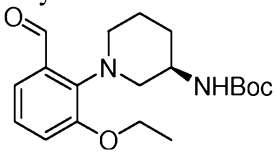
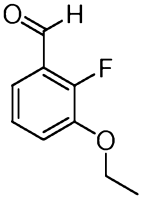
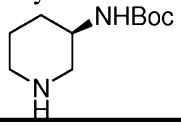
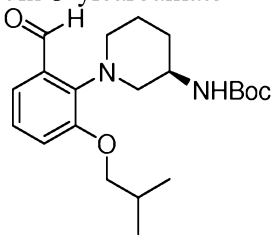
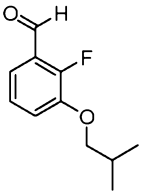
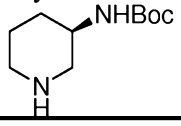
82	*tert*-butyl 4-(3-formylpyridin-2-yl)piperazine-1-carboxylate 		292	2-fluoronicotinaldehyde  and *tert*-butyl piperazine-1-carboxylate 
83	*tert*-butyl [(3*S*)-1-(2-formyl-6-methoxyphenyl)pyrrolidin-3-yl]carbamate 		322	2-fluoro-3-methoxybenzaldehyde  and *tert*-butyl (3*S*)-pyrrolidin-3-ylcarbamate 
84	*tert*-butyl 4-(2-formyl-6-methoxyphenyl)piperazine-1-carboxylate 		321	2-fluoro-3-methoxybenzaldehyde  and *tert*-butyl piperazine-1-carboxylate 

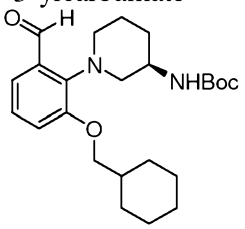
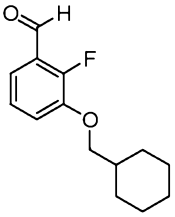
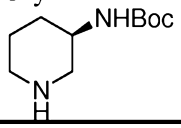
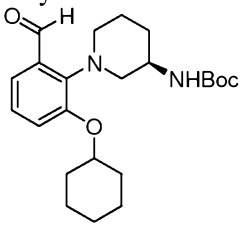
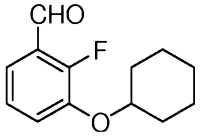
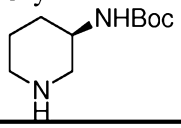
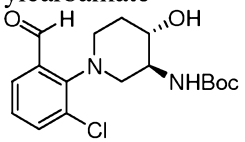
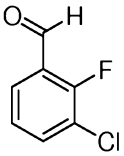
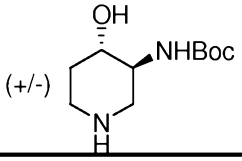
85	*tert*-butyl 4-(2-chloro-6-formylphenyl)piperazine-1-carboxylate 		326	3-chloro-2-fluorobenzaldehyde  and *tert*-butyl piperazine-1-carboxylate 
86	*tert*-butyl (1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-yl)methylcarbamate 		365	2-fluoro-4,5-dimethoxybenzaldehyde  and *tert*-butyl (pyrrolidin-3-ylmethyl)carbamate 
87	(*R*)-*tert*-butyl 1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate 		351	2-fluoro-4,5-dimethoxybenzaldehyde  and *tert*-butyl (3*R*)-pyrrolidin-3-ylcarbamate 

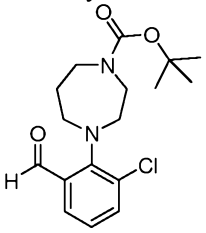
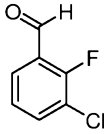
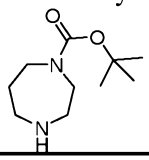
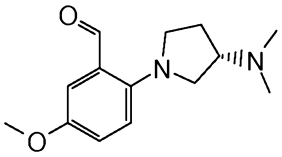
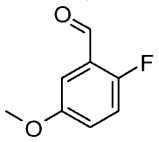
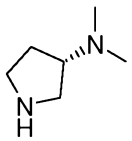
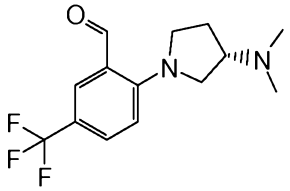
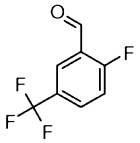
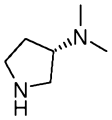
88	(*S*)-*tert*-butyl 1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate 		351	2-fluoro-4,5-dimethoxybenzaldehyde  and *tert*-butyl (3*S*)-pyrrolidin-3-ylcarbamate 
89	*tert*-butyl 4-(2-formylphenyl)-1,4-diazepane-1-carboxylate 		305	2-fluorobenzaldehyde  and *tert*-butyl 1,4-diazepane-1-carboxylate 
90	*tert*-butyl 1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate 		351	2-fluoro-4,5-dimethoxybenzaldehyde  and *tert*-butyl pyrrolidin-3-ylcarbamate 

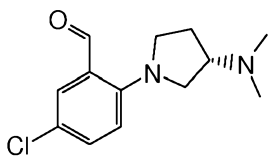
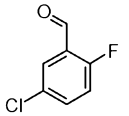
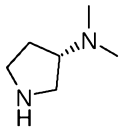
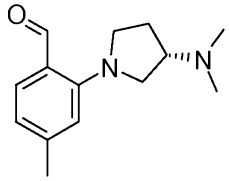
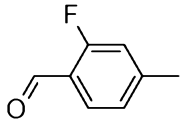
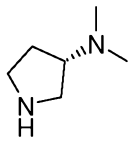
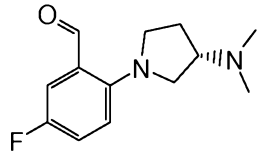
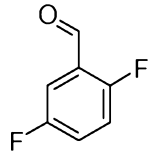
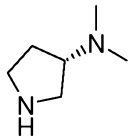
91	(*R*)-*tert*-butyl (1-(2-chloro-6-formylphenyl)pyrrolidin-3-yl)methylcarbamate 		339	3-chloro-2-fluorobenzaldehyde  and (*S*)-*tert*-butyl pyrrolidin-3-ylmethylcarbamate 
92	(*S*)-*tert*-butyl (1-(2-chloro-6-formylphenyl)pyrrolidin-3-yl)methylcarbamate 		339	3-chloro-2-fluorobenzaldehyde  and *(R)*-*tert*-butyl pyrrolidin-3-ylmethylcarbamate 
93	(*R*)-*tert*-butyl 1-(2-chloro-6-formylphenyl)piperidin-3-ylcarbamate 		339	3-chloro-2-fluorobenzaldehyde  and (*R*)-*tert*-butyl piperidin-3-ylcarbamate 

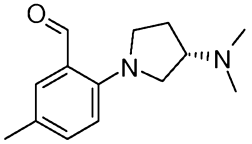
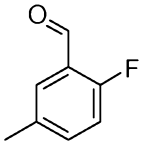
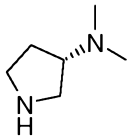
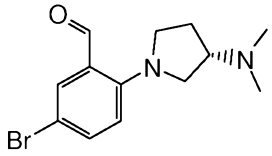
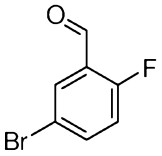
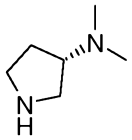
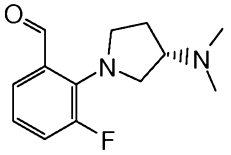
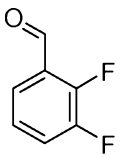
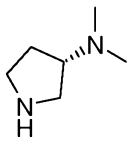
94	(*R*)-*tert*-butyl 1-(2-formyl-6-methoxyphenyl)piperidin-3-ylcarbamate 		335	2-fluoro-3-methoxybenzaldehyde  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
95	(*R*)-*tert*-butyl 1-(2-bromo-6-formylphenyl)piperidin-3-ylcarbamate 		385	3-bromo-2-fluorobenzaldehyde  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
96	(*R*)-*tert*-butyl 1-(2-chloro-6-formylphenyl)pyrrolidin-3-ylcarbamate 		325	3-chloro-2-fluorobenzaldehyde  and (*R*)-*tert*–butyl pyrrolidin-3-ylcarbamate 

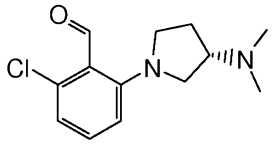
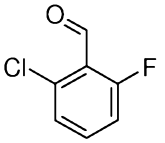
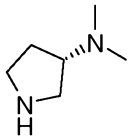
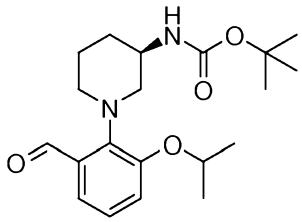
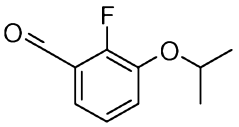
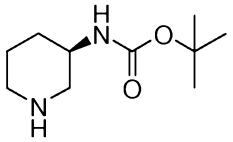
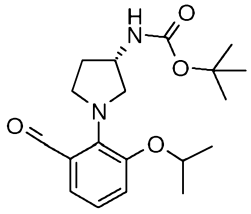
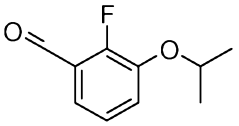
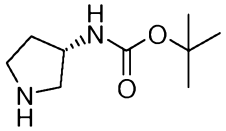
97	(*S*)-*tert*-butyl 1-(2-bromo-6-formylphenyl)pyrrolidin-3-ylcarbamate 		371	3-bromo-2-fluorobenzaldehyde  And (*S*)-*tert*-butyl pyrrolidin-3-ylcarbamate 
98	(*R*)-*tert*-butyl 1-(2-ethoxy-6-formylphenyl)piperidin-3-ylcarbamate 		349	3-ethoxy-2-fluorobenzaldehyde Method 172  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
99	(*R*)-*tert*-butyl 1-(2-formyl-6-isobutoxyphenyl)piperidin-3-ylcarbamate 		377	2-fluoro-3-isobutoxybenzaldehyde Method 173  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 

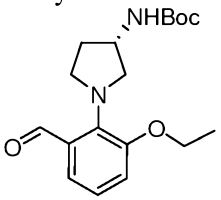
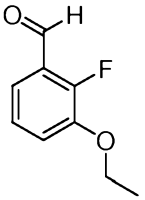
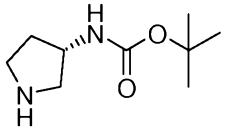
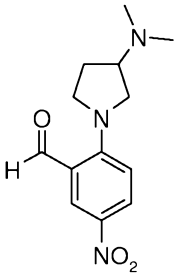
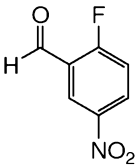
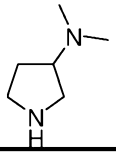
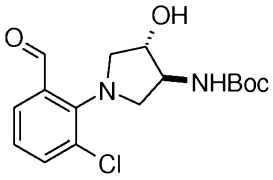
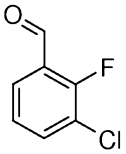
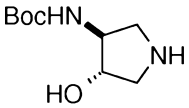
100	(*R*)-*tert*-butyl 1-(2-(cyclohexylmethoxy)-6-formylphenyl)piperidin-3-ylcarbamate 		417	3-(cyclohexylmethoxy)-2-fluorobenzaldehyde Method 174  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
101	(*R*)-*tert*-butyl 1-(2-(cyclohexyloxy)-6-formylphenyl)piperidin-3-ylcarbamate 		403	3-(cyclohexyloxy)-2-fluorobenzaldehyde Method 175  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
102	(±)-*tert*-butyl-1-(2-chloro-6-formylphenyl)-4-hydroxypiperidin-3-ylcarbamate 		354	3-chloro-2-fluorobenzaldehyde  and (±)-*tert*-butyl-4-hydroxypiperidin-3-ylcarbamate Method 189 

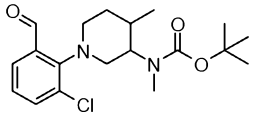
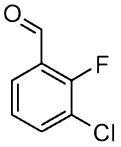
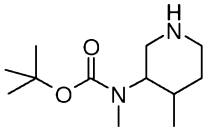
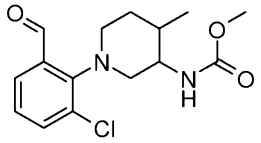
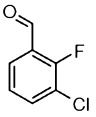
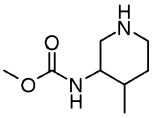
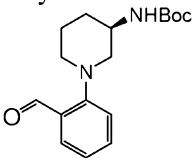
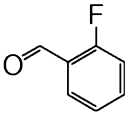
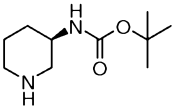
103	*tert*-butyl 4-(2-chloro-6-formylphenyl)-1,4-diazepane-1-carboxylate 	10.49 (s, 1 H), 7.75 (d, 1 H), 7.63 (d, 1 H), 7.25 (t, 1 H), 3.37 (brs, 4 H), 1.88 (brs, 2 H), 1.53 (s, 9 H)	339	3-chloro-2-fluorobenzaldehyde  and *tert*-butyl 1,4-diazepane-1-carboxylate 
104	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methoxybenzaldehyde 		249	2-fluoro-5-methoxybenzaldehyde  and (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
105	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzaldehyde 		287	2-fluoro-5-(trifluoromethyl)benzaldehyde  and (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 

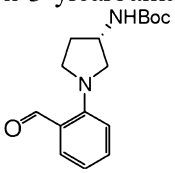
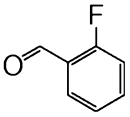
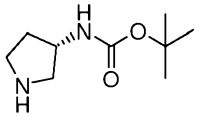
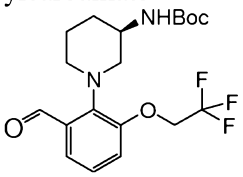
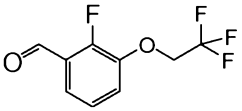
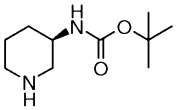
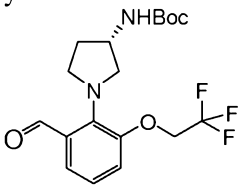
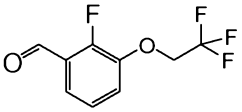
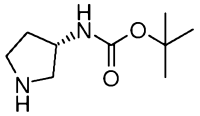
106	(*S*)-5-chloro-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehydeMethod 		253	5-chloro-2-fluorobenzaldehyde  and (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
107	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-4-methylbenzaldehyde 		233	2-fluoro-4-methylbenzaldehyde  And (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
108	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-fluorobenzaldehyde 		237	2,5-difluorobenzaldehyde  And (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 

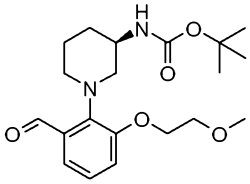
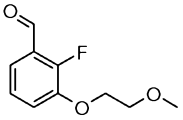
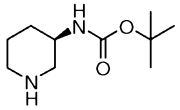
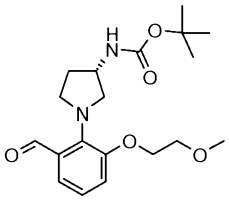
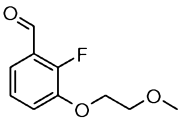
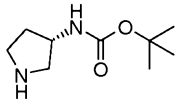
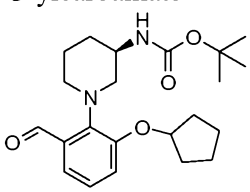
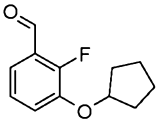
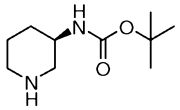
109	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-5-methylbenzaldehyde 		233	2-fluoro-5-methylbenzaldehyde  And (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
110	(*S*)-5-bromo-2-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde 		298	5-bromo-2-fluorobenzaldehyde  And (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
111	(*S*)-2-(3-(dimethylamino)pyrrolidin-1-yl)-3-fluorobenzaldehyde 		237	2,3-difluorobenzaldehyde  And (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 

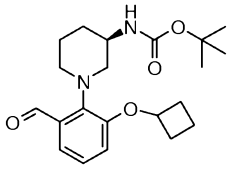
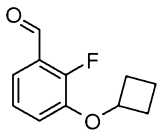
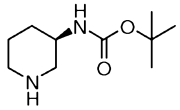
112	(S)-2-chloro-6-(3-(dimethylamino)pyrrolidin-1-yl)benzaldehyde 		253	2-chloro-6-fluorobenzaldehyde  And (*S*)-*N*,*N*-dimethylpyrrolidin-3-amine 
113	(*R*)-*tert*-butyl 1-(2-formyl-6-isopropoxyphenyl)piperidin-3-ylcarbamate 		363	2-fluoro-3-isopropoxybenzaldehyde Method 176  (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
114	(*S*)-*tert*-butyl 1-(2-formyl-6-isopropoxyphenyl)pyrrolidin-3-ylcarbamate 		349	2-fluoro-3-isopropoxybenzaldehyde Method 176  (*S*)-*tert*-butyl pyrrolidin-3-ylcarbamate 

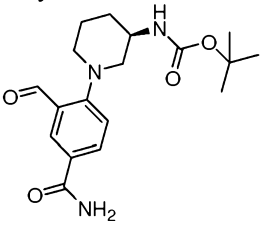
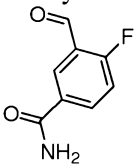
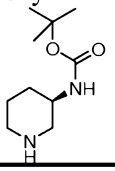
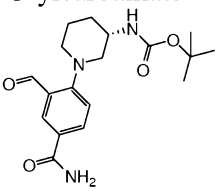
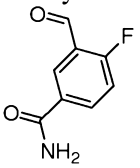
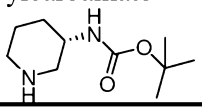
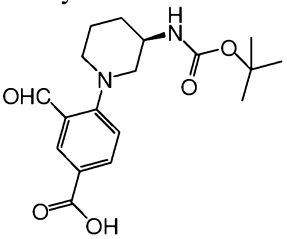
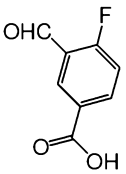
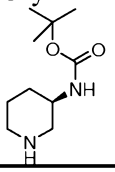
115	(*S*)-*tert*-butyl 1-(2-ethoxy-6-formylphenyl)pyrrolidin-3-ylcarbamate 		334	3-ethoxy-2-fluorobenzaldehyde Method 172  And (*S*)-*tert*-butyl pyrrolidin-3-ylcarbamate 
116	2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzaldehyde 		263	2-fluoro-5-nitrobenzaldehyde  and *N,N*-dimethylpyrrolidin-3-amine 
117	(±)-*tert*-butyl-1-(2-chloro-6-formylphenyl)-4-hydroxypyrrolidin-3-ylcarbamate 	10.30 (s, 1 H) 7.76 (dd, 1 H) 7.65 (dd, 1 H) 7.29-7.24(m, 1 H) 5.05 (brs, 1 H) 4.41 (brs, 1 H) 4.20 (brs, 1 H) 3.87 (dd, 1 H) 3.78 (dd, 1 H) 3.64-3.47 (m, 1 H) 3.36 (brs, 1 H) 3.21 (dd, 1 H) 1.50 (s, 9 H)	341	3-chloro-2-fluorobenzaldehyde  And (±)-*tert*-butyl-4-hydroxypyrrolidin-3-ylcarbamate Method 188 

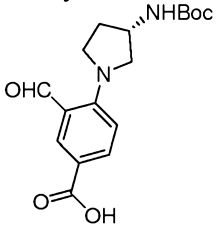
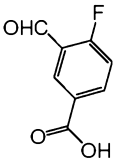
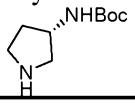
118	*tert*-butyl 1-(2-chloro-6-formylphenyl)-4-methylpiperidin-3-yl(methyl)carbamate 		367	3-chloro-2-fluorobenzaldehyde  *tert*-butyl methyl(4-methylpiperidin-3-yl)carbamate 
119	methyl 1-(2-chloro-6-formylphenyl)-4-methylpiperidin-3-ylcarbamate 		310	3-chloro-2-fluorobenzaldehyde  methyl 4-methylpiperidin-3-ylcarbamate 
120	*(R)-tert*-butyl 1-(2-formylphenyl)piperidin-3-ylcarbamate 		305	2-fluorobenzaldehyde  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 

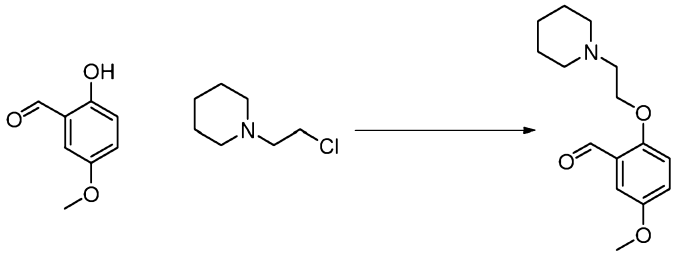
121	(*S*)-*tert*-butyl 1-(2-formylphenyl)pyrrolidin-3-ylcarbamate 		291	2-fluorobenzaldehyde  And (*S*)-*tert*-butyl pyrrolidin-3-ylcarbamate 
122	(*R*)-*tert*-butyl 1-(2-formyl-6-(2,2,2-trifluoroethoxy)phenyl) piperidin-3-ylcarbamate 		403	2-fluoro-3-(2,2,2-trifluoroethoxy)benzaldehyde Method 177  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
123	(*S*)-*tert*-butyl 1-(2-formyl-6-(2,2,2-trifluoroethoxy)phenyl) pyrrolidin-3-ylcarbamate 		389	2-fluoro-3-(2,2,2-trifluoroethoxy)benzaldehyde Method 177  And (*S*)-*tert*-butyl pyrrolidin-3-ylcarbamate 

124	(*R*)-*tert*-butyl 1-(2-formyl-6-(2-methoxyethoxy)phenyl)piperidin-3-ylcarbamate 		379	2-fluoro-3-(2-methoxyethoxy)benzaldehyde Method 178  and And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
125	(*S*)-*tert*-butyl 1-(2-formyl-6-(2-methoxyethoxy)phenyl)pyrrolidin-3-ylcarbamate 		365	2-fluoro-3-(2-methoxyethoxy)benzaldehyde Method 178  and (S)-tert-butyl pyrrolidin-3-ylcarbamate 
126	(*R*)-*tert*-butyl 1-(2-(cyclopentyloxy)-6-formylphenyl)piperidin-3-ylcarbamate 		389	3-(cyclopentyloxy)-2-fluorobenzaldehyde Method 179  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 

127	(*R*)-*tert*-butyl 1-(2-cyclobutoxy-6-formylphenyl)piperidin-3-ylcarbamate 		375	3-cyclobutoxy-2-fluorobenzaldehyde Method 180  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 

128	(*R*)-*tert*-butyl 1-(4-carbamoyl-2-formylphenyl)piperidin-3-ylcarbamate 		348	4-fluoro-3-formylbenzamide  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 
129	(*S*)-*tert*-butyl 1-(4-carbamoyl-2-formylphenyl)piperidin-3-ylcarbamate 		348	4-fluoro-3-formylbenzamide  And (*S*)-*tert*-butyl piperidin-3-ylcarbamate 
130	(*R*)-4-(3-(*tert*-butoxycarbonylamino) piperidin-1-yl)-3-formylbenzoic acid 		348	4-fluoro-3-formylbenzoic acid  And (*R*)-*tert*-butyl piperidin-3-ylcarbamate 

131	(*S*)-4-(3-(*tert*-butoxycarbonylamino) pyrrolidin-1-yl)-3-formylbenzoic acid 		334	4-fluoro-3-formylbenzoic acid  And (*S*)-*tert*-butyl pyrrolidin-3-ylcarbamate 



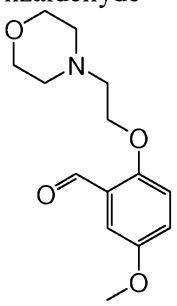
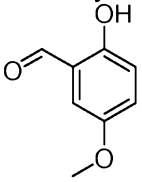
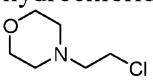
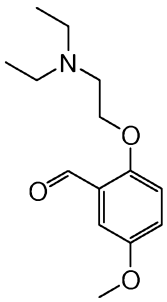
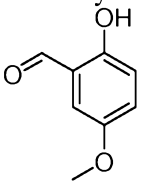
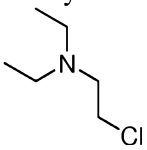
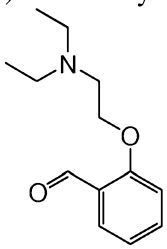
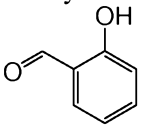
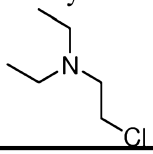
Method 27:

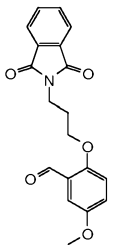
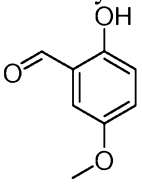
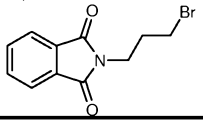
5-methoxy-2-(2-(piperidin-1-yl)ethoxy)benzaldehyde:

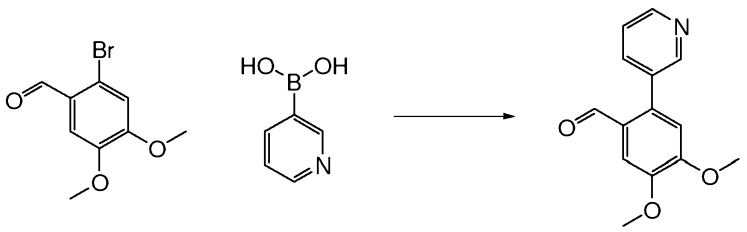
A mixture of 2-hydroxy-5-methoxybenzaldehyde (0.761 g, 5 mmol), 1-(2-chloroethyl)piperidine hydrochloride (0.921 g, 5.00 mmol), K_2CO_3 (2.07 g, 14.99 mmol), and sodium iodide (0.075 g, 0.50 mmol) in acetonitrile (40 mL) was stirred at 100 °C overnight. The reaction was allowed to cool to ambient temperature and sat'd aqueous K_2CO_3 was added to the reaction mixture. The mixture was poured into a separatory funnel and extracted with EtOAc. The organic phase was dried over anhydrous $MgSO_4$, filtered through a bed of Celite, and conc. *in vacuo* to yield the product which was purified via silica gel chromatography (80 g) using EtOAc/hexanes (4:1) as eluent to yield the title compound as a brown oil (0.551 g, 42 %); *m/z* 264.

The following intermediates were prepared by the procedure of Method 27, using the

appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
28	5-methoxy-2-(2-morpholinoethoxy)benzaldehyde 		266	2-hydroxy-5-methoxybenzaldehyde  and 4-(2-chloroethyl)morpholine hydrochloride 
29	2-(2-(diethylamino)ethoxy)-5-methoxybenzaldehyde 		252	2-hydroxy-5-methoxybenzaldehyde  and 2-chloro-*N*,*N*-diethylethanamine 
30A	2-(2-(diethylamino)ethoxy)benzaldehyde 		222	Salicylaldehyde  and 2-chloro-*N*,*N*-diethylethanamine 

30B	2-(3-(1,3-dioxoisoindolin-2-yl)propoxy)-5-methoxybenzaldehyde 	10.18 (s, 1 H) 7.69 (m, 4 H) 7.11 (m, 2 H) 6.97 (d, 1 H) 4.05 (m, 2 H) 3.83 (m, 2 H) 3.67 (s, 3 H) 2.12 (m, 2 H)	340	2-hydroxy-5-methoxybenzaldehyde  and 2-(3-bromopropyl)isoindoline-1,3-dione 

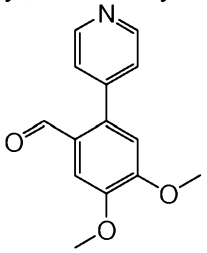
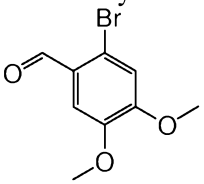
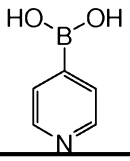
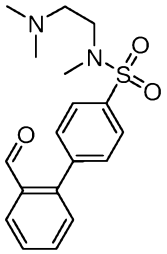
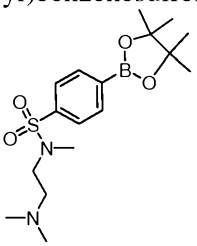
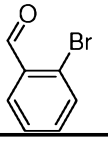


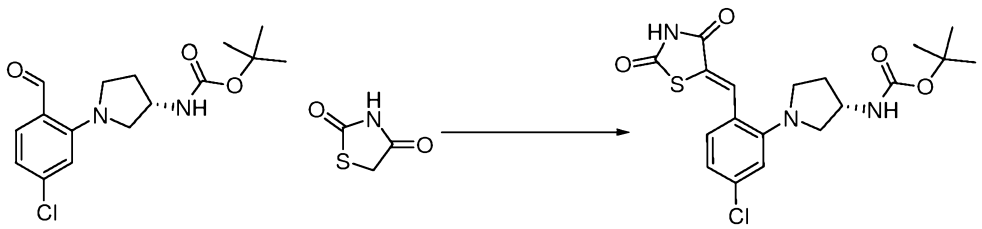
Method 31:

4,5-dimethoxy-2-(pyridin-3-yl)benzaldehyde:

A mixture of 2-bromo-4,5-dimethoxybenzaldehyde (0.368 g, 1.5 mmol), pyridin-3-ylboronic acid (0.246 g, 2.0 mmol), $Pd(PPh_3)_4$ (0.173 g, 0.150 mmol), and cesium carbonate (0.977 g, 3 mmol) were suspended in dioxane (4 mL) and water (1 mL). The mixture was heated to 140 °C in a microwave for 1 h. The reaction vessel was allowed to cool to ambient temperature, diluted with ethyl acetate (~ 25 mL), filtered through a bed of Celite, and conc. *in vacuo* to afford the aldehyde which was purified via SiO_2 chromatography (40 g) using ethyl acetate / hexanes (5:1) as eluent to afford the title compound as a white solid (0.340 g, 93 %); *m/z* 244.

The following intermediates were prepared by the procedure of Method 31, using the appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
32A	4,5-dimethoxy-2-(pyridin-4-yl)benzaldehyde 		244	2-bromo-4,5-dimethoxybenzaldehyde  and pyridin-4-ylboronic acid 
32B	*N*-(2-(dimethylamino)ethyl)-2'-formyl-*N*-methylbiphenyl-4-sulfonamide 	9.95 (s, 1 H), 8.05 (d, 1 H), 7.96 (d,2 H), 7.72 – 7.83 (m, 1 H), 7.57 – 7.72 (m, 3 H), 7.53 (d, 1 H), 3.24 (t, 2 H), 2.79 – 2.91 (m, 3 H), 2.65 (t, 2 H), 2.37 (s, 6 H)	346	*N*-(2-(dimethylamino)ethyl)-N-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenesulfonamide  And 2-bromobenzaldehyde 

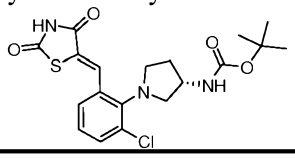
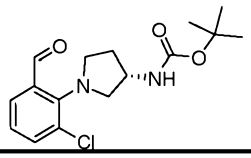
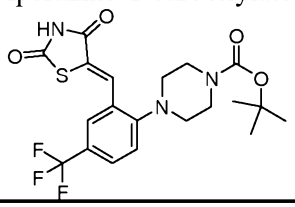
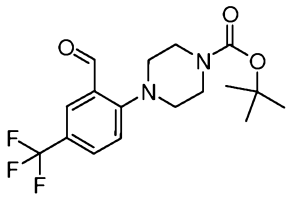
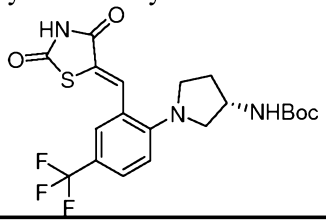
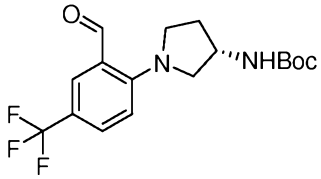
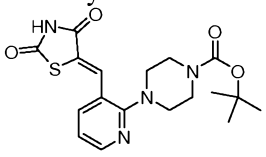
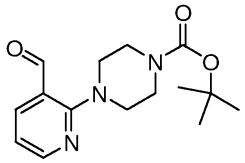


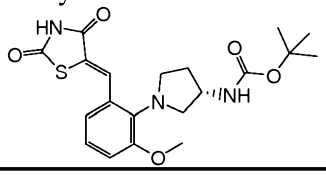
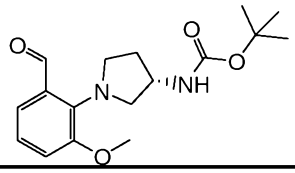
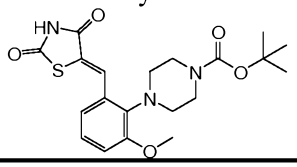
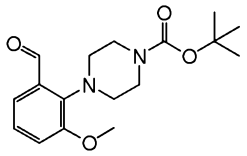
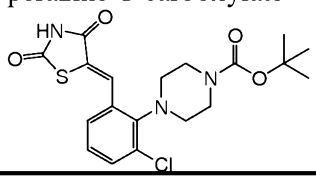
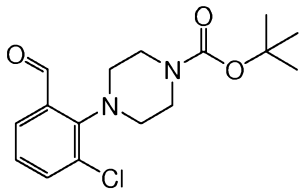
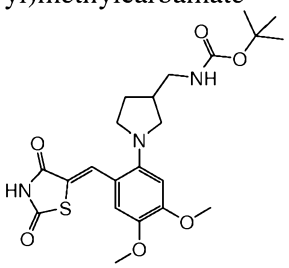
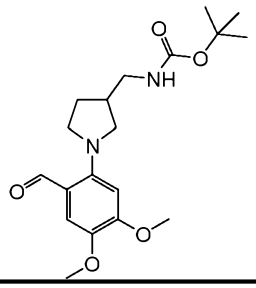
Method 33:

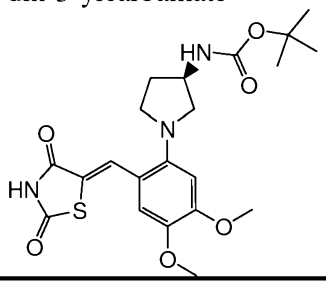
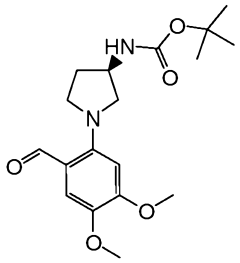
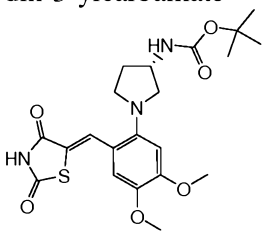
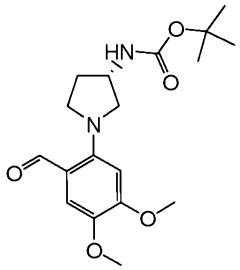
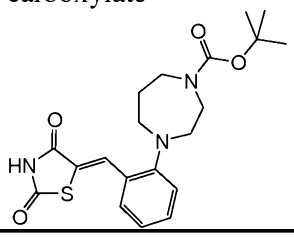
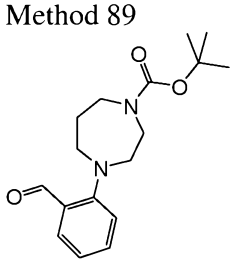
(*S,Z*)-*tert*-butyl 1-(5-chloro-2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate:

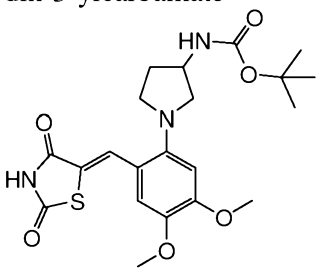
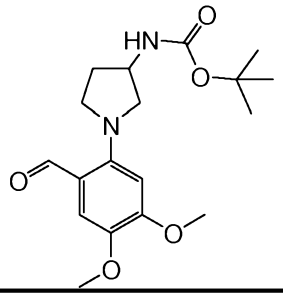
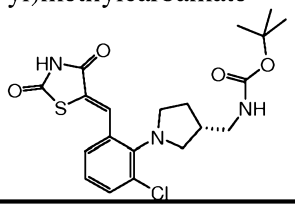
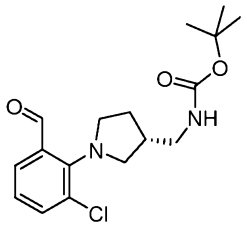
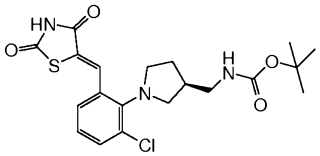
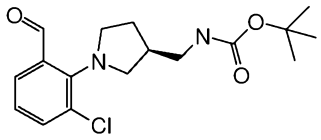
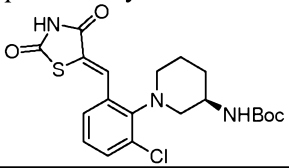
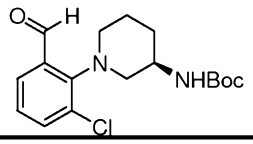
A 100 mL round bottom flask was charged with a magnetic stir bar, (*S*)-*tert*-butyl 1-(5-chloro-2-formylphenyl)pyrrolidin-3-ylcarbamate (Method 78) (1.100 g, 3.39 mmol), thiazolidine-2,4-dione (0.397 g, 3.39 mmol), and ethanol (11.29 ml). Piperidine (0.034 mL, 0.34 mmol) was added and the reaction was heated to reflux for 2 h. Once the reaction was judged to be complete by LCMS, it was allowed to cool to ambient temperature and conc. *in vacuo* to afford the title compound (1.310 g, 91 %) which was used in the next step without further purification.; *m/z* 425.

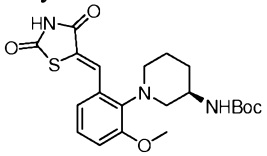
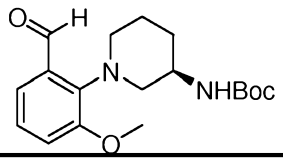
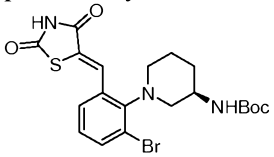
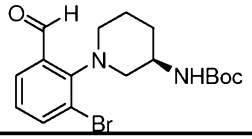
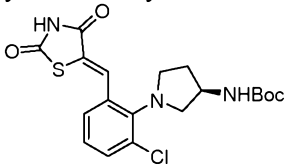
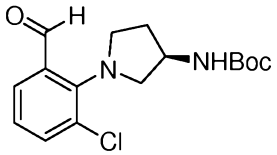
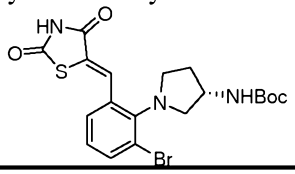
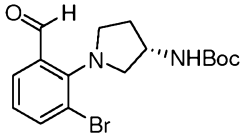
The following intermediates were prepared by the procedure of Method 33, using the appropriate starting materials.

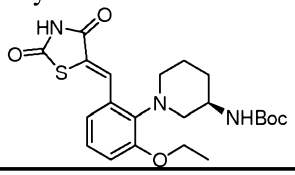
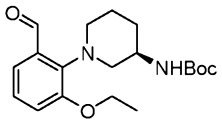
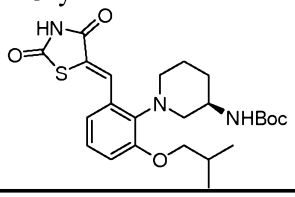
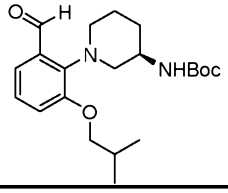
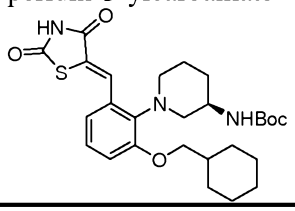
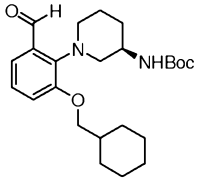
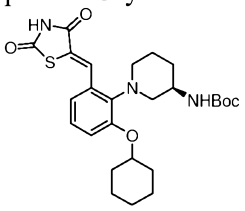
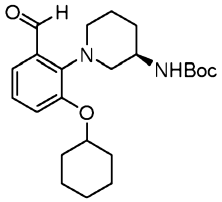
Method	Compound	^{1}H NMR	m/z	SM
34	(*S,Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate 		425	*tert*-butyl [(3*S*)-1-(2-chloro-6-formylphenyl)pyrrolidin-3-yl]carbamate Method 79 
35	(*Z*)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazine-1-carboxylate 		459	*tert*-butyl4-[2-formyl-4-(trifluoromethyl)phenyl]piperazine-1-carboxylate Method 80 
36	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)pyrrolidin-3-ylcarbamate 		459	*tert*-butyl{(3*S*)-1-[2-formyl-4-(trifluoromethyl)phenyl]pyrrolidin-3-yl}carbamate Method 81 
37	(*Z*)-*tert*-butyl 4-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)pyridin-2-yl)piperazine-1-carboxylate 		391	*tert*-butyl 4-(3-formylpyridin-2-yl)piperazine-1-carboxylate Method 82 

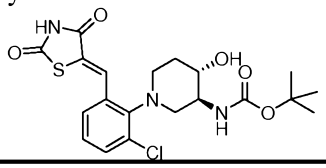
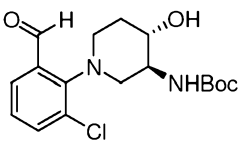
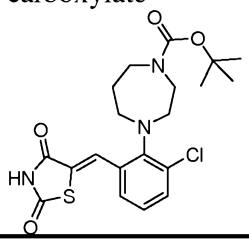
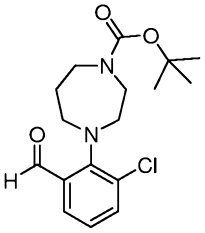
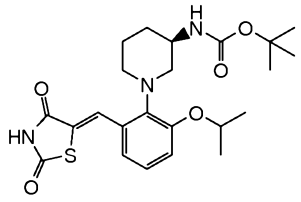
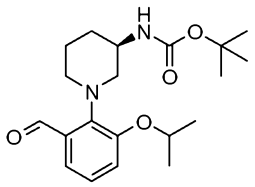
44	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)pyrrolidin-3-ylcarbamate 		421	*tert*-butyl [(3*S*)-1-(2-formyl-6-methoxyphenyl)pyrrolidin-3-yl]carbamate Method 83 
45	(*Z*)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)piperazine-1-carboxylate 		421	*tert*-butyl 4-(2-formyl-6-methoxyphenyl)piperazine-1-carboxylate Method 84 
46	(*Z*)-*tert*-butyl 4-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carboxylate 		425	*tert*-butyl 4-(2-chloro-6-formylphenyl)piperazine-1-carboxylate Method 85 
47	(*Z*)-*tert*-butyl (1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)methylcarbamate 		465	*tert*-butyl (1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-yl)methylcarbamate Method 86 

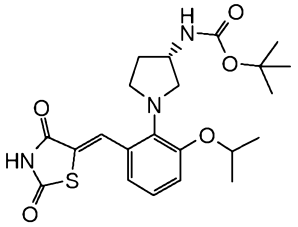
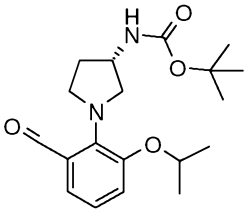
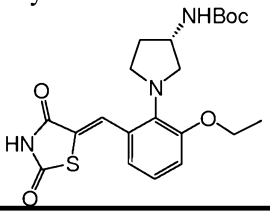
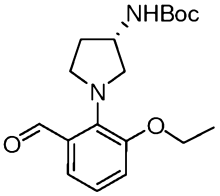
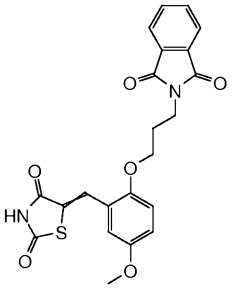
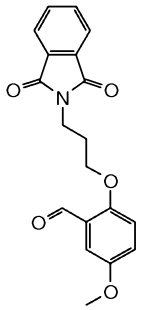
48	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate 		451	(*R*)-*tert*-butyl 1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate Method 87 
49	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate 		451	(*S*)-*tert*-butyl 1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate Method 88 
54	(*Z*)-*tert*-butyl 4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepane-1-carboxylate 		404	*tert*-butyl 4-(2-formylphenyl)-1,4-diazepane-1-carboxylate Method 89 

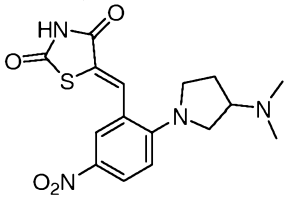
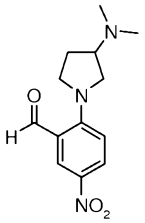
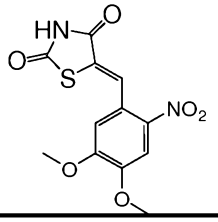
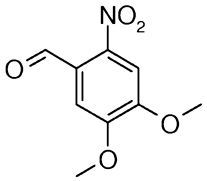
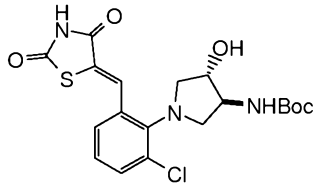
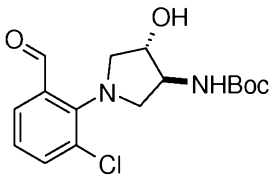
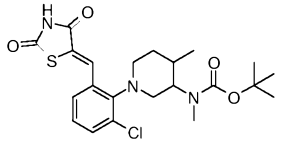
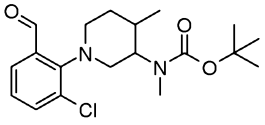
65	*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate 		451	*tert*-butyl 1-(2-formyl-4,5-dimethoxyphenyl)pyrrolidin-3-ylcarbamate Method 90 
132	(*R*,*Z*)-*tert*-butyl (1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)methylcarbamate 		439	(*R*)-*tert*-butyl (1-(2-chloro-6-formylphenyl)pyrrolidin-3-yl)methylcarbamate Method 91 
133	(*S*,*Z*)-*tert*-butyl (1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-yl)methylcarbamate 		439	(*S*)-*tert*-butyl (1-(2-chloro-6-formylphenyl)pyrrolidin-3-yl)methylcarbamate Method 92 
134	(*R*,*Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		438	*(R)-tert*-butyl 1-(2-chloro-6-formylphenyl)piperidin-3-ylcarbamate Method 93 

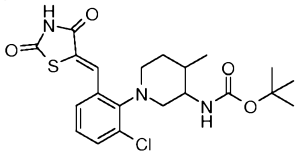
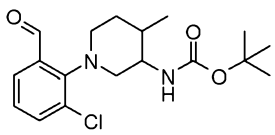
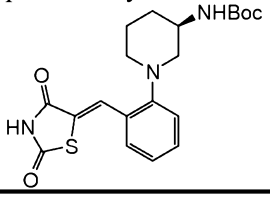
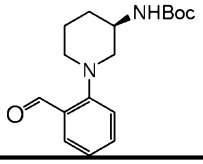
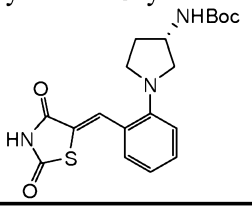
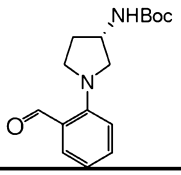
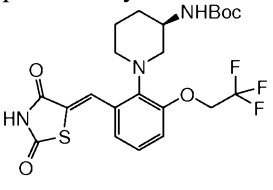
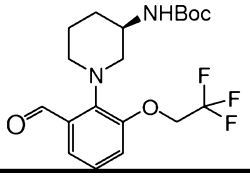
135	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)piperidin-3-ylcarbamate 		434	(*R*)-*tert*-butyl 1-(2-formyl-6-methoxyphenyl)piperidin-3-ylcarbamate Method 94 
136	(*R,Z*)-*tert*-butyl 1-(2-bromo-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		484	(*R*)-*tert*-butyl 1-(2-bromo-6-formylphenyl)piperidin-3-ylcarbamate Method 95 
137	(*R,Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate 		424	(*R*)-*tert*-butyl 1-(2-chloro-6-formylphenyl)pyrrolidin-3-ylcarbamate Method 96 
138	(*S,Z*)-*tert*-butyl 1-(2-bromo-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate 		470	(*S*)-*tert*-butyl 1-(2-bromo-6-formylphenyl)pyrrolidin-3-ylcarbamate Method 97 

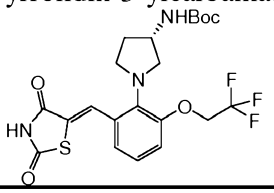
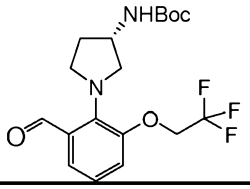
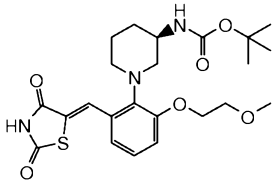
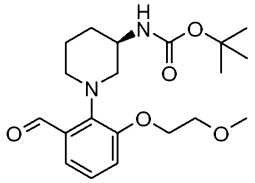
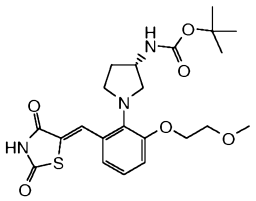
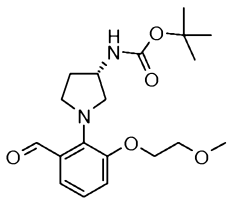
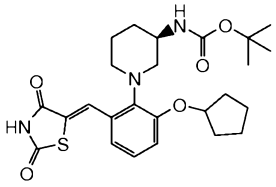
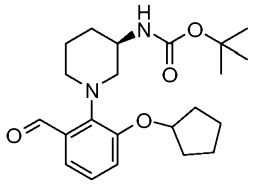
139	(*R*,*Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-ethoxyphenyl)piperidin-3-ylcarbamate 		448	(*R*)-*tert*-butyl 1-(2-ethoxy-6-formylphenyl)piperidin-3-ylcarbamate Method 98 
140	(*R*,*Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isobutoxyphenyl)piperidin-3-ylcarbamate 		476	(*R*)-*tert*-butyl 1-(2-formyl-6-isobutoxyphenyl)piperidin-3-ylcarbamate Method 99 
141	(*R*,*Z*)-*tert*-butyl 1-(2-(cyclohexylmethoxy)-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		516	(*R*)-*tert*-butyl 1-(2-(cyclohexylmethoxy)-6-formylphenyl)piperidin-3-ylcarbamate Method 100 
142	(*R*,*Z*)-*tert*-butyl 1-(2-(cyclohexyloxy)-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		501	(*R*)-*tert*-butyl 1-(2-(cyclohexyloxy)-6-formylphenyl)piperidin-3-ylcarbamate Method 101 

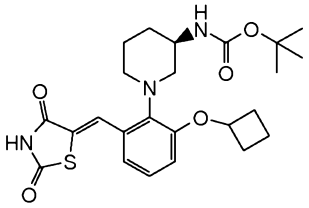
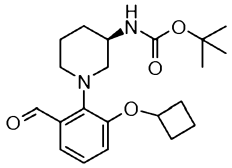
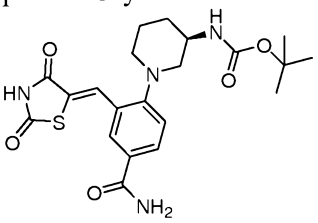
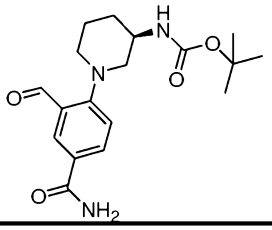
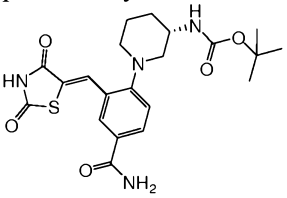
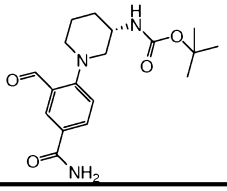
143	(±)-*tert*-butyl-1-(2-chloro-6-((*Z*)-(2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-hydroxypiperidin-3-ylcarbamate 		454	(±)-*tert*-butyl-1-(2-chloro-6-formylphenyl)-4-hydroxypiperidin-3-ylcarbamate Method 102 
144	(*Z*)-*tert*-butyl 4-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepane-1-carboxylate 	8.66 (brs, 1 H), 8.36 (brs, 1 H), 7.47 (d, 1 H), 7.39 (d, 1 H), 7.22 (t, 1 H), 3.61 (brs, 3 H), 3.52 (brs, 2 H), 3.27 (brs, 3 H), 1.91 (brs, 2 H), 1.52 (s, 9 H)	438	*tert*-butyl 4-(2-chloro-6-formylphenyl)-1,4-diazepane-1-carboxylate Method 103 
145	(*R*,*Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isopropoxyphenyl)piperidin-3-ylcarbamate 		462	(*R*)-*tert*-butyl 1-(2-formyl-6-isopropoxyphenyl)piperidin-3-ylcarbamate Method 113 

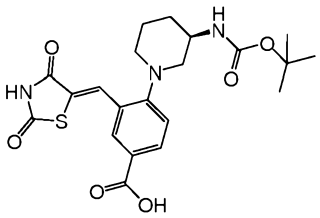
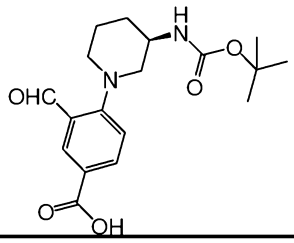
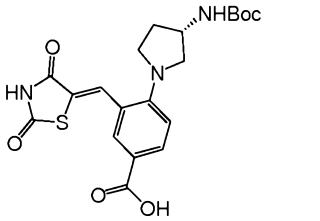
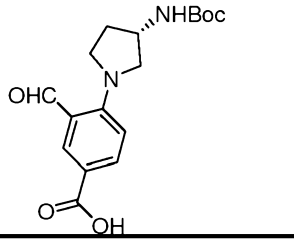
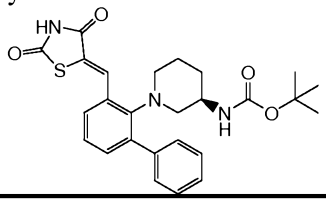
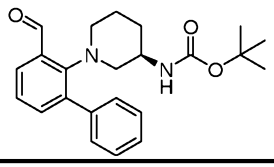
146	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-isopropoxyphenyl)pyrrolidin-3-ylcarbamate 		448	(*S*)-*tert*-butyl 1-(2-formyl-6-isopropoxyphenyl)pyrrolidin-3-ylcarbamate Method 114 
147	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-ethoxyphenyl)pyrrolidin-3-ylcarbamate 		334	(*S*)-*tert*-butyl 1-(2-ethoxy-6-formylphenyl)pyrrolidin-3-ylcarbamate Method 115 
148	5-(2-(3-(1,3-dioxoisoindolin-2-yl)propoxy)-5-methoxybenzylidene)thiazolidine-2,4-dione 	12.54 (s, 1 H) 7.83-7.79 (m, 5 H) 7.04 (s, 2 H) 6.86 (s, 1 H) 4.08 (m, 2 H) 3.80-3.75 (m, 5 H) 2.11 (m, 2 H)	438	2-(3-(1,3-dioxoisoindolin-2-yl)propoxy)-5-methoxybenzaldehyde Method 30B 

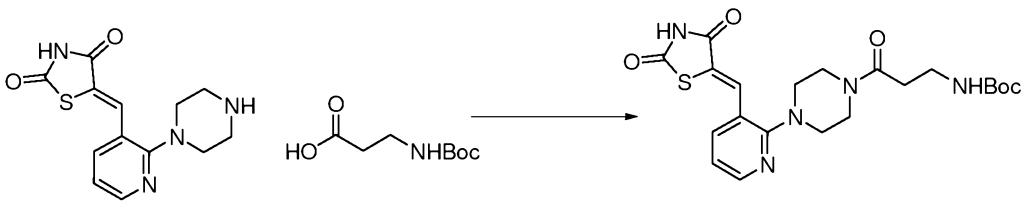
149	5-(2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzylidene)thiazolidine-2,4-dione 	8.20 (s, 1 H) 8.07 (d, 1 H) 7.82 (s, 1 H) 6.96 (d, 1H) 3.58-3.51 (m, 3H) 3.36 (m, 1 H) 3.04 (m, 1 H) 2.51 (s, 6 H), 2.40 (m, 1 H), 1.86 (m, 1 H)	363	2-(3-(dimethylamino)pyrrolidin-1-yl)-5-nitrobenzaldehyde Method 116 
150	(Z)-5-(4,5-dimethoxy-2-nitrobenzylidene)thiazolidine-2,4-dione 	8.32 (s, 1 H) 8.25 (brs, 1 H) 7.79 (s, 1 H) 7.02 (s, 1 H) 4.03 (s, 6 H)	309	4,5-dimethoxy-2-nitrobenzaldehyde 
151	*tert*-butyl (3*S*,4*S*)-1-(2-chloro-6-((*Z*)-(2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-hydroxypyrrolidin-3-ylcarbamate 	8.30 (s, 1 H) 7.49 (d, 1 H) 7.42 (d, 1 H) 7.28-7.20 (m, 1 H) 5.01 (d, 1 H) 4.39 (brs, 1 H) 4.27 (brs, 1 H) 4.05 (s, 1 H) 3.83 (dd, 1 H) 3.69 (dd, 1 H) 3.27 (brs, 1 H) 3.19 (dd, 1 H), 1.50 (s, 9 H)	439	*tert*-butyl (3*S*,4*S*)-1-(2-chloro-6-formylphenyl)-4-hydroxypyrrolidin-3-ylcarbamate Method 117 
152	(*Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-methylpiperidin-3-yl(methyl)carbamate 		465	*tert*-butyl 1-(2-chloro-6-formylphenyl)-4-methylpiperidin-3-yl(methyl)carbamate Method 118 

153	(*Z*)-*tert*-butyl 1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-4-methylpiperidin-3-ylcarbamate 		451	*tert*-butyl 1-(2-chloro-6-formylphenyl)-4-methylpiperidin-3-ylcarbamate Method 119 
154	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		404	(*R*)-*tert*-butyl 1-(2-formylphenyl)piperidin-3-ylcarbamate Method 120 
155	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)pyrrolidin-3-ylcarbamate 		390	(*S*)-*tert*-butyl 1-(2-formylphenyl)pyrrolidin-3-ylcarbamate Method 121 
156	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2,2,2-trifluoroethoxy)phenyl)piperidin-3-ylcarbamate 		502	(*R*)-*tert*-butyl 1-(2-formyl-6-(2,2,2-trifluoroethoxy)phenyl)piperidin-3-ylcarbamate Method 122 

157	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2,2,2-trifluoroethoxy)phenyl)pyrrolidin-3-ylcarbamate 		488	(*S*)-*tert*-butyl 1-(2-formyl-6-(2,2,2-trifluoroethoxy)phenyl)pyrrolidin-3-ylcarbamate Method 123 
158	(*R,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2-methoxyethoxy)phenyl)piperidin-3-ylcarbamate 		478	(*R*)-*tert*-butyl 1-(2-formyl-6-(2-methoxyethoxy)phenyl)piperidin-3-ylcarbamate Method 124 
159	(*S,Z*)-*tert*-butyl 1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-(2-methoxyethoxy)phenyl)pyrrolidin-3-ylcarbamate 		464	(*S*)-*tert*-butyl 1-(2-formyl-6-(2-methoxyethoxy)phenyl)pyrrolidin-3-ylcarbamate Method 125 
160	(*R,Z*)-*ter*t-butyl 1-(2-(cyclopentyloxy)-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		488	(*R*)-*tert*-butyl 1-(2-(cyclopentyloxy)-6-formylphenyl)piperidin-3-ylcarbamate Method 126 

161	(*R,Z*)-*tert*-butyl 1-(2-cyclobutoxy-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		474	(*R*)-*tert*-butyl 1-(2-cyclobutoxy-6-formylphenyl)piperidin-3-ylcarbamate Method 127 
162	(*R,Z*)-*tert*-butyl 1-(4-carbamoyl-2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		447	(*R*)-*tert*-butyl 1-(4-carbamoyl-2-formylphenyl)piperidin-3-ylcarbamate Method 128 
163	(*S,Z*)-*tert*-butyl 1-(4-carbamoyl-2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylcarbamate 		447	(*S*)-*tert*-butyl 1-(4-carbamoyl-2-formylphenyl)piperidin-3-ylcarbamate Method 129 

164	(*R*,*Z*)-4-(3-(*tert*-butoxycarbonylamino)piperidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzoic acid 		447	(*R*)-4-(3-(*tert*-butoxycarbonylamino)piperidin-1-yl)-3-formylbenzoic acid Method 130 
165	(*S*,*Z*)-4-(3-(*tert*-butoxycarbonylamino)pyrrolidin-1-yl)-3-((2,4-dioxothiazolidin-5-ylidene)methyl)benzoic acid 		433	(*S*)-4-(3-(*tert*-butoxycarbonylamino)pyrrolidin-1-yl)-3-formylbenzoic acid Method 131 
166	(*R*,*Z*)-*tert*-butyl 1-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)biphenyl-2-yl)piperidin-3-ylcarbamate 		480	(*R*)-*tert*-butyl 1-(3-formylbiphenyl-2-yl)piperidin-3-ylcarbamate Method 201 

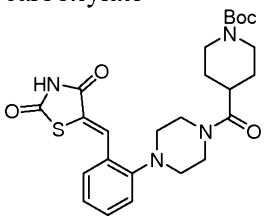
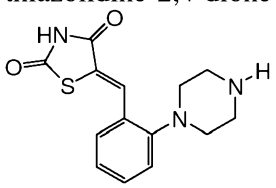
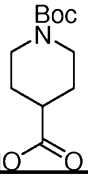
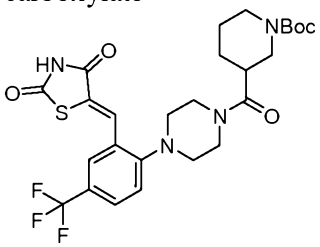
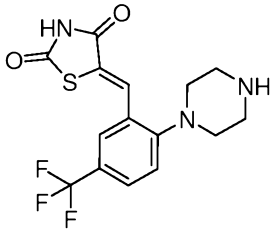
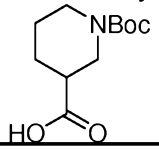


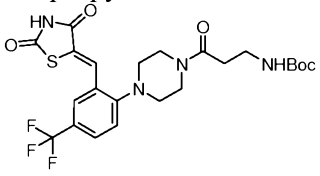
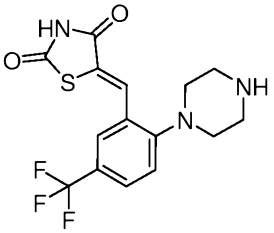
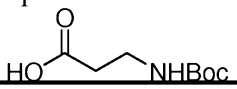
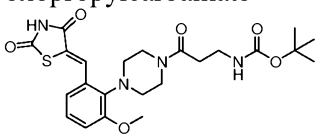
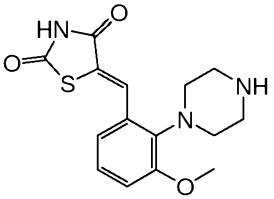
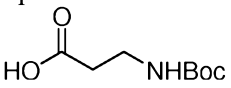
Method 38:

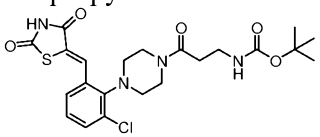
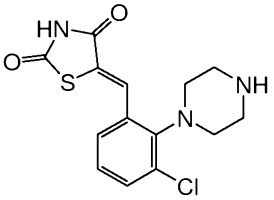
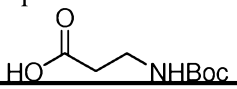
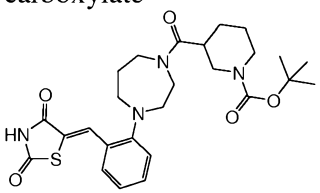
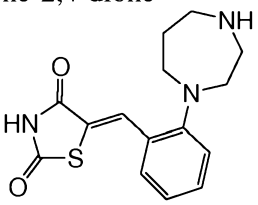
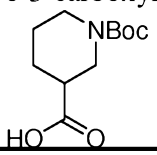
(*Z*)-*tert*-butyl 3-(4-(3-((2,4-dioxothiazolidin-5-ylidene)methyl)pyridin-2-yl)piperazin-1-yl)-3-oxopropylcarbamate:

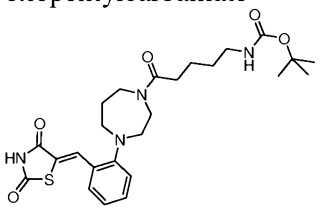
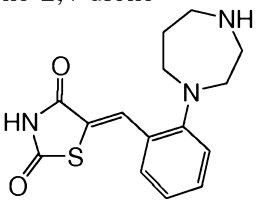
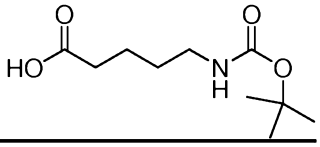
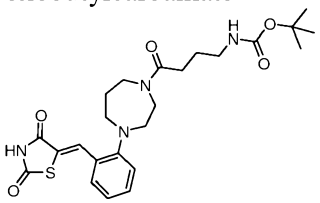
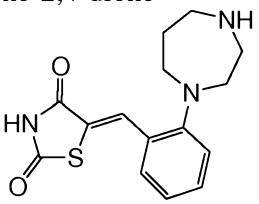
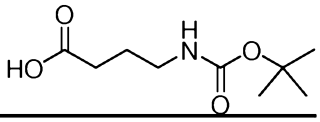
A 50 mL vial was charged with a magnetic spin bar, (*Z*)-5-((2-(piperazin-1-yl)pyridin-3-yl)methylene)thiazolidine-2,4-dione hydrochloride (Example 89) (0.125 g, 0.38 mmol), 3-(*tert*-butoxycarbonylamino)propanoic acid (0.109 g, 0.57 mmol), DMF (1.912 ml), and diisopropylethylamine (0.334 ml, 1.91 mmol). With stirring, HATU (0.291 g, 0.76 mmol) was added and the reaction was warmed to 50 °C for 3 h. The reaction was then diluted with water and extracted with ethyl acetate (3 X 50 mL). The combined organic extract was dried with $MgSO_4$, filtered through a bed of Celite, and conc. *in vacuo* to yield the product which was purified via silica gel chromatography (80 g) using ethyl acetate/hexanes (1:1) as eluent to provide the title compound as an off white solid. (0.080 g, 45.3 %); *m/z* 462.

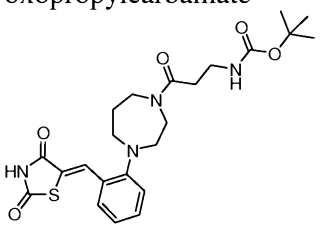
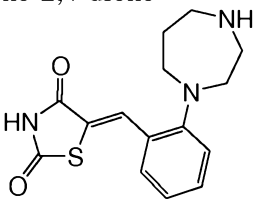
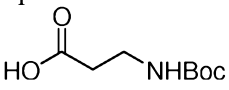
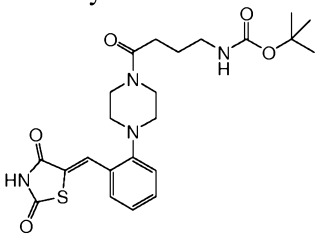
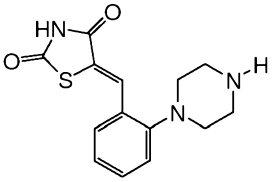
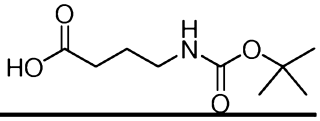
The following intermediates were prepared by the procedure of Method 38, using the appropriate starting materials.

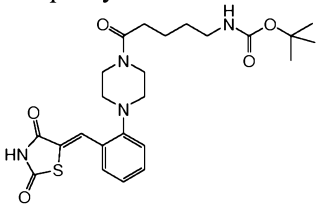
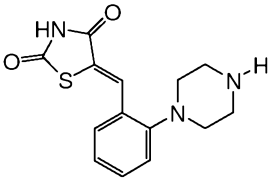
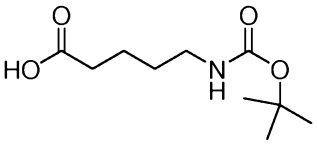
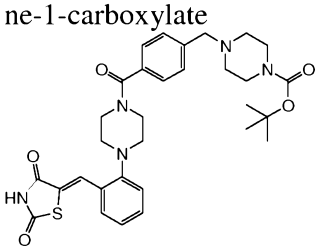
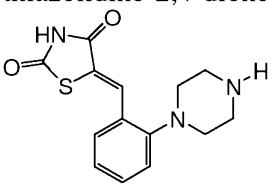
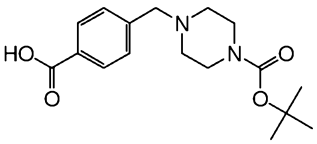
Method	Compound	^{1}H NMR	m/z	SM
39	(Z)-*tert*-butyl 4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)piperidine-1-carboxylate 		502	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid 
40	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazine-1-carbonyl)piperidine-1-carboxylate 		560	(Z)-5-(2-(piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione  Example 87 and 1-(*tert*-butoxycarbonyl)piperidine-3-carboxylic acid 

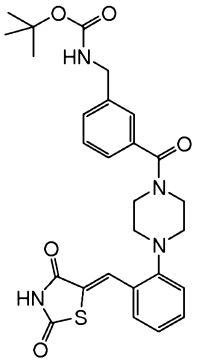
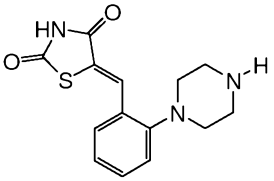
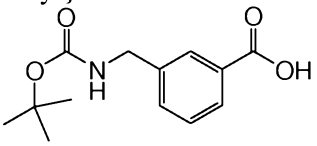
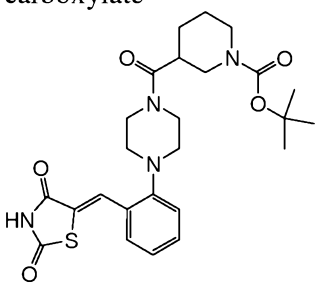
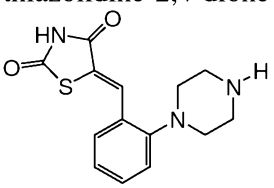
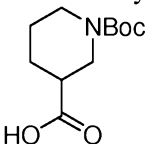
41	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4-(trifluoromethyl)phenyl)piperazin-1-yl)-3-oxopropylcarbamate 		530	(Z)-5-(2-(piperazin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione  Example 87 and 3-[(*tert*-butoxycarbonyl)amino]propanoic acid 
42	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-6-methoxyphenyl)piperazin-1-yl)-3-oxopropylcarbamate 		492	(Z)-5-(3-methoxy-2-(piperazin-1-yl)benzylidene)thiazolidine-2,4-dione  Example 97 and 3-[(*tert*-butoxycarbonyl)amino]propanoic acid 

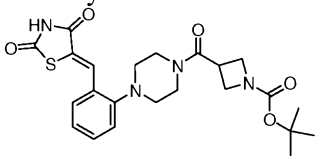
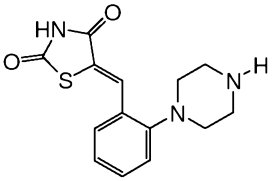
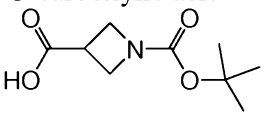
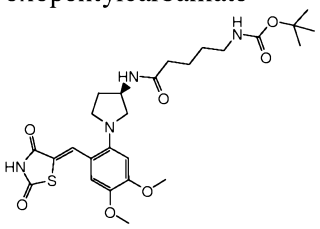
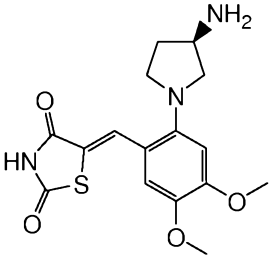
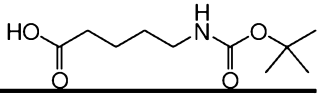
43	(Z)-*tert*-butyl 3-(4-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)-3-oxopropylcarbamate 		496	(Z)-5-(3-chloro-2-(piperazin-1-yl)benzylidene)thiazolidine-2,4-dione  Example 98 and 3-[(*tert*-butoxycarbonyl)amino]propanoic acid 
50	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepane-1-carbonyl)piperidine-1-carboxylate 		516	(Z)-5-(2-(1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione  Example 106 and 1-(*tert*-butoxycarbonyl)piperidine-3-carboxylic acid 

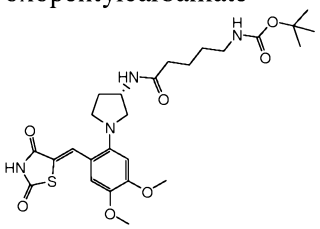
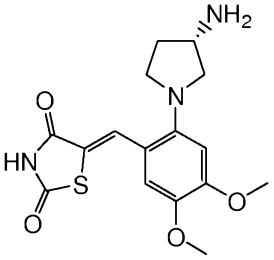
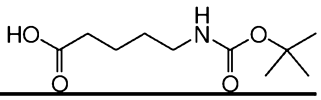
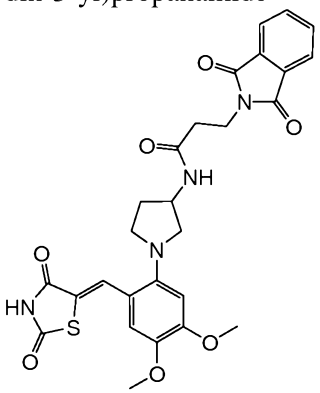
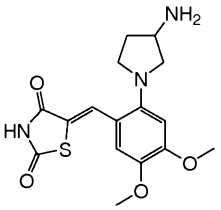
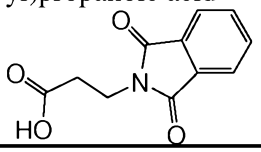
51	(Z)-*tert*-butyl 5-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepan-1-yl)-5-oxopentylcarbamate 		504	(Z)-5-(2-(1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione  Example 106 and 5-[(*tert*-butoxycarbonyl)amino]pentanoic acid 
52	(Z)-*tert*-butyl 4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepan-1-yl)-4-oxobutylcarbamate 		490	(Z)-5-(2-(1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione  Example 106 and 4-[(*tert*-butoxycarbonyl)amino]butanoic acid 

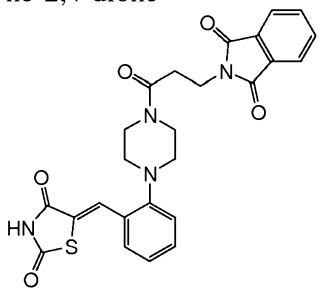
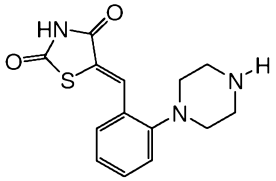
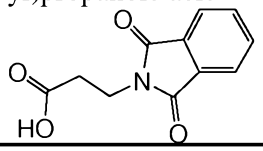
53	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)-1,4-diazepan-1-yl)-3-oxopropylcarbamate 		475	(Z)-5-(2-(1,4-diazepan-1-yl)benzylidene)thiazolidine-2,4-dione  Example 106 and 3-[(*tert*-butoxycarbonyl)amino]propanoic acid 
55	(Z)-*tert*-butyl 4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)-4-oxobutylcarbamate 		476	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and 4-[(*tert*-butoxycarbonyl)amino]butanoic acid 

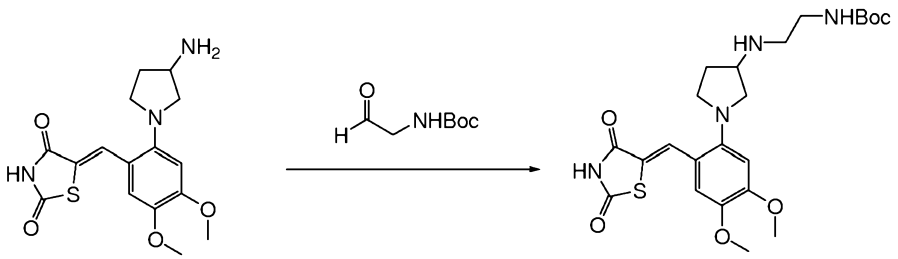
56	(Z)-*tert*-butyl 5-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)-5-oxopentylcarbamate 		490	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and nd 5-[(*tert*-butoxycarbonyl)amino]pentanoic acid 
57	(Z)-*tert*-butyl 4-(4-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)benzyl)piperazine-1-carboxylate 		593	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and 4-{[4-(*tert*-butoxycarbonyl)piperazin-1-yl]methyl}benzoic acid 

58	(Z)-*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)benzylcarbamate 		524	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and 3-{[(*tert*-butoxycarbonyl)amino]methyl}benzoic acid 
63	*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)piperidine-1-carboxylate 		501	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 And 1-(*tert*-butoxycarbonyl)piperidine-3-carboxylic acid 

64	*tert*-butyl 3-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazine-1-carbonyl)azetidine-1-carboxylate 		473	(5*Z*)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 And 1-(*tert*-butoxycarbonyl)azetidine-3-carboxylic acid 
66	(*R*,*Z*)-*tert*-butyl 5-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)-5-oxopentylcarbamate 		550	(*R*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione  Example 100 And 5-[(*tert*-butoxycarbonyl)amino]pentanoic acid 

67	(*S,Z*)-*tert*-butyl 5-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)-5-oxopentylcarbamate 		550	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione  Example 101 And 5-[(*tert*-butoxycarbonyl)amino]pentanoic acid 
75	(*Z*)-3-(1,3-dioxoisoindolin-2-yl)-N-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-yl)propanamide 		552	(5*Z*)-5-[2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene]-1,3-thiazolidine-2,4-dione  Example 118 and 3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanoic acid 

76	5Z)-(2-(4-(3-(1,3-dioxoisoindolin-2-yl)propanoyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione 			(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and 3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanoic acid 

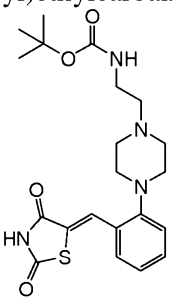
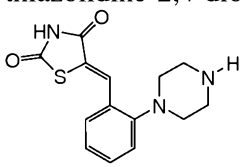
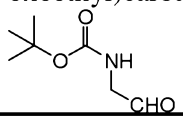
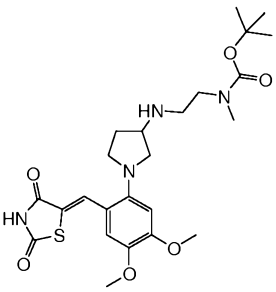
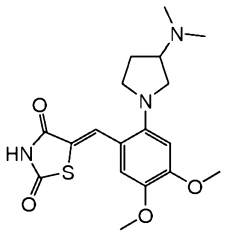
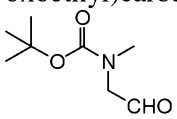


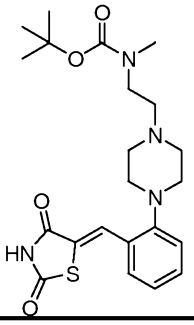
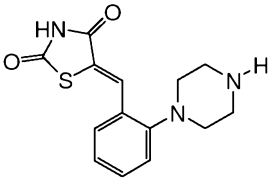
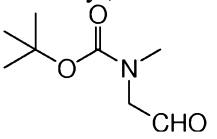
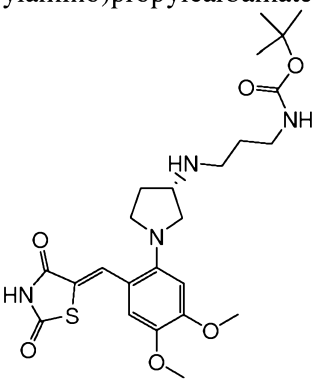
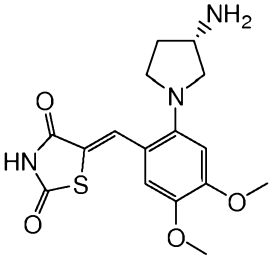
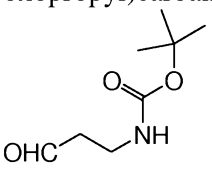
Method 59:

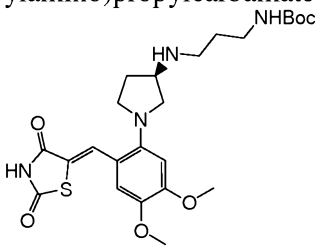
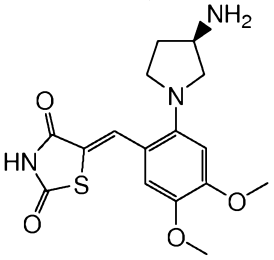
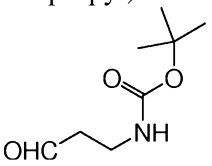
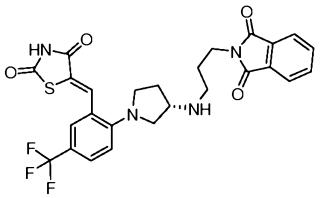
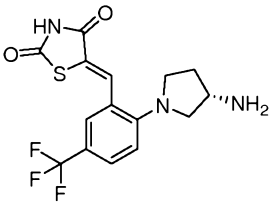
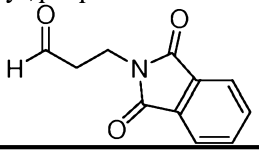
(*Z*)-*tert*-butyl 2-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)ethylcarbamate:

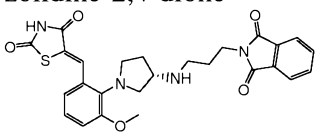
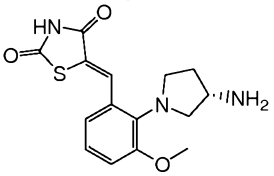
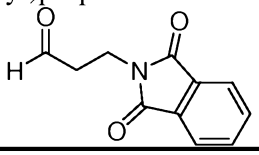
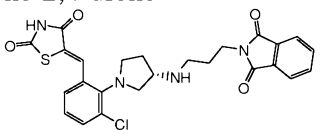
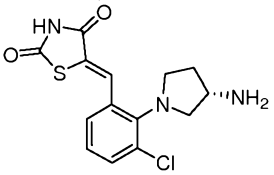
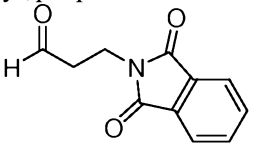
A mixture of (5*Z*)-5-{2-[3-(dimethylamino)pyrrolidin-1-yl]-4,5-dimethoxybenzylidene}-1,3-thiazolidine-2,4-dione (Example 52)(120 mg, 0.31 mmol) and *tert*-butyl 2-oxoethylcarbamate (198 mg, 1.24 mmol) in CH_2Cl_2 (20 mL) were heated to reflux for 15 min followed by the addition of sodium triacetoxyhydroborate (65.9 mg, 0.31 mmol). The reaction mixture was refluxed overnight before being allowed to cool to ambient temperature. Water (~ 0.5 mL) was added and the mixture was allowed to stir for 15 min before being loaded onto a silica gel column which was eluted with ethyl acetate/hexane (10:1) to yield the title compound as an orange solid as (60.0 mg, 39.2 %); *m/z* 493.

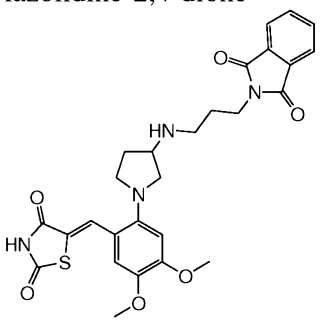
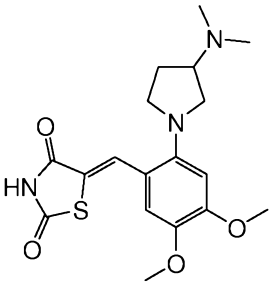
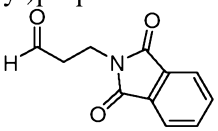
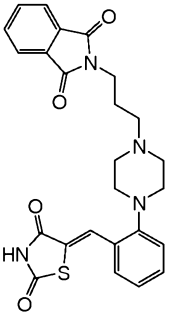
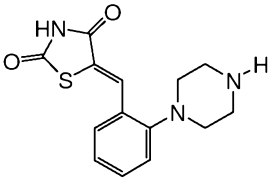
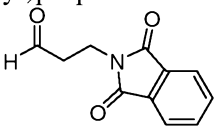
The following intermediates were prepared by the procedure of Method 59, using the appropriate starting materials.

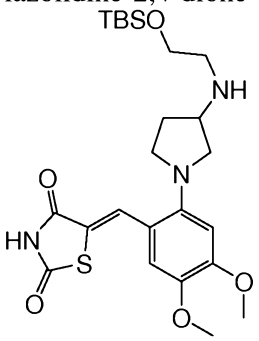
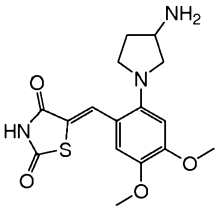
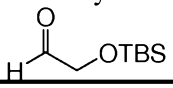
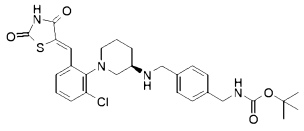
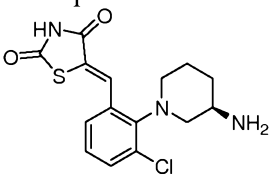
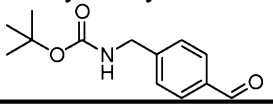
Method	Compound	^{1}H NMR	m/z	SM
60	(Z)-*tert*-butyl 2-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)ethylcarbamate 		433	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and *tert*-butyl (2-oxoethyl)carbamate 
61	(Z)-*tert*-butyl 2-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)ethyl(methyl)carbamate 		507	(5Z)-5-{2-[3-(dimethylamino)pyrrolidin-1-yl]-4,5-dimethoxybenzylidene}-1,3-thiazolidine-2,4-dione  Example 52 and *tert*-butyl methyl(2-oxoethyl)carbamate 

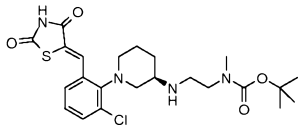
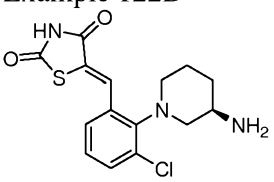
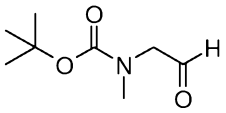
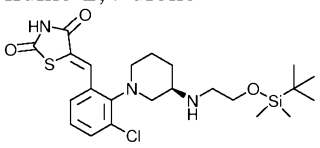
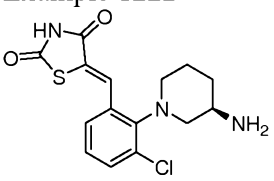
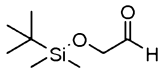
62	(*Z*)-*tert*-butyl 2-(4-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperazin-1-yl)ethyl(methyl)carbamate Method 62 		448	(5*Z*)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and *tert*-butyl methyl(2-oxoethyl)carbamate 
68	(*S,Z*)-*tert*-butyl 3-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)propylcarbamate 		507	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione  Example 101 and *tert*-butyl (3-oxopropyl)carbamate 

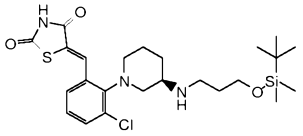
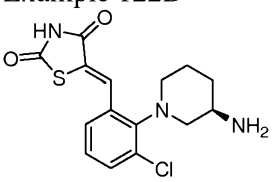
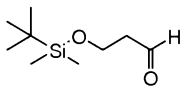
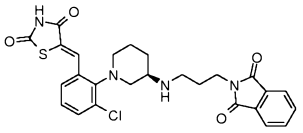
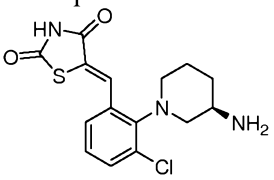
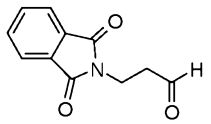
69	(*R,Z*)-*tert*-butyl 3-(1-(2-((2,4-dioxothiazolidin-5-ylidene)methyl)-4,5-dimethoxyphenyl)pyrrolidin-3-ylamino)propylcarbamate 		507	(*R,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione  Example 100 and *tert*-butyl (3-oxopropyl)carbamate 
70	(*S,Z*)-5-(2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione 		545	(*S,Z*)-5-(2-(3-aminopyrrolidin-1-yl)-5-(trifluoromethyl)benzylidene)thiazolidine-2,4-dione  Example 88 and 3-(1,3-dioxoisoindolin-2-yl)propanal 

71	(*S*,*Z*)-5-(2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)-3-methoxybenzylidene)thiazolidine-2,4-dione 		508	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-methoxybenzylidene)thiazolidine-2,4-dione  Example 96 and 3-(1,3-dioxoisoindolin-2-yl)propanal 
72	(*S*,*Z*)-5-(3-chloro-2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)benzylidene)thiazolidine-2,4-dione 		512	(*S*,*Z*)-5-(2-(3-aminopyrrolidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione  Example 86 and 3-(1,3-dioxoisoindolin-2-yl)propanal 

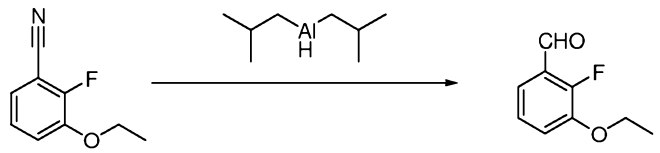
73	(Z)-5-(2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione 		507	(5Z)-5-{2-[3-(dimethylamino)pyrrolidin-1-yl]-4,5-dimethoxybenzylidene}-1,3-thiazolidine-2,4-dione  Example 52 and 3-(1,3-dioxoisoindolin-2-yl)propanal 
74	(Z)-5-(2-(4-(3-(1,3-dioxoisoindolin-2-yl)propyl)piperazin-1-yl)benzylidene)thiazolidine-2,4-dione 		477	(5Z)-5-(2-piperazin-1-ylbenzylidene)-1,3-thiazolidine-2,4-dione  Example 115 and 3-(1,3-dioxoisoindolin-2-yl)propanal 

77	(*Z*)-5-(2-(3-(2-(*tert*-butyldimethylsilyloxy)ethylamino)pyrrolidin-1-yl)-4,5-dimethoxybenzylidene)thiazolidine-2,4-dione 		509	(5*Z*)-5-[2-(3-aminopyrrolidin-1-yl)-4,5-dimethoxybenzylidene]-1,3-thiazolidine-2,4-dione  Example 118 and 2-(*tert*-butyldimethylsilyloxy)acetaldehyde 
167	(*R*,*Z*)-*tert*-butyl 4-((1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylamino)methyl)benzylcarbamate 		557	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride Example 122D  And *tert*-butyl 4-formylbenzylcarbamate 

168	(*R*,*Z*)-*tert*-butyl 2-(1-(2-chloro-6-((2,4-dioxothiazolidin-5-ylidene)methyl)phenyl)piperidin-3-ylamino)ethyl(methyl)carbamate 		496	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride Example 122D  and *tert*-butyl methyl (2-oxoethyl)carbamate 
169	(*R*,*Z*)-5-(2-(3-(2-*(tert*-butyldimethylsilyloxy)ethylamino)piperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione 		496	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride Example 122D  and 2-(*tert*-butyldimethylsilyloxy)acetaldehyde 

170	(*R*,*Z*)-5-(2-(3-(3-(*tert*-butyldimethylsilyloxy)propylamino)piperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione 		510	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride Example 122D  and 3-(*tert*-butyldimethylsilyloxy)propanal 
171	(*R*,*Z*)-5-(3-chloro-2-(3-(3-(1,3-dioxoisoindolin-2-yl)propylamino)piperidin-1-yl)benzylidene)thiazolidine-2,4-dione 		525	(*R*,*Z*)-5-(2-(3-aminopiperidin-1-yl)-3-chlorobenzylidene)thiazolidine-2,4-dione hydrochloride Example 122D  3-(1,3-dioxoisoindolin-2-yl)propanal 

Method 172

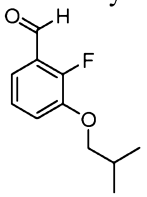
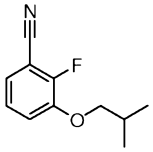
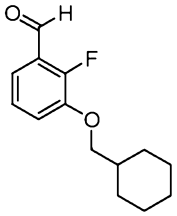
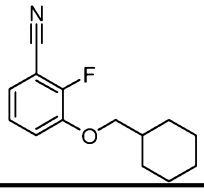
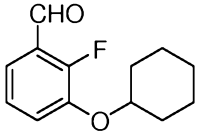
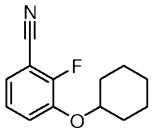
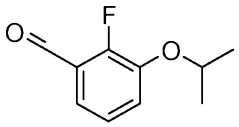
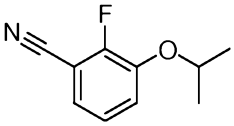
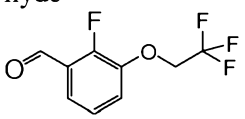
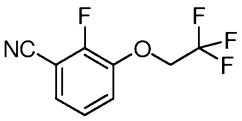


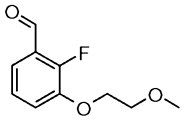
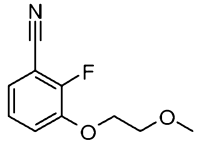
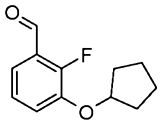
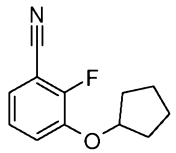
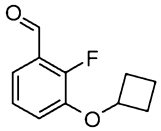
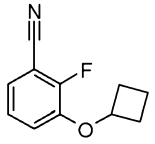
3-ethoxy-2-fluorobenzaldehyde:

A 200 mL round bottom flask was charged with a magnetic stir bar, 3-ethoxy-2-fluorobenzonitrile (1.000 g, 6.05 mmol), and anhydrous toluene (12.92 ml). The sol'n

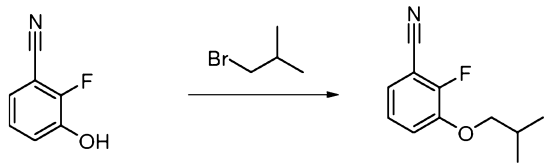
was placed under argon and cooled to 0 °C with an ice bath. DIBAL-H (7.27 ml, 7.27 mmol) (1M in PhMe) was then added drop wise via syringe and the reaction was allowed to stir to rt overnight. To this mixture was added 10 % HCl until the sol'n reached a pH of ~ 2. The resulting mixture was then left to stir for 0.5 h. and was then poured into a separatory funnel and extracted with ethyl acetate (2 x 200 mL). The combined organic extract was dried with $MgSO_4$, filtered, and conc. *in vacuo* to yield the crude product which was purified via silica gel chromatography (80 g) using ethyl acetate/hexanes (1:4) as eluent to provide pure 3-ethoxy-2-fluorobenzaldehyde (0.810 g, 80 %). *m/z* 196.

The following intermediates were prepared by the procedure of Method 172, using the appropriate starting materials.

173	2-fluoro-3-isobutoxybenzaldehyde 		197	2-fluoro-3-isobutoxybenzonitrile Method 181 
174	3-(cyclohexylmethoxy)-2-fluorobenzaldehyde 		237	3-(cyclohexylmethoxy)-2-fluorobenzonitrile Method 182 
175	3-(cyclohexyloxy)-2-fluorobenzaldehyde 		223	3-(cyclohexyloxy)-2-fluorobenzonitrile Method 183 
176	2-fluoro-3-isopropoxybenzaldehyde 		183	2-fluoro-3-isopropoxybenzonitrile Method 184 
177	2-fluoro-3-(2,2,2-trifluoroethoxy)benzaldehyde 		223	2-fluoro-3-(2,2,2-trifluoroethoxy)benzonitrile Method 200 

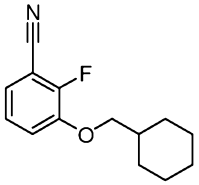
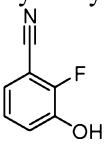
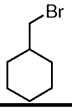
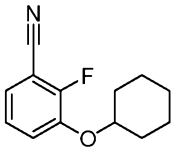
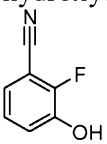
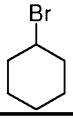
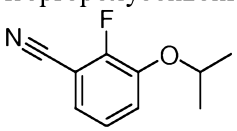
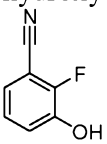
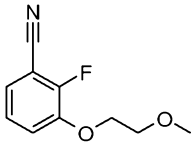
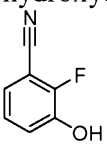
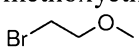
178	2-fluoro-3-(2-methoxyethoxy)benzaldehyde 	10.32 (s, 1 H) 7.56-7.35 (m, 2 H) 7.13-6.96 (m, 1 H) 4.33-4.22 (m, 2 H) 3.84-3.77 (m, 2 H) 3.42 (s, 3 H)	199	2-fluoro-3-(2-methoxyethoxy)benzonitrile Method 185 
179	3-(cyclopentyloxy)-2-fluorobenzaldehyde 		195	3-(cyclopentyloxy)-2-fluorobenzonitrile Method 187 
180	3-cyclobutoxy-2-fluorobenzaldehyde 	10.31 (s, 1 H) 7.41-7.36 (m, 2 H) 7.05-7.03 (m, 1 H) 4.94-4.85 (m, 1 H) 2.01-1.83 (m, 8 H)	209	3-cyclobutoxy-2-fluorobenzonitrile Method 186 

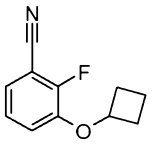
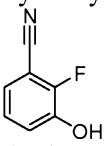
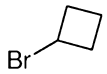
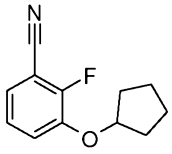
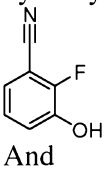
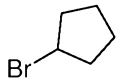
Method 181



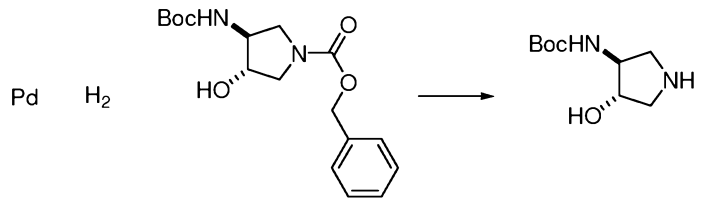
A 100 mL round bottom flask was charged with a magnetic stir bar, 2-fluoro-3-hydroxybenzonitrile (0.500 g, 3.65 mmol), MeCN (13.89 ml), 1-bromo-2-methylpropane (0.699 ml, 7.29 mmol), and K_2CO_3 (1.008 g, 7.29 mmol). The mixture was then placed in an oil bath and heated to 60 °C with stirring overnight. This mixture was then cooled to rt, filtered through a bed of Celite, and conc. *In vacuo*. The crude material was purified via silica gel chromatography (40 g) using ethyl acetate/hexanes (1:4) as eluent to afford pure 2-fluoro-3-isobutoxybenzonitrile (0.610 g, 87 %) as a colorless oil. *M/z* 194.

The following intermediates were prepared by the procedure of Method 181, using the appropriate starting materials.

182	3-(cyclohexylmethoxy)-2-fluorobenzonitrile 		234	2-fluoro-3-hydroxybenzonitrile  And (bromomethyl)cyclohexane 
183	3-(cyclohexyloxy)-2-fluorobenzonitrile 		220	2-fluoro-3-hydroxybenzonitrile  And Bromocyclohexane 
184	2-fluoro-3-isopropoxybenzonitrile 		179	2-fluoro-3-hydroxybenzonitrile  And 2-iodopropane 
185	2-fluoro-3-(2-methoxyethoxy)benzonitrile 		196	2-fluoro-3-hydroxybenzonitrile  And 1-bromo-2-methoxyethane 

186	3-cyclobutoxy-2-fluorobenzonitrile 		192	2-fluoro-3-hydroxybenzonitrile  And Bromocyclobutane 
187	3-(cyclopentyloxy)-2-fluorobenzonitrile 			2-fluoro-3-hydroxybenzonitrile  And bromocyclopentane 

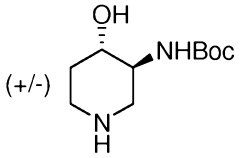
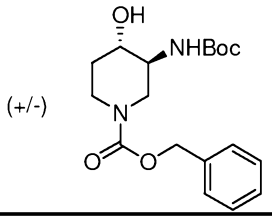
Method 188



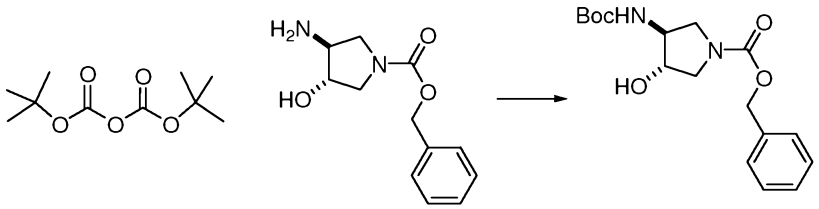
(±)-*tert*-butyl-4-hydroxypyrrolidin-3-ylcarbamate

A racemic mixture of *trans*-benzyl 3-(*tert*-butoxycarbonylamino)-4-hydroxypyrrolidine-1-carboxylate (3.36 g, 9.99 mmol) (Method 190) in MeOH (40 mL) was degassed, then 10 wt % Pd/C (3.19 g, 3.00 mmol) was added. The mixture was degassed, charged with H_2, and stirred overnight. The mixture was filtered through a bed of Celite, washed with methanol, the filtrate was dried over anhydrous Na_2SO_4, filtered and conc. *in vacuo* to yield a white solid as racemic *tert*-butyl-4-hydroxypyrrolidin-3-ylcarbamate (2.020 g, 100 %). ^{1}H NMR (400 MHz, MeOD) δ ppm 4.13 (dt, 1 H), 3.89-3.75 (m, 1 H), 3.35 (brs, 1 H), 3.14 (dd, 1 H), 2.93-2.73 (m, 2 H), 1.46 (s, 10 H); *m/z* 203.

The following intermediates were prepared by the procedure of Method 188, using the appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
189	(±)-*tert*-butyl-4-hydroxypiperidin-3-ylcarbamate 		216	(±)-benzyl 3-(*tert*-butoxycarbonylamino)-4-hydroxypiperidine-1-carboxylate Method 191 

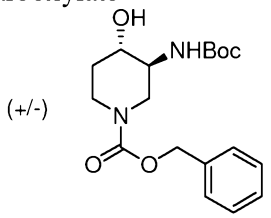
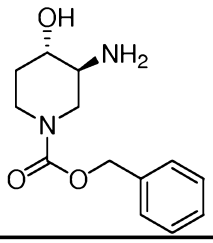
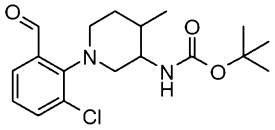
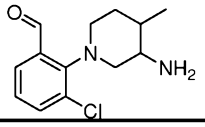
Method 190



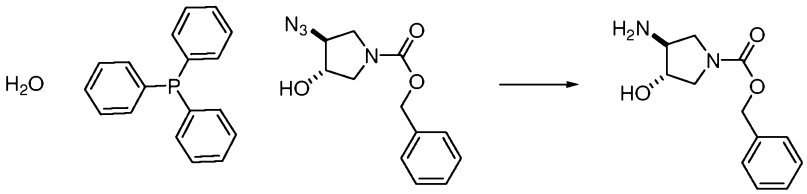
(±)-benzyl 3-(*tert*-butoxycarbonylamino)-4-hydroxypyrrolidine-1-carboxylate

To a mixture of racemic *trans*-benzyl 3-amino-4-hydroxypyrrolidine-1-carboxylate (2.67 g, 11.30 mmol)(Method 193) and di-*tert*-butyl dicarbonate (3.70 g, 16.95 mmol) in CH_2Cl_2 (50 mL) was added Et_3N (4.73 mL, 33.90 mmol) at 0 °C. The mixture was then stirred at rt for 48 h. The reaction mixture was then conc. *in vacuo* giving a residue which was purified via silica gel chromatography (40% to 90% ethyl acetate/hexane) to yield a white solid as (±)-benzyl 3-(*tert*-butoxycarbonylamino)-4-hydroxypyrrolidine-1-carboxylate (3.36 g, 88 %). ^{1}H NMR (400 MHz, Dichloromethane-d2) δ ppm 7.48-7.32 (m, 5 H), 5.21-5.00 (m, 2 H), 4.78 (brs, 1 H), 4.29-4.18 (m, 1 H), 3.84 (dd, 1 H), 3.74 (d, 1 H), 3.41-3.12 (m, 2 H), 1.49-1.33 (m, 9 H); *m/z* 337

The following starting materials were prepared by the procedure of Method 190 using the appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
191	(±)-benzyl 3-(*tert*-butoxycarbonylamino)-4-hydroxypiperidine-1-carboxylate 		350	(±)-benzyl 3-amino-4-hydroxypiperidine-1-carboxylate Method 194 
192	*tert*-butyl 1-(2-chloro-6-formylphenyl)-4-methylpiperidin-3-ylcarbamate 		352	2-(3-amino-4-methylpiperidin-1-yl)-3-chlorobenzaldehyde Method 199 

Method 193

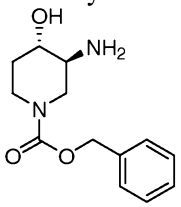
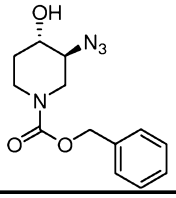


(±)-benzyl 3-amino-4-hydroxypyrrolidine-1-carboxylate:

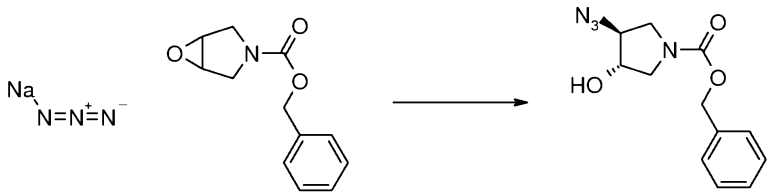
A mixture of racemic *trans*-benzyl 3-azido-4-hydroxypyrrolidine-1-carboxylate (2.96 g, 11.29 mmol) (Method 195) and triphenylphosphine (3.11 g, 11.85 mmol) in THF (25 mL) was stirred at rt for 7 h. Water (2 mL, 111 mmol) was then added and the mixture then stirred at 50 °C overnight. The mixture was then concentrated under reduced pressure, and the residue was purified via silica gel chromatography (100% DCM to 37:3:60/methanol:Et_3N:DCM) to yield the title compound (2.96 g, 11.29 mmol) as an oil.

^{1}H NMR (400 MHz, Dichloromethane-d2) δ ppm 7.38-7.19 (m, 5 H), 5.02 (s, 2 H), 3.89 (brs, 1 H), 3.62 (dd, 2 H), 3.29-3.15 (m, 2 H), 3.12-3.01 (m, 1 H); *m/z* 236.

The following starting materials were prepared by the procedure of Method 193 using the appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
194	(±)-benzyl 3-amino-4-hydroxypiperidine-1-carboxylate 		250	(±)-benzyl 3-azido-4-hydroxypiperidine-1-carboxylate Method 196 

Method 195

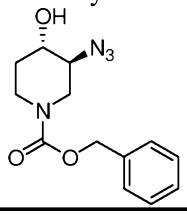
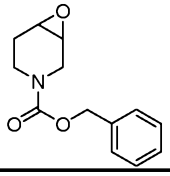


(±)-benzyl 3-azido-4-hydroxypyrrolidine-1-carboxylate

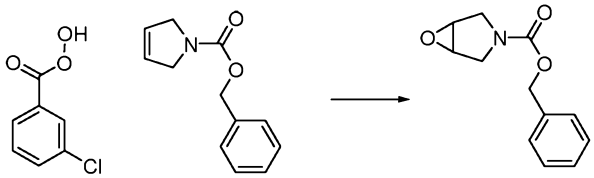
To a stirred mixture of benzyl 6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (5.2 g, 23.72 mmol) (Method 197) in DMF (30 mL) was added sodium azide (2.313 g, 35.58 mmol) in a mixture of acetone (20.00 mL) and water (10.00 mL). The resulting mixture was stirred at 80 °C for 24 h. The mixture was then diluted with water and ether, separated, and the organic layer was washed with brine, dried and conc. invacuo. The resulting material was purified via silica gel chromatography (eluted with 15% to 35% ethyl acetate/hexane), yielding the title compound as a yellow solid (4.10 g, 65.9 %). ^{1}H NMR (400 MHz, dichloromethane-d2) δ ppm 7.50-7.25 (m, 5 H), 5.43-5.25 (m, 2 H),

4.31 (brs, 1 H), 4.00 (brs, 1 H), 3.77 (dd, 1 H), 3.69 (dd, 1 H), 3.53 (d, 1 H), 3.44 (dd, 1 H), 2.17 (brs, 1 H); *m/z* 263.

The following starting materials were prepared by the procedure of Method 195 using the appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
196	(±)-benzyl 3-azido-4-hydroxypiperidine-1-carboxylate 		276	benzyl 7-oxa-3-azabicyclo[4.1.0]heptane-3-carboxylate Method 198 

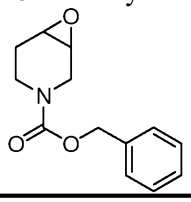
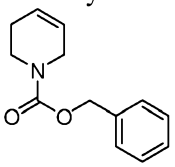
Method 197



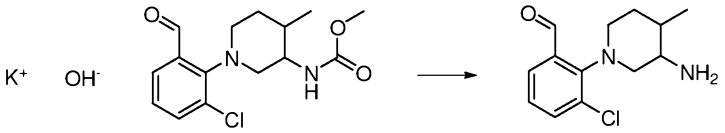
benzyl 6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate

To a stirred mixture of benzyl 2,5-dihydro-1H-pyrrole-1-carboxylate (5 g, 24.60 mmol) in DCM (80 mL) was added 3-chlorobenzoperoxoic acid (6.89 g, 30.75 mmol) at 0 °C. The mixture was then stirred at rt overnight. The reaction mixture was then filtered through a bed of Celite and the filtrate was washed with sat'd aqueous Na_2CO_3 and brine. The organic was then separated and dried over anhydrous Na_2SO_4, filtered, and conc. *in vacuo* to yield the title compound that was used for next step without further purification.

The following starting materials were prepared by the procedure of Method 197 using the appropriate starting materials.

Method	Compound	^{1}H NMR	m/z	SM
198	benzyl 7-oxa-3-azabicyclo[4.1.0]heptane-3-carboxylate 		217	Benzyl 5,6-dihydropyridine-1(2H)-carboxylate 

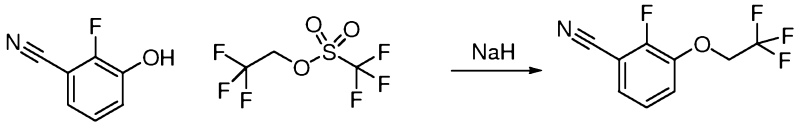
Method 199:



2-(3-amino-4-methylpiperidin-1-yl)-3-chlorobenzaldehyde

To a stirred solution of methyl 1-(2-chloro-6-formylphenyl)-4-methylpiperidin-3-ylcarbamate (220 mg, 0.71 mmol) (Method 119) in MeOH (3 ml) was added 40 % aqueous solution of KOH (10ml) drop wise, and the resulting mixture was heated at reflux for 16 h. The mixture was allowed to cool to rt, diluted with water, and extracted with DCM. The combined organic extract was dried over anhydrous Na_2SO_4, filtered, and conc. *in vacuo*. The resulting residue was purified via silica gel chromatography (100 % ethyl acetate to 10 % methanol in ethyl acetate) to yield the title compound as a light yellow gum (0.057 g, 31.9 %). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.44 (s, 1 H), 7.40 (t, 2 H), 7.07 (t, 1 H), 4.29 (d, 1 H), 3.58 (ddd, 1 H), 3.38 (dd, 1 H), 3.11 (td, 1 H), 2.81 (d, 1 H), 2.20-1.91 (m, 1 H), 1.31-1.14 (m, 1 H), 1.08 (d, 3 H), 0.63-0.37 (m,1 H).

Method 200

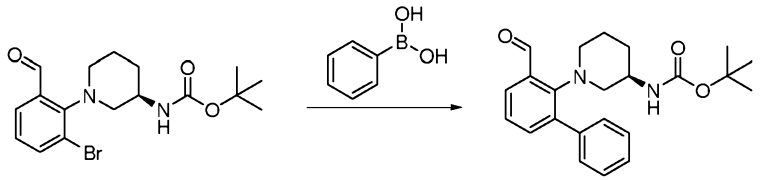


2-fluoro-3-(2,2,2-trifluoroethoxy)benzonitrile:

A stirred solution of 2-fluoro-3-hydroxybenzonitrile (800 mg, 5.83 mmol) in DMF (10 mL) at 0 °C was treated portionwise with NaH (280 mg, 7.00 mmol) (60% oil dispersion). The reaction mixture was then stirred for 0.5 h and 2,2,2-trifluoroethyl trifluoromethanesulfonate (1490 mg, 6.42 mmol) was added. The reaction was allowed to warm to rt overnight with stirring. The reaction mixture was then treated with water (40 mL) and brine (5 mL) and extracted with ethyl acetate (~ 50 mL). The organic extract was washed with water, dried over anhydrous Na_2SO_4, filtered and conc. *in vacuo* to afford a residue which was purified via silica gel chromatography (10 % to 30 % ethyl acetate/hexanes) to yield the title compound as a white solid (1040 mg, 81 %). ^{1}H NMR (400 MHz, MeOD) δ ppm 7.56 (td, 1 H), 7.47-7.38 (m, 1 H), 7.38-7.24 (m, 1 H), 4.73 (q, 2 H); *m/z* 220.

Method 201:

(*R*)-*tert*-butyl 1-(3-formylbiphenyl-2-yl)piperidin-3-ylcarbamate:



A mixture of (*R*)-*tert*-butyl 1-(2-bromo-6-formylphenyl)piperidin-3-yl carbamate (Method 95) (300 mg, 0.78 mmol), phenylboronic acid (143 mg, 1.17 mmol), 1,1'-bis(di-*tert*-butyllphosphino)ferrocenedichloro palladium (II) complex (40.8 mg, 0.06 mmol), and Na_2CO_3 (124 mg, 1.17 mmol) was suspended in dioxane (5 mL) and water (1.50 mL) and stirred at 110 °C for overnight under an atmosphere of nitrogen. The reaction was cooled to rt and water (~ 50 mL) and ethyl acetate (~ 50 mL) was added to the mixture. The organic phase was separated, dried over anhydrous $MgSO_4$, filtered, and conc. *in vacuo* affording a residue purified with via silica gel chromatography (40 g) using a gradient of 5% to 30% ethyl acetate/hexanes to yield the title compound as a low melting solid (168 mg, 56.4 %); *m/z* 381.

One may purify examples provided above by reverse-phase HPLC in a solvent

contain varying concentrations of trifluoroacetic acid or hydrochloric acid. Thus the examples above may be isolated as, the freebase, hydrochloride salt, or trifluoroacetate salt.

PIM 1 and 2 enzyme assay descriptions:

PIM1 in-vitro mobility shift assay

One may determine the activity of purified human His-PIM1 [2-313] enzyme *in-vitro* using a mobility shift assay on a Caliper LC3000 reader (Caliper, MA), which measures fluorescence of a phosphorylated and unphosphorylated FL-Ahx-Bad (FITC-(AHX)RSRHSSYPAGT-COOH, Primm 200606-00289, Primm Biotech, MA) and calculates a ratiometric value to determine percent turnover. One may express PIM1 (University of Dundee, Scotland) in baculovirus system with a typical yield of >85% purity.

One determines phosphorylation of the FL-Ahx-Bad in the presence and absence of the compound of interest. One preincubates 5ul of Enzyme/Substrate/adenosine triphosphate (ATP) mix consisting of 2.4nM PIM1, 3.6uM FL-Ahx-Bad, and 240uM ATP in 1.2x buffer with 2ul of compound for 20 minutes at 25 °C. One initiates reactions with 5ul of Metal mix consisting of 24mM $MgCl_2$ in 1.2x buffer and incubated at 25 °C for 90 minutes and stops the reactions by addition of 5ul of Stop mix consisting of 100mM HEPES, 121mM ethylenediamine tetraacetic acid, 0.8% Coatin Reagent 3 (Caliper, MA), and 0.01% Tween. One detects phosphorylated and unphosphorylated substrate by a Caliper LC3000 reader (Caliper, MA) in the presence of separation buffer consisting of 100mM HEPES, 16mM ethylenediamine tetraacetic acid, 0.1% Coatin Reagent 3 (Caliper, MA), 0.015% Brij-35, 5% DMSO, and 5.6mM $MgCl_2$. One may use the following separation conditions for a Caliper LC3000: -1.0 PSI, -2000 V upstream voltage, -400 V downstream voltage, 0.2 second sample sip, 45 second post sip, 10% laser strength.

PIM2 in-vitro mobility shift assay

One may determine the activity of purified human His-PIM2 [23-299] enzyme *in-vitro* using a mobility shift assay on a Caliper LC3000 reader (Caliper, MA), which measures fluorescence of a phosphorylated and unphosphorylated FL-Ahx-Bad (FITC-(AHX)RSRHSSYPAGT-COOH, Primm 200606-00289, Primm Biotech, MA) and calculates a ratiometric value to determine percent turnover. One may express PIM2 (produced at AstraZeneca, R&D Boston) in *E. coli* cells with a typical yield of >90% purity.

One determines phosphorylation of the FL-Ahx-Bad in the presence and absence of the compound of interest. One preincubates 5uL of Enzyme/Substrate/adenosine triphosphate (ATP) mix consisting of 2.4nM PIM1, 3.6uM FL-Ahx-Bad, and 12uM ATP in 1.2x buffer with 2ul of compound for 20 minutes at 25 °C. One initiates reactions with 5uL of Metal mix consisting of 24mM $MgCl_2$ in 1.2x buffer and incubates at 25 °C for 90 minutes. One stops reactions by addition of 5uL of Stop mix consisting of 100mM HEPES, 121mM ethylenediamine tetraacetic acid, 0.8% Coatin Reagent 3 (Caliper, MA), and 0.01% Tween. One detects phosphorylated and unphosphorylated substrate by a Caliper LC3000 reader (Caliper, MA) in the presence of separation buffer consisting of 100mM HEPES, 16mM ethylenediamine tetraacetic acid, 0.1% Coatin Reagent 3 (Caliper, MA), 0.015% Brij-35, 5% DMSO, and 5.6mM $MgCl_2$. One may use the following separation conditions for a Caliper LC3000: -1.0 PSI, -2000 V upstream voltage, -400 V downstream voltage, 0.2 second sample sip, 45 second post sip, 10% laser strength.

Using the above described assays, or appropriate modifications thereof, preferred compounds disclosed herein generally have an IC_{50} for PIM1 of less that 5 micromolar (uM), and even more preferred of less than 1 micromolar. The table 1 below provides the percent inhibition of PIM1 at 0.3 micromolar for Examples provided herein. Several examples were tested more than once. Variations in the experimental outcomes, negative values, or values over 100% inhibition are presumably due to experimental error inherent in the assay.

Table 1.

Example number	PIM1 %I at 0.3 uM	PIM2 %I at 0.3 uM
1	>95	77.7
2	>95	>95
3	>95	58.0
4	>95	79.6
5A	>95	79.9
5B	>95	>95
6	79.4	9.5
7	5.4	<5
8	16.3	<5
9	6.9	<5
10	>95	50.1
11	89.4	17.9
12	80.2	<5
13	<5	<5
14	>95	69.9
15	12.9	<5
16	13.9	<5
17	29.8	<5
18	<5	<5
19	>95	38.3

20	86.5	19.1
21	82.9	15.8
22	81.9	8.5
23	87.6	19.7
24	>95	44.3
25	>95	68.4
26	>95	49.6
27	90.8	25.1
28	90.0	27.4
29	92.8	
30	90.8	15.6
31	92.8	23.3
32	94.0	31.9
33	>95	>95
34	>95	39.3
35	<5	<5
36	>95	>95
37	89.7	69.4
38	>95	92.9
39	89.4	57.3
40	>95	89.8
41	74.0	25.1

42	58.8	23.3
43	55.4	14.7
44	83.8	46.7
45	40.1	14.3
46	13.4	15.7
47	50.0	26.3
48	84.4	41.3
49	>95	86.3
50	93.7	45.4
51	85.5	80.6
52	>95	93.5
53	92.3	82.1
54	88.1	73.1
55	11.0	<5
56	90.7	33.5
57	53.3	42.6
58	16.0	7.1
59	<5	6.6
60	35.4	11.3
61	81.8	28.1
62	62.1	17.5
63	79.2	21.5

64	86.5	25.7
65	45.3	18.9
66	50.3	20.9
67		<5
68	41.9	9.0
69	<5	16.3
70	<5	<5
71	<5	<5
72	<5	<5
73	<5	<5
74		
75	>95	69.5
76	59.6	27.6
77	51.2	22.7
78	71.4	30.0
79	90.0	60.7
80	<5	
81	<5	
82	87.4	58.2
83	34.0	
84A	92.9	54.3
84B		

84C	47.8	29.6
84D	27.8	<5
84E	11.7	6.1
84F	87.4	52.4
84G	92.0	63.0
84H	>95	67.0
84I	>95	82.7
84J	93.3	40.4
84K	>95	90.8
84L	>95	55.2
84M	>95	80.9
84N	92.8	81.4
84O	<5	<5
85	>95	82.4
86	>95	>95
87	>95	84.2
88	>95	88.4
89	48.4	21.5
90	78.2	86.3
91	6.6	16.4
92	>95	81.5
93	>95	66.3

94	>95	>95
95	>95	>95
96	>95	>95
97	>95	86.4
98	>95	81.4
99	>95	>95
100	93.0	93.9
101	>95	>95
102	93.3	91.9
103	>95	88.7
104	>95	92.4
105	>95	92.4
106	>95	92.8
107	>95	>95
108	>95	>95
109	64.2	65.8
110	90.9	90.7
111	>95	>95
112	>95	>95
113	>95	>95
114	>95	>95
115	93.3	76.1

116	>95	>95
117	>95	>95
118	>95	>95
119	56.2	20.1
120	58.9	22.2
121	>95	87.4
122A	88.2	55.0
122B	>95	92.3
122C	>95	>95
122D	>95	>95
122E	>95	>95
122F	>95	>95
122G	>95	92.1
122H	>95	>95
122I	>95	>95
122J	>95	>95
122K	>95	>95
122L	>95	>95
122M	>95	>95
122N	>95	>95
1220	>95	>95
122P	>95	>95

122Q	>95	>95
122R	>95	89.6
122S	>95	>95
122T	>95	>95
122U	>95	>95
122V	>95	>95
122W	>95	>95
122X	>95	67.1
122Y	>95	>95
122Z	>95	>95
122AA	>95	>95
122AB	>95	>95
122AC	>95	>95
122AD	>95	>95
122AE	>95	>95
122AF	83.9	87.9
122AG	68.9	86.7
122AH	19.0	14.0
122AI	>95	>95
123	>95	>95
124	>95	>95
125	>95	>95

126	>95	>95
127	>95	>95
128	81.2	49.0
129A	>95	>95
129B	>95	>95
129C	85.0	52.1
130	66.2	45.5
131A	27.1	<5
131B	<5	<5
132	93.0	88.1
133	>95	93.4
134	>95	85.2
135	42.5	10.8
136	82.8	44.6
137	55.1	18.6
138	87.9	63.2
139	58.1	15.1
140	73.3	52.0
141	34.9	<5
142	86.1	75.2
143	85.9	49.8
144	63.2	21.2

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145	>95	80.1
146	88.9	48.5
147	74.3	36.4
148	91.5	60.8
149	>95	75.4
150	79.8	31.7
151	31.5	13.5
152	10.8	16.7

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A compound selected from:

5-({2-[(3S)-3-aminopiperidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3R)-3-aminopiperidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[2-(4-aminopiperidin-1-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({2-[3-(aminomethyl)piperidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(1,4-diazepan-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-cyclopentylpiperazin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(4-fluorophenyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(3-methyl-1,2,4-oxadiazol-5-yl)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-pyrrolidin-1-ylpiperidin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(1-methylethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-methylpropyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-hydroxyethyl)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(4-chloro-2-fluorophenyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[3-(3-methyl-1,2,4-oxadiazol-5-yl)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(pyridin-4-ylmethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-chlorobenzyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(1-methylpiperidin-4-yl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-morpholin-4-ylethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(cyclopropylmethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-morpholin-4-ylpiperidin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(3-hydroxypropyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(dimethylamino)piperidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-{[3-(dimethylamino)propyl](methyl)amino}-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-hydroxyethyl)-1,4-diazepan-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[2-(4-butyl-1,4-diazepan-1-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-chloro-2-[4-(2-hydroxyethyl)piperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-morpholin-4-yl-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[2-(4-tert-butylpiperazin-1-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[2-(1,4'-bipiperidin-1'-yl)-3-chloro-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-{[3-chloro-2-(4-methylpiperazin-1-yl)-5-(trifluoromethyl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

5-({3-bromo-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-chloro-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-[3-(4-methylpiperazin-1-yl)propoxy]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

2-{3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenoxy}acetamide;

(5Z)-5-{[3-(3-piperidin-1-ylpropoxy)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-[(4-methylpiperazin-1-yl)methyl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

N-[2-(dimethylamino)ethyl]-2'-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-N-methylbiphenyl-4-sulfonamide;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-methoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-(trifluoromethyl)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({5-chloro-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-4-methylphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-methylphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({5-bromo-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-3-fluorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

5-({2-chloro-6-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-(aminomethyl)pyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-(aminomethyl)pyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-methoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-bromophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-bromophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-ethoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(2-methylpropoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclohexylmethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclohexyloxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R,4R)-3-amino-4-hydroxypiperidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-{[3-chloro-2-(1,4-diazepan-1-yl)phenyl]methylidene}-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(1-methylethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-(1-methylethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-ethoxyphenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-{[4-(aminomethyl)benzyl]amino}piperidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-chloro-2-[(3R)-3-{[2-(methylamino)ethyl]amino}piperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S,4S)-3-amino-4-hydroxypyrrolidin-1-yl]-3-chlorophenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({3-chloro-2-[4-methyl-3-(methylamino)piperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-{[2-(3-amino-4-methylpiperidin-1-yl)-3-chlorophenyl]methylidene}-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(2,2,2-trifluoroethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-(2,2,2-trifluoroethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(2-methoxyethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3S)-3-aminopyrrolidin-1-yl]-3-(2-methoxyethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclopentyloxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(cyclobutyloxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

4-[(3R)-3-aminopiperidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzamide;

4-[(3S)-3-aminopiperidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzamide;

4-[(3R)-3-aminopiperidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzoic acid;

4-[(3S)-3-aminopyrrolidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]benzoic acid;

(5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]biphenyl-3-yl}methylidene)-1,3-thiazolidine-2,4-dione;

5-{[2-(3-aminopropoxy)-5-methoxyphenyl]methylidene}-1,3-thiazolidine-2,4-dione;

N-{4-[3-(dimethylamino)pyrrolidin-1-yl]-3-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}acetamide;

(5Z)-5-[(3-chloro-2-{(3R)-3-[(2-hydroxyethyl)amino]piperidin-1-yl}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

(5Z)-5-[(3-chloro-2-{(3R)-3-[(3-hydroxypropyl)amino]piperidin-1-yl}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-1-methyl-1H-imidazole-2-carboxamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-methoxyacetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-1-methyl-1H-pyrazole-3-carboxamide;

N^2-carbamoyl-N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]glycinamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-pyridin-3-ylacetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-pyridin-4-ylacetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-1-methyl-1H-pyrazole-4-carboxamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-(1-oxidothiomorpholin-4-yl)acetamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-4-sulfamoylbutanamide;

N'-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-N,N-dimethylbutanediamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-N~2~,N~2~-dimethylglycinamide;

N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]-2-cyanoacetamide;

N^2-acetyl-N-[(3S)-1-{2-chloro-6-[(Z)-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]phenyl}pyrrolidin-3-yl]glycinamide;

(5Z)-5-({3-chloro-2-[(3R)-3-(dipropylamino)piperidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione;

(5Z)-5-[(3-chloro-2-{(3R)-3-[(3,3,3-trifluoropropyl)amino]piperidin-1-yl}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

5-[(5-methoxy-2-{3-[(1-methylethyl)amino]propoxy}phenyl)methylidene]-1,3-thiazolidine-2,4-dione;

(5Z)-5-({5-amino-2-[3-(dimethylamino)pyrrolidin-1-yl]phenyl}methylidene)-1,3-thiazolidine-2,4-dione; and

5-[(2-amino-4,5-dimethoxyphenyl)methylidene]-1,3-thiazolidine-2,4-dione,

or salts thereof.

2. A pharmaceutical composition comprising a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof.

3. The use of a compound or a pharmaceutically acceptable salt thereof, as claimed in Claim 1, for the manufacture of a medicament for the production of an anti-cancer effect in a subject.

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4. A compound according to claim 1 which is (5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]biphenyl-3-yl}methylidene)-1,3-thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof.

5. A pharmaceutical composition comprising a compound as defined in Claim 4, or a pharmaceutically acceptable salt thereof.

6. A compound according to claim 1 which is (5Z)-5-({2-[(3R)-3-aminopiperidin-1-yl]-3-(1-methylethoxy)phenyl}methylidene)-1,3-thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof.

7. A pharmaceutical composition comprising a compound as defined in Claim 6, or a pharmaceutically acceptable salt thereof.

8. The use of a compound of claim 4, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the production of an anti-cancer effect in a subject.

9. The use of a compound of claim 6, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the production of an anti-cancer effect in a subject.

10. A method for the production of an anti-cancer effect in a subject in need thereof comprising administering to said subject a compound according to claim 1 or a salt thereof.

11. A compound according to claim 1; or a pharmaceutical composition according to claim 2; or a use according to claim 3; or a method according to claim 10 substantially as hereinbefore described with reference to the Examples.