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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 April 2015 (30.04.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/061518 A1

(51) International Patent Classification:
C07D 263/56 (2006.01) *C07D 233/54* (2006.01)
C07D 215/08 (2006.01) *C07D 401/04* (2006.01)
C07D 311/04 (2006.01) *C07D 311/58* (2006.01)
C07D 317/66 (2006.01) *C07D 409/12* (2006.01)
C07D 231/12 (2006.01) *C07D 249/08* (2006.01)
C07D 333/18 (2006.01) *C07D 261/08* (2006.01)
C07D 333/28 (2006.01) *C07D 205/04* (2006.01)
C07D 233/38 (2006.01)

(21) International Application Number:
PCT/US2014/061870

(22) International Filing Date:
23 October 2014 (23.10.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/895,102 24 October 2013 (24.10.2013) US

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

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

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

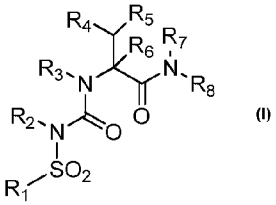
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

— *of inventorship (Rule 4.17(iv))*

Published:

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

(54) Title: INHIBITORS OF HUMAN IMMUNODEFICIENCY VIRUS REPLICATION



(I)

(57) Abstract: Compounds of Formula I with activity against HIV, including pharmaceutical compositions and methods for using these compounds in treating human immunodeficiency virus (HIV) infection, are set forth: Formula :(I)

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INHIBITORS OF HUMAN IMMUNODEFICIENCY VIRUS REPLICATION

CROSS REFERENCE TO RELATED APPLICATION

This application claims the priority of U.S. Provisional Application Serial No. 61/895,102 filed October 24, 2013 which is herein incorporated by reference in its entirety.

FIELD OF THE INVENTION

The invention relates to compounds, compositions, and methods for the treatment of human immunodeficiency virus (HIV) infection. More particularly, the invention provides novel inhibitors of HIV, pharmaceutical compositions containing such compounds, and methods for using these compounds in the treatment of HIV infection.

BACKGROUND OF THE INVENTION

HIV (human immunodeficiency virus) infection/acquired immunodeficiency syndrome (HIV/AIDS) is the result of infection by HIV. It remains a major medical problem, with an estimated 34 million people infected worldwide at the end of 2011, 3.3 million of them under the age of 15. In 2011, there were 2.5 million new infections, with, 1.7 million people dying from complications due to HIV/AIDS.

Current therapy for HIV-infected individuals consists of a combination of approved anti-retroviral agents. Over two dozen drugs are currently approved for HIV infection, either as single agents or as fixed dose combinations or single tablet regimens, the latter two containing 2-4 approved agents. These agents belong to a number of different classes, targeting either a viral enzyme or the function of a viral protein during the virus life cycle. Thus, agents are classified as either nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleotide reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors (INIs), or entry inhibitors (one, maraviroc, targets the host CCR5 protein, while the other,

enfuvirtide, is a peptide that targets the gp41 region of the viral gp160 protein). In addition, a pharmacokinetic enhancer with no antiviral activity (cobicistat) has recently been approved for use in combinations with antiretroviral agents (ARVs) that require boosting.

Despite the armamentarium of agents and drug combinations, there remains a medical need for new anti-retroviral agents, due in part to the need for chronic dosing to combat infection. Significant problems related to long-term toxicities are documented, creating a need to address and prevent these co-morbidities (e.g. CNS, CV/metabolic, renal disease). Also, increasing failure rates on current therapies continue to be a problem, due either to the presence or emergence of resistant strains or to non-compliance attributed to drug holidays or adverse side effects. For example, despite therapy, it has been estimated that 63% of subjects receiving combination therapy remained viremic, as they had viral loads >500 copies/ml (Oette, M, Kaiser, R, Däumer, M, et al. Primary HIV Drug Resistance and Efficacy of First-Line Antiretroviral Therapy Guided by Resistance Testing. J Acq Imm Def Synd 2006; 41(5):573-581). Among these patients, 76% had viruses that were resistant to one or more classes of antiretroviral agents.

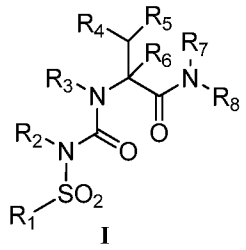
As a result, new drugs are needed that are easier to take, have high genetic barriers to the development of resistance and have improved safety over current agents. In this panoply of choices, novel MOAs that can be used as part of the preferred HAART regimen can still have a major role to play since they should be effective against viruses resistant to current agents.

The invention provides technical advantages, for example, the compounds are novel and are useful in the treatment of HIV. Additionally, the compounds provide advantages for pharmaceutical uses, for example, with regard to one or more of their mechanism of action, binding, inhibition efficacy, target selectivity, solubility, safety profiles, or bioavailability.

SUMMARY OF THE INVENTION

The invention encompasses compounds of Formula I, including pharmaceutically acceptable salts, their pharmaceutical compositions, and their use in inhibiting HIV and treating those infected with HIV or AIDS.

One aspect of the invention is a compound of Formula I, including pharmaceutically acceptable salts thereof:



I

wherein:

R^1 is alkyl, aryl, arylalkyl, cycloalkyl or heteroaryl; wherein said aryl, arylalkyl or heteroaryl moieties are linked to the parent molecule through their respective carbon atoms, and further wherein said R^1 groups are substituted with 0-4 groups independently selected from the group of alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylamino, alkyl, alkylsulphonyl, alkylthioxy, aminocarbonyl, alkynyl, carboxylic acid, cyano, halo, haloalkyl, haloalkoxy, hydroxy, hydroxyalkyl, thioxy, -SO_2alkyl, heteroaryl, and nitro;

R^2 is -H, C_1-C_4 alkyl or C_3-C_4 cycloalkyl;
or R^1 and R^2 together with the atoms to which they are attached form a heterocyclic ring optionally substituted with 0-2 alkyl groups;

R^3 is -H, C_1-C_4 alkyl or C_3-C_4 cycloalkyl;

R^4 is -H, alkyl, aryl, C_5-C_{10} bicycloalkyl, cycloalkyl or heteroaryl which is substituted with 0-3 groups independently selected from the group of alkenoxy,

alkenyl, alkoxy, alkoxycarbonyl, alkyl, benzyloxy, carboamide, cyano, halo, haloalkyl, haloalkoxy, -NHCO(alkyl), -SO_2N-heterocycle, -OH, nitro, and -CH_2OH;

R^5 and R^6 are independently selected from H or alkyl, or R^5 and R^4 together with the atom to which they are attached form an aryl group; or R^5 and R^6 together with the atoms to which they are attached form a C_3-C_4 cycloalkyl;

R^7 is -H, alkyl, aryl, heteroaryl, heteroarylalkyl, C_3-C_7 cycloalkyl or dialkylaminoalkyl, wherein said aryl or heteroaryl is substituted with 0-3 groups independently selected from the group of -OH, -NHCOalkyl, -NHCON(alkyl)$_2$, -NHCO$_2$-alkyl, -CONH$_2$, -CN, -SO_2N(alkyl)$_2$, alkoxy, alkyl, halo, haloalkoxy, and haloalkyl; and

R^8 is -H, alkyl, arylalkyl, cycloalkyl, haloalkyl or heteroarylalkyl; or $R^7$and R^8 together with the nitrogen atom to which they are attached form a heterocycle which is substituted with 0-3 groups independently selected from the group of alkyl, alkoxy, halo, -OH, -CN, and -SO_2N(alkyl)$_2$.

For a compound of Formula I, the scope of any instance of a variable substituent can be used independently with the scope of any other instance of a variable substituent. As such, the invention includes combinations of the different aspects.

The invention also relates to pharmaceutical compositions comprising a compound of Formula I, including pharmaceutically acceptable salts thereof, and a pharmaceutically acceptable carrier, excipient, and/or diluent.

In addition, the invention provides one or more methods of treating HIV infection comprising administering a therapeutically effective amount of a compound of Formula I to a patient.

Also provided as part of the invention are one or more methods for making the compounds of Formula I.

The present invention is directed to these, as well as other important ends, hereinafter described.

DETAILED DESCRIPTION OF THE EMBODIMENTS

The singular forms "a", "an", and "the" include plural reference unless the context dictates otherwise.

Unless otherwise expressly set forth elsewhere in the application, the following terms shall have the following meanings:

"Alkenyl" means a straight or branched alkyl group comprised of 2 to 10 carbons with at least one double bond and optionally substituted with 0-3 halo or alkoxy group.

"Alkenyloxy" means an alkenyl group attached to the parent structure by an oxygen atom.

"Alkoxy" means an alkyl group attached to the parent structure by an oxygen atom.

"Alkoxycarbonyl" means an alkoxy group attached to the parent structure by a carbonyl moiety.

"Alkoxycarbonylamino" means alkoxycabonyl group attached to the parent structure by nitrogen where the nitrogen is optionally substituted with an alkyl group.

"Alkyl" means a straight or branched saturated hydrocarbon comprised of 1 to 10 carbons, and preferably 1 to 6 carbons.

"Alkylsulphonyl" means an alkyl group attached to the parent structure through $-SO_2-$ moiety.

"Alkylthioxy" means an alkyl group attached to the parent structure through a sulfur atom.

"Alkynyl" means an optionally substituted straight or branched alkyl group comprised of 2 to 10 carbons and containing at least one triple bond.

"Aminocabonyl" means an amine group attached to the parent structure through a carbonyl moiety where the amine is optionally substituted with one or two alkyl groups.

"Aryl" mean a carbocyclic group comprised of 1-3 rings that are fused and/or bonded and at least one or a combination of which is aromatic. The non-aromatic carbocyclic portion, where present, will be comprised of C_3 to C_7 alkyl group. Examples of an aromatic group include phenyl, biphenyl, dihydroindene, naphthalene, and tetrahydronaphthalene. The aryl group can be attached to the parent structure through any substitutable carbon atom in the group.

"Arylalkyl" is a C_1-C_5 alkyl group attached to 1 to 2 aryl groups and linked to the parent structure through the alkyl moiety and where the aryl component is further substituted with 0-4 groups selected from halo, alkyl, alkoxy, haloalkyl, haloalkoxy or cyano. Examples include, but are not limited to, $-(CH_2)_nPh$ and $-CH(CH_3)Ph$ with n = 1-5.

"Benzyloxy" means a benzyl group attached to the parent structure through an oxygen atom. The phenyl group of the benzyl moiety could be optionally substituted by 1-3 moieties independently selected from the group of alkyl, alkoxy, halo, haloalkyl, haloalkoxy and cyano.

"C_5-C_{10} bicycloalkyl" means a bicyclic ring system comprised of 5 to 10 carbons. Examples include bicyclo[2.2.2]octane.

"C_3-C_4 cycloalkyl" means a monocyclic ring system comprised of 3 to 4 carbons.

"Cycloalkyl" means carbocycle with 1-2 rings optionally substituted with an alkyl or benzyl group.

"Cyano" refers to -CN.

"Dialkylaminoalkyl" means a dialkylamino group attached to the parent structure through a C_2 to C_3 alkyl moiety.

"Halo" or "halogen" refers to -F, -Cl, -Br, or -I.

"Haloalkyl" means an alkyl group substituted by any combination of one to six halogen atoms.

"Haloalkoxy" means a haloalkyl group attached to the parent structure through an oxygen atom.

"Hydroxy" refers to –OH.

"Heteroaryl" is a subset of heterocyclic group as defined below and is comprised of 1-3 rings where at least one or a combination of which is aromatic and

that the aromatic group contains at least one atom chosen from a group of oxygen, nitrogen or sulfur.

"Heteroarylalkyl" is a heteroaryl moiety attached to the parent structure through C_1-C_5 alkyl group and where the aryl moiety is further substituted with halo, alkyl, alkoxy, haloalkyl, haloalkoxy or cyano. Examples include, but are not limited to, -$(CH_2)_n$-pyridine, -$(CH_2)_n$-thiazole, -$(CH_2)_n$-quinoline, -$(CH_2)_n$-phenyl-pyrazole, -$(CH_2)_n$-(2-methylbenzimidazole), -$(CH_2)_n$-(N-methylimidazole), -$(CH_2)_n$-(methyloxadiazole), -$CH(CH_3)$-(pyridine) with n = 1-5.

"Heterocyclic" means a cyclic group of 1-3 rings comprised of carbon and at least one other atom selected independently from the group of oxygen, nitrogen and sulfur. The rings could be fused and/or bonded, through a direct or spiro attachment, with the option to have one or a combination thereof be aromatic. Examples include, but are not limited to, azaindole, azaindoline, azetidine, benzimidazole, bezodioxolyl, benzoxazole, benzothiophene, benzothiazole, chroman, dihydro-benzo[1,4]oxazine, dihalobezodioxolyl, dihydrobenzofuran, furanylphenyl, imidazo[1,2-a]pyridine, indazole, indole, indoline, isoquinoline, isoquinolinone, isothiazolidine 1,1-dioxide, morpholine, 2-oxa-5-azabicyclo[2.2.1]heptanes, oxadiazole-phenyl, pyrrazole-phenyl, pyridine-phenyl, pyridinylpyrrolidine, pyrimidine-phenyl, quinazoline, quinoxaline, quinoline, tetrahydroisoquinoline, tetrahydrothieno[3,2-c]pyridine, thiophene, thiophene-phenyl, triazole. Unless otherwise specifically set forth, the heterocyclic group can be attached to the parent structure through any suitable atom in the group that results in a stable compound.

Substituents which are illustrated by chemical drawing to bond at variable positions on a multiple ring system (for example a bicyclic ring system) are intended to bond to the ring where they are drawn to append. Parenthetic and multiparenthetic terms are intended to clarify bonding relationships to those skilled in the art. For example, a term such as ((R)alkyl) means an alkyl substituent further substituted with the substituent R.

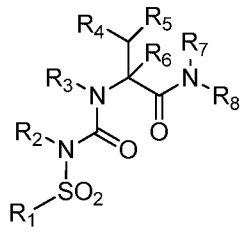
Those terms not specifically set forth herein shall have the meaning which is commonly understood and accepted in the art.

The invention includes all pharmaceutically acceptable salt forms of the compounds. Pharmaceutically acceptable salts are those in which the counter ions do not contribute significantly to the physiological activity or toxicity of the compounds and as such function as pharmacological equivalents. These salts can be made according to common organic techniques employing commercially available reagents. Some anionic salt forms include acetate, acistrate, besylate, bromide, chloride, citrate, fumarate, glucouronate, hydrobromide, hydrochloride, hydroiodide, iodide, lactate, maleate, mesylate, nitrate, pamoate, phosphate, succinate, sulfate, tartrate, tosylate, and xinofoate. Some cationic salt forms include ammonium, aluminum, benzathine, bismuth, calcium, choline, diethylamine, diethanolamine, lithium, magnesium, meglumine, 4-phenylcyclohexylamine, piperazine, potassium, sodium, tromethamine, and zinc.

Some of the compounds of the invention exist in stereoisomeric forms. The invention includes all stereoisomeric forms of the compounds including enantiomers and diastereromers. Methods of making and separating stereoisomers are known in the art. The invention includes all tautomeric forms of the compounds. The invention includes atropisomers and rotational isomers.

The invention is intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include deuterium and tritium. Isotopes of carbon include ^{13}C and ^{14}C. Isotopically-labeled compounds of the invention can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described herein, using an appropriate isotopically-labeled reagent in place of the non-labeled reagent otherwise employed. Such compounds may have a variety of potential uses, for example as standards and reagents in determining biological activity. In the case of stable isotopes, such compounds may have the potential to favorably modify biological, pharmacological, or pharmacokinetic properties.

As set forth above, the invention is directed to a compound of Formula I, including pharmaceutically acceptable salts thereof:



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wherein:

R^1 is alkyl, aryl, arylalkyl, cycloalkyl or heteroaryl; wherein said aryl, arylalkyl or heteroaryl moieties are linked to the parent molecule through their respective carbon atoms, and further wherein said R^1 groups are substituted with 0-4 groups independently selected from the group of alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylamino, alkyl, alkylsulphonyl, alkylthioxy, aminocarbonyl, alkynyl, carboxylic acid, cyano, halo, haloalkyl, haloalkoxy, hydroxy, hydroxyalkyl, thioxy, -SO_2alkyl, heteroaryl, and nitro;

R^2 is -H, C_1-C_4 alkyl or C_3-C_4 cycloalkyl;
or R^1 and R^2 together with the atoms to which they are attached form a heterocyclic ring optionally substituted with 0-2 alkyl groups;

R^3 is -H, C_1-C_4 alkyl or C_3-C_4 cycloalkyl;

R^4 is -H, alkyl, aryl, C_5-C_{10} bicycloalkyl, cycloalkyl or heteroaryl which is substituted with 0-3 groups independently selected from the group of alkenoxy, alkenyl, alkoxy, alkoxycarbonyl, alkyl, benzyloxy, carboamide, cyano, halo, haloalkyl, haloalkoxy, -NHCO(alkyl), -SO_2N-heterocycle, -OH, nitro, and -CH_2OH;

R^5 and R^6 are independently selected from H or alkyl, or R^5 and R^4 together with the atom to which they are attached form an aryl group; or R^5 and R^6 together with the atoms to which they are attached form a C_3-C_4 cycloalkyl;

R^7 is -H, alkyl, aryl, heteroaryl, heteroarylalkyl, C_3-C_7 cycloalkyl or dialkylaminoalkyl, wherein said aryl or heteroaryl is substituted with 0-3 groups independently selected from the group of -OH, -NHCOalkyl, -NHCON(alkyl)$_2$, -NHCO$_2$-alkyl, -CONH$_2$, -CN, -SO$_2$N(alkyl)$_2$, alkoxy, alkyl, halo, haloalkoxy, and haloalkyl; and

R^8 is -H, alkyl, arylalkyl, cycloalkyl, haloalkyl or heteroarylalkyl; or $R^7$and R^8 together with the nitrogen atom to which they are attached form a heterocycle which is substituted with 0-3 groups independently selected from the group of alkyl, alkoxy, halo, -OH, -CN, and -SO$_2$N(alkyl)$_2$.

In a preferred embodiment of the invention, R^1 is aryl. More preferably, R^1 is aryl which is selected from the group of phenyl, biphenyl, and naphthalenyl.

In a further embodiment, R^1 is heteroaryl. More preferably, R^1 is selected from the group of thiophene, pyrrazolophenyl, furanylphenyl, pyridinylphenyl, pyrimidinylphenyl, thiophenylphenyl, benzothiophene, oxadiazolephenyl, indole, and andazaindole.

In a further preferred embodiment, R^1 and R^2 form a heteroaryl ring. More preferably, the heteroaryl ring is isothiazolidine 1,1-dioxide.

It is also preferred that R^4 is aryl. More preferably, R^4 is phenyl, naphthalenyl, or biaryl.

In another embodiment it is preferred that R^4 is heteroaryl. More preferably, R^4 is triazole or thiophene.

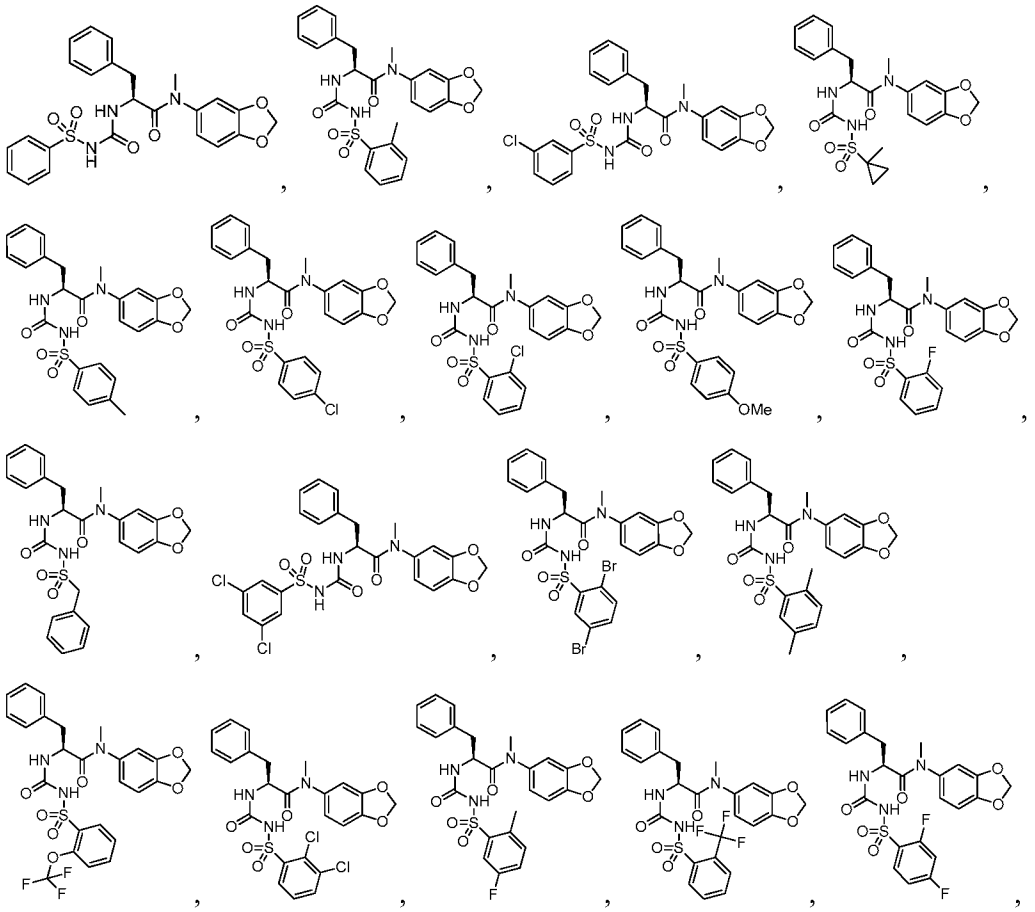
It is further preferred that R^7 is aryl. More preferably, R^7 is phenyl or naphthalenyl.

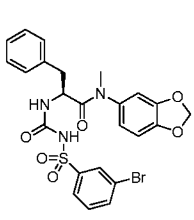
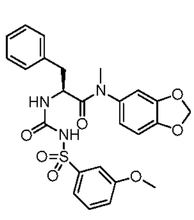
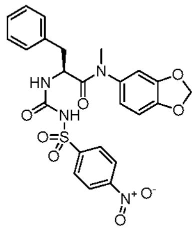
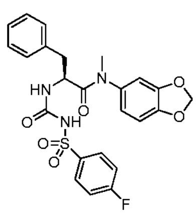
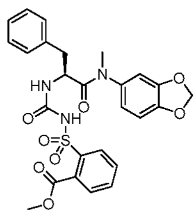
In another embodiment it is preferred that R^7 is heteroaryl. More preferably R^7 is selected from the group of bezodioxolyl, dihalobezodioxolyl, benzothiazole,

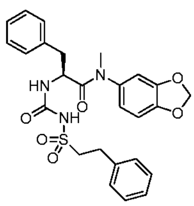
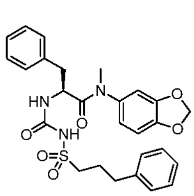
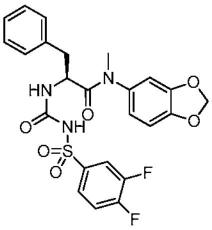
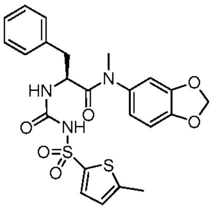
quinoline, benzothiazole, benzimidazole, quinazoline, quinoxaline, dihydrobenzofuran, chroman, benzoxazole, isoquinoline, and isoquinolinone.

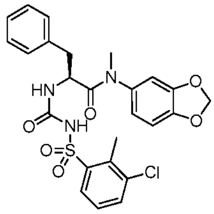
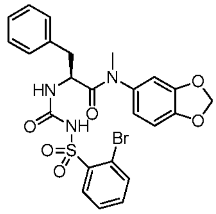
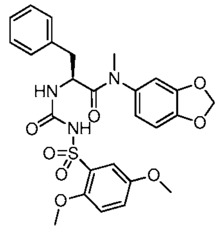
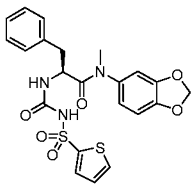
In a further embodiment of the invention, R^7 and R^8 form a heterocycle. More preferably, the heterocycle is selected from the group of tetrahydroisoquinoline, dihydro-benzo[1,4]oxazine, dihydroindole, tetrahydrothieno[3,2-c]pyridine, 2-oxa-5-azabicyclo[2.2.1]heptanes, azetidine, and pyridinylpyrrolidine.

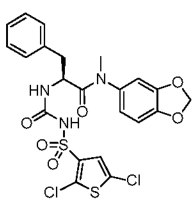
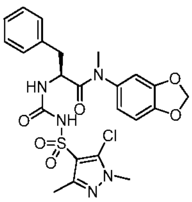
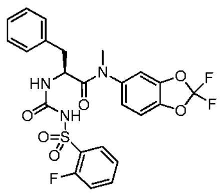
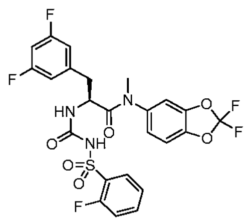
Preferred compounds of the invention, including pharmaceutically acceptable salts thereof, are selected from the group of:

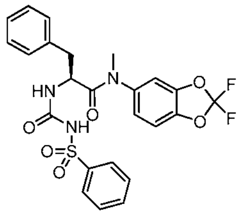
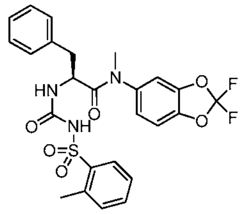
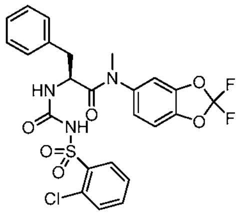
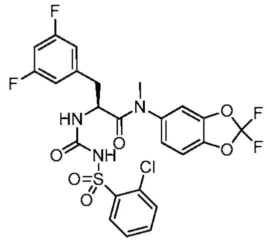


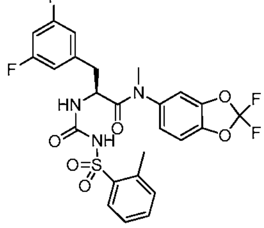
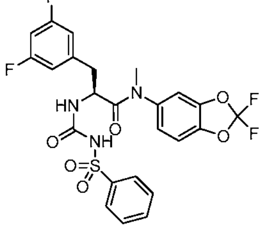
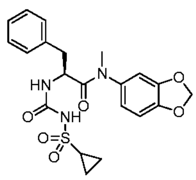
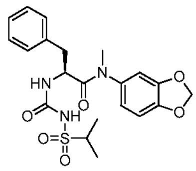
 ,  ,  ,  ,  ,

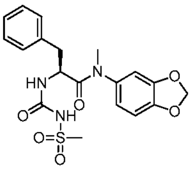
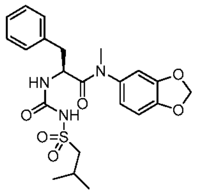
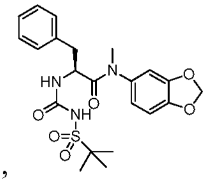
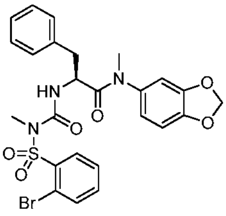
 ,  ,  ,  ,

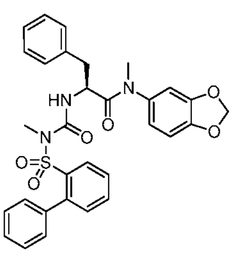
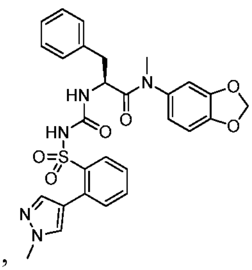
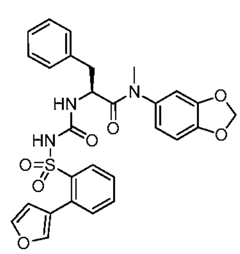
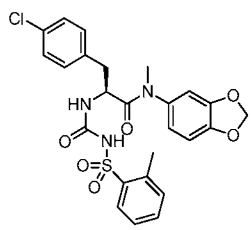
 ,  ,  ,  ,

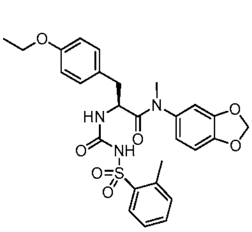
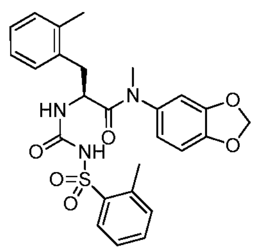
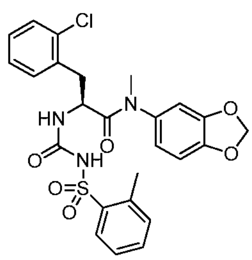
 ,  ,  ,  ,

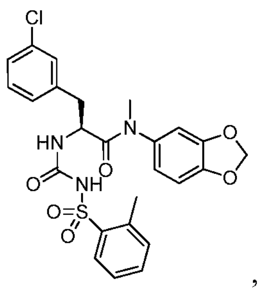
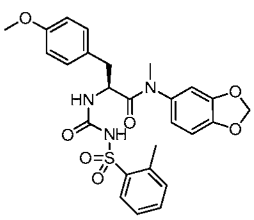
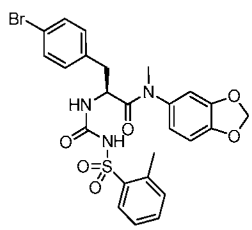
 ,  ,  ,  ,

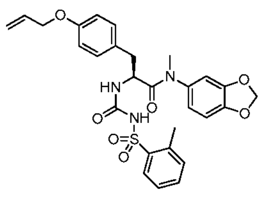
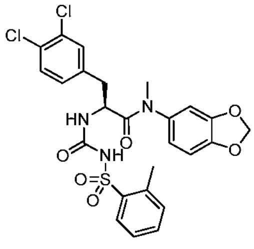
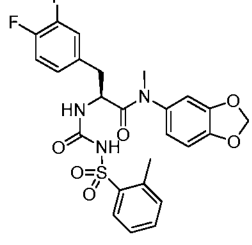
 ,  ,  ,  ,

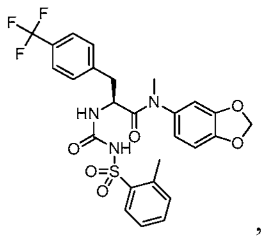
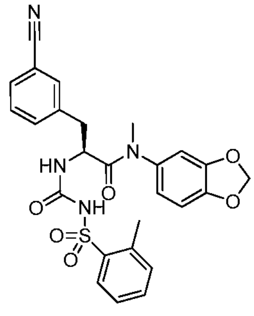
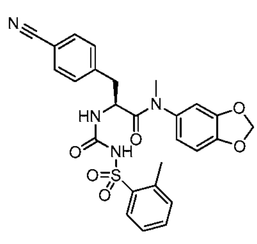
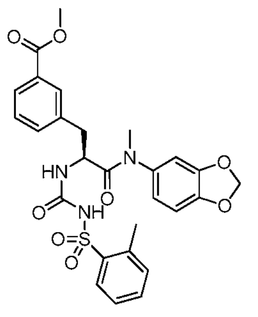
 ,  ,  ,  ,

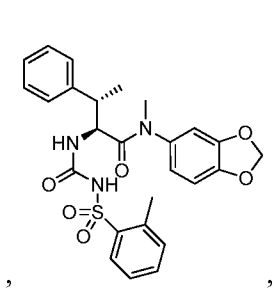
 ,  ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  , 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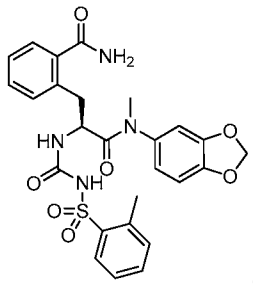
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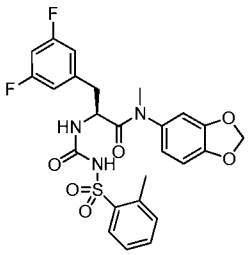
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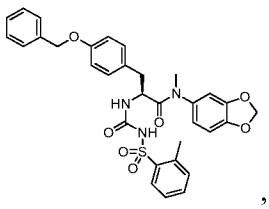
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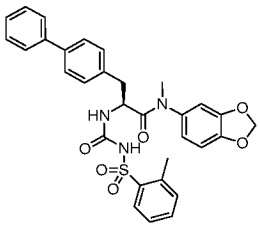
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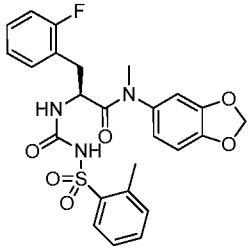
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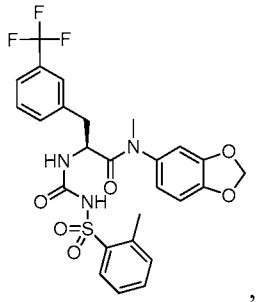
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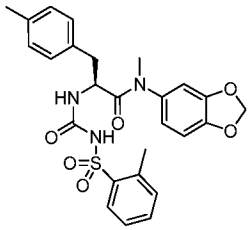
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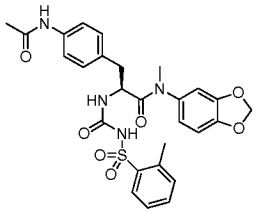
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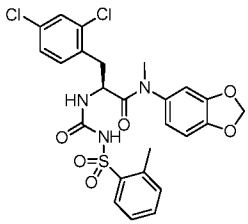
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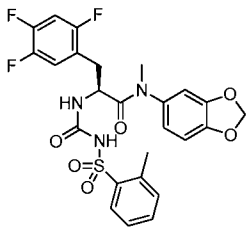
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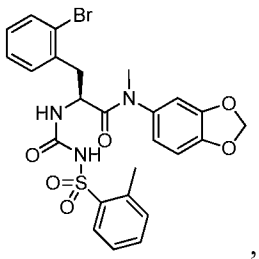
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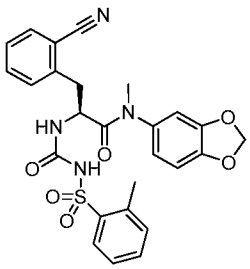
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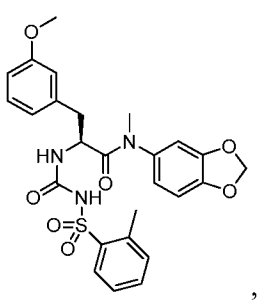
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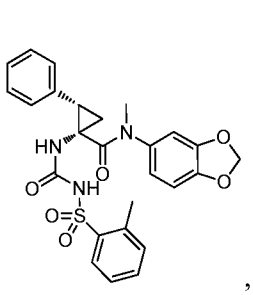
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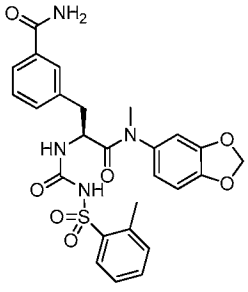
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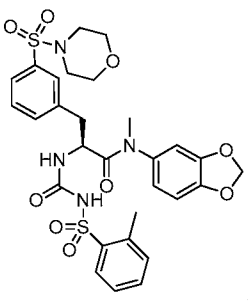
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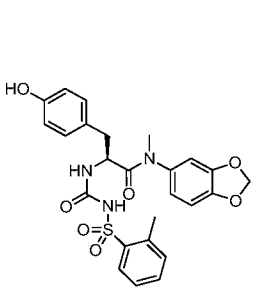
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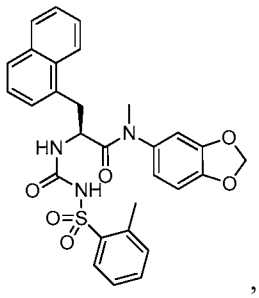
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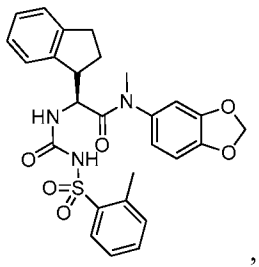
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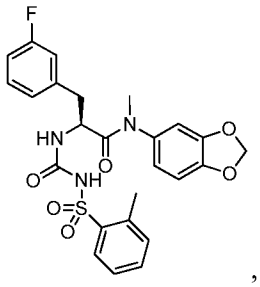
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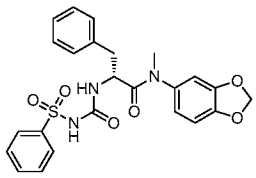
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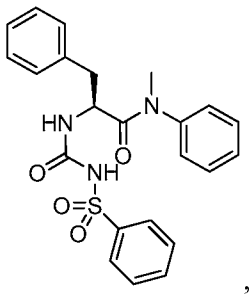
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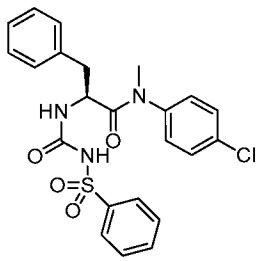
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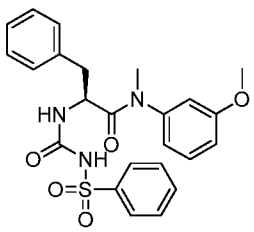
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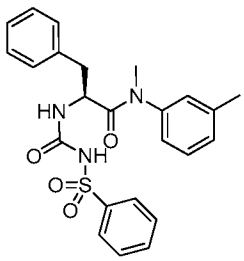
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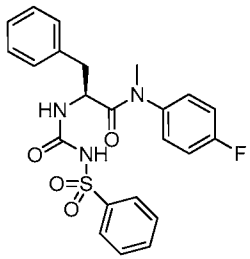
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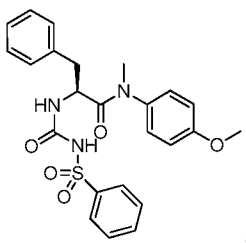
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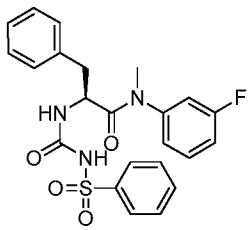
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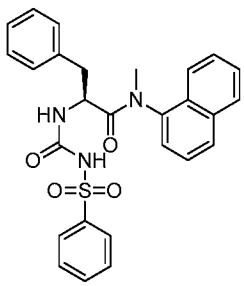
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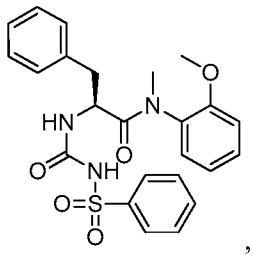
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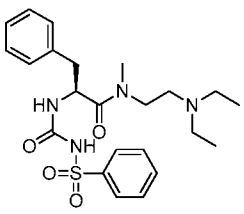
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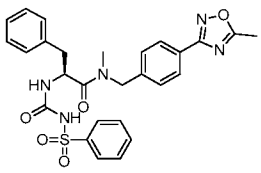
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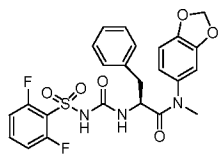
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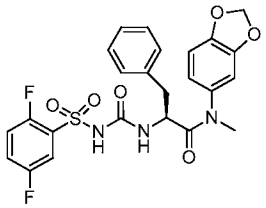
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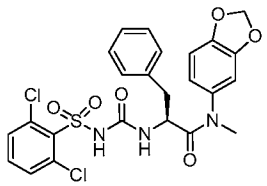
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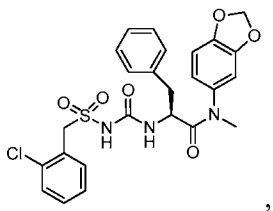
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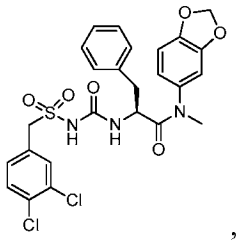
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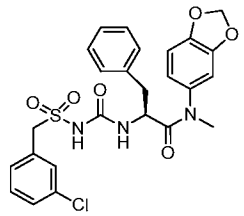
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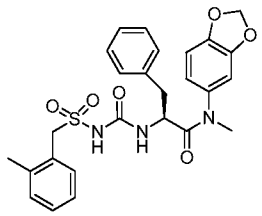
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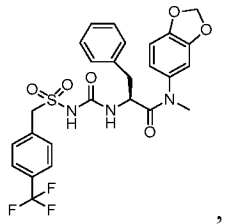
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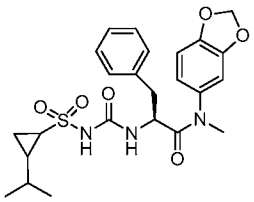
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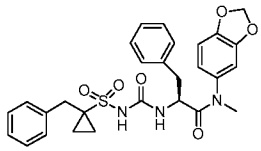
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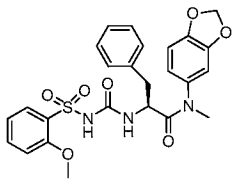
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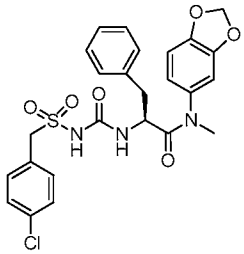
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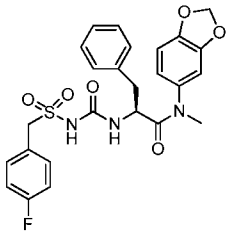
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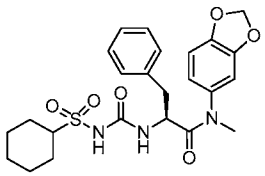
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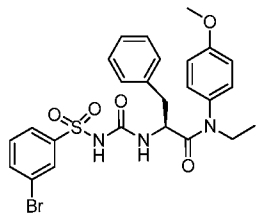
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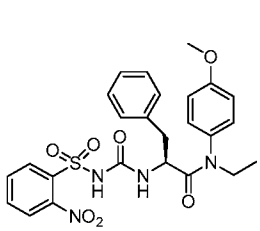
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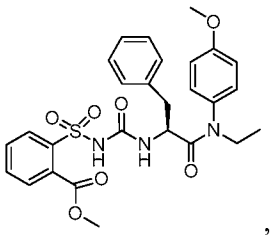
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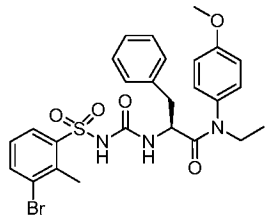
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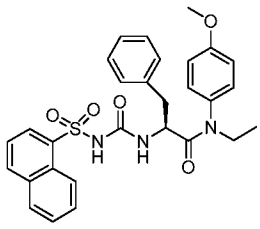
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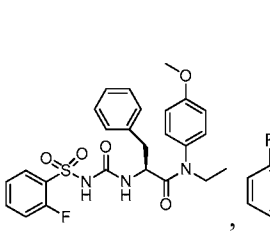
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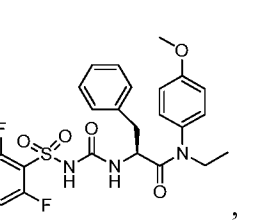
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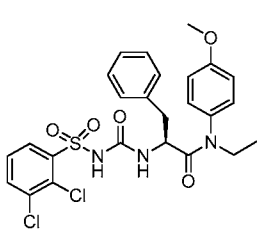
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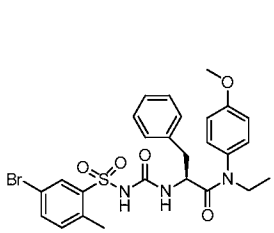
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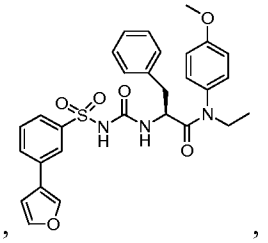
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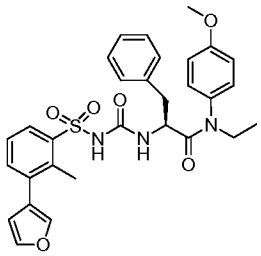
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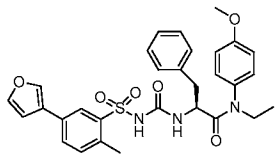
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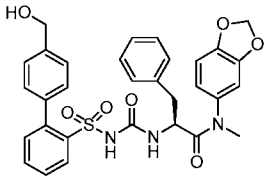
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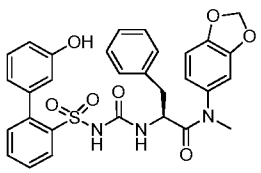
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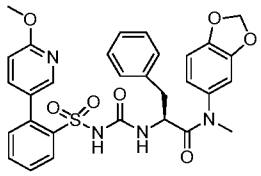
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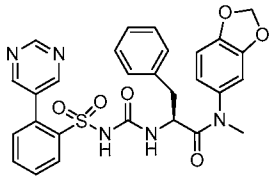
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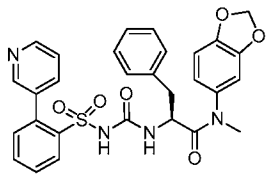
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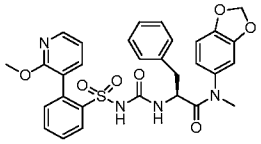
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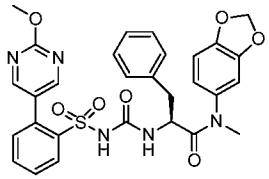
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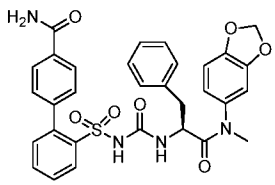
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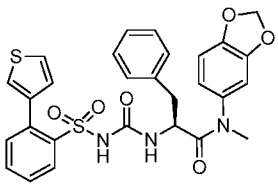
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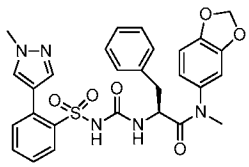
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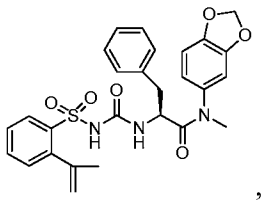
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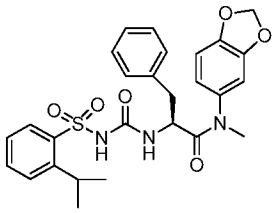
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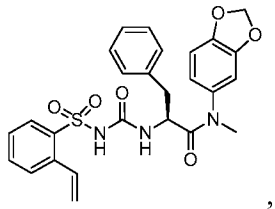
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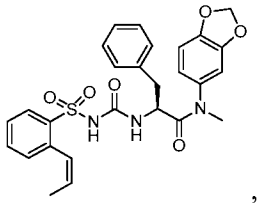
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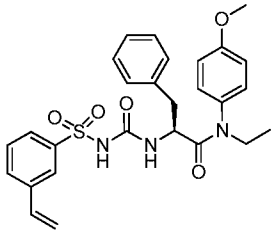
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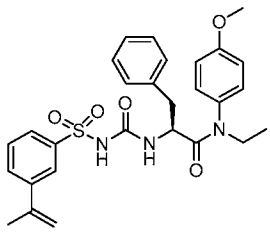
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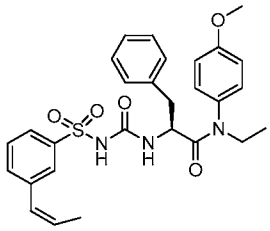
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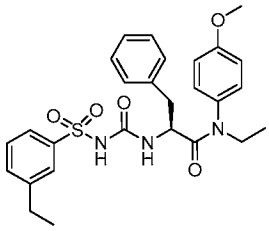
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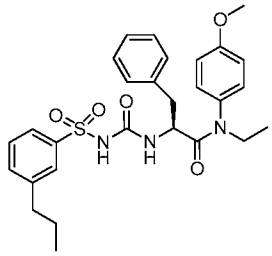
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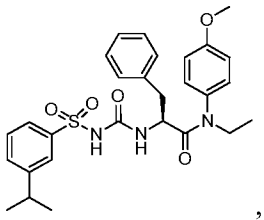
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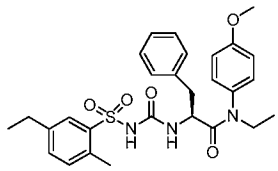
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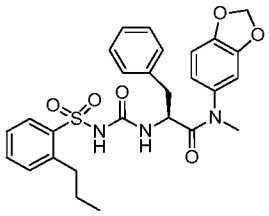
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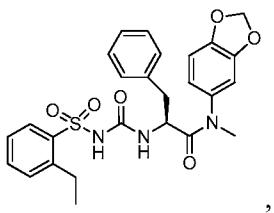
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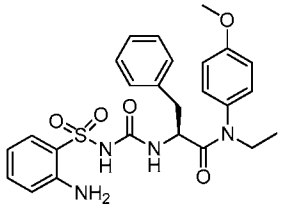
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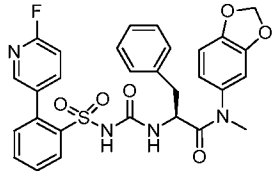
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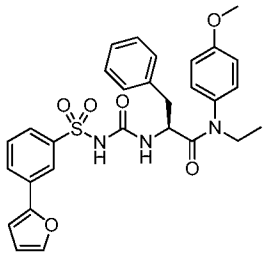
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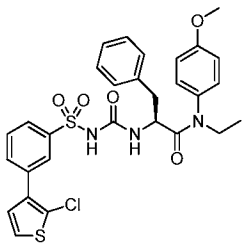
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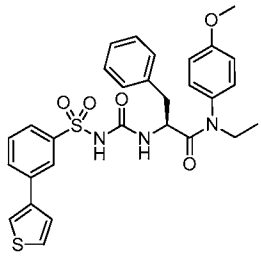
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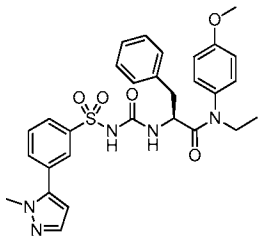
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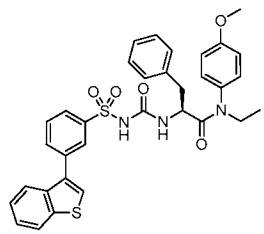
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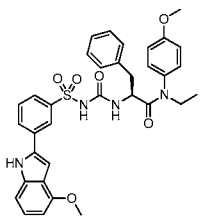
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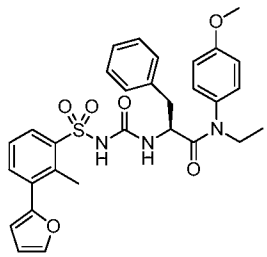
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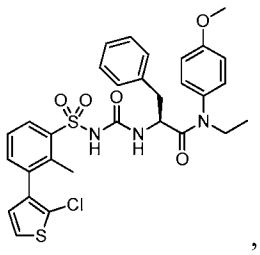
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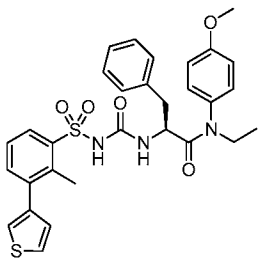
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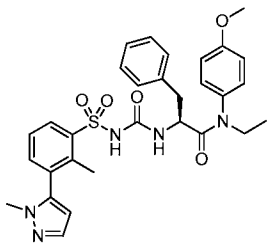
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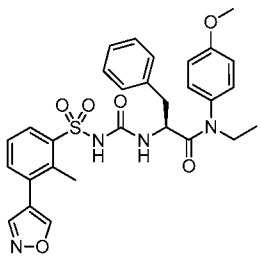
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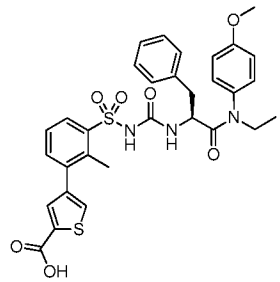
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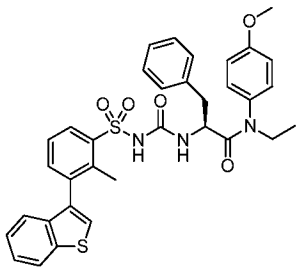
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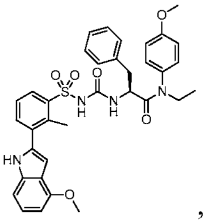
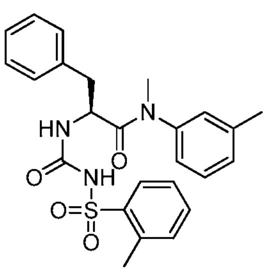
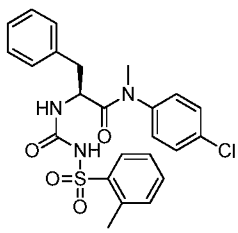
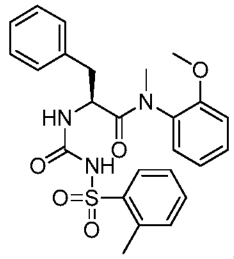
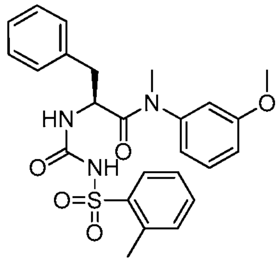
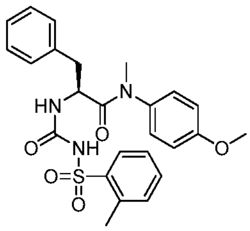
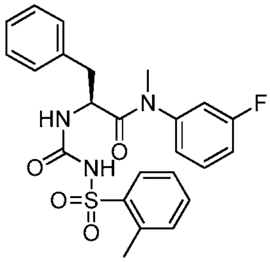
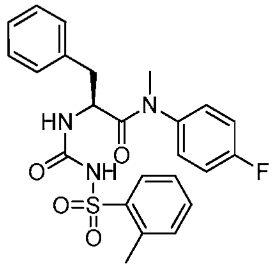
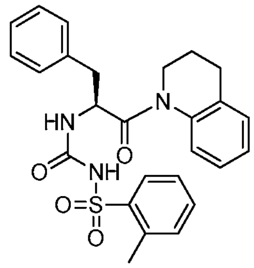
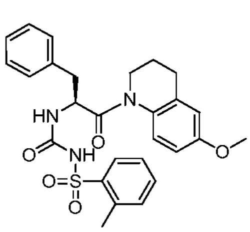
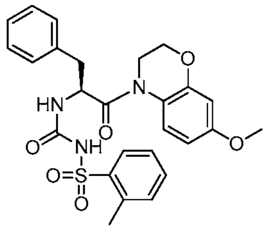
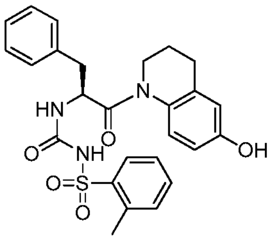
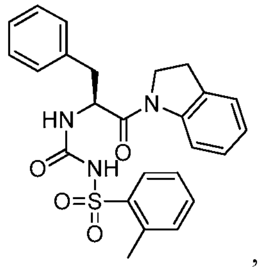
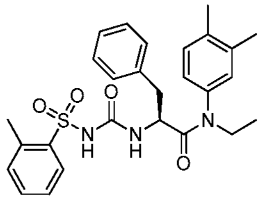
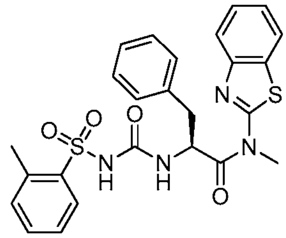
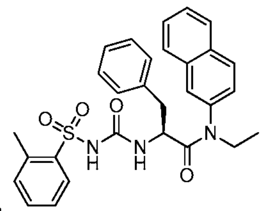
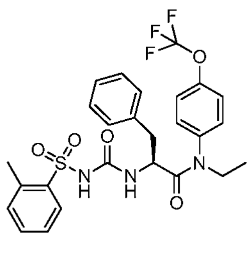
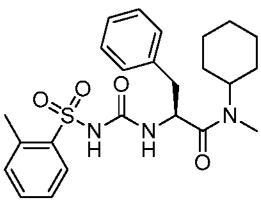
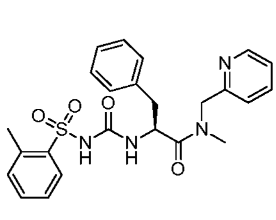
 ,  ,  ,  ,

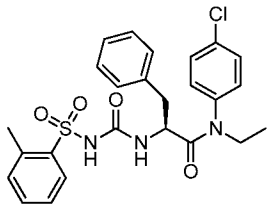
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,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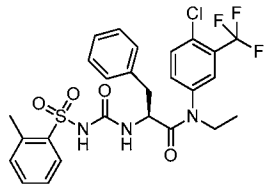
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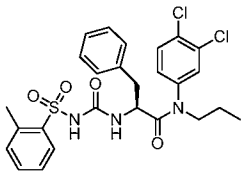
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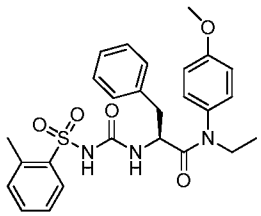
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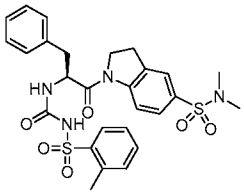
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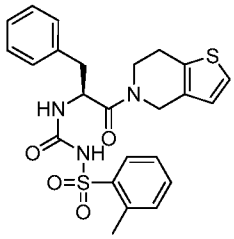
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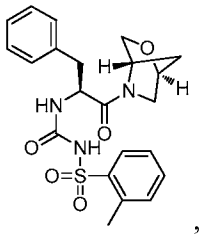
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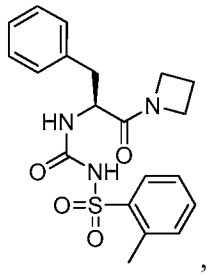
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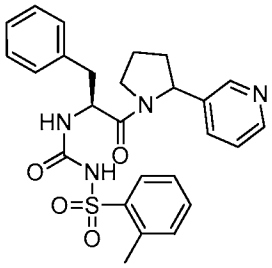
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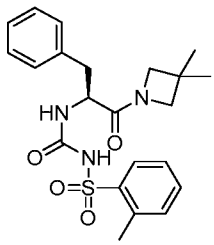
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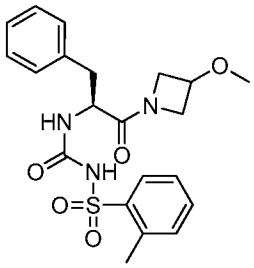
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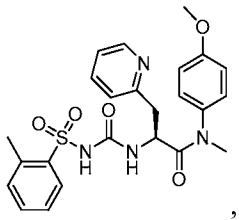
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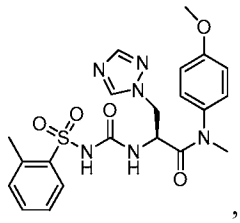
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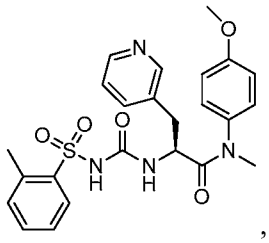
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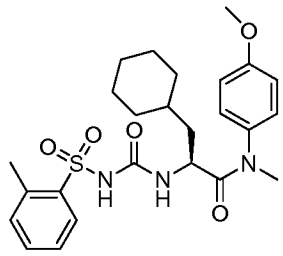
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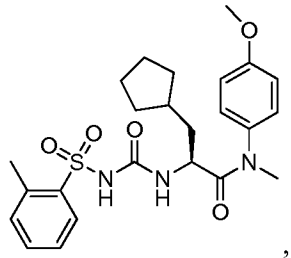
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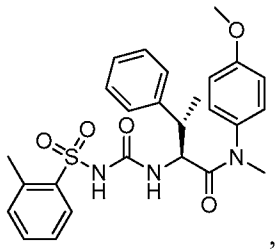
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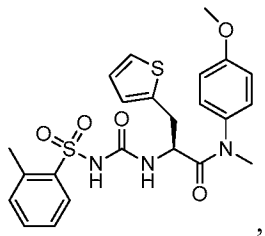
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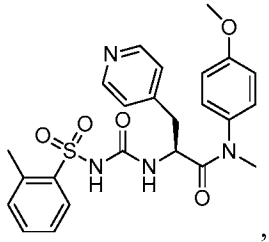
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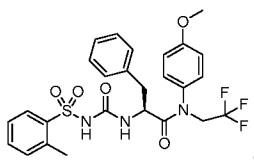
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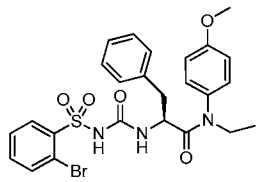
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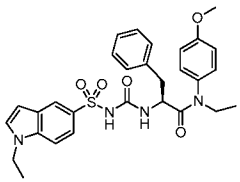
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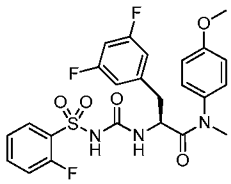
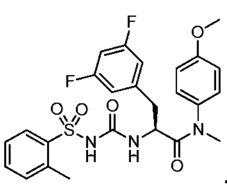
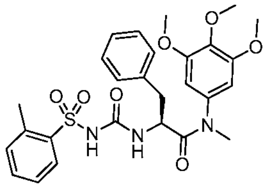
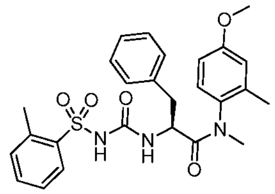
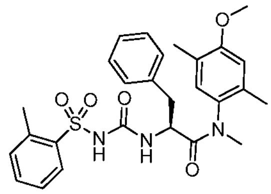
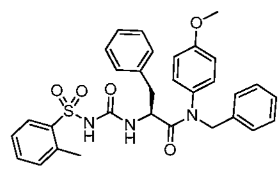
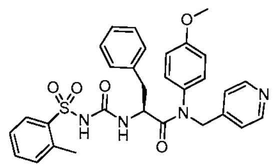
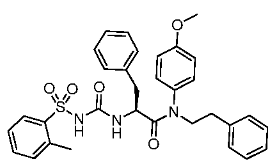
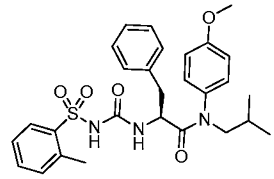
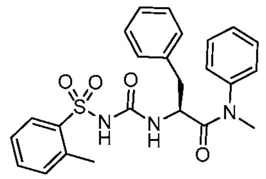
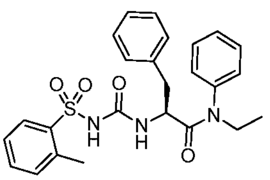
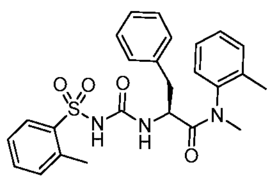
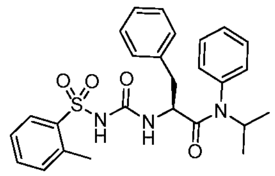
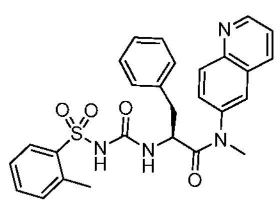
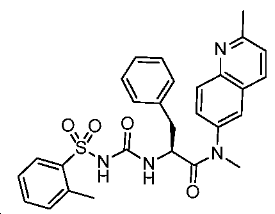
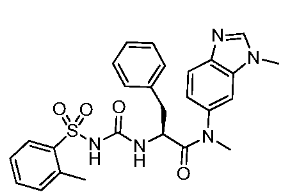
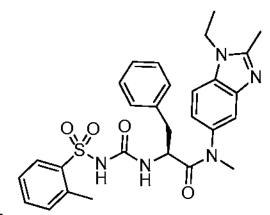
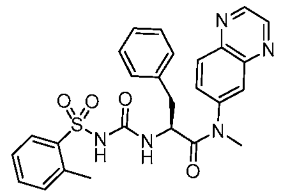
 ,  ,  ,

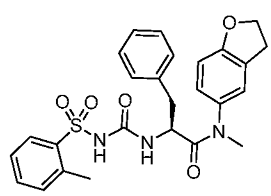
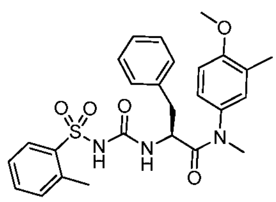
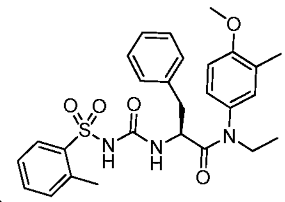
 ,  ,  ,

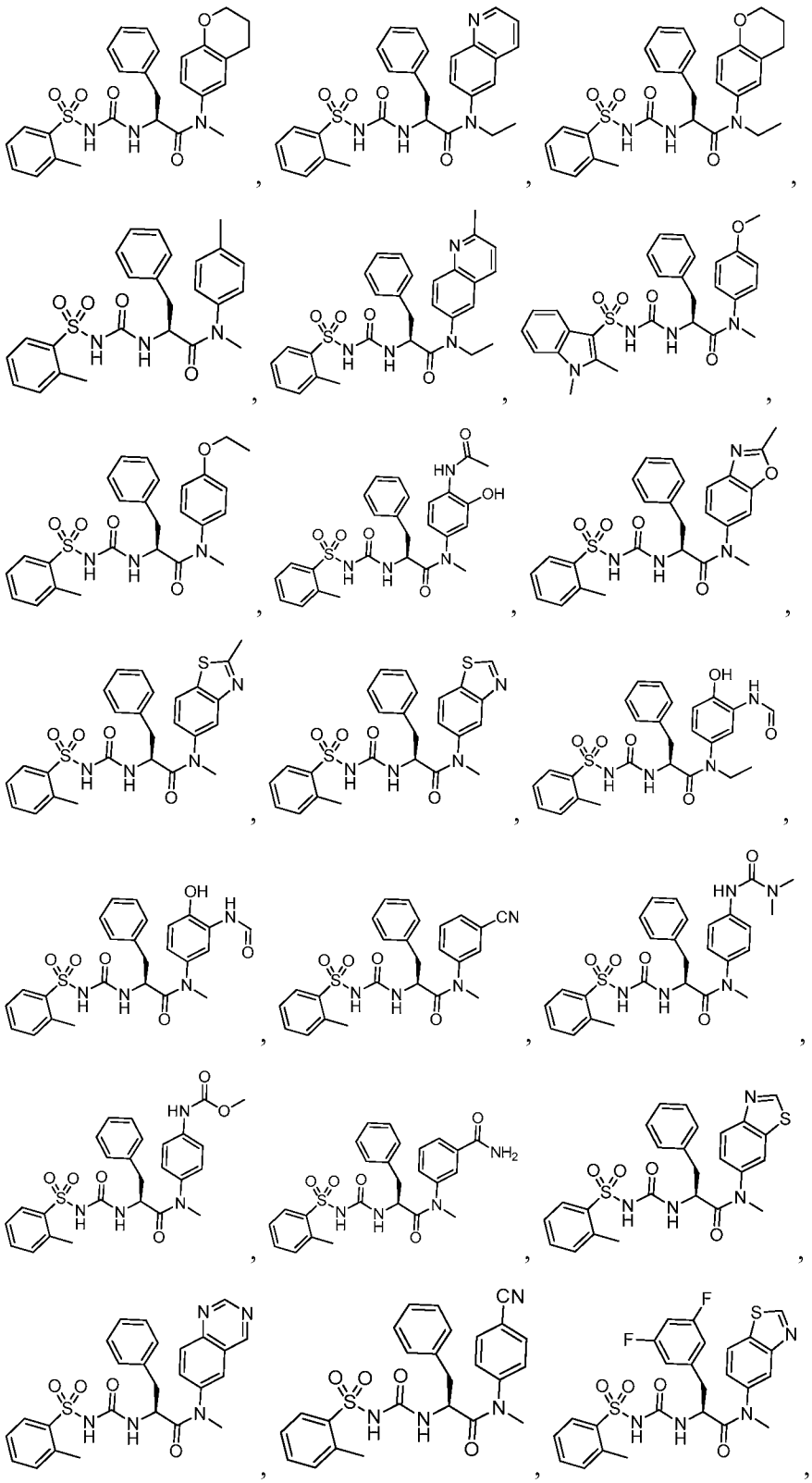
 ,  ,  ,

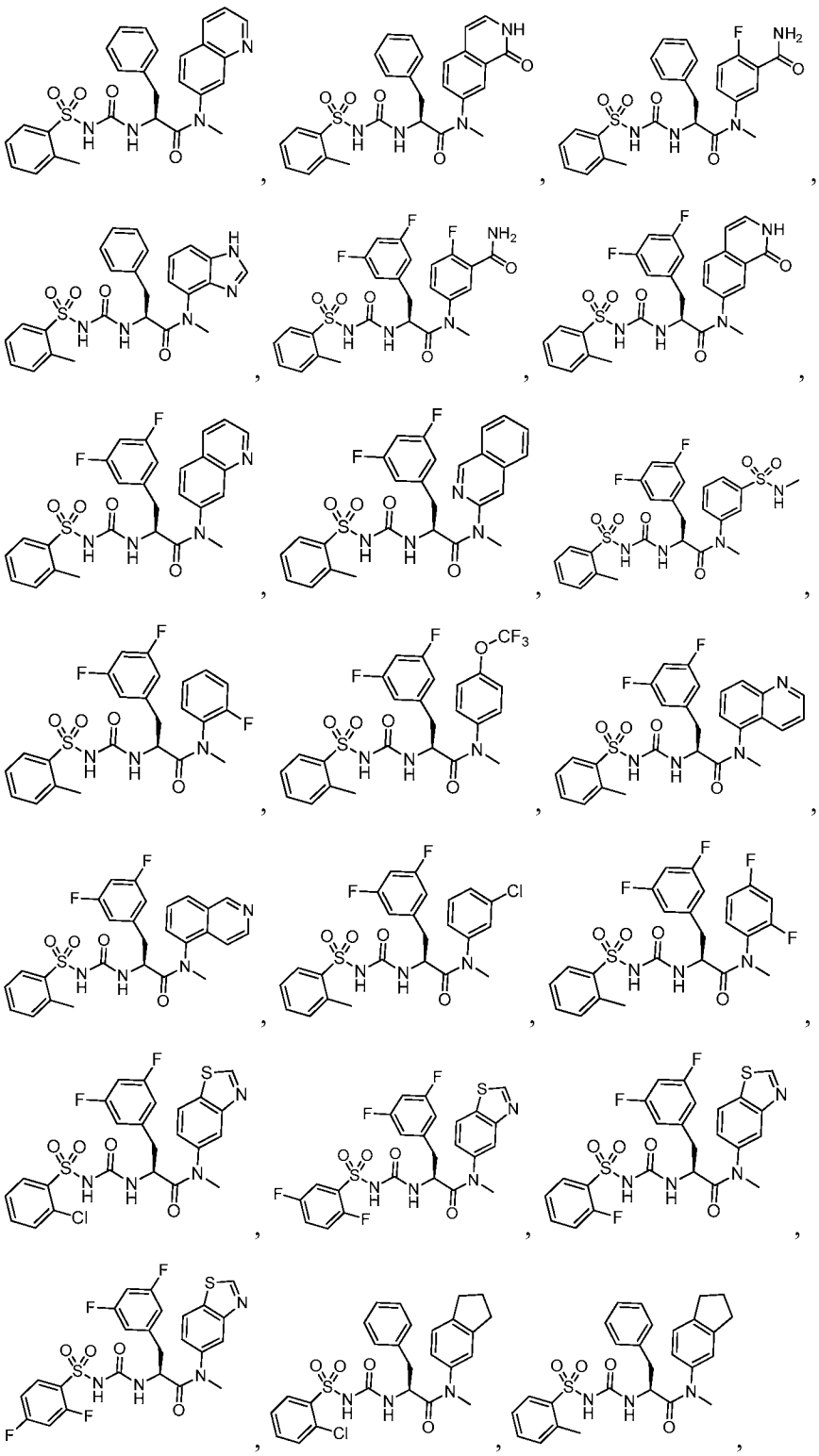
 ,  ,  ,

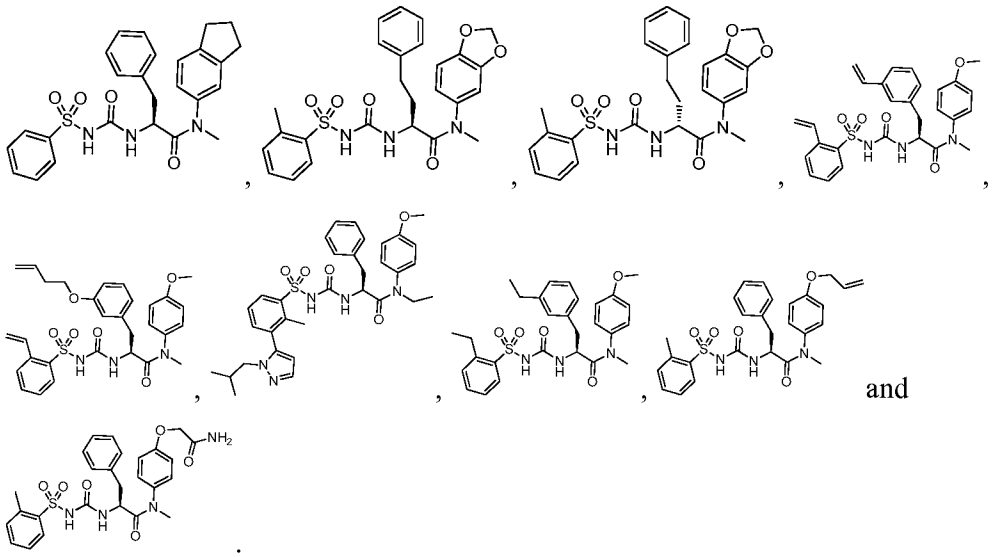
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,







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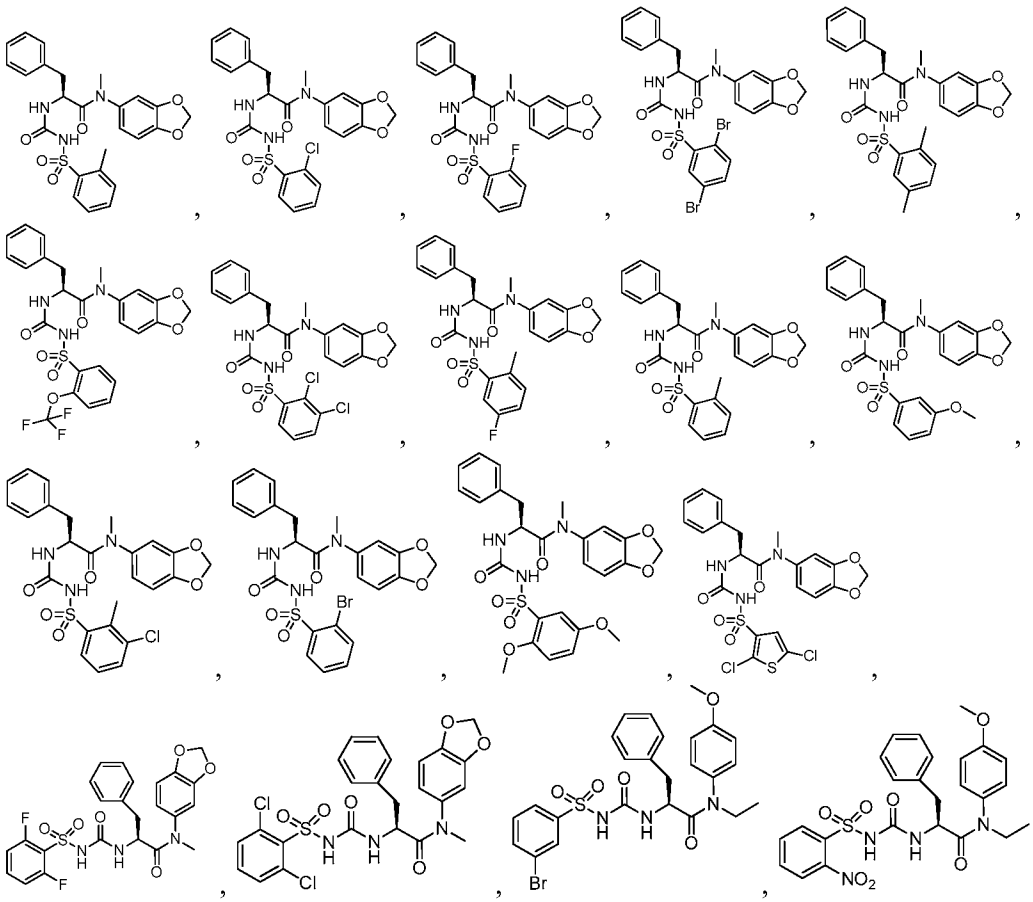

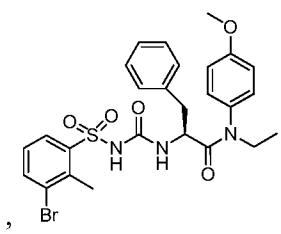
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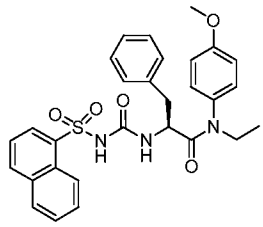
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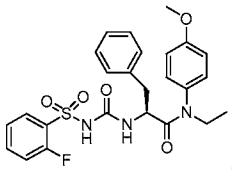
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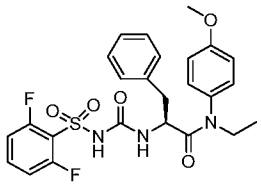
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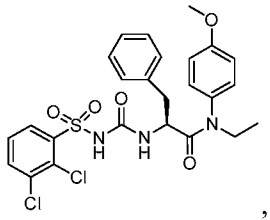
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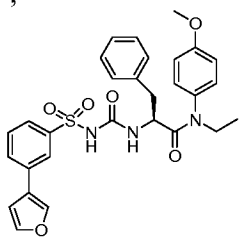
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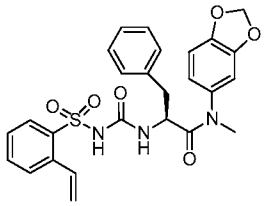
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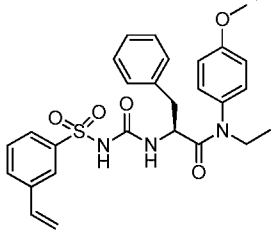
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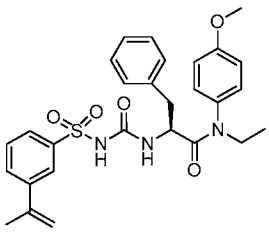
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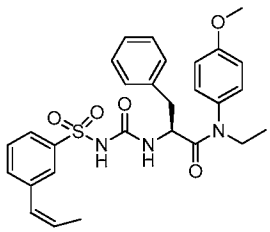
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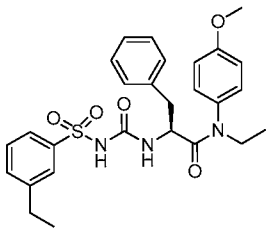
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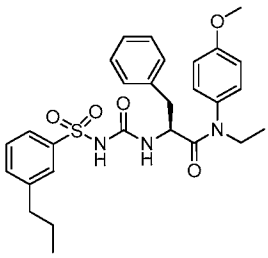
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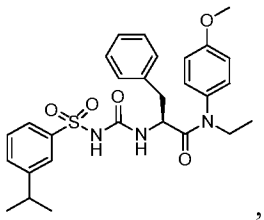
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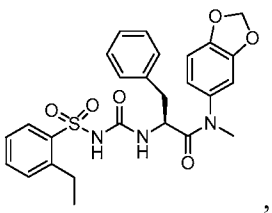
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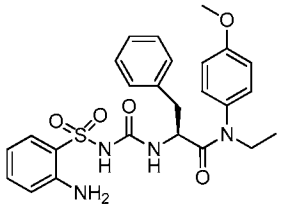
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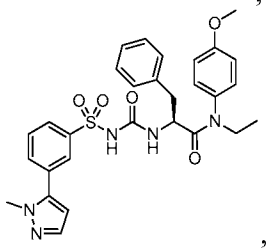
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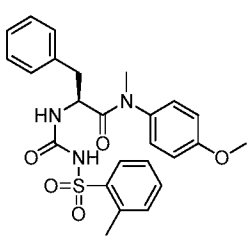
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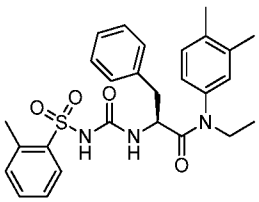
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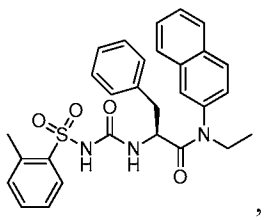
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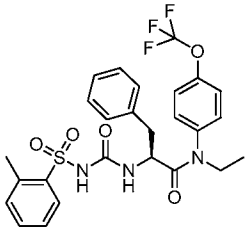
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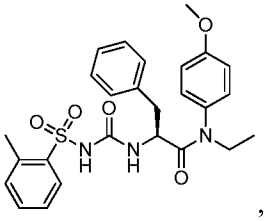
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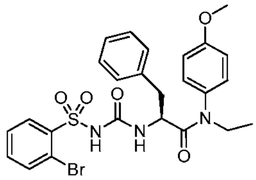
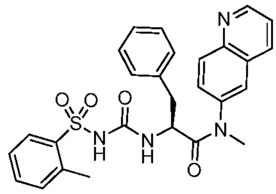
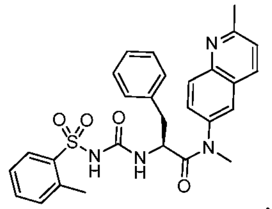
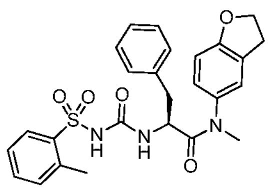
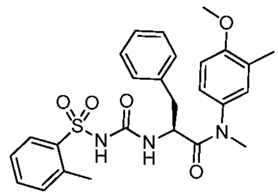
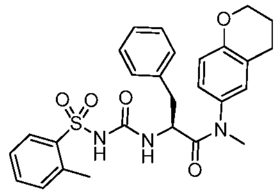
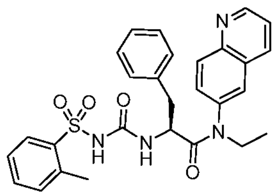
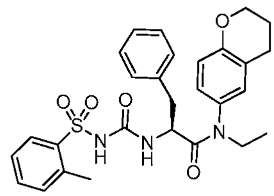
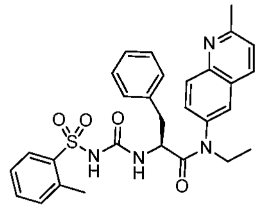
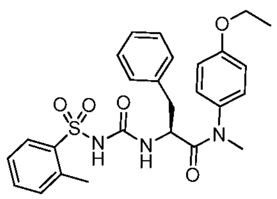
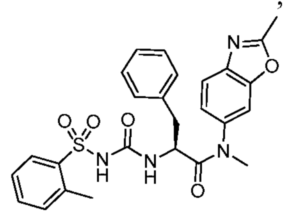
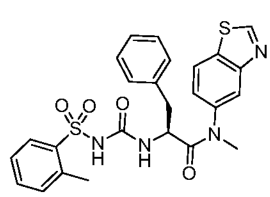
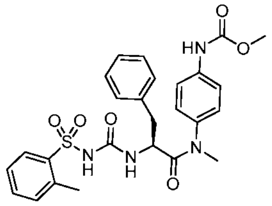
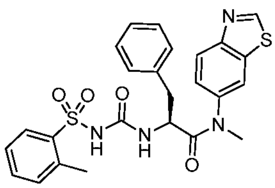
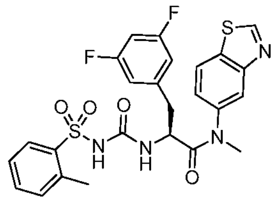
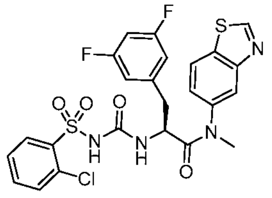
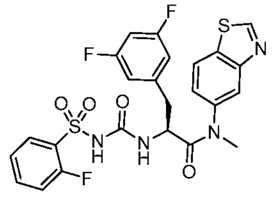
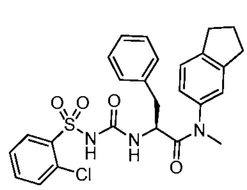
 ,  ,  ,

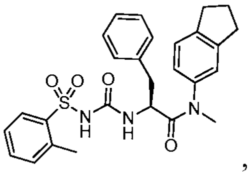
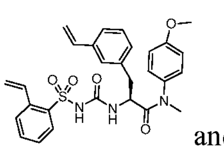
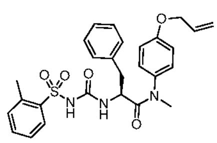
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  and  .

Pharmaceutical Compositions and Methods of Use

The compounds of the invention herein described and set forth are generally given as pharmaceutical compositions. These compositions are comprised of a therapeutically effective amount of a compound of Formula I or its pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier and may contain one or more carriers, excipients and/or diluents. A therapeutically effective amount is that which is needed to provide a meaningful patient benefit. Pharmaceutically acceptable carriers are those conventionally known carriers having acceptable safety profiles. Compositions encompass all common solid and liquid forms including capsules, tablets, lozenges, and powders as well as liquid suspensions, syrups, elixirs, and solutions. Compositions are made using available formulation techniques, and available excipients (such as binding and wetting agents) and vehicles (such as water and alcohols) are generally used for compositions. See, for example, *Remington's Pharmaceutical Sciences*, 17th edition, Mack Publishing Company, Easton, PA (1985).

Solid compositions are normally formulated in dosage units and compositions providing from about 1 to 1000 mg of the active ingredient per dose are preferred. Some examples of dosages are 1 mg, 10 mg, 100 mg, 250 mg, 500 mg, and 1000 mg. Generally, other antiretroviral agents will be present in a unit range similar to agents of that class used clinically. Typically, this is 0.25-1000 mg/unit.

Liquid compositions are usually in dosage unit ranges. Generally, the liquid composition will be in a unit dosage range of 1-100 mg/mL. Some examples of dosages are 1 mg/mL, 10 mg/mL, 25 mg/mL, 50 mg/mL, and 100 mg/mL. Generally, other antiretroviral agents will be present in a unit range similar to agents of that class used clinically. Typically, this is 1-100 mg/mL.

The invention encompasses all conventional modes of administration; oral and parenteral methods are preferred. Generally, the dosing regimen will be similar to other antiretroviral agents used clinically. Typically, the daily dose will be 1-100 mg/kg body weight daily. Generally, more compound is required orally and less

parenterally. The specific dosing regimen, however, will be determined by a physician using sound medical judgment.

The compounds of this invention have activity against HIV. Accordingly, another aspect of the invention is a method for treating HIV infection in a human patient comprising administering a therapeutically effective amount of a compound of Formula I, including a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable carrier, excipient and/or diluent.

The invention also encompasses methods where the compound is given in combination therapy. That is, the compound can be used in conjunction with, but separately from, other agents useful in treating AIDS and HIV infection. The compound can also be used in combination therapy wherein the compound and one or more of the other agents are physically together in a fixed-dose combination (FDC). Some of these agents include HIV attachment inhibitors, CCR5 inhibitors, CXCR4 inhibitors, HIV cell fusion inhibitors, HIV integrase inhibitors, HIV nucleoside reverse transcriptase inhibitors, HIV non-nucleoside reverse transcriptase inhibitors, HIV protease inhibitors, budding and maturation inhibitors, immunomodulators, and anti-infectives. In these combination methods, the compound of Formula I will generally be given in a daily dose of 1-100 mg/kg body weight daily in conjunction with other agents. The other agents generally will be given in the amounts used therapeutically. The specific dosing regimen, however, will be determined by a physician using sound medical judgment.

"Combination," "coadministration," "concurrent" and similar terms referring to the administration of a compound of Formula I with at least one anti-HIV agent mean that the components are part of a combination antiretroviral therapy or highly active antiretroviral therapy (HAART) as understood by practitioners in the field of AIDS and HIV infection.

"Therapeutically effective" means the amount of agent required to provide a meaningful patient benefit as understood by practitioners in the field of AIDS and HIV infection. In general, the goals of treatment are suppression of viral load,

restoration and preservation of immunologic function, improved quality of life, and reduction of HIV-related morbidity and mortality.

"Patient" means a person infected with the HIV virus and suitable for therapy as understood by practitioners in the field of AIDS and HIV infection.

"Treatment," "therapy," "regimen," "HIV infection," "ARC," "AIDS" and related terms are used as understood by practitioners in the field of AIDS and HIV infection.

Thus, as set forth above, contemplated herein are combinations of the compounds of Formula I, together with one or more agents useful in the treatment of AIDS. For example, the compounds of the invention may be effectively administered, whether at periods of pre-exposure and/or post-exposure, in combination with effective amounts of the AIDS antivirals, immunomodulators, anti-infectives, or vaccines, such as those in the following non-limiting table:

ANTIVIRALS

Drug Name	Manufacturer	Indication
Rilpivirine	Tibotec	HIV infection, AIDS, ARC (non-nucleoside reverse transcriptase inhibitor)
COMPLERA®	Gilead	HIV infection, AIDS, ARC; combination with emtricitabine, rilpivirine, and tenofovir disoproxil fumarate

097	Hoechst/Bayer	HIV infection, AIDS, ARC (non-nucleoside reverse trans-criptase (RT) inhibitor)
Amprenavir 141 W94 GW 141	Glaxo Wellcome	HIV infection, AIDS, ARC (protease inhibitor)
Abacavir (1592U89) GW 1592	Glaxo Wellcome	HIV infection, AIDS, ARC (RT inhibitor)
Acemannan	Carrington Labs (Irving, TX)	ARC
Acyclovir	Burroughs Wellcome	HIV infection, AIDS, ARC
AD-439	Tanox Biosystems	HIV infection, AIDS, ARC
AD-519	Tanox Biosystems	HIV infection, AIDS, ARC
Adefovir dipivoxil AL-721	Gilead Sciences Ethigen (Los Angeles, CA)	HIV infection ARC, PGL HIV positive, AIDS
Alpha Interferon	Glaxo Wellcome	Kaposi's sarcoma,

		HIV in combination w/Retrovir
Ansamycin LM 427	Adria Laboratories (Dublin, OH) Erbamont (Stamford, CT)	ARC
Antibody which Neutralizes pH Labile alpha aberrant Interferon	Advanced Biotherapy Concepts (Rockville, MD)	AIDS, ARC
AR177	Aronex Pharm	HIV infection, AIDS, ARC
Beta-fluoro-ddA	Nat'l Cancer Institute	AIDS-associated diseases
BMS-234475 (CGP-61755)	Bristol-Myers Squibb/ Novartis	HIV infection, AIDS, ARC (protease inhibitor)
CI-1012	Warner-Lambert	HIV-1 infection
Cidofovir	Gilead Science	CMV retinitis, herpes, papillomavirus
Curdlan sulfate	AJI Pharma USA	HIV infection
Cytomegalovirus Immune globin	MedImmune	CMV retinitis

Cytovene	Syntex	Sight threatening
Ganciclovir		CMV peripheral CMV retinitis
Darunavir	Tibotec- J & J	HIV infection, AIDS, ARC (protease inhibitor)
Delaviridine	Pharmacia-Upjohn	HIV infection, AIDS, ARC (RT inhibitor)
Dextran Sulfate	Ueno Fine Chem. Ind. Ltd. (Osaka, Japan)	AIDS, ARC, HIV positive asymptomatic
ddC Dideoxycytidine	Hoffman-La Roche	HIV infection, AIDS, ARC
ddI Dideoxyinosine	Bristol-Myers Squibb	HIV infection, AIDS, ARC; combination with AZT/d4T
DMP-450	AVID (Camden, NJ)	HIV infection, AIDS, ARC (protease inhibitor)

Efavirenz (DMP 266, SUSTIVA®) (-)6-Chloro-4-(S)-cyclopropylethynyl-4(S)-trifluoro-methyl-1,4-dihydro-2H-3,1-benzoxazin-2-one, STOCRINE	Bristol Myers Squibb	HIV infection, AIDS, ARC (non-nucleoside RT inhibitor)
EL10	Elan Corp, PLC (Gainesville, GA)	HIV infection
Etravirine	Tibotec/ J & J	HIV infection, AIDS, ARC (non-nucleoside reverse transcriptase inhibitor)
Famciclovir	Smith Kline	herpes zoster, herpes simplex
GS 840	Gilead	HIV infection, AIDS, ARC (reverse transcriptase inhibitor)
HBY097	Hoechst Marion Roussel	HIV infection, AIDS, ARC (non-nucleoside reverse transcriptase inhibitor)
Hypericin	VIMRx Pharm.	HIV infection, AIDS, ARC

Recombinant Human Interferon Beta	Triton Biosciences (Almeda, CA)	AIDS, Kaposi's sarcoma, ARC
Interferon alfa-n3	Interferon Sciences	ARC, AIDS
Indinavir	Merck	HIV infection, AIDS, ARC, asymptomatic HIV positive, also in combination with AZT/ddI/ddC
ISIS 2922	ISIS Pharmaceuticals	CMV retinitis
KNI-272	Nat'l Cancer Institute	HIV-assoc. diseases
Lamivudine, 3TC	Glaxo Wellcome	HIV infection, AIDS, ARC (reverse transcriptase inhibitor); also with AZT
Lobucavir	Bristol-Myers Squibb	CMV infection
Nelfinavir	Agouron Pharmaceuticals	HIV infection, AIDS, ARC (protease inhibitor)
Nevirapine	Boeheringer Ingleheim	HIV infection, AIDS, ARC (RT inhibitor)

Novapren	Novaferon Labs, Inc. (Akron, OH)	HIV inhibitor
Peptide T Octapeptide Sequence	Peninsula Labs (Belmont, CA)	AIDS
Trisodium Phosphonoformate	Astra Pharm. Products, Inc.	CMV retinitis, HIV infection, other CMV infections
PNU-140690	Pharmacia Upjohn	HIV infection, AIDS, ARC (protease inhibitor)
Probucol	Vyrex	HIV infection, AIDS
RBC-CD4	Sheffield Med. Tech (Houston, TX)	HIV infection, AIDS, ARC
Ritonavir	Abbott	HIV infection, AIDS, ARC (protease inhibitor)
Saquinavir	Hoffmann-LaRoche	HIV infection, AIDS, ARC (protease inhibitor)
Stavudine; d4T Didehydrodeoxy-Thymidine	Bristol-Myers Squibb	HIV infection, AIDS, ARC

Tipranavir	Boehringer Ingelheim	HIV infection, AIDS, ARC (protease inhibitor)
Valaciclovir	Glaxo Wellcome	Genital HSV & CMV Infections
Virazole Ribavirin	Viratek/ICN (Costa Mesa, CA)	asymptomatic HIV positive, LAS, ARC
VX-478	Vertex	HIV infection, AIDS, ARC
Zalcitabine	Hoffmann-LaRoche	HIV infection, AIDS, ARC, with AZT
Zidovudine; AZT	Glaxo Wellcome	HIV infection, AIDS, ARC, Kaposi's sarcoma, in combination with other therapies
Tenofovir disoproxil, fumarate salt (VIREAD®)	Gilead	HIV infection, AIDS, (reverse transcriptase inhibitor)
EMTRIVA® (Emtricitabine) (FTC)	Gilead	HIV infection, AIDS, (reverse transcriptase inhibitor)

COMBIVIR®	GSK	HIV infection, AIDS, (reverse transcriptase inhibitor)
Abacavir succinate (or ZIAGEN®)	GSK	HIV infection, AIDS, (reverse transcriptase inhibitor)
REYATAZ® (or atazanavir)	Bristol-Myers Squibb	HIV infection AIDs, protease inhibitor
FUZEON® (Enfuvirtide or T-20)	Roche / Trimeris	HIV infection AIDs, viral Fusion inhibitor
LEXIVA® (or Fosamprenavir calcium)	GSK/Vertex	HIV infection AIDs, viral protease inhibitor
SELZENTRY™ Maraviroc; (UK 427857)	Pfizer	HIV infection AIDs, (CCR5 antagonist, in development)
TRIZIVIR®	GSK	HIV infection AIDs, (three drug combination)

Sch-417690 (vicriviroc)	Schering-Plough	HIV infection AIDs, (CCR5 antagonist, in development)
TAK-652	Takeda	HIV infection AIDs, (CCR5 antagonist, in development)
GSK 873140 (ONO-4128)	GSK/ONO	HIV infection AIDs, (CCR5 antagonist, in development)
Integrase Inhibitor MK-0518 Raltegravir	Merck	HIV infection AIDs
TRUVADA® EMTRIVA®	Gilead	Combination of Tenofovir disoproxil fumarate salt (VIREAD®) and (Emtricitabine)
Integrase Inhibitor GS917/JTK-303 Elvitegravir	Gilead/Japan Tobacco	HIV Infection AIDs in development
Triple drug combination ATRIPLA®	Gilead/Bristol-Myers Squibb	Combination of Tenofovir disoproxil fumarate salt (VIREAD®), EMTRIVA® (Emtricitabine), and SUSTIVA® (Efavirenz)

FESTINAVIR®	Oncolys BioPharma	HIV infection AIDs in development
CMX-157 Lipid conjugate of nucleotide tenofovir	Chimerix	HIV infection AIDs
GSK1349572 Integrase inhibitor	GSK	HIV infection AIDs

IMMUNOMODULATORS

Drug Name	*Manufacturer*	*Indication*
AS-101	Wyeth-Ayerst	AIDS
Bropirimine	Pharmacia Upjohn	Advanced AIDS
Acemannan	Carrington Labs, Inc. (Irving, TX)	AIDS, ARC
CL246,738	Wyeth Lederle Labs	AIDS, Kaposi's sarcoma
FP-21399	Fuki ImmunoPharm	Blocks HIV fusion with CD4+ cells
Gamma Interferon	Genentech	ARC, in combination w/TNF (tumor necrosis factor)

Granulocyte Macrophage Colony Stimulating Factor	Genetics Institute Sandoz	AIDS
Granulocyte Macrophage Colony Stimulating Factor	Hoechst-Roussel Immunex	AIDS
Granulocyte Macrophage Colony Stimulating Factor	Schering-Plough	AIDS, combination w/AZT
HIV Core Particle Immunostimulant	Rorer	Seropositive HIV
IL-2 Interleukin-2	Cetus	AIDS, in combination w/AZT
IL-2 Interleukin-2	Hoffman-LaRoche Immunex	AIDS, ARC, HIV, in combination w/AZT
IL-2 Interleukin-2 (aldeslukin)	Chiron	AIDS, increase in CD4 cell counts
Immune Globulin Intravenous (human)	Cutter Biological (Berkeley, CA)	Pediatric AIDS, in combination w/AZT
IMREG-1	Imreg (New Orleans, LA)	AIDS, Kaposi's sarcoma, ARC, PGL

IMREG-2	Imreg (New Orleans, LA)	AIDS, Kaposi's sarcoma, ARC, PGL
Imuthiol Diethyl Dithio Carbamate	Merieux Institute	AIDS, ARC
Alpha-2 Interferon	Schering Plough	Kaposi's sarcoma w/AZT, AIDS
Methionine-Enkephalin	TNI Pharmaceutical (Chicago, IL)	AIDS, ARC
MTP-PE Muramyl-Tripeptide	Ciba-Geigy Corp.	Kaposi's sarcoma
Granulocyte Colony Stimulating Factor	Amgen	AIDS, in combination w/AZT
Remune	Immune Response Corp.	Immunotherapeutic
rCD4 Recombinant Soluble Human CD4	Genentech	AIDS, ARC
rCD4-IgG hybrids		AIDS, ARC
Recombinant Soluble Human CD4	Biogen	AIDS, ARC
Interferon	Hoffman-La Roche	Kaposi's sarcoma

Alfa 2a		AIDS, ARC, in combination w/AZT
SK&F106528 Soluble T4	Smith Kline	HIV infection
Thymopentin	Immunobiology Research Institute (Annandale, NJ)	HIV infection
Tumor Necrosis Factor; TNF	Genentech	ARC, in combination w/gamma Interferon

ANTI-INFECTIVES

Drug Name	*Manufacturer*	*Indication*
Clindamycin with Primaquine	Pharmacia Upjohn	PCP
Fluconazole	Pfizer	Cryptococcal meningitis, candidiasis
Pastille Nystatin Pastille	Squibb Corp.	Prevention of oral candidiasis
Ornidyl Eflornithine	Merrell Dow	PCP
Pentamidine Isethionate (IM & IV)	LyphoMed (Rosemont, IL)	PCP treatment
Trimethoprim		Antibacterial

Trimethoprim/sulfa		Antibacterial
Piritrexim	Burroughs Wellcome	PCP treatment
Pentamidine Isethionate for Inhalation	Fisons Corporation	PCP prophylaxis
Spiramycin	Rhone-Poulenc diarrhea	Cryptosporidial
Intraconazole-R51211	Janssen-Pharm.	Histoplasmosis; cryptococcal meningitis
Trimetrexate	Warner-Lambert	PCP
Daunorubicin	NeXstar, Sequus	Kaposi's sarcoma
Recombinant Human Erythropoietin	Ortho Pharm. Corp.	Severe anemia assoc. with AZT therapy
Recombinant Human Growth Hormone	Serono	AIDS-related wasting, cachexia
Megestrol Acetate	Bristol-Myers Squibb	Treatment of anorexia assoc. W/AIDS
Testosterone	Alza, Smith Kline	AIDS-related wasting

Total Enteral Nutrition	Norwich Eaton Pharmaceuticals	Diarrhea and malabsorption related to AIDS

Synthetic Methods

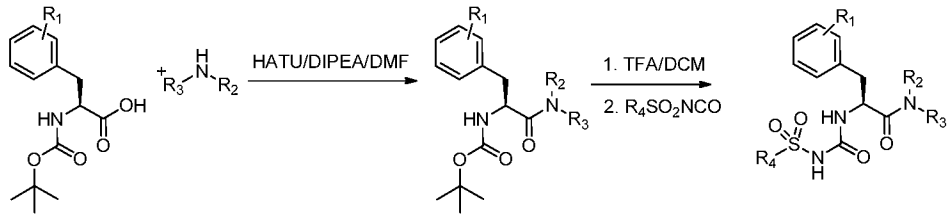
The compounds of the invention can be made by various methods available in the art including those of the following scheme and in the specific embodiments section which follows. The structure numbering and variable numbering shown in the synthetic schemes are distinct from, and should not be confused with, the structure or variable numbering in the claims or the rest of the specification. The variables in the schemes are meant only to illustrate how to make some of the compounds of the invention.

Abbreviations used in the schemes generally follow conventions used in the art. Chemical abbreviations used in the specification and examples are defined as follows: "DMF" for N,N-dimethylformamide; “MeOH” for methanol; “Ar” for aryl; "TFA" for trifluoroacetic acid; “BOC” for t-butoxycarbonate, “DMSO” for dimethylsulfoxide; “h” for hours; “rt” for room temperature or retention time (context will dictate); “min” for minutes; "EtOAc" for ethyl acetate; "THF" for tetrahydrofuran; “Et_2O” for diethyl ether; "DMAP" for 4-dimethylaminopyridine; “DCE” for 1,2-dichloroethane; “ACN” for acetonitrile; “DME” for 1,2-dimethoxyethane; “HATU” for (1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3- oxid hexafluorophosphate) “DIEA” for diisopropylethylamine.

Abbreviations as used herein, are defined as follows: “1 x” for once, “2 x” for twice, “3 x” for thrice, "°C" for degrees Celsius, “eq” for equivalent or equivalents, “g” for gram or grams, “mg” for milligram or milligrams, “L” for liter or liters, “mL” for milliliter or milliliters, “μL” for microliter or microliters, “N” for normal, “M” for molar, “mmol” for millimole or millimoles, “min” for minute or minutes, “h” for hour or hours, “rt” for room temperature, “RT” for retention time, “atm” for atmosphere, “psi” for pounds per square inch, “conc.” for concentrate, “sat” or “sat’d

" for saturated, "MW" for molecular weight, "mp" for melting point, "ee" for enantiomeric excess, "MS" or "Mass Spec" for mass spectrometry, "ESI" for electrospray ionization mass spectroscopy, "HR" for high resolution, "HRMS" for high resolution mass spectrometry , "LCMS" for liquid chromatography mass spectrometry, "HPLC" for high pressure liquid chromatography, "RP HPLC" for reverse phase HPLC, "TLC" or "tlc" for thin layer chromatography, "NMR" for nuclear magnetic resonance spectroscopy, "^{1}H" for proton, "δ" for delta, "s" for singlet, "d" for doublet, "t" for triplet, "q" for quartet, "m" for multiplet, "br" for broad, "Hz" for hertz, and "α", "β", "R", "S", "E", and "Z" are stereochemical designations familiar to one skilled in the art.

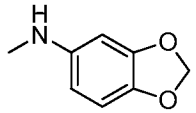
Scheme 1.



EXAMPLES

The following examples are provided by way of illustration only, and should not be construed as limiting the scope of the invention.

Intermediate 1



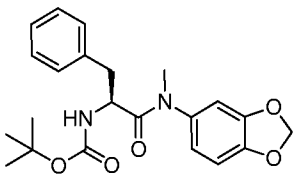
N-methylbenzo[d][1,3]dioxol-5-amine

Benzo[d][1,3]dioxol-5-amine (1.6 g, 12 mmol) was added to a solution of 25% wt. sodium methoxide (12.6 g, 58.3 mmol) in MeOH and paraformaldehyde (3.50 g, 117 mmol) in MeOH (50 mL). The reaction mixture was stirred at r.t. for 18 h and then sodium borohydride (1.32 g, 35.0 mmol) was added in portions and the reaction was

heated at 40 °C for 3 h, cooled to r.t., and then concentrated. The residue was dissolved into EtOAc (~60 mL), washed with water (50 mL) and brine (50 mL) and then dried ($MgSO_4$), filtered and concentrated. The residue was purified using a Biotage Horizon (40 g SiO_2, 10-25% EtOAc/hexanes) to afford the title compound (1.43 g) as amber oil. ^1H NMR (400 MHZ, $CDCl_3$) δ 6.69 (d, *J*=8.3 Hz, 1H), 6.26 (d, *J*=2.5 Hz, 1H), 6.06 (dd, *J*=8.3, 2.5 Hz, 1H), 5.87 (s, 2H), 2.80 (s, 3H).

MS $(M+H)^+$ Calcd.	152.1
MS $(M+H)^+$ Observ.	152.2
Retention Time	0.298 min
	LC Condition
Solvent A	10 % acetonitrile : 90% Water : 0.1% TFA
Solvent B	90 % acetonitrile : 10% Water : 0.1% TFA
Start % B	0
Final % B	100
Gradient Time	2 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Phenomenex LUNA C18 30 x 2 mm, 3 μ

Intermediate 2



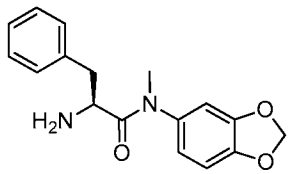
(S)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (3.02 g, 7.94 mmol) was added to a stirred solution of (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (1.93 g, 7.28 mmol) and N-methylbenzo[d][1,3]dioxol-5-amine (1.0 g, 6.6 mmol) in diisopropylethylamine (2.3 mL, 13 mmol) and DMF (35 mL) and the reaction solution was stirred at r.t. for 18 h. The reaction was concentrated to dryness and partitioned between 1/2 sat. $NaHCO_3$

(aq) (50 mL) and EtOAc (100 mL). The organic layer was washed with brine (50 mL), dried ($MgSO_4$) filtered and concentrated. The residue was purified using a Biotage Horizon (80 g SiO_2, 10-40% EtOAc) to afford the title compound (2.15 g) as tan solidified foam. ^1H NMR (400 MHZ, $CDCl_3$) δ 7.34 - 7.20 (m, 4H), 7.02 (br. s., 2H), 6.70 (d, *J*=7.5 Hz, 1H), 6.36 - 6.19 (m, 1H), 6.01 (s, 2H), 5.19 (d, *J*=7.0 Hz, 1H), 4.53 (d, *J*=7.0 Hz, 1H), 3.15 (s, 3H), 2.92 - 2.77 (m, 2H), 1.40 (s, 9H).

MS $(M+H)^+$ Calcd.	399.2
MS $(M+H)^+$ Observ.	399.3
Retention Time	1.68 min
	LC Condition
Solvent A	10 % acetonitrile : 90% Water : 0.1% TFA
Solvent B	90 % acetonitrile : 10% Water : 0.1% TFA
Start % B	0
Final % B	100
Gradient Time	2 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Phenomenex LUNA C18 30 x 2 mm, 3 μ

Intermediate 3

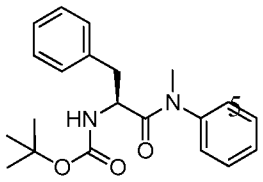


(S)-2-amino-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenylpropanamide

To (S)-*tert*-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (1070 mg, 2.69 mmol) was added 50% TFA in DCM (2 mL). The reaction mixture was stirred at r.t. for 1 hr. The solvent was evaporated to give the title compound (1090 mg) as a TFA salt.

MS $(M+H)^+$ Calcd.	299.1
MS $(M+H)^+$ Observ.	299.2
Retention Time	0.99 min
	LC Condition
Solvent A	10% acetonitrile : 90% Water : 0.1% TFA
Solvent B	90 % acetonitrile : 10% Water : 0.1% TFA
Start % B	0
Final % B	100
Gradient Time	2 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Phenomenex Luna 30 x 2.0 MM 3u

Intermediate 4



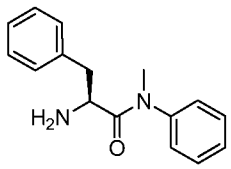
(S)-tert-butyl (1-(methyl(phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

A solution of (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (26.5 mg, 0.100 mmol), N-methylaniline (11.77 mg, 0.110 mmol), HATU (38 mg, 0.100 mmol) and DIPEA (0.053 mL, 0.300 mmol) in DMF (1 mL) was stirred at room temperature for 18h. The reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (10 mL) and ethyl acetate (20 mL). The organic component was washed with brine (10 mL), dried ($MgSO_4$) filtered and concentrated. The residue was used without purification.

MS $(M+H)^+$ Calcd.	355.2
MS $(M+H)^+$ Observ.	355.3
Retention Time	1.88 min
	LC Condition
Solvent A	10 % acetonitrile : 90% Water : 0.1% TFA

Solvent B	90 % acetonitrile : 10% Water : 0.1% TFA
Start % B	0
Final % B	100
Gradient Time	2 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Phenomenex LUNA C18 30 x 2 mm, 3 μ

Intermediate 5

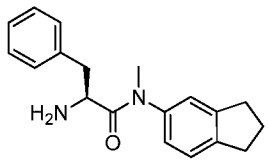


(S)-2-amino-N-methyl-N,3-diphenylpropanamide

To (S)-tert-butyl (1-(methyl(phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (20 mg, 0.056 mmol) was added 50% TFA in DCM (2 mL). The reaction mixture was stirred at r.t. for 1 hr. The solvent was evaporated to give the title compound (14.5 mg) as a TFA salt.

MS $(M+H)^+$ Calcd.	255.1
MS $(M+H)^+$ Observ.	255.2
Retention Time	1.19 min
	LC Condition
Solvent A	10 % acetonitrile : 90% Water : 0.1% TFA
Solvent B	90 % acetonitrile : 10% Water : 0.1% TFA
Start % B	0
Final % B	100
Gradient Time	2 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Phenomenex LUNA C18 30 x 2 mm, 3 μ

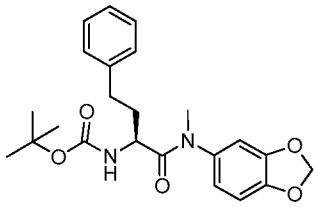
Intermediate 6



(S)-2-amino-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenylpropanamide

Intermediate 6 was prepared using the analogous procedures for the preparation of Intermediates 1-3 where the benzo[d][1,3]dioxol-5-amine used in the preparation of Intermediate 1 was replaced with 2,3-dihydro-1H-inden-5-amine and then carried through the subsequent steps. LC-MS retention time = 1.17 min; m/z = 295.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 90% Water:10% Acetonitrile: 0.1% TFA. Solvent B = 10% Water:90% Acetonitrile: 0.1% TFA. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 2 min. Wavelength = 220).

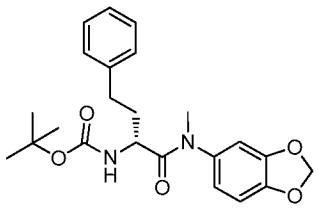
Intermediate 7



(S)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-4-phenylbutan-2-yl)carbamate

Intermediate 7 was prepared using the analogous procedure for the preparation of Intermediates 2 where the (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid was replaced with (S)-2-((tert-butoxycarbonyl)amino)-4-phenylbutanoic acid. LC-MS retention time = 1.68 min; m/z = 413.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 90% Water:10% Acetonitrile: 0.1% TFA. Solvent B = 10% Water:90% Acetonitrile: 0.1% TFA. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 2 min. Wavelength = 220).

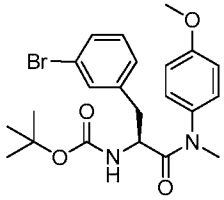
Intermediate 8



(R)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-4-phenylbutan-2-yl)carbamate

Intermediate 8 was prepared using the analogous procedure for the preparation of Intermediates 2 where the (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid was replaced with (R)-2-((tert-butoxycarbonyl)amino)-4-phenylbutanoic acid. LC-MS retention time = 1.67 min; m/z = 413.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 90% Water:10% Acetonitrile: 0.1% TFA. Solvent B = 10% Water:90% Acetonitrile: 0.1% TFA. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 2 min. Wavelength = 220).

Intermediate 9

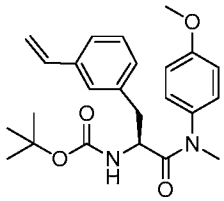


(S)-tert-butyl (3-(3-bromophenyl)-1-((4-methoxyphenyl)(methyl)amino)-1-oxopropan-2-yl)carbamate

HATU (2.00 g, 5.26 mmol) was added to a stirred solution of 4-methoxy-N-methylaniline (0.601 g, 4.38 mmol), (S)-3-(3-bromophenyl)-2-((tert-butoxycarbonyl)amino)propanoic acid (1.508 g, 4.38 mmol) and DIPEA (2.3 mL, 13 mmol) in DMF (15 mL) and the reaction mixture was stirred at RT overnight. The reaction was diluted with water (50 mL), extracted by EtOAc (2 X 40 mL) and the combined organic component was concentrated to dryness to yield the title compound (1.9 g) which was used without further purification. LC-MS retention time = 2.40 min; m/z = 363.1 $[M+H\text{-}Boc]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate =

1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220).

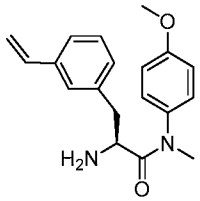
Intermediate 10



(S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-(3-vinylphenyl)propan-2-yl)carbamate

A solution of (S)-tert-butyl (3-(3-bromophenyl)-1-((4-methoxyphenyl)(methyl)amino)-1-oxopropan-2-yl)carbamate (0.740 g, 1.56 mmol), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (0.295 g, 1.92 mmol), 3M aqueous Na_2CO_3 (2.66 mL, 7.99 mmol) and $PdCl_2$(dppf) (0.117 g, 0.160 mmol) in DMF (2 mL) was degassed and heated at 110 °C for 2 h. The reaction mixture was allowed to cool, diluted with water (150 mL) and extracted with EtOAc (2 X 150 mL). The combined organic component was purified by silica gel chromatography (TLC (50% EtAOc/ Hexanes, R*f* 0.66)) to yield the title compound (0.43 g). LC-MS retention time = 2.38 min; m/z = 411.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220). ^{1}H NMR (400MHz, CHLOROFORM-d) δ 7.23 - 7.15 (m, 1H), 7.01 - 6.55 (m, 7H), 5.68 (d, *J*=17.6 Hz, 1H), 5.23 (d, *J*=11.0 Hz, 2H), 4.52 (d, *J*=7.6 Hz, 1H), 3.81 (s, 3H), 3.16 (s, 3H), 2.94 - 2.82 (m, 1H), 2.72 (dd, *J*=12.6, 6.7 Hz, 1H), 1.57 (s, 9H).

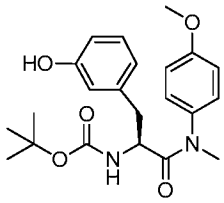
Intermediate 11



(S)-2-amino-N-(4-methoxyphenyl)-N-methyl-3-(3-vinylphenyl)propanamide

A solution of (S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-(3-vinylphenyl)propan-2-yl)carbamate (0.430 g, 1.047 mmol) and TFA (3 mL, 38.9 mmol) in DCM (6 mL) was stirred at RT for 1 h. Solvent was evaporated to yield a TFA salt of the title compound (0.445g) which was used without further purification. LC-MS retention time = 1.77 min; m/z = 311.2 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220).

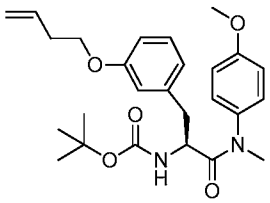
Intermediate 12



(S)-tert-butyl (3-(3-hydroxyphenyl)-1-((4-methoxyphenyl)(methyl)amino)-1-oxopropan-2-yl)carbamate

HATU (0.800 g, 2.10 mmol) was added to a stirred solution of 4-methoxy-N-methylaniline (0.240 g, 1.75 mmol), (S)-2-((tert-butoxycarbonyl)amino)-3-(3-hydroxyphenyl)propanoic acid (0.493 g, 1.75 mmol) and DIPEA (0.92 mL, 5.3 mmol) in DMF (5 mL) and the reaction mixture was stirred at RT overnight. The reaction was diluted with water (50 mL), extracted with EtOAc (2 X 40 mL) and the combined organic component was concentrated to dryness and purified (40g SiO_2, 0-30% EtOAc/DCM) to yield the title compound (0.58 g). LC-MS retention time = 1.99 min; m/z = 399.3 $[M-H]^-$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220). ^1H NMR (400MHz, CHLOROFORM-d) δ 7.10 (t, *J*=7.8 Hz, 1H), 6.91 - 6.66 (m, 5H), 6.52 (d, *J*=7.6 Hz, 1H), 6.46 (s, 1H), 5.57 (br. s., 1H), 5.20 (d, *J*=7.6 Hz, 1H), 4.52 (d, *J*=7.8 Hz, 1H), 3.81 (s, 3H), 3.19 (s, 3H), 2.84 (dd, *J*=13.0, 7.8 Hz, 1H), 2.68 (dd, *J*=12.8, 6.2 Hz, 1H), 1.40 (br. s., 9H).

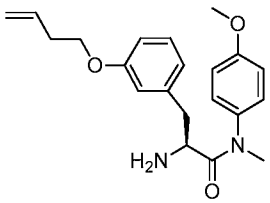
Intermediate 13



(S)-tert-butyl (3-(3-(but-3-en-1-yloxy)phenyl)-1-((4-methoxyphenyl)(methyl)amino)-1-oxopropan-2-yl)carbamate

The reaction mixture of (S)-tert-butyl (3-(3-hydroxyphenyl)-1-((4-methoxyphenyl)(methyl)amino)-1-oxopropan-2-yl)carbamate (0.52 g, 1.3 mmol), 4-bromo-2-butene (0.26 mL, 2.6 mmol) and Cs_2CO_3 (0.465 g, 1.43 mmol) in THF (8 mL), EtOH(8 mL) and H_2O (8 mL) was stirred at 85 °C for 22 h. The reaction was diluted with water (80 mL), extracted with EtOAc (2 X 100 mL) and the combined organic component was concentrated to dryness and purified (24g SiO_2, 0-40% EtOAc/DCM) to yield the title compound (0.28 g). LC-MS retention time = 2.51min; m/z = 355.1 $[M+H-Boc]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220). ^1H NMR (400MHz, CHLOROFORM-d) δ 7.12 (t, *J*=7.8 Hz, 1H), 6.93 - 6.67 (m, 5H), 6.55 (d, *J*=7.3 Hz, 1H), 6.44 (br. s., 1H), 5.91 (ddt, *J*=17.1, 10.4, 6.7 Hz, 1H), 5.22 - 5.09 (m, 3H), 4.52 (d, *J*=8.1 Hz, 1H), 3.90 (td, *J*=6.7, 3.4 Hz, 2H), 3.82 (s, 3H), 3.18 (s, 3H), 2.89 - 2.80 (m, 1H), 2.68 (dd, *J*=12.6, 6.0 Hz, 1H), 2.52 (q, *J*=6.6 Hz, 2H), 1.55 (s, 9H).

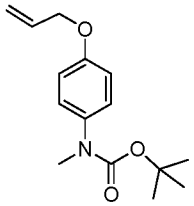
Intermediate 14



(S)-2-amino-3-(3-(but-3-en-1-yloxy)phenyl)-N-(4-methoxyphenyl)-N-methylpropanamide

A solution of (S)-tert-butyl (3-(3-(but-3-en-1-yloxy)phenyl)-1-((4-methoxyphenyl)(methyl)amino)-1-oxopropan-2-yl)carbamate (0.280 g, 0.616 mmol) in TFA (1.0 mL, 13 mmol) and DCM (2 mL) was stirred at RT for 1 h. The solvent was removed to yield a TFA salt of the title compound (0.445g) which was used without further purification. LC-MS retention time = 1.87 min; m/z = 355.1 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220).

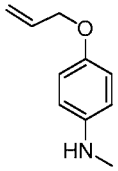
Intermediate 15



tert-butyl (4-(allyloxy)phenyl)(methyl)carbamate

A mixture of tert-butyl (4-hydroxyphenyl)(methyl)carbamate (1.00 g, 4.48 mmol), allyl bromide (0.58 mL, 6.7 mmol) and Cs_2CO_3 (2.92 g, 8.96 mmol) in acetone (40 mL) was sealed and heated to gentle reflux for 4 h. The reaction mixture was allowed to cool to rt, filtered and concentrated. The residue was taken up into EtOAc, washed with 5% citric acid and then brine, dried over $MgSO_4$, filtered, and concentrated. The residue was taken up into DCM and purified by flash column chromatography. ^1H NMR (400MHz, CHLOROFORM-d) δ 7.14 (d, *J*=8.3 Hz, 1H), 6.91 - 6.85 (m, 1H), 6.08 (ddt, *J*=17.3, 10.6, 5.3 Hz, 1H), 5.44 (dq, *J*=17.2, 1.6 Hz, 1H), 5.34 - 5.28 (m, 1H), 4.54 (dt, *J*=5.3, 1.5 Hz, 2H), 3.24 (s, 3H), 1.45 (s, 9H).

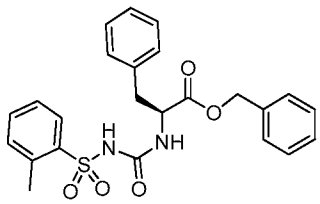
Intermediate 16



4-(allyloxy)-N-methylaniline

A solution of 2 M HCl in ether (0.949 mL, 1.899 mmol) was added to tert-butyl (4-(allyloxy)phenyl)-(methyl)carbamate (50 mg, 0.190 mmol) and stirred at RT overnight. The reaction was concentrated under a stream of nitrogen to yield the title compound which was used without further purification. LC-MS retention time = 0.73 min; m/z = 164.2 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

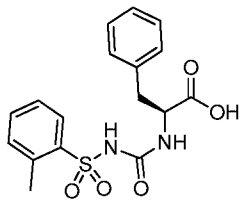
Intermediate 17



(S)-benzyl 3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanoate

2-Methylbenzenesulfonyl isocyanate (0.52 mL, 3.4 mmol) was added dropwise to an ice bath cooled mixture of (S)-benzyl 2-amino-3-phenylpropanoate, HCl (1.00 g, 3.43 mmol) and DIPEA (2.4 mL, 14 mmol) in acetonitrile (20 mL) and the resulting solution was stirred at RT for 2 h. The reaction mixture was concentrated and the residual oil was taken into EtOAc (100 mL) and washed with 5% citric acid and brine, dried over $MgSO_4$, filtered and concentrated. The residual oil was purified by flash column chromatography (80 g silica gel cartridge, eluted with gradient 30%~70% acetone-hexanes) to afford the title compound (1.20 g) as a white solid. LC-MS retention time = 1.28 min; m/z = 453.3 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

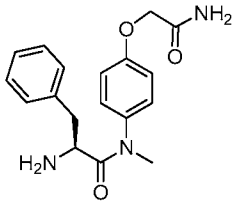
Intermediate 18



(S)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanoic acid

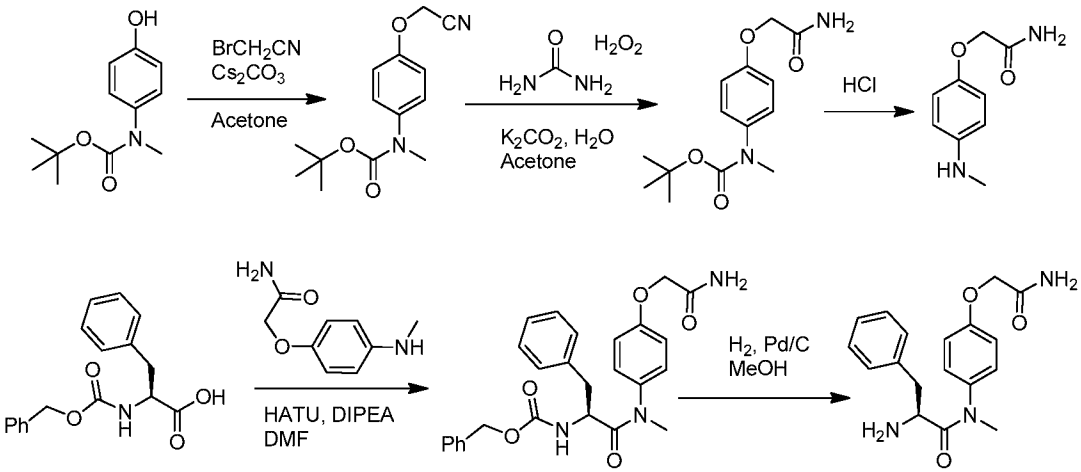
A mixture of (S)-benzyl 3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanoate (1.00 g, 2.21 mmol) and 10% Pd-C (0.118 g, 0.110 mmol) in EtOAc (15 mL) and MeOH (15 mL) was placed under a balloon of hydrogen and stirred at RT for 2 h. The reaction was filtered through celite and concentrated to dryness to yield the title compound (750 mg) as a white solid. LC-MS retention time = 0.99 min; m/z = 363.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

Intermediate 19



(S)-2-amino-N-(4-(2-amino-2-oxoethoxy)phenyl)-N-methyl-3-phenylpropanamide

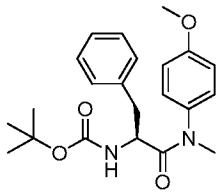
Intermediate 19 was prepared using the chemical procedures displayed in the following scheme:



LC-MS retention time = 0.73 min; m/z = 328.2 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 100% Water : 0.05% TFA.

Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

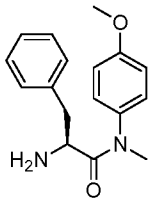
Intermediate JB-1



(S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (1.5 g, 4.0 mmol) was added to a stirred solution of 4-methoxy-N-methylaniline (500 mg, 3.64 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (1.06 g, 4.0 mmol) in DMF (20 mL) and DIPEA (1.3 mL, 7.3 mmol) and the reaction mixture was stirred at RT for 4h. The reaction was concentrated and the residual crude oil was partitioned between EtOAc (~60 mL) and 1/2 sat. $NaHCO_3$ (aq) (~60 mL). The organic component was washed with brine (~40 mL), dried ($MgSO_4$), filtered, concentrated and purified using a Biotage Horizon (80g SiO_2, 10-40% EtOAc/hexanes) to yield (S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (1.34 g) as a clear amber viscous oil. LC-MS retention time = 3.17 min; m/z = 385.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 50mm 3 µm. Solvent A = 95% Water:5% Acetonitrile:10 mM NH_4OAc. Solvent B = 5% Water:95% Acetonitrile:10 mM NH_4OAc. Flow Rate = 0.8 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 4 min. Wavelength = 220). ^1H NMR (400MHz, $CDCl_3$) δ 7.25 - 7.20 (m, 3H), 7.03 - 6.64 (m, 6H), 5.20 (d, *J*=8.8 Hz, 1H), 4.53 (q, *J*=7.4 Hz, 1H), 3.83 (s, 3H), 3.18 (s, 3H), 2.89 (dd, *J*=13.1, 7.5 Hz, 1H), 2.71 (dd, *J*=13.1, 6.5 Hz, 1H), 1.39 (s, 9H).

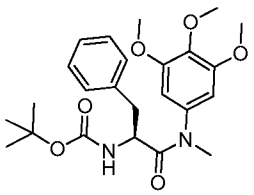
Intermediate JB-2



(S)-2-amino-N-(4-methoxyphenyl)-N-methyl-3-phenylpropanamide

A 4M HCl (15 mL, 60.0 mmol) in dioxanes solution was added to a stirred solution of (S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (Intermediate JB-1) (1.34 g, 3.49 mmol) in THF (10 mL) and the reaction mixture was stirred at RT for 5h. The reaction mixture was concentrated to dryness under vacuum to yield an HCl salt of (S)-2-amino-N-(4-methoxyphenyl)-N-methyl-3-phenylpropanamide (1.11 g) as a solidified foam which was used without additional purification. LC-MS retention time = 2.33 min; m/z = 285.2 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 50mm 3 µm. Solvent A = 95% Water:5% Acetonitrile:10 mM NH_4OAc. Solvent B = 5% Water:95% Acetonitrile:10 mM NH_4OAc. Flow Rate = 0.8 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 4 min. Wavelength = 220).

Intermediate JB-7

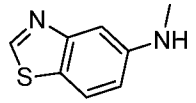


(S)-tert-butyl (1-(methyl(3,4,5-trimethoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (776 mg, 2.04 mmol) was added to a stirred solution of 3,4,5-trimethoxy-N-methylaniline (350 mg, 1.78 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (518 mg, 1.95 mmol) in DMF (10 mL) and DIPEA (0.62 mL, 3.6 mmol) and stirred at RT ON. The reaction mixture was concentrated and the crude oil was partitioned between EtOAc (~40 mL) and 1/2 sat $NaHCO_3$ (aq) (~40 mL). The organic component was washed with brine (~30 mL), dried ($MgSO_4$), filtered and concentrated. The crude residue was then purified using a Biotage

Horizon (80g SiO_2, 10-40% EtOAc/hexanes) to yield(S)-tert-butyl (1-(methyl(3,4,5-trimethoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (474 mg) as a clear colorless solidified oil. Used without further purification. LC-MS retention time = 1.60 min; m/z = 385.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 50mm 3 µm. Solvent A = 90% Water:10% Acetonitrile: 0.1% TFA. Solvent B = 10% Water:90% Acetonitrile: 0.1% TFA. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 2 min. Wavelength = 220). ^1H NMR (400MHz, CHLOROFORM-d) δ 7.27 - 7.17 (m, 3H), 7.01 (d, J=6.3 Hz, 2H), 6.11 (br. s., 2H), 5.21 (d, J=9.0 Hz, 1H), 4.76 - 4.64 (m, 1H), 3.86 (s, 3H), 3.77 (br. s., 6H), 3.17 (s, 3H), 3.01 - 2.87 (m, 1H), 2.77 (dd, J=12.8, 6.3 Hz, 1H), 1.40 (s, 9H).

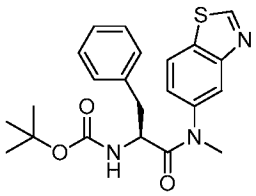
Intermediate ZY-1



N-methylbenzo[d]thiazol-5-amine

Paraformaldehyde (80 mg, 2.7 mmol) was added to a stirred solution of benzo[d]thiazol-5-amine (200 mg, 1.332 mmol) in MeOH (5 mL) The resulting suspension was then treated with 25%w/w NaOMe in MeOH (1.5 mL, 6.7 mmol) and the clear reaction mixture was stirred at 60 °C for 16 h. The reaction was allowed to cool to RT and then treated with $NaBH_4$ (126 mg, 3.33 mmol) and stirred at RT for 16 h. The reaction mixture was diluted with water (10 mL) and extracted with $CHCl_3$ (3 x 20 mL). The combined organic component was concentrated and purified using a Biotage Horizon (12g SiO_2, 0-50% EtOAc/hexanes) to yield N-methylbenzo[d]thiazol-5-amine (217 mg) as yellow gum. .LC-MS retention time = 0.67 min; m/z = 165.05 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^1H NMR (400MHz, CHLOROFORM-d) δ 8.92 (s, 1H), 7.69 (d, *J*=8.5 Hz, 1H), 7.31 (d, *J*=2.3 Hz, 1H), 6.82 (dd, *J*=8.8, 2.3 Hz, 1H), 3.93 (br. s., 1H), 2.94 (s, 3H).

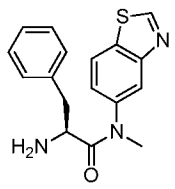
Intermediate ZY-2



(S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (1.90 g, 5.01 mmol) was added to a solution of N-methylbenzo[d]thiazol-5-amine (Intermediate ZY-1) (685 mg, 4.17 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (1.33 g, 5.01 mmol) in DMF (20 mL) and DIPEA (2.18 mL, 12.5 mmol) and the reaction mixture was stirred at RT for 6 h. The crude reaction mixture was diluted with sat. aq. $NaHCO_3$ (20 mL) and extracted with EtOAc (3 x 50 mL). The combined organic component was washed with brine (~60 mL), dried (Na_2SO_4), filtered and concentrated. The crude material was then purified using a Biotage Horizon (12g SiO_2, 0-40%-50% EtOAc/hexanes) to yield (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (1.7 g) as a white solid. LC-MS retention time = 1.19 min; m/z = 412.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^1H NMR (400MHz, CHLOROFORM-d) δ 9.07 (s, 1H), 7.90 (d, *J*=8.3 Hz, 1H), 7.38 (d, *J*=7.5 Hz, 1H), 7.27 - 7.19 (m, 3H), 6.94 (d, *J*=6.8 Hz, 3H), 5.22 (d, *J*=8.8 Hz, 1H), 4.58 - 4.48 (m, 1H), 3.26 (s, 3H), 2.93 (dd, *J*=12.9, 8.4 Hz, 1H), 2.78 (dd, *J*=12.4, 5.9 Hz, 1H), 1.40 (s, 9H).

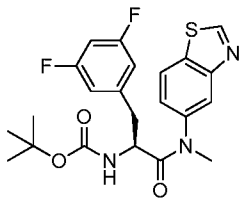
Intermediate ZY-3



(S)-2-amino-N-(benzo[d]thiazol-5-yl)-N-methyl-3-phenylpropanamide

A solution of 4M HCl (10 mL, 40.0 mmol) in dioxanes was added to a stirred solution of (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (Intermediate ZY-2) (1.7 g, 4.13 mmol) in THF (10 mL) and the reaction mixture was stirred at RT for 16 h. The reaction mixture was concentrated, redissolved in EtOH/toluene, and then reconcentrated (3x) to yield an HCl salt of (S)-2-amino-N-(benzo[d]thiazol-5-yl)-N-methyl-3-phenylpropanamide (1.7 g, 4.42 mmol, 107 % yield) as a pink sticky solid. LC-MS retention time = 0.83 min; m/z = 312.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^{1}H NMR (400MHz, METHANOL-d_4) δ 9.42 (s, 1H), 8.10 (d, *J*=8.3 Hz, 1H), 7.39 - 7.08 (m, 6H), 6.91 (d, *J*=7.0 Hz, 2H), 4.10 (dd, *J*=8.0, 6.5 Hz, 1H), 3.63 - 3.56 (m, 2H), 3.11 (dd, *J*=13.4, 8.2 Hz, 1H), 2.92 (dd, *J*=13.3, 6.5 Hz, 1H), 2.87 (s, 3H).

Intermediate ZY-4

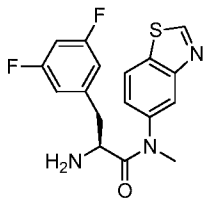


(S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-3-(3,5-difluorophenyl)-1-oxopropan-2-yl)carbamate

HATU (592 mg, 1.556 mmol) was added to a stirred solution of N-methylbenzo[d]thiazol-5-amine (Intermediate ZY-1) (213 mg, 1.30 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-(3,5-difluorophenyl)propanoic acid (469 mg, 1.56 mmol) in DMF (7 mL) and DIPEA (0.45 mL, 2.6 mmol) and the reaction mixture was stirred at RT for 16 h. The crude reaction mixture was diluted with sat. aq. $NaHCO_3$ (20 mL) and extracted with EtOAc (3 x 50 mL). The combined organic component was washed with brine (~60 mL), dried (Na_2SO_4), filtered and concentrated. The crude material was then purified using a Biotage Horizon (24g SiO_2, 0-50% EtOAc/hexanes) yield (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-3-(3,5-difluorophenyl)-1-oxopropan-2-yl)carbamate (581 mg) as a

white solid. LC-MS retention time = 1.23 min; m/z = 448.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^1H NMR (400MHz, CHLOROFORM-d) δ 9.10 (s, 1H), 7.98 (d, *J*=8.3 Hz, 1H), 7.68 (br. s., 1H), 7.05 (br. s., 1H), 6.68 (t, *J*=8.9 Hz, 1H), 6.44 (d, *J*=6.3 Hz, 2H), 5.25 (d, *J*=9.0 Hz, 1H), 4.54 (q, *J*=7.3 Hz, 1H), 2.94 - 2.86 (m, 1H), 2.81 (s, 3H), 2.72 (dd, *J*=13.1, 6.5 Hz, 1H), 1.39 (s, 9H).

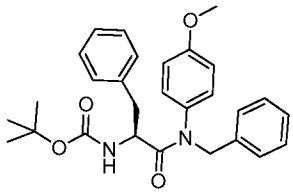
Intermediate ZY-5



(S)-2-amino-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-N-methylpropanamide

TFA (1.0 mL, 13 mmol) was added to a stirred solution of (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-3-(3,5-difluorophenyl)-1-oxopropan-2-yl)carbamate (Intermediate ZY-4) (0.58 g, 1.23 mmol) in DCM (2 mL) and the reaction mixture was stirred at RT for 16 h. The crude reaction mixture was concentrated and the residue was dissolved in MeOH/DCM and 4 M HCl in dioxane (2 mL) and reconcentrated. The residue was redissolved in EtOH/toluene, and then reconcentrated (3x) to yield an HCl salt of (S)-2-amino-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-N-methylpropanamide (0.55 g) as a white solid. LC-MS retention time = 0.83 min; m/z = 348.1$[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

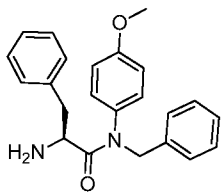
Intermediate ZY-6



(S)-tert-butyl (1-(benzyl(4-methoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

BOP-Cl (131 mg, 0.516 mmol) was added to a stirred solution of (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (124 mg, 0.469 mmol) and N-benzyl-4-methoxyaniline (100 mg, 0.469 mmol) in DCM (3 mL), and DIPEA (0.25 mL, 1.4 mmol) and the reaction mixture was stirred at RT for 16h. The crude reaction mixture was concentrated and the residue was purified using a Biotage Horizon (12 g SiO_2, 0 - 50% Et_2O/hexanes) to yield the title compound (125 mg). LC-MS retention time = 1.43 min; m/z = 461.4 $[M+H]^+$. (Column: Waters Aquity BEH C18 2.1 X 50 mm 1.7U. Solvent A = 100% Water / 0.05% TFA. Solvent B = 100% Acetonitrile / 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

Intermediate ZY-7

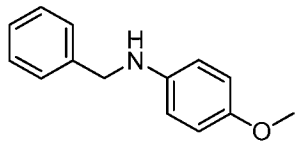


(S)-2-amino-N-benzyl-N-(4-methoxyphenyl)-3-phenylpropanamide

A 4M solution of HCl (1.3 mL, 5.2 mmol) in dioxane was added to a stirred solution of (S)-tert-butyl (1-(benzyl(4-methoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (Intermediate ZY-6) (120 mg, 0.261 mmol) in THF (1.3 mL) and the reaction mixture was stirred at RT for 2h. The reaction mixture concentrated to yield an HCl salt of the title compound (117 mg). LC-MS retention time = 0.99 min; m/z = 361.2 $[M+H]^+$. (Column: Waters Aquity BEH C18 2.1 X 50 mm 1.7U. Solvent A = 100% Water / 0.05% TFA. Solvent B = 100% Acetonitrile / 0.05% TFA. Flow Rate

= 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

Intermediate ZY-8

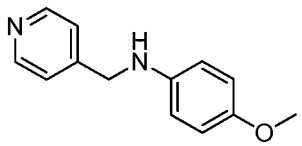


N-benzyl-4-methoxyaniline

Diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (0.617 g, 2.44 mmol) was added to a stirred solution of scandium trifluoromethanesulfonate (0.024 g, 0.049 mmol), benzaldehyde (0.248 mL, 2.44 mmol) and 4-methoxyaniline (0.300 g, 2.44 mmol) in DCM (10 mL) and the reaction mixture was stirred at RT for 16 h. The reaction was then concentrated and the residue was purified by silica gel chromatography (0 - 20% Et_2O/hexanes) to yield the title compound (503 mg) as yellow oil.

MS $(M+H)^+$ Calcd.	214.1
MS $(M+H)^+$ Observ.	214.1
Retention Time	0.824 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-9

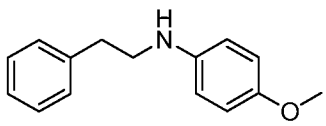


4-methoxy-N-(pyridin-4-ylmethyl)aniline

Diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (0.617 g, 2.44 mmol) was added to a stirred solution of scandium trifluoromethanesulfonate (0.024 g, 0.049 mmol), isonicotinaldehyde (0.229 mL, 2.44 mmol) and 4-methoxyaniline (0.300 g, 2.44 mmol) in DCM (10 mL) and the reaction mixture was stirred at RT for 16 h. The reaction was then concentrated and the residue was purified by silica gel chromatography (24 g SiO_2, 0 - 100% Et_2O/hexanes) to yield the title compound (447 mg) as yellow solid.

MS $(M+H)^+$ Calcd.	215.1
MS $(M+H)^+$ Observ.	215.1
Retention Time	0.719 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-10

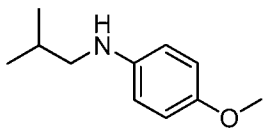


4-methoxy-N-phenethylaniline

Diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1.03 g, 4.06 mmol) was added to a stirred solution of scandium trifluoromethanesulfonate (0.040 g, 0.081 mmol), 2-phenylacetaldehyde (0.488 g, 4.06 mmol) and 4-methoxyaniline (0.500 g, 4.06 mmol) in DCM (10 mL) and the reaction mixture was stirred at RT for 16 h and then heated at 50° C for 2h. Additional 2-phenylacetaldehyde (0.488 g, 4.06 mmol), and diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1.03 g, 4.06 mmol) were added and heating at 50° C was continued for 1h. The reaction was then concentrated and the residue was purified by silica gel chromatography (24 g SiO_2, 0 - 20% Et_2O/hexanes) to yield the title compound (2.25 g) contaminated with and impurity, but used without additional purification, as red/orange oil.

MS $(M+H)^+$ Calcd.	228.1
MS $(M+H)^+$ Observ.	228.1
Retention Time	0.867 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-11



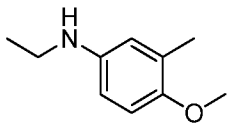
N-isobutyl-4-methoxyaniline

Diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (2.06 g, 8.12 mmol) was added to a stirred solution of scandium trifluoromethanesulfonate (0.080 g, 0.16 mmol), isobutyraldehyde (0.74 mL, 8.1 mmol) and 4-methoxyaniline (0.300 g, 2.44 mmol) in DCM (10 mL) and the reaction mixture was stirred at RT for 16 h. The

reaction was then concentrated and the residue was purified by silica gel chromatography (40 g SiO_2, 0 - 20% Et_2O/hexanes) to yield the title compound (1.02 g) as clear colorless oil.

MS $(M+H)^+$ Calcd.	180.1
MS $(M+H)^+$ Observ.	180.1
Retention Time	0.774 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-12



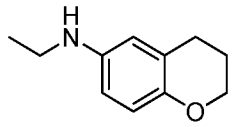
N-ethyl-4-methoxy-3-methylaniline

Acetic acid (0.042 mL, 0.73 mmol) was added to a stirred solution of 4-methoxy-3-methylaniline (100 mg, 0.729 mmol) and acetaldehyde (0.054 mL, 0.948 mmol) in DCM (3 mL) and the reaction mixture was stirred at RT for 5 min. Sodium triacetoxyborohydride (232 mg, 1.09 mmol) was then added to the reaction mixture and the reaction was stirred at RT for 16 h. The reaction was quenched with 1N aq. NaOH (4 mL), extracted with chloroform (3 x 10 mL) and the combined organic component was concentrated and purified by preparative HPLC (H_2O-MeOH with 0.1% TFA buffer) to yield a TFA salt of the title compound (27 mg) as dark pink oil.

MS $(M+H)^+$ Calcd.	166.1
MS $(M+H)^+$ Observ.	166.1

Retention Time	0.787 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-13

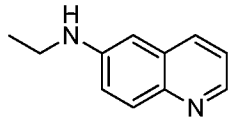


N-ethylchroman-6-amine

Prepared using the procedure outlined for Intermediate ZY-12 where 4-methoxy-3-methylaniline was replaced with chroman-6-amine.

MS $(M+H)^+$ Calcd.	178.1
MS $(M+H)^+$ Observ.	178.1
Retention Time	0.774 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-14

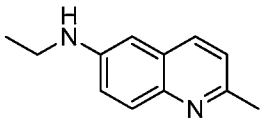


N-ethylquinolin-6-amine

Prepared using the procedure outlined for Intermediate ZY-12 where 4-methoxy-3-methylaniline was replaced with quinoline-6-amine.

MS $(M+H)^+$ Calcd.	173.1
MS $(M+H)^+$ Observ.	173.1
Retention Time	0.775 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Intermediate ZY-15



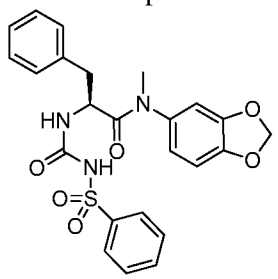
N-ethyl-2-methylquinolin-6-amine

10% Pd-C (0.135 g, 0.126 mmol) was added to a mixture of 2-methylquinolin-6-amine (0.200 g, 1.26 mmol) in MeOH (10 mL) and MeCN (6.6 mL). The reaction mixture was vacuum flushed with N_2 (3X) followed by H_2 (3X) and then shaken at RT under 20 psi H_2 for 4 h. The reaction mixture was filtered through celite, concentrated and purified by flash silica chromatography (12 g SiO_2, 0 - 35% EtOAc/hexanes) to yield N-ethyl-2-methylquinolin-6-amine (192 mg) as brown solid.

MS $(M+H)^+$ Calcd.	187.1

MS $(M+H)^+$ Observ.	187.1
Retention Time	0.809 min
	LC Condition
Solvent A	100% Water : 0.05% TFA
Solvent B	100 % acetonitrile : 0.05% TFA
Start % B	2
Final % B	98
Gradient Time	1.5 min
Flow Rate	0.8 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Waters Aquity BEH C18 2.1 X 50 mm 1.7U

Example 1



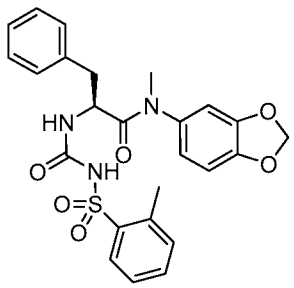
(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-(phenylsulfonyl)ureido)propanamide

2M HCl (0.5 mL, 1 mmol) in dioxane was added to (S)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (49 mg, 0.12 mmol) and the reaction was stirred 3 h at r.t and then concentrated. The residue was dissolved into acetonitrile (0.5 mL) and treated with diisopropylethylamine (0.054 mL, 0.31 mmol) and then benzenesulfonyl isocyanate (33.8 mg, 0.184 mmol) (exothermic reaction observed). The reaction was stirred 3 h, diluted with MeOH (0.5 mL) and then concentrated. The residue was partitioned between water (1.5 mL) and EtOAc (3 x 1 mL). The combined organic component was concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to afford the title compound (45.9 mg). ^{1}H NMR (600 MHZ, DMSO-d_6) δ 7.79 (d,

J=7.7 Hz, 2H), 7.71 - 7.62 (m, 1H), 7.61 - 7.52 (m, 2H), 7.20 – 1.14 (m, 3H), 6.90 (d, *J*=8.1 Hz, 1H), 6.80 (d, *J*=3.3 Hz, 2H), 6.69 (d, *J*=8.1 Hz, 2H), 6.59 (d, *J*=7.7 Hz, 1H), 6.08 (s, 2H), 4.31 (d, *J*=6.2 Hz, 1H), 3.07 (s, 3H), 2.83 - 2.77 (m, 1H), 2.58 - 2.52 (m, 1H).

MS $(M+H)^+$ Calcd.	482.1
MS $(M+H)^+$ Observ.	482.2
Retention Time	1.30 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µ particles

Example 2



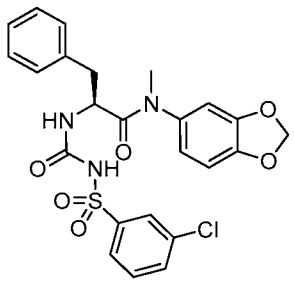
(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

To a solution of (S)-2-amino-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenylpropanamide, TFA (40 mg, 0.097 mmol) in dichloromethane (2 mL) was

added diisopropylethylamine (0.051 mL, 0.291 mmol) followed by a solution of 2-methylbenzenesulfonyl isocyanate (28.7 mg, 0.146 mmol) in dichloromethane (2 mL). The reaction mixture was stirred at r.t. for 1 hr. The solvent was evaporated and the residue was purified by preparative HPLC to afford) of the title compound (34.4mg. ^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 (d, *J*=7.6 Hz, 1H), 7.48 - 7.01 (m, 7H), 6.87 -6.81 (m, 3H), 6.73 - 6.17 (m, 2H), 6.06 (s, 2H), 4.26 (br. s., 1H), 3.05 (s, 3H), 2.94 - 2.62 (m, 2H), 2.51 (s, 3H).

MS $(M+H)^+$ Calcd.	496.2
MS $(M+H)^+$ Observ.	496.3
Retention Time	1.46 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 3



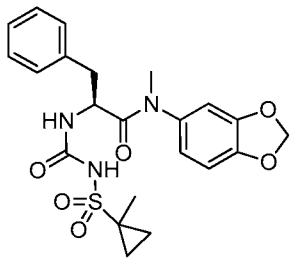
(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3-chlorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

To a solution of 3-chlorobenzenesulfonamide (100 mg, 0.522 mmol) in toluene (1 mL) was added 1-isocyanatobutane (5.05 mg, 0.051 mmol) followed by triphosgene (52.9 mg, 0.178 mmol). The reaction mixture was stirred at 110°C for 24 hrs. The reaction mixture was allowed to cool and the solvent was evaporated to afford 3-chlorobenzenesulfonyl isocyanate which was used in the subsequent step without further purification. To a solution of (S)-2-amino-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenylpropanamide, TFA (30 mg, 0.073 mmol) in dichloromethane (0.5 mL) was added diisopropylethylamine (0.04 mL, 0.22 mmol) followed by 3-chlorobenzenesulfonyl isocyanate (23.8 mg, 0.11 mmol) in dichloromethane (0.5 mL). The reaction mixture was stirred at r.t. for 1 hr. The solvent was evaporated and the residue was purified by preparative HPLC to afford the title compound (15.2 mg). ^{1}H NMR (600 MHZ, DMSO-d_6) δ 7.68 (br. s., 1H), 7.60 (d, *J*=7.3 Hz, 1H), 7.51 - 7.35 (m, 2H), 7.17 - 7.15 (m, 3H), 6.90 - 6.81 (m, 3H), 6.71 - 6.50 (m, 2H), 6.06 – 6.01 (m, 3H), 4.26 (br. s., 1H), 3.05 (s, 3H), 2.73 - 2.52 (m, 2H).

MS $(M+H)^+$ Calcd.	516.1
MS $(M+H)^+$ Observ.	516.4
Retention Time	1.36 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm

particles

Example 4



(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-((1-methylcyclopropyl)sulfonyl)ureido)-3-phenylpropanamide

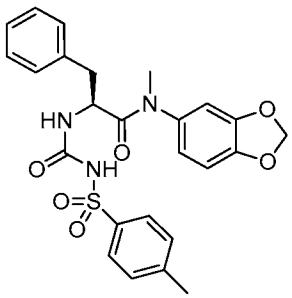
To a solution of 1-methylcyclopropane-1-sulfonamide (49.2 mg, 0.36 mmol) in toluene (1 mL) was added 1-isocyanatobutane (5.05 mg, 0.051 mmol) followed by triphosgene (34.5 mg, 0.12 mmol). The reaction mixture was stirred at 110°C for 20 hrs. The reaction mixture (0.2 mL) was allowed to cool and then added to a solution of (S)-2-amino-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenylpropanamide, TFA (30 mg, 0.073 mmol) and diisopropylethylamine (0.04 mL, 0.22 mmol) in toluene (0.5 mL). The reaction mixture was stirred at r.t. for 1 hr. The solvent was evaporated and the residue was purified by preparative HPLC to afford the title compound (22.4 mg). ^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.35 - 7.13 (m, 3H), 7.05 - 6.86 (m, 3H), 6.82 - 6.60 (m, 3H), 6.11 (d, *J*=5.5 Hz, 2H), 4.45 (d, *J*=5.5 Hz, 1H), 3.11 (s, 3H), 2.96 - 2.55 (m, 2H), 1.34 (s, 3H), 1.27 - 1.11 (m, 2H), 0.91 - 0.69 (m, 2H).

MS $(M+H)^+$ Calcd.	460.2
MS $(M+H)^+$ Observ.	460.3
Retention Time	1.43 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate

Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Examples 5 – 7 were synthesized using the procedure described above for Example 2.

Example 5



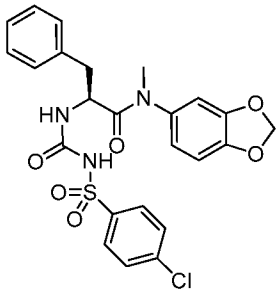
(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-tosylureido)propanamide

MS $(M+H)^+$ Calcd.	496.2
MS $(M+H)^+$ Observ.	496.2
Retention Time	1.65 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220

Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (600 MHZ, DMSO-d_6) δ 7.65 (d, *J*=7.7 Hz, 2H), 7.33 (d, *J*=7.3 Hz, 2H), 7.18 – 7.16 (m, 3H), 6.89 (d, *J*=8.1 Hz, 1H), 6.81 (br. s., 2H), 6.73 - 6.50 (m, 3H), 6.08 (s, 2H), 4.30 (d, *J*=5.5 Hz, 1H), 3.07 (s, 3H), 2.84 - 2.52 (m, 2H), 2.37 (s, 3H).

Example 6

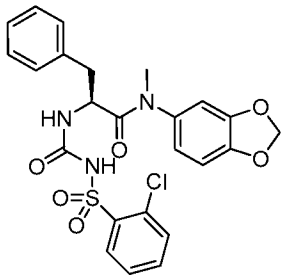


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((4-chlorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	516.1
MS $(M+H)^+$ Observ.	516.2
Retention Time	1.62 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (600 MHZ, DMSO-d_6) δ 7.79 (d, *J*=8.1 Hz, 2H), 7.63 (d, *J*=8.1 Hz, 2H), 7.16 – 7.15 (m, 3H), 6.91 (d, *J*=8.1 Hz, 1H), 6.85 - 6.53 (m, 5H), 6.08 (s, 2H), 4.31 (d, *J*=5.5 Hz, 1H), 3.08 (s, 3H), 2.85 - 2.53 (m, 2H).

Example 7



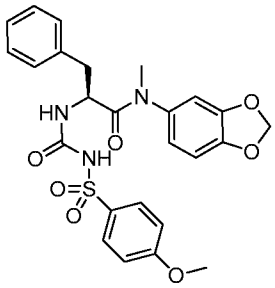
(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-chlorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	516.1
MS $(M+H)^+$ Observ.	516.5
Retention Time	1.27 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (600 MHZ, DMSO-d_6) δ 7.95 (d, *J*=4.4 Hz, 1H), 7.66 (br. s., 2H), 7.51 (br. s., 1H), 7.23 - 7.09 (m, 3H), 6.88 (d, *J*=8.1 Hz, 1H), 6.82 (d, *J*=6.6 Hz, 2H), 6.76 - 6.54 (m, 3H), 6.06 (s, 2H), 4.29 (d, *J*=5.5 Hz, 1H), 3.08 (s, 3H), 2.83 - 2.52 (m, 2H).

Examples 8 – 35 were synthesized using the procedure described above for Example 3.

Example 8

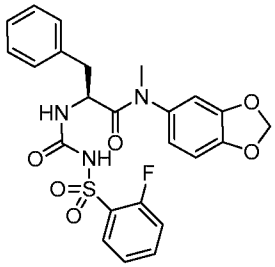


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((4-methoxyphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	512.1
MS $(M+H)^+$ Observ.	512.2
Retention Time	1.57 min
	LC Condition
Solvent A	10 % acetonitrile : 90% Water : 0.1% TFA
Solvent B	90 % acetonitrile : 10% Water : 0.1% TFA
Start % B	0
Final % B	100
Gradient Time	2 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : TFA
Column	Phenomenex Luna 30 x 2.0 MM 3u

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.79 (d, *J*=9.0 Hz, 2H), 7.26 - 7.18 (m, 3H), 7.04 (d, *J*=9.0 Hz, 2H), 6.92 (d, *J*=3.0 Hz, 2H), 6.74 (d, *J*=8.3 Hz, 1H), 6.37 (br.s., 2H), 6.00 (d, *J*=3.3 Hz, 2H), 4.55 - 4.44 (m, 1H), 3.88 (s, 3H), 3.13 (s, 3H), 2.97 - 2.62 (m, 2H).

Example 9

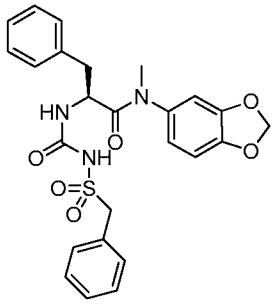


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-fluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	500.1
MS $(M+H)^+$ Observ.	500.2
Retention Time	1.48 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.95 (s, 1H), 7.81 - 7.55 (m, 2H), 7.46 - 7.02 (m, 5H), 6.94 - 6.74 (m, 3H), 6.72 - 6.37 (m, 3H), 6.06 (s, 2H), 4.28 (d, *J*=4.6 Hz, 1H), 3.06 (s, 3H), 2.82 - 2.51 (m, 2H).

Example 10

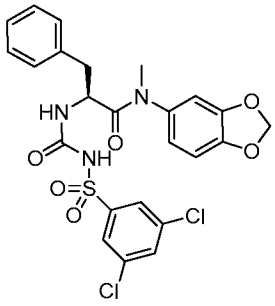


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-(benzylsulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	496.2
MS $(M+H)^+$ Observ.	496.3
Retention Time	1.78 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.35 – 7.31 (m, 3H), 7.26 – 7.22 (m, 3H), 7.16 (d, *J*=6.7 Hz, 2H), 6.98 - 6.92 (m, 1H), 6.87 (d, *J*=6.7 Hz, 2H), 6.78 - 6.61 (m, 2H), 6.58 - 6.51 (m, 1H), 6.06 (d, *J*=7.6 Hz, 2H), 4.49 – 4.44 (m, 3H), 3.10 (s, 3H), 2.90 - 2.54 (m, 2H).

Example 11

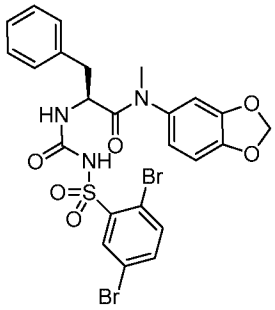


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3,5-dichlorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	550.1
MS $(M+H)^+$ Observ.	550.2
Retention Time	1.82 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.95 (s, 1H), 7.80 - 7.53 (m, 3H), 7.21 - 7.06 (m, 3H), 6.95 - 6.76 (m, 3H), 6.73 - 6.15 (m, 2H), 6.07 (s, 2H), 4.25 (d, *J*=5.2 Hz, 1H), 3.05 (s, 3H), 2.93 - 2.53 (m, 2H).

Example 12

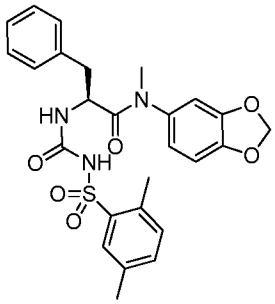


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,5-dibromophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	638.0
MS $(M+H)^+$ Observ.	638.1
Retention Time	1.88 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.00 (s, 1H), 7.73 - 7.55 (m, 2H), 7.16 (d, *J*=7.3 Hz, 3H), 6.91 - 6.82 (m, 3H), 6.72 - 6.48 (m, 2H), 6.39 - 6.13 (m, 1H), 6.06 (s, 2H), 4.27 (br. s., 1H), 3.06 (s, 3H), 2.96 - 2.53 (m, 2H).

Example 13

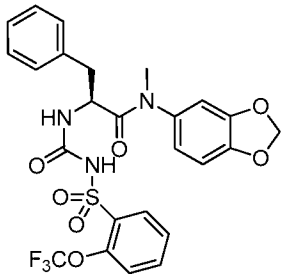


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,5-dimethylphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.75 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.62 (s, 1H), 7.38 - 7.07 (m, 5H), 6.93 - 6.74 (m, 3H), 6.71 - 6.48 (m, 3H), 6.06 (s, 2H), 4.28 (d, *J*=5.2 Hz, 1H), 3.07 (s, 3H), 2.81 - 2.47 (m, 2H), 2.45 (s, 3H), 2.31 (s, 3H).

Example 14

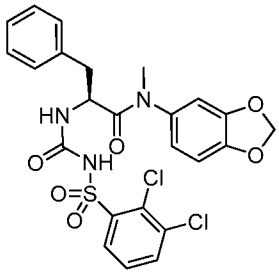


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(trifluoromethoxy)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	566.1
MS $(M+H)^+$ Observ.	566.2
Retention Time	1.78 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.91 (d, *J*=7.9 Hz, 1H), 7.82 (br. s., 1H), 7.66 - 7.48 (m, 2H), 7.17 (br. s., 3H), 6.89 (d, *J*=8.2 Hz, 1H), 6.85 - 6.63 (m, 4H), 6.60 (d, *J*=7.3 Hz, 1H), 6.07 (s, 2H), 4.30 (d, *J*=5.8 Hz, 1H), 3.08 (s, 3H), 2.81 – 2.49 (m, 2H).

Example 15

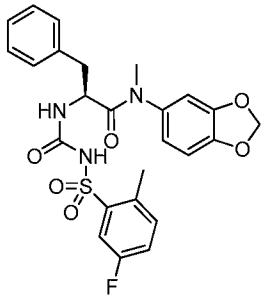


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,3-dichlorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	550.1
MS $(M+H)^+$ Observ.	550.2
Retention Time	1.41 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.92 - 7.79 (m, 2H), 7.46 (br. s., 1H), 7.20 - 7.06 (m, 3H), 6.88 (d, *J*=7.9 Hz, 1H), 6.82 (d, *J*=6.4 Hz, 2H), 6.76 - 6.39 (m, 3H), 6.06 (s, 2H), 4.28 (br. s., 1H), 3.08 (s, 3H), 2.82 - 2.53 (m, 2H).

Example 16

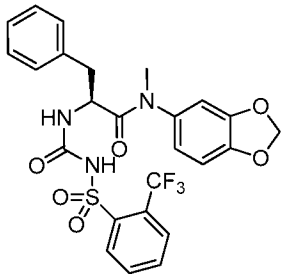


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((5-fluoro-2-methylphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	514.1
MS $(M+H)^+$ Observ.	514.3
Retention Time	1.57 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.50 (d, *J*=7.6 Hz, 1H), 7.41 - 7.25 (m, 2H), 7.22 - 7.06 (m, 3H), 6.88 (d, *J*=8.2 Hz, 1H), 6.83 - 6.27 (m, 5H), 6.06 (s, 2H), 4.28 (br. s., 1H), 3.06 (s, 3H), 2.78 - 2.48 (m, 2H), 2.46 (s, 3H).

Example 17

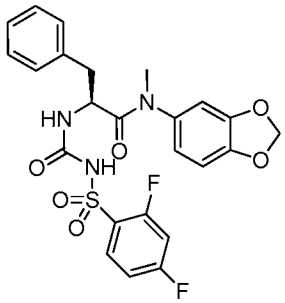


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(trifluoromethyl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	550.1
MS $(M+H)^+$ Observ.	550.3
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.06 (br. s., 1H), 7.93 - 7.68 (m, 3H), 7.12 (br. s., 3H), 6.88 (d, *J*=8.2 Hz, 1H), 6.83 - 6.40 (m, 5H), 6.06 (s, 2H), 4.29 (d, *J*=5.5 Hz, 1H), 3.06 (s, 3H), 2.77 - 2.48 (m, 2H).

Example 18

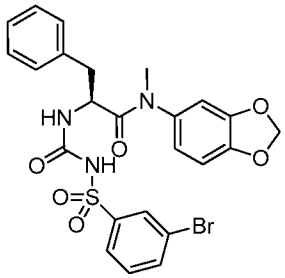


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,4-difluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	518.1
MS $(M+H)^+$ Observ.	518.2
Retention Time	1.54 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.71 (br. s., 1H), 7.42 - 6.99 (m, 6H), 6.92 - 6.77 (m, 3H), 6.73 - 6.39 (m, 2H), 6.06 (s, 2H), 4.26 (br. s., 1H), 3.06 (s, 3H), 2.74 - 2.48 (m, 2H).

Example 19

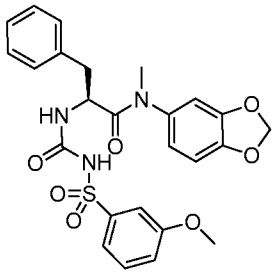


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3-bromophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	560.0
MS $(M+H)^+$ Observ.	560.1
Retention Time	1.63 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.87 (br. s., 1H), 7.71 (d, *J*=8.2 Hz, 2H), 7.44 (br. s., 1H), 7.21 - 7.09 (m, 3H), 6.93 - 6.78 (m, 3H), 6.74 - 6.26 (m, 3H), 6.07 (s, 2H), 4.27 (d, *J*=6.4 Hz, 1H), 3.06 (s, 3H), 2.75 - 2.53 (m, 2H).

Example 20

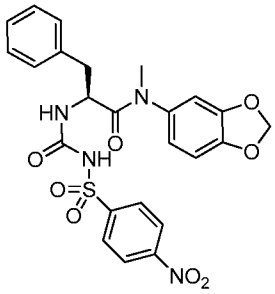


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3-methoxyphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	512.1
MS $(M+H)^+$ Observ.	512.2
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.41 (d, *J*=8.1 Hz, 1H), 7.36 - 7.25 (m, 2H), 7.16 (m, 5H), 6.92 - 6.78 (m, 3H), 6.72 - 6.46 (m, 2H), 6.08 (s, 2H), 4.30 (d, *J*=5.9 Hz, 1H), 3.80 (s, 3H), 3.07 (s, 3H), 2.77 - 2.53 (m, 2H).

Example 21

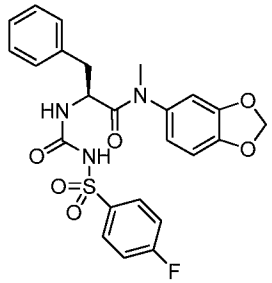


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-((4-nitrophenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	527.1
MS $(M+H)^+$ Observ.	527.2
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.22 (d, *J*=7.6 Hz, 2H), 7.90 (d, *J*=7.9 Hz, 2H), 7.22 - 7.05 (m, 3H), 6.95 - 6.75 (m, 3H), 6.74 - 6.50 (m, 2H), 6.11 (br. s., 1H), 6.05 (s, 2H), 4.24 (br. s., 1H), 3.04 (s, 3H), 2.70 - 2.52 (m, 2H).

Example 22

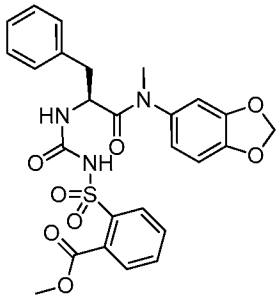


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((4-fluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	500.1
MS $(M+H)^+$ Observ.	500.3
Retention Time	1.32 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.89 (dd, *J*=8.6, 5.1 Hz, 2H), 7.33 - 7.11 (m, 6H), 6.91 (br. s., 2H), 6.73 (d, *J*=8.3 Hz, 1H), 6.59 - 6.17 (m, 2H), 5.99 (d, *J*=2.7 Hz, 2H), 4.57 - 4.40 (m, 1H), 3.11 (s, 3H), 2.93 - 2.64 (m, 2H).

Example 23

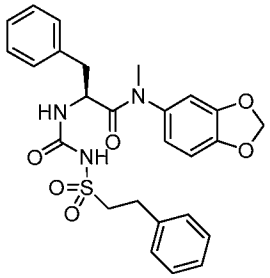


(S)-methyl 2-(N-((1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamoyl)sulfamoyl)benzoate

MS $(M+H)^+$ Calcd.	540.1
MS $(M+H)^+$ Observ.	540.4
Retention Time	1.32 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.85 (d, *J*=7.7 Hz, 1H), 7.69 - 7.42 (m, 3H), 7.36 - 7.08 (m, 3H), 6.99 - 6.80 (m, 3H), 6.64 - 6.41 (m, 3H), 6.06 (s, 2H), 4.30 (br. s., 1H), 3.78 (s, 3H), 3.06 (s, 3H), 2.81 - 2.52 (m, 2H).

Example 24

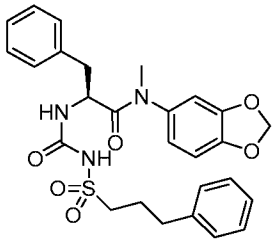


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(phenethylsulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.57 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.40 - 7.08 (m, 9H), 7.00 - 6.84 (m, 3H), 6.81 - 6.31 (m, 2H), 6.09 (s, 2H), 4.39 (br. s., 1H), 3.10 (s, 3H), 2.88 - 2.82 (m, 4H), 2.61 - 2.52 (m, 2H).

Example 25

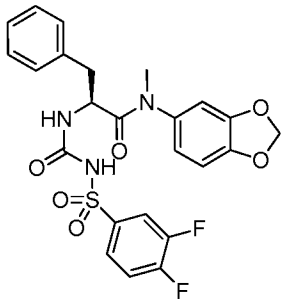


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((3-phenylpropyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	524.2
MS $(M+H)^+$ Observ.	524.3
Retention Time	1.68 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.33 - 7.25 (m, 3H), 7.24 - 7.14 (m, 6H), 6.96 (d, *J*=8.1 Hz, 1H), 6.90 (d, *J*=6.6 Hz, 2H), 6.80 - 6.60 (m, 2H), 6.11 (s, 2H), 4.41 (d, *J*=5.5 Hz, 1H), 3.23 - 3.15 (m, 2H), 3.11 (s, 3H), 2.87 (dd, *J*=13.6, 4.8 Hz, 1H), 2.68 - 2.54 (m, 3H), 1.91 - 1.79 (m, 2H).

Example 26

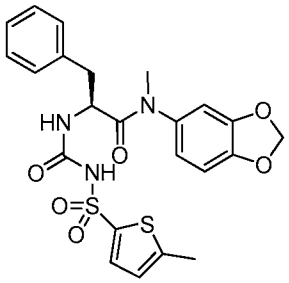


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3,4-difluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	518.1
MS $(M+H)^+$ Observ.	518.2
Retention Time	1.37 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 - 7.42 (m, 3H), 7.22 - 7.11 (m, 3H), 6.90 (d, *J*=7.7 Hz, 1H), 6.83 (d, *J*=5.1 Hz, 2H), 6.76 - 6.17 (m, 2H), 6.08 (s, 2H), 4.27 (d, *J*=5.1 Hz, 1H), 3.07 (s, 3H), 2.80 - 2.52 (m, 2H).

Example 27

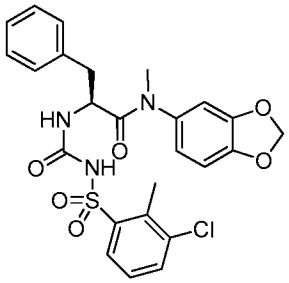


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-((5-methylthiophen-2-yl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	502.1
MS $(M+H)^+$ Observ.	502.3
Retention Time	1.35 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.17 (br. s., 4H), 6.97 - 6.80 (m, 3H), 6.76 - 6.53 (m, 3H), 6.22 (br. s., 1H), 6.08 (s, 2H), 4.32 (d, *J*=4.8 Hz, 1H), 3.07 (s, 3H), 2.82 - 2.53 (m, 2H), 2.43 (s, 3H).

Example 28

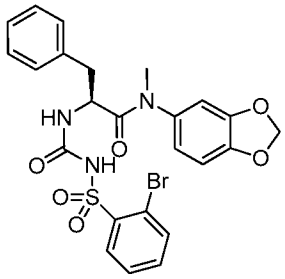


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3-chloro-2-methylphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.4
Retention Time	1.53 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=8.1 Hz, 1H), 7.62 (d, *J*=7.7 Hz, 1H), 7.30 (br. s., 1H), 7.20 - 7.03 (m, 4H), 6.88 (d, *J*=8.1 Hz, 1H), 6.79 (d, *J*=6.6 Hz, 2H), 6.73 - 6.31 (m, 2H), 6.06 (s, 2H), 4.26 (br. s., 1H), 3.06 (s, 3H), 2.80 - 2.55 (m, 2H), 2.53 (s, 3H).

Example 29

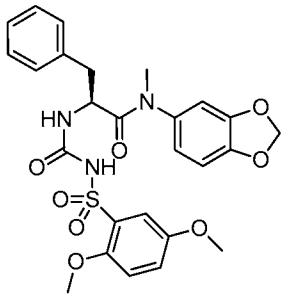


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-bromophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	560.0
MS $(M+H)^+$ Observ.	560.3
Retention Time	1.35 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.94 (d, *J*=7.7 Hz, 1H), 7.77 (d, *J*=6.2 Hz, 1H), 7.48 (br. s., 2H), 7.34 - 7.09 (m, 3H), 6.85 (dd, *J*=13.0, 7.5 Hz, 3H), 6.72 - 6.46 (m, 3H), 6.06 (s, 2H), 4.28 (d, *J*=4.8 Hz, 1H), 3.07 (s, 3H), 2.81 - 2.52 (m, 2H).

Example 30

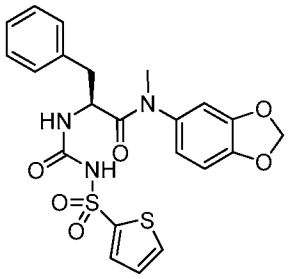


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,5-dimethoxyphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	542.2
MS $(M+H)^+$ Observ.	542.5
Retention Time	1.50 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.30 - 7.10 (m, 7H), 6.92 - 6.77 (m, 3H), 6.75 - 6.47 (m, 3H), 6.07 (s, 2H), 4.29 (d, *J*=4.8 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.06 (s, 3H), 2.85 - 2.52 (m, 2H).

Example 31

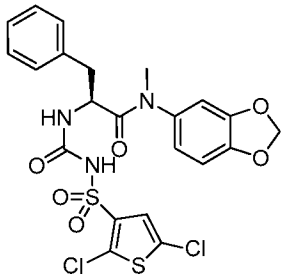


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-(thiophen-2-ylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	488.1
MS $(M+H)^+$ Observ.	488.2
Retention Time	1.19 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.85 (br. s., 1H), 7.52 (br. s., 1H), 7.31 - 7.00 (m, 4H), 6.97 - 6.77 (m, 3H), 6.74 - 6.41 (m, 3H), 6.08 (s, 2H), 4.35 (d, *J*=6.1 Hz, 1H), 3.08 (s, 3H), 2.84 - 2.53 (m, 2H).

Example 32

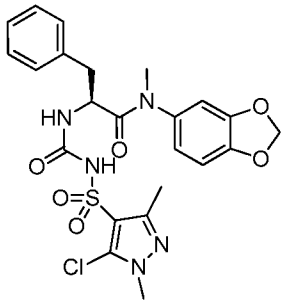


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,5-dichlorothiophen-3-yl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	556.0
MS $(M+H)^+$ Observ.	556.2
Retention Time	1.42 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.25 - 7.08 (m, 4H), 6.91 (d, *J*=7.9 Hz, 1H), 6.85 (d, *J*=6.7 Hz, 2H), 6.77 - 6.41 (m, 2H), 6.08 (s, 2H), 4.32 (d, *J*=5.2 Hz, 1H), 3.08 (s, 3H), 2.84 - 2.52 (m, 2H).

Example 33

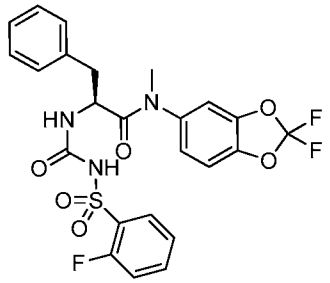


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	534.1
MS $(M+H)^+$ Observ.	534.3
Retention Time	1.18 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.18 (br. s., 3H), 6.91 (d, *J*=7.9 Hz, 1H), 6.84 (d, *J*=5.2 Hz, 2H), 6.77 - 6.38 (m, 3H), 6.08 (s, 2H), 4.31 (d, *J*=5.8 Hz, 1H), 3.74 (s, 3H), 3.08 (s, 3H), 2.84 - 2.53 (m, 2H), 2.24 (s, 3H).

Example 34

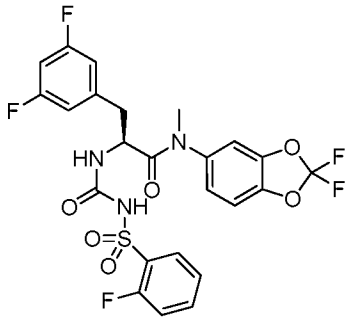


(S)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-2-(3-((2-fluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	536.1
MS $(M+H)^+$ Observ.	536.2
Retention Time	2.54 min
	LC Condition
Solvent A	5 % Methanol : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % Methanol : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	Methanol : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.69 (br. s., 1H), 7.51 (br. s., 1H), 7.36 (d, *J*=8.1 Hz, 1H), 7.30 - 7.00 (m, 6H), 6.95 - 6.77 (m, 2H), 6.30 (br. s., 1H), 4.20 (br. s., 1H), 3.08 (s, 3H), 2.77 - 2.53 (m, 2H).

Example 35



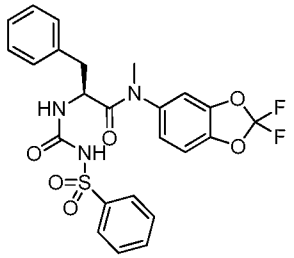
(S)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-3-(3,5-difluorophenyl)-2-(3-((2-fluorophenyl)sulfonyl)ureido)-N-methylpropanamide

MS $(M+H)^+$ Calcd.	572.1
MS $(M+H)^+$ Observ.	572.4
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.69 (br. s., 1H), 7.55 (br. s., 1H), 7.41 (d, *J*=8.4 Hz, 1H), 7.36 (br. s., 1H), 7.24 (d, *J*=7.7 Hz, 2H), 7.10 (br. s., 1H), 6.99 (br. s., 1H), 6.58 - 6.29 (m, 3H), 4.23 (d, *J*=5.5 Hz, 1H), 3.11 (s, 3H), 2.83 - 2.56 (m, 2H).

Examples 36 – 41 were synthesized using the procedure described above for Example 2.

Example 36

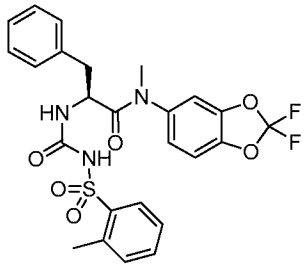


(S)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-(phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	518.1
MS $(M+H)^+$ Observ.	518.3
Retention Time	1.65 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.80 (d, *J*=7.3 Hz, 2H), 7.67 - 7.50 (m, 3H), 7.41 (d, *J*=8.4 Hz, 1H), 7.28 - 7.01 (m, 4H), 6.99 - 6.63 (m, 4H), 4.23 (d, *J*=7.3 Hz, 1H), 3.09 (s, 3H), 2.84 - 2.53 (m, 2H).

Example 37

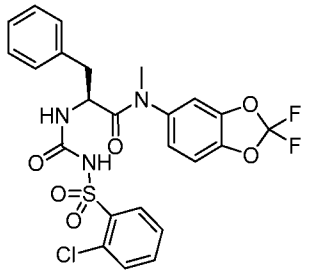


(S)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	532.1
MS $(M+H)^+$ Observ.	532.4
Retention Time	1.68 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.81 (d, *J*=7.7 Hz, 1H), 7.60 - 7.48 (m, 1H), 7.44 - 7.31 (m, 3H), 7.24 - 7.06 (m, 4H), 6.95 (d, *J*=8.1 Hz, 1H), 6.81 (d, *J*=3.7 Hz, 2H), 6.68 (d, *J*=7.7 Hz, 1H), 4.23 (d, *J*=6.6 Hz, 1H), 3.10 (s, 3H), 2.85 - 2.55 (m, 2H), 2.53 (s, 3H).

Example 38

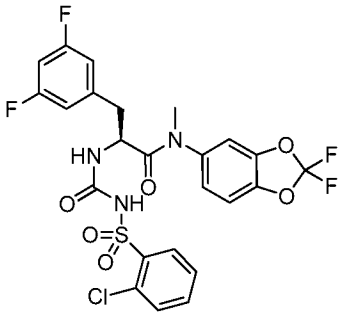


(S)-2-(3-((2-chlorophenyl)sulfonyl)ureido)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	552.1
MS $(M+H)^+$ Observ.	552.4
Retention Time	1.59 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.89 (d, *J*=6.6 Hz, 1H), 7.50 (br. s., 2H), 7.43 - 7.00 (m, 8H), 6.96 - 6.77 (m, 2H), 6.48 - 6.22 (m, 1H), 4.20 (br. s., 1H), 3.08 (s, 3H), 2.79 - 2.53 (m, 2H).

Example 39

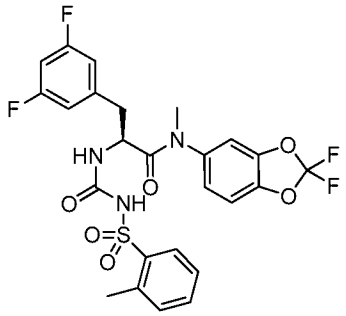


(S)-2-(3-((2-chlorophenyl)sulfonyl)ureido)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-3-(3,5-difluorophenyl)-N-methylpropanamide

MS $(M+H)^+$ Calcd.	588.1
MS $(M+H)^+$ Observ.	588.4
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.88 (d, *J*=7.0 Hz, 1H), 7.58 - 7.18 (m, 5H), 7.16 - 6.89 (m, 2H), 6.51 (br. s., 3H), 4.25 (br. s., 1H), 3.12 (s, 3H), 2.83 - 2.57 (m, 2H).

Example 40

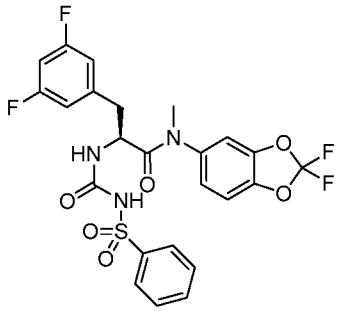


(S)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	568.1
MS $(M+H)^+$ Observ.	568.4
Retention Time	1.71 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=7.0 Hz, 1H), 7.49 - 7.34 (m, 3H), 7.29 (d, *J*=5.9 Hz, 2H), 7.17 - 6.90 (m, 2H), 6.64 - 6.38 (m, 3H), 4.24 (br. s., 1H), 3.12 (s, 3H), 2.85 - 2.55 (m, 2H), 2.51 (s, 3H).

Example 41



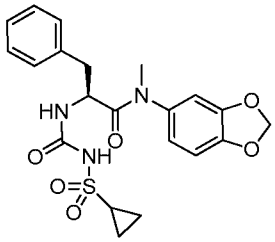
(S)-N-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	554.1
MS $(M+H)^+$ Observ.	554.3
Retention Time	1.62 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.80 (d, *J*=7.7 Hz, 2H), 7.70 - 7.62 (m, 1H), 7.60 - 7.51 (m, 2H), 7.45 (d, *J*=8.4 Hz, 1H), 7.39 (br. s., 1H), 7.11 (d, *J*=8.4 Hz, 1H), 7.01 (t, *J*=8.8 Hz, 1H), 6.81 (d, *J*=7.7 Hz, 1H), 6.51 (d, *J*=7.0 Hz, 2H), 4.28 (d, *J*=5.5 Hz, 1H), 3.13 (s, 3H), 2.87 - 2.58 (m, 2H).

Examples 42 – 46 were synthesized using the procedure described above for Example 4.

Example 42

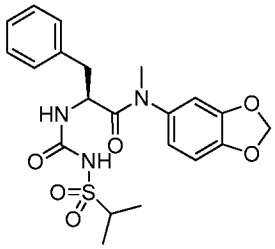


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-(cyclopropylsulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	446.1
MS $(M+H)^+$ Observ.	446.2
Retention Time	1.71 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.29 - 7.14 (m, 3H), 6.96 (d, *J*=8.2 Hz, 1H), 6.90 (d, *J*=7.0 Hz, 2H), 6.80 - 6.59 (m, 3H), 6.10 (d, *J*=3.4 Hz, 2H), 4.42 (d, *J*=5.8 Hz, 1H), 3.10 (s, 3H), 2.87 - 2.54 (m, 3H), 1.04 - 0.89 (m, 4H).

Example 43

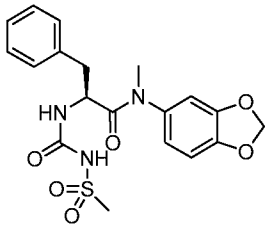


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-(isopropylsulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	448.2
MS $(M+H)^+$ Observ.	448.2
Retention Time	1.72 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.25 - 7.20 (m, 3H), 6.97 (d, *J*=8.2 Hz, 1H), 6.90 (d, *J*=7.0 Hz, 2H), 6.83 - 6.58 (m, 3H), 6.11 (s, 2H), 4.43 (d, *J*=5.5 Hz, 1H), 3.11 (s, 3H), 2.88 - 2.55 (m, 3H), 1.27 - 1.07 (m, 6H).

Example 44

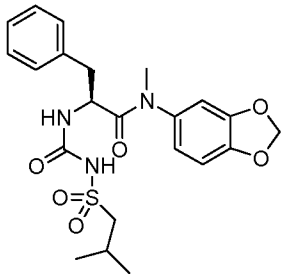


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(methylsulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	420.1
MS $(M+H)^+$ Observ.	420.2
Retention Time	1.42 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.31 - 7.15 (m, 3H), 6.97 (d, *J*=8.2 Hz, 1H), 6.91 (d, *J*=7.0 Hz, 2H), 6.81 - 6.56 (m, 3H), 6.11 (d, *J*=2.1 Hz, 2H), 4.42 (d, *J*=5.8 Hz, 1H), 3.11 (s, 3H), 3.08 (s, 3H), 2.89 - 2.55 (m, 2H).

Example 45

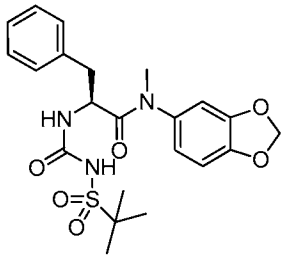


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-(isobutylsulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	462.2
MS $(M+H)^+$ Observ.	462.3
Retention Time	1.45 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (s, 1H), 7.01 - 6.96 (m, 3H), 6.73 (d, *J*=7.9 Hz, 1H), 6.66 (d, *J*=7.0 Hz, 2H), 6.58 - 6.31 (m, 3H), 5.87 (d, *J*=4.0 Hz, 2H), 4.19 (d, *J*=4.9 Hz, 1H), 2.87 (s, 3H), 2.70 - 2.30 (m, 4H), 1.74 (dt, *J*=13.0, 6.4 Hz, 1H), 0.71 (dd, *J*=17.5, 6.6 Hz, 6H).

Example 46

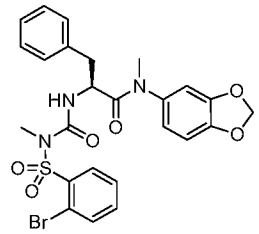


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-(tert-butylsulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	462.2
MS $(M+H)^+$ Observ.	462.3
Retention Time	1.52 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.34 - 7.13 (m, 3H), 6.95 (d, *J*=7.9 Hz, 1H), 6.91 - 6.81 (m, 3H), 6.77 - 6.60 (m, 2H), 6.10 (d, *J*=4.9 Hz, 2H), 4.44 (d, *J*=5.5 Hz, 1H), 3.09 (s, 3H), 2.94 - 2.54 (m, 2H), 1.21 (s, 9H).

Example 47



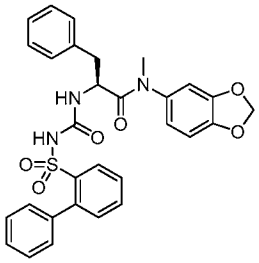
(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-bromophenyl)sulfonyl)-3-methylureido)-N-methyl-3-phenylpropanamid

To a solution of (S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-bromophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide (30 mg, 0.054 mmol) in acetonitrile (1 mL) was added K_2CO_3 (74.0 mg, 0.535 mmol) followed by iodomethane (76 mg, 0.535 mmol). The reaction mixture was stirred at r.t. for 20 hrs. The solvent was filtered and evaporated and the residue was purified by preparative HPLC to afford the title compound (15.7 mg). ^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.05 - 7.95 (m, 1H), 7.86 (d, *J*=8.4 Hz, 1H), 7.66 - 7.56 (m, 2H), 7.53 (d, *J*=7.3 Hz, 1H), 7.27 - 7.12 (m, 3H), 6.92 (d, *J*=8.1 Hz, 1H), 6.83 (d, *J*=6.2 Hz, 2H), 6.73 - 6.66 (m, 1H), 6.63 (d, *J*=8.1 Hz, 1H), 6.08 (s, 2H), 4.35 (d, *J*=3.7 Hz, 1H), 3.16 (s, 3H), 3.09 (s, 3H), 2.94 - 2.66 (m, 2H).

MS $(M+H)^+$ Calcd.	574.1
MS $(M+H)^+$ Observ.	574.5
Retention Time	1.98 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220

Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 48



(S)-2-(3-([1,1'-biphenyl]-2-ylsulfonyl)ureido)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenylpropanamide

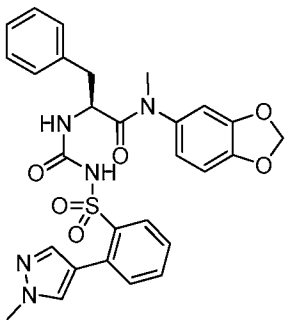
To a 0.5-2 mL microwave tube was added (S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-bromophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide (17 mg, 0.030 mmol), phenylboronic acid (7.40 mg, 0.061 mmol), $Pd(PPh_3)_4$ (3.51 mg, 3.03 µmol) and DMF (1 mL), followed by 2M aq. Na_2CO_3 (50µl). The reaction mixture was heated in a microwave reactor at 125°C for 15 min. The reaction mixture was filtered and the filtrate was purified by preparative HPLC to afford of the title compound (8.8 mg). ^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.91 (d, *J*=7.0 Hz, 1H), 7.56 - 7.10 (m, 12H), 6.87 (d, *J*=6.2 Hz, 3H), 6.70 - 6.49 (m, 2H), 6.20 - 6.11 (m, 1H), 6.07 (s, 2H), 4.29 (br. s., 1H), 3.06 (s, 3H), 2.80 - 2.53 (m, 2H).

MS $(M+H)^+$ Calcd.	558.2
MS $(M+H)^+$ Observ.	558.3
Retention Time	1.74 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100

Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Examples 49 – 50 were synthesized using the procedure described above for Example 48.

Example 49



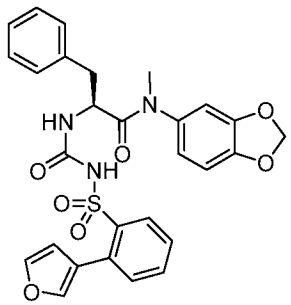
(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-((2-(1-methyl-1H-pyrazol-4-yl)phenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	562.2
MS $(M+H)^+$ Observ.	562.3
Retention Time	1.43 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220

Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.00 (br. s., 1H), 7.89 (d, *J*=7.7 Hz, 1H), 7.62 (br. s., 1H), 7.52 (br. s., 1H), 7.38 (d, *J*=7.7 Hz, 2H), 7.17 (br. s., 3H), 6.92 - 6.78 (m, 3H), 6.69 - 6.29 (m, 3H), 6.06 (s, 2H), 4.27 (br. s., 1H), 3.88 (s, 3H), 3.06 (s, 3H), 2.73 - 2.47 (m, 2H).

Example 50



(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-(furan-3-yl)phenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

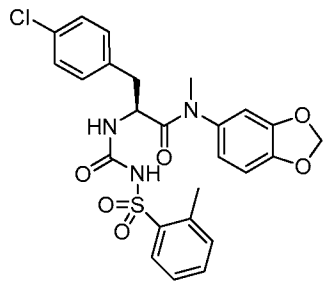
MS $(M+H)^+$ Calcd.	548.1
MS $(M+H)^+$ Observ.	548.3
Retention Time	1.58 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm

particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.93 (d, *J*=7.7 Hz, 1H), 7.81 - 7.61 (m, 3H), 7.52 (t, *J*=7.3 Hz, 1H), 7.42 (d, *J*=7.3 Hz, 1H), 7.27 - 7.11 (m, 3H), 6.90 (d, *J*=8.1 Hz, 1H), 6.83 (d, *J*=5.5 Hz, 2H), 6.69 - 6.48 (m, 4H), 6.07 (s, 2H), 4.28 (d, *J*=5.9 Hz, 1H), 3.07 (s, 3H), 2.84 - 2.43 (m, 2H).

Examples 51 – 85 were synthesized using the procedure described above for Example 2.

Example 51



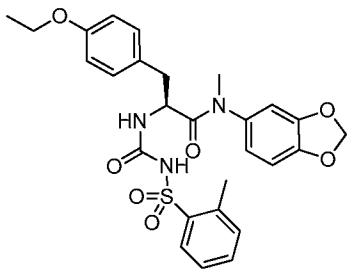
(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-chlorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.3
Retention Time	1.60 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm

particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 (d, *J*=7.7 Hz, 1H), 7.54 - 7.08 (m, 5H), 6.98 - 6.59 (m, 5H), 6.52 - 6.31 (m, 1H), 6.07 (s, 2H), 4.27 (br. s., 1H), 3.07 (s, 3H), 2.73 - 2.54 (m, 2H), 2.51 (s, 3H).

Example 52

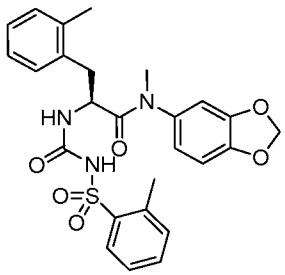


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-ethoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	540.2
MS $(M+H)^+$ Observ.	540.3
Retention Time	1.55 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=8.1 Hz, 1H), 7.42 (br. s., 1H), 7.29 (br. s., 2H), 6.87 (d, *J*=8.1 Hz, 1H), 6.76 - 6.26 (m, 6H), 6.07 (s, 2H), 4.22 (br. s., 1H), 3.96 (q, *J*=6.7 Hz, 2H), 3.06 (s, 3H), 2.72 - 2.35 (m, 5H), 1.31 (t, *J*=6.6 Hz, 3H).

Example 53

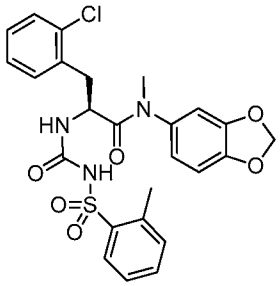


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-(o-tolyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.65 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 (d, *J*=7.7 Hz, 1H), 7.43 (br. s., 1H), 7.29 (d, *J*=7.0 Hz, 2H), 7.10 - 7.04 (m, 1H), 7.03 - 6.96 (m, 2H), 6.80 (t, *J*=8.4 Hz, 2H), 6.40 (br. s., 2H), 6.04 (d, *J*=5.5 Hz, 2H), 4.38 (d, *J*=6.6 Hz, 1H), 3.02 (s, 3H), 2.77 - 2.48 (m, 5H), 1.82 (s, 3H).

Example 54

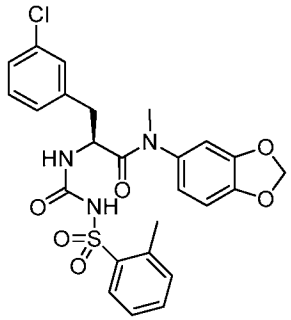


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(2-chlorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.3
Retention Time	1.59 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (d, *J*=7.7 Hz, 1H), 7.40 (br. s., 1H), 7.32 - 7.08 (m, 6H), 7.01 (br. s., 1H), 6.84 (d, *J*=7.3 Hz, 1H), 6.73 - 6.27 (m, 2H), 6.04 (d, *J*=7.0 Hz, 2H), 4.51 (br. s., 1H), 3.06 (s, 3H), 2.89 - 2.60 (m, 2H), 2.50 (s, 3H).

Example 55

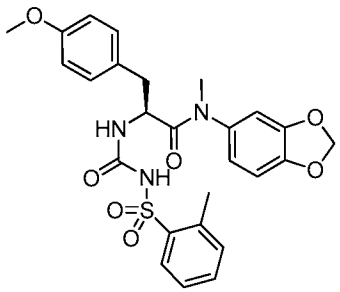


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3-chlorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.2
Retention Time	1.64 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 (d, *J*=7.0 Hz, 1H), 7.44 - 7.32 (m, 1H), 7.31 - 7.12 (m, 4H), 6.89 (d, *J*=8.4 Hz, 1H), 6.85 - 6.25 (m, 4H), 6.07 (d, *J*=5.9 Hz, 2H), 4.32 - 4.17 (m, 1H), 3.07 (s, 3H), 2.75 - 2.48 (m, 5H).

Example 56

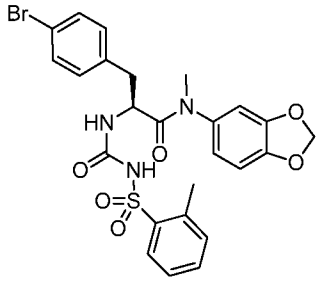


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-methoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	526.2
MS $(M+H)^+$ Observ.	526.3
Retention Time	1.51 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 - 7.69 (m, 1H), 7.45 - 7.17 (m, 3H), 6.90 - 6.83 (m, 1H), 6.71 (s, 4H), 6.66 - 6.31 (m, 2H), 6.04 (s, 2H), 4.29 - 4.12 (m, 1H), 3.69 (s, 3H), 3.04 (s, 3H), 2.71 - 2.35 (m, 5H).

Example 57

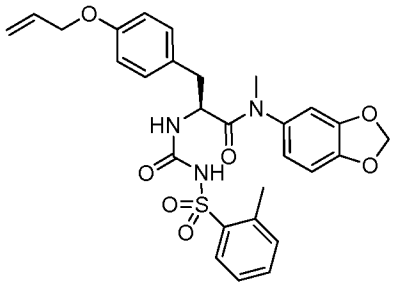


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-bromophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	574.1
MS $(M+H)^+$ Observ.	574.3
Retention Time	1.64 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (d, *J*=7.7 Hz, 1H), 7.49 - 7.07 (m, 5H), 6.87 (d, *J*=7.7 Hz, 1H), 6.80 - 6.34 (m, 4H), 6.06 (s, 2H), 4.26 (br. s., 1H), 3.06 (s, 3H), 2.79 - 2.34 (m, 5H).

Example 58

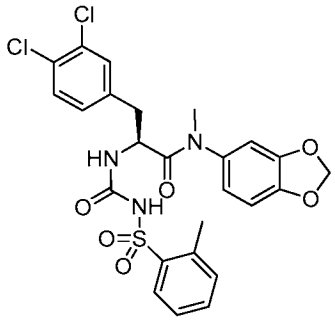


(S)-3-(4-(allyloxy)phenyl)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	552.2
MS $(M+H)^+$ Observ.	552.4
Retention Time	1.64 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=7.3 Hz, 1H), 7.54 - 7.25 (m, 3H), 6.89 (d, *J*=8.4 Hz, 1H), 6.78 - 6.66 (m, 5H), 6.63 - 6.45 (m, 2H), 6.13 - 5.96 (m, 3H), 5.45 - 5.17 (m, 2H), 4.51 (d, *J*=5.1 Hz, 2H), 4.24 (d, *J*=5.1 Hz, 1H), 3.07 (s, 3H), 2.78 - 2.38 (m, 5H).

Example 59

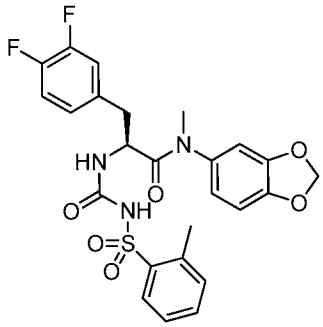


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3,4-dichlorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.2
Retention Time	1.69 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.73 (d, *J*=7.7 Hz, 1H), 7.51 - 7.06 (m, 5H), 7.00 (br. s., 1H), 6.90 (d, *J*=8.1 Hz, 1H), 6.85 - 6.66 (m, 3H), 6.42 (br. s., 1H), 6.08 (d, *J*=7.7 Hz, 2H), 4.29 (br. s., 1H), 3.08 (s, 3H), 2.79 - 2.46 (m, 5H).

Example 60

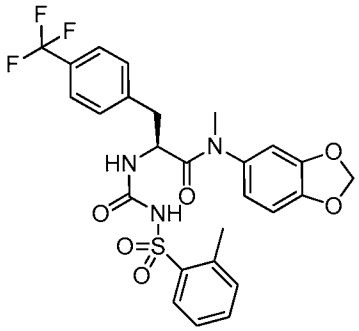


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3,4-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	532.1
MS $(M+H)^+$ Observ.	532.2
Retention Time	1.71 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=8.1 Hz, 1H), 7.51 (t, *J*=7.2 Hz, 1H), 7.40 - 7.29 (m, 2H), 7.24 - 7.13 (m, 1H), 6.93 (d, *J*=8.1 Hz, 1H), 6.86 (s, 1H), 6.82 - 6.47 (m, 4H), 6.08 (d, *J*=7.3 Hz, 2H), 4.31 (d, *J*=4.0 Hz, 1H), 3.09 (s, 3H), 2.84 - 2.45 (m, 5H).

Example 61

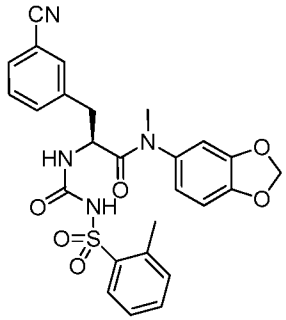


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)-3-(4-(trifluoromethyl)phenyl)propanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.2
Retention Time	1.69 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.3 Hz, 1H), 7.55 - 7.42 (m, 3H), 7.38 - 7.26 (m, 2H), 7.00 (d, *J*=7.7 Hz, 2H), 6.90 (d, *J*=8.1 Hz, 1H), 6.83 - 6.55 (m, 3H), 6.08 (d, *J*=2.6 Hz, 2H), 4.34 (d, *J*=4.8 Hz, 1H), 3.09 (s, 3H), 2.92 - 2.57 (m, 2H), 2.50 (s, 3H).

Example 62

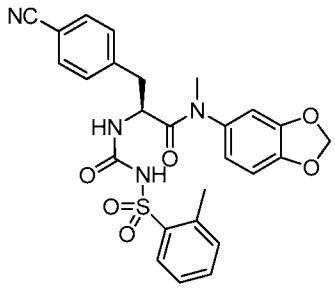


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3-cyanophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	521.1
MS $(M+H)^+$ Observ.	521.3
Retention Time	1.35 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.71 (d, *J*=7.7 Hz, 1H), 7.60 (d, *J*=7.7 Hz, 1H), 7.45 - 7.04 (m, 6H), 6.89 (d, *J*=8.1 Hz, 1H), 6.79 - 6.28 (m, 2H), 6.06 (d, *J*=8.1 Hz, 2H), 4.28 (br. s., 1H), 3.06 (br. s., 3H), 2.83 - 2.55 (m, 2H), 2.48 (s, 3H).

Example 63

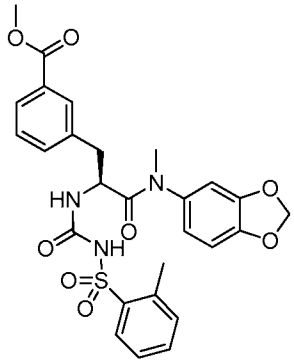


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-cyanophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	521.1
MS $(M+H)^+$ Observ.	521.3
Retention Time	1.60 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.75 - 7.51 (m, 3H), 7.41 - 7.07 (m, 3H), 6.98 (d, *J*=5.1 Hz, 2H), 6.88 (d, *J*=8.1 Hz, 1H), 6.78 - 6.17 (m, 2H), 6.06 (br. s., 2H), 4.29 (br. s., 1H), 3.06 (s, 3H), 2.84 - 2.56 (m, 2H), 2.48 (s, 3H).

Example 64

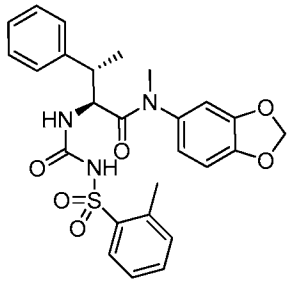


(S)-methyl 3-(3-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-3-oxo-2-(3-(o-tolylsulfonyl)ureido)propyl)benzoate

MS $(M+H)^+$ Calcd.	554.2
MS $(M+H)^+$ Observ.	554.3
Retention Time	1.48 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (dd, *J*=19.6, 7.5 Hz, 2H), 7.42 - 7.04 (m, 6H), 6.91 - 6.24 (m, 3H), 6.05 (d, *J*=10.6 Hz, 2H), 4.27 (br. s., 1H), 3.83 (s, 3H), 3.05 (s, 3H), 2.85 - 2.54 (m, 2H), 2.47 (s, 3H).

Example 65

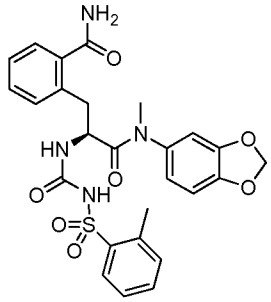


(2S,3S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)butanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.48 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.71 (d, *J*=8.1 Hz, 1H), 7.41 (br. s., 1H), 7.33 - 7.10 (m, 6H), 6.94 (d, *J*=6.6 Hz, 2H), 6.90 - 6.57 (m, 3H), 6.08 (s, 2H), 4.45 (br. s., 1H), 3.08 (s, 3H), 2.85 (t, *J*=7.0 Hz, 1H), 2.51 (s, 3H), 0.94 (d, *J*=7.0 Hz, 3H).

Example 66

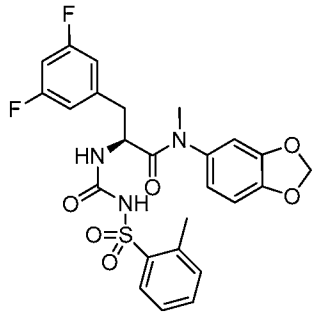


(S)-2-(3-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-3-oxo-2-(3-(o-tolylsulfonyl)ureido)propyl)benzamide

MS $(M+H)^+$ Calcd.	539.2
MS $(M+H)^+$ Observ.	539.3
Retention Time	1.41 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.71 (br. s., 2H), 7.54 - 7.03 (m, 7H), 6.99 - 6.78 (m, 1H), 6.64 (br. s., 2H), 6.07 (s, 2H), 4.33 (br. s., 1H), 3.08 (s, 3H), 2.90 - 2.62 (m, 2H), 2.48 (s, 3H).

Example 67

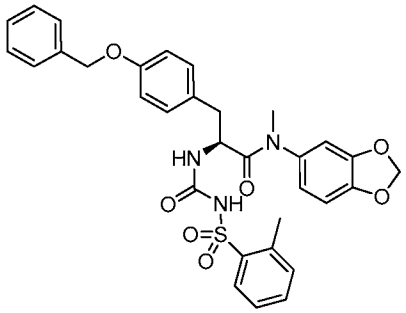


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	532.1
MS $(M+H)^+$ Observ.	532.2
Retention Time	1.52 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.73 (d, *J*=7.7 Hz, 1H), 7.37 (br. s., 1H), 7.23 (br. s., 2H), 7.04 - 6.80 (m, 3H), 6.78 - 6.65 (m, 1H), 6.48 (d, *J*=7.0 Hz, 2H), 6.36 (br. s., 1H), 6.07 (d, *J*=6.6 Hz, 2H), 4.29 (br. s., 1H), 3.08 (s, 3H), 2.82 - 2.54 (m, 2H), 2.49 (s, 3H).

Example 68

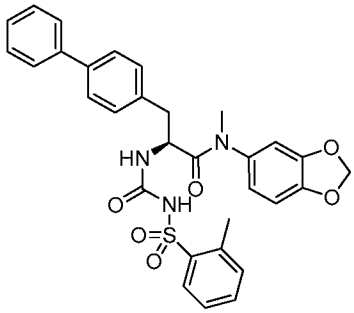


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-(benzyloxy)phenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	602.2
MS $(M+H)^+$ Observ.	602.3
Retention Time	1.81 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=7.3 Hz, 1H), 7.53 - 7.22 (m, 8H), 6.90 - 6.77 (m, 3H), 6.71 (d, *J*=8.4 Hz, 3H), 6.62 - 6.39 (m, 2H), 6.07 (s, 2H), 5.05 (s, 2H), 4.24 (br. s., 1H), 3.06 (s, 3H), 2.75 - 2.35 (m, 5H).

Example 69

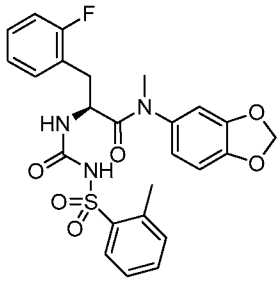


(S)-3-([1,1'-biphenyl]-4-yl)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	572.2
MS $(M+H)^+$ Observ.	572.4
Retention Time	1.81 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=6.6 Hz, 1H), 7.62 (d, *J*=7.3 Hz, 2H), 7.46 (d, *J*=7.3 Hz, 4H), 7.41 - 7.18 (m, 4H), 6.90 (d, *J*=7.0 Hz, 3H), 6.79 - 6.38 (m, 3H), 6.08 (s, 2H), 4.32 (br. s., 1H), 3.09 (s, 3H), 2.86 - 2.42 (m, 5H).

Example 70

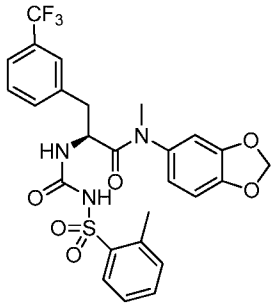


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(2-fluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	514.1
MS $(M+H)^+$ Observ.	514.3
Retention Time	1.49 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.73 (d, *J*=7.7 Hz, 1H), 7.41 (br. s., 1H), 7.33 - 7.16 (m, 3H), 7.05 - 6.95 (m, 2H), 6.94 - 6.81 (m, 2H), 6.77 - 6.25 (m, 3H), 6.07 (s, 2H), 4.37 (br. s., 1H), 3.06 (s, 3H), 2.80 - 2.54 (m, 2H), 2.51 (s, 3H).

Example 71

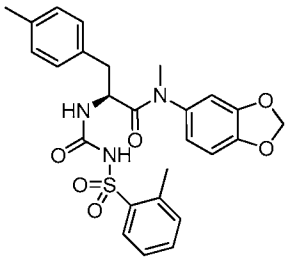


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)-3-(3-(trifluoromethyl)phenyl)propanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.3
Retention Time	1.64 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (d, *J*=7.7 Hz, 1H), 7.50 (br. s., 1H), 7.39 (t, *J*=7.7 Hz, 1H), 7.34 (br. s., 1H), 7.27 - 7.02 (m, 5H), 6.86 (d, *J*=8.1 Hz, 1H), 6.78 - 6.24 (m, 2H), 6.13 - 5.94 (m, 2H), 4.34 - 4.18 (m, 1H), 3.06 (s, 3H), 2.85 - 2.59 (m, 2H), 2.49 (s, 3H).

Example 72

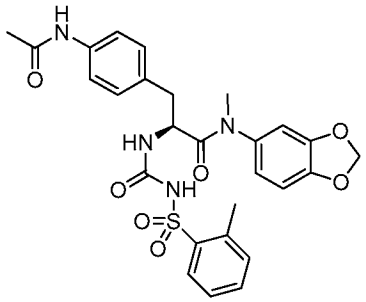


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-(p-tolyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.58 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.7 Hz, 1H), 7.46 (d, *J*=7.0 Hz, 1H), 7.37 - 7.24 (m, 2H), 6.96 (d, *J*=7.7 Hz, 2H), 6.88 (d, *J*=8.1 Hz, 1H), 6.74 - 6.39 (m, 5H), 6.07 (s, 2H), 4.25 (d, *J*=5.9 Hz, 1H), 3.06 (s, 3H), 2.77 - 2.39 (m, 5H), 2.23 (s, 3H).

Example 73

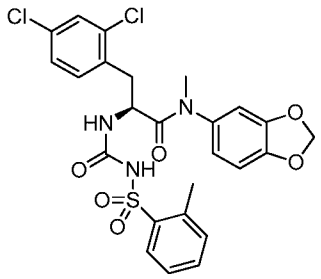


(S)-3-(4-acetamidophenyl)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	553.2
MS $(M+H)^+$ Observ.	553.3
Retention Time	1.33 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 9.86 (br. s., 1H), 7.71 (d, *J*=7.7 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.21 (br. s., 2H), 6.84 (d, *J*=8.1 Hz, 1H), 6.77 - 6.15 (m, 4H), 6.03 (s, 2H), 4.21 (br. s., 1H), 3.03 (s, 3H), 2.65 - 2.41 (m, 5H), 2.01 (s, 3H).

Example 74

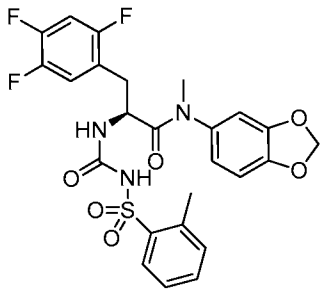


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(2,4-dichlorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.3
Retention Time	1.71 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (d, *J*=7.7 Hz, 1H), 7.49 (t, *J*=7.2 Hz, 1H), 7.39 - 7.26 (m, 3H), 7.18 (d, *J*=8.1 Hz, 1H), 6.96 (d, *J*=8.1 Hz, 1H), 6.90 (d, *J*=8.1 Hz, 1H), 6.83 - 6.52 (m, 3H), 6.06 (d, *J*=8.8 Hz, 2H), 4.53 (d, *J*=4.4 Hz, 1H), 3.10 (s, 3H), 2.92 - 2.56 (m, 2H), 2.51 (s, 3H).

Example 75

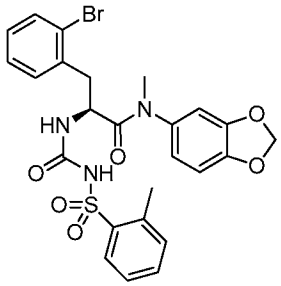


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)-3-(2,4,5-trifluorophenyl)propanamide

MS $(M+H)^+$ Calcd.	550.1
MS $(M+H)^+$ Observ.	550.3
Retention Time	1.56 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.73 (d, *J*=7.7 Hz, 1H), 7.54 - 7.43 (m, 1H), 7.38 - 7.17 (m, 3H), 7.03 - 6.46 (m, 5H), 6.08 (d, *J*=7.0 Hz, 2H), 4.41 (d, *J*=4.0 Hz, 1H), 3.11 (s, 3H), 2.87 - 2.52 (m, 2H), 2.49 (s, 3H).

Example 76

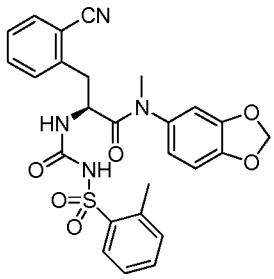


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(2-bromophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	574.1
MS $(M+H)^+$ Observ.	574.2
Retention Time	1.72 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.70 (d, *J*=7.3 Hz, 1H), 7.41 (d, *J*=7.7 Hz, 1H), 7.38 - 7.29 (m, 1H), 7.20 (br. s., 3H), 7.12 (d, *J*=7.3 Hz, 1H), 6.77 (br. s., 4H), 6.01 (d, *J*=8.8 Hz, 2H), 4.54 - 4.38 (m, 1H), 3.02 (s, 3H), 2.81 - 2.66 (m, 2H), 2.49 (br. s., 3H).

Example 77

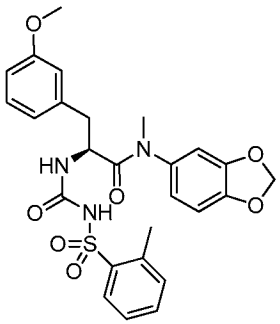


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(2-cyanophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	521.1
MS $(M+H)^+$ Observ.	521.3
Retention Time	1.42 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 - 7.59 (m, 2H), 7.53 - 7.30 (m, 3H), 7.28 - 7.13 (m, 2H), 7.00 - 6.78 (m, 2H), 6.71 (br. s., 2H), 6.21 - 6.09 (m, 1H), 6.04 (d, *J*=8.4 Hz, 2H), 4.54 - 4.39 (m, 1H), 3.05 (s, 3H), 2.93 - 2.74 (m, 2H), 2.49 (s, 3H).

Example 78

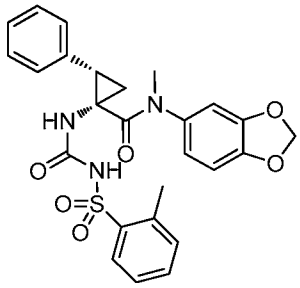


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3-methoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	526.2
MS $(M+H)^+$ Observ.	526.3
Retention Time	1.50 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (d, *J*=7.7 Hz, 1H), 7.48 - 7.01 (m, 4H), 6.86 (d, *J*=8.1 Hz, 1H), 6.77 - 6.53 (m, 2H), 6.42 (d, *J*=7.3 Hz, 1H), 6.32 (br. s., 2H), 6.03 (s, 2H), 4.24 (br. s., 1H), 3.63 (s, 3H), 3.05 (s, 3H), 2.78 - 2.34 (m, 5H).

Example 79

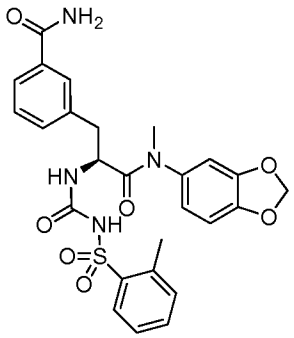


(1S,2S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-phenyl-1-(3-(o-tolylsulfonyl)ureido)cyclopropanecarboxamide

MS $(M+H)^+$ Calcd.	508.2
MS $(M+H)^+$ Observ.	508.3
Retention Time	1.42 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.65 (d, *J*=7.7 Hz, 1H), 7.48 - 7.33 (m, 1H), 7.30 - 7.15 (m, 5H), 7.07 (br. s., 2H), 6.79 - 6.48 (m, 3H), 5.98 (d, *J*=17.2 Hz, 2H), 3.01 (s, 3H), 2.81 - 2.62 (m, 1H), 2.37 (s, 3H), 1.99 - 1.92 (m, 1H), 1.19 - 1.07 (m, 1H).

Example 80

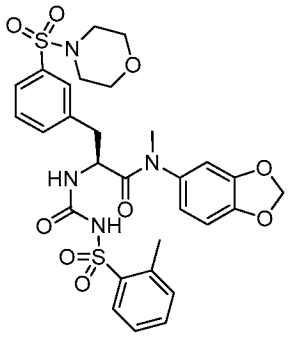


(S)-3-(3-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-3-oxo-2-(3-(o-tolylsulfonyl)ureido)propyl)benzamide

MS $(M+H)^+$ Calcd.	539.2
MS $(M+H)^+$ Observ.	539.3
Retention Time	1.30 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.93 - 7.55 (m, 3H), 7.47 - 7.04 (m, 6H), 6.93 (d, *J*=7.3 Hz, 1H), 6.80 (d, *J*=8.1 Hz, 1H), 6.67 - 6.18 (m, 2H), 6.04 (d, *J*=9.9 Hz, 2H), 4.28 (br. s., 1H), 3.04 (s, 3H), 2.83 - 2.37 (m, 5H).

Example 81

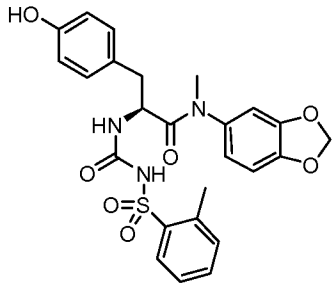


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-(3-(morpholinosulfonyl)phenyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	645.2
MS $(M+H)^+$ Observ.	645.3
Retention Time	1.37 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.75 - 7.66 (m, 1H), 7.47 (s, 8H), 6.91 - 6.82 (m, 1H), 6.81 - 6.30 (m, 2H), 6.05 (d, *J*=6.6 Hz, 2H), 3.62 (br. s., 4H), 3.07 (br. s., 3H), 2.87 – 2.61 (m, 6H), 2.50 - 2.35 (m, 4H).

Example 82

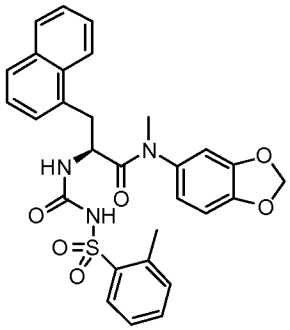


(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(4-hydroxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	512.1
MS $(M+H)^+$ Observ.	512.3
Retention Time	1.45 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.72 (d, *J*=7.7 Hz, 1H), 7.47 - 7.09 (m, 3H), 6.84 (d, *J*=8.1 Hz, 1H), 6.71 - 6.48 (m, 5H), 6.32 - 6.16 (m, 1H), 6.04 (s, 2H), 4.28 - 4.10 (m, 1H), 3.04 (s, 3H), 2.68 - 2.30 (m, 5H).

Example 83

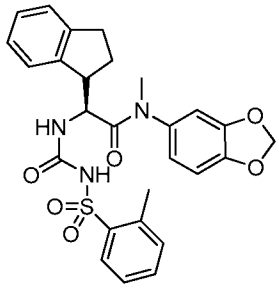


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-(naphthalen-1-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	546.2
MS $(M+H)^+$ Observ.	546.3
Retention Time	1.68 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.84 (d, *J*=8.1 Hz, 1H), 7.76 (d, *J*=7.7 Hz, 1H), 7.67 (br. s., 1H), 7.48 - 7.08 (m, 8H), 6.75 - 6.20 (m, 3H), 6.07 - 5.89 (m, 2H), 4.57 (br. s., 1H), 3.00 (br. s., 4H), 2.48 (s, 3H), 2.37 (br. s., 1H).

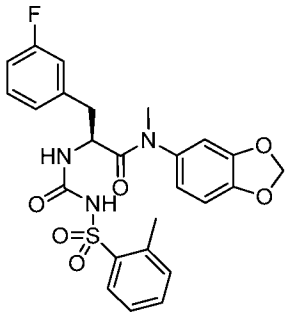
Example 84



(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-((S)-2,3-dihydro-1H-inden-1-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)acetamide

MS $(M+H)^+$ Calcd.	522.2
MS $(M+H)^+$ Observ.	522.3
Retention Time	1.87 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 85



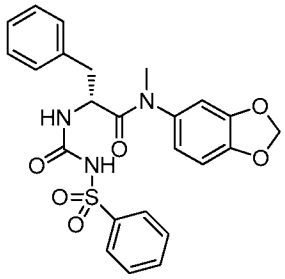
(S)-N-(benzo[d][1,3]dioxol-5-yl)-3-(3-fluoorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	514.1
MS $(M+H)^+$ Observ.	514.2
Retention Time	1.51 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.95 (d, *J*=7.6 Hz, 1H), 7.54 - 7.41 (m, 1H), 7.39 - 7.27 (m, 2H), 7.25 - 7.12 (m, 1H), 6.92 (d, *J*=2.2 Hz, 1H), 6.73 (dd, *J*=13.1, 7.9 Hz, 2H), 6.63 (d, *J*=9.8 Hz, 1H), 6.50 - 6.23 (m, 2H), 6.00 (s, 2H), 4.57 - 4.43 (m, 1H), 3.13 (s, 3H), 2.95 - 2.57 (m, 5H).

Example 86 was synthesized using the procedure described above for Example 2 starting from (*R*)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

Example 86

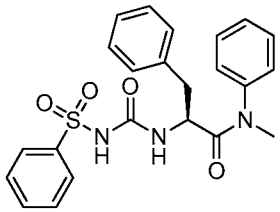


(R)-N-(benzo[d][1,3]dioxol-5-yl)- N-methyl-3-phenyl2-(3phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	482.1
MS $(M+H)^+$ Observ.	482.2
Retention Time	1.67 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.66 (dd, *J*=7.8, 1.5 Hz, 2H), 7.36-7.31 (m, 3H), 7.23 - 7.10 (m, 4H), 6.93 - 6.76 (m, 4H), 6.64-6.56 (m, 2H), 6.06-5.98 (m, 2H), 4.27 (br. s., 1H), 3.05 (br. s., 3H), 2.76 - 2.51 (m, 2H)

Example 87



(S)-N-methyl-N,3-diphenyl-2-(3-(phenylsulfonyl)ureido)propanamide

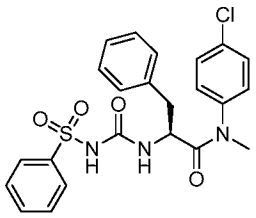
To a solution of (S)-tert-butyl (1methyl(phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate, TFA (12.7 mg, 0.050 mmol) in dichloromethane (2 mL) was added diisopropylethylamine (0.026 mL, 0.15 mmol) followed by a solution of 2-methylbenzenesulfonyl isocyanate (13.7 mg, 0.075 mmol) in dichloromethane (2 mL). The reaction mixture was stirred at r.t. for 1 hr. The solvent was evaporated and the residue was purified by preparative HPLC to afford the title compound (16.9 mg).

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=6.6 Hz, 2H), 7.64 - 7.33 (m, 6H), 7.14 (br. s., 5H), 6.72 (br. s., 2H), 6.58 (br. s., 1H), 4.29 (br. s., 1H), 3.13 (s, 3H), 2.73 (d, *J*=6.2 Hz, 2H).

MS $(M+H)^+$ Calcd.	438.1
MS $(M+H)^+$ Observ.	438.3
Retention Time	1.36 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm

Examples 88-97 were synthesized using the procedure described above for Example 87.

Example 88

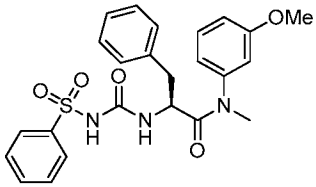


(S)-N-(4-chlorophenyl)-N-methyl-3-phenyl-2(3-phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	472.1
MS $(M+H)^+$ Observ.	472.2
Retention Time	1.56 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=6.2 Hz, 2H), 7.60 (d, *J*=6.2 Hz, 1H), 7.54 (d, *J*=7.0 Hz, 2H), 7.43 (d, *J*=8.1 Hz, 2H), 7.23 - 7.05 (m, 5H), 6.79 (br. s., 2H), 6.63 (br. s., 1H), 4.24 (br. s., 1H), 3.09 (s, 3H), 2.81 - 2.64 (m, 2H).

Example 89

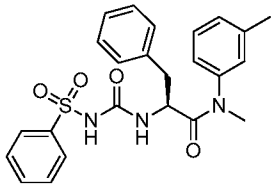


(S)-N-(3-methoxyphenyl)-N-methyl-3-phenyl-2-(3-phenylsulfonyl)ureido)-propanamide

MS $(M+H)^+$ Calcd.	468.2
MS $(M+H)^+$ Observ.	468.3
Retention Time	1.44 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=7.0 Hz, 2H), 7.62 - 7.43 (m, 3H), 7.28 (t, *J*=7.9 Hz, 1H), 7.15 (br. s., 3H), 6.92 (d, *J*=7.3 Hz, 1H), 6.77 (br. s., 3H), 6.66 - 6.46 (m, 2H), 4.34 (br. s., 1H), 3.70 (s, 3H), 3.11 (s, 3H), 2.81 - 2.68 (m, 2H).

Example 90

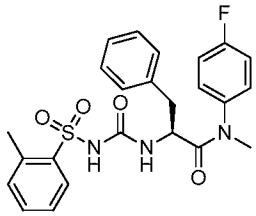


(S)-N-methyl-3-phenyl-2-(3-phenylsulfonyl)ureido)-N-(m-tolyl)propanamide

MS $(M+H)^+$ Calcd.	452.2
MS $(M+H)^+$ Observ.	452.3
Retention Time	1.50 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.79 (d, *J*=7.7 Hz, 2H), 7.70 - 7.47 (m, 3H), 7.32 - 7.23 (m, 1H), 7.17 (br. s., 4H), 6.91 - 6.72 (m, 4H), 6.66 (d, *J*=7.0 Hz, 1H), 4.27 (br. s., 4H), 3.09 (s, 3H), 2.81 - 2.68 (m, 2H), 2.51 (s, 3H).

Example 91

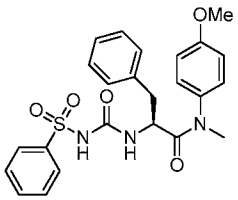


(S)-N-(4-fluorophenyl)-N-methyl-3-phenyl-2(3-phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	456.1
MS $(M+H)^+$ Observ.	456.3
Retention Time	1.40 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.7 Hz, 2H), 7.68 - 7.48 (m, 3H), 7.30 - 7.04 (m, 7H), 6.77 (br. s., 2H), 6.64 (d, *J*=6.6 Hz, 1H), 4.22 (d, *J*=5.5 Hz, 1H), 3.10 (s, 3H), 2.82 - 2.67 (m, 2H).

Example 92



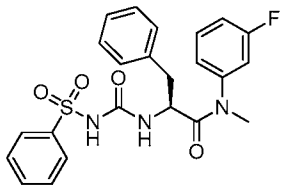
(S)-N-(4-methoxyphenyl)-N-methyl-3-phenyl-2(3-phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	468.2
MS $(M+H)^+$ Observ.	468.3
Retention Time	1.39 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM

	Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.7 Hz, 2H), 7.67 - 7.50 (m, 3H), 7.15 (d, *J*=2.9 Hz, 3H), 7.07 - 6.89 (m, 4H), 6.76 (br. s., 2H), 6.63 (d, *J*=7.7 Hz, 1H), 4.27 (br. s., 1H), 3.78 (s, 3H), 3.09 (s, 3H), 2.81 - 2.66 (m, 2H).

Example 93



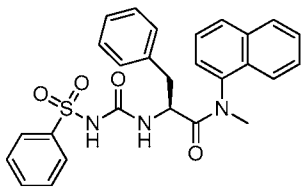
(S)-N-(3-fluorophenyl)-N-methyl-3-phenyl-2(3-phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	456.1
MS $(M+H)^+$ Observ.	456.1
Retention Time	1.41 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100

Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.88 (d, *J*=7.6 Hz, 2H), 7.65 - 7.46 (m, 3H), 7.39 - 7.29 (m, 1H), 7.26 - 7.17 (m, 3H), 7.09 (br. s., 1H), 6.90 (d, *J*=5.1 Hz, 2H), 6.81 - 6.74 (m, 1H), 6.59 - 6.46 (m, 1H), 4.47 (br. s., 1H), 3.16 (s, 3H), 2.96 - 2.63 (m, 2H).

Example 94



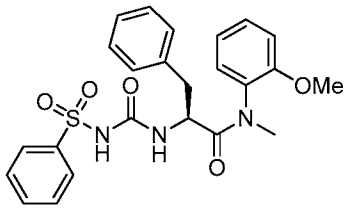
(S)-N-methyl-N-(naphthalen-1-yl)-3-phenyl-2-(3-(phenylsulfonyl)ureido)-propanamide

MS $(M+H)^+$ Calcd.	488.2
MS $(M+H)^+$ Observ.	488.2
Retention Time	1.47 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm

particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.09 - 7.76 (m, 3H), 7.68 (br. s., 3H), 7.58 (br. s., 2H), 7.50 - 7.35 (m, 3H), 7.32 - 7.18 (m, 2H), 7.14 - 7.03 (m, 2H), 6.61 (d, *J*=7.0 Hz, 1H), 6.51 (d, *J*=7.0 Hz, 1H), 4.19 (d, *J*=4.8 Hz, 1H), 3.23 - 3.08 (m, 3H), 2.86 (br. s., 2H).

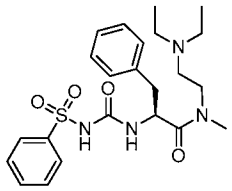
Example 95



(S)-N-(2-methoxyphenyl)-N-methyl-3-phenyl-2-(3(phenylsulfonyl)ureido)-propanamide

MS $(M+H)^+$ Calcd.	468.2
MS $(M+H)^+$ Observ.	468.2
Retention Time	1.48 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

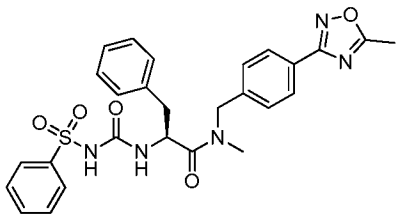
Example 96



(S)-N-(2-(diethylamino)ethyl)-N-methyl-3-phenyl-2-(3-(phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	461.2
MS $(M+H)^+$ Observ.	461.4
Retention Time	1.84 min
	LC Condition
Solvent A	5 % Methanol : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % Methanol : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 97



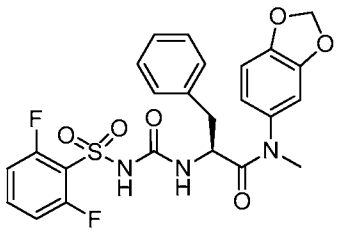
(S)-N-methyl-N-(4-(5-methyl-1,2,4-oxadiazol-3-yl)benzyl)-3-phenyl-2-(3-(phenylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	534.2
MS $(M+H)^+$ Observ.	534.3
Retention Time	2.37 min
	LC Condition
Solvent A	5 % Methanol : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % Methanol : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 8.07 - 7.88 (m, 4H), 7.63 - 7.43 (m, 3H), 7.31 - 6.92 (m, 7H), 4.60 - 4.31 (m, 3H), 3.22 - 2.90 (m, 2H), 2.80 (s, 3H), 2.67 (s, 3H).

Examples 98 – 120 were synthesized using the procedure described above for Example 3.

Example 98



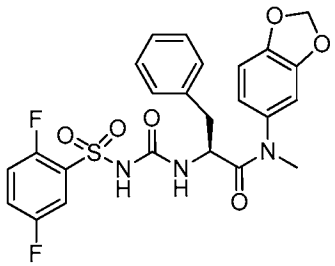
(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,6-difluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	518.1
MS $(M+H)^+$ Observ.	518.4
Retention Time	1.65 min
	LC Condition

Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.41 (br. s., 1H), 7.31 - 7.09 (m, 4H), 7.07 - 6.78 (m, 5H), 6.73 - 6.42 (m, 2H), 6.05 (s, 2H), 4.27 (br. s., 1H), 3.18 (s, 3H), 2.73 - 2.52 (m, 2H).

Example 99



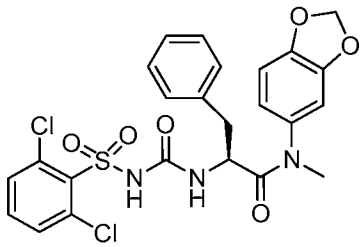
(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,5-difluorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	518.1
MS $(M+H)^+$ Observ.	518.3
Retention Time	1.48 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate

Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.49 - 7.09 (m, 7H), 6.92 - 6.78 (m, 3H), 6.73 - 6.52 (m, 2H), 6.06 (s, 2H), 4.26 (br. s., 1H), 3.06 (s, 3H), 2.79 - 2.53 (m, 2H).

Example 100



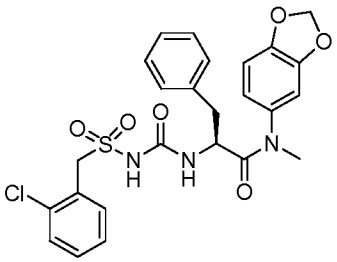
(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2,6-dichlorophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	550.1
MS $(M+H)^+$ Observ.	550.4
Retention Time	1.55 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate

Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.68 - 7.41 (m, 3H), 7.17 (d, *J*=7.3 Hz, 4H), 6.96 - 6.79 (m, 3H), 6.75 - 6.47 (m, 2H), 6.07 (s, 2H), 4.30 (br. s., 1H), 3.08 (s, 3H), 2.79 - 2.53 (m, 2H).

Example 101

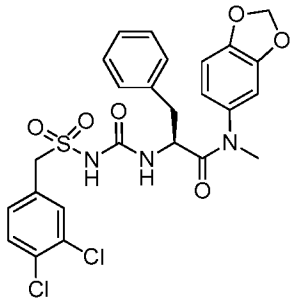


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-chlorobenzyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.4
Retention Time	1.39 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.46 (d, *J*=8.4 Hz, 1H), 7.38 - 7.14 (m, 7H), 7.02 - 6.88 (m, 3H), 6.82 - 6.57 (m, 2H), 6.11 (s, 2H), 4.72 - 4.46 (m, 3H), 3.11 (s, 3H), 2.89 - 2.56 (m, 2H).

Example 102

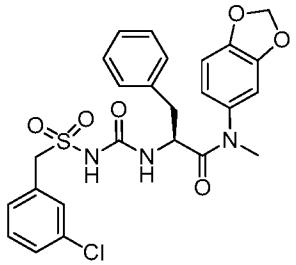


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3,4-dichlorobenzyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.4
Retention Time	1.53 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.60 - 7.42 (m, 2H), 7.32 - 7.11 (m, 4H), 7.03 - 6.85 (m, 3H), 6.83 - 6.58 (m, 2H), 6.10 (s, 2H), 4.51 - 4.26 (m, 3H), 3.11 (s, 3H), 2.85 - 2.55 (m, 2H).

Example 103



(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3-chlorobenzyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.2
Retention Time	1.55 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.49 - 7.07 (m, 7H), 7.02 - 6.84 (m, 3H), 6.68 – 6.26 (m, 3H), 6.11 (s, 2H), 4.48 (br. s., 3H), 3.11 (s, 3H), 2.88 - 2.56 (m, 2H).

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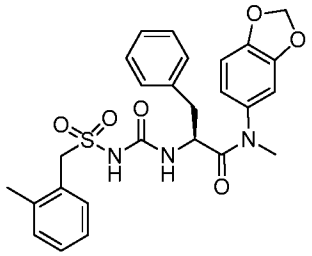
Example 104

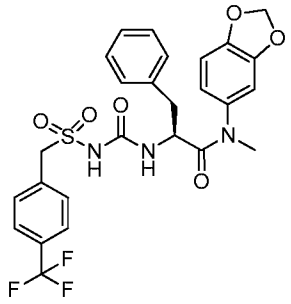


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-((2-methylbenzyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.35 - 7.04 (m, 8H), 7.01 - 6.86 (m, 3H), 6.83 - 6.60 (m, 2H), 6.11 (s, 2H), 4.58 - 4.38 (m, 3H), 3.12 (s, 3H), 2.89 - 2.56 (m, 2H), 2.31 (s, 3H).

Example 105

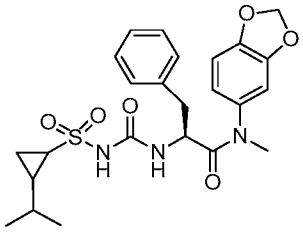


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((4-(trifluoromethyl)benzyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.2
Retention Time	1.63 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.64 (d, *J*=6.6 Hz, 2H), 7.41 (d, *J*=7.7 Hz, 2H), 7.27 – 7.21 (m, 3H), 7.03 - 6.64 (m, 5H), 6.11 (br. s., 2H), 4.64 - 4.36 (m, 3H), 3.13 (s, 3H), 2.87 - 2.54 (m, 2H).

Example 106

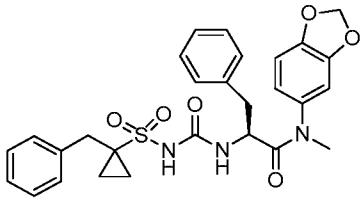


(2S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-isopropylcyclopropyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	488.2
MS $(M+H)^+$ Observ.	488.5
Retention Time	1.60 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.31 - 7.16 (m, 3H), 7.00 - 6.83 (m, 3H), 6.80 - 6.52 (m, 3H), 6.10 (s, 2H), 4.43 (br. s., 1H), 3.09 (s, 3H), 2.89 - 2.56 (m, 2H), 1.28 - 1.00 (m, 3H), 0.96 - 0.74 (m, 8H).

Example 107

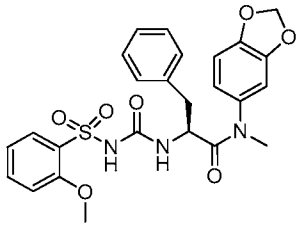


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((1-benzylcyclopropyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	536.2
MS $(M+H)^+$ Observ.	536.3
Retention Time	1.82 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.34 - 7.16 (m, 6H), 7.13 (d, *J*=7.0 Hz, 2H), 7.00 - 6.85 (m, 3H), 6.81 - 6.55 (m, 3H), 6.11 (d, *J*=4.8 Hz, 2H), 4.45 (d, *J*=5.9 Hz, 1H), 3.22 - 3.06 (m, 5H), 2.89 - 2.55 (m, 2H), 1.34 - 1.11 (m, 2H), 0.57 (br. s., 2H).

Example 108

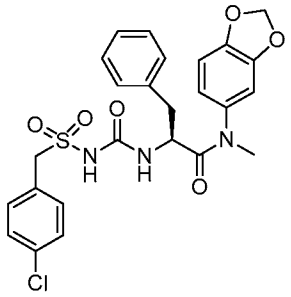


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-methoxyphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	512.1
MS $(M+H)^+$ Observ.	512.2
Retention Time	1.51 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.69 (d, *J*=8.8 Hz, 1H), 7.62 - 7.52 (m, 1H), 7.18 (d, *J*=7.0 Hz, 4H), 7.04 (t, *J*=7.3 Hz, 1H), 6.91 - 6.77 (m, 3H), 6.70 - 6.45 (m, 3H), 6.06 (s, 2H), 4.28 (d, *J*=5.9 Hz, 1H), 3.81 (s, 3H), 3.06 (s, 3H), 2.85 - 2.45 (m, 2H).

Example 109

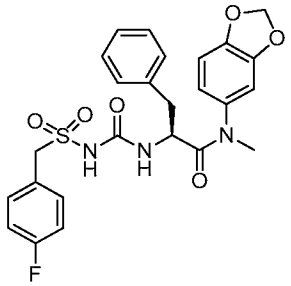


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((4-chlorobenzyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	530.1
MS $(M+H)^+$ Observ.	530.2
Retention Time	1.56 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.40 (d, *J*=8.4 Hz, 2H), 7.33 - 7.15 (m, 5H), 7.00 (d, *J*=8.1 Hz, 1H), 6.92 (d, *J*=7.0 Hz, 2H), 6.85 - 6.49 (m, 3H), 6.13 (d, *J*=5.1 Hz, 2H), 4.64 - 4.44 (m, 3H), 3.14 (s, 3H), 2.95 - 2.56 (m, 2H).

Example 110

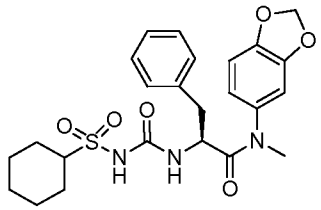


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((4-fluorobenzyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	514.1
MS $(M+H)^+$ Observ.	514.2
Retention Time	1.49 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.23 (d, *J*=5.9 Hz, 6H), 7.10 (br. s., 2H), 7.01 - 6.87 (m, 3H), 6.85 - 6.61 (m, 2H), 6.11 (s, 2H), 4.52 - 4.26 (m, 3H), 3.12 (s, 3H), 2.87 - 2.55 (m, 2H).

Example 111

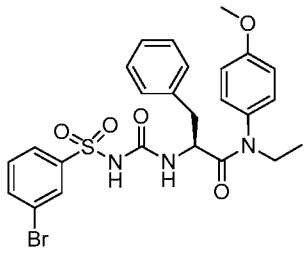


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-(cyclohexylsulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	488.2
MS $(M+H)^+$ Observ.	488.5
Retention Time	1.54 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.31 - 7.20 (m, 3H), 6.97 (dd, *J*=7.3, 2.0 Hz, 2H), 6.84 (d, *J*=8.3 Hz, 1H), 6.59 (d, *J*=9.8 Hz, 2H), 6.04 (s, 2H), 4.61 (br. s., 1H), 3.33 (dt, *J*=3.2, 1.7 Hz, 1H), 3.19 (s, 3H), 2.73 (dd, *J*=13.4, 8.3 Hz, 2H), 2.09 - 1.17 (m, 10H).

Example 112

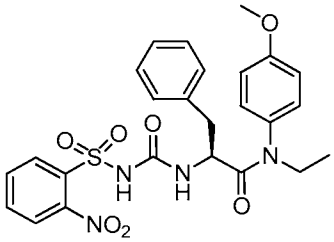


(S)-2-(3-((3-bromophenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	560.1
MS $(M+H)^+$ Observ.	560.2
Retention Time	1.62 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.90 (br. s., 1H), 7.85 - 7.68 (m, 2H), 7.48 (t, *J*=8.3 Hz, 1H), 7.15 (d, *J*=2.2 Hz, 3H), 6.93 (br. s., 4H), 6.80 (br. s., 2H), 6.48 (br. s., 1H), 4.17 (d, *J*=6.6 Hz, 1H), 3.79 (s, 3H), 3.67 - 3.41 (m, 2H), 2.80 - 2.45 (m, 2H), 0.95 (t, *J*=7.0 Hz, 3H).

Example 113

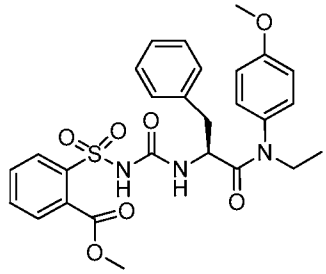


(S)-N-ethyl-N-(4-methoxyphenyl)-2-(3-((2-nitrophenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	527.2
MS $(M+H)^+$ Observ.	527.2
Retention Time	1.49 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.06 - 7.95 (m, 2H), 7.91 (t, *J*=7.2 Hz, 1H), 7.85 - 7.78 (m, 1H), 7.18 - 7.07 (m, 3H), 7.04 - 6.90 (m, 4H), 6.89 - 6.73 (m, 3H), 4.26 - 4.15 (m, 1H), 3.79 (s, 3H), 3.68 - 3.43 (m, 2H), 2.83 - 2.44 (m, 2H), 0.96 (t, *J*=7.2 Hz, 3H).

Example 114

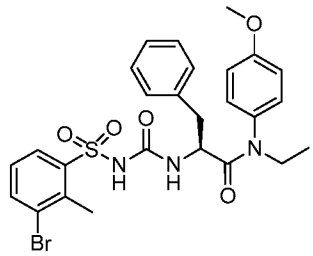


(S)-methyl 2-(N-((1-(ethyl(4-methoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamoyl)sulfamoyl)benzoate

MS $(M+H)^+$ Calcd.	540.2
MS $(M+H)^+$ Observ.	540.2
Retention Time	1.50 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.93 (d, *J*=7.7 Hz, 1H), 7.80 - 7.73 (m, 1H), 7.69 (d, *J*=5.1 Hz, 2H), 7.17 - 7.09 (m, 3H), 7.03 - 6.85 (m, 5H), 6.80 (d, *J*=3.3 Hz, 2H), 4.24 - 4.13 (m, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.67 - 3.44 (m, 2H), 2.82 - 2.43 (m, 2H), 0.96 (t, *J*=7.2 Hz, 3H).

Example 115

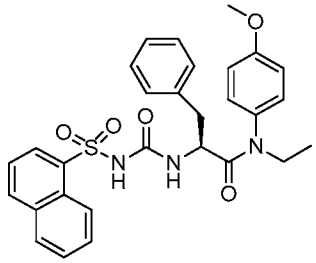


(S)-2-(3-((3-bromo-2-methylphenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	574.1
MS $(M+H)^+$ Observ.	574.2
Retention Time	1.70 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.3 Hz, 1H), 7.69 (br. s., 1H), 7.14 (br. s., 5H), 7.00 - 6.73 (m, 6H), 4.12 (d, *J*=5.9 Hz, 1H), 3.77 (s, 3H), 3.66 - 3.41 (m, 2H), 2.72 - 2.44 (m, 5H), 0.94 (br. s., 3H).

Example 116

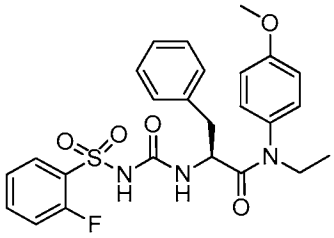


(S)-N-ethyl-N-(4-methoxyphenyl)-2-(3-(naphthalen-1-ylsulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	532.2
MS $(M+H)^+$ Observ.	532.2
Retention Time	1.65 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.59 (d, *J*=7.7 Hz, 1H), 8.22 (d, *J*=8.1 Hz, 1H), 8.11 (d, *J*=7.0 Hz, 2H), 7.78 - 7.54 (m, 3H), 7.12 - 7.04 (m, 1H), 7.03 - 6.95 (m, 2H), 6.81 (br. s., 4H), 6.66 (d, *J*=7.3 Hz, 2H), 4.13 - 4.01 (m, 1H), 3.73 (s, 3H), 3.62 - 3.37 (m, 2H), 2.69 - 2.33 (m, 2H), 0.91 (t, *J*=7.0 Hz, 3H).

Example 117

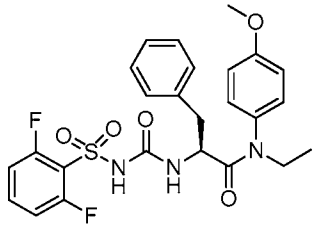


(S)-N-ethyl-2-(3-((2-fluorophenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	500.2
MS $(M+H)^+$ Observ.	500.1
Retention Time	1.40 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.63 (t, *J*=7.7 Hz, 1H), 7.42 (br. s., 1H), 7.22 - 7.08 (m, 6H), 6.93 - 6.78 (m, 6H), 4.15 (br. s., 1H), 3.77 (s, 3H), 3.66 - 3.25 (m, 2H), 2.72 - 2.52 (m, 2H), 0.94 (t, *J*=6.2 Hz, 3H).

Example 118

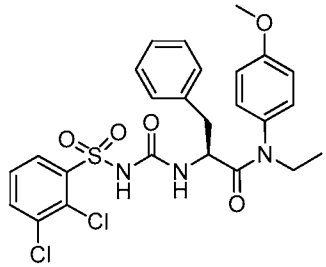


(S)-2-(3-((2,6-difluorophenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	518.2
MS $(M+H)^+$ Observ.	518.1
Retention Time	1.47 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.45 (br. s., 1H), 7.22 - 7.11 (m, 4H), 7.04 (br. s., 2H), 6.94 - 6.79 (m, 6H), 4.17 (br. s., 1H), 3.76 (s, 3H), 3.60 - 3.44 (m, 2H), 2.73 - 2.46 (m, 2H), 0.93 (t, *J*=5.9 Hz, 3H).

Example 119

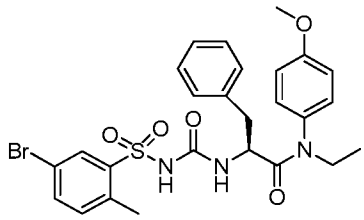


(S)-2-(3-((2,3-dichlorophenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	550.1
MS $(M+H)^+$ Observ.	550.2
Retention Time	1.62 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.84 (d, *J*=7.7 Hz, 1H), 7.74 (br. s., 1H), 7.38 (br. s., 1H), 7.19 - 7.11 (m, 3H), 6.98 - 6.76 (m, 6H), 4.19 - 4.09 (m, 1H), 3.76 (s, 3H), 3.69 - 3.40 (m, 2H), 2.76 - 2.45 (m, 2H), 0.95 (t, *J*=6.6 Hz, 3H).

Example 120



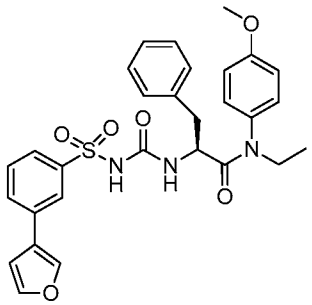
(S)-2-(3-((5-bromo-2-methylphenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	574.1
MS $(M+H)^+$ Observ.	574.2
Retention Time	1.76 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.87 (s, 1H), 7.71 (d, *J*=7.3 Hz, 1H), 7.34 (d, *J*=8.1 Hz, 1H), 7.15 - 7.14 (m, 3H), 6.93 (br. s., 4H), 6.77 (d, *J*=3.3 Hz, 2H), 6.50 (br. s., 1H), 4.16 (d, *J*=7.0 Hz, 1H), 3.78 (s, 3H), 3.67 - 3.43 (m, 2H), 2.79 - 2.38 (m, 5H), 0.95 (t, *J*=7.2 Hz, 3H).

Examples 121 – 133 were synthesized using the procedure described above for Example 48.

Example 121

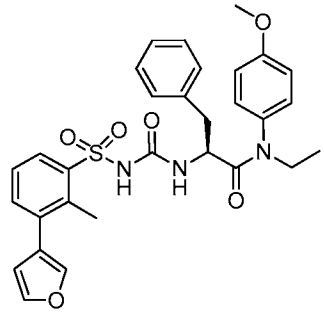


(S)-N-ethyl-2-(3-((3-(furan-3-yl)phenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	548.2
MS $(M+H)^+$ Observ.	548.2
Retention Time	1.67 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.31 (s, 1H), 7.98 (br. s., 1H), 7.86 (d, *J*=6.6 Hz, 1H), 7.81 (s, 1H), 7.65 (d, *J*=7.3 Hz, 1H), 7.55 (t, *J*=7.7 Hz, 1H), 7.13 (br. s., 3H), 7.00 (s, 1H), 6.97 - 6.55 (m, 7H), 4.22 - 4.11 (m, 1H), 3.75 (s, 3H), 3.66 - 3.42 (m, 2H), 2.80 - 2.46 (m, 2H), 0.92 (t, *J*=7.0 Hz, 3H).

Example 122

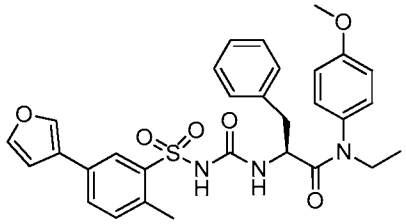


(S)-N-ethyl-2-(3-((3-(furan-3-yl)-2-methylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	562.2
MS $(M+H)^+$ Observ.	562.3
Retention Time	1.74 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.88 (s, 1H), 7.83 - 7.76 (m, 2H), 7.54 (d, *J*=7.3 Hz, 1H), 7.36 (t, *J*=7.9 Hz, 1H), 7.13 (d, *J*=2.6 Hz, 3H), 7.02 - 6.86 (m, 4H), 6.82 - 6.43 (m, 4H), 4.21 - 4.09 (m, 1H), 3.77 (s, 3H), 3.68 - 3.41 (m, 2H), 2.81 - 2.45 (m, 5H), 0.93 (t, *J*=7.0 Hz, 3H).

Example 123

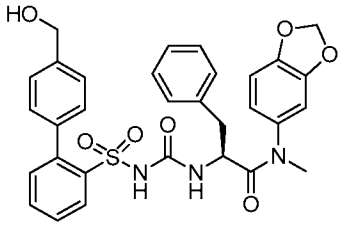


(S)-N-ethyl-2-(3-((5-(furan-3-yl)-2-methylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	562.2
MS $(M+H)^+$ Observ.	562.3
Retention Time	1.87 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.26 (s, 1H), 7.98 (s, 1H), 7.83 - 7.74 (m, 2H), 7.43 (d, *J*=8.1 Hz, 1H), 7.21 - 7.09 (m, 3H), 7.00 - 6.83 (m, 5H), 6.76 (br. s., 2H), 6.70 (d, *J*=8.4 Hz, 1H), 4.22 - 4.07 (m, 1H), 3.73 (s, 3H), 3.67 - 3.41 (m, 2H), 2.80 - 2.42 (m, 5H), 0.93 (t, *J*=7.2 Hz, 3H).

Example 124

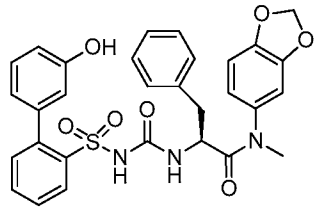


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((4'-(hydroxymethyl)-[1,1'-biphenyl]-2-yl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	588.2
MS $(M+H)^+$ Observ.	588.2
Retention Time	1.57 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.92 (d, *J*=8.1 Hz, 1H), 7.70 - 7.59 (m, 1H), 7.53 (d, *J*=7.3 Hz, 1H), 7.36 - 7.08 (m, 9H), 6.91 (d, *J*=7.7 Hz, 1H), 6.86 (d, *J*=7.0 Hz, 2H), 6.71 - 6.48 (m, 3H), 6.08 (s, 2H), 4.58 (br. s., 2H), 4.31 (br. s., 1H), 3.08 (s, 3H), 2.98 - 2.77 (m, 2H).

Example 125

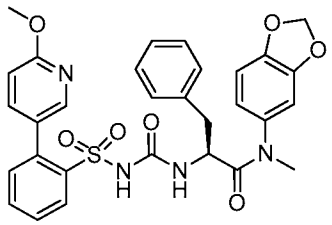


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((3'-hydroxy-[1,1'-biphenyl]-2-yl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	574.2
MS $(M+H)^+$ Observ.	574.2
Retention Time	1.56 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.90 (d, *J*=7.3 Hz, 1H), 7.69 - 7.61 (m, 1H), 7.54 (t, *J*=7.9 Hz, 1H), 7.33 - 7.03 (m, 8H), 6.94 - 6.75 (m, 3H), 6.67 (br. s., 2H), 6.60 - 6.45 (m, 2H), 6.07 (s, 2H), 4.30 (d, *J*=6.6 Hz, 1H), 3.06 (s, 3H), 2.99 - 2.76 (m, 2H).

Example 126

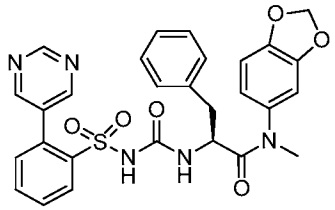


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-(6-methoxypyridin-3-yl)phenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	589.2
MS $(M+H)^+$ Observ.	589.2
Retention Time	1.55 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.00 - 7.92 (m, 1H), 7.70 (s, 1H), 7.59 (s, 1H), 7.53 - 7.46 (m, 1H), 7.33 (d, *J*=7.3 Hz, 2H), 7.23 - 7.18 (m, 6H), 6.91 (d, *J*=8.4 Hz, 1H), 6.87 - 6.79 (m, 2H), 6.70 - 6.49 (m, 2H), 6.08 (s, 2H), 4.35 - 4.24 (m, 1H), 3.93 (s, 3H), 3.07 (s, 3H), 2.98 - 2.75 (m, 2H).

Example 127

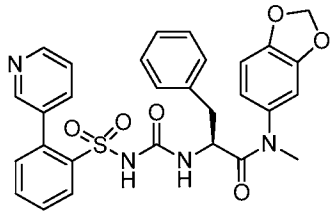


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(pyrimidin-5-yl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	560.2
MS $(M+H)^+$ Observ.	560.2
Retention Time	1.35 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 9.25 (s, 1H), 8.65 (br. s., 2H), 8.00 (d, *J*=8.1 Hz, 1H), 7.77 (s, 1H), 7.69 (d, *J*=8.1 Hz, 1H), 7.44 (d, *J*=7.3 Hz, 1H), 7.23 - 7.20 (m, 3H), 6.92 (d, *J*=8.1 Hz, 1H), 6.85 (d, *J*=7.0 Hz, 2H), 6.72 - 6.53 (m, 3H), 6.08 (s, 2H), 4.29 (d, *J*=6.6 Hz, 1H), 3.07 (s, 3H), 2.98 - 2.76 (m, 2H).

Example 128

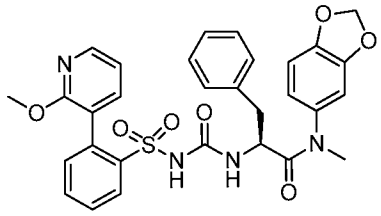


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(pyridin-3-yl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	559.2
MS $(M+H)^+$ Observ.	559.2
Retention Time	1.39 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.64 (d, *J*=3.7 Hz, 1H), 8.43 (s, 1H), 7.97 (d, *J*=8.1 Hz, 1H), 7.77 - 7.69 (m, 1H), 7.67 - 7.56 (m, 2H), 7.44 (dd, *J*=7.7, 5.1 Hz, 1H), 7.36 (d, *J*=7.7 Hz, 1H), 7.24 - 7.19 (m, 3H), 6.92 (d, *J*=8.1 Hz, 1H), 6.85 (d, *J*=6.6 Hz, 2H), 6.71 - 6.54 (m, 3H), 6.08 (s, 2H), 4.30 (d, *J*=5.5 Hz, 1H), 3.08 (s, 3H), 2.86 - 2.52 (m, 2H).

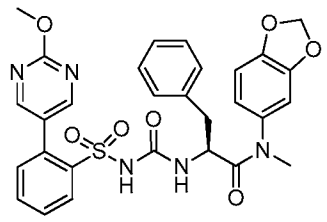
Example 129



(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-(2-methoxypyridin-3-yl)phenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	589.2
MS $(M+H)^+$ Observ.	589.2
Retention Time	1.63 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 130

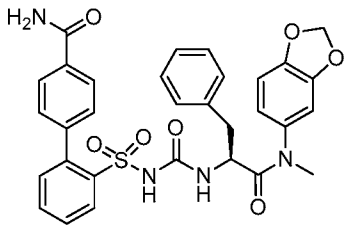


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-(2-methoxypyrimidin-5-yl)phenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	590.2
MS $(M+H)^+$ Observ.	590.2
Retention Time	1.34 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.41 (s, 2H), 7.99 (d, *J*=8.1 Hz, 1H), 7.74 (d, *J*=7.0 Hz, 1H), 7.66 (d, *J*=8.1 Hz, 1H), 7.41 (d, *J*=7.3 Hz, 1H), 7.22 – 7.19 (m, 3H), 6.91 (d, *J*=8.1 Hz, 1H), 6.85 (d, *J*=6.6 Hz, 2H), 6.58 (d, *J*=7.3 Hz, 3H), 6.08 (s, 2H), 4.35 - 4.21 (m, 1H), 4.01 (s, 3H), 3.07 (s, 3H), 2.94 - 2.77 (m, 2H).

Example 131



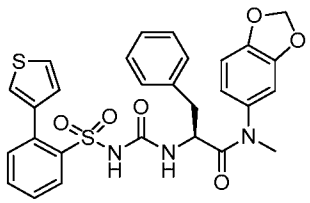
(S)-2'-(N-((1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamoyl)sulfamoyl)-[1,1'-biphenyl]-4-carboxamide

MS $(M+H)^+$ Calcd.	601.2
MS $(M+H)^+$ Observ.	601.3
Retention Time	1.36 min
	LC Condition

Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.08 (br. s., 1H), 7.95 - 7.88 (m, 2H), 7.74 - 7.67 (m, 1H), 7.62 - 7.56 (m, 1H), 7.45 (br. s., 1H), 7.32 - 7.18 (m, 6H), 6.92 (d, *J*=8.1 Hz, 1H), 6.86 (d, *J*=6.6 Hz, 2H), 6.69 - 6.55 (m, 3H), 6.08 (s, 2H), 4.32 (d, *J*=5.9 Hz, 1H), 3.08 (s, 3H), 2.86 - 2.52 (m, 2H).

Example 132



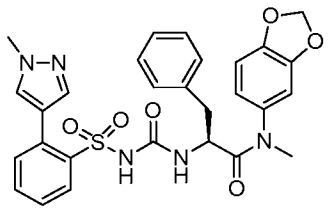
(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(thiophen-3-yl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	564.1
MS $(M+H)^+$ Observ.	564.2
Retention Time	1.63 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate

Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.92 (d, *J*=7.7 Hz, 1H), 7.68 - 7.63 (m, 1H), 7.60 - 7.51 (m, 2H), 7.38 - 7.03 (m, 6H), 6.91 (d, *J*=8.1 Hz, 1H), 6.84 (d, *J*=5.9 Hz, 2H), 6.75 - 6.55 (m, *J*=8.1 Hz, 3H), 6.08 (s, 2H), 4.30 (d, *J*=8.4 Hz, 1H), 3.07 (s, 3H), 2.85 - 2.51 (m, 2H).

Example 133

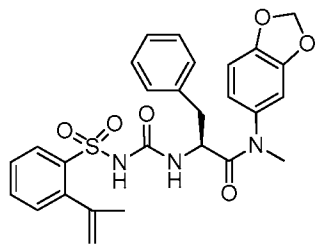


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-(3-((2-(1-methyl-1H-pyrazol-4-yl)phenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	562.2
MS $(M+H)^+$ Observ.	562.1
Retention Time	1.38 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min

Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 134



(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(prop-1-en-2-yl)phenyl)sulfonyl)ureido)propanamide

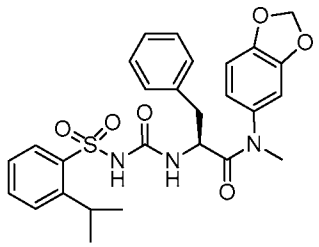
To a 0.5-2 mL microwave tube was added (S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-bromophenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide (30 mg, 0.054 mmol), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (0.1 mL, 0.080 mmol), $Pd(PPh_3)_4$ (6.19 mg, 5.35 µmol), DMF (1 mL), followed by 2M K_2CO_3 (60 µl, 0.120 mmol). The reaction mixture was heated in a microwave reactor at 125°C for 15min. The reaction mixture was filtered and the filtrate was purified by preparative HPLC to afford the title compound (13.4 mg).

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.81 (d, *J*=7.7 Hz, 1H), 7.50 (br. s., 1H), 7.36 (br. s., 1H), 7.16 (br. s., 4H), 6.88 (d, *J*=7.7 Hz, 1H), 6.82 (d, *J*=4.4 Hz, 2H), 6.69 - 6.39 (m, 3H), 6.06 (s, 2H), 5.12 (br. s., 1H), 4.67 (br. s., 1H), 4.27 (d, *J*=5.1 Hz, 1H), 3.06 (s, 3H), 2.82 - 2.43 (m, 2H), 1.99 (s, 3H).

MS $(M+H)^+$ Calcd.	522.2
MS $(M+H)^+$ Observ.	522.2
Retention Time	1.79 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM

	Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

Example 135



(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-isopropylphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

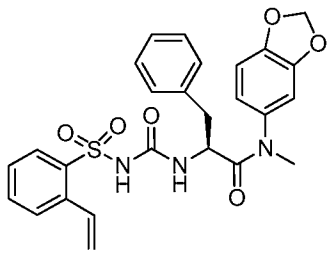
A mixture of 10% palladium on carbon (1.0 mg, 0.94 μmol) in methanol (1 mL) was stirred under H_2 balloon for 5 min. (S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(prop-1-en-2-yl)phenyl)sulfonyl)ureido)propanamide (15 mg, 0.029 mmol) in methanol (1 mL) was added. The reaction mixture was stirred under H_2 balloon for 16 hrs. The palladium catalyst was filtered off and the solvent was evaporated. The residue was purified by preparative HPLC to afford the title compound (8.2 mg). ^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 (d, *J*=7.3 Hz, 1H), 7.44 (br. s., 2H), 7.29 - 7.03 (m, 5H), 6.90 - 6.77 (m, 3H), 6.64 - 6.45 (m, 2H), 6.05 (br. s., 2H), 4.23 (d, *J*=5.9 Hz, 1H), 4.01 - 3.91 (m, 1H), 3.14 - 2.68 (m, 5H), 1.20 - 0.95 (m, 6H).

MS $(M+H)^+$ Calcd.	524.2
MS $(M+H)^+$ Observ.	524.3
Retention Time	1.72 min

	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Examples 136 – 140 were synthesized using the procedure described above for Example 134.

Example 136



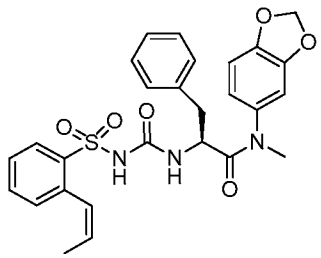
(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-vinylphenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	508.2
MS $(M+H)^+$ Observ.	508.1
Retention Time	1.56 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate

Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=7.7 Hz, 1H), 7.68 (br. s., 1H), 7.62 - 7.41 (m, 2H), 7.39 - 7.05 (m, 5H), 6.92 - 6.76 (m, 3H), 6.72 - 6.42 (m, 2H), 6.05 (s, 2H), 5.75 (d, *J*=15.4 Hz, 1H), 5.32 (d, *J*=11.4 Hz, 1H), 4.24 (br. s., 1H), 3.05 (s, 3H), 2.73 - 2.42 (m, 2H).

Example 137



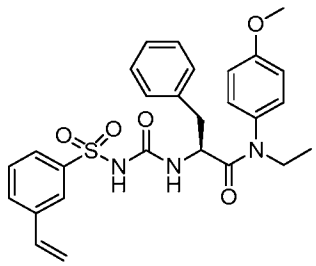
(S,Z)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-(prop-1-en-1-yl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	522.2
MS $(M+H)^+$ Observ.	522.2
Retention Time	1.76 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min

Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.84 (d, *J*=7.3 Hz, 1H), 7.55 (br. s., 1H), 7.39 (br. s., 1H), 7.32 (d, *J*=7.0 Hz, 1H), 7.17 (br. s., 3H), 6.91 - 6.76 (m, 4H), 6.64 - 6.37 (m, 3H), 6.06 (s, 2H), 5.83 (dd, *J*=11.6, 7.9 Hz, 1H), 4.25 (br. s., 1H), 3.05 (s, 3H), 2.80 - 2.38 (m, 2H), 1.60 (d, *J*=6.6 Hz, 3H).

Example 138



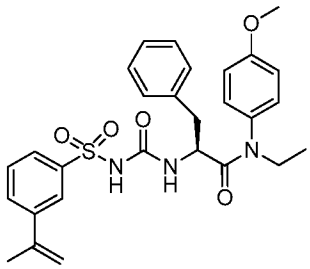
(S)-N-ethyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-((3-vinylphenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	508.2
MS $(M+H)^+$ Observ.	508.2
Retention Time	1.62 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate

Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.85 (s, 1H), 7.74 (d, *J*=7.3 Hz, 1H), 7.66 (d, *J*=7.0 Hz, 1H), 7.58 - 7.40 (m, 1H), 7.15 (d, *J*=2.9 Hz, 3H), 7.00 - 6.73 (m, 7H), 6.59 (br. s., 1H), 5.93 (d, *J*=17.6 Hz, 1H), 5.40 (d, *J*=11.0 Hz, 1H), 4.24 - 4.10 (m, *J*=5.9 Hz, 1H), 3.78 (s, 3H), 3.67 - 3.39 (m, 2H), 2.83 - 2.43 (m, 2H), 0.94 (t, *J*=7.0 Hz, 3H).

Example 139

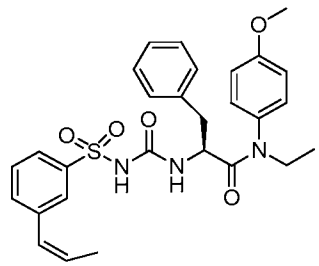


(S)-N-ethyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-((3-(prop-1-en-2-yl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	522.2
MS $(M+H)^+$ Observ.	522.2
Retention Time	1.68 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.91 (s, 1H), 7.82 (d, *J*=7.7 Hz, 1H), 7.72 (d, *J*=7.7 Hz, 1H), 7.62 - 7.50 (m, 1H), 7.20 - 7.08 (m, 3H), 6.92 (br. s., 4H), 6.83 - 6.66 (m, 3H), 5.52 (s, 1H), 5.26 (s, 1H), 4.24 - 4.12 (m, 1H), 3.78 (s, 3H), 3.66 - 3.41 (m, 2H), 2.86 - 2.44 (m, 2H), 2.14 (s, 3H), 0.94 (t, *J*=7.0 Hz, 3H).

Example 140



(S,Z)-N-ethyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-((3-(prop-1-en-1-yl)phenyl)sulfonyl)ureido)propanamide

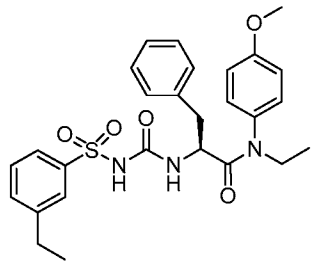
MS (M+H)$^+$ Calcd.	522.2
MS (M+H)$^+$ Observ.	522.2
Retention Time	1.70 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (s, 1H), 7.67 (d, *J*=7.0 Hz, 1H), 7.63 - 7.54 (m, 2H), 7.15 (br. s., 3H), 6.93 (br. s., 4H), 6.82 - 6.64 (m, 3H), 6.51 (d, *J*=11.4 Hz,

1H), 5.93 (dd, *J*=11.6, 7.2 Hz, 1H), 4.18 (q, *J*=7.1 Hz, 1H), 3.78 (s, 3H), 3.68 - 3.42 (m, 2H), 2.82 - 2.45 (m, 2H), 1.86 (d, *J*=7.0 Hz, 3H), 0.94 (t, *J*=7.2 Hz, 3H).

Examples 141 – 146 were synthesized using the procedure described above for Example 135.

Example 141



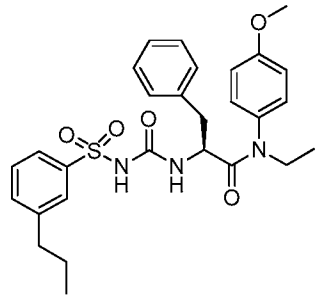
(S)-N-ethyl-2-(3-((3-ethylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.2
Retention Time	1.81 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.66 (s, 1H), 7.61 (d, *J*=7.3 Hz, 1H), 7.56 - 7.45 (m, 2H), 7.21 - 7.11 (m, 3H), 6.93 (br. s., 4H), 6.82 - 6.66 (m, 3H), 4.23 - 4.14 (m,

1H), 3.78 (s, 3H), 3.67 - 3.42 (m, 2H), 2.81 - 2.46 (m, 4H), 1.19 (t, *J*=7.7 Hz, 3H), 0.95 (t, *J*=7.2 Hz, 3H).

Example 142

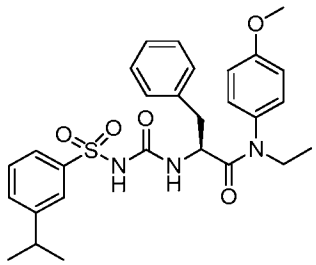


(S)-N-ethyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-((3-propylphenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	524.2
MS $(M+H)^+$ Observ.	524.3
Retention Time	1.91 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.66 - 7.57 (m, 2H), 7.54 - 7.45 (m, 2H), 7.16 (d, *J*=3.7 Hz, 3H), 6.93 (br. s., 4H), 6.77 (d, *J*=3.7 Hz, 2H), 6.72 (d, *J*=8.1 Hz, 1H), 4.22 - 4.14 (m, 1H), 3.78 (s, 3H), 3.65 - 3.46 (m, 2H), 2.81 - 2.42 (m, 4H), 1.65 - 1.52 (m, 2H), 0.94 (t, *J*=7.0 Hz, 3H), 0.88 (t, *J*=7.3 Hz, 3H).

Example 143

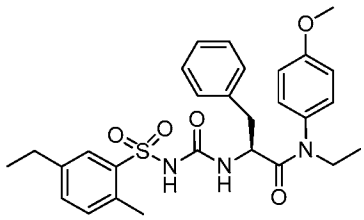


(S)-N-ethyl-2-(3-((3-isopropylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	524.2
MS $(M+H)^+$ Observ.	524.2
Retention Time	1.85 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.81 (s, 1H), 7.71 - 7.65 (m, 1H), 7.53 (s, 1H), 7.47 (d, *J*=7.8 Hz, 1H), 7.24 - 7.15 (m, 3H), 6.93 - 6.83 (m, 6H), 4.41 (s, 1H), 3.82 (s, 3H), 3.75 - 3.45 (m, 2H), 3.02 (dt, *J*=13.9, 6.9 Hz, 1H), 2.94 - 2.60 (m, 2H), 1.30 (dd, *J*=6.8, 1.5 Hz, 6H), 1.04 (t, *J*=7.2 Hz, 3H).

Example 144

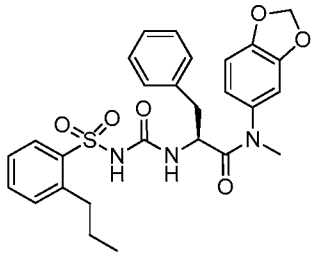


(S)-N-ethyl-2-(3-((5-ethyl-2-methylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	524.2
MS $(M+H)^+$ Observ.	524.3
Retention Time	1.89 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 7.83 (d, *J*=1.5 Hz, 1H), 7.40 - 7.24 (m, 2H), 7.21 - 7.12 (m, 3H), 6.89 - 6.79 (m, 6H), 4.40 (t, *J*=6.7 Hz, 1H), 3.80 (s, 3H), 3.73 - 3.47 (m, 2H), 2.70 (d, *J*=7.8 Hz, 4H), 1.97 (s, 3H), 1.26 (t, *J*=7.6 Hz, 3H), 1.02 (t, *J*=7.2 Hz, 3H).

Example 145

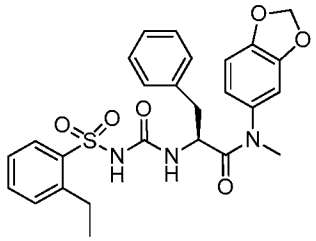


(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-3-phenyl-2-(3-((2-propylphenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	524.2
MS $(M+H)^+$ Observ.	524.3
Retention Time	1.88 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=8.1 Hz, 1H), 7.55 - 7.08 (m, 7H), 6.91 - 6.78 (m, 3H), 6.70 - 6.40 (m, 2H), 6.06 (br. s., 2H), 4.27 (d, *J*=6.2 Hz, 1H), 3.06 (s, 3H), 2.94 - 2.69 (m, 2H), 2.58 - 2.41 (m, 2H), 1.62 - 1.42 (m, 2H), 0.94 (t, *J*=6.8 Hz, 3H).

Example 146

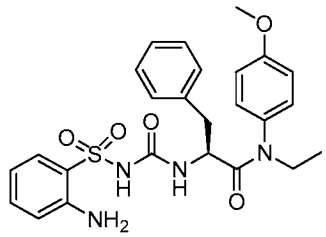


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-ethylphenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.3
Retention Time	1.73 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.7 Hz, 1H), 7.56 - 7.07 (m, 7H), 6.88 (d, *J*=8.4 Hz, 1H), 6.80 (d, *J*=2.9 Hz, 2H), 6.71 - 6.35 (m, 2H), 6.06 (s, 2H), 4.27 (d, *J*=5.5 Hz, 1H), 3.06 (s, 3H), 2.94 (q, *J*=7.2 Hz, 2H), 2.82 - 2.45 (m, 2H), 1.14 (t, *J*=7.2 Hz, 3H).

Example 147



(S)-2-(3-((2-aminophenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

A mixture of 10% palladium on carbon (4.0 mg, 3.8 μmol) in methanol (4 mL) was stirred under H_2 balloon for 5 min. (S)-N-ethyl-N-(4-methoxyphenyl)-2-(3-((2-nitrophenyl)sulfonyl)ureido)-3-phenylpropanamide (20 mg, 0.038 mmol) in methanol (1 mL) was added. The reaction mixture was stirred under a H_2 balloon for 3 hrs. The palladium catalyst was filtered off and the solvent was evaporated. The residue was purified by preparative HPLC to afford the title compound (14 mg).

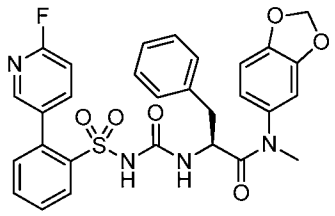
^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.47 (d, *J*=8.1 Hz, 1H), 7.28 - 7.12 (m, 4H), 6.90 (br. s., 4H), 6.83 - 6.72 (m, 3H), 6.63 - 6.48 (m, 2H), 4.21 - 4.11 (m, *J*=6.6 Hz, 1H), 3.77 (s, 3H), 3.67 - 3.43 (m, 2H), 2.79 - 2.46 (m, 2H), 0.95 (t, *J*=7.2 Hz, 3H).

MS $(M+H)^+$ Calcd.	497.2
MS $(M+H)^+$ Observ.	497.2
Retention Time	1.49 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate

Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 148 was synthesized using the procedure described above for Example 48.

Example 148

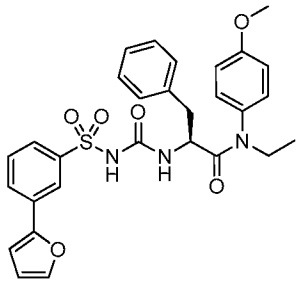


(S)-N-(benzo[d][1,3]dioxol-5-yl)-2-(3-((2-(6-fluoropyridin-3-yl)phenyl)sulfonyl)ureido)-N-methyl-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	577.2
MS $(M+H)^+$ Observ.	577.2
Retention Time	1.54 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.08 (s, 1H), 7.96 (s, 1H), 7.85 (br. s., 1H), 7.68 - 7.51 (m, 2H), 7.34 - 7.08 (m, 6H), 6.95 - 6.80 (m, 3H), 6.71 - 6.48 (m, 2H), 6.07 (s, 2H), 4.29 (d, *J*=5.1 Hz, 1H), 3.06 (s, 3H), 2.83 - 2.52 (m, 2H).

Example 149



(S)-N-ethyl-2-(3-(((3furan-2-phenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

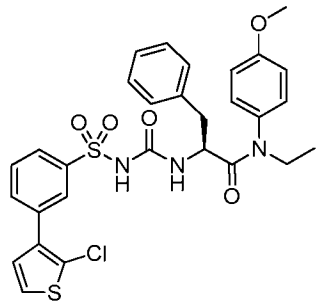
To a 0.5-2 mL microwave tube was added (S)-2-(3-((3-bromophenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide (18.5 mg, 0.033 mmol), 2-(furan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11.6 mg, 0.060 mmol), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)chloride dichloromethane complex (1.23 mg, 1.05 μmol), 1,4-dioxane (1 mL), followed by 2M K_3PO_4 (100 μL). The reaction mixture was heated in a microwave reactor at 100°C for 15 min. The reaction mixture was filtered and the filtrate was purified by preparative HPLC to afford the title compound (8.8 mg).

MS $(M+H)^+$ Calcd.	548.1
MS $(M+H)^+$ Observ.	548.1
Retention Time	1.73 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate

Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Examples 150 – 154 were synthesized using the procedure described above for Example 149.

Example 150

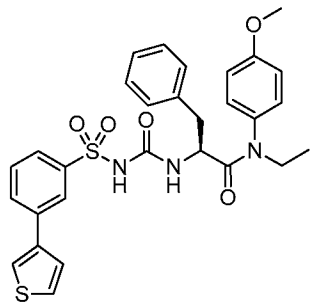


(S)-2-(3-((3-(2-chlorothiophen-3-yl)phenyl)sulfonyl)ureido)-N-ethyl-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	598.1
MS $(M+H)^+$ Observ.	598.1
Retention Time	1.82 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Solvent Pair	acetonitrile : Water : Ammonium Acetate
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.02 (br. s., 1H), 7.89 - 7.78 (m, 2H), 7.72 - 7.57 (m, 3H), 7.28 (d, *J*=5.9 Hz, 2H), 7.12 (br. s., 3H), 6.90 (br. s., 4H), 6.78 (br. s., 2H), 4.18 (d, *J*=6.6 Hz, 1H), 3.77 (s, 3H), 3.66 - 3.45 (m, 2H), 2.80 - 2.51 (m, 2H), 2.51 (s, 3H), 0.93 (t, *J*=7.0 Hz, 4H).

Example 151

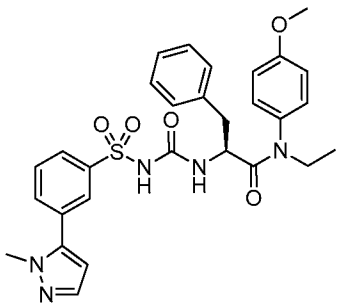


(S)-N-ethyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-((3-(thiophen-3-yl)phenyl)sulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	564.2
MS $(M+H)^+$ Observ.	564.2
Retention Time	1.75 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.08 (br. s., 1H), 8.01 - 7.88 (m, 1H), 7.77 - 7.66 (m, 2H), 7.58 (d, *J*=5.5 Hz, 2H), 7.20 - 7.08 (m, 3H), 6.88 (br. s., 4H), 6.79 (br. s., 2H), 6.58 (br. s., 1H), 4.17 (d, *J*=6.2 Hz, 1H), 3.75 (s, 3H), 3.64 - 3.42 (m, 2H), 2.79 - 2.44 (m, 2H), 2.51 (s, 3H), 0.92 (t, *J*=6.8 Hz, 3H).

Example 152



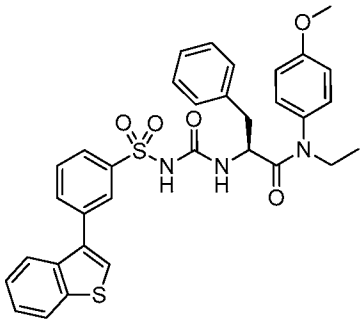
(S)-N-ethyl-N-(4-methoxyphenyl)-2-(3-((3-(1-methyl-1H-pyrazol-5-yl)phenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	562.4
MS $(M+H)^+$ Observ.	562.4
Retention Time	1.59 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.90 (br. s., 1H), 7.83 - 7.74 (m, 2H), 7.71 - 7.61 (m, 1H), 7.52 (s, 1H), 7.21 - 7.09 (m, 3H), 6.91 (br. s., 4H), 6.78 (br. s., 2H), 6.58 -

6.41 (m, 2H), 4.17 (d, *J*=5.9 Hz, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 3.64 - 3.44 (m, 2H), 2.79 - 2.38 (m, 2H), 0.93 (t, *J*=7.2 Hz, 3H).

Example 153

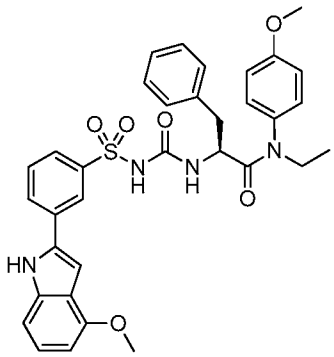


(S)-2-(3-((3-(benzo[b]thiophen-3-yl)phenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	614.2
MS $(M+H)^+$ Observ.	614.2
Retention Time	1.94 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.12 (s, 1H), 8.05 (s, 1H), 7.93 - 7.82 (m, 3H), 7.78 - 7.66 (m, 1H), 7.53 - 7.34 (m, 2H), 7.06 (d, *J*=3.3 Hz, 3H), 6.95 - 6.83 (m, 4H), 6.76 (d, *J*=3.7 Hz, 2H), 6.67 (br. s., 1H), 4.26 - 4.13 (m, 1H), 3.73 (s, 3H), 3.61 - 3.36 (m, 2H), 2.81 - 2.45 (m, 2H), 0.90 (t, *J*=7.2 Hz, 3H).

Example 154

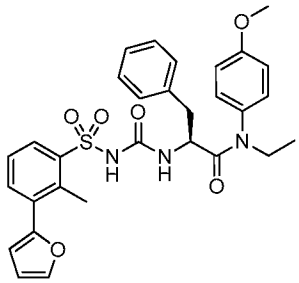


(S)-N-ethyl-2-(3-((3-(4-methoxy-1H-indol-2-yl)phenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	627.2
MS $(M+H)^+$ Observ.	627.2
Retention Time	2.79 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 11.75 (br. s., 1H), 8.25 (br. s., 1H), 8.03 (br. s., 1H), 7.70 - 7.45 (m, 3H), 7.11 (br. s., 2H), 7.06 - 7.03 (m, 2H), 6.98 (br. s., 1H), 6.86 - 6.78 (m, 4H), 6.52 (d, *J*=5.5 Hz, 1H), 4.18 (br. s., 1H), 3.89 (s, 3H), 3.69 (br. s., 3H), 3.62 - 3.37 (m, 2H), 2.82 - 2.45 (m, 2H), 0.90 (br. s., 3H).

Example 155



(S)-N-ethyl-2-(3-(((3furan-2-phenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

To a 0.5-2 mL microwave tube was added (S)-2-(3-((3-bromo-2-methylphenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide (17.3 mg, 0.030 mmol), 2-(furan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11.6 mg, 0.060 mmol), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)chloride dichloromethane complex (1.2 mg, 1.5 μmol), 1,4-dioxane (1 mL), followed by 2M K_3PO_4 (100 μL). The reaction mixture was heated in a microwave reactor at 100°C for 15 min. The reaction mixture was filtered and the filtrate was purified by preparative HPLC to afford the title compound (5.5 mg).

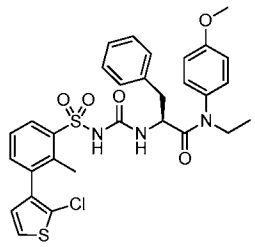
MS $(M+H)^+$ Calcd.	562.2
MS $(M+H)^+$ Observ.	562.2
Retention Time	1.78 min
	LC condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220

Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.89 - 7.74 (m, 2H), 7.63 (br. s., 1H), 7.30 (br. s., 1H), 7.12 (d, *J*=4.0 Hz, 3H), 6.93 - 6.78 (m, 6H), 6.74 - 6.56 (m, 2H), 4.14 (br. s., 1H), 3.75 (br. s., 3H), 3.63 - 3.41 (m, 2H), 2.76 - 2.52 (m, 2H), 2.59 (s, 3H), 0.92 (br. s., 3H).

Examples 156 – 162 were synthesized using the procedure described above for Example 149.

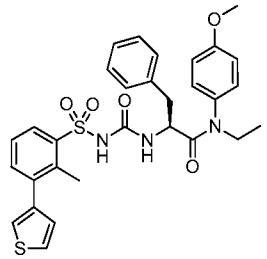
Example 156



(S)-2-(3-((3-(2-chlorothiophen-3-yl)-2-methylphenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	612.1
MS $(M+H)^+$ Observ.	612.3
Retention Time	1.93 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 157

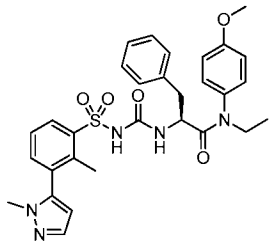


(S)-N-ethyl-N-(4-methoxyphenyl)-2-(3-((2-methyl-3-(thiophen-3-yl)phenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	578.2
MS $(M+H)^+$ Observ.	578.3
Retention Time	1.93 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.82 (d, *J*=8.1 Hz, 1H), 7.68 (br. s., 1H), 7.58 - 7.48 (m, 2H), 7.36 (br. s., 1H), 7.27 - 7.11 (m, 4H), 7.05 - 6.90 (m, 4H), 6.79 (br. s., 2H), 4.17 (br. s., 1H), 3.77 (s, 3H), 3.67 - 3.43 (m, 2H), 2.79 - 2.48 (m, 2H), 2.57 (s, 3H), 0.93 (t, *J*=7.0 Hz, 3H).

Example 158

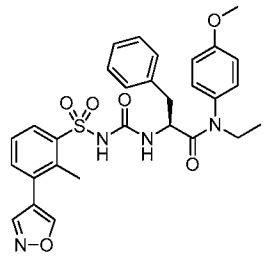


(S)-N-ethyl-N-(4-methoxyphenyl)-2-(3-((2-methyl-3-(1-methyl-1H-pyrazol-5-yl)phenyl)sulfonyl)ureido)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	576.2
MS $(M+H)^+$ Observ.	576.3
Retention Time	1.58 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.88 (d, *J*=8.8 Hz, 1H), 7.51 (s, 1H), 7.33 (br. s., 2H), 7.14 (br. s., 3H), 6.97 - 6.88 (m, 4H), 6.80 (br. s., 2H), 6.23 (br. s., 1H), 4.15 (br. s., 1H), 3.78 (s, 3H), 3.51 (s, 3H), 3.51-3.45 (m, 2H), 2.76 - 2.47 (m, 2H), 2.51 (s, 3H) 0.93 (t, *J*=7.0 Hz, 3H).

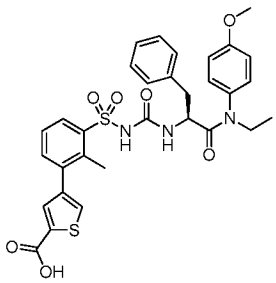
Example 159



(S)-N-ethyl-2-(3-((3-(isoxazol-4-yl)-2-methylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	563.2
MS $(M+H)^+$ Observ.	563.3
Retention Time	1.63 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

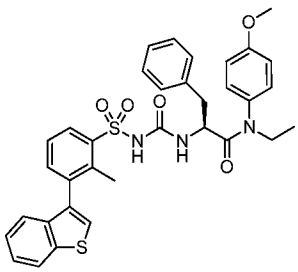
Example 160



(S)-4-(3-(N-((1-(ethyl(4-methoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamoyl)sulfamoyl)-2-methylphenyl)thiophene-2-carboxylic acid

MS $(M+H)^+$ Calcd.	622.2
MS $(M+H)^+$ Observ.	622.3
Retention Time	1.45 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 161



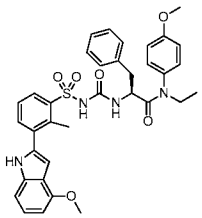
(S)-2-(3-((3-(benzo[b]thiophen-3-yl)-2-methylphenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	628.3
MS $(M+H)^+$ Observ.	628.3
Retention Time	2.05 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM

	Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.10 (d, *J*=8.1 Hz, 1H), 7.76 (br. s., 1H), 7.59 - 7.53 (m, 1H), 7.49 (d, *J*=7.3 Hz, 1H), 7.46 - 7.40 (m, 1H), 7.26 (d, *J*=15.0 Hz, 2H), 7.14 (br. s., 3H), 6.95 (br. s., 4H), 6.81 (br. s., 2H), 6.60 (br. s., 1H), 4.22 (br. s., 1H), 3.78 (s, 3H), 3.69 - 3.46 (m, 2H), 2.82 - 2.53 (m, 2H), 2.31 (s, 3H), 0.94 (t, *J*=7.0 Hz, 3H).

Example 162



(S)-N-ethyl-2-(3-((3-(4-methoxy-1H-indol-2-yl)-2-methylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

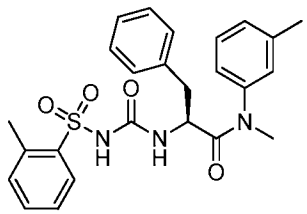
MS $(M+H)^+$ Calcd.	641.2
MS $(M+H)^+$ Observ.	641.3
Retention Time	1.88 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min

Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 11.39 (br. s., 1H), 7.96 (s, 1H), 7.87 (d, *J*=7.7 Hz, 1H), 7.69 (d, *J*=8.4 Hz, 1H), 7.52 - 7.38 (m, 1H), 7.14 (br. s., 3H), 7.09 - 6.87 (m, 5H), 6.80 (d, *J*=3.7 Hz, 2H), 6.58 - 6.39 (m, 2H), 4.18 (br. s., 1H), 3.87 (s, 3H), 3.77 (s, 3H), 3.68 - 3.43 (m, 2H), 2.82 - 2.56 (m, 2H), 2.61 (s, 3H), 0.94 (t, *J*=7.2 Hz, 3H).

Examples 163 – 205 were synthesized using the procedure described above for Example 87.

Example 163



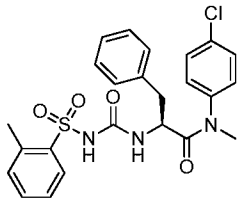
(S)-N-methyl-3-phenyl-N-(m-tolyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	466.2
MS $(M+H)^+$ Observ.	466.2
Retention Time	1.47 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm

particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.79 (d, *J*=7.7 Hz, 2H), 7.63 (d, *J*=7.0 Hz, 1H), 7.60 - 7.51 (m, 2H), 7.32 - 7.23 (m, 1H), 7.17 (br. s., 5H), 6.88 (d, *J*=6.2 Hz, 1H), 6.76 (br. s., 1H), 6.66 (d, *J*=7.0 Hz, 1H), 4.27 (br. s., 1H), 3.09 (s, 3H), 2.51 (s, 3H), 2.81 - 2.42 (m, 2H), 2.24 (s, 3H).

Example 164

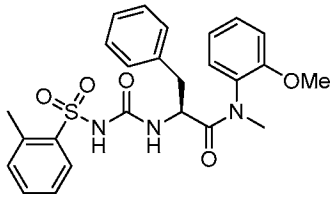


(S)-N-(4-chlorophenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	486.1
MS $(M+H)^+$ Observ.	486.3
Retention Time	1.60 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=5.9 Hz, 1H), 7.41 (d, *J*=7.7 Hz, 4H), 7.29 (br. s., 3H), 7.20 - 7.06 (m, 3H), 6.79 (br. s., 2H), 6.42 (br. s., 1H), 4.22 (br. s., 1H), 3.09 (br. s., 3H), 2.77 - 2.56 (m, 2H), 2.51 (s, 3H),

Example 165

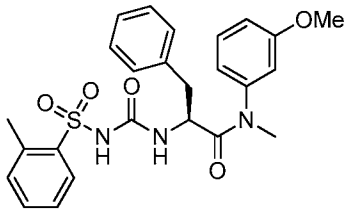


(S)-N-(2-methoxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	482.5
MS $(M+H)^+$ Observ.	482.5
Retention Time	1.49 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.79 (dd, *J*=17.8, 7.9 Hz, 2H), 7.59 - 7.08 (m, 5H), 7.04 - 6.98 (m, 2H), 6.87 (t, *J*=7.5 Hz, 1H), 6.78 - 6.59 (m, 3H), 6.52 (br. s., 1H), 4.28 (br. s., 1H), 3.85 (s, 3H), 3.06 (s, 3H), 2.77 - 2.56 (m, 2H), 2.55 (s, 3H).

Example 166

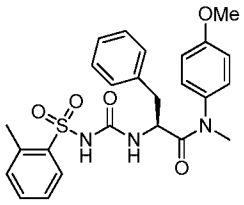


(S)-N-(3-methoxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	482.2
MS $(M+H)^+$ Observ.	482.2
Retention Time	1.59 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.75 (d, *J*=7.3 Hz, 2H), 7.37 (br. s., 1H), 7.24 (d, *J*=7.7 Hz, 3H), 7.14 (br. s., 3H), 6.90 (br. s., 1H), 6.76 (br. s., 2H), 6.59 (br. s., 1H), 6.30 (br. s., 1H), 4.30 (br. s., 1H), 3.67 (br. s., 3H), 3.10 (br. s., 3H), 2.79 - 2.34 (m, 2H), 2.51 (br. s., 3H),

Example 167

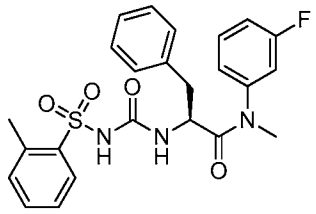


(S)-N-(4-methoxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	482.2
MS $(M+H)^+$ Observ.	482.5
Retention Time	1.34 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=8.1 Hz, 1H), 7.50 (br. s., 1H), 7.40 - 7.28 (m, 2H), 7.15 (br. s., 3H), 7.05 (d, *J*=8.1 Hz, 2H), 6.93 (d, *J*=8.4 Hz, 2H), 6.75 (br. s., 2H), 6.55 (d, *J*=7.3 Hz, 1H), 4.26 (br. s., 1H), 3.77 (s, 3H), 3.09 (s, 3H), 2.79 - 2.34 (m, 2H), 2.51 (s, 3H).

Example 168

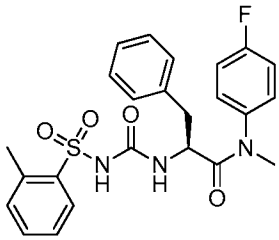


(S)-N-(3-fluorophenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	470.2
MS $(M+H)^+$ Observ.	470.2
Retention Time	1.58 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.79 (d, *J*=7.0 Hz, 1H), 7.52 - 7.38 (m, 3H), 7.36 - 7.29 (m, 2H), 7.26 - 7.10 (m, 4H), 7.03 - 6.92 (m, 2H), 6.77 (br. s., 2H), 6.54 (br. s., 1H), 4.27 (br. s., 1H), 3.12 (br. s., 3H), 2.51 (s, 3H), 2.76 - 2.41 (m, 2H).

Example 169

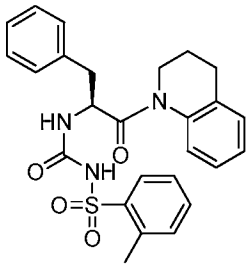


(S)-N-(4-fluorophenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	470.2
MS $(M+H)^+$ Observ.	470.3
Retention Time	1.50 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=7.7 Hz, 1H), 7.45 (br. s., 1H), 7.31 (br. s., 2H), 7.23 - 7.05 (m, 7H), 6.77 (br. s., 2H), 6.46 (br. s., 1H), 4.21 (br. s., 1H), 3.10 (s, 3H), 2.51 (s, 3H), 2.76 - 2.41 (m, 2H).

Example 170

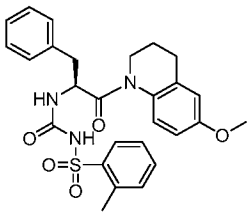


(S)-N-((1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	478.2
MS $(M+H)^+$ Observ.	478.4
Retention Time	1.51 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.7 Hz, 1H), 7.32 (br. s., 2H), 7.21 (br. s., 2H), 7.09 (d, *J*=8.8 Hz, 5H), 6.77 (br. s., 1H), 6.31 (br. s., 1H), 4.93 (br. s., 1H), 3.91-3.81 (m, 2H), 3.39-3.27 (m, 2H), 2.61-2.35 (m, 2H), 2.54 (br. s., 3H), 1.72 - 1.48 (m, 2H).

Example 171

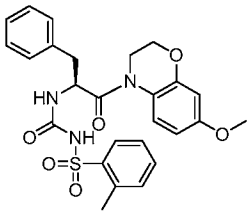


(S)-N-((1-(6-methoxy-3,4-dihydroquinolin-1(2H)-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	508.5
MS $(M+H)^+$ Observ.	508.5
Retention Time	1.48 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.84 (d, *J*=6.6 Hz, 1H), 7.52 (d, *J*=7.3 Hz, 1H), 7.45 - 7.34 (m, 2H), 7.27 - 6.98 (m, 4H), 6.81 - 6.51 (m, 4H), 4.92 (br. s., 1H), 3.95 - 3.83 (m, 2H), 3.73 (s, 3H), 3.41 - 3.29 (m, 2H), 2.70 - 2.35 (m, 2H), 2.55 (s, 3H), 1.80 - 1.44 (m, 2H).

Example 172

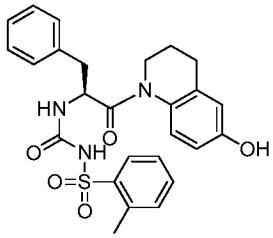


(S)-N-((1-(7-methoxy-2H-benzo[b][1,4]oxazin-4(3H)-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	510.2
MS $(M+H)^+$ Observ.	510.2
Retention Time	1.52 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.85 (br. s., 1H), 7.64 (br. s., 1H), 7.51 (d, *J*=6.6 Hz, 1H), 7.41 - 7.34 (m, 2H), 7.26 - 7.01 (m, 4H), 6.84 (br. s., 1H), 6.74 (br. s., 1H), 6.50 - 6.32 (m, 2H), 4.85 (br. s., 1H), 4.03 (br. s., 2H), 3.70 (br. s., 3H), 3.51 - 3.38 (m, 4H), 2.55 (s, 3H).

Example 173

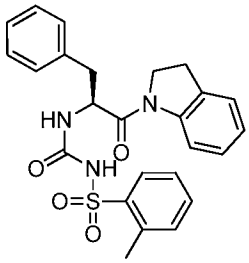


(S)-N-((1-(6-hydroxy-3,4-dihydroquinolin-1(2H)-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	494.2
MS $(M+H)^+$ Observ.	494.5
Retention Time	1.20 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.82 (br. s., 1H), 7.47 (br. s., 1H), 7.33 (br. s., 3H), 7.25 - 7.08 (m, 2H), 6.94 (br. s., 1H), 6.75 (br. s., 1H), 6.60 - 6.29 (m, 3H), 4.92 (br. s., 1H), 3.91 - 3.36 (m, 2H), 2.54 (s, 3H), 2.70 - 2.35 (m, 2H), 2.45 - 2.29 (m, 2H), 1.74 - 1.48 (m, 2H).

Example 174

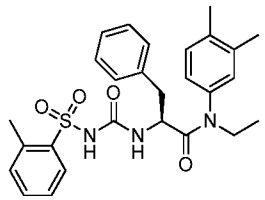


(S)-N-((1-(indolin-1-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	464.2
MS $(M+H)^+$ Observ.	464.4
Retention Time	1.43 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.05 (d, *J*=8.1 Hz, 1H), 7.81 (d, *J*=7.7 Hz, 1H), 7.53 - 7.29 (m, 2H), 7.25 - 7.09 (m, 7H), 7.02 (d, *J*=6.6 Hz, 1H), 6.68 (br. s., 1H), 4.58 (br. s., 1H), 4.21 - 3.76 (m, 2H), 3.42 - 2.68 (m, 4H), 2.58 (s, 3H).

Example 175

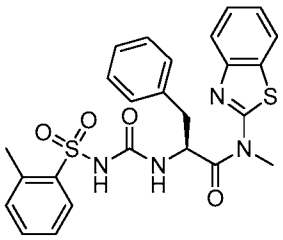


(S)-N-(3,4-dimethylphenyl)-N-ethyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	494.2
MS $(M+H)^+$ Observ.	494.3
Retention Time	1.94 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.81 (d, *J*=8.1 Hz, 1H), 7.62 - 7.48 (m, 1H), 7.46 - 7.35 (m, 2H), 7.17 (d, *J*=3.3 Hz, 3H), 7.11 (d, *J*=8.1 Hz, 1H), 6.81 - 6.57 (m, 4H), 4.22 - 4.08 (m, 1H), 3.66 - 3.45 (m, 2H), 3.14 - 2.81 (m, 2H), 2.53 (s, 3H), 2.21 (s, 3H), 2.14 (s, 3H), 0.94 (t, *J*=7.2 Hz, 3H).

Example 176

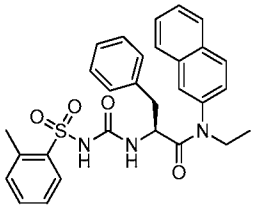


(S)-N-(benzo[d]thiazol-2-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	509.1
MS $(M+H)^+$ Observ.	509.3
Retention Time	1.71 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 8.00 (d, *J*=1.0 Hz, 1H), 7.69 (d, *J*=7.8 Hz, 1H), 7.61 (d, *J*=7.6, Hz, 1H), 7.49 (d, *J*=8.1 Hz, 1H), 7.43 - 7.36 (m, 2H), 7.33 (d, *J*=7.6 Hz, 1H), 7.26 - 7.19 (m, 3H), 7.15 (t, *J*=7.5 Hz, 2H), 7.01 (d, *J*=7.3 Hz, 2H), 4.48 (s, 1H), 3.13 (s, 3H), 3.09 - 2.93 (m, 2H), 2.27 (s, 3H).

Example 177

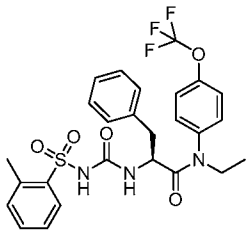


(S)-N-ethyl-N-(naphthalen-2-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	516.2
MS $(M+H)^+$ Observ.	516.3
Retention Time	1.82 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.66 (d, *J*=4.4 Hz, 1H), 7.77 (d, *J*=7.7 Hz, 1H), 7.61 (d, *J*=7.7 Hz, 1H), 7.52 (t, *J*=7.5 Hz, 1H), 7.44 (dd, *J*=7.7, 4.8 Hz, 1H), 7.37 (t, *J*=4.2 Hz, 2H), 7.34 (d, *J*=9.5 Hz, 2H), 7.13 (d, *J*=8.8 Hz, 1H), 7.08 - 7.02 (m, 3H), 6.93 (t, *J*=9.2 Hz, 1H), 6.33 (d, *J*=6.6 Hz, 2H), 4.7 (s, 1H), 3.81-3.6 (m, 2H), 3.01 - 2.70 (m, 2H), 2.51 (br s, 3H), 1.17 (t, *J*=7.3 Hz, 3H).

Example 178

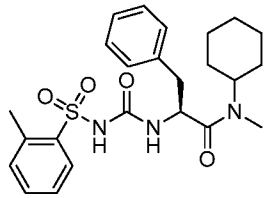


(S)-N-ethyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)-N-(4-(trifluoromethoxy)phenyl)propanamide

MS $(M+H)^+$ Calcd.	550.2
MS $(M+H)^+$ Observ.	550.5
Retention Time	1.81 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.80 (d, *J*=7.7 Hz, 1H), 7.59 - 7.50 (m, 1H), 7.45 - 7.33 (m, 4H), 7.22 (d, *J*=8.1 Hz, 2H), 7.14 (d, *J*=7.0 Hz, 3H), 6.77 - 6.56 (m, 3H), 4.12 (d, *J*=4.8 Hz, 1H), 3.78 - 3.43 (m, 2H), 2.99 - 2.68 (m, 2H), 2.52 (br s., 3H), 0.96 (t, *J*=7.0 Hz, 3H).

Example 179

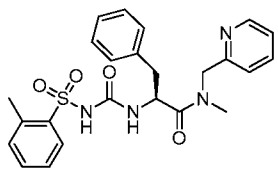


(S)-N-cyclohexyl-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	458.2
MS $(M+H)^+$ Observ.	458.5
Retention Time	1.54 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 8.01 (dd, *J*=8.1, 2.0 Hz, 1H), 7.62 - 7.53 (m, 1H), 7.46 - 7.38 (m, 2H), 7.30 - 7.17 (m, 3H), 7.15 - 7.05 (m, 2H), 4.82 (t, *J*=7.1 Hz, 1H), 4.28 - 4.17 (m, 1H), 2.97 - 2.80 (m, 2H), 2.64 (s, 3H), 2.60 (s, 3H), 1.84 - 0.80 (m, 10H).

Example 180

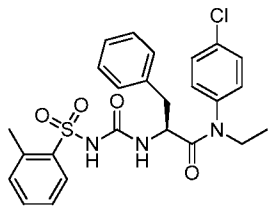


(S)-N-methyl-3-phenyl-N-(pyridin-2-ylmethyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	467.2
MS $(M+H)^+$ Observ.	467.3
Retention Time	1.27 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.48 (d, *J*=4.8 Hz, 1H), 7.79 (d, *J*=7.7 Hz, 1H), 7.75 - 7.60 (m, 2H), 7.36 (br. s., 1H), 7.29 - 7.18 (m, 3H), 7.17 - 7.10 (m, 2H), 7.07 (br. s., 1H), 6.98 (br. s., 1H), 6.90 (d, *J*=8.1 Hz, 1H), 6.37 (br. s., 1H), 4.93 - 4.64 (m, 1H), 4.60 - 4.29 (m, 2H), 3.18 (s, 3H), 2.87 (br. s., 3H), 2.85-2.63 (m, 2H).

Example 181



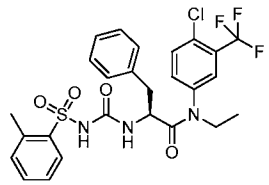
(S)-N-(4-chlorophenyl)-N-ethyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	500.1
MS $(M+H)^+$ Observ.	500.2
Retention Time	1.72 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM

	Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.80 (d, *J*=8.1 Hz, 1H), 7.62 - 7.53 (m, 1H), 7.48 - 7.29 (m, 5H), 7.18 (br. s., 3H), 7.03 (d, *J*=7.3 Hz, 2H), 6.79 (br. s., 2H), 6.66 (d, *J*=7.0 Hz, 1H), 4.12 (d, *J*=7.0 Hz, 1H), 3.70 - 3.48 (m, 2H), 2.83 - 2.56 (m, 2H), 2.52 (s, 3H), 0.94 (t, *J*=7.0 Hz, 3H).

Example 182



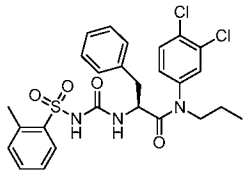
(S)-N-(4-chloro-3-(trifluoromethyl)phenyl)-N-ethyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	568.1
MS $(M+H)^+$ Observ.	568.5
Retention Time	1.87 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100

Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.84 (d, *J*=7.3 Hz, 1H), 7.68 (d, *J*=7.7 Hz, 1H), 7.60 - 7.50 (m, 1H), 7.45 - 7.33 (m, 3H), 7.20 (br. s., 4H), 6.84 (br. s., 2H), 6.75 (d, *J*=7.7 Hz, 1H), 4.03 (d, *J*=7.7 Hz, 1H), 3.69 - 3.45 (m, 2H), 2.83 - 2.56 (m, 2H), 2.53 (s, 3H), 0.91 (t, *J*=6.8 Hz, 3H).

Example 183

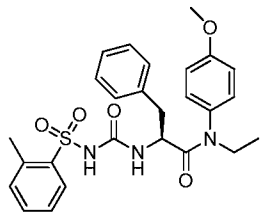


(S)-N-(3,4-dichlorophenyl)-3-phenyl-N-propyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	548.11
MS $(M+H)^+$ Observ.	548.5
Retention Time	1.91 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.84 (d, *J*=7.3 Hz, 1H), 7.68 (d, *J*=7.7 Hz, 1H), 7.60 - 7.50 (m, 1H), 7.45 - 7.33 (m, 3H), 7.20 (br. s., 4H), 6.84 (br. s., 2H), 6.75 (d, *J*=7.7 Hz, 1H), 4.03 (d, *J*=7.7 Hz, 1H), 3.69 - 3.45 (m, 2H), 2.83 - 2.56 (m, 2H), 2.53 (s, 3H), 1.29 (m. 2H), 0.91 (t, *J*=6.8 Hz, 3H).

Example 184

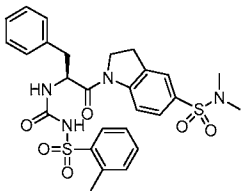


(S)-N-ethyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	496.2
MS $(M+H)^+$ Observ.	496.3
Retention Time	1.58 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.79 (d, *J*=7.7 Hz, 1H), 7.60 - 7.50 (m, 1H), 7.43 - 7.31 (m, 2H), 7.16-7.14 (m, 3H), 7.03 - 6.90 (m, 4H), 6.77-6.75 (m, 2H), 6.62 (d, *J*=8.8 Hz, 1H), 4.24 (br. s., 1H), 3.77 (s, 3H), 3.69 - 3.40 (m, 2H), 2.80 - 2.50 (m, 2H), 2.55 (s, 3H), 0.95 (t, *J*=7.0 Hz, 3H).

Example 185

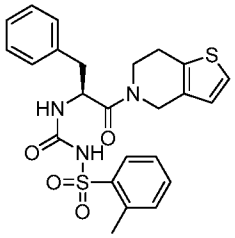


(S)-N,N-dimethyl-1-(3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanoyl)indoline-5-sulfonamide

MS $(M+H)^+$ Calcd.	571.2
MS $(M+H)^+$ Observ.	571.5
Retention Time	2.27 min
	LC Condition
Solvent A	5 % Methanol : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % Methanol : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (400 MHZ, MeOH-d_4) δ 8.52 (br. s., 1H), 8.29 (d, *J*=8.1 Hz, 2H), 7.95 (d, *J*=6.8 Hz, 2H), 7.64 - 7.53 (m, 2H), 7.47 - 7.37 (m, 3H), 7.29-7.26 (m, 3H), 4.75 (br. s., 1H), 4.20 (br. s., 1H), 3.63 (br. s., 1H), 3.16 - 2.87 (m, 4H), 2.70 (s, 3H), 2.67 (s, 3H), 2.64 (S, 3H).

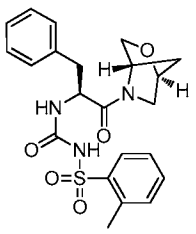
Example 186



(S)-N-((1-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	484.1
MS $(M+H)^+$ Observ.	484.2
Retention Time	1.73 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 187

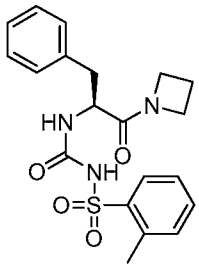


N-(((S)-1-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	444.2

MS $(M+H)^+$ Observ.	444.2
Retention Time	1.11 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 188



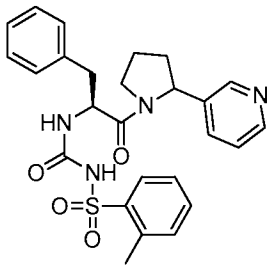
(S)-N-((1-(azetidin-1-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	402.1
MS $(M+H)^+$ Observ.	402.2
Retention Time	1.14 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0

Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.83 (d, *J*=7.7 Hz, 1H), 7.48 (br. s., 1H), 7.35 (br. s., 1H), 7.24-7.26 (m, 4H), 7.08 (d, *J*=7.3 Hz, 2H), 6.47 (br. s., 1H), 4.17 (d, *J*=6.6 Hz, 1H), 3.85 - 3.68 (m, 2H), 3.66 - 3.54 (m, 2H), 2.82 - 2.63 (m, 2H), 2.51 (m, 3H), 2.16 - 1.90 (m, 2H).

Example 189

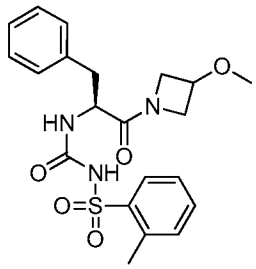


2-methyl-N-(((2S)-1-oxo-3-phenyl-1-(2-(pyridin-3-yl)pyrrolidin-1-yl)propan-2-yl)carbamoyl)benzenesulfonamide

MS $(M+H)^+$ Calcd.	493.2
MS $(M+H)^+$ Observ.	493.2
Retention Time	1.28 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220

Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 190

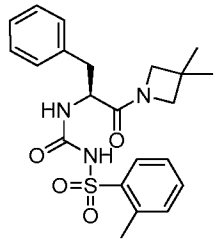


(S)-N-((1-(3-methoxyazetidin-1-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	432.2
MS $(M+H)^+$ Observ.	432.4
Retention Time	1.98 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.75 (d, *J*=7.3 Hz, 1H), 7.36 - 7.06 (m, 8H), 6.16 (br. s., 1H), 4.15 (br. s., 1H), 4.07 - 3.74 (m, 4H), 3.61 - 3.23 (m, 2H), 3.12 (s, 3H), 2.51 (s, 3H).

Example 191

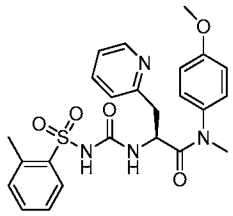


(S)-N-((1-(3,3-dimethylazetidin-1-yl)-1-oxo-3-phenylpropan-2-yl)carbamoyl)-2-methylbenzenesulfonamide

MS $(M+H)^+$ Calcd.	430.2
MS $(M+H)^+$ Observ.	430.3
Retention Time	1.36 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.77 (d, *J*=7.3 Hz, 1H), 7.36 - 7.03 (m, 8H), 6.12 (br. s., 1H), 4.12 (br. s., 1H), 3.67 - 3.00 (m, 6H), 2.51 (s, 3H), 1.07 (s, 3H), 0.91 (s, 3H).

Example 192

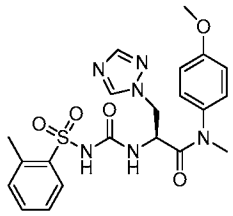


(S)-N-(4-methoxyphenyl)-N-methyl-3-(pyridin-2-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	483.2
MS $(M+H)^+$ Observ.	483.2
Retention Time	1.22 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.34 (d, *J*=4.0 Hz, 1H), 7.77 (d, *J*=8.1 Hz, 1H), 7.58 (t, *J*=7.3 Hz, 1H), 7.54 - 7.47 (m, 1H), 7.39 - 7.31 (m, 2H), 7.21 - 7.14 (m, 1H), 7.07 (d, *J*=8.1 Hz, 2H), 6.97 - 6.82 (m, 3H), 6.61 (br. s., 1H), 4.44 (br. s., 1H), 3.76 (s, 3H), 3.07 (s, 3H), 2.93-2.63 (m, 2H), 2.5 (s *J*=13.4, 3H).

Example 193

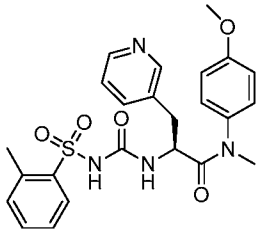


(S)-N-(4-methoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)-3-(1H-1,2,4-triazol-1-yl)propanamide

MS $(M+H)^+$ Calcd.	473.2
MS $(M+H)^+$ Observ.	473.1
Retention Time	1.85 min
	LC Condition
Solvent A	5 % Methanol : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % Methanol : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.24 (s, 1H), 7.87 - 7.74 (m, 2H), 7.53 (d, *J*=6.6 Hz, 1H), 7.44 - 7.33 (m, 2H), 7.15-7.11 (m, 3H), 6.92 (d, *J*=8.4 Hz, 2H), 6.83 (br. s., 1H), 4.46 (br. s., 1H), 4.31 - 4.02 (m, 2H), 3.76 (s, 3H), 3.09 (s, 3H), 2.54 (s, 3H).

Example 194

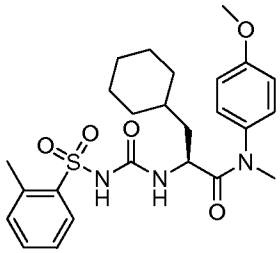


(S)-N-(4-methoxyphenyl)-N-methyl-3-(pyridin-3-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	483.2
MS $(M+H)^+$ Observ.	483.2
Retention Time	1.15
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.34 (br. s., 1H), 7.72 (d, *J*=7.7 Hz, 1H), 7.36 (br. s., 1H), 7.24 (br. s., 2H), 7.15-7.11 (m, 4H), 6.91-6.94 (m, 3H), 6.29 (br. s., 1H), 4.25 (br. s., 1H), 3.77 (br. s., 3H), 3.09 (s, 3H), 2.76 - 2.49 (m, 2H), 2.5 (s, 3H).

Example 195

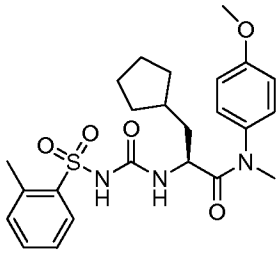


(S)-3-cyclohexyl-N-(4-methoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	488.2
MS $(M+H)^+$ Observ.	488.2
Retention Time	1.72 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.86 (d, *J*=7.7 Hz, 1H), 7.59 - 7.48 (m, 1H), 7.43 - 7.32 (m, 2H), 7.19 (d, *J*=8.4 Hz, 2H), 6.96 (d, *J*=8.4 Hz, 2H), 6.51 (br. s., 1H), 4.21 (t, *J*=7.7 Hz, 1H), 3.75 (s, 3H), 3.09 (s, 3H), 2.56 (s, 3H), 1.54 - 1.37 (m, 2H), 1.35 - 1.17 (m, 4H), 1.06 - 0.85 (m, 7H).

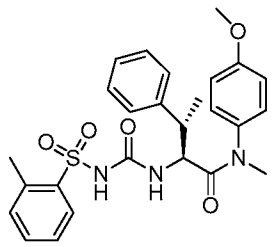
Example 196



(S)-3-cyclopentyl-N-(4-methoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	474.2
MS $(M+H)^+$ Observ.	474.2
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

Example 197

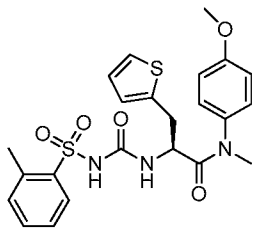


(2S,3S)-N-(4-methoxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)butanamide

MS $(M+H)^+$ Calcd.	496.2
MS $(M+H)^+$ Observ.	496.2
Retention Time	1.73 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.76 (d, *J*=7.7 Hz, 1H), 7.59 - 7.52 (m, 1H), 7.42 - 7.34 (m, 2H), 7.21 - 7.12 (m, 4H), 6.98 - 6.81 (m, 4H), 6.38 (br. s., 1H), 4.40-4.43 (m, 1H), 3.78 (s, 3H), 3.11 (s, 3H), 2.84-2.87 (m, 1H), 2.46 (s, 3H), 0.90 (d, *J*=7.3 Hz, 3H).

Example 198



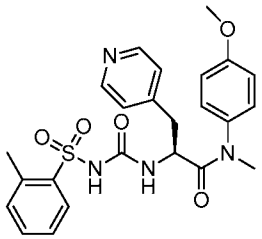
(S)-N-(4-methoxyphenyl)-N-methyl-3-(thiophen-2-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	488.1
MS $(M+H)^+$ Observ.	488.1
Retention Time	1.4 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM

	Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.81 (d, *J*=7.7 Hz, 1H), 7.51 (br. s., 1H), 7.42 - 7.32 (m, 2H), 7.25 (d, *J*=4.8 Hz, 1H), 7.07 (d, *J*=8.1 Hz, 2H), 6.93 (s, 1H), 6.87 - 6.81 (m, 1H), 6.66 - 6.49 (m, 2H), 4.24 (br. s., 1H), 3.76 (s, 3H), 3.09 (s, 3H), 2.99 - 2.67 (m, 2H), 2.55 (s, 3H).

Example 199



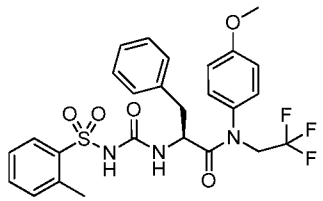
(S)-N-(4-methoxyphenyl)-N-methyl-3-(pyridin-4-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	483.3
MS $(M+H)^+$ Observ.	483.1
Retention Time	1.09 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0

Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.31 (d, *J*=5.5 Hz, 1H), 7.73 (d, *J*=7.7 Hz, 1H), 7.43 - 7.22 (m, 3H), 7.13 (d, *J*=7.3 Hz, 2H), 6.94 (d, *J*=8.4 Hz, 2H), 6.75 (d, *J*=5.1 Hz, 2H), 6.36 (br. s., 1H), 4.29 (br. s., 1H), 3.78 (br. s., 3H), 3.10 (s, 3H), 2.74 - 2.54 (m, 2H), 2.5 (s, 3H).

Example 200

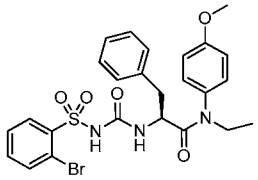


(S)-N-(4-methoxyphenyl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)-N-(2,2,2-trifluoroethyl)propanamide

MS $(M+H)^+$ Calcd.	550.2
MS $(M+H)^+$ Observ.	550.3
Retention Time	2.0 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm

particles

Example 201

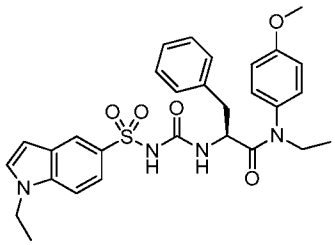


(S)-2-(3-((2-bromophenyl)sulfonyl)ureido)-N-ethyl-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	560.1
MS $(M+H)^+$ Observ.	560.1
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.89 (d, *J*=7.7 Hz, 1H), 7.70 (d, *J*=7.3 Hz, 1H), 7.46 - 7.31 (m, 2H), 7.15 (br. s., 3H), 6.94 - 6.72 (m, 5H), 6.33 (br. s., 1H), 4.15 (br. s., 1H), 3.70 (s, 3H), 3.69 - 3.41 (m, 2H), 2.77 - 2.4 (m, 2H), 0.94 (t, *J*=7.0 Hz, 3H).

Example 203

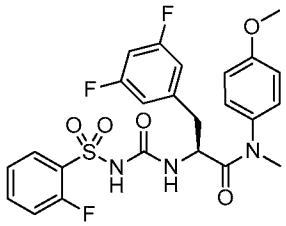


(S)-N-ethyl-2-(3-((1-ethyl-1H-indol-5-yl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

MS $(M+H)^+$ Calcd.	549.2
MS $(M+H)^+$ Observ.	549.4
Retention Time	2.62 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 8.00 (br. s., 1H), 7.53 (br. s., 4H), 7.11 (br. s., 4H), 6.91 - 6.74 (m, 6H), 6.59 (br. s., 1H), 6.41 (br. s., 1H), 4.32 - 4.10 (m, 1H), 3.74 (br. s., 3H), 3.35 (br. s., 2H), 2.95 - 2.65 (m, 4H), 1.34 (br. s., 3H), 0.92 (br. s., 3H).

Example 204

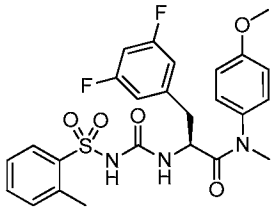


(S)-3-(3,5-difluorophenyl)-2-(3-((2-fluorophenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-N-methylpropanamide

MS $(M+H)^+$ Calcd.	522.1
MS $(M+H)^+$ Observ.	522.2
Retention Time	1.61 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.74 - 7.50 (m, 2H), 7.32 - 7.15 (m, 4H), 6.96-6.97 (m, 3H), 6.41-6.43 (m, 3H), 4.28 (br. s., 1H), 3.78 (s, 3H), 3.10 (s, 3H), 2.77 - 2.52 (m, 2H).

Example 205

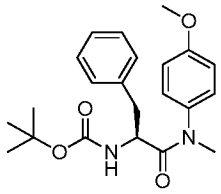


(S)-3-(3,5-difluorophenyl)-N-(4-methoxyphenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

MS $(M+H)^+$ Calcd.	518.2
MS $(M+H)^+$ Observ.	518.2
Retention Time	1.73 min
	LC Condition
Solvent A	5 % acetonitrile : 95% Water : 10mM Ammonium Acetate
Solvent B	95 % acetonitrile : 5% Water : 10mM Ammonium Acetate
Start % B	0
Final % B	100
Gradient Time	3 min
Flow Rate	1 mL/min
Wavelength	220
Column	Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles

^{1}H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=8.1 Hz, 1H), 7.53 (t, *J*=7.2 Hz, 1H), 7.36 (d, *J*=7.7 Hz, 2H), 7.19 (d, *J*=8.8 Hz, 2H), 6.97-7.00 (m, 3H), 6.68 (d, *J*=8.1 Hz, 1H), 6.38 (d, *J*=6.6 Hz, 2H), 4.33 - 4.20 (m, 1H), 3.78 (s, 3H), 3.12 (s, 3H), 2.81 - 2.53 (m, 2H), 2.50 (s, 3H).

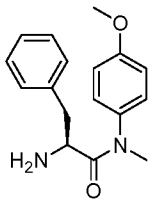
Intermediate JB-1



(S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (1.5 g, 4.0 mmol) was added to a stirred solution of 4-methoxy-N-methylaniline (500 mg, 3.64 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (1.06 g, 4.0 mmol) in DMF (20 mL) and DIPEA (1.3 mL, 7.3 mmol) and the reaction mixture was stirred at rt for 4h. The reaction was concentrated and the residual crude oil was partitioned between EtOAc (~60 mL) and 1/2 sat. $NaHCO_3$ (aq) (~60 mL). The organic component was washed with brine (~40 mL), dried ($MgSO_4$), filtered, concentrated and purified using a Biotage Horizon (80g SiO_2, 10-40% EtOAc/hexanes) to yield (S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (1.34 g) as a clear amber viscous oil. LC-MS retention time = 3.17 min; m/z = 385.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 50mm 3 µm. Solvent A = 95% Water:5% Acetonitrile:10 mM NH_4OAc. Solvent B = 5% Water:95% Acetonitrile:10 mM NH_4OAc. Flow Rate = 0.8 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 4 min. Wavelength = 220). ^1H NMR (400 MHZ, $CDCl_3$) δ 7.25 - 7.20 (m, 3H), 7.03 - 6.64 (m, 6H), 5.20 (d, *J*=8.8 Hz, 1H), 4.53 (q, *J*=7.4 Hz, 1H), 3.83 (s, 3H), 3.18 (s, 3H), 2.89 (dd, *J*=13.1, 7.5 Hz, 1H), 2.71 (dd, *J*=13.1, 6.5 Hz, 1H), 1.39 (s, 9H).

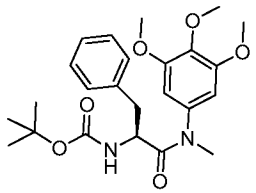
Intermediate JB-2



(S)-2-amino-N-(4-methoxyphenyl)-N-methyl-3-phenylpropanamide

A 4M HCl (15 mL, 60.0 mmol) in dioxanes solution was added to a stirred solution of (S)-tert-butyl (1-((4-methoxyphenyl)(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (Intermediate JB-1) (1.34 g, 3.49 mmol) in THF (10 mL) and the reaction mixture was stirred at rt for 5h. The reaction mixture was concentrated to dryness under vacuum to yield an HCl salt of (S)-2-amino-N-(4-methoxyphenyl)-N-methyl-3-phenylpropanamide (1.11 g) as a solidified foam which was used without additional purification. LC-MS retention time = 2.33 min; m/z = 285.2 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 50mm 3 µm. Solvent A = 95% Water:5% Acetonitrile:10 mM NH_4OAc. Solvent B = 5% Water:95% Acetonitrile:10 mM NH_4OAc. Flow Rate = 0.8 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 4 min. Wavelength = 220).

Intermediate JB-7

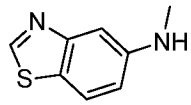


(S)-tert-butyl (1-(methyl(3,4,5-trimethoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (776 mg, 2.04 mmol) was added to a stirred solution of 3,4,5-trimethoxy-N-methylaniline (350 mg, 1.78 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (518 mg, 1.95 mmol) in DMF (10 mL) and DIPEA (0.62 mL, 3.6 mmol) and stirred at rt ON. The reaction mixture was concentrated and the crude oil was partitioned between EtOAc (~40 mL) and 1/2 sat $NaHCO_3$ (aq) (~40 mL). The organic component was washed with brine (~30 mL), dried ($MgSO_4$), filtered and concentrated. The crude residue was then purified using a Biotage Horizon (80g SiO_2, 10-40% EtOAc/hexanes) to yield(S)-tert-butyl (1-(methyl(3,4,5-trimethoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (474 mg) as a clear colorless solidified oil. Used without further purification. LC-MS retention time = 1.60 min; m/z = 385.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 50mm 3 µm.

Solvent A = 90% Water:10% Acetonitrile: 0.1% TFA. Solvent B = 10% Water:90% Acetonitrile: 0.1% TFA. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 2 min. Wavelength = 220). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.27 - 7.17 (m, 3H), 7.01 (d, J=6.3 Hz, 2H), 6.11 (br. s., 2H), 5.21 (d, J=9.0 Hz, 1H), 4.76 - 4.64 (m, 1H), 3.86 (s, 3H), 3.77 (br. s., 6H), 3.17 (s, 3H), 3.01 - 2.87 (m, 1H), 2.77 (dd, J=12.8, 6.3 Hz, 1H), 1.40 (s, 9H).

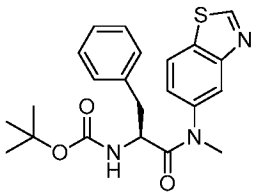
Intermediate ZY-1



N-methylbenzo[d]thiazol-5-amine

Paraformaldehyde (80 mg, 2.7 mmol) was added to a stirred solution of benzo[d]thiazol-5-amine (200 mg, 1.332 mmol) in MeOH (5 mL) The resulting suspension was then treated with 25%w/w NaOMe in MeOH (1.5 mL, 6.7 mmol) and the clear reaction mixture was stirred at 60 °C for 16 h. The reaction was allowed to cool to rt and then treated with $NaBH_4$ (126 mg, 3.33 mmol) and stirred at rt for 16 h. The reaction mixture was diluted with water (10 mL) and extracted with $CHCl_3$ (3 x 20 mL). The combined organic component was concentrated and purified using a Biotage Horizon (12g SiO_2, 0-50% EtOAc/hexanes) to yield N-methylbenzo[d]thiazol-5-amine (217 mg) as yellow gum. .LC-MS retention time = 0.67 min; m/z = 165.05 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.69 (d, *J*=8.5 Hz, 1H), 7.31 (d, *J*=2.3 Hz, 1H), 6.82 (dd, *J*=8.8, 2.3 Hz, 1H), 3.93 (br. s., 1H), 2.94 (s, 3H).

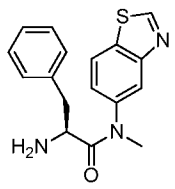
Intermediate ZY-2



(S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

HATU (1.90 g, 5.01 mmol) was added to a solution of N-methylbenzo[d]thiazol-5-amine (Intermediate ZY-1) (685 mg, 4.17 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (1.33 g, 5.01 mmol) in DMF (20 mL) and DIPEA (2.18 mL, 12.5 mmol) and the reaction mixture was stirred at rt for 6 h. The crude reaction mixture was diluted with sat. aq. $NaHCO_3$ (20 mL) and extracted with EtOAc (3 x 50 mL). The combined organic component was washed with brine (~60 mL), dried (Na_2SO_4), filtered and concentrated. The crude material was then purified using a Biotage Horizon (12g SiO_2, 0-40%-50% EtOAc/hexanes) to yield (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (1.7 g) as a white solid. LC-MS retention time = 1.19 min; m/z = 412.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^1H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.90 (d, *J*=8.3 Hz, 1H), 7.38 (d, *J*=7.5 Hz, 1H), 7.27 - 7.19 (m, 3H), 6.94 (d, *J*=6.8 Hz, 3H), 5.22 (d, *J*=8.8 Hz, 1H), 4.58 - 4.48 (m, 1H), 3.26 (s, 3H), 2.93 (dd, *J*=12.9, 8.4 Hz, 1H), 2.78 (dd, *J*=12.4, 5.9 Hz, 1H), 1.40 (s, 9H).

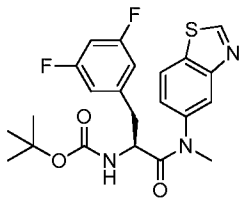
Intermediate ZY-3



(S)-2-amino-N-(benzo[d]thiazol-5-yl)-N-methyl-3-phenylpropanamide

A solution of 4M HCl (10 mL, 40.0 mmol) in dioxanes was added to a stirred solution of (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (Intermediate ZY-2) (1.7 g, 4.13 mmol) in THF (10 mL) and the reaction mixture was stirred at rt for 16 h. The reaction mixture was concentrated, redissolved in EtOH/toluene, and then reconcentrated (3x) to yield an HCl salt of (S)-2-amino-N-(benzo[d]thiazol-5-yl)-N-methyl-3-phenylpropanamide (1.7 g, 4.42 mmol, 107 % yield) as a pink sticky solid. LC-MS retention time = 0.83 min; m/z = 312.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^{1}H NMR (400 MHZ, MeOH-d_4) δ 9.42 (s, 1H), 8.10 (d, *J*=8.3 Hz, 1H), 7.39 - 7.08 (m, 6H), 6.91 (d, *J*=7.0 Hz, 2H), 4.10 (dd, *J*=8.0, 6.5 Hz, 1H), 3.63 - 3.56 (m, 2H), 3.11 (dd, *J*=13.4, 8.2 Hz, 1H), 2.92 (dd, *J*=13.3, 6.5 Hz, 1H), 2.87 (s, 3H).

Intermediate ZY-4

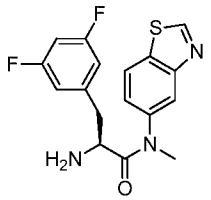


(S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-3-(3,5-difluorophenyl)-1-oxopropan-2-yl)carbamate

HATU (592 mg, 1.556 mmol) was added to a stirred solution of N-methylbenzo[d]thiazol-5-amine (Intermediate ZY-1) (213 mg, 1.30 mmol) and (S)-2-((tert-butoxycarbonyl)amino)-3-(3,5-difluorophenyl)propanoic acid (469 mg, 1.56 mmol) in DMF (7 mL) and DIPEA (0.45 mL, 2.6 mmol) and the reaction mixture was stirred at rt for 16 h. The crude reaction mixture was diluted with sat. aq. $NaHCO_3$ (20 mL) and extracted with EtOAc (3 x 50 mL). The combined organic component was washed with brine (~60 mL), dried (Na_2SO_4), filtered and concentrated. The crude material was then purified using a Biotage Horizon (24g

SiO_2, 0-50% EtOAc/hexanes) yield (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-3-(3,5-difluorophenyl)-1-oxopropan-2-yl)carbamate (581 mg) as a white solid. LC-MS retention time = 1.23 min; m/z = 448.0 $[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220). ^1H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.98 (d, *J*=8.3 Hz, 1H), 7.68 (br. s., 1H), 7.05 (br. s., 1H), 6.68 (t, *J*=8.9 Hz, 1H), 6.44 (d, *J*=6.3 Hz, 2H), 5.25 (d, *J*=9.0 Hz, 1H), 4.54 (q, *J*=7.3 Hz, 1H), 2.94 - 2.86 (m, 1H), 2.81 (s, 3H), 2.72 (dd, *J*=13.1, 6.5 Hz, 1H), 1.39 (s, 9H).

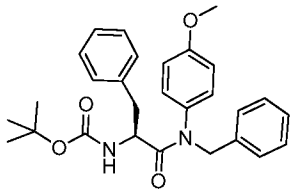
Intermediate ZY-5



(S)-2-amino-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-N-methylpropanamide

TFA (1.0 mL, 13 mmol) was added to a stirred solution of (S)-tert-butyl (1-(benzo[d]thiazol-5-yl(methyl)amino)-3-(3,5-difluorophenyl)-1-oxopropan-2-yl)carbamate (Intermediate ZY-4) (0.58 g, 1.23 mmol) in DCM (2 mL) and the reaction mixture was stirred at rt for 16 h. The crude reaction mixture was concentrated and the residue was dissolved in MeOH/DCM and 4 M HCl in dioxane (2 mL) and reconcentrated. The residue was redissolved in EtOH/toluene, and then reconcentrated (3x) to yield an HCl salt of (S)-2-amino-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-N-methylpropanamide (0.55 g) as a white solid. LC-MS retention time = 0.83 min; m/z = 348.1$[M+H]^+$. (Column: Waters Aquity BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 100% Water : 0.05% TFA. Solvent B = 100% Acetonitrile : 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

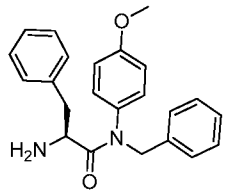
Intermediate ZY-6



(S)-tert-butyl (1-(benzyl(4-methoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

BOP-Cl (131 mg, 0.516 mmol) was added to a stirred solution of (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (124 mg, 0.469 mmol) and N-benzyl-4-methoxyaniline (100 mg, 0.469 mmol) in DCM (3 mL), and DIPEA (0.25 mL, 1.4 mmol) and the reaction mixture was stirred at rt for 16h. The crude reaction mixture was concentrated and the residue was purified using a Biotage Horizon (12 g SiO_2, 0 - 50% Et_2O/hexanes) to yield the title compound (125 mg). LC-MS retention time = 1.43 min; m/z = 461.4 $[M+H]^+$. (Column: Waters Aquity BEH C18 2.1 X 50 mm 1.7U. Solvent A = 100% Water / 0.05% TFA. Solvent B = 100% Acetonitrile / 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

Intermediate ZY-7

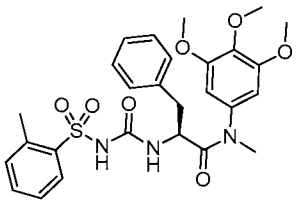


(S)-2-amino-N-benzyl-N-(4-methoxyphenyl)-3-phenylpropanamide

A 4M solution of HCl (1.3 mL, 5.2 mmol) in dioxane was added to a stirred solution of (S)-tert-butyl (1-(benzyl(4-methoxyphenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (Intermediate ZY-6) (120 mg, 0.261 mmol) in THF (1.3 mL) and the reaction mixture was stirred at rt for 2h. The reaction mixture concentrated to yield an HCl salt of the title compound (117 mg). LC-MS retention time = 0.99 min; m/z = 361.2 $[M+H]^+$. (Column: Waters Aquity BEH C18 2.1 X 50 mm 1.7U. Solvent A =

100% Water / 0.05% TFA. Solvent B = 100% Acetonitrile / 0.05% TFA. Flow Rate = 0.8 mL/min. Start % B = 2. Final % B = 98. Gradient Time = 1.5 min. Wavelength = 220).

Example JB-82

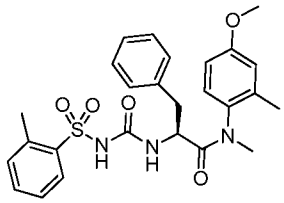


(S)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)-N-(3,4,5-trimethoxyphenyl)propanamide

A solution of 4M HCl (1 mL, 4.0 mmol) in dioxane was added to a stirred solution of Intermediate JB-7 (77 mg, 0.17 mmol) was dissolved into THF (1 mL) and the reaction was stirred at rt for 3h. The reaction mixture was concentrated to dryness dissolved into CH_3CN (1 mL) and Hunig's Base (0.11 mL, 0.61 mmol) and then treated with 2-methylbenzenesulfonyl isocyanate (51 mg, 0.26 mmol) and stirred at rt for 3h. The reaction mixture was quenched with MeOH (5 mL), stirred 5 min. and then concentrated to dryness. The residue was partitioned between EtOAc (10 mL) and water (5 mL) and the organic component was further washed with brine (5 mL) and concentrated. The residue was dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (50.3 mg). LC-MS retention time = 1.98 min; m/z = 542.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Examples JB-83 and JB-84 were prepared using the procedure detailed for Example JB-82 where the 3,4,5-trimethoxy-N-methylaniline used in the preparation of Intermediate JB-7 was replaced with the appropriate amine.

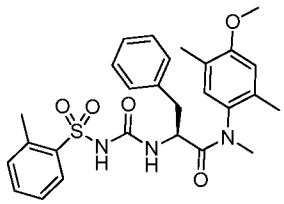
Example JB-83



(S)-N-(4-methoxy-2-methylphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.97 min; m/z = 496.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

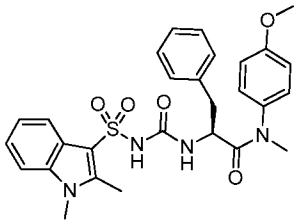
Example JB-84



(S)-N-(4-methoxy-2,5-dimethylphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.03 min; m/z = 510.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

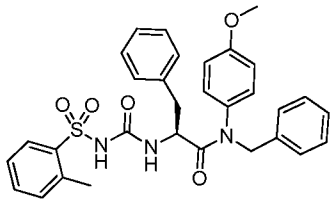
Example JB-85



(S)-2-(3-((1,2-dimethyl-1H-indol-3-yl)sulfonyl)ureido)-N-(4-methoxyphenyl)-N-methyl-3-phenylpropanamide

A solution of sulfurisocyanatidic chloride (0.048 mL, 0.56 mmol) in DCM (1.5 mL) was added dropwise at 0 °C to a stirred solution of Intermediate JB-2 (140 mg, 0.37 mmol) in DCM (~1 mL) and the reaction mixture was stirred at 0 °C for 1h. Then TEA (0.17 mL, 1.2 mmol) in DCM (0.6 mL) was added and reaction mixture was stirred at 0 °C for 3 min. A portion of this crude reaction mixture (~0.8 mL, 25%) was added to a stirred solution of 1,2-dimethyl-1H-indole (43.1 mg, 0.297 mmol) in DCM (1 mL) and stirred at rt for 2 h. The reaction was concentrated diluted with EtOAc (~2 mL) and washed with sat. aq. $NaHCO_3$ (aq) (1mL) and brine (1 mL). The organic component was concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (10.8 mg). LC-MS retention time = 1.74 min; m/z = 535.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (500 MHZ, DMSO-d_6) δ 7.78 (d, *J*=8.1 Hz, 1H), 7.56 (d, *J*=8.1 Hz, 1H), 7.29 - 7.24 (m, 1H), 7.24 - 7.20 (m, 1H), 7.11 - 7.07 (m, 1H), 7.04 - 6.99 (m, 2H), 6.98 - 6.94 (m, 2H), 6.88 (d, *J*=8.8 Hz, 2H), 6.64 (d, *J*=7.3 Hz, 2H), 6.57 (d, *J*=8.1 Hz, 1H), 4.26 - 4.19 (m, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.06 (s, 3H), 2.69 (dd, *J*=13.8, 5.3 Hz, 1H), 2.61 (s, 3H), 2.41 (dd, *J*=13.4, 7.5 Hz, 1H).

Example ZY-3

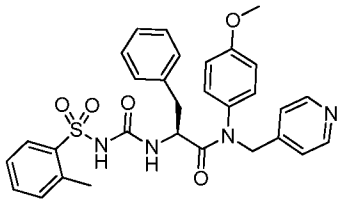


(S)-N-benzyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

To a stirred solution of Intermediate ZY-7 (32 mg, 0.081 mmol) in CH_3CN (1 mL) and DIPEA (0.042 mL, 0.242 mmol) was added 2-methylbenzenesulfonyl isocyanate (24 mg, 0.12 mmol) and the reaction mixture was stirred at rt for 16 h. The reaction mixture was concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (44.6 mg). LC-MS retention time = 1.91 min; m/z = 558.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (500 MHZ, DMSO-d_6) δ 7.80 (d, *J*=7.7 Hz, 1H), 7.49 (d, *J*=7.0 Hz, 1H), 7.38 - 7.31 (m, 2H), 7.27 - 7.12 (m, 7H), 7.06 (br. s., 2H), 6.79 (br. s., 6H), 4.87 (d, *J*=15.0 Hz, 1H), 4.63 (d, *J*=14.3 Hz, 1H), 4.23 (d, *J*=6.2 Hz, 1H), 3.71 (s, 3H), 2.81 (dd, *J*=13.6, 5.1 Hz, 1H), 2.59 - 2.53 (m, 4H).

Examples ZY-4 through ZY-6 were prepared using the procedure detailed for Example ZY-3 where the N-benzyl-4-methoxyaniline used in the preparation of Intermediate ZY-6 was replaced with the appropriate amine.

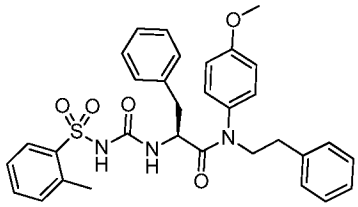
Example ZY-4



(S)-N-(4-methoxyphenyl)-3-phenyl-N-(pyridin-4-ylmethyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.48 min; m/z = 559.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

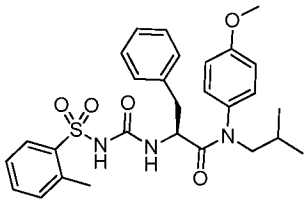
Example ZY-5



(S)-N-(4-methoxyphenyl)-N-phenethyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.87 min; m/z = 572.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

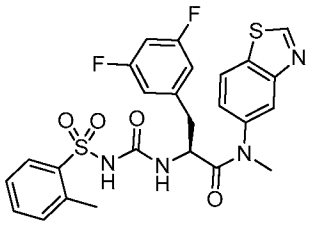
Example ZY-6



(S)-N-isobutyl-N-(4-methoxyphenyl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.84 min; m/z = 524.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (600 MHZ, DMSO-d_6) δ 7.76 (d, *J*=7.7 Hz, 1H), 7.47 (d, *J*=6.6 Hz, 1H), 7.36 - 7.27 (m, 2H), 7.17 - 6.86 (m, 7H), 6.80 - 6.53 (m, 3H), 4.18 (d, *J*=5.9 Hz, 1H), 3.76 (s, 3H), 3.58 - 3.16 (m, 2H), 2.78 - 2.72 (m, 2H), 1.58 - 1.49 (m, 1H), 0.76 (dd, *J*=17.8, 6.4 Hz, 6H).

Example ZY-7



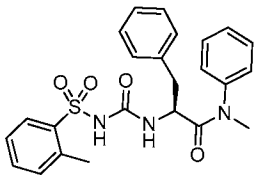
(S)-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

2-Methylbenzenesulfonyl isocyanate (28.4 mg, 0.144 mmol) was added to a stirred solution of an HCl salt of Intermediate ZY-5 (55 mg, 0.131 mmol) in CH_3CN (1 mL) and DIPEA (0.11 mL, 0.65 mmol) and the reaction mixture was stirred at rt ON. Additional 2-methylbenzenesulfonyl isocyanate (20mg) was added and the reaction mixture was stirred at rt for 2h. The reaction mixture was concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (49.8 mg).

LC-MS retention time = 2.33 min; m/z = 545.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (500 MHZ, DMSO-d_6) δ 9.49 (s, 1H), 8.23 (d, *J*=8.4 Hz, 1H), 8.04 (s, 1H), 7.78 (d, *J*=7.7 Hz, 1H), 7.54 - 7.48 (m, 1H), 7.41 - 7.30 (m, 3H), 6.95 (t, *J*=9.2 Hz, 1H), 6.74 (d, *J*=8.1 Hz, 1H), 6.35 (d, *J*=6.6 Hz, 2H), 4.31 (d, *J*=4.4 Hz, 1H), 3.23 (s, 3H), 2.90 - 2.80 (m, 1H), 2.60 (dd, *J*=13.6, 8.8 Hz, 1H), 2.50 (br. s., 3H).

For Examples CA-67 through CA-101, the following procedure was used:
A solution of $POCl_3$ (0.15 mmol) in pyridine (0.5 mL) was added to a solution of the appropriate aniline (0.11 mol) and (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (0.10 mmol) in pyridine (0.5 mL) at 0°C. The reaction mixture was allowed to warm to rt while being shaken ON.
The reaction was cooled using ice bath, quenched with MeOH (0.5 mL) and concentrated to dryness. The crude residue was treated with DCM (0.5 mL) and TFA (0.5 mL) and the reaction mixture was shaken at rt for 4h. The reaction mixture was concentrated to dryness and the crude residue was dissolved into DIPEA (0.3 mmol) in DCM (0.5 mL) and treated with a solution of 2-methylbenzenesulfonyl isocyanate (0.15 mmol) in DCM (0.5 mL). The reaction mixture was shaken at rt for 2h, diluted with MeOH (0.5 mL) and concentrated to dryness. The crude residue was dissolved into DMF (1 mL), filtered and purified by preparative HPLC to yield the title compound.

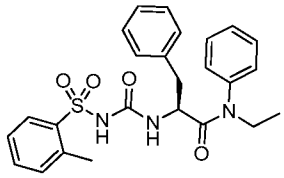
Example CA-67



(S)-N-methyl-N,3-diphenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.42 min; m/z = 452.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

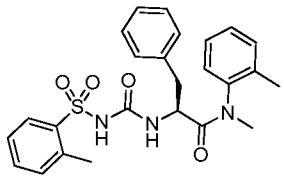
Example CA-68



(S)-N-ethyl-N,3-diphenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.54 min; m/z = 466.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

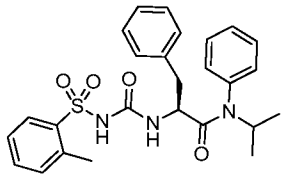
Example CA-69



(S)-N-methyl-3-phenyl-N-(o-tolyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.52 min; m/z = 466.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

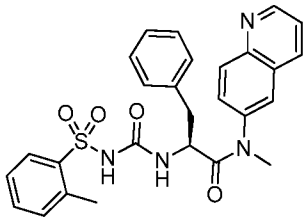
Example CA-70



(S)-N-isopropyl-N,3-diphenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 3.06 min; m/z = 480.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

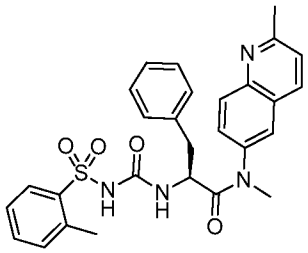
Example CA-71



(S)-N-methyl-3-phenyl-N-(quinolin-6-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.22 min; m/z = 503.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

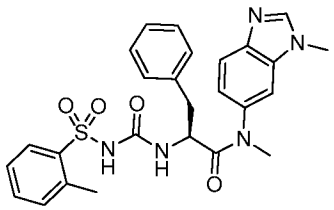
Example CA-72



(S)-N-methyl-N-(2-methylquinolin-6-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.50 min; m/z = 517.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

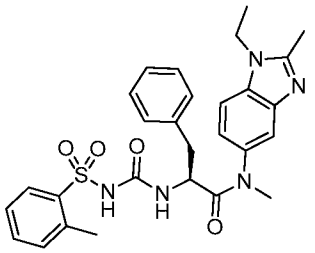
Example CA-73



(S)-N-methyl-N-(1-methyl-1H-benzo[d]imidazol-6-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.07 min; m/z = 506.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

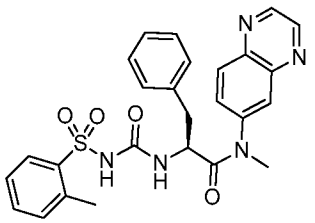
Example CA-74



(S)-N-(1-ethyl-2-methyl-1H-benzo[d]imidazol-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.23 min; m/z = 534.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

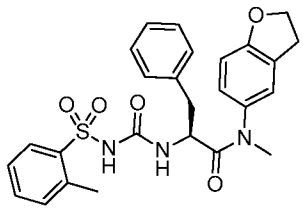
Example CA-75



(S)-N-methyl-3-phenyl-N-(quinoxalin-6-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.15 min; m/z = 504.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

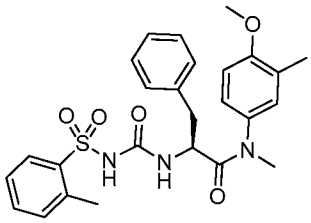
Example CA-76



(S)-N-(2,3-dihydrobenzofuran-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.38 min; m/z = 494.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

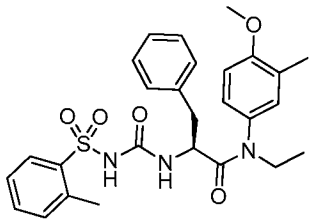
Example CA-77



(S)-N-(4-methoxy-3-methylphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.56 min; m/z = 496.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

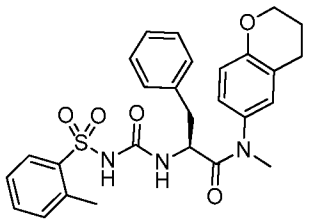
Example CA-78



(S)-N-ethyl-N-(4-methoxy-3-methylphenyl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.67 min; m/z = 510.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

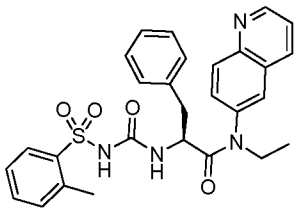
Example CA-79



(S)-N-(chroman-6-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.65 min; m/z = 508.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

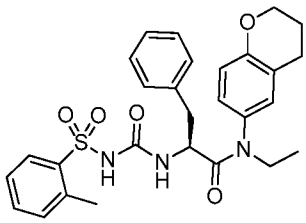
Example CA-80



(S)-N-ethyl-3-phenyl-N-(quinolin-6-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.48 min; m/z = 517.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

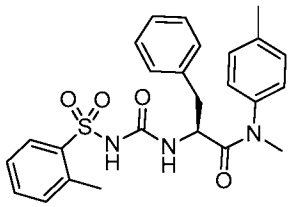
Example CA-81



(S)-N-(chroman-6-yl)-N-ethyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.66 min; m/z = 522.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

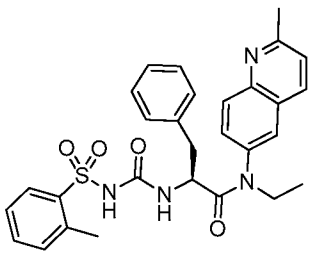
Example CA-82



(S)-N-methyl-3-phenyl-N-(p-tolyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.76 min; m/z = 466.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

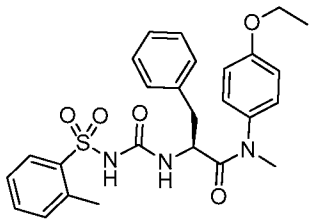
Example CA-83



(S)-N-ethyl-N-(2-methylquinolin-6-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.66 min; m/z = 531.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

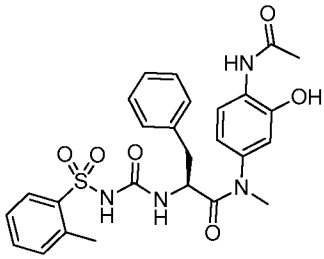
Example CA-84



(S)-N-(4-ethoxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.54 min; m/z = 496.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

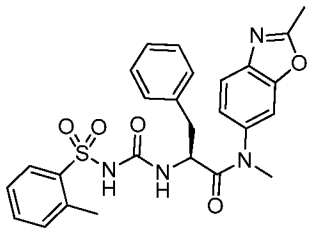
Example CA-85



(S)-N-(4-acetamido-3-hydroxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.43 min; m/z = 525.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

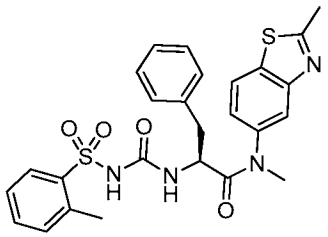
Example CA-86



(S)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.49 min; m/z = 507.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

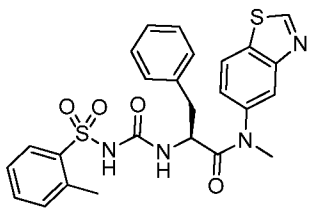
Example CA-87



(S)-N-methyl-N-(2-methylbenzo[d]thiazol-5-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.69 min; m/z = 523.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

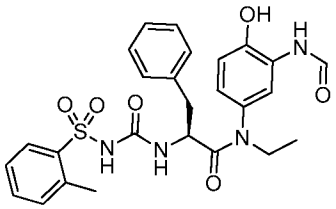
Example CA-88



(S)-N-(benzo[d]thiazol-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.22 min; m/z = 509.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

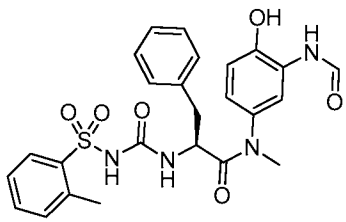
Example CA-89



(S)-N-ethyl-N-(3-formamido-4-hydroxyphenyl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.31 min; m/z = 525.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

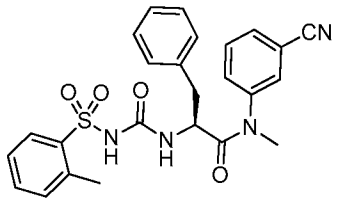
Example CA-90



(S)-N-(3-formamido-4-hydroxyphenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.96 min; m/z = 511.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

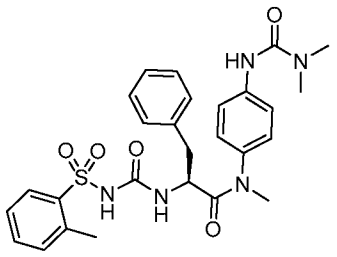
Example CA-91



(S)-N-(3-cyanophenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.28 min; m/z = 477.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

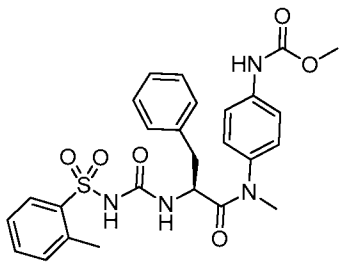
Example CA-92



(S)-N-(4-(3,3-dimethylureido)phenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.08 min; m/z = 538.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (500 MHZ, DMSO-d_6) δ 8.41 (br. s., 1H), 7.76 (d, *J*=8.8 Hz, 1H), 7.47 (d, *J*=7.7 Hz, 3H), 7.30 (br. s., 2H), 7.15 (br. s., 3H), 6.92 (d, *J*=7.0 Hz, 2H), 6.78 (br. s., 2H), 6.45 (br. s., 1H), 4.29 (br. s., 1H), 3.08 (s, 3H), 2.93 (s, 6H), 2.73 - 2.69 (m, 1H), 2.55 - 2.46 (m, 4H).

Example CA-93

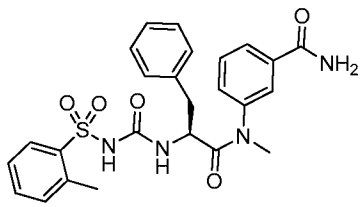


(S)-methyl (4-(N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamido)phenyl)carbamate

LC-MS retention time = 2.73 min; m/z = 525.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (500 MHZ, DMSO-d_6) δ

9.81 (s, 1H), 7.79 (d, *J*=7.7 Hz, 1H), 7.57 - 7.51 (m, 1H), 7.48 - 7.34 (m, 4H), 7.15 (d, *J*=4.0 Hz, 3H), 7.02 (d, *J*=8.4 Hz, 2H), 6.74 (d, *J*=4.0 Hz, 2H), 6.65 (d, *J*=8.1 Hz, 1H), 4.32 - 4.24 (m, 1H), 3.68 (s, 3H), 3.09 (s, 3H), 2.78 - 2.71 (m, 1H), 2.50 (s, 3H), 2.50 - 2.45 (m, 1H).

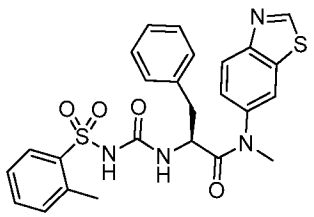
Example CA-94



(S)-3-(N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamido)benzamide

LC-MS retention time = 2.05 min; m/z = 495.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Example CA-95

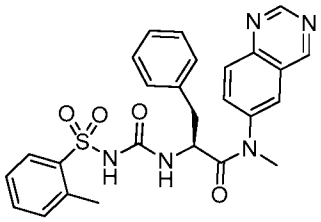


(S)-N-(benzo[d]thiazol-6-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.19 min; m/z = 509.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220). ^1H NMR (500 MHZ, DMSO-d_6) δ 9.46 (s, 1H), 8.06 (d, *J*=8.8 Hz, 1H), 7.79 (d, *J*=7.7 Hz, 1H), 7.72 (br. s., 1H), 7.51 (d,

J=6.6 Hz, 1H), 7.42 - 7.32 (m, 2H), 7.26 (d, *J*=7.7 Hz, 1H), 7.14 (d, *J*=7.0 Hz, 3H), 6.73 (d, *J*=6.6 Hz, 2H), 6.65 (br. s., 1H), 4.21 (d, *J*=5.5 Hz, 1H), 3.18 (s, 3H), 2.80 (d, *J*=7.3 Hz, 1H), 2.57 - 2.47 (m, 4H).

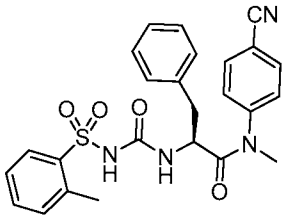
Example CA-96



(S)-N-methyl-3-phenyl-N-(quinazolin-6-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.00 min; m/z = 504.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

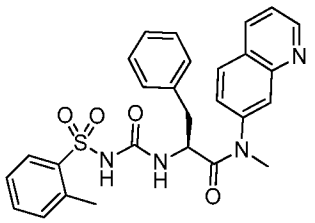
Example CA-97



(S)-N-(4-cyanophenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.61 min; m/z = 476.9 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

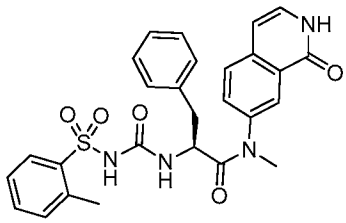
Example CA-98



(S)-N-methyl-3-phenyl-N-(quinolin-7-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.22 min; m/z = 503.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

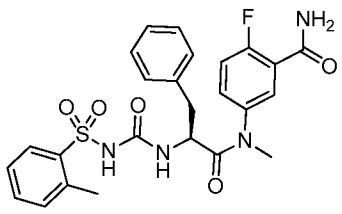
Example CA-99



(S)-N-methyl-N-(1-oxo-1,2-dihydroisoquinolin-7-yl)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.48 min; m/z = 519.0 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

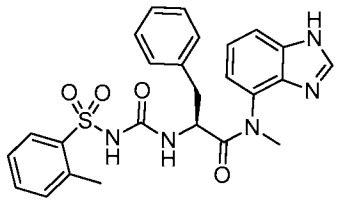
Example CA-100



(S)-2-fluoro-5-(N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamido)benzamide

LC-MS retention time = 1.23 min; m/z = 513.0 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Example CA-101



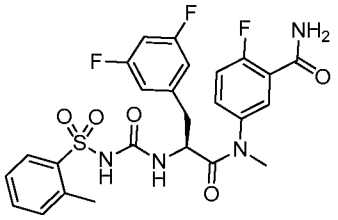
(S)-N-(1H-benzo[d]imidazol-4-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.26 min; m/z = 492.0 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

For Examples CA-102 through CA-112, the following procedure was utilized:
A solution of $POCl_3$ (0.15 mmol) in pyridine (0.5 mL) was added to a solution of the appropriate aniline (0.11 mol) and (S)-2-((tert-butoxycarbonyl)amino)-3-(3,5-difluorophenyl)propanoic acid (0.10 mmol) in pyridine (0.5 mL) at 0°C. The

reaction mixture was allowed to warm to rt while being shaken ON. The reaction was cooled using ice bath, quenched with MeOH (0.5 mL) and concentrated to dryness. The crude residue was treated with DCM (0.5 mL) and TFA (0.5 mL) and the reaction mixture was shaken at rt for 4h. The reaction mixture was concentrated to dryness and the crude residue was dissolved into DIPEA (0.3 mmol) in DCM (0.5 mL) and treated with a solution of 2-methylbenzenesulfonyl isocyanate (0.15 mmol) in DCM (0.5 mL). The reaction mixture was shaken at rt for 2h, diluted with MeOH (0.5 mL) and concentrated to dryness. The crude residue was dissolved into DMF (1 mL), filtered and purified by preparative HPLC to yield the title compound.

Example CA-102

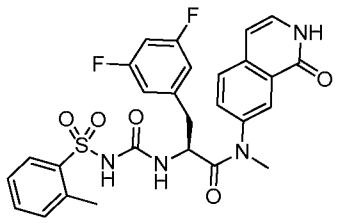


(S)-5-(3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamido)-2-fluorobenzamide

A solution of (S)-2-((tert-butoxycarbonyl)amino)-3-(3,5-difluorophenyl)propanoic acid (30.1 mg, 100 µmol) and HATU (41.8 mg, 110 µmol) in DMF (0.5 mL) was added to a solution of 2-fluoro-5-(methylamino)benzamide (16.8 mg, 100 µmol) in DIPEA (0.044 mL, 250 µmol) and DMF (0.5 mL) and the reaction mixture was shaken at rt ON. The reaction mixture was concentrated to dryness, dissolved into DCM (0.5 mL) and TFA (0.5 mL) and the reaction mixture was shaken at rt for 4h. The reaction mixture was concentrated to dryness. The crude residue was dissolved into DCM (1.0 mL) and treated with DIPEA (0.052 mL, 300 µmol) and 2-methylbenzenesulfonyl isocyanate (0.023 mL, 150 µmol), and then the reaction mixture was shaken at rt for 2h and concentrated to dryness. The crude residue was dissolved into DMF (1 mL), filtered and purified by preparative HPLC to yield the title compound (19.4 mg). LC-MS retention time = 1.14 min; m/z = 549.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10

mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

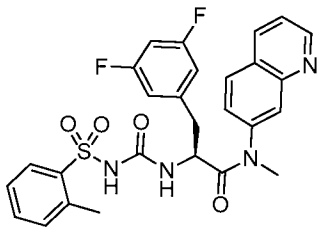
Example CA-103



(S)-3-(3,5-difluorophenyl)-N-methyl-N-(1-oxo-1,2-dihydroisoquinolin-7-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.11 min; m/z = 555.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

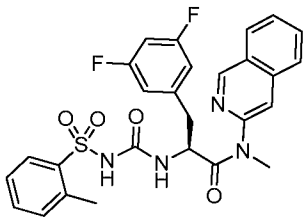
Example CA-104



(S)-3-(3,5-difluorophenyl)-N-methyl-N-(quinolin-7-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.32 min; m/z = 539.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

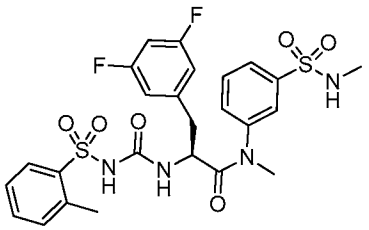
Example CA-105



(S)-3-(3,5-difluorophenyl)-N-(isoquinolin-3-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.46 min; m/z = 539.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

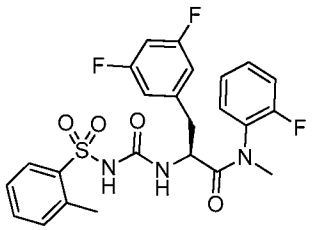
Example CA-106



(S)-3-(3,5-difluorophenyl)-N-methyl-N-(3-(N-methylsulfamoyl)phenyl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.32 min; m/z = 581.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

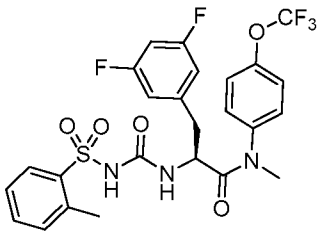
Example CA-107



(S)-3-(3,5-difluorophenyl)-N-(2-fluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.47 min; m/z = 506.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

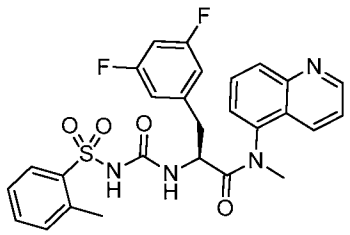
Example CA-108



(S)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)-N-(4-(trifluoromethoxy)phenyl)propanamide

LC-MS retention time = 1.83 min; m/z = 572.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

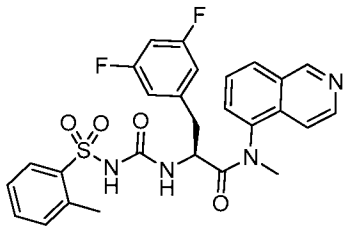
Example CA-109



(S)-3-(3,5-difluorophenyl)-N-methyl-N-(quinolin-5-yl)-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.36 min; m/z = 539.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

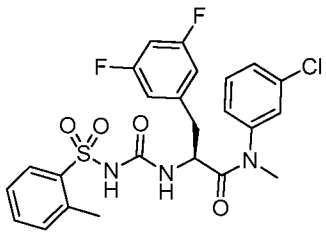
Example CA-110



(S)-3-(3,5-difluorophenyl)-N-(isoquinolin-5-yl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.34 min; m/z = 539.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

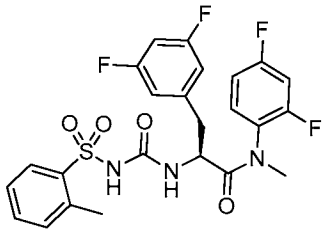
Example CA-111



(S)-N-(3-chlorophenyl)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 2.66 min; m/z = 522.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

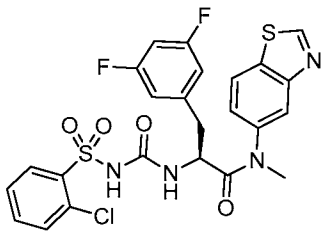
Example CA-112



(S)-N-(2,4-difluorophenyl)-3-(3,5-difluorophenyl)-N-methyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

LC-MS retention time = 1.56 min; m/z = 524.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

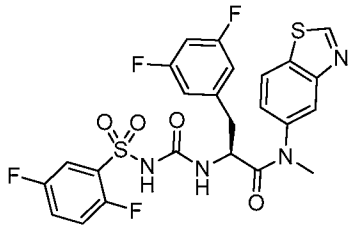
Example ZY-13



(S)-N-(benzo[d]thiazol-5-yl)-2-(3-((2-chlorophenyl)sulfonyl)ureido)-3-(3,5-difluorophenyl)-N-methylpropanamide

Prepared using the procedure described for Example ZY-7 where 2-methylbenzenesulfonyl isocyanate was replaced by 2-chlorobenzenesulfonyl isocyanate. LC-MS retention time = 2.23 min; m/z = 565.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Example ZY-14

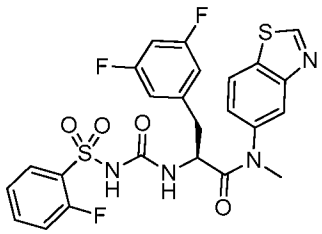


(S)-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-2-(3-((2,5-difluorophenyl)sulfonyl)ureido)-N-methylpropanamide

Triphosgene (0.051 g, 0.17 mmol) was added to a stirred suspension of 2,5-difluorobenzenesulfonamide (0.10 g, 0.52 mmol) and 1-isocyanatobutane (5.8 μl, 0.052 mmol) in toluene (2 mL) and the reaction mixture was heated at 110 °C for 16 h. The reaction mixture was allowed to cool to rt, and ½ (1 mL) of the crude solution was added to a solution of an HCL salt of Intermediate ZY-5 (30 mg, 0.071 mmol) in CH_3CN (1 mL) and DIPEA (0.050 mL, 0.29 mmol) and stirred at rt for 2 h. The reaction mixture was concentrated, dissolved into MeOH, filtered and purified by

preparative HPLC to yield the title compound (23.1 mg). LC-MS retention time = 2.61 min; m/z = 566.9 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

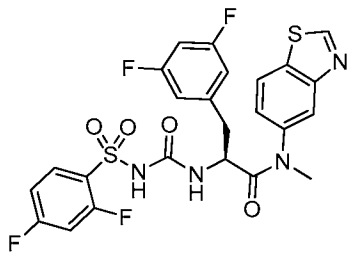
Example ZY-16



(S)-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-2-(3-((2-fluorophenyl)sulfonyl)ureido)-N-methylpropanamide

Prepared using the procedure described for Example ZY-14 where 2,5-difluorobenzenesulfonamide was replaced by 2-fluorobenzenesulfonamide. LC-MS retention time = 1.28 min; m/z = 549.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

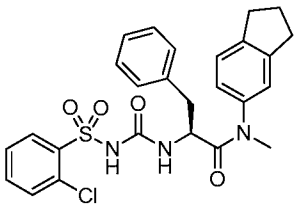
Example ZY-17



(S)-N-(benzo[d]thiazol-5-yl)-3-(3,5-difluorophenyl)-2-(3-((2,4-difluorophenyl)sulfonyl)ureido)-N-methylpropanamide

Prepared using the procedure described for Example ZY-14 where 2,5-difluorobenzenesulfonamide was replaced by 2,4-difluorobenzenesulfonamide. LC-MS retention time = 2.23 min; m/z = 567.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

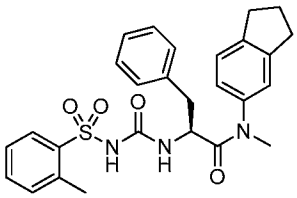
Example 206



(S)-2-(3-((2-chlorophenyl)sulfonyl)ureido)-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenylpropanamide

A solution of 2-chlorobenzenesulfonyl isocyanate (21 mg, 0.098 mmol) in DCM (0.5 mL) was added dropwise to a stirred solution of a TFA salt of (S)-2-amino-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenylpropanamide (Intermediate 6) (40 mg, 0.098 mmol) and triethylamine (40 mg, 0.39 mmol) in DCM (1 mL) at RT and the reaction mixture was stirred at RT for 1 h. The reaction mixture was concentrated, dissolved into DMF, filtered and purified by preparative HPLC to yield the title compound (23.6 mg). LC-MS retention time = 1.57 min; m/z = 512.5 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

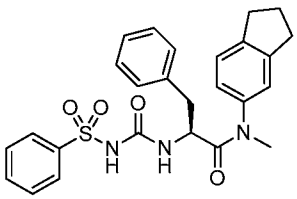
Example 207



(S)-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

A solution of 2-methylbenzenesulfonyl isocyanate (19 mg, 0.098 mmol) in DCM (0.5 mL) was added dropwise to a stirred solution of a TFA salt of (S)-2-amino-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenylpropanamide (Intermediate 6) (40 mg, 0.098 mmol) and triethylamine (40 mg, 0.39 mmol) in DCM (1 mL) at RT and the reaction mixture was stirred at RT for 1 h. The reaction mixture was concentrated, dissolved into DMF, filtered and purified by preparative HPLC to yield the title compound (36.5 mg). LC-MS retention time = 1.90 min; m/z = 492.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Example 208

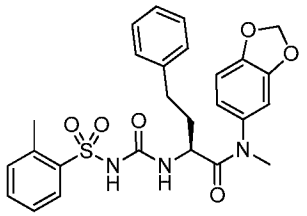


(S)-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenyl-2-(3-(phenylsulfonyl)ureido)propanamide

A solution of benzenesulfonyl isocyanate (18 mg, 0.098 mmol) in DCM (0.5 mL) was added dropwise to a stirred solution of a TFA salt of (S)-2-amino-N-(2,3-dihydro-1H-inden-5-yl)-N-methyl-3-phenylpropanamide (Intermediate 6) (40 mg, 0.098 mmol) and triethylamine (40 mg, 0.39 mmol) in DCM (1 mL) at RT and the reaction mixture was stirred at RT for 1 h. The reaction mixture was concentrated, dissolved into DMF, filtered and purified by preparative HPLC to yield the title

compound (34.4 mg). LC-MS retention time = 1.81 min; m/z = 478.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

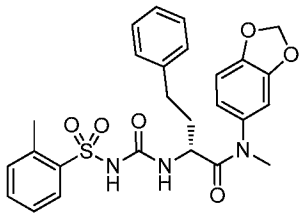
Example 209



(S)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-4-phenyl-2-(3-(o-tolylsulfonyl)ureido)butanamide

A solution of 4M HCl (0.67 mL, 2.7 mmol) in dioxane was added to a stirred solution of (S)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-4-phenylbutan-2-yl)carbamate (Intermediate 7) (110 mg, 0.267 mmol) in dioxane (0.67 mL) and the reaction mixture was stirred at RT for 2h. The crude reaction mixture was concentrated to dryness and the residue was dissolved into acetonitrile (1.1 mL) and DIPEA (0.116 mL, 0.667 mmol) and then treated with 2-methylbenzenesulfonyl isocyanate (79 mg, 0.40 mmol) and stirred at RT for 2.5 h. The reaction was quenched with MeOH (~5 mL), concentrated and the residue was partitioned between EtOAc (~8 mL) and water (~5 mL). The organic component was washed with brine (5 mL), concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (63.1 mg). LC-MS retention time = 1.88 min; m/z = 510.3 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

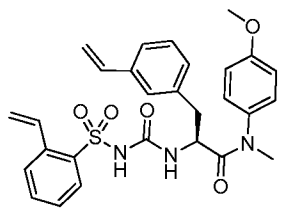
Example 210



(R)-N-(benzo[d][1,3]dioxol-5-yl)-N-methyl-4-phenyl-2-(3-(o-tolylsulfonyl)ureido)butanamide

A solution of 4M HCl (0.54 mL, 2.2 mmol) in dioxane was added to a stirred solution of (R)-tert-butyl (1-(benzo[d][1,3]dioxol-5-yl(methyl)amino)-1-oxo-4-phenylbutan-2-yl)carbamate (Intermediate 8) (89 mg, 0.22 mmol) in dioxane (0.54 mL) and the reaction mixture was stirred at RT for 2h. The crude reaction mixture was concentrated to dryness and the residue was dissolved into acetonitrile (1 mL) and DIPEA (0.0.94 mL, 0.54 mmol) and then treated with 2-methylbenzenesulfonyl isocyanate (64 mg, 0.32 mmol) and stirred at RT for 2.5 h. The reaction was quenched with MeOH (~5 mL), concentrated and the residue was partitioned between EtOAc (~8 mL) and water (~5 mL). The organic component was washed with brine (5 mL), concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (58.7 mg). LC-MS retention time = 2.44 min; m/z = 510.2 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% MeOH : 10 mM NH_4OAc. Solvent B = 5% Water : 95% MeOH : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

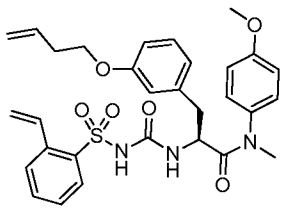
Example 212



(S)-N-(4-methoxyphenyl)-N-methyl-3-(3-vinylphenyl)-2-(3-((2-vinylphenyl)sulfonyl)ureido)propanamide

A suspension of 2-vinylbenzenesulfonamide (77.4 mg, 0.422 mmol) in toluene (1 mL) in an 8-mL glass vial was treated with butyl isocyanante (4.2 mg, 0.042 mmol) and triphosgene (44 mg, 0.15 mmol). The vial was sealed and the reaction mixture was stirred at 115 °C overnight. The crude reaction mixture was concentrated to dryness, dissolved into DCM (1 mL) and added dropwise to a suspension of (S)-2-amino-N-(4-methoxyphenyl)-N-methyl-3-(3-vinylphenyl)propanamide, TFA (Intermediate 11) (179 mg, 0.422 mmol) in DIPEA (0.368 mL, 2.11 mmol) and DCM (5 mL) and the resulting reaction solution was stirred at RT for 1 h. The reaction was concentrated and purified by preparative HPLC (0.1% TFA, MeOH/ H_2O) to yield the title compound (76 mg). LC-MS retention time = 1.97 min; m/z = 520.2 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220). ^{1}H NMR (400MHz, DMSO-d_6) δ 10.66 (s, 1H), 7.82 (dd, *J*=7.8, 1.0 Hz, 1H), 7.76 (d, *J*=7.3 Hz, 1H), 7.64 (t, *J*=7.5 Hz, 1H), 7.49 - 7.43 (m, 1H), 7.35 (dd, *J*=17.4, 11.0 Hz, 1H), 7.24 (d, *J*=7.8 Hz, 1H), 7.12 (t, *J*=7.6 Hz, 1H), 7.01 (d, *J*=8.8 Hz, 2H), 6.91 (d, *J*=9.0 Hz, 2H), 6.75 (s, 1H), 6.71 - 6.54 (m, 3H), 5.83 (d, *J*=17.1 Hz, 1H), 5.67 (d, *J*=17.4 Hz, 1H), 5.45 (d, *J*=11.5 Hz, 1H), 5.22 (d, *J*=11.2 Hz, 1H), 4.23 (td, *J*=8.0, 5.3 Hz, 1H), 3.75 (s, 3H), 3.08 (s, 3H), 2.74 (dd, *J*=13.4, 5.1 Hz, 1H), 2.46 (d, *J*=8.1 Hz, 1H).

Example 213

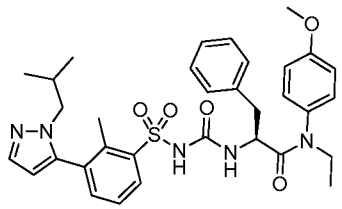


(S)-3-(3-(but-3-en-1-yloxy)phenyl)-N-(4-methoxyphenyl)-N-methyl-2-(3-((2-vinylphenyl)sulfonyl)ureido)propanamide

A suspension of 2-vinylbenzenesulfonamide (121 mg, 0.66 mmol) in toluene (1.4 mL) in an 8-mL glass vial was treated with butyl isocyanante (6.6 mg, 0.066 mmol) and triphosgene (69 mg, 0.23 mmol). The vial was sealed and the reaction mixture was stirred at 115 °C overnight. The crude reaction mixture was concentrated under

a stream of nitrogen, dissolved into DCM (1 mL) and added dropwise to a suspension of (S)-2-amino-3-(3-(but-3-en-1-yloxy)phenyl)-N-(4-methoxyphenyl)-N-methylpropanamide, TFA (136 mg, 0.290 mmol) (Intermediate 14) in DIPEA (0.253 mL, 1.45 mmol) and DCM (5 mL) and the resulting reaction solution was stirred at RT for 1 h. The reaction was concentrated and purified by preparative HPLC (0.1% TFA, MeOH/ H_2O) to yield the title compound (96 mg). LC-MS retention time = 2.11 min; m/z = 564.3 $[M+H]^+$. (Column: Phenonenex-Luna C18 2.0 x 30mm 3 µm. Solvent A = 95% Water:5% Acetonitrile: 10 µM ammonium acetate. Solvent B = 5% Water:95% Acetonitrile: 10 µM ammonium acetate. Flow Rate = 1.0 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 min. Wavelength = 220). ^1H NMR (400MHz, DMSO-d_6) δ 10.56 (s, 1H), 7.88 (s, 1H), 7.81 (d, *J*=7.8 Hz, 1H), 7.70 (d, *J*=7.8 Hz, 1H), 7.60 - 7.53 (m, 1H), 7.08 - 7.01 (m, 3H), 6.94 (d, *J*=8.8 Hz, 2H), 6.90 - 6.68 (m, 3H), 6.37 (d, *J*=7.6 Hz, 1H), 6.24 (s, 1H), 6.00 - 5.80 (m, 2H), 5.43 (d, *J*=11.0 Hz, 1H), 5.22 - 5.05 (m, 2H), 4.28 (td, *J*=8.2, 5.1 Hz, 1H), 3.86 (t, *J*=6.5 Hz, 2H), 3.78 (s, 3H), 3.09 (s, 3H), 2.75 (dd, *J*=13.6, 5.0 Hz, 1H), 2.48 - 2.41 (m, 3H).

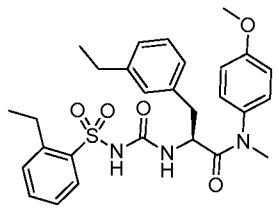
Example 214



(S)-N-ethyl-2-(3-((3-(1-isobutyl-1H-pyrazol-5-yl)-2-methylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-3-phenylpropanamide

Example 214 was synthesized using the procedure described above for Example 149. LC-MS retention time = 1.64 min; m/z = 618.1 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-µm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

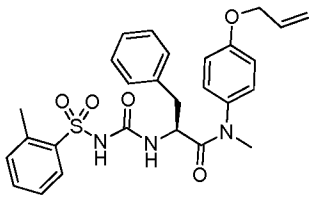
Example 215



(S)-3-(3-ethylphenyl)-2-(3-((2-ethylphenyl)sulfonyl)ureido)-N-(4-methoxyphenyl)-N-methylpropanamide

10% Palladium on carbon (7.4 mg, 6.9 μmol) was added to a solution of (S)-N-(4-methoxyphenyl)-N-methyl-3-(3-vinylphenyl)-2-(3-((2-vinylphenyl)sulfonyl)ureido)propanamide (18 mg, 0.035 mmol) in MeOH (4 mL) and DCM (3 mL) and the reaction mixture was stirred under a balloon of hydrogen at RT for 1 h. The catalyst was removed by filtration and the reaction mixture was concentrated to dryness. The reaction mixture was concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (8.2 mg). LC-MS retention time = 2.13 min; m/z = 524.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Example 216

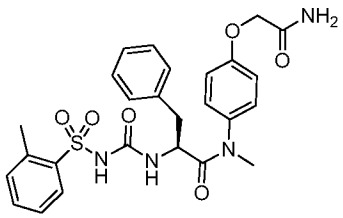


(S)-N-(4-(allyloxy)phenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

HATU (63.5 mg, 0.167 mmol) was added to a solution of 4-(allyloxy)-N-methylaniline, HCl (36.4 mg, 0.182 mmol), (S)-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanoic acid (55 mg, 0.15 mmol) and DIPEA (0.11 mL, 0.61 mmol) in DMF (1.4 mL) and the reaction mixture was stirred at RT for 2 h. The reaction mixture was transferred into a microwave vial and heated in a microwave system at 65° C for 2 h. The reaction mixture was filtered and purified by preparative HPLC to yield the title compound (8.3 mg). LC-MS retention time = 1.48 min; m/z

= 508.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Example 217



(S)-N-(4-(2-amino-2-oxoethoxy)phenyl)-N-methyl-3-phenyl-2-(3-(o-tolylsulfonyl)ureido)propanamide

2-Methylbenzenesulfonyl isocyanate (0.015 mL, 0.10 mmol) was added dropwise to an ice bath cooled stirred solution of (S)-2-amino-N-(4-(2-amino-2-oxoethoxy)phenyl)-N-methyl-3-phenylpropanamide (33 mg, 0.10 mmol) and DIPEA (0.070 mL, 0.40 mmol) in acetonitrile (1 mL) and the resulting reaction solution was stirred at RT overnight. The reaction mixture was concentrated, dissolved into MeOH, filtered and purified by preparative HPLC to yield the title compound (17.6 mg). LC-MS retention time = 1.04 min; m/z = 525.4 $[M+H]^+$. (Column: Waters BEH C18, 2.0 x 50 mm, 1.7-μm particles. Solvent A = 95% Water : 5% Acetonitrile : 10 mM NH_4OAc. Solvent B = 5% Water : 95% Acetonitrile : 10 mM NH_4OAc. Flow Rate = 0.5 mL/min. Start % B = 0. Final % B = 100. Gradient Time = 3 minutes, then a 0.5-minute hold at 100% B. Wavelength = 220).

Biological Methods

HIV cell culture assay - MT-2 cells, 293T cells and the proviral DNA clone of NL_{4-3} virus were obtained from the NIH AIDS Research and Reference Reagent Program. MT-2 cells were propagated in RPMI 1640 media supplemented with 10% heat inactivated fetal bovine serum (FBS), 100 ug/ml penicillin G and up to 100 units/ml streptomycin. The 293T cells were propagated in DMEM media supplemented with 10% heat inactivated FBS, 100 ug/ml penicillin G and 100 ug/ml

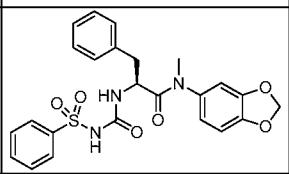
streptomycin. A recombinant NL_{4-3} proviral clone, in which a section of the nef gene was replaced with the Renilla luciferase gene, was used to make the reference virus used in these studies. The recombinant virus was prepared through transfection of the recombinant NL_{4-3} proviral clone into 293T cells using Transit-293 Transfection Reagent from Mirus Bio LLC (Madison, WI). Supernatent was harvested after 2-3 days after transfection, and the amount of virus present was titered in MT-2 cells using luciferase enzyme activity as a marker. Luciferase activity was quantitated using the EnduRen Live Cell Substrate from Promega (Madison, WI). Antiviral activities of compounds toward the recombinant virus were quantified by measuring luciferase activity in MT-2 cells infected for 4-5 days with the recombinant virus in the presence of serial dilutions of the compound.

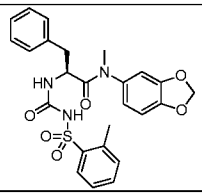
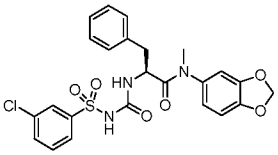
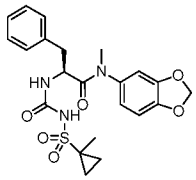
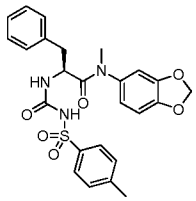
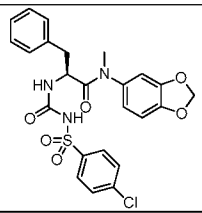
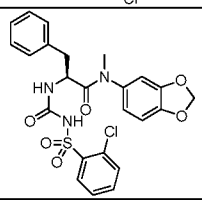
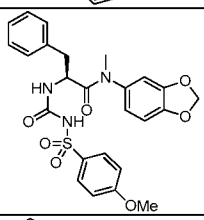
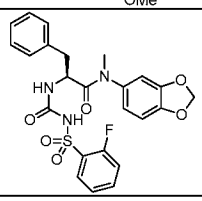
The 50% effective concentration (EC_{50}) was calculated by using the exponential form of the median effect equation where (Fa) = 1/[1+ (ED_{50}/drug conc.)^m] (Johnson VA, Byington RT. Infectivity Assay. In *Techniques in HIV Research*. ed. Aldovini A, Walker BD. 71-76. New York: Stockton Press.1990).

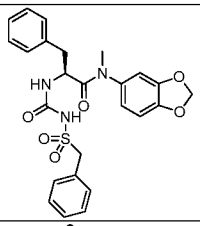
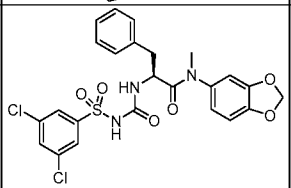
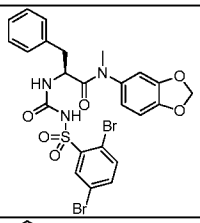
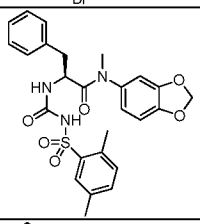
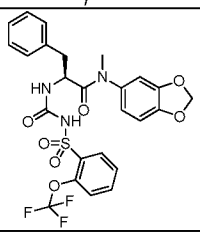
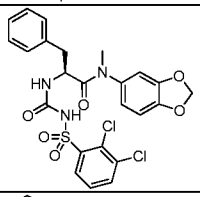
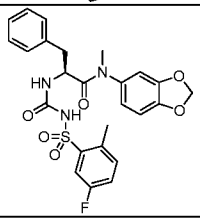
Compound cytotoxicity and the corresponding CC_{50} values were determined using the same protocol as described in the antiviral assay except that uninfected cells were used. Cytotoxicity was assessed on day 4 in uninfected MT2 cells by using a XTT-based (2,3-bis[2-Methoxy-4-nitro-5-sulfophenyl]-2H-tetrazolium-5-carboxyanilide inner salt)-based colorimetric assay (Sigma-Aldrich, St Louis, Mo).

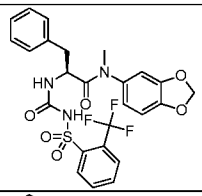
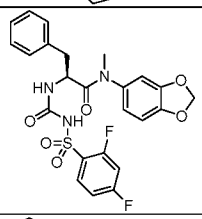
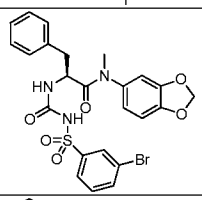
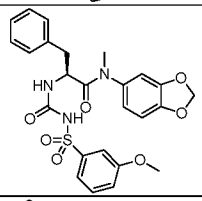
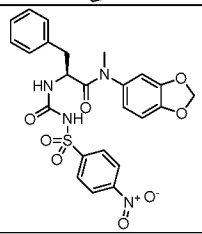
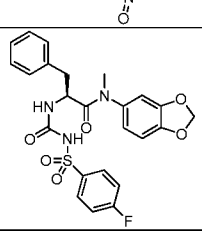
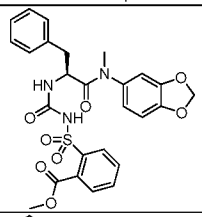
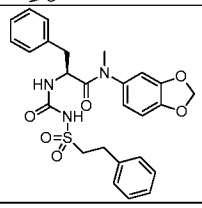
Compounds demonstrated antiviral activity as depicted in the table below. Activity equal to A refers to a compound having an EC_{50} value which is <0.1 μM, B is 0.1 to <1.0 μM, C is 1.0 to <10 μM, and D is 10 to <100 μM.

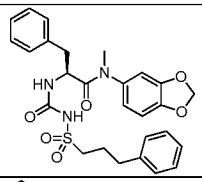
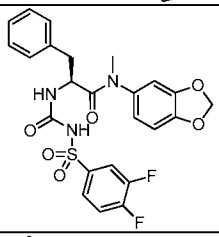
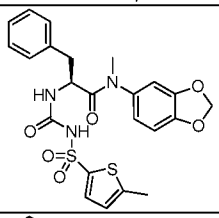
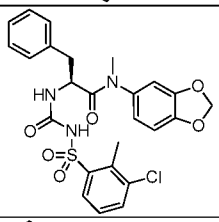
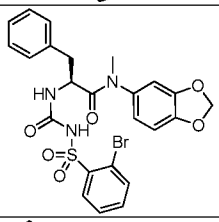
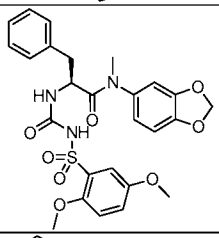
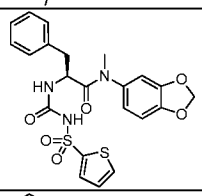
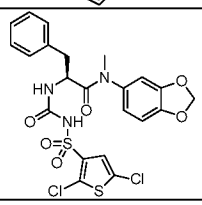
Table 1.

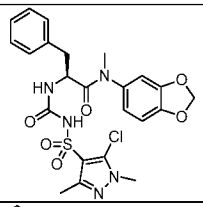
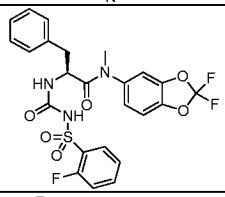
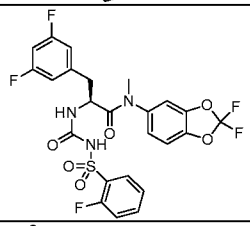
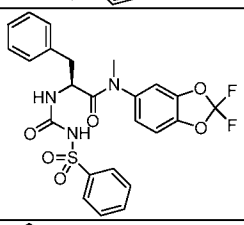
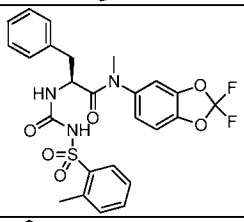
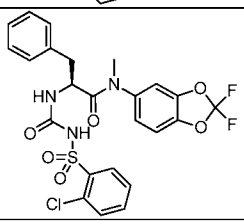
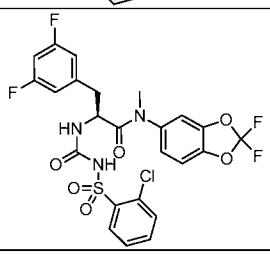
Example	Structure	Activity	EC_{50} (μM)
1		B	0.26

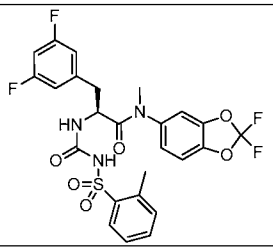
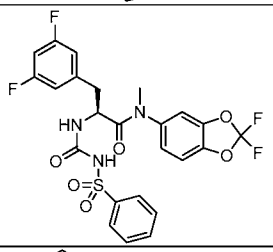
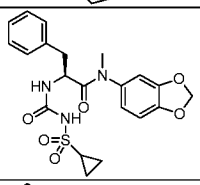
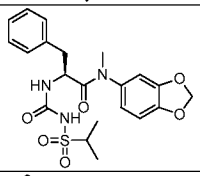
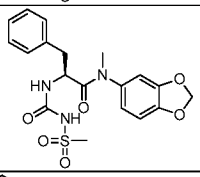
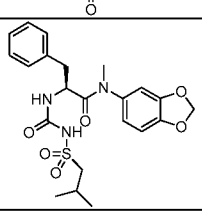
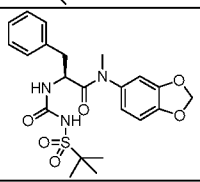
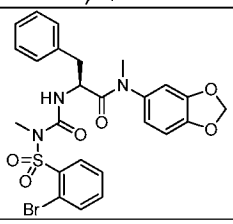
Example	Structure	Activity	EC_{50} (μM)
2		A	0.07
3		B	
4		C	1.11
5		B	
6		B	
7		A	
8		B	0.18
9		A	

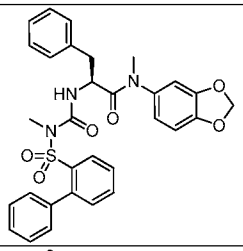
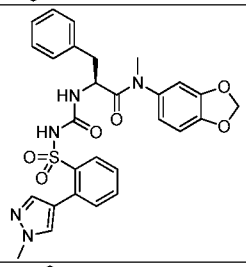
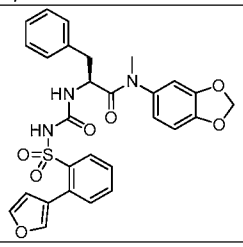
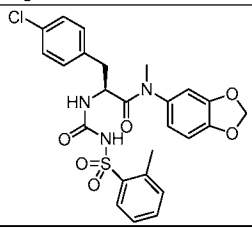
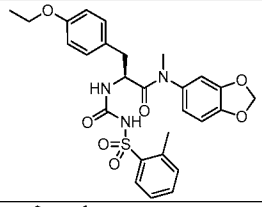
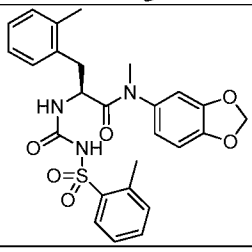
Example	Structure	Activity	EC_{50} (μM)
10		B	
11		B	
12		A	
13		A	0.05
14		A	
15		A	
16		A	

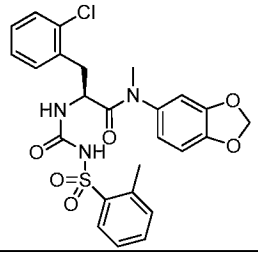
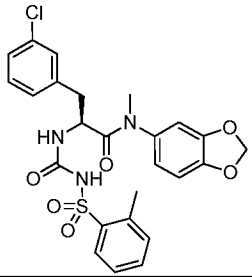
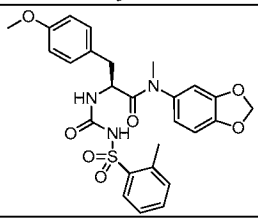
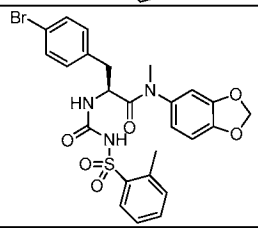
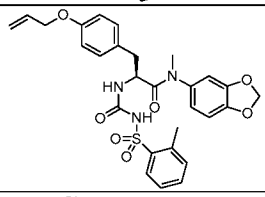
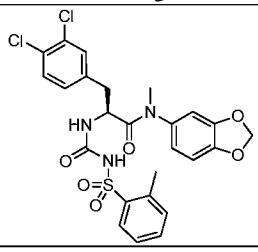
Example	Structure	Activity	EC_{50} (μM)
17		B	
18		B	0.20
19		B	
20		A	0.09
21		C	
22		B	
23		C	
24		B	

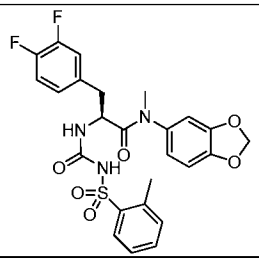
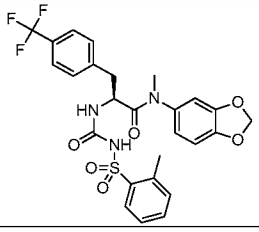
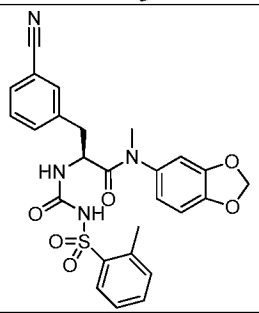
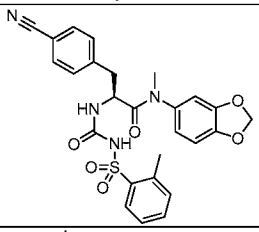
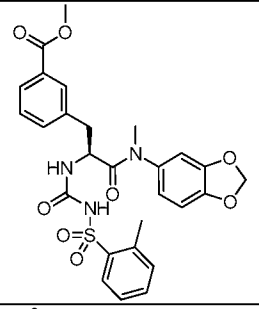
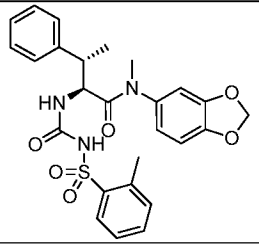
Example	Structure	Activity	EC_{50} (μM)
25		B	0.93
26		B	
27		B	
28		A	
29		A	
30		A	
31		B	
32		A	0.07

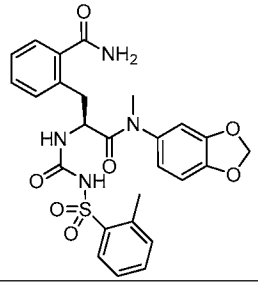
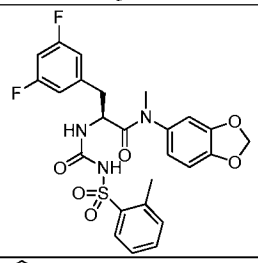
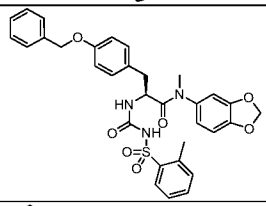
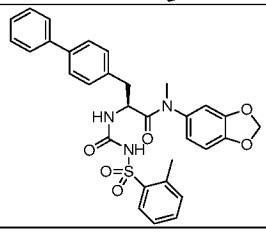
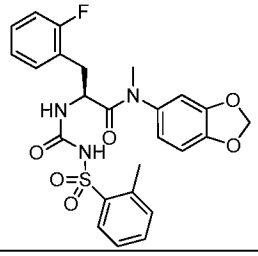
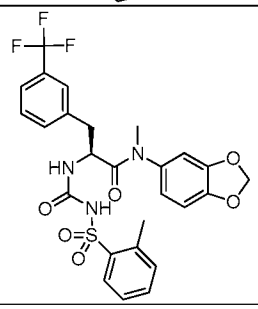
Example	Structure	Activity	EC_{50} (μM)
33		B	0.21
34		B	
35		B	
36		C	
37		B	
38		B	0.31
39		B	

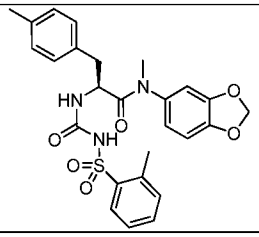
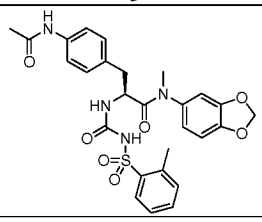
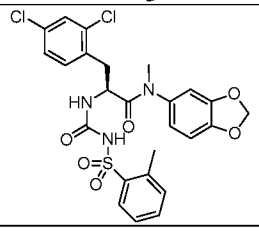
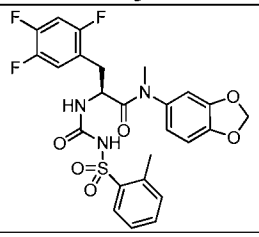
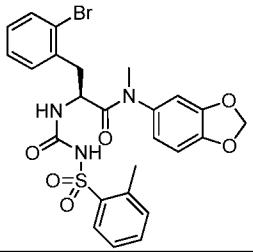
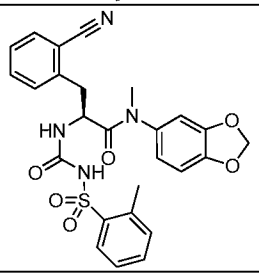
Example	Structure	Activity	EC_{50} (μM)
40		B	
41		B	
42		B	0.48
43		B	
44		C	2.48
45		B	
46		C	
47		C	

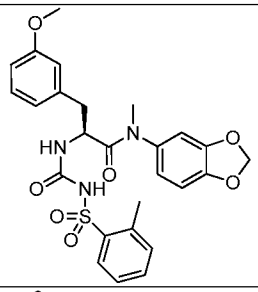
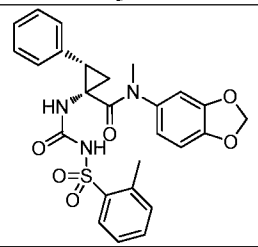
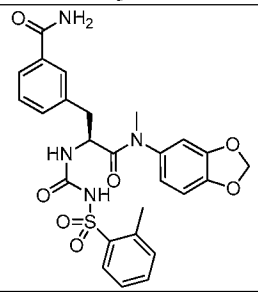
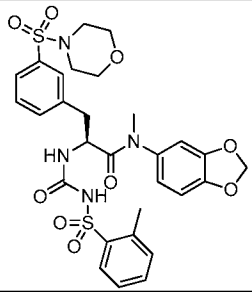
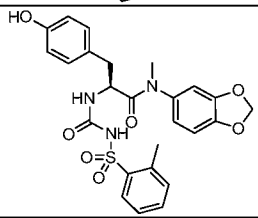
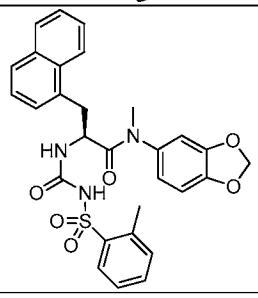
Example	Structure	Activity	EC_{50} (μM)
48		C	
49		C	1.34
50		B	
51		B	0.49
52		C	6.23
53		B	

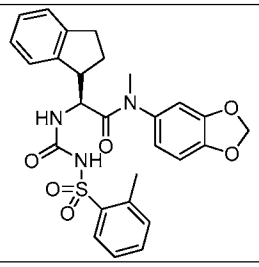
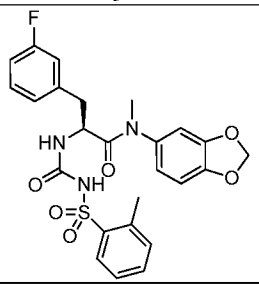
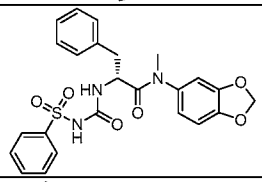
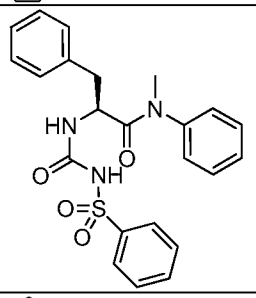
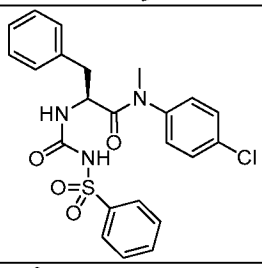
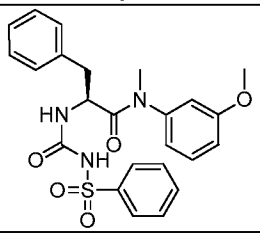
Example	Structure	Activity	EC_{50} (μM)
54		B	
55		B	
56		C	
57		C	
58		C	
59		C	1.04

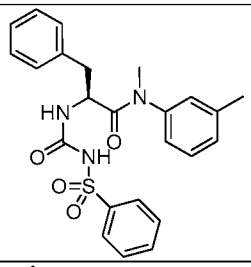
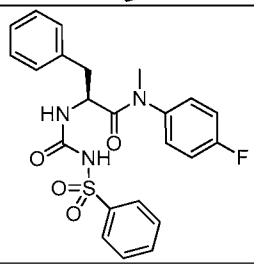
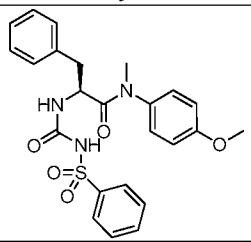
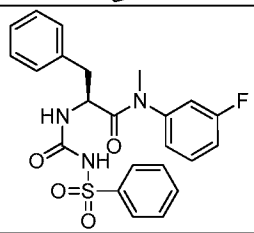
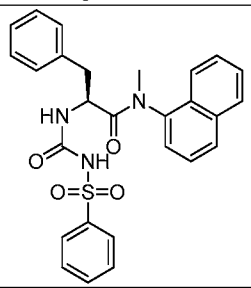
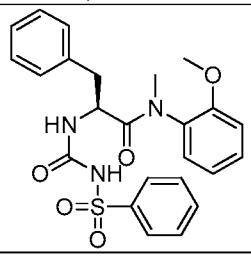
Example	Structure	Activity	EC_{50} (μM)
60		B	0.23
61		C	6.62
62		C	
63		C	
64		C	
65		C	6.83

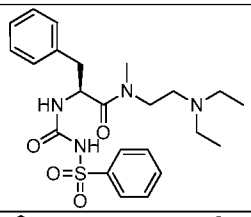
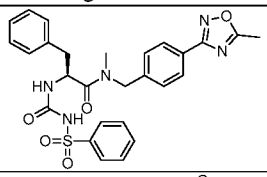
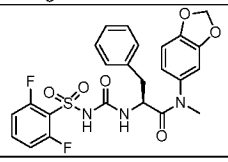
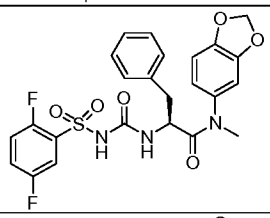
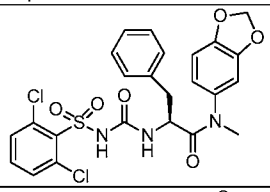
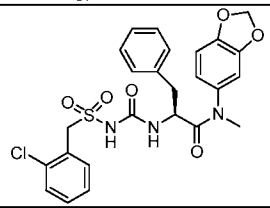
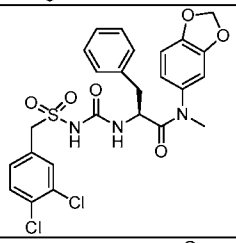
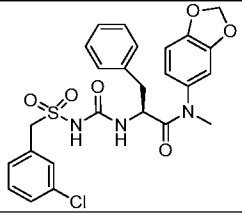
Example	Structure	Activity	EC_{50} (μM)
66			>100
67		B	
68		D	16.0
69		D	
70		B	
71		B	

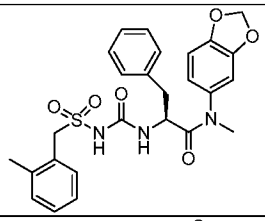
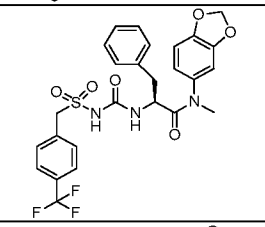
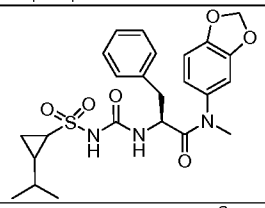
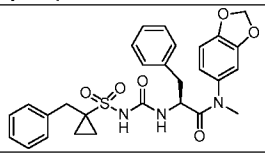
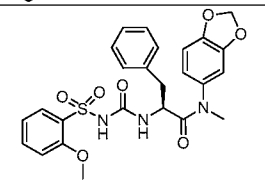
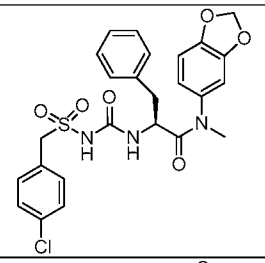
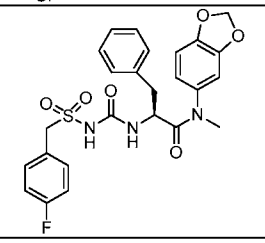
Example	Structure	Activity	EC_{50} (μM)
72		B	0.58
73			>100
74		C	3.88
75		B	0.29
76		C	
77		C	

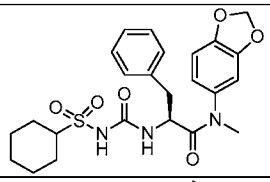
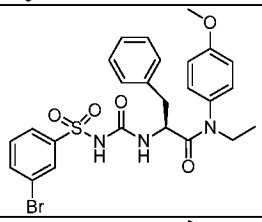
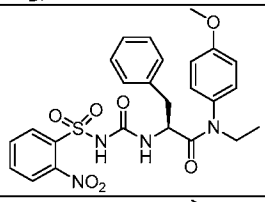
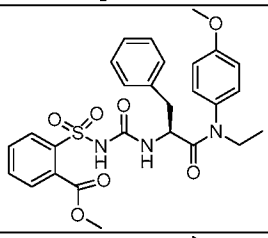
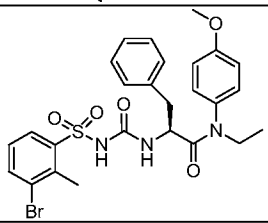
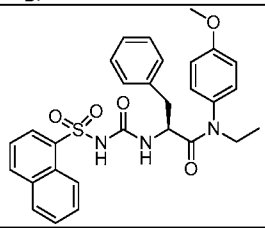
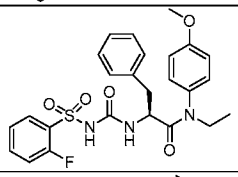
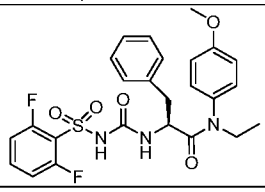
Example	Structure	Activity	EC_{50} (μM)
78		B	
79		D	
80			>100
81		D	
82		C	
83		C	4.28

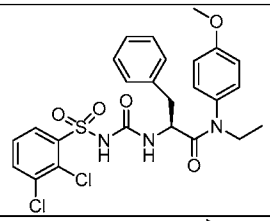
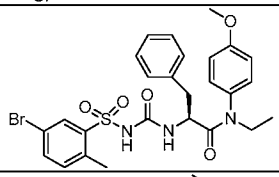
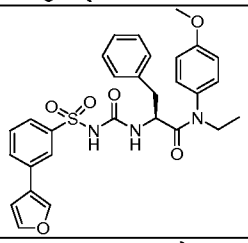
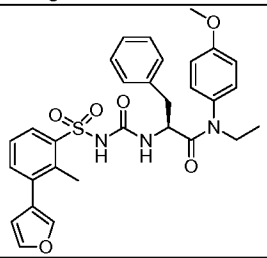
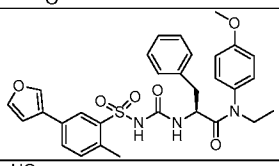
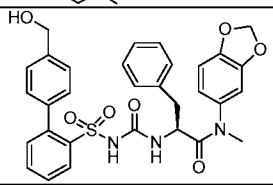
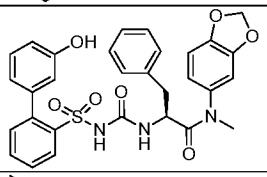
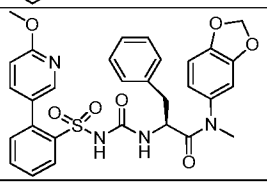
Example	Structure	Activity	EC_{50} (μM)
84		D	22.1
85		B	
86		D	
87		B	
88		B	0.45
89		B	

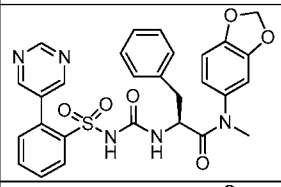
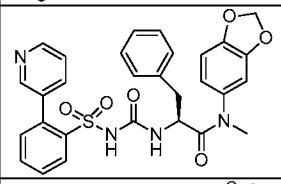
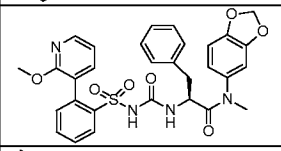
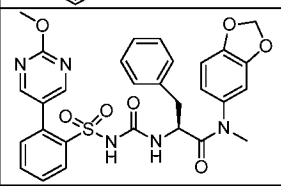
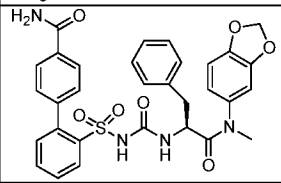
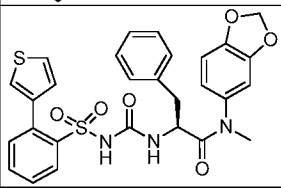
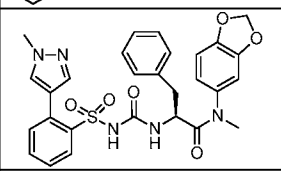
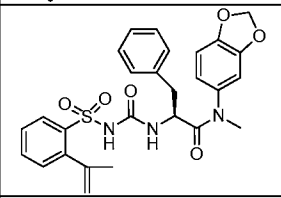
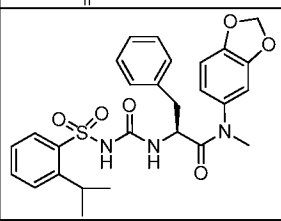
Example	Structure	Activity	EC_{50} (μM)
90		B	
91		B	
92		B	
93		C	1.59
94		D	
95		C	

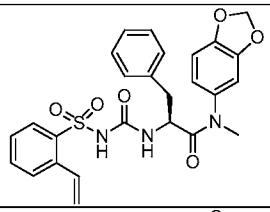
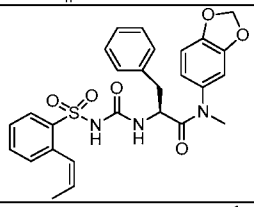
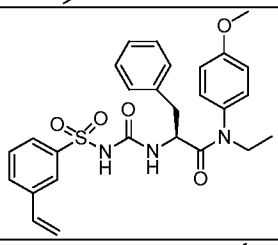
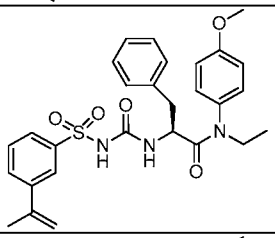
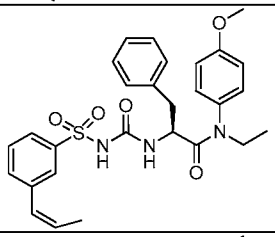
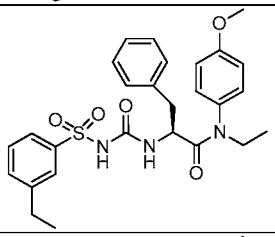
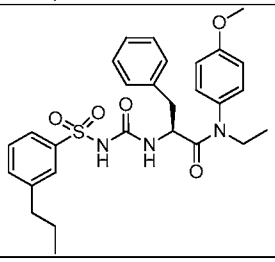
Example	Structure	Activity	EC_{50} (μM)
96			>100
97		C	
98		A	0.09
99		B	0.15
100		A	
101		B	
102		B	
103		B	

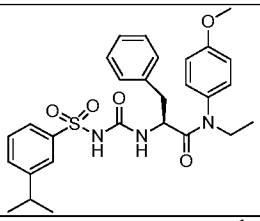
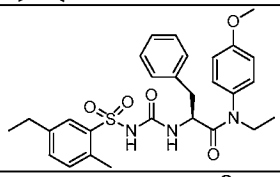
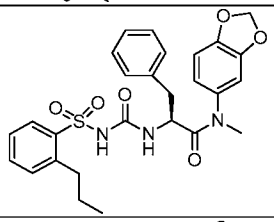
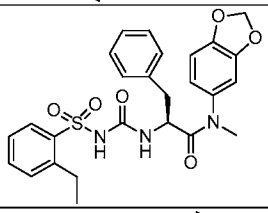
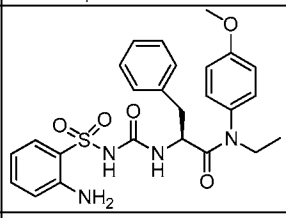
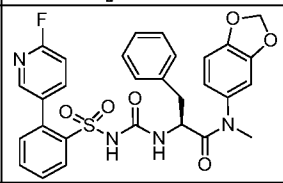
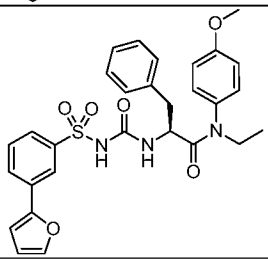
Example	Structure	Activity	EC_{50} (μM)
104		B	0.62
105		B	
106		B	
107		C	
108		B	
109		B	
110		B	0.16

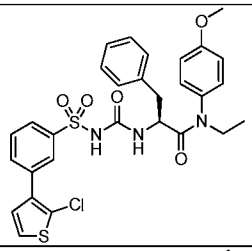
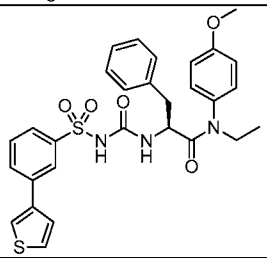
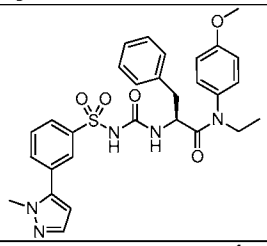
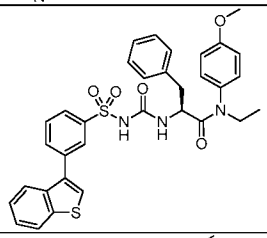
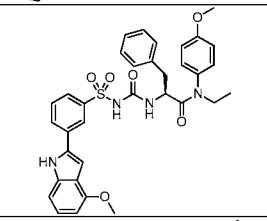
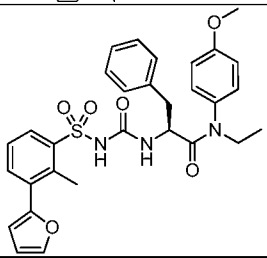
Example	Structure	Activity	EC_{50} (μM)
111		B	
112		A	
113		A	
114		C	1.06
115		A	
116		A	
117		A	
118		A	0.04

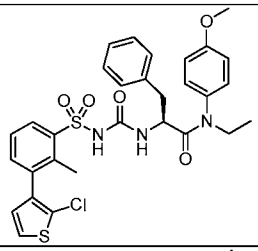
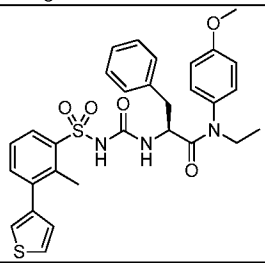
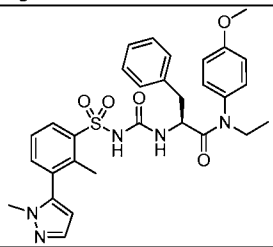
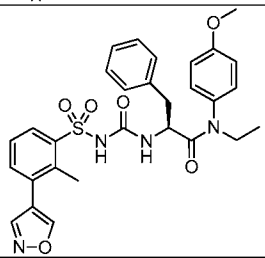
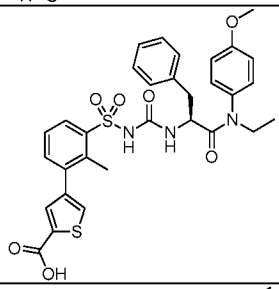
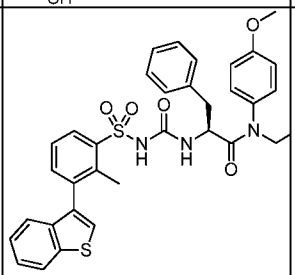
Example	Structure	Activity	EC_{50} (μM)
119		A	
120		B	
121		A	
122		B	
123		B	0.66
124		C	
125		C	
126		D	

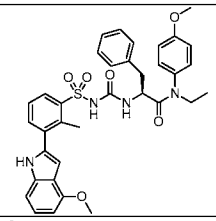
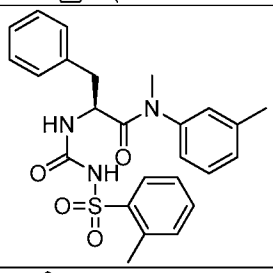
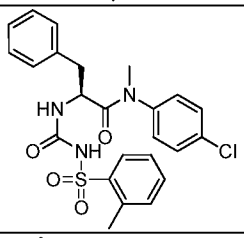
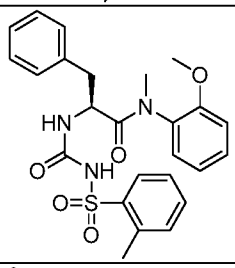
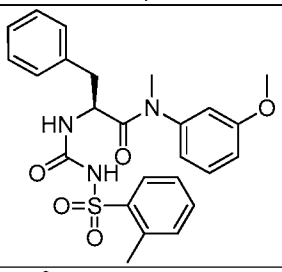
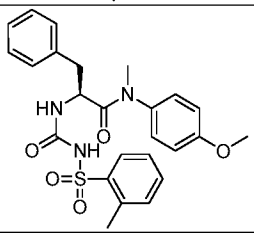
Example	Structure	Activity	EC_{50} (μM)
127		D	21.74
128		C	
129		C	5.52
130		C	
131		D	
132		D	
133		B	
134		C	
135		B	

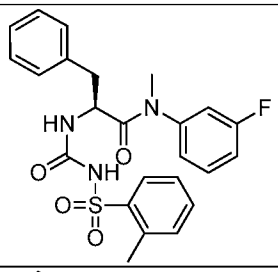
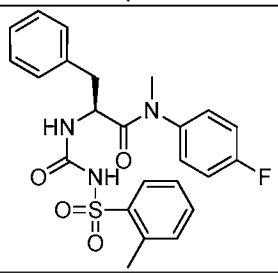
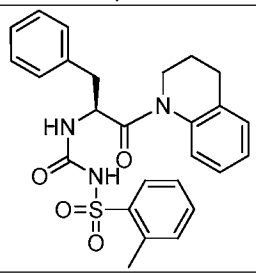
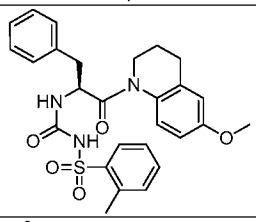
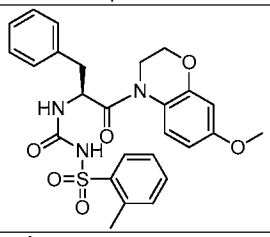
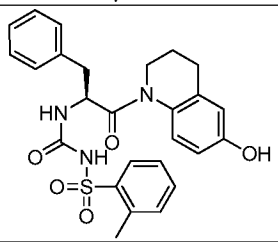
Example	Structure	Activity	EC_{50} (μM)
136		A	
137		B	
138		A	0.05
139		A	
140		A	
141		A	
142		A	0.06

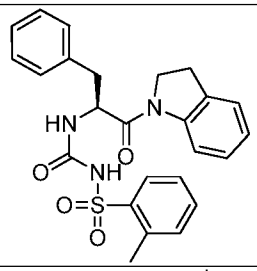
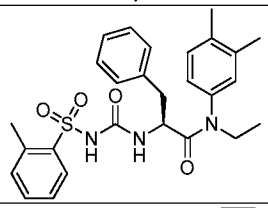
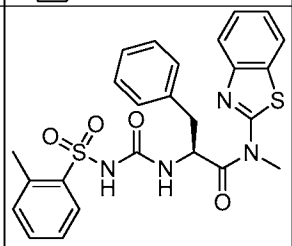
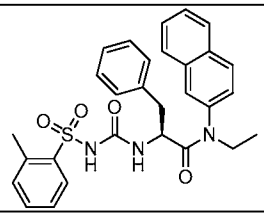
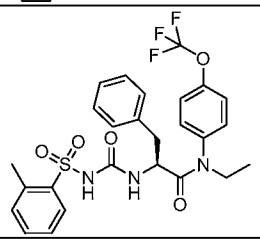
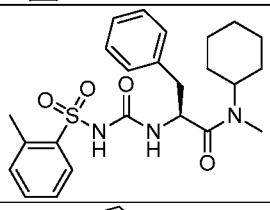
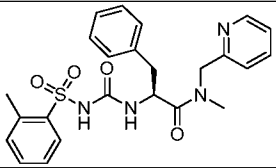
Example	Structure	Activity	EC_{50} (μM)
143		A	
144		B	0.62
145		B	
146		A	
147		A	
148		C	
149		B	

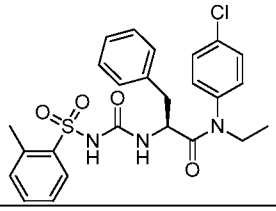
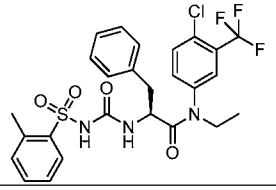
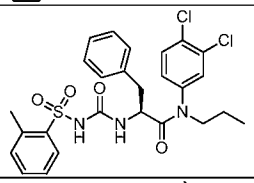
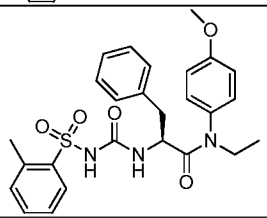
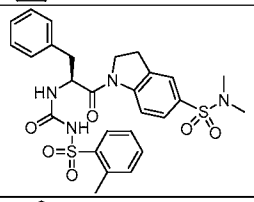
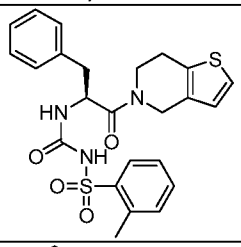
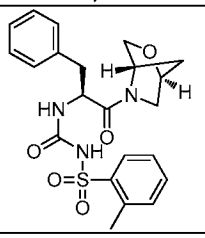
Example	Structure	Activity	EC_{50} (μM)
150		B	
151		B	0.11
152		A	0.09
153		B	
154		B	0.67
155		C	

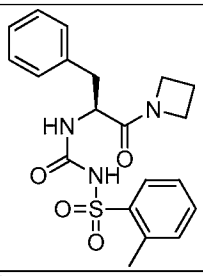
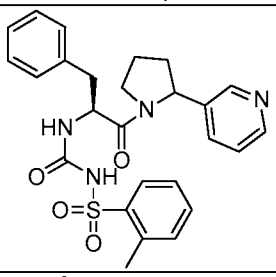
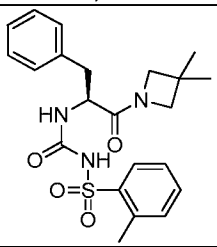
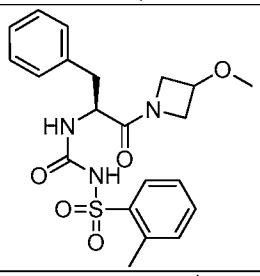
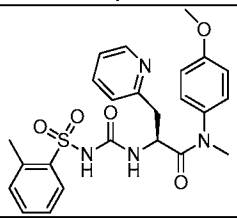
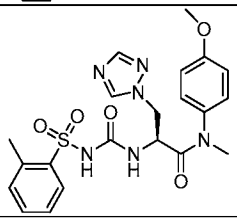
Example	Structure	Activity	EC_{50} (μM)
156		B	
157		B	
158		B	0.23
159		B	
160		C	5.64
161		C	

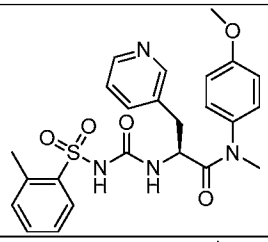
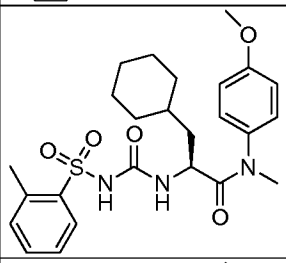
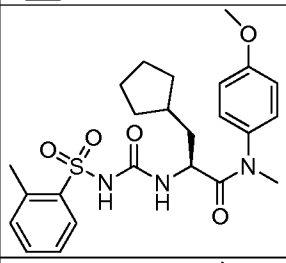
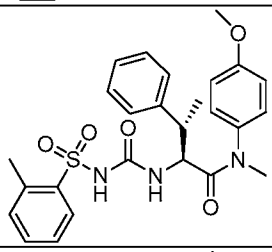
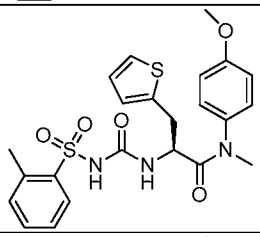
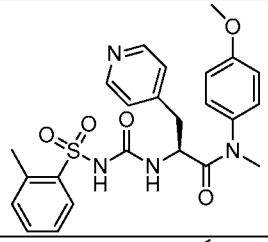
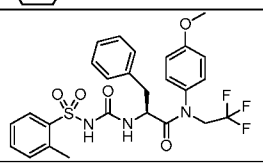
Example	Structure	Activity	EC_{50} (μM)
162		C	
163		B	
164		B	
165		C	
166		B	0.24
167		A	

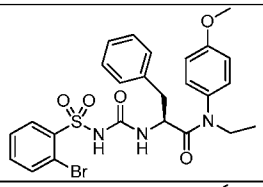
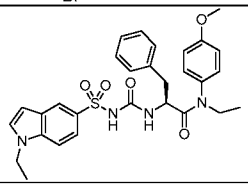
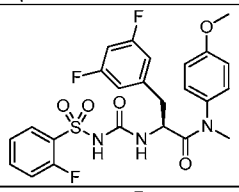
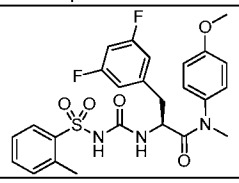
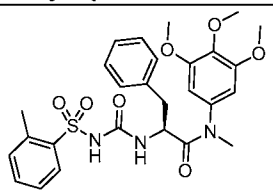
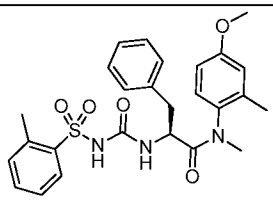
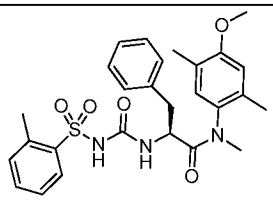
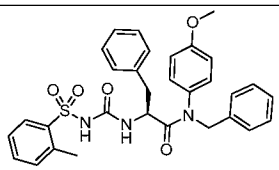
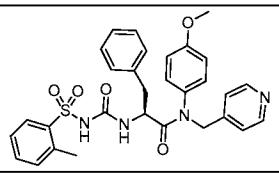
Example	Structure	Activity	EC_{50} (μM)
168		B	
169		B	
170		C	
171		B	
172		B	0.27
173		B	

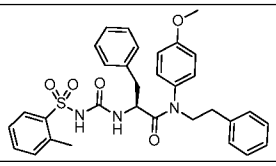
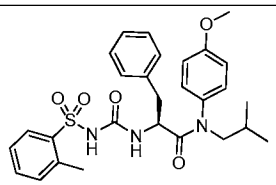
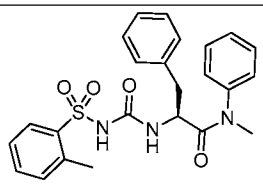
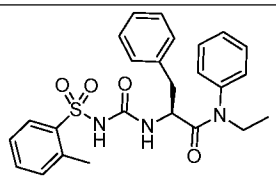
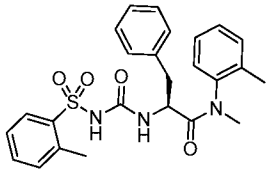
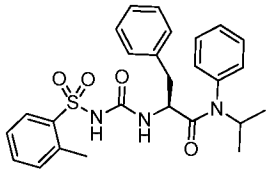
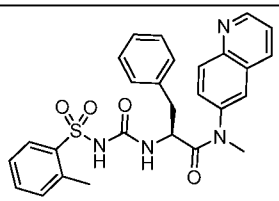
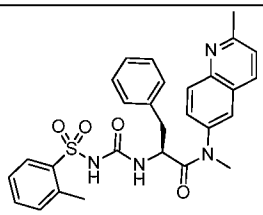
Example	Structure	Activity	EC_{50} (μM)
174		C	3.84
175		A	
176		D	
177		A	
178		A	0.08
179		C	
180		C	

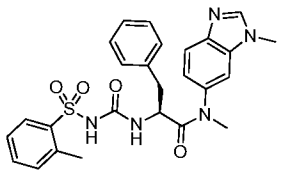
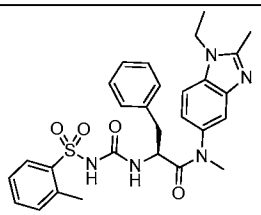
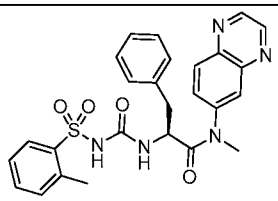
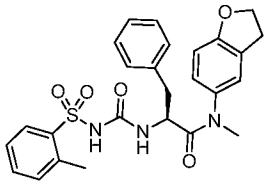
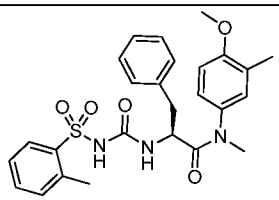
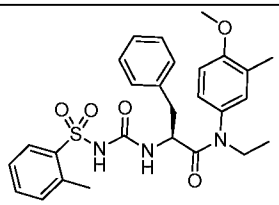
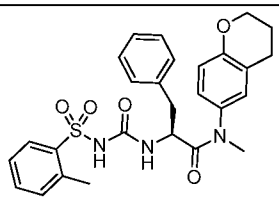
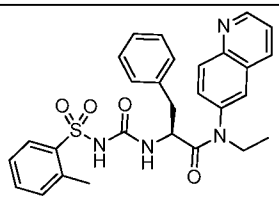
Example	Structure	Activity	EC_{50} (μM)
181		B	
182		B	
183		B	0.31
184		A	
185		C	
186		C	3.59
187			>33.3

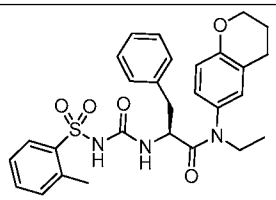
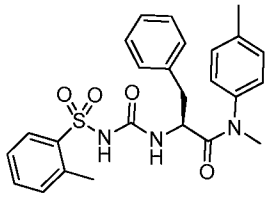
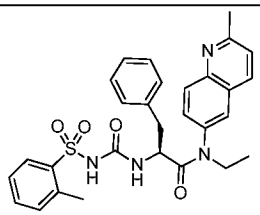
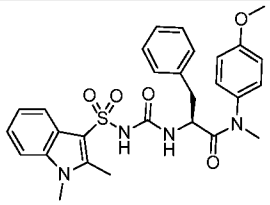
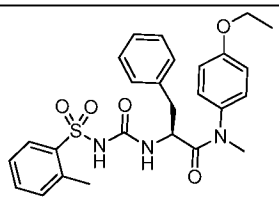
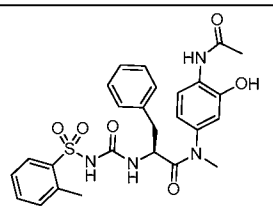
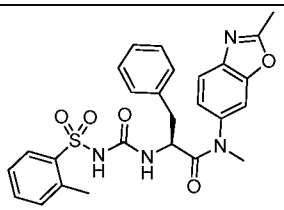
Example	Structure	Activity	EC_{50} (μM)
188		D	27.5
189		C	
190			>100
191			>100
192		D	
193			>100

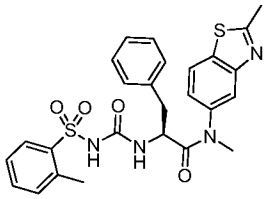
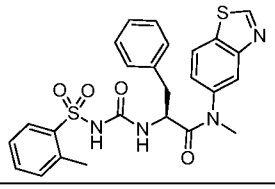
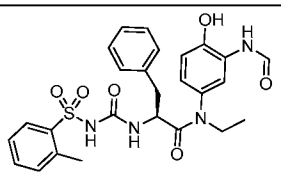
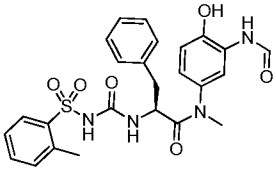
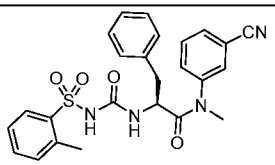
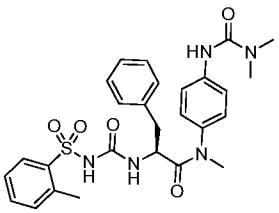
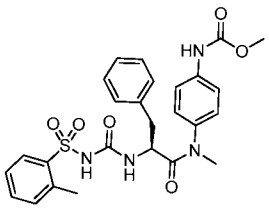
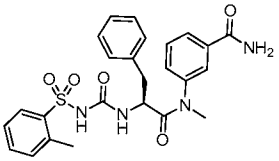
Example	Structure	Activity	EC_{50} (μM)
194		D	
195		C	
196		D	
197		D	11.5
198		B	0.27
199		D	
200		B	

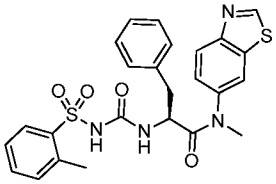
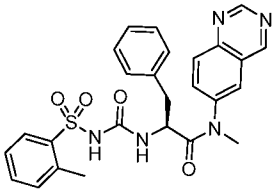
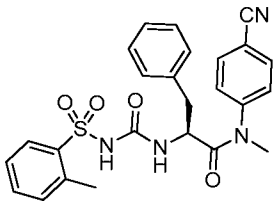
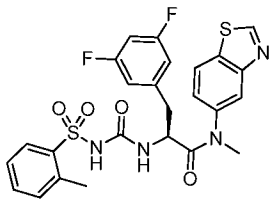
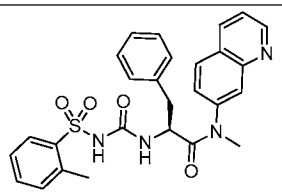
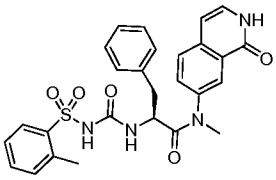
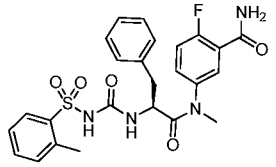
Example	Structure	Activity	EC_{50} (μM)
201		A	
203		B	
204		B	
205		B	0.11
JB-82		C	
JB-83		B	
JB-84		B	
ZY-3		C	3.61
ZY-4		C	

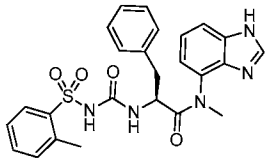
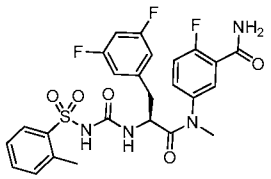
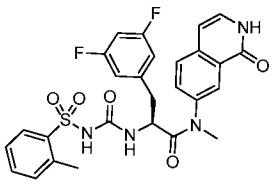
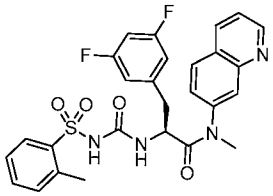
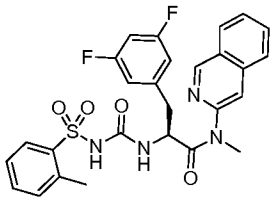
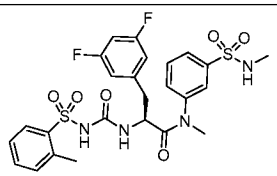
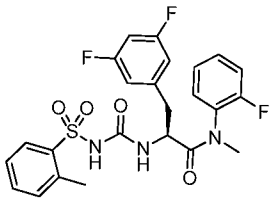
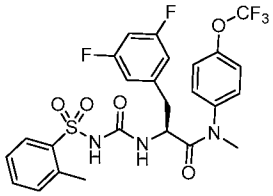
Example	Structure	Activity	EC_{50} (μM)
ZY-5		D	11.42
ZY-6		C	
CA-67		B	0.49
CA-68		B	
CA-69		C	
CA-70		B	
CA-71		A	
CA-72		A	0.03

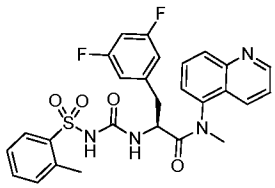
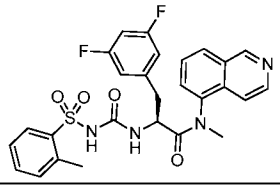
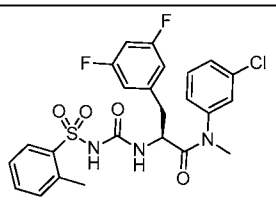
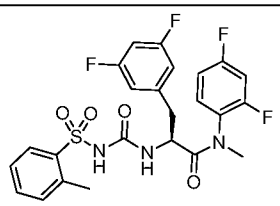
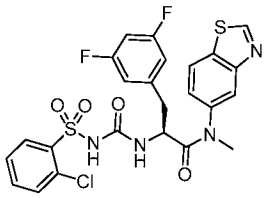
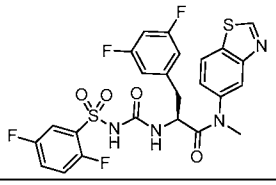
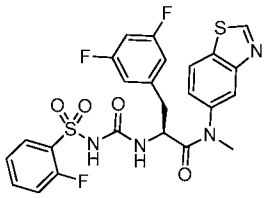
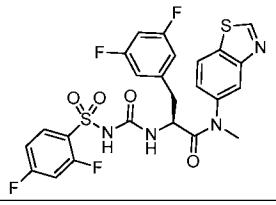
Example	Structure	Activity	EC_{50} (μM)
CA-73		B	
CA-74		C	2.03
CA-75		B	
CA-76		A	
CA-77		A	
CA-78		B	0.12
CA-79		A	
CA-80		A	0.03

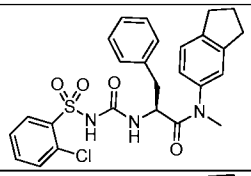
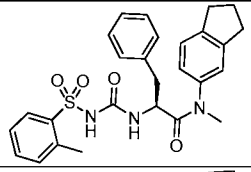
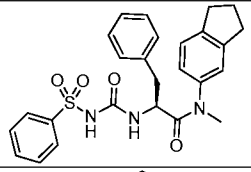
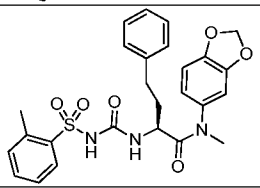
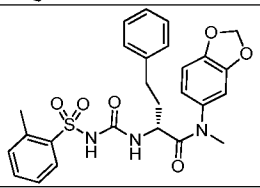
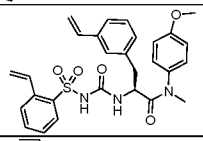
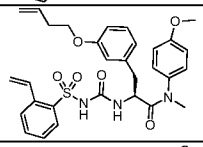
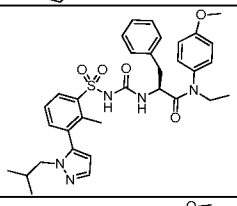
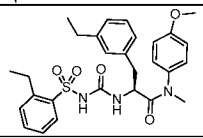
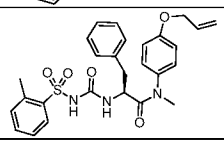
Example	Structure	Activity	EC_{50} (μM)
CA-81		A	0.04
CA-82		B	
CA-83		A	
JB-85		B	
CA-84		A	
CA-85		C	
CA-86		A	

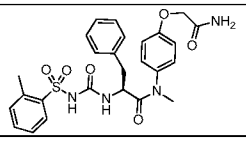
Example	Structure	Activity	EC_{50} (μM)
CA-87		B	
CA-88		A	0.06
CA-89		B	0.60
CA-90		C	
CA-91		B	
CA-92		C	
CA-93		A	
CA-94		C	3.26

Example	Structure	Activity	EC_{50} (μM)
CA-95		A	
CA-96		B	
CA-97		B	
ZY-7		A	
CA-98		B	0.12
CA-99		C	
CA-100		C	

Example	Structure	Activity	EC_{50} (μM)
CA-101		C	
CA-102		C	2.58
CA-103		C	1.33
CA-104		B	
CA-105		B	
CA-106		C	
CA-107		C	
CA-108		B	

Example	Structure	Activity	EC_{50} (μM)
CA-109		B	0.37
CA-110		B	
CA-111		C	
CA-112		C	1.29
ZY-13		A	0.03
ZY-14		B	
ZY-16		A	
ZY-17		B	

Example	Structure	Activity	EC_{50} (μM)
206		A	
207		A	
208		B	
209		D	
210		D	
212		A	0.058
213		C	5.07
214		B	0.87
215		B	
216		A	

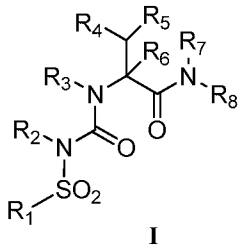
Example	Structure	Activity	EC_{50} (μM)
217		B	

It will be evident to one skilled in the art that the present disclosure is not limited to the foregoing illustrative examples, and that it can be embodied in other specific forms without departing from the essential attributes thereof. It is therefore desired that the examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing examples, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

CLAIMS

What is claimed is:

1. A compound of Formula I, including pharmaceutically acceptable salts thereof:



I

wherein:

R^1 is alkyl, aryl, arylalkyl, cycloalkyl or heteroaryl; wherein said aryl, arylalkyl or heteroaryl moieties are linked to the parent molecule through their respective carbon atoms, and further wherein said R^1 groups are substituted with 0-4 groups independently selected from the group of alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylamino, alkyl, alkylsulphonyl, alkylthioxy, aminocarbonyl, alkynyl, carboxylic acid, cyano, halo, haloalkyl, haloalkoxy, hydroxy, hydroxyalkyl, thioxy, -SO_2alkyl, heteroaryl, and nitro;

R^2 is -H, C_1-C_4 alkyl or C_3-C_4 cycloalkyl;
or R^1 and R^2 together with the atoms to which they are attached form a heterocyclic ring optionally substituted with 0-2 alkyl groups;

R^3 is -H, C_1-C_4 alkyl or C_3-C_4 cycloalkyl;

R^4 is -H, alkyl, aryl, C_5-C_{10} bicycloalkyl, cycloalkyl or heteroaryl which is substituted with 0-3 groups independently selected from the group of alkenoxy, alkenyl, alkoxy, alkoxycarbonyl, alkyl, benzyloxy, carboamide, cyano, halo, haloalkyl, haloalkoxy, -NHCO(alkyl), -SO_2N-heterocycle, -OH, nitro, and -CH_2OH;

R^5 and R^6 are independently selected from H or alkyl, or R^5 and R^4 together with the atom to which they are attached form an aryl group, or R^5 and R^6 together with the atoms to which they are attached form a C_3-C_4 cycloalkyl;

R^7 is -H, alkyl, aryl, heteroaryl, heteroarylalkyl, C_3-C_7 cycloalkyl or dialkylaminoalkyl, wherein said aryl or heteroaryl is substituted with 0-3 groups independently selected from the group of -OH, -NHCOalkyl, -NHCON(alkyl)$_2$, -NHCO$_2$-alkyl, -CONH$_2$, -CN, -SO$_2$N(alkyl)$_2$, alkoxy, alkyl, halo, haloalkoxy, and haloalkyl; and

R^8 is -H, alkyl, arylalkyl, cycloalkyl, haloalkyl or heteroarylalkyl;
or $R^7$and R^8 together with the nitrogen atom to which they are attached form a heterocycle which is substituted with 0-3 groups independently selected from the group of alkyl, alkoxy, halo, -OH, -CN, and -SO$_2$N(alkyl)$_2$.

2. A compound of claim 1, wherein R^1 is aryl.

3. A compound of claim 2, wherein R^1 is phenyl, biphenyl or naphthalenyl.

4. A compound of claim 1, wherein R^1 is heteroaryl.

5. A compound of claim 4, wherein R^1 is selected from the group of thiophene, pyrrazolophenyl, furanylphenyl, pyridinylphenyl, pyrimidinylphenyl, thiophenylphenyl, benzothiophene, oxadiazolephenyl, indole, and azaindole.

6. A compound of claim 1, wherein R^1 and R^2 form a heteroaryl ring.

7. A compound of claim 6, wherein said heteroaryl ring is isothiazolidine 1,1-dioxide.

8. A compound of claim 1, wherein R^4 is aryl.

9. A compound of claim 8, wherein R^4 is phenyl, naphthanenyl, or biaryl.

10. A compound of claim 1, wherein R^4 is heteroaryl.

11. A compound of claim 10, wherein R^4 is triazole or thiophene.

12. A compound of claim 1, wherein R^7 is aryl.

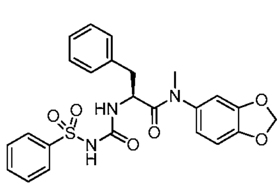
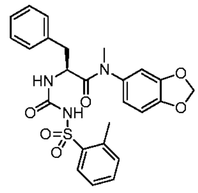
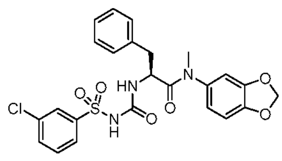
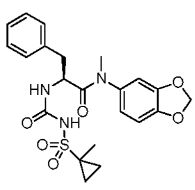
13. A compound of claim 12, wherein R^7 is phenyl or naphthalenyl.

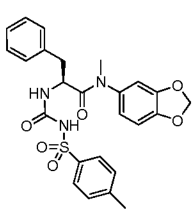
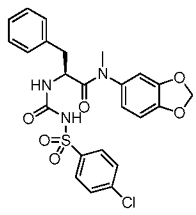
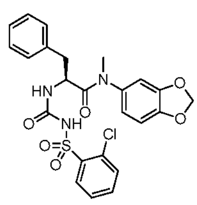
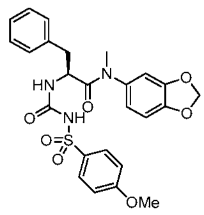
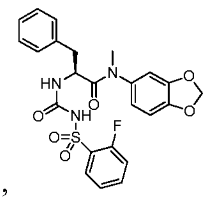
14. A compound of claim 1, wherein R^7 is heteroaryl.

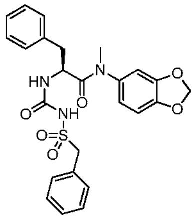
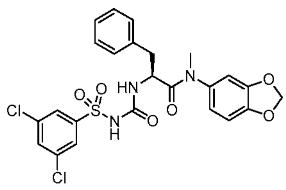
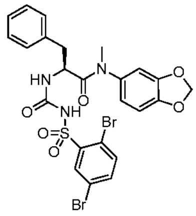
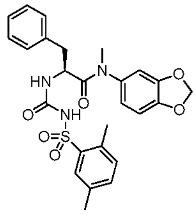
15. A compound of claim 14, wherein R^7 is selected from the group of bezodioxolyl, dihalobezodioxolyl, benzothiazole, quinoline, benzothiazole, benzimidazole, quinazoline, quinoxaline, dihydrobenzofuran, chroman, benzoxazole, isoquinoline, and isoquinolinone.

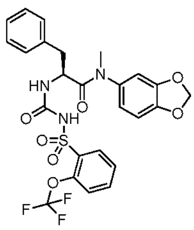
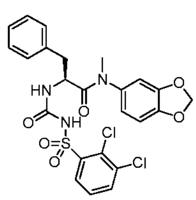
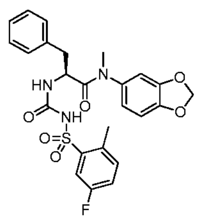
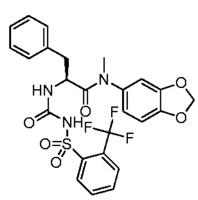
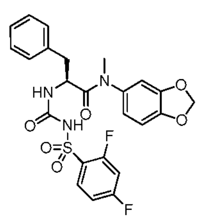
16. A compound of claim 1, wherein R^7 and R^8 together form a heterocycle which is selected from the group of tetrahydroisoquinoline, dihydro-benzo[1,4]oxazine, dihydroindole, tetrahydrothieno[3,2-c]pyridine, 2-oxa-5-azabicyclo[2.2.1]heptanes, azetidine, and pyridinylpyrrolidine.

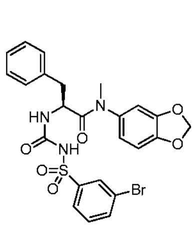
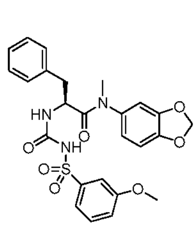
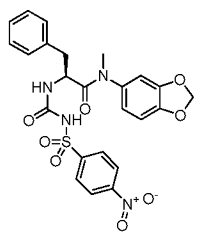
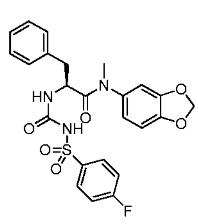
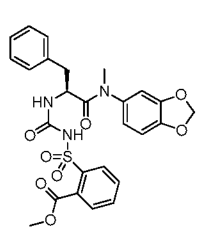
17. A compound, including pharmaceutically acceptable salts thereof, which is selected from the group of:

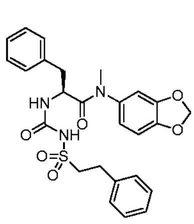
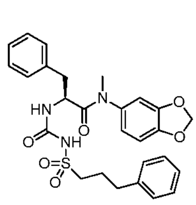
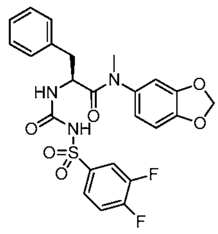
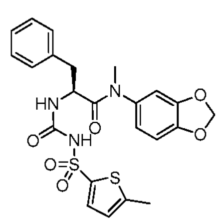
 ,  ,  ,  ,

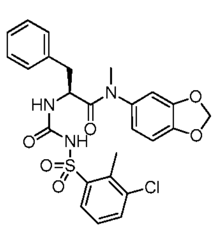
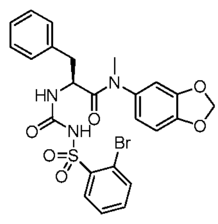
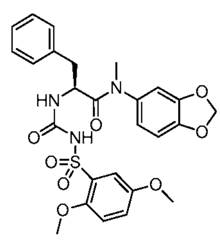
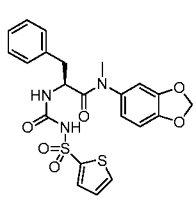
 ,  ,  ,  ,  ,

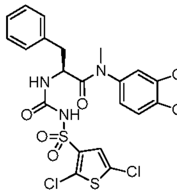
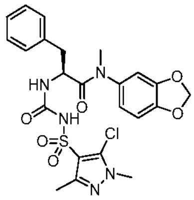
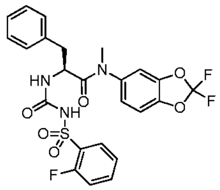
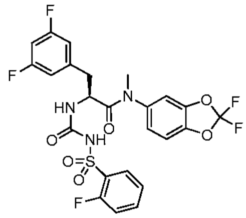
 ,  ,  ,  ,

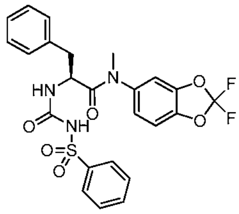
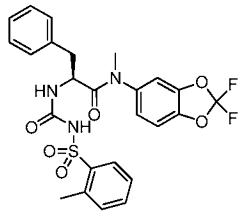
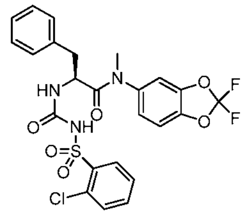
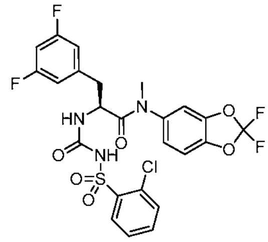
 ,  ,  ,  ,  ,

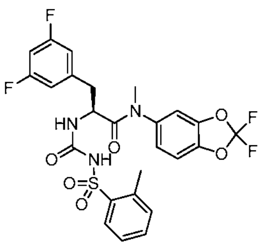
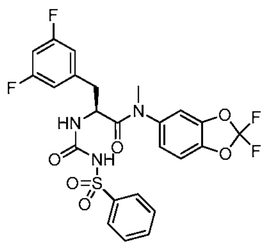
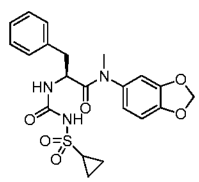
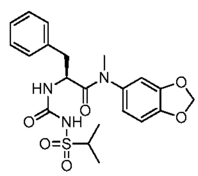
 ,  ,  ,  ,  ,

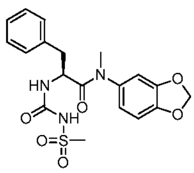
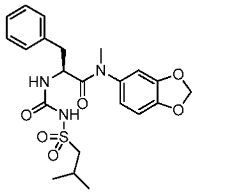
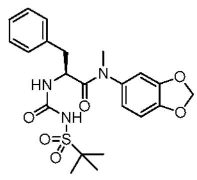
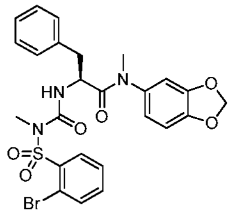
 ,  ,  ,  ,

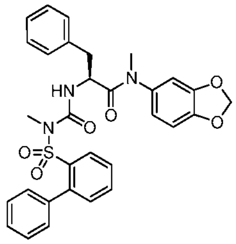
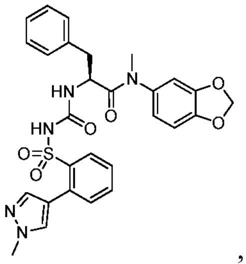
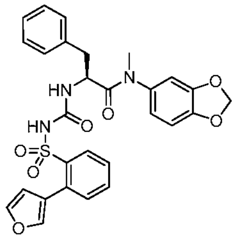
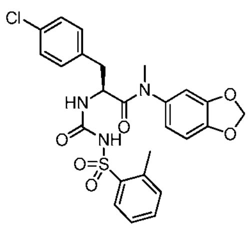
 ,  ,  ,  ,

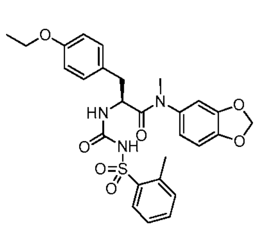
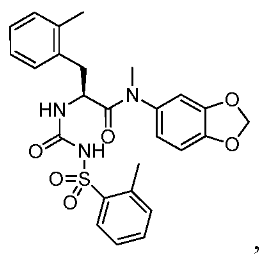
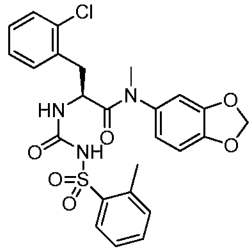
 ,
 ,
 ,
 ,

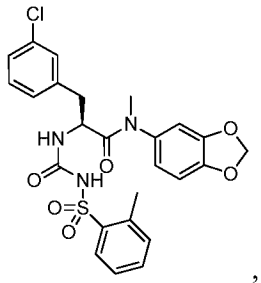
 ,
 ,
 ,
 ,

 ,
 ,
 ,
 ,

 ,
 ,
 ,
 ,

 ,
 ,
 ,
 ,

 ,
 ,
 ,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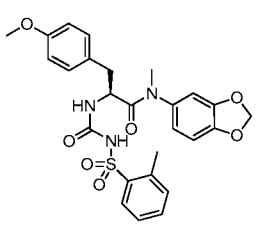
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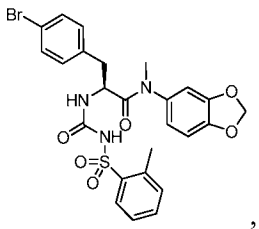
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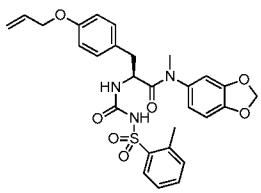
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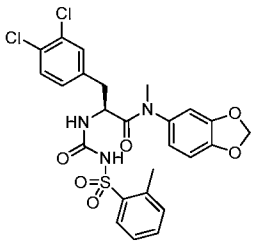
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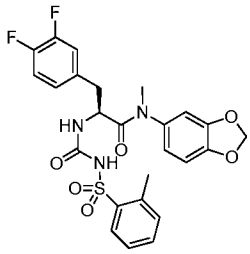
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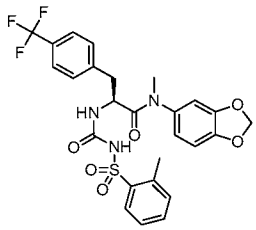
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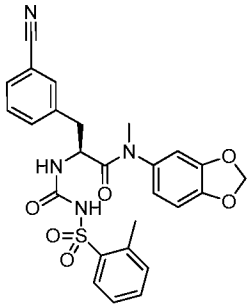
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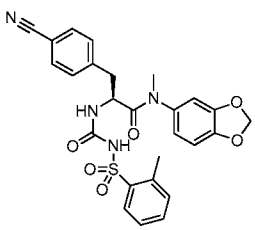
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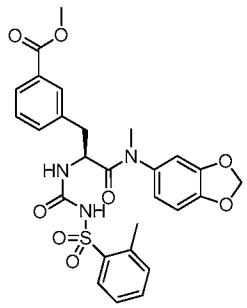
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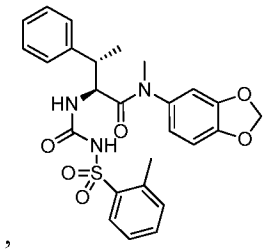
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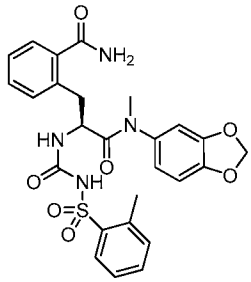
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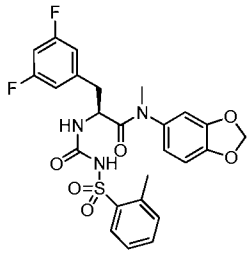
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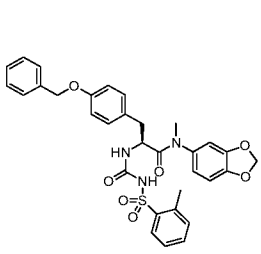
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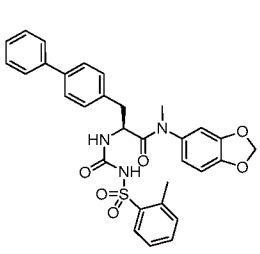
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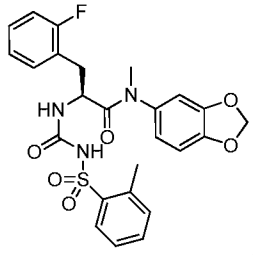
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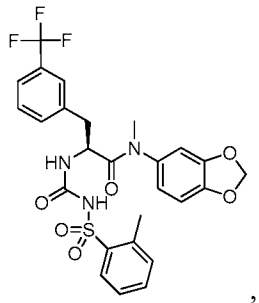
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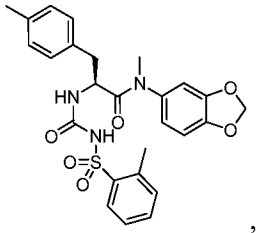
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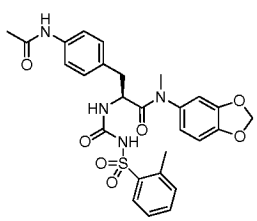
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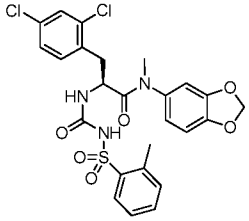
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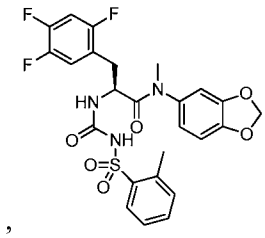
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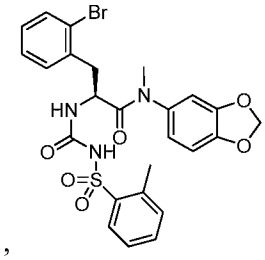
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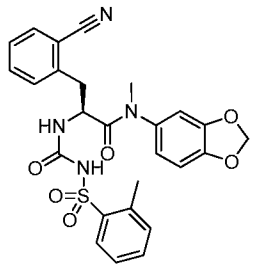
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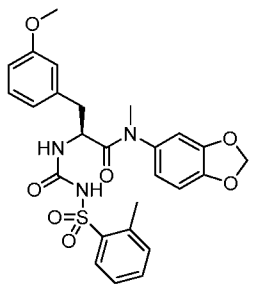
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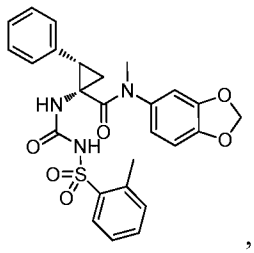
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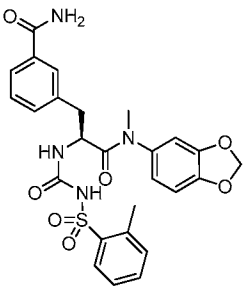
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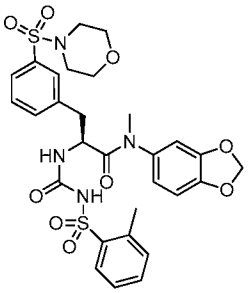
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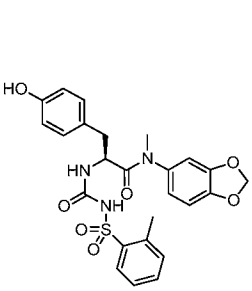
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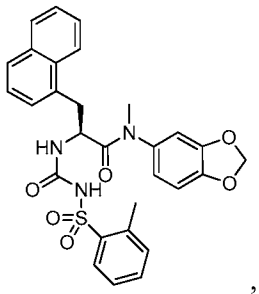
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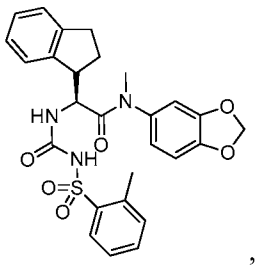
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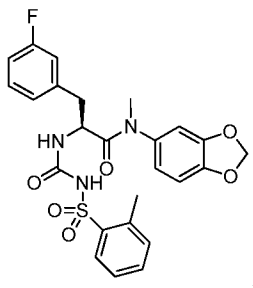
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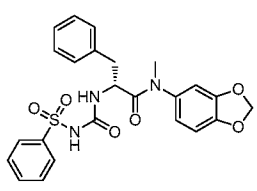
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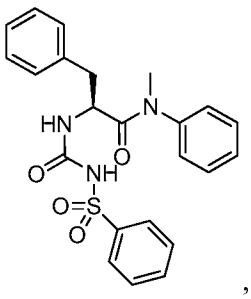
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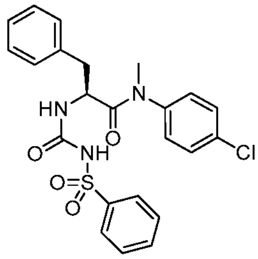
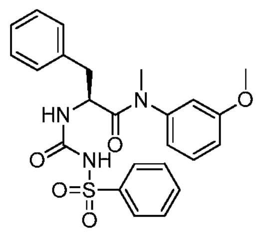
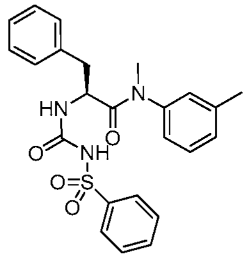
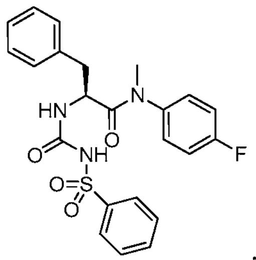
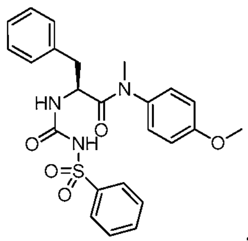
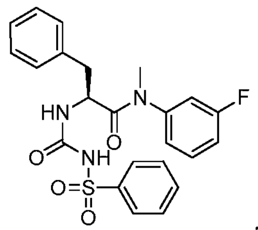
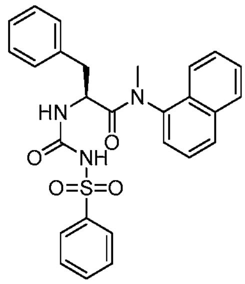
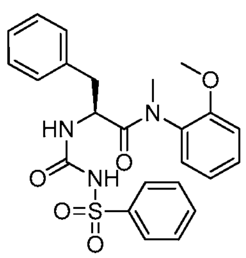
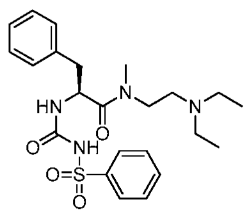
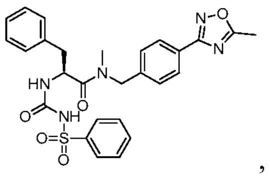
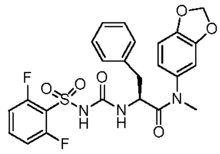
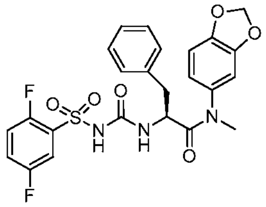
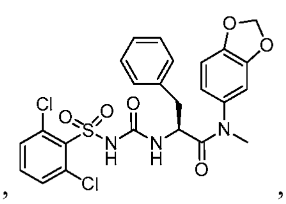
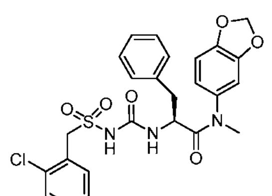
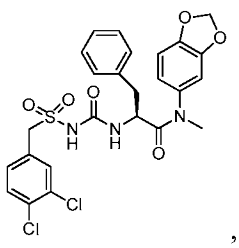
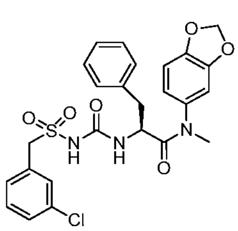
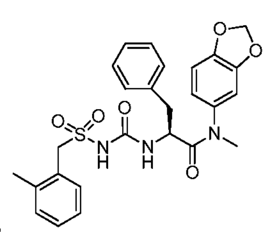
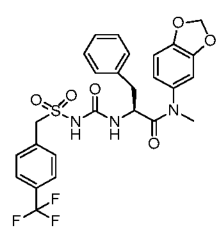
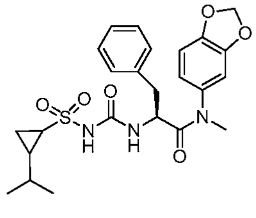
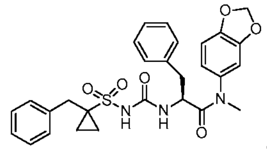
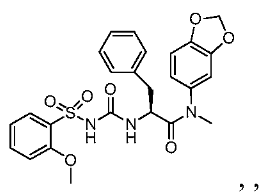
 ,  ,  ,

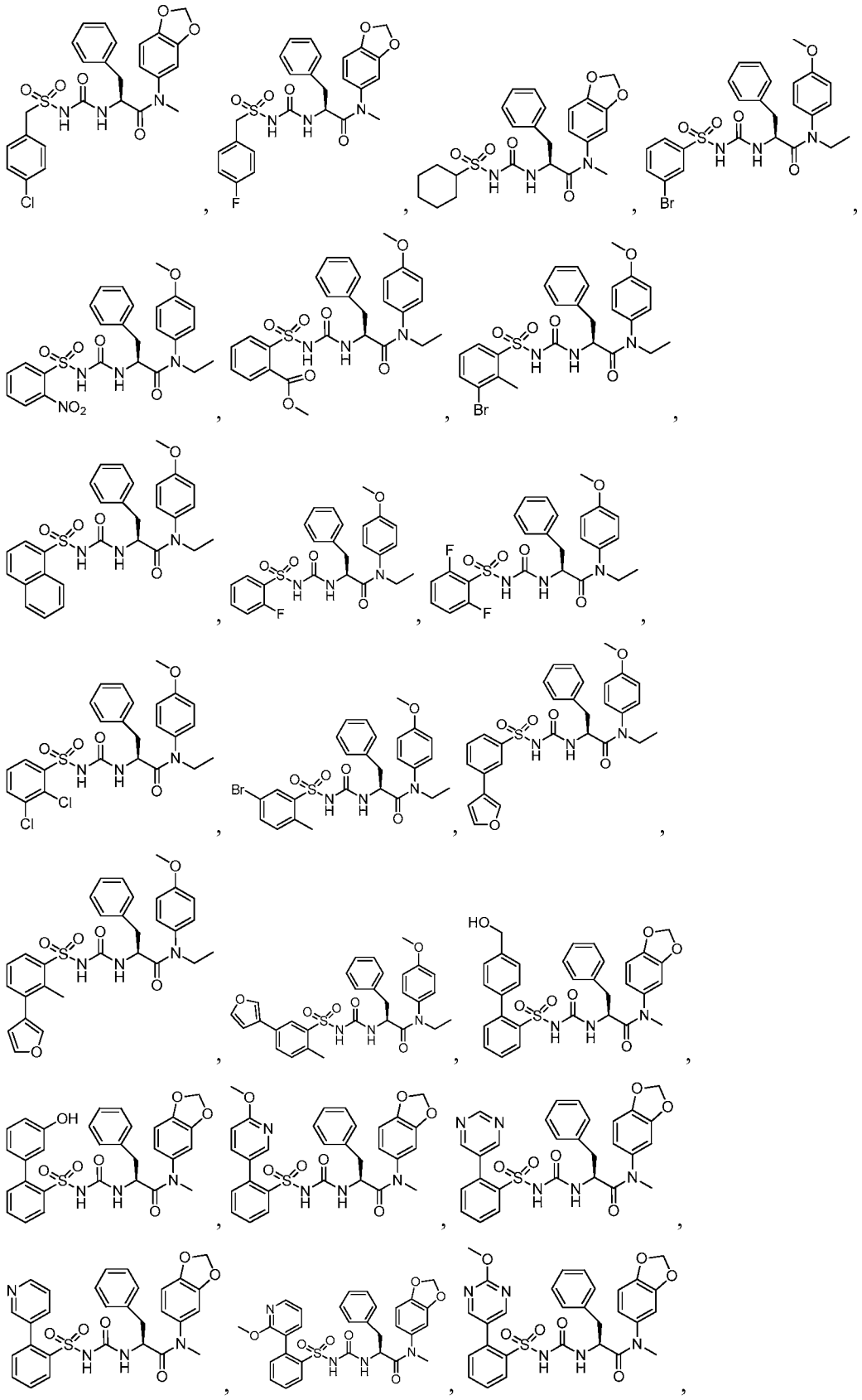
 ,  ,  ,  ,

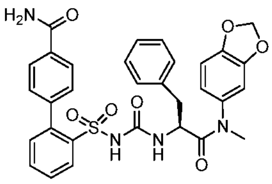
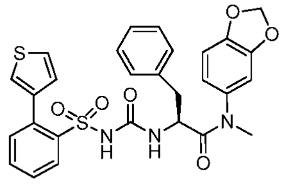
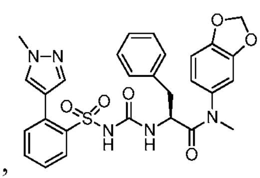
 ,  ,  ,  ,

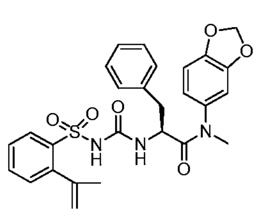
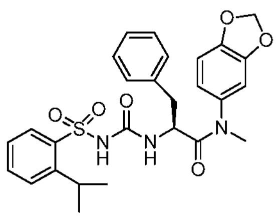
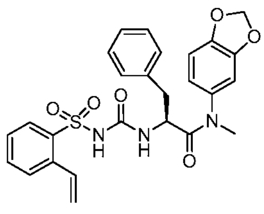
 ,  ,  ,

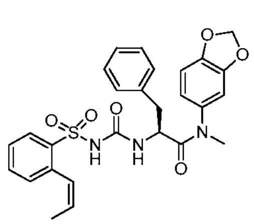
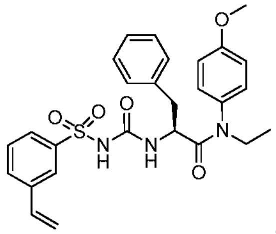
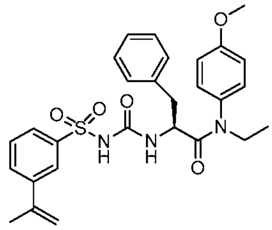
 ,  ,  ,  ,

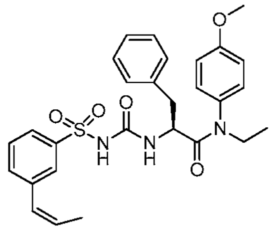
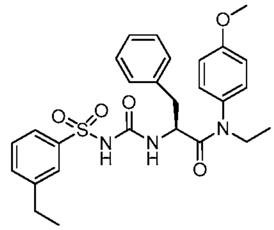
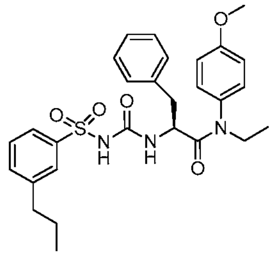
 ,  ,  , ,

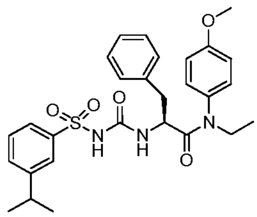
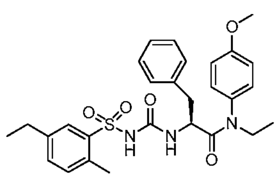
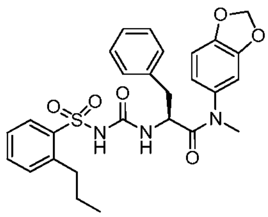


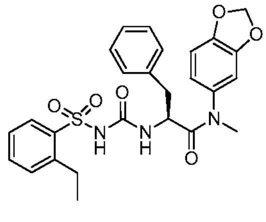
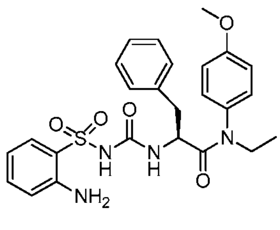
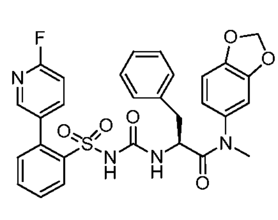
 ,
 ,
 ,

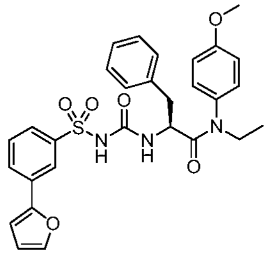
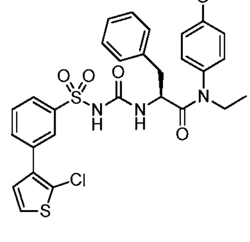
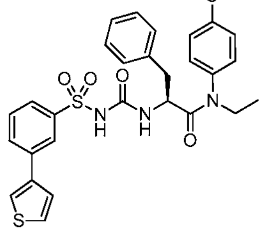
 ,
 ,
 ,

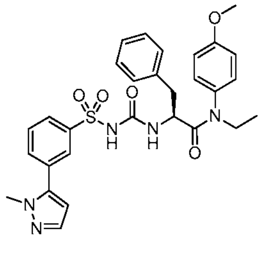
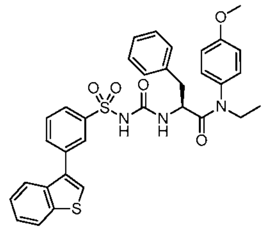
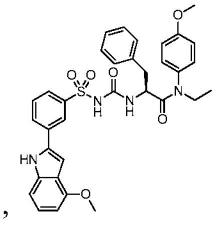
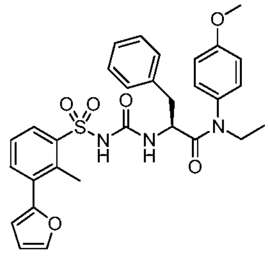
 ,
 ,
 ,

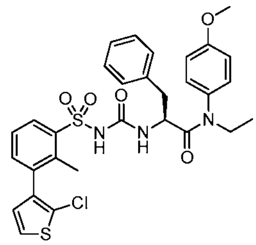
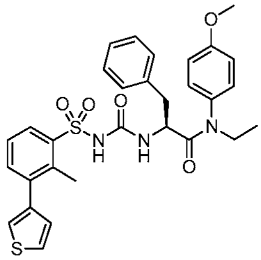
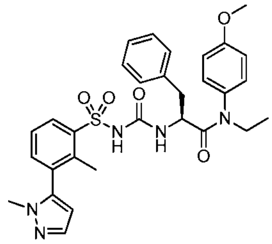
 ,
 ,
 ,

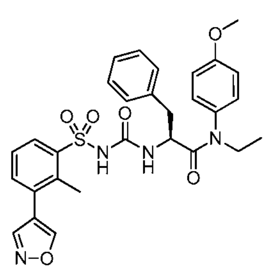
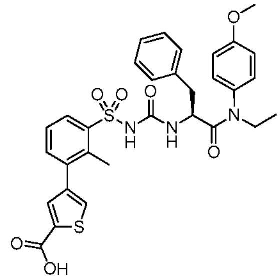
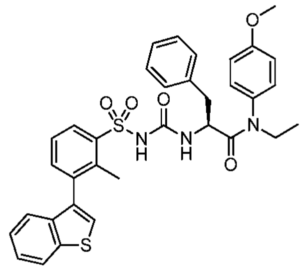
 ,
 ,
 ,

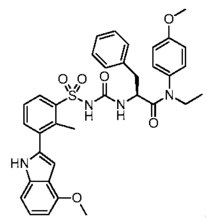
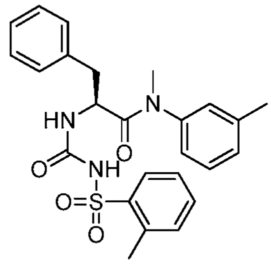
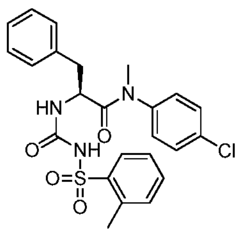
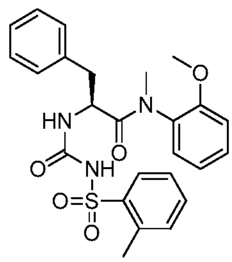
 ,
 ,
 ,

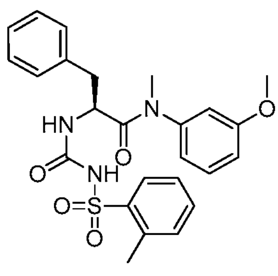
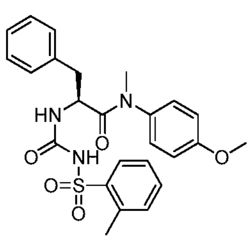
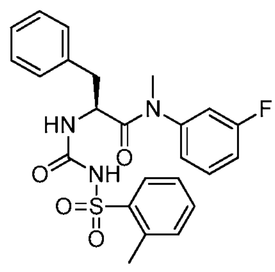
 ,
 ,
 ,

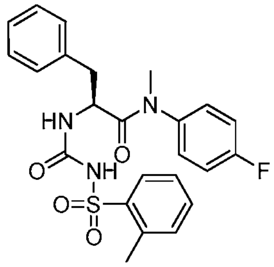
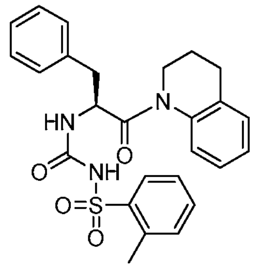
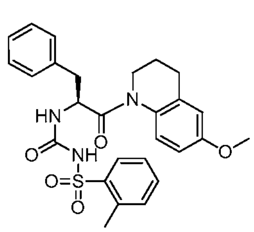
 ,
 ,
 ,
 ,

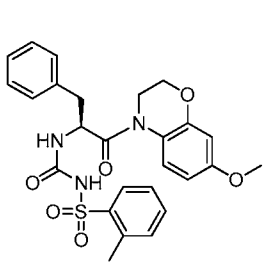
 ,
 ,
 ,

 ,
 ,
 ,

 ,
 ,
 ,
 ,

 ,
 ,
 ,

 ,
 ,
 ,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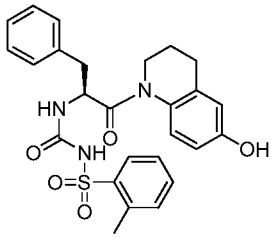
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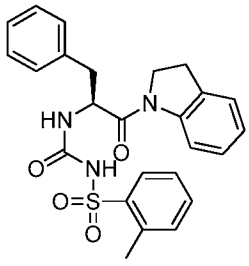
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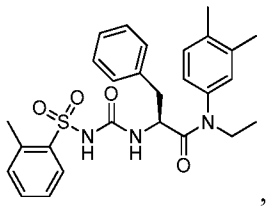
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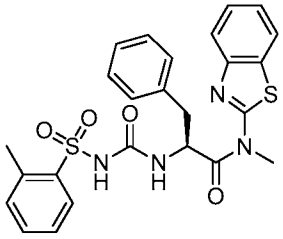
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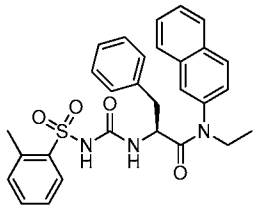
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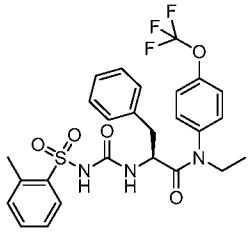
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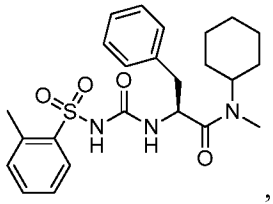
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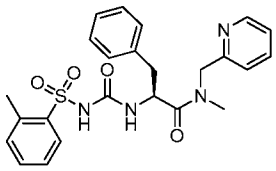
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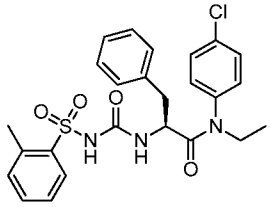
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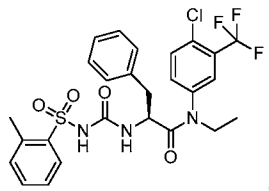
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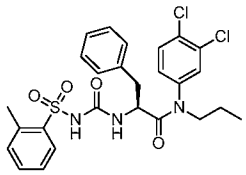
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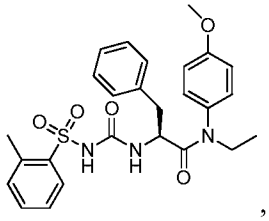
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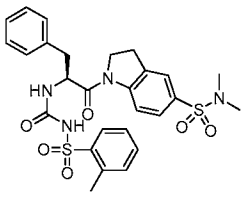
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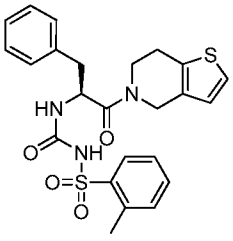
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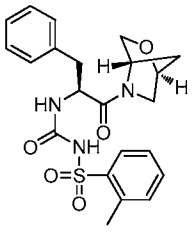
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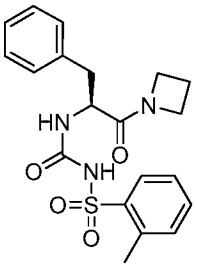
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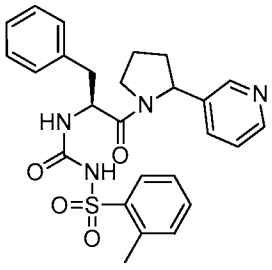
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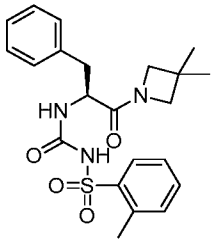
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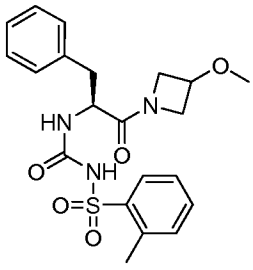
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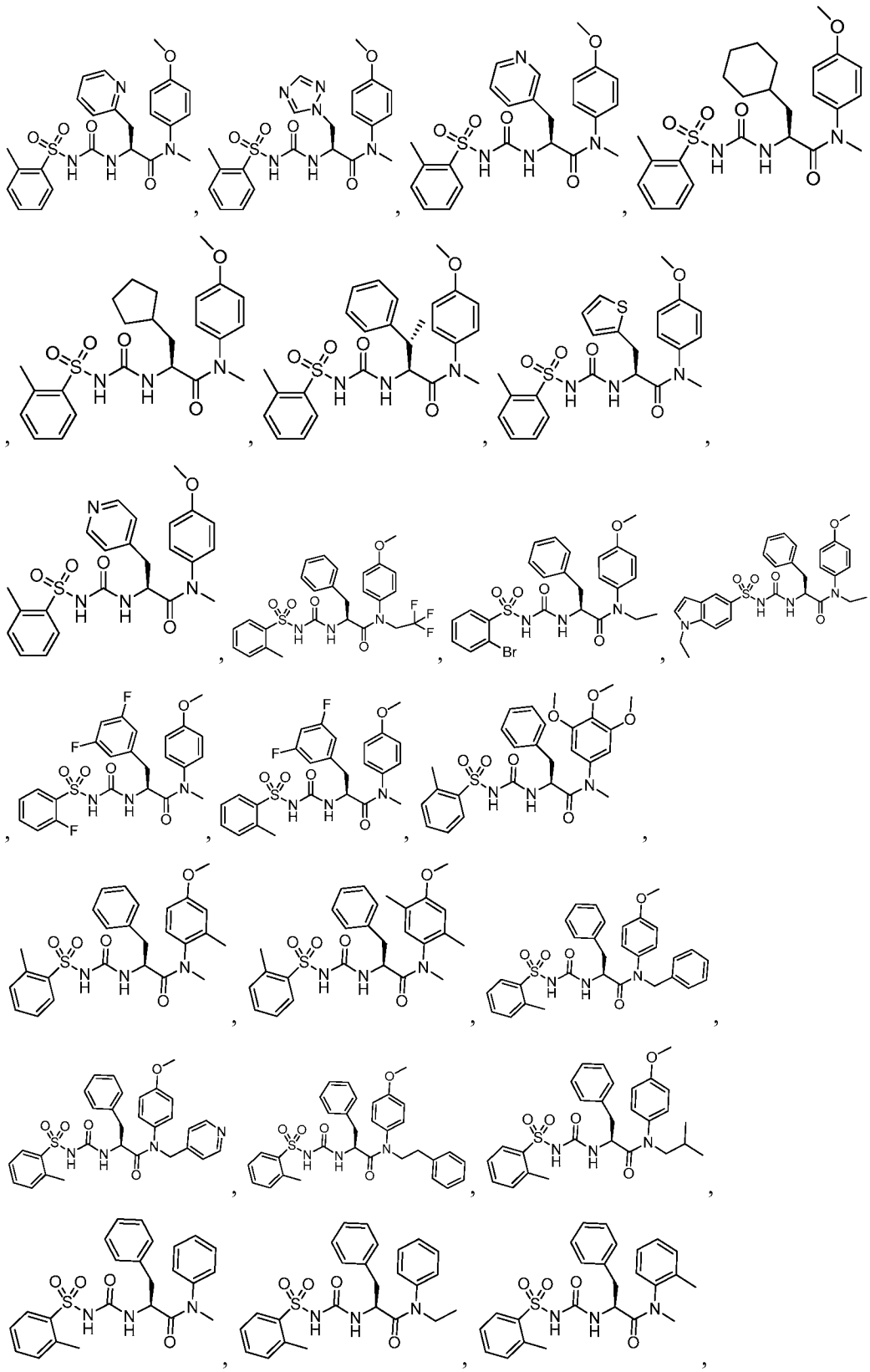
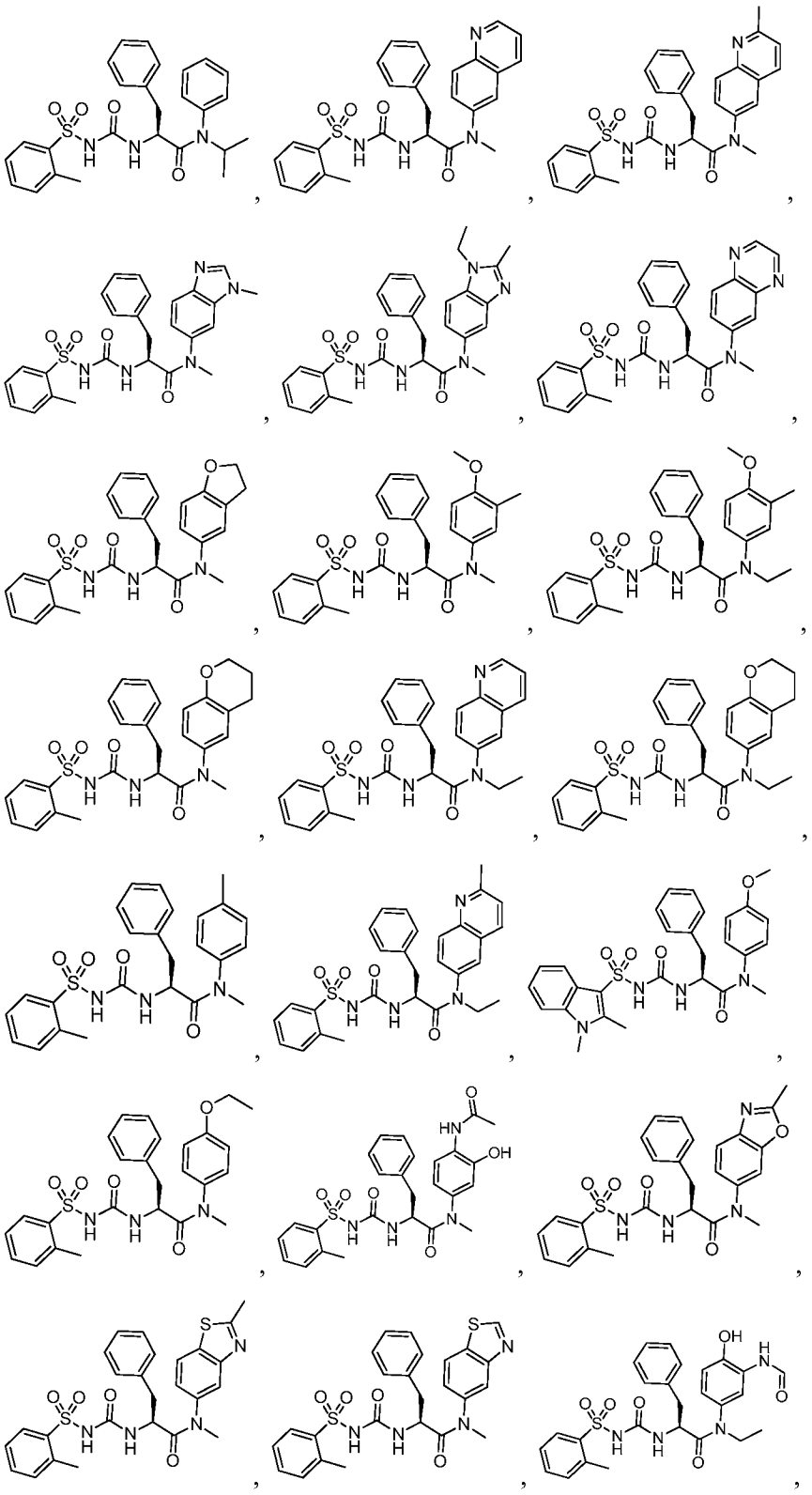
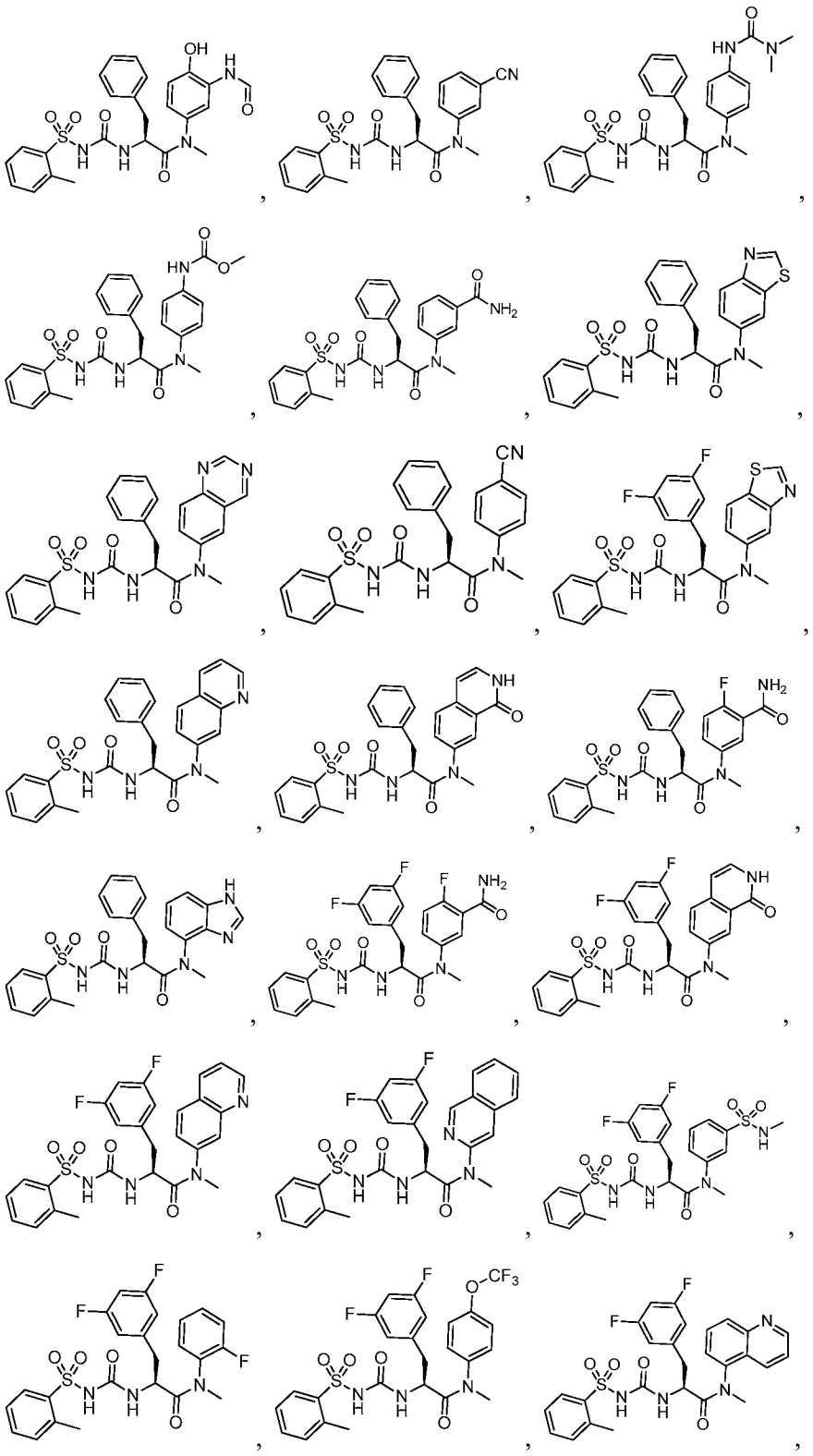
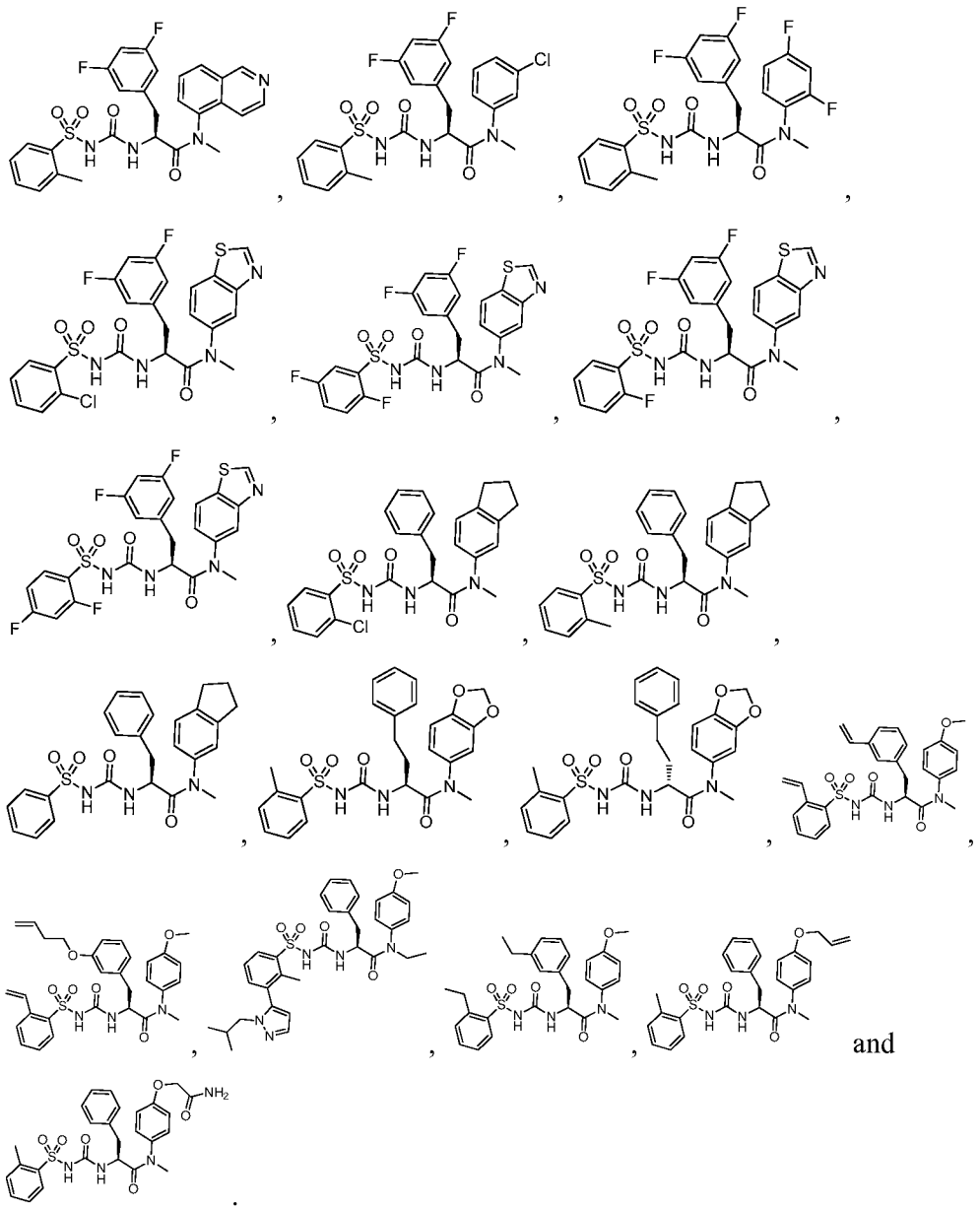


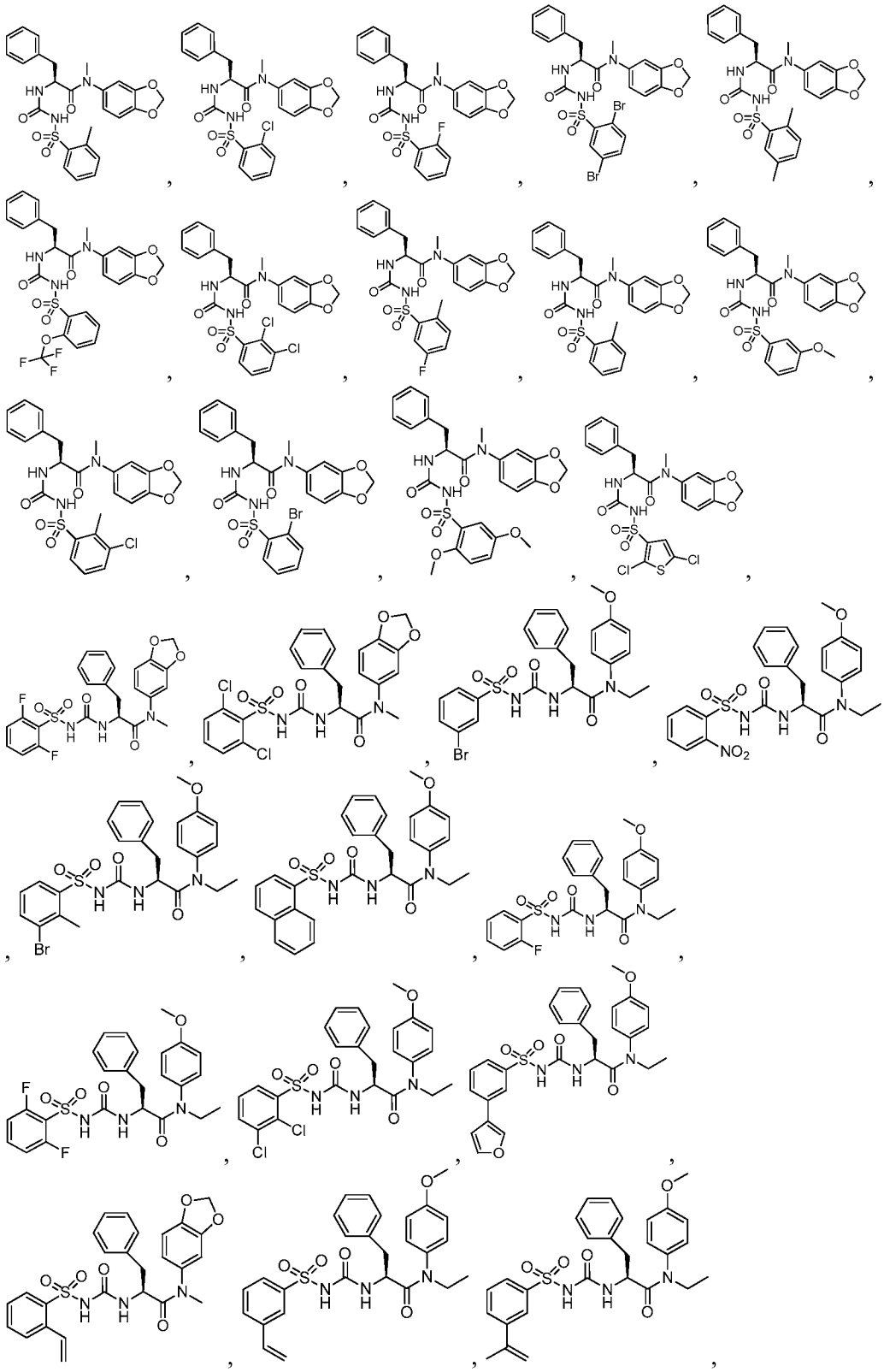


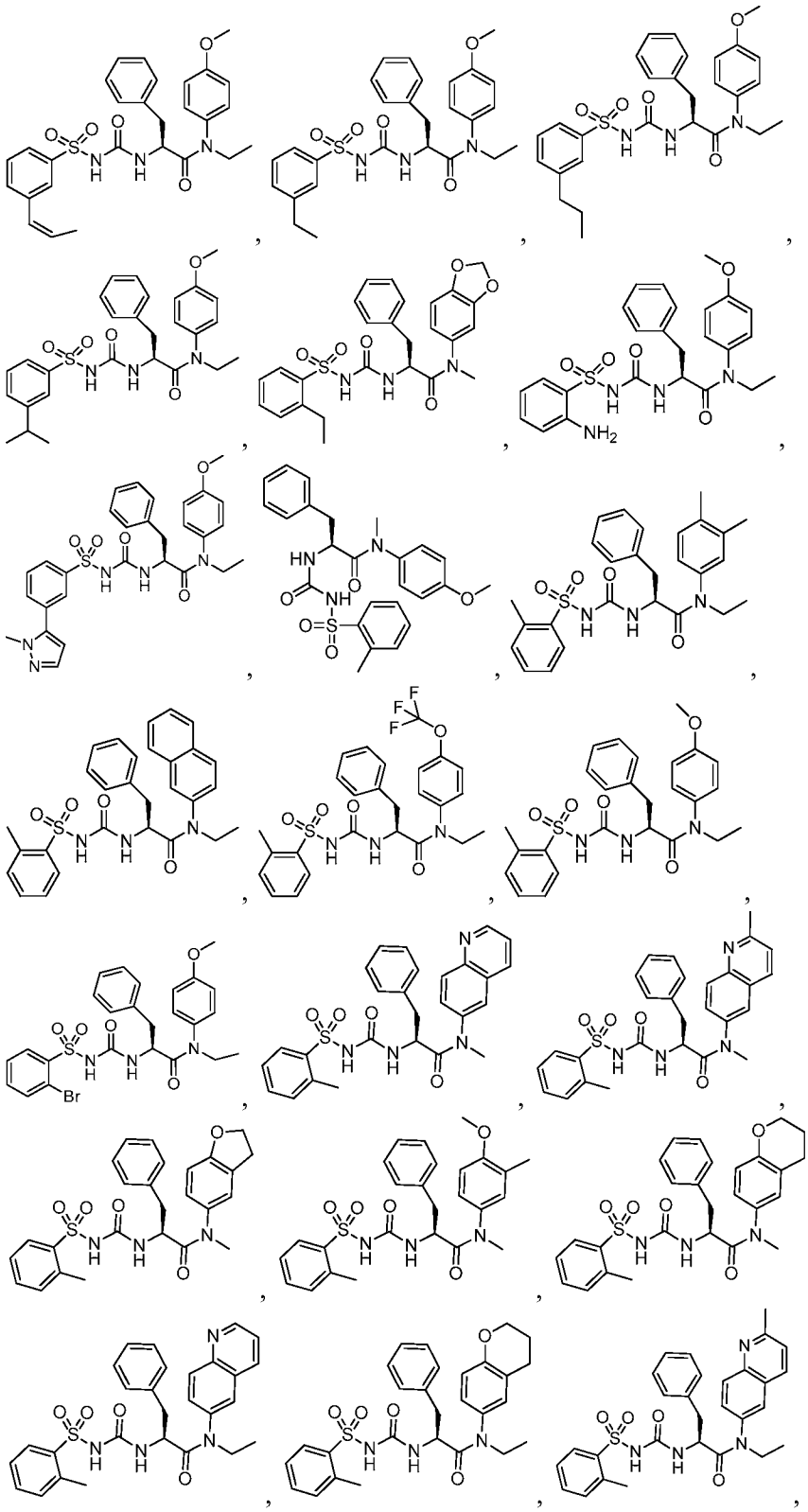


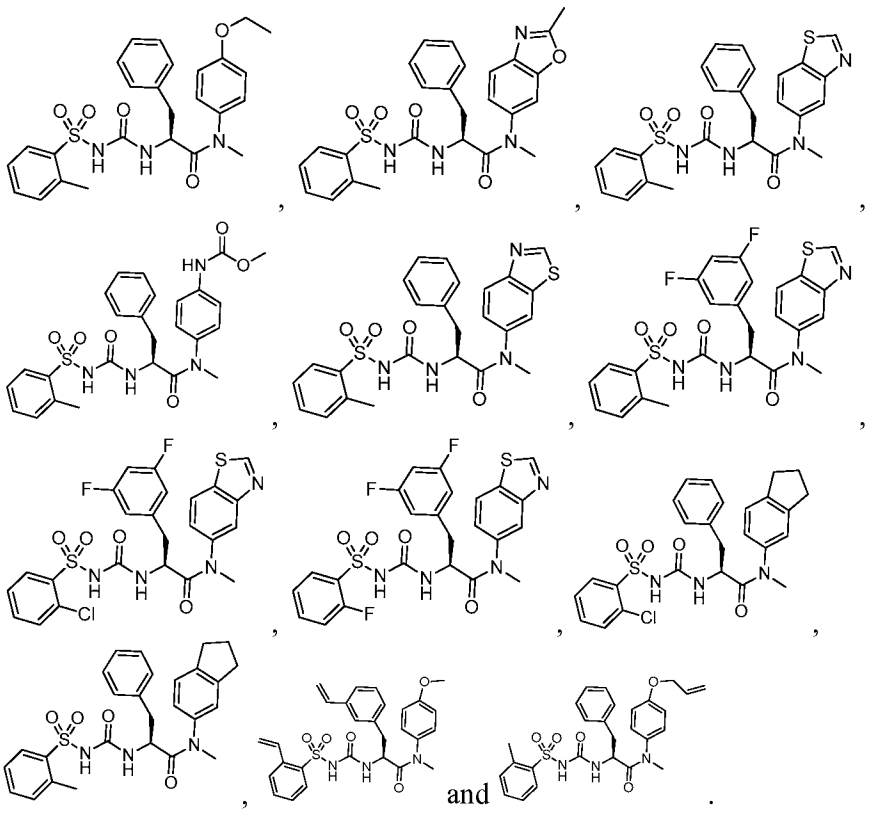


and

18. A compound, including pharmaceutically acceptable salts thereof, which is selected from the group of:







and

19. A composition useful for treating HIV infection comprising a therapeutic amount of a compound of claim 1 and a pharmaceutically acceptable carrier, excipient and/or diluent.

20. A method for treating HIV infection comprising administering a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, to a patient in need thereof.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/061870

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D263/56 C07D215/08 C07D311/04 C07D317/66 C07D231/12
C07D333/18 C07D333/28 C07D233/38 C07D233/54 C07D401/04
C07C311/58 C07D409/12 C07D249/08 C07D261/08 C07D205/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C C07D A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ANDREA SCOZZAFAVA ET AL: "Carbonic anhydrase activators", EUROPEAN JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 10, no. 1, 1 March 2000 (2000-03-01), pages 29-41, XP55013480, ISSN: 0928-0987, DOI: 10.1016/S0928-0987(99)00086-X compounds A1-A20	1-3,8-10
A	WO 95/09614 A1 (ABBOTT LAB [US]) 13 April 1995 (1995-04-13) the whole document	1-20

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 December 2014	07/01/2015

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/061870

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SCOZZAFAVA, A. ET AL.: "Carbonic anhydrase activators: synthesis of high affinity isozymes I, II and IV activators, derivatives of 4-(4-tosylureido-amino acyl)ehtyl-1H-imidazole (histamine derivatives)", J.ENZYME INHIBITION, vol. 15, 2000, pages 139-161, XP008173956, table I ----- 	1-3,8-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2014/061870

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		JP H09503501 A	08-04-1997
		PT 721330 E	28-09-2001
		US 5559158 A	24-09-1996
		US 5610193 A	11-03-1997
		WO 9509614 A1	13-04-1995