

PRODRUGS OF MYELOPEROXIDASE INHIBITORS

CROSS-REFERENCE TO RELATED APPLICATIONS

5 The application claims priority to U.S. Provisional Patent Application No. 62/913417 filed on October 10, 2019 in the United States Patent and Trademark Office (USPTO), and all the benefits accruing therefrom under 35 U.S.C. § 119, the content of which is incorporated herein in its entirety by reference.

FIELD OF THE INVENTION

10 The present invention relates to prodrugs of myeloperoxidase (MPO) inhibitors and their use in treating MPO-related disorders, such as multiple system atrophy (MSA), amyotrophic lateral sclerosis (ALS) or Huntington disease (HD). The present invention further relates to the use of prodrugs of MPO inhibitors for neuroprotection.

15 BACKGROUND OF THE INVENTION

Prodrugs are molecules with little or no pharmacological activity that are converted to the active parent drug *in vivo* by enzymatic or chemical reactions or by a combination of the two. Prodrugs are often designed to improve bioavailability when a drug itself is poorly absorbed from the gastrointestinal tract. Since 2008, at least 30 prodrugs have been approved by the U.S. Food and Drug Administration
20 (FDA). See, *e.g.*, Rautio, Jarkko; Meanwell, Nicholas A.; Di, Li; Hageman, Michael J., *Nature Reviews Drug Discovery*, volume 17, pages 559–587 (2018).

Myeloperoxidase (MPO) is a heme-containing enzyme found predominantly in polymorphonuclear leukocytes (PMNs). MPO is one member of a diverse protein family of mammalian peroxidases that also includes eosinophil peroxidase, thyroid peroxidase, salivary peroxidase,
25 lactoperoxidase, prostaglandin H synthase, and others. The mature enzyme is a dimer of identical halves. Each half molecule contains a covalently bound heme that exhibits unusual spectral properties responsible for the characteristic green color of MPO. Cleavage of the disulfide bridge linking the two halves of MPO yields the hemi-enzyme that exhibits spectral and catalytic properties indistinguishable from those of the intact enzyme. The enzyme uses hydrogen peroxide to oxidize chloride to
30 hypochlorous acid. Other halides and pseudohalides (like thiocyanate) are also physiological substrates to MPO.

PMNs are of particular importance for combating infections. These cells contain MPO, with well-documented microbicidal action. PMNs act non-specifically by phagocytosis to engulf microorganisms, incorporate them into vacuoles, termed phagosomes, which fuse with granules containing myeloperoxidase to form phagolysosomes. In phagolysosomes, the enzymatic activity of the myeloperoxidase leads to the formation of hypochlorous acid, a potent bactericidal compound. Hypochlorous acid is oxidizing in itself, and reacts most avidly with thiols and thioethers, but also converts amines into chloramines, and chlorinates aromatic amino acids. Macrophages are large phagocytic cells, which, like PMNs, are capable of phagocytosing microorganisms. Macrophages can generate hydrogen peroxide and upon activation also produce myeloperoxidase. MPO and hydrogen peroxide can also be released to the outside of the cells where the reaction with chloride can induce damage to adjacent tissue.

Linkage of myeloperoxidase activity to disease has been implicated in neurological diseases with a neuroinflammatory response including multiple sclerosis such as amyotrophic lateral sclerosis, Alzheimer's disease, and Parkinson's disease.

MPO positive cells are immensely present in the circulation and in tissue undergoing inflammation. More specifically, MPO containing macrophages, microglia, astrocytes and/or neurons have been documented in the CNS during disease; multiple sclerosis (Nagra et al. *Journal of Neuroimmunology* 1997; 78(1-2):97-107; Marik et al. *Brain* 2007; 130: 2800-15; Gray et al. *Brain Pathology* 2008; 18: 86-95), Parkinson's disease (Choi et al. *J. Neurosci.* 2005; 25(28):6594-600), and Alzheimer's disease (Reynolds et al. *Experimental Neurology* 1999; 155:31-41; Green et al. *Journal of Neurochemistry* 2004; 90(3):724-33). It is supposed that some aspects of a chronic ongoing inflammation result in an overwhelming destruction where agents from MPO reactions have an important role.

The enzyme is released both extracellularly as well as into phagolysosomes in the neutrophils (Hampton et al. *Blood* 1998; 92(9):3007-17). A prerequisite for the MPO activity is the presence of hydrogen peroxide, generated by NADPH oxidase and a subsequent superoxide dismutation. The oxidized enzyme is able to use a plethora of different substrates of which chloride is most recognized. From this reaction the strong non-radical oxidant—hypochlorous acid (HOCl)—is formed. HOCl oxidizes sulfur-containing amino acids like cysteine and methionine very efficiently (Peskin et al. *Free Radical Biology and Medicine* 2001; 30(5):572-9). It also forms chloramines with amino groups, both in proteins and other biomolecules (Peskin et al. *Free Radical Biology and Medicine* 2004; 37(10):1622-30). It

chlorinates phenols (like tyrosine) (Hazen et al. *Mass Free Radical Biology and Medicine* 1997; 23(6):909-16) and unsaturated bonds in lipids (Albert et al. *J. Biol. Chem.* 2001; 276(26):23733-41), oxidizes iron centers (Rosen et al. *Journal of Biological Chemistry* 1982; 257(22):13731-354) and crosslinks proteins (Fu et al. *Biochemistry* 2002; 41(4):1293-301). Various compounds that are MPO inhibitors are disclosed
5 in WO 2001/085146 published November 15, 2001, *J. Heterocyclic Chemistry*, 1992, 29, 343-354, *J. Chem. Soc.*, 1962, 1863, WO 2003/089430 published October 30, 2003, and WO 2006/062465 published June 15, 2006.

Multiple system atrophy (MSA) is a neurodegenerative disorder presenting with autonomic failure and with motor impairment resulting from L-DOPA-unresponsive Parkinsonism, cerebellar ataxia,
10 and pyramidal signs. Histologically, there is neuron loss in the striatum, substantia nigra pars compacta, cerebellum, pons, inferior olives, and intermediolateral column of the spinal cord. Glial pathology includes astrogliosis, microglial activation and α -synuclein containing oligodendroglial cytoplasmic inclusions. The pronounced neuroinflammation with activated microglia contribution as well as cytoplasmic inclusion bodies, containing aggregated and oxidatively modified proteins, makes it
15 plausible to consider a significant contribution of MPO activity in the progressive neurodegeneration characterizing the MSA pathology.

Support for MPO inhibition in an MSA-like pathology can be generated through the use of preclinical disease models for MSA, like transgenic mice with oligodendroglial overexpression of human α -synuclein with or without a toxin addition like 3-nitropropionic acid.

20 Huntington's disease (HD) is a hereditary progressive neurodegenerative disorder characterized clinically by motor and psychiatric disturbances and pathologically by neuronal loss and gliosis (reactive astrogliosis), particularly, in the striatum and cerebral cortex. HD is a neurodegenerative disorder caused by expansion of a CAG repeat in the HD gene, coding for polyglutamine in the huntingtin protein. Explanations to the pathological mechanisms include oxidative stress, impaired energy metabolism, and
25 abnormal protein-protein interactions. Such mechanisms are possible to link to MPO activity, which might be manifested through its observed overexpression in pathological HD tissue (Choi et al. *J. Neurosci.* 2005; 25(28):6594-600).

Support for MPO inhibition in an HD-like pathology can be generated through the use of preclinical disease models for HD. Such models might be mice or rats treated with mitochondrial toxins
30 like 3-nitropropionic acid or malonate (Matthews et al. *J. Neurosci.* 1998; 18:156-63). Useful models

might also be transgenic mice expressing mutants of the huntingtin protein with or without a toxin addition like 3-nitropropionic acid (Bogdanov et al. *J. Neurochem.* 1998; 71:2642-44).

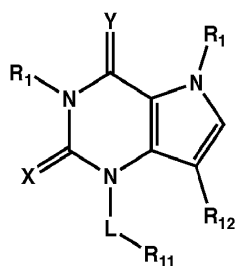
There is a large unmet need for medications that can be used for the treatment of Huntington's disease, for the treatment of multiple system atrophy and/or for neuroprotection. Several earlier stage MPO inhibitors are currently in development, such as disclosed, for example, in US 2009/0054468 published August 21, 2008. Among them, BHV-3241 is a first-in-class, brain-penetrant, irreversible myeloperoxidase (MPO) inhibitor that is being developed for the treatment of multiple system atrophy (MSA) and amyotrophic lateral sclerosis (ALS). However, certain MPO inhibitors may have pharmacokinetic properties that render them challenging to prepare in oral and/or parenteral dosage forms. Enhancing the oral bioavailability, modifying the pharmacokinetic profile or increasing the aqueous solubility of such compounds would therefore be desirable.

SUMMARY OF THE INVENTION

The present invention is directed to the treatment of MPO-related disorders, *e.g.*, multiple system atrophy, amyotrophic lateral sclerosis, and Huntington's disease, and methods of neuroprotection, which include administering to a patient in need thereof the prodrugs, pharmaceutical compositions including the prodrugs, and kits including the pharmaceutical compositions and instructions for use.

In an aspect of the invention, there is provided a compound having one of General Formula (1):

General Formula (1)



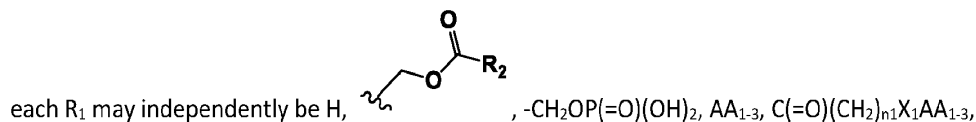
In General Formula (1):

at least one of X and Y may represent S, and the other may represent O or S;

L may represent a direct bond or C1 to C7 alkylene group as described below;

R¹¹ may be hydrogen or an unsubstituted or substituted carbocyclic, heterocyclic, or aromatic ring as described below;

R¹² may be hydrogen, a halogen, or a carbon optionally substituted with one to three halogen atoms;



or C(=O)AA, provided that at least one R₁ may not be H; wherein

5 AA₁₋₃ may be a moiety consisting of 1 to 3 natural amino acids linked through a peptide bond,

n₁ may be an integer of 1 to 5,

X₁ may be S, O, or NH, and

and R₂ may be -[C(R₃)₂]_nR₄, -NR₃R₄, or -OR₄, wherein each R₃ may independently be hydrogen or C1-C10 alkyl wherein R₃ may be optionally connected to form a ring, and R₄ may be a substituted or

10 unsubstituted C1-C20 alkyl group, a substituted or unsubstituted C2-C20 alkenyl group, a substituted or unsubstituted C2-C20 alkynyl group, a substituted or unsubstituted C1-C20 heteroalkyl group, a substituted or unsubstituted C2-C20 heteroalkenyl group, a substituted or unsubstituted C2-C20 heteroalkynyl group, a substituted or unsubstituted C3-C20 cycloalkyl group, a substituted or unsubstituted C3-C20 heterocycloalkyl group, a substituted or unsubstituted C6-C20 aryl group, or a

15 substituted or unsubstituted C1-C20 heteroaryl group, and n may be 0 or 1.

In an aspect of the invention, there is provided a pharmaceutical composition including a therapeutically effective amount of the compound in accordance with the invention described herein.

In an aspect of the invention, there is provided a method of treating multiple system atrophy in a patient in need thereof, which includes administering to the patient a pharmaceutical composition

20 including a therapeutically effective amount of a compound in accordance with the invention described herein.

In an aspect of the invention, there is provided a method of treating Huntington's disease in a patient in need thereof, which includes administering to the patient a pharmaceutical composition including a therapeutically effective amount of a compound in accordance with the invention described

25 herein.

In an aspect of the invention, there is provided a method for neuroprotection, which includes administering to the patient a pharmaceutical composition including a therapeutically effective amount of a compound in accordance with the invention described herein.

In an aspect of the invention, there is provided a kit for treating multiple system atrophy, the kit

30 comprising:

(a) a pharmaceutical composition comprising a therapeutically effective amount of a compound in accordance with the invention described herein; and

(b) instructions for administering the pharmaceutical composition.

5 In an aspect of the invention, there is provided a kit for treating Huntington's disease, the kit comprising:

(a) a pharmaceutical composition comprising a therapeutically effective amount of a compound in accordance with the invention described herein; and

(b) instructions for administering the pharmaceutical composition.

In an aspect of the invention, there is provided a kit for neuroprotection, the kit comprising:

10 (a) a pharmaceutical composition comprising a therapeutically effective amount of a compound in accordance with the invention described herein; and

(b) instructions for administering the pharmaceutical composition.

DETAILED DESCRIPTION OF THE INVENTION

15 The following detailed description is provided to aid those skilled in the art in practicing the present invention. Those of ordinary skill in the art may make modifications and variations in the embodiments described herein without departing from the spirit or scope of the present disclosure. Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. The

20 terminology used in the description is for describing particular embodiments only and is not intended to be limiting. Terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the relevant art and the present disclosure, and will not be interpreted in an idealized or overly formal sense unless expressly so defined herein.

25 As used in this application, except as otherwise expressly provided herein, each of the following terms shall have the meaning set forth below. Additional definitions are set forth throughout the application. In instances where a term is not specifically defined herein, that term is given an art-recognized meaning by those of ordinary skill applying that term in context to its use in describing the present invention.

The articles "a" and "an" refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article unless the context clearly indicates otherwise. By way of example, "an element" means one element or more than one element.

5 The term "or" means "and/or." It will be further understood that the terms "comprises" and/or "comprising," or "includes" and/or "including" when used in this specification, specify the presence of stated features, regions, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, regions, integers, steps, operations, elements, components, and/or groups thereof.

10 The term "about" refers to a value or composition that is within an acceptable error range for the particular value or composition as determined by one of ordinary skill in the art, which will depend in part on how the value or composition is measured or determined, *i.e.*, the limitations of the measurement system. For example, "about" can mean within 1 or more than 1 standard deviation per the practice in the art. Alternatively, "about" can mean a range of up to 10% or 20% (*i.e.*, $\pm 10\%$ or $\pm 20\%$). For example, about 3 mg can include any number between 2.7 mg and 3.3 mg (for 10%) or
15 between 2.4 mg and 3.6 mg (for 20%). Furthermore, particularly with respect to biological systems or processes, the terms can mean up to an order of magnitude or up to 5-fold of a value. When particular values or compositions are provided in the application and claims, unless otherwise stated, the meaning of "about" should be assumed to be within an acceptable error range for that particular value or composition.

20 The term "administering" refers to the physical introduction of a composition comprising a therapeutic agent to a subject, using any of the various methods and delivery systems known to those skilled in the art. Administering can also be performed, for example, once, a plurality of times, and/or over one or more extended periods and can be a therapeutically effective dose or a subtherapeutic dose.

25 The term "AUC" (area under the curve) refers to a total amount of drug absorbed or exposed to a subject. Generally, AUC may be obtained from mathematical method in a plot of drug concentration in the subject over time until the concentration is negligible. The term "AUC" (area under the curve) could also refer to partial AUC at specified time intervals.

30 The term " $C_{\max}$ " refers to a maximum concentration of a drug in blood, serum, a specified compartment or test area of a subject between administration of a first dose and administration of a second dose. The term $C_{\max}$ could also refer to dose normalized ratios if specified.

The term "dosing interval," refers to the amount of time that elapses between multiple doses of a formulation disclosed herein being administered to a subject. Dosing interval can thus be indicated as ranges.

5 The term "dosing frequency" refers to the frequency of administering doses of a formulation disclosed herein in a given time. Dosing frequency can be indicated as the number of doses per a given time, *e.g.*, once a week or once in two weeks.

The terms "in combination with" and "in conjunction with" refer to administration of one treatment modality in addition to another treatment modality. As such, "in combination with" or "in conjunction with" refers to administration of one treatment modality before, during, or after
10 administration of the other treatment modality to the subject.

The term "pharmaceutically acceptable salt" refers to a salt form of one or more of the compounds or prodrugs described herein which are presented to increase the solubility of the compound in the gastric or gastroenteric juices of the patient's gastrointestinal tract in order to promote dissolution and the bioavailability of the compounds. Pharmaceutically acceptable salts
15 include those derived from pharmaceutically acceptable inorganic or organic bases and acids, where applicable. Suitable salts include those derived from alkali metals such as potassium and sodium, alkaline earth metals such as calcium, magnesium and ammonium salts, among numerous other acids and bases well known in the pharmaceutical art.

The terms "subject" and "patient" refer any human or non-human animal. The term "non-
20 human animal" includes, but is not limited to, vertebrates such as non-human primates, sheep, dogs, and rodents such as mice, rats and guinea pigs. In some embodiments, the subject is a human. The terms, "subject" and "patient" are used interchangeably herein.

The terms "effective amount", "therapeutically effective amount", "therapeutically effective dosage" and "therapeutically effective dose" of an agent (also sometimes referred to herein as a "drug")
25 refers to any amount of the agent that, when used alone or in combination with another agent, protects a subject against the onset of a disease or promotes disease regression evidenced by a decrease in severity of disease symptoms, an increase in frequency and duration of disease symptom-free periods, or a prevention of impairment or disability due to the disease affliction. The therapeutically effective amount of an agent can be evaluated using a variety of methods known to the skilled practitioner, such
30 as in human subjects during clinical trials, in animal model systems predictive of efficacy in humans, or by assaying the activity of the agent in *in vitro* assays.

The term " $T_{\max}$ " refers to a time or period after administration of a drug when the maximum concentration ($C_{\max}$) is reached in blood, serum, a specified compartment or test area of a subject.

The term "treatment" refers to any treatment of a condition or disease in a subject and may include: (i) preventing the disease or condition from occurring in the subject which may be predisposed to the disease but has not yet been diagnosed as having it; (ii) inhibiting the disease or condition, *i.e.*, arresting its development; relieving the disease or condition, *i.e.*, causing regression of the condition; or (iii) ameliorating or relieving the conditions caused by the disease, *i.e.*, symptoms of the disease. Treatment could be used in combination with other standard therapies or alone. Treatment or "therapy" of a subject also includes any type of intervention or process performed on, or the administration of an agent to, the subject with the objective of reversing, alleviating, ameliorating, inhibiting, slowing down or preventing the onset, progression, development, severity or recurrence of a symptom, complication or condition, or biochemical indicia associated with a disease.

With respect to multiple system atrophy and Huntington's disease, "treatment" is an approach for obtaining beneficial or desired clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, one or more of the following: improvement in any aspect of a major symptom including lessening severity, alleviation of major symptom intensity, and other associated symptoms, reducing frequency of recurrence, increasing the quality of life of those suffering from the symptom, and decreasing dose of other medications required to treat the symptom.

An "alkyl group" as used herein refers to a linear or branched aliphatic hydrocarbon monovalent group having a specified number of carbon atoms. Non-limiting examples of the "alkyl group" are a methyl group, an ethyl group, a propyl group, an iso-butyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an iso-amyl group, and a hexyl group. An "alkylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the alkyl group.

An "alkenyl group" as used herein refers to a hydrocarbon monovalent group containing at least one carbon-carbon double bond in the middle or at the terminal thereof and having a specified number of carbon atoms. Non-limiting examples thereof are an ethenyl group, a propenyl group, and a butenyl group. An "alkenylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the alkenyl group.

An "alkynyl group" as used herein refers to a hydrocarbon monovalent group containing at least one carbon-carbon triple bond in the middle or at the terminal thereof and having a specified number of carbon atoms. Non-limiting examples thereof are an ethynyl group and a propynyl group. An

"alkynylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the alkynyl group.

A "heteroalkyl group" as used herein refers to an alkyl group as defined above, in which at least one carbon atom is replaced with a heteroatom selected from N, O, P, and S or in which at least one
5 carbon atom is replaced with a group containing at least one of the above heteroatoms. Non-limiting examples thereof are a methoxyethyl group and a dimethylaminoethyl group. A "heteroalkylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the heteroalkyl group.

A "heteroalkenyl group" as used herein refers to an alkenyl group as defined above, in which at least one carbon atom is replaced with a heteroatom selected from N, O, P, and S. Non-limiting
10 examples thereof are a methoxybutenyl group and a dimethylaminobutenyl group. A "heteroalkenylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the heteroalkenyl group.

A "heteroalkynyl group" as used herein refers to an alkynyl group as defined above, in which at least one carbon atom is replaced with a heteroatom selected from N, O, P, and S. Non-limiting
15 examples thereof are a methoxybutynyl group and a dimethylaminobutynyl group. A "heteroalkynylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the heteroalkynyl group.

A "cycloalkyl group" as used herein refers to a monovalent hydrocarbon monocyclic group having a specified number of carbon atoms. Non-limiting examples thereof are a cyclopropyl group, a
20 cyclobutyl group, a cyclopentyl group, a cyclohexyl group, and a cycloheptyl group. A "cycloalkylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the cycloalkyl group.

A "heterocycloalkyl group" as used herein refers to a monovalent monocyclic group having at least one heteroatom selected from N, O, P, and S as a ring-forming atom and specified number of
25 carbon atoms. Non-limiting examples thereof are a tetrahydrofuran group, and a tetrahydrothiophenyl group. A "heterocycloalkylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the heterocycloalkyl group.

An "aryl group" as used herein refers to a monovalent group having a carbocyclic aromatic system having a specified number of carbon atoms. Non-limiting examples of the aryl group are a
30 phenyl group, a naphthyl group, an anthracenyl group, a phenanthrenyl group, a pyrenyl group, and a chrysenyl group. When the aryl group includes two or more rings, the rings may be fused to each other.

An "arylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the aryl group.

A "heteroaryl group" as used herein refers to a monovalent carbocyclic aromatic system having at least one heteroatom selected from N, O, P, and S as a ring-forming atom and a specified number of carbon atoms. Non-limiting examples of the heteroaryl group are a pyridinyl group, a pyrimidinyl group, a pyrazinyl group, a pyridazinyl group, a triazinyl group, a quinolinyl group, and an isoquinolinyl group.

When the heteroaryl group includes two or more rings, the rings may be fused to each other. A "heteroarylene group" as used herein refers to a divalent group formed by abstraction of hydrogen from the heteroaryl group.

At least one of substituents of the substituted alkyl group, substituted alkenyl group, substituted alkynyl group, substituted cycloalkyl group, substituted heterocycloalkyl group, substituted aryl group, and substituted heteroaryl group may be selected from:

deuterium, -F, -Cl, -Br, -I, a hydroxyl group, a cyano group, a nitro group, an amino group, an amidino group, a hydrazine group, a hydrazone group, a carboxylic acid group or a salt thereof, a sulfonic acid group or a salt thereof, a phosphoric acid group or a salt thereof, a C1-C10 alkyl group, a C2-C10 alkenyl group, a C2-C10 alkynyl group, and C1-C10 alkoxy group;

a C1-C10 alkyl group, a C2-C10 alkenyl group, a C2-C10 alkynyl group, and C1-C10 alkoxy group, each substituted with at least one selected from deuterium, -F, -Cl, -Br, -I, a hydroxyl group, a cyano group, a nitro group, an amino group, an amidino group, a hydrazine group, a hydrazone group, a carboxylic acid group or a salt thereof, a sulfonic acid group or a salt thereof, a phosphoric acid group or a salt thereof, a C3-C10 cycloalkyl group, a C1-C10 heterocycloalkyl group, a C3-C10 cycloalkenyl group, a C1-C10 heterocycloalkenyl group, a C6-C20 aryl group, a C6-C20 aryloxy group, a C6-C20 arylthio group, and a C1-C20 heteroaryl group;

a C3-C10 cycloalkyl group, a C1-C10 heterocycloalkyl group, a C3-C10 cycloalkenyl group, a C1-C10 heterocycloalkenyl group, a C6-C20 aryl group, a C6-C20 aryloxy group, a C6-C20 arylthio group, and a C1-C20 heteroaryl group; and

a C3-C10 cycloalkyl group, a C1-C10 heterocycloalkyl group, a C3-C10 cycloalkenyl group, a C1-C10 heterocycloalkenyl group, a C6-C20 aryl group, a C6-C20 aryloxy group, a C6-C20 arylthio group, and a C1-C20 heteroaryl group, each substituted with at least one selected from deuterium, -F, -Cl, -Br, -I, a hydroxyl group, a cyano group, a nitro group, an amino group, an amidino group, a hydrazine group, a hydrazone group, a carboxylic acid group or a salt thereof, a sulfonic acid group or a salt thereof, a

phosphoric acid group or a salt thereof, a C1-C10 alkyl group, a C2-C10 alkenyl group, a C2-C10 alkynyl group, and a C1-C10 alkoxy group, a C3-C10 cycloalkyl group, a C1-C10 heterocycloalkyl group, a C3-C10 cycloalkenyl group, a C1-C10 heterocycloalkenyl group, a C6-C20 aryl group, a C6-C20 aryloxy group, a C6-C20 arylthio group, and a C1-C20 heteroaryl group.

5 For example, at least one of substituents of the substituted alkyl group, substituted alkenyl group, substituted alkynyl group, substituted alkoxy group, substituted cycloalkyl group, substituted heterocycloalkyl group, substituted aryl group, and substituted C1-C30 heteroaryl group may be selected from:

deuterium, -F, -Cl, -Br, -I, a hydroxyl group, a cyano group, a nitro group, an amino group, an
10 amidino group, a hydrazine group, a hydrazone group, a carboxylic acid group or a salt thereof, a sulfonic acid group or a salt thereof, a phosphoric acid group or a salt thereof, a C1-C10 alkyl group, a C2-C10 alkenyl group, a C2-C10 alkynyl group, and C1-C10 alkoxy group;

a C1-C10 alkyl group, a C2-C10 alkenyl group, a C2-C10 alkynyl group, and C1-C10 alkoxy group,
each substituted with at least one selected from deuterium, -F, -Cl, -Br, -I, a hydroxyl group, a cyano
15 group, a nitro group, an amino group, an amidino group, a hydrazine group, a hydrazone group, a carboxylic acid group or a salt thereof, a sulfonic acid group or a salt thereof, a phosphoric acid group or a salt thereof, a C3-C10 cycloalkyl group, a C1-C10 heterocycloalkyl group, a C3-C10 cycloalkenyl group, a C1-C10 heterocycloalkenyl group, a C6-C20 aryl group, a C6-C20 aryloxy group, a C6-C20 arylthio group, and a C1-C20 heteroaryl group;

20 a phenyl group, a pentalenyl group, an indenyl group, a naphthyl group, an azulenyl group, a heptalenyl group, an indacenyl group, an acenaphthyl group, a fluorenyl group, a spiro-fluorenyl group, a phenalenyl group, a phenanthrenyl group, an anthracenyl group, a fluoranthenyl group, a triphenylenyl group, a pyrenyl group, a chrysenyl group, a naphthacenyl group, a picenyl group, a perylenyl group, a pentaphenyl group, a hexacenyl group, a pyrrolyl group, an imidazolyl group, a
25 pyrazolyl group, a pyridinyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, an isoindolyl group, an indolyl group, an indazolyl group, a purinyl group, a quinolinyl group, an isoquinolinyl group, a benzoquinolinyl group, a phthalazinyl group, a naphthyridinyl group, a quinoxalinyl group, a quinazolinyl group, a cinnolinyl group, a carbazolyl group, a phenanthridinyl group, an acridinyl group, a phenanthrolinyl group, a phenazinyl group, a benzoxazolyl group, a benzoimidazolyl
30 group, a furanyl group, a benzofuranyl group, a thiophenyl group, a benzothiophenyl group, a thiazolyl group, an isothiazolyl group, a benzothiazolyl group, an isoxazolyl group, an oxazolyl group, a triazolyl

group, a tetrazolyl group, an oxadiazolyl group, a triazinyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzocarbazolyl group, a dibenzocarbazolyl group, an imidazopyrimidinyl group and an imidazopyridinyl group, each substituted with at least one selected from a cyclopentyl group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group, a cyclopentenyl group, a cyclohexenyl group, a cycloheptenyl group, a phenyl group, a naphthyl group, an anthracenyl group, a pyrenyl group, a phenanthrenyl group, a fluorenyl group, a carbazolyl group, a benzocarbazolyl group, a dibenzocarbazolyl group, a pyridinyl group, a pyrimidinyl group, a pyrazinyl group, a pyridazinyl group, a triazinyl group, a quinolinyl group, an isoquinolinyl group, a phthalazinyl group, a quinoxalinyl group, a cinnolinyl group, and a quinazolinyl group; and

10 a phenyl group, a pentalenyl group, an indenyl group, a naphthyl group, an azulenyl group, a heptalenyl group, an indacenyl group, an acenaphthyl group, a fluorenyl group, a spiro-fluorenyl group, a phenalenyl group, a phenanthrenyl group, an anthracenyl group, a fluoranthenyl group, a triphenylenyl group, a pyrenyl group, a chrysenyl group, a naphthacenyl group, a picenyl group, a perylenyl group, a pentaphenyl group, a hexacenyl group, a pyrrolyl group, an imidazolyl group, a pyrazolyl group, a pyridinyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, an

15 isoindolyl group, an indolyl group, an indazolyl group, a purinyl group, a quinolinyl group, an isoquinolinyl group, a benzoquinolinyl group, a phthalazinyl group, a naphthyridinyl group, a quinoxalinyl group, a quinazolinyl group, a cinnolinyl group, a carbazolyl group, a phenanthridinyl group, an acridinyl group, a phenanthrolinyl group, a phenazinyl group, a benzoxazolyl group, a benzoimidazolyl

20 group, a furanyl group, a benzofuranyl group, a thiophenyl group, a benzothiophenyl group, a thiazolyl group, an isothiazolyl group, a benzothiazolyl group, an isoxazolyl group, an oxazolyl group, a triazolyl group, a tetrazolyl group, an oxadiazolyl group, a triazinyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzocarbazolyl group, a dibenzocarbazolyl group, an imidazopyrimidinyl group, and an imidazopyridinyl group, each substituted with at least one selected from a cyclopentyl

25 group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group, a cyclopentenyl group, a cyclohexenyl group, a cycloheptenyl group, a phenyl group, a naphthyl group, an anthracenyl group, a pyrenyl group, a phenanthrenyl group, a fluorenyl group, a carbazolyl group, a benzocarbazolyl group, a dibenzocarbazolyl group, a pyridinyl group, a pyrimidinyl group, a pyrazinyl group, a pyridazinyl group, a triazinyl group, a quinolinyl group, an isoquinolinyl group, a phthalazinyl group, a quinoxalinyl group, a cinnolinyl group, and a quinazolinyl group, each substituted with at least one selected from deuterium, -

30 F, -Cl, -Br, -I, a hydroxyl group, a cyano group, a nitro group, an amino group, an amidino group, a

hydrazine group, a hydrazone group, a carboxylic acid group or a salt thereof, a sulfonic acid group or a salt thereof, a phosphoric acid group or a salt thereof, a C1-C10 alkyl group, a C2-C10 alkenyl group, a C2-C10 alkynyl group, and C1-C10 alkoxy group, a C3-C10 cycloalkyl group, a C1-C10 heterocycloalkyl group, a C3-C10 cycloalkenyl group, a C1-C10 heterocycloalkenyl group, a C6-C20 aryl group, a C6-C20 aryloxy group, a C6-C20 arylthio group, and a C1-C20 heteroaryl group.

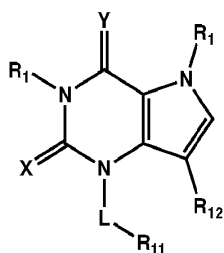
When a group containing a specified number of carbon atoms is substituted with any of the groups listed in the preceding paragraph, the number of carbon atoms in the resulting "substituted" group is defined as the sum of the carbon atoms contained in the original (unsubstituted) group and the carbon atoms (if any) contained in the substituent. For example, when the term "substituted C1-C20 alkyl" refers to a C1-C20 alkyl group substituted with C6-C20 aryl group, the total number of carbon atoms in the resulting aryl substituted alkyl group is C7-C40.

The starting materials useful for making the compounds and pharmaceutical compositions of the present invention are readily commercially available or can be prepared by those skilled in the art.

The subject compounds are useful as prodrugs in a method of inhibiting MPO in a patient, such as mammal in need of such inhibition, wherein the method comprises the administration of an effective amount of the compound. Embodiments of the present invention are directed to the use of the compounds disclosed herein as prodrugs of MPO inhibitors. In addition to primate, especially humans, a variety of other mammals can be treated according to the method of the present invention.

An embodiment of the present invention provides a compound having General Formula (1):

General Formula (1)



In General Formula (1), at least one of X and Y may represent S, and the other may represent O or S. L may represent a direct bond or C1 to C7 alkylene group, wherein the C1 to C7 alkylene group may optionally incorporate a heteroatom selected from O, S(O)_n (wherein n represents an integer 0, 1, or 2), and NR¹⁶. The C1 to C7 alkylene group may optionally incorporate one or two carbon-carbon double bonds, and the C1 to C7 alkylene group may be optionally substituted with one or more substituents selected independently from OH, a halogen, CN and NR¹⁴R¹⁵, a C1 to C6 alkyl group and a

C1 to C6 alkoxy group, wherein the C1 to C6 alkoxy group optionally incorporates a carbonyl group adjacent to the oxygen.

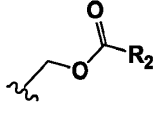
In some embodiments, R^{11} may be hydrogen. In other embodiments, R^{11} may be a saturated or partially unsaturated 3 to 7 membered ring optionally incorporating one or two heteroatoms selected independently from O, N, and S, and optionally incorporating a carbonyl group. The ring may be optionally substituted with one or more substituents independently selected from a halogen, SO_2R^9 , $SO_2NR^9R^{10}$, OH, a C1 to C7 alkyl group, a C1 to C7 alkoxy group, CN, $CONR^{22}R^{23}$, $NR^{22}COR^{23}$ and COR^{23} , wherein the C1 to C7 alkoxy group may be further substituted with a C1 to C6 alkoxy group and may optionally incorporate a carbonyl group adjacent to the oxygen. The C1 to C7 alkyl group may be further substituted with hydroxy or a C1 to C6 alkoxy group, and the C1 to C7 alkyl group or the C1 to C6 alkoxy group may optionally incorporate a carbonyl group adjacent to the oxygen or at any position in the C1 to C7 alkyl group.

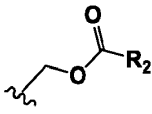
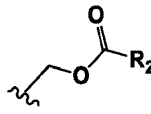
In some other embodiments, R^{11} may be an aromatic ring system selected from phenyl, biphenyl, naphthyl or a monocyclic or bicyclic heteroaromatic ring structure containing 1 to 3 heteroatoms independently selected from O, N, and S. The aromatic ring system may be optionally substituted with one or more substituents independently selected from a halogen, SO_2R^9 , $SO_2NR^9R^{10}$, OH, a C1 to C7 alkyl group, a C1 to C7 alkoxy group, CN, $CONR^{22}R^{23}$, $NR^{22}COR^{23}$ and COR^{23} , wherein the C1 to C7 alkoxy group may optionally be further substituted with a C1 to C6 alkoxy group, and the C1 to C6 alkoxy group may optionally incorporate a carbonyl group adjacent to the oxygen. The C1 to C7 alkyl group may be further substituted with hydroxy or a C1 to C6 alkoxy group, and the C1 to C7 alkyl group and the C1 to C6 alkoxy group may optionally incorporate a carbonyl group adjacent to the oxygen or at any position in the alkyl group.

R^{12} may represent hydrogen, a halogen, or a carbon optionally substituted with one to three halogen atoms.

At each occurrence, R^9 , R^{10} , R^{14} , R^{15} , R^{16} , R^{22} , and R^{23} may independently represent hydrogen, a C1 to C6 alkyl group or a C1 to C6 alkoxy group, wherein the alkoxy group may optionally incorporate a carbonyl group adjacent to the oxygen. The C1 to C6 alkyl group may be further substituted with a halogen, a C1 to C6 alkoxy group, CHO, a C2 to C6 alkanoyl group, OH, $CONR^7R^8$, and NR^7COR^8 . In some embodiments, the groups NR^9R^{10} , $NR^{14}R^{15}$, and $NR^{22}R^{23}$ may each independently represent a 5 to 7 membered saturated azacyclic ring optionally incorporating one additional heteroatom selected from O, S and NR¹¹, wherein the azacyclic ring may be optionally substituted with a halogen, a C1 to C6 alkoxy

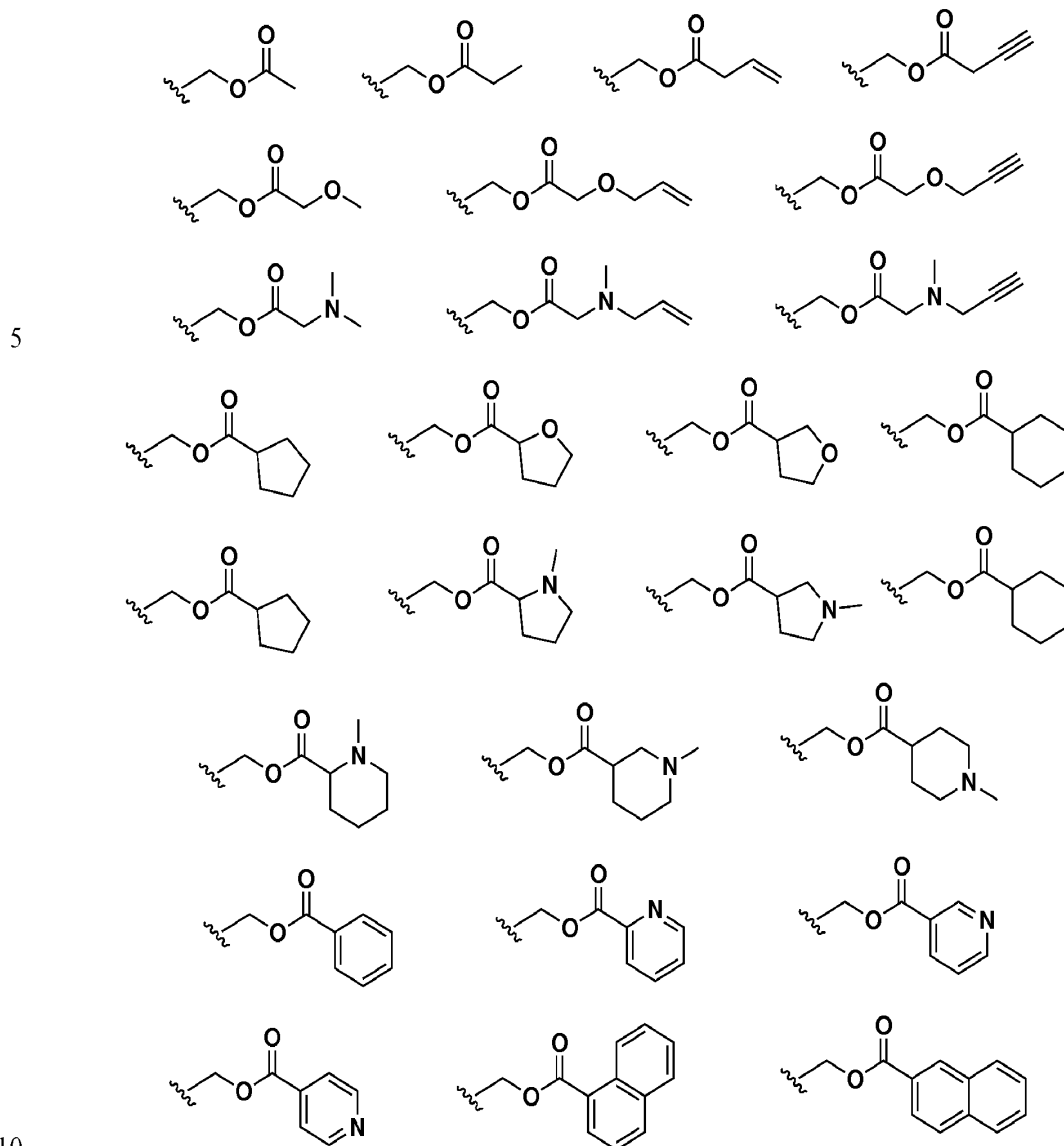
group, CHO, a C2 to C6 alkanoyl group, OH, CONR^7R^8 and NR^7COR^8 . At each occurrence, R^7 , R^8 and R^{11} may independently represent hydrogen or a C1 to C6 alkyl group, or the group NR^7R^8 may represent a 5- to 7-membered saturated azacyclic ring may optionally incorporate one additional heteroatom selected from O, S, and NR^{11} .

5 In some embodiments, each R_1 may independently be H or , provided that at

least one R_1 is . When each R_1 is , R_2 may be optionally connected to form a ring.

R_2 may be $-\text{C}(\text{R}_3)_2\text{R}_4$, $-\text{NR}_3\text{R}_4$, or $-\text{OR}_4$. R_3 may independently be hydrogen or a C1-C10 alkyl group. When each R_3 is a C1-C10 alkyl group, R_3 may be optionally connected with a single bond to form a ring. R_4 may be a substituted or unsubstituted C1-C20 alkyl group, a substituted or unsubstituted C2-C20 alkenyl group, a substituted or unsubstituted C2-C20 alkynyl group, a substituted or unsubstituted C1-C20 heteroalkyl group, a substituted or unsubstituted C2-C20 heteroalkenyl group, a substituted or unsubstituted C2-C20 heteroalkynyl group, a substituted or unsubstituted C3-C20 cycloalkyl group, a substituted or unsubstituted C3-C20 heterocycloalkyl group, a substituted or unsubstituted C6-C20 aryl group, or a substituted or unsubstituted C1-C20 heteroaryl group. For example, R_4 may be a substituted or unsubstituted C1-C15 alkyl group, a substituted or unsubstituted C2-C15 alkenyl group, a substituted or unsubstituted C2-C15 alkynyl group, a substituted or unsubstituted C1-C15 heteroalkyl group, a substituted or unsubstituted C2-C15 heteroalkenyl group, a substituted or unsubstituted C2-C15 heteroalkynyl group, a substituted or unsubstituted C3-C15 cycloalkyl group, a substituted or unsubstituted C3-C15 heterocycloalkyl group, a substituted or unsubstituted C6-C15 aryl group, or a substituted or unsubstituted C1-C15 heteroaryl group. In another example, R_4 may be a substituted or unsubstituted C1-C10 alkyl group, a substituted or unsubstituted C2-C10 alkenyl group, a substituted or unsubstituted C2-C10 alkynyl group, a substituted or unsubstituted C1-C10 heteroalkyl group, a substituted or unsubstituted C2-C10 heteroalkenyl group, a substituted or unsubstituted C2-C10 heteroalkynyl group, a substituted or unsubstituted C3-C10 cycloalkyl group, a substituted or unsubstituted C3-C10 heterocycloalkyl group, a substituted or unsubstituted C6-C10 aryl group, or a substituted or unsubstituted C1-C10 heteroaryl group.

In formula -[C(R₃)₂]_nR₄, n may be 0 or 1. When n is 0, moiety [C(R₃)₂] is absent, and R₂ may be the same as R₄ described above. When n is 0, examples of R₁ groups may include:



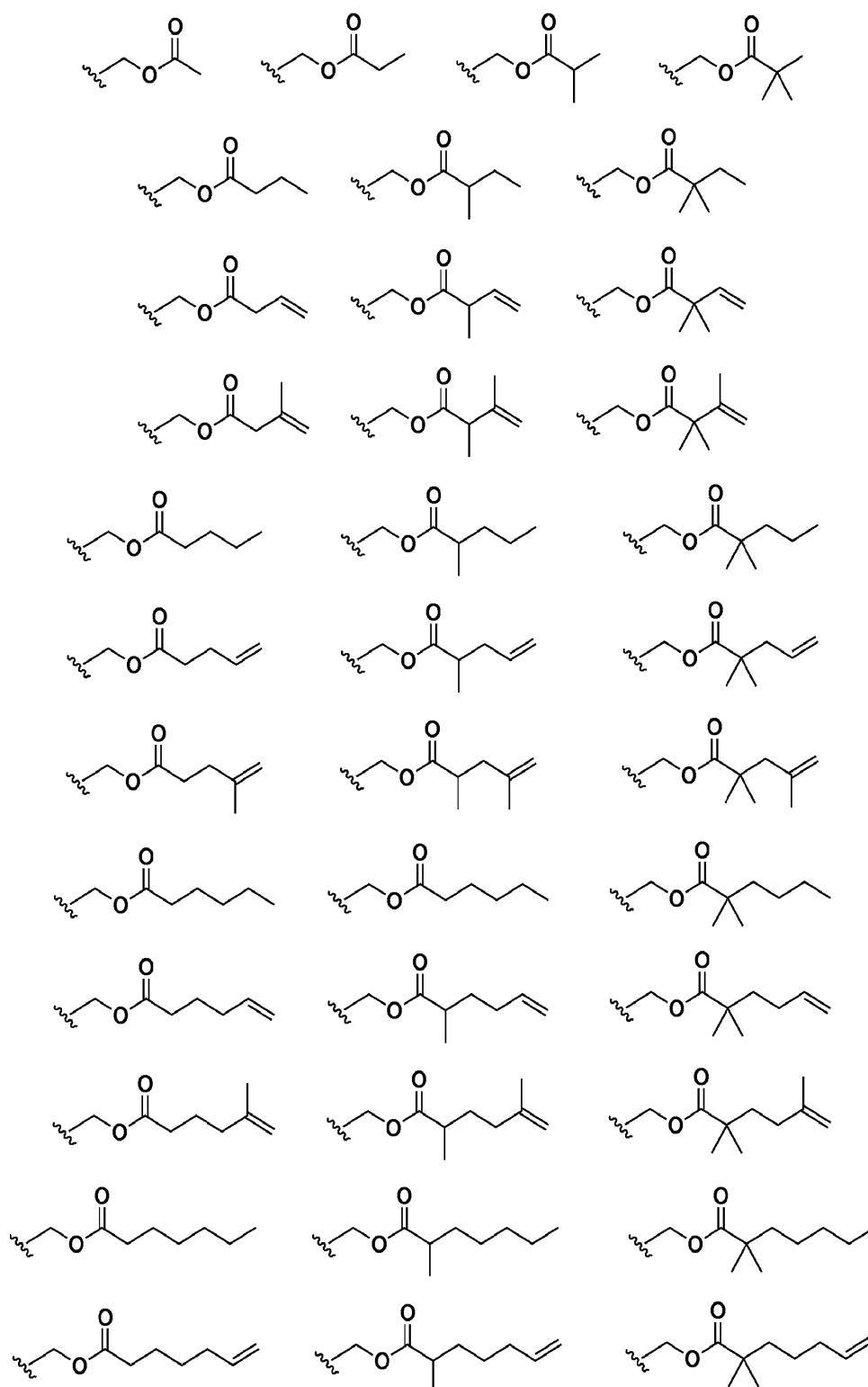
Each of the above groups may be substituted or unsubstituted.

When n in formula $-\text{C}(\text{R}_3)_2\text{R}_4$ is 1, moiety $[\text{C}(\text{R}_3)_2]$ is present. In some embodiments, each R_3 in moiety $[\text{C}(\text{R}_3)_2]$ may be hydrogen. In other embodiments, one R_3 may be hydrogen and the other R_3 may be a C1-C10 alkyl group. In some other embodiments, each R_3 may be a C1-C10 alkyl group.

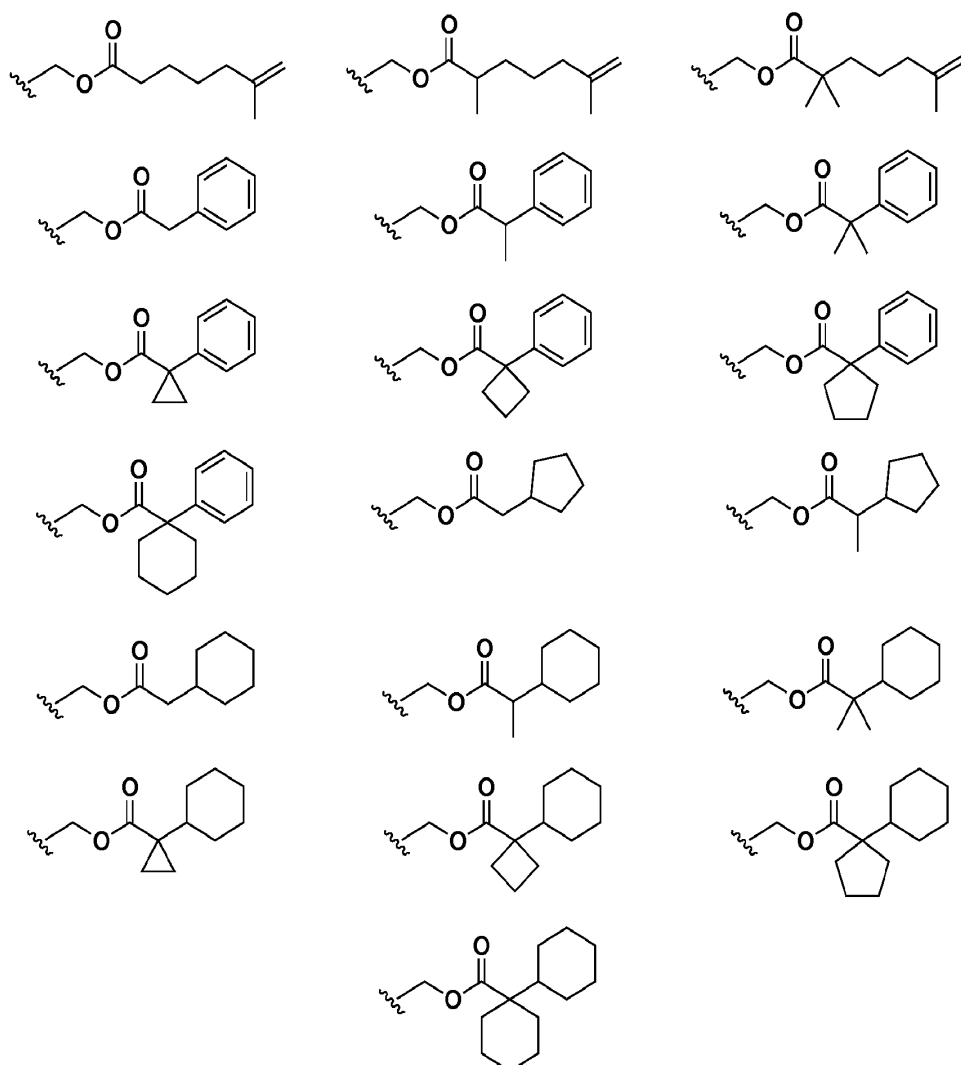
When n is 1, examples of R_1 groups may include:

5

10

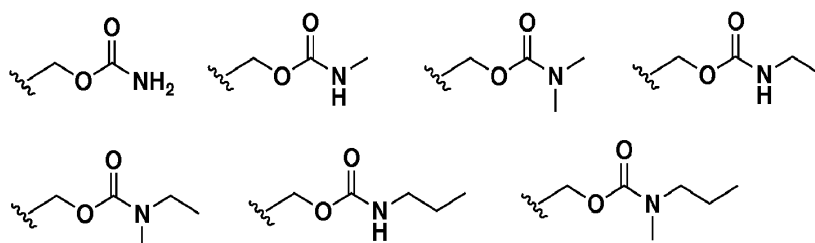


5

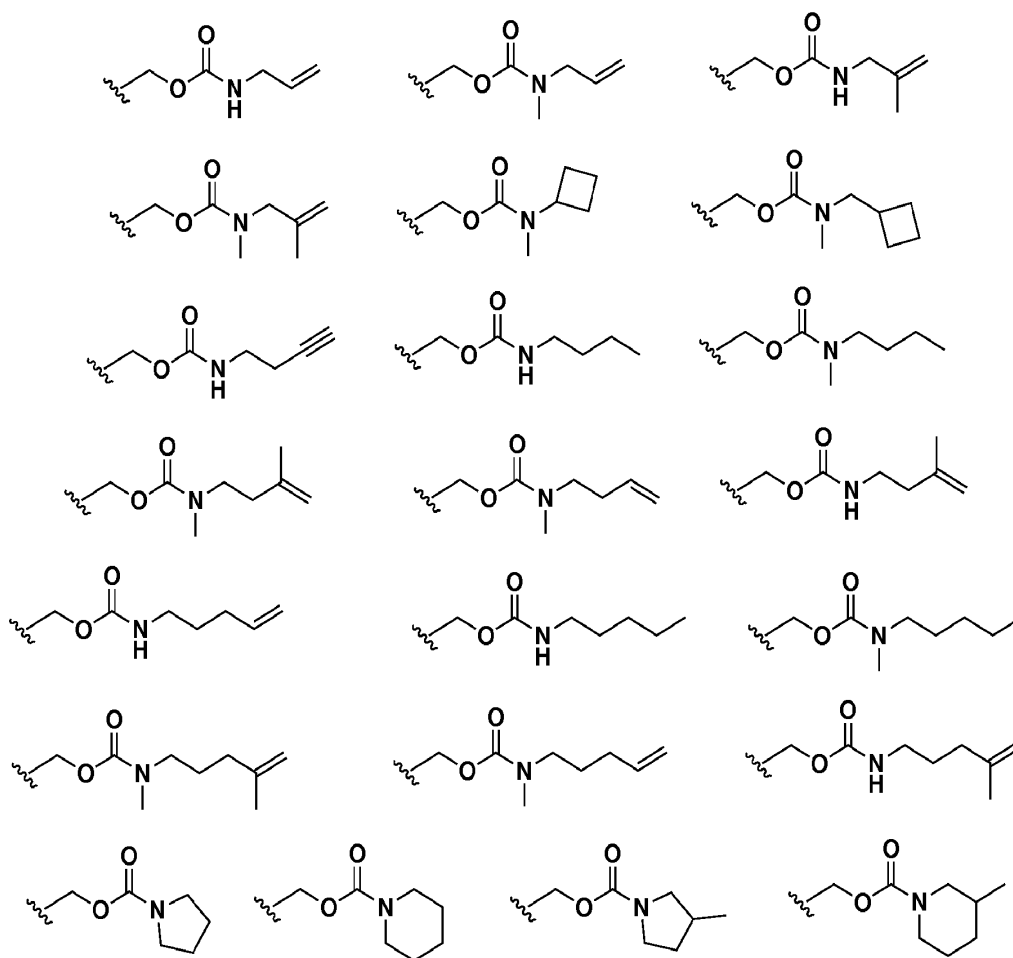


Each of the above groups may be substituted or unsubstituted.

10 In General Formula (1), R_2 may be $-NR_3R_4$, wherein R_3 and R_4 may be the same as described above. In an embodiment, R_3 and R_4 may be individual substituents. In another embodiment, R_3 and R_4 may be connected to form a ring. When R_2 is $-NR_3R_4$, examples of R_1 groups may include:



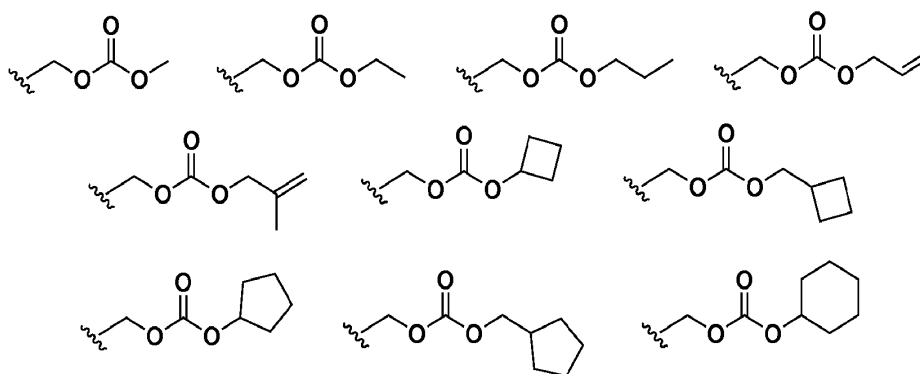
5

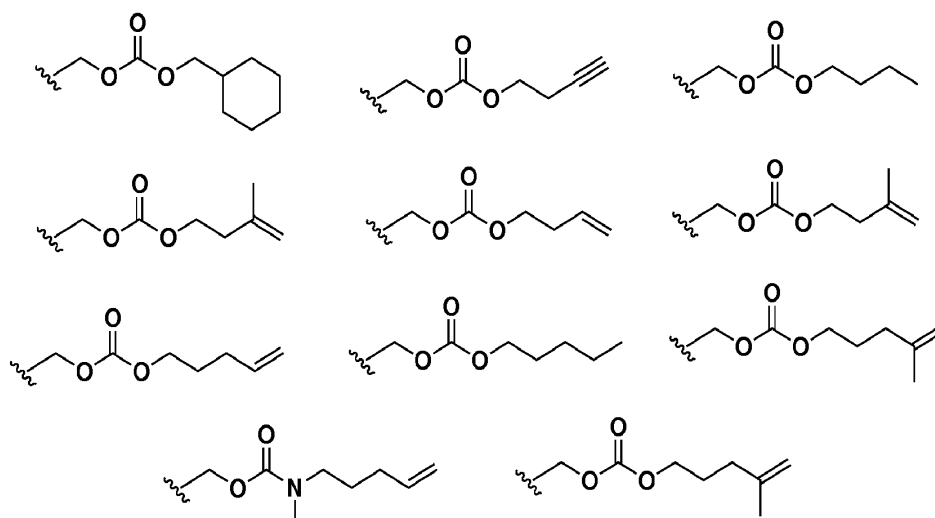


Each of the above groups may be substituted or unsubstituted.

In General Formula (1), R_2 may be $-OR_4$, wherein R_4 may be the same as described above. When

10 R_2 is $-OR_4$, examples of R_4 groups may include:



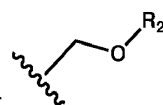


5 Each of the above groups may be substituted or unsubstituted.

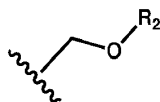
In an embodiment, R_4 may be substituted with a natural amino acid that is linked to R_4 through an oxygen atom of a carboxylic acid group. The natural amino acid may be glycine, alanine, valine, leucine, isoleucine, serine, threonine, cysteine, cystine, methionine, aspartic acid, glutamic acid, asparagine, glutamine, lysine, hydroxylysine, arginine, histidine, phenylalanine, tyrosine, tryptophan, proline, or hydroxyproline. The natural amino acid may be attached at the terminal or internal carbon atom of the R_4 group.

In General Formula 1, R_1 may be $-\text{CH}_2\text{OP}(=\text{O})(\text{OR}^b)_2$, $-\text{CH}_2\text{OP}(=\text{O})(\text{OR}^b)\text{R}^a$, $-\text{CH}_2\text{OP}(=\text{O})\text{R}^a\text{R}^b$, or $-\text{CH}_2\text{OP}(=\text{O})(\text{OR}^b)-\text{OP}(=\text{O})(\text{OR}^b)_2$. In these formulae, R^a and R^b may be independently selected from hydrogen, a substituted or unsubstituted C1-C20 alkyl group, a substituted or unsubstituted C3-C20 cycloalkyl group, a substituted or unsubstituted C6-C20 aryl group, a substituted or unsubstituted C1-C20 heteroaryl group. In an embodiment, R_1 may be $-\text{CH}_2\text{OP}(=\text{O})(\text{OH})_2$.

In some other embodiments, R_1 may independently be H or



provided that at



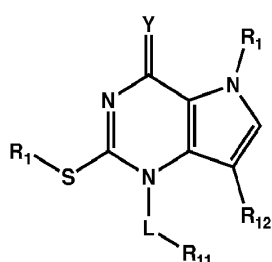
least one R_1 is . R_2 may be AA_{1-3} , $\text{C}(=\text{O})(\text{CH}_2)_n\text{X}_1\text{AA}_{1-3}$, or $\text{C}(=\text{O})\text{AA}$. AA_{1-3} may be a moiety consisting of 1 to 3 natural amino acids linked through a peptide bond. The natural amino acids may be the same as those described in connection with group R_4 above. n may be an integer of 1 to 5. X_1 may be S, O, or NH. R_3 and R_4 may each independently be H, a substituted or unsubstituted C1-C10 alkyl

group, a substituted or unsubstituted C2-C10 alkenyl group, a substituted or unsubstituted C2-C10 alkynyl group, a substituted or unsubstituted C1-C10 heteroalkyl group, a substituted or unsubstituted C2-C10 heteroalkenyl group, or a substituted or unsubstituted C2-C10 heteroalkynyl group. AA may be a natural amino acid linked through a peptide bond.

5 General Formula (1) may include pharmaceutically acceptable salts of the compound, solvates of the compound, or solvates of salts of the compound.

Another embodiment of the present invention provides a compound having General Formula (2):

General Formula (2)



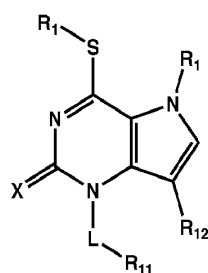
10

In General Formula (2), Y, L, R₁, R₁₁, and R₁₂ may be the same as that described above in connection with General Formula (1).

Another embodiment of the present invention provides a compound having General Formula (3):

15

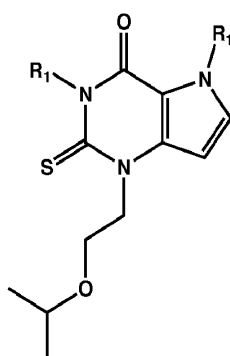
General Formula (3)



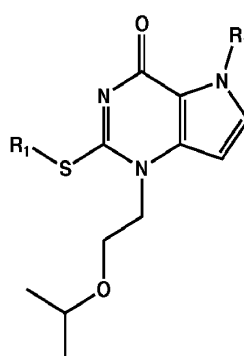
In General Formula (3), X, L, R₁, R₁₁, and R₁₂ may be the same as that described above in connection with General Formula (1).

20 The number of R₁ substituents in General Formulae (1), (2), and (3) can be determined by one skilled in the art, *e.g.*, the desired degree of bioavailability. One or two R₁ groups may be present in the compound. If two R₁ groups are present, the R₁ groups may be the same or different.

In an embodiment, the compound may be represented by Formula (I) or Formula (II):

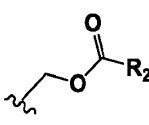


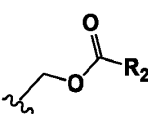
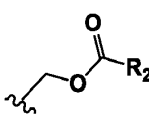
(I)

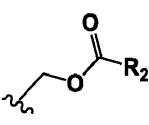


(II)

In Formulae (I) and (II),

each R_1 may independently be H or , provided that at least one R_1 is

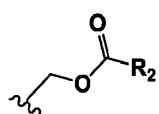
5 . Thus, Formulae (I) and (II) require the presence of at least one group .

In Formulae (I) and (II), each R_1 may be .

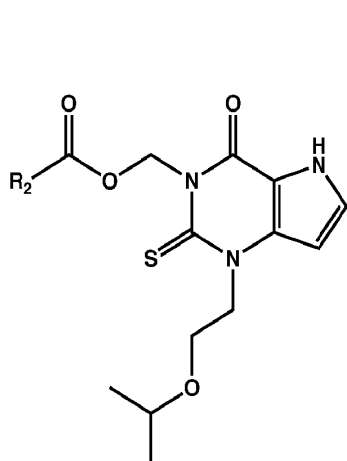
In Formulae (I) and (II), R_2 may be the same as that described in connection with General Formula (1) above.

In formula $-[C(R_3)_2]_nR_4$, at least one R_3 may not be hydrogen, or each R_3 may not be hydrogen.

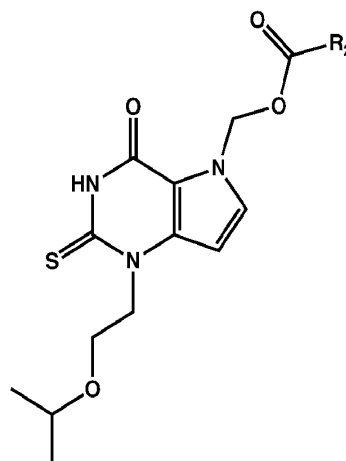
- 10 For example, at least one R_3 may be a methyl group or each R_3 may be a methyl group. In these embodiments, R_2 may independently be $-C(H)(CH_3)R_4$ or $-C(CH_3)_2R_4$, wherein R_4 may be the same as that described above. In an embodiment, R_4 may each independently be a substituted or unsubstituted C1-C15 alkyl group, a substituted or unsubstituted C2-C15 alkenyl group, a substituted or unsubstituted C2-C15 alkynyl group, a substituted or unsubstituted C1-C15 heteroalkyl group, a substituted or
- 15 unsubstituted C2-C15 heteroalkenyl group, a substituted or unsubstituted C2-C15 heteroalkynyl group, or a substituted or unsubstituted C6-C20 aryl group. In another embodiment, R_4 may each independently be a substituted or unsubstituted C1-C10 alkyl group, a substituted or unsubstituted C2-C10 alkenyl group, a substituted or unsubstituted C2-C10 alkynyl group, a substituted or unsubstituted C1-C10 heteroalkyl group, a substituted or unsubstituted C2-C10 heteroalkenyl group, a substituted or
- 20 unsubstituted C2-C10 heteroalkynyl group, or a substituted or unsubstituted C6-C20 aryl group.

In Formulae (I) and (II), when each R_1 is , R_2 may be connected to form a ring.

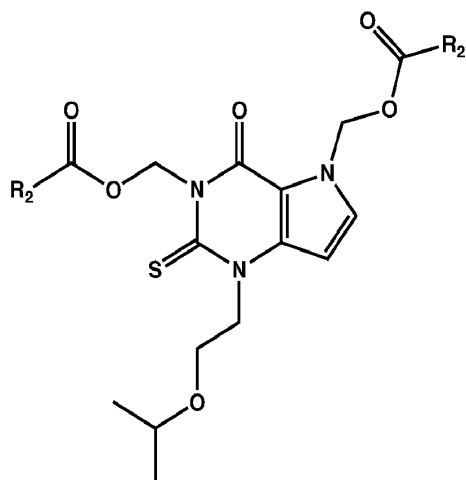
When the compound has Formula (I), the compound may be represented by one of Formulae (Ia), (Ib), and (Ic):



(Ia)



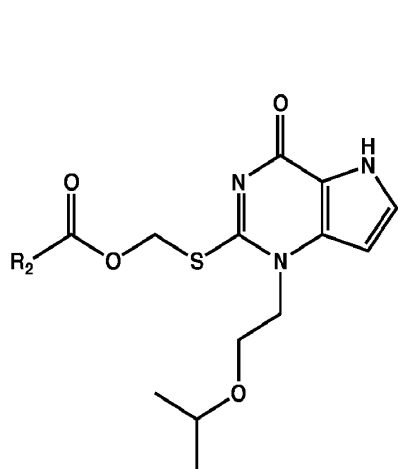
(Ib)



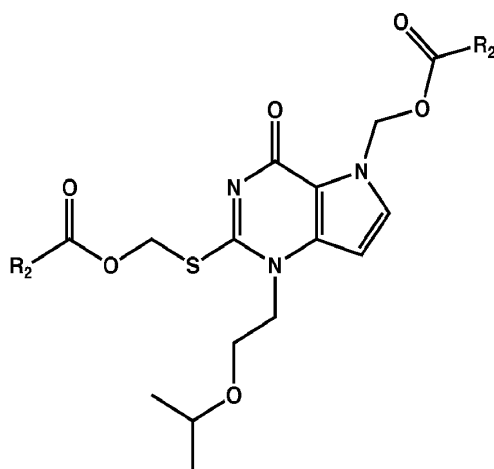
(Ic)

In Formulae (Ia), (Ib), and (Ic), groups R_2 may be the same as those described in connection with Formula (I).

When the compound has Formula (II), the compound may be represented by one of Formulae (IIa) and (IIb):



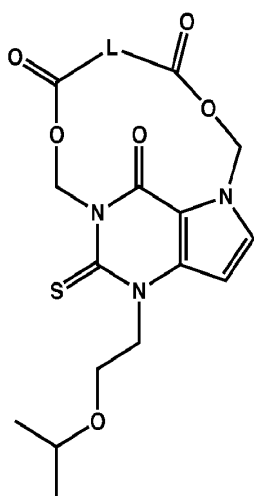
(IIa)



(IIb)

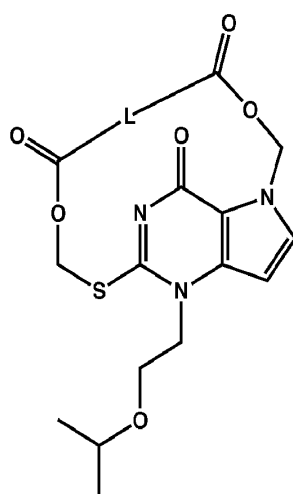
In Formulae (IIa) and (IIb), groups R₂ may be the same as those described in connection with Formula (II).

- 5 When the compound is represented by Formula (Ic), groups R₂ may be connected with a single bond to form a linking group L, as in Formula (Id):



(Id)

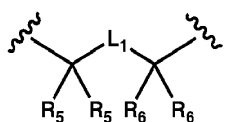
- 10 When the compound is represented by Formula (IIb), groups R₂ may be connected with a single bond to form a linking group L, as in Formula (IIc):



(IIc)

In the Formulae (Ic) and (IIb), the linking group L may be a substituted or unsubstituted C1-C10 alkylene group, a substituted or unsubstituted C2-C10 alkenylene group, a substituted or unsubstituted C2-C10 alkynylene group, a substituted or unsubstituted C1-C10 heteroalkylene group, a substituted or unsubstituted C2-C10 heteroalkenylene group, a substituted or unsubstituted C2-C10 heteroalkynylene group, a substituted or unsubstituted C3-C10 cycloalkylene group, a substituted or unsubstituted C3-C10 heterocycloalkylene group, a substituted or unsubstituted C6-C10 arylene group, or a substituted or unsubstituted C1-C10 heteroarylene group, or any combination thereof.

In the Formulae (Ic) and (IIb), the linking group L may be composed of two groups R_2 and may have the structure $-R_2-R_2-$. For example, the linking group may be represented by Formula (L-1):

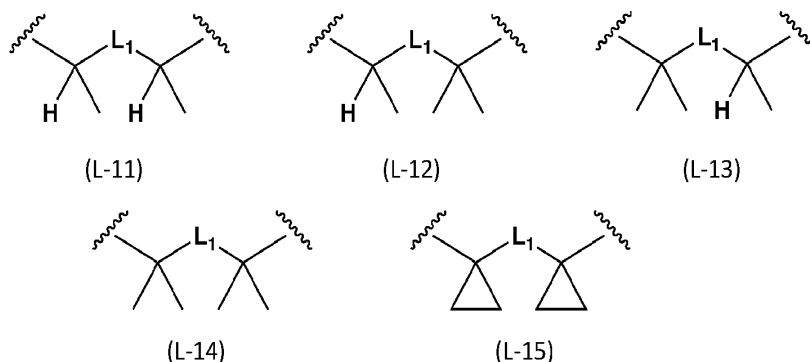


(L-1)

In Formula (L-1), L_1 may be a substituted or unsubstituted C1-C10 alkylene group, a substituted or unsubstituted C2-C10 alkenylene group, a substituted or unsubstituted C2-C10 alkynylene group, a substituted or unsubstituted C1-C10 heteroalkylene group, a substituted or unsubstituted C2-C10 heteroalkenylene group, a substituted or unsubstituted C2-C10 heteroalkynylene group, or a substituted or unsubstituted C6-C20 aryl group. For example, L_1 may be a substituted or unsubstituted C1-C10 alkylene group or a substituted or unsubstituted C2-C10 alkenylene group. R_5 and R_6 may each

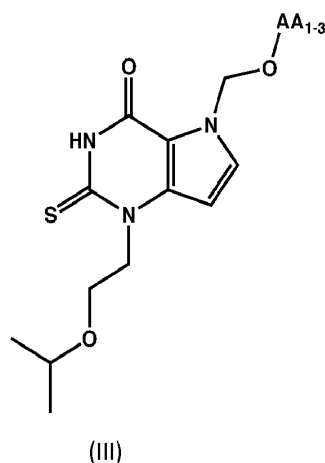
independently be hydrogen or a C1-C10 alkyl group, for example, a C1-C5 alkyl group, or a C1-C3 alkyl group.

In Formula (L-1), at least one R_5 may not hydrogen and at least one R_6 may not hydrogen. For example, at least one R_5 may be a methyl group and at least one R_6 may be a methyl group. Two geminal groups R_5 may be optionally connected with a single bond to form a ring. Also, two geminal groups R_6 may be optionally connected with a single bond to form a ring. In some embodiments, the linking group L may have one of Formulae (L-11), (L-12), (L-13), (L-14), and (L-15):



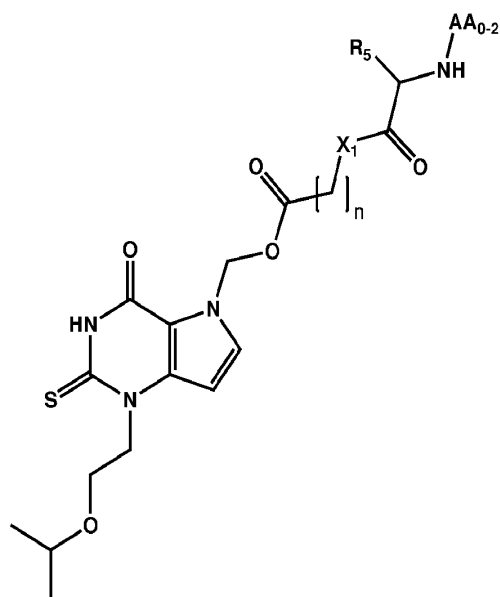
In Formulae (L-11) to (L-15) above, L_1 may be the same as that described in connection with Formula (L-1).

In an embodiment, the compound may be represented by Formula (III):



In Formula (III), AA_{1-3} may be a moiety consisting of 1 to 3 natural amino acids linked through a peptide bond.

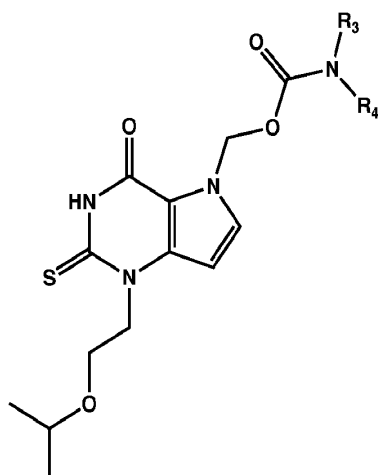
In another embodiment, the compound may be represented by Formula (IV):



(IV)

In Formula (IV), X_1 may be S, O, or NH, R_5 may be H or a side-chain group present in a natural amino acid, AA_{0-2} may be H or a moiety consisting of 1 or 2 natural amino acids, which may be the same or different, that are linked through a peptide bond. n may be an integer of 1 to 5. The moiety AA_{0-2} may include any combination of the natural amino acids.

In still another embodiment, the compound may be represented by Formula (V):

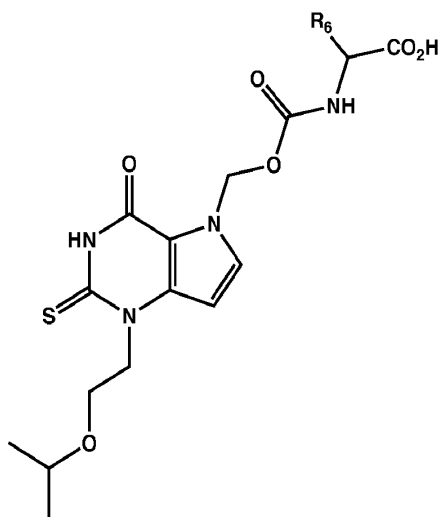


(V)

In Formula (V), R_3 and R_4 are each independently H, a substituted or unsubstituted C1-C10 alkyl group, a substituted or unsubstituted C2-C10 alkenyl group, a substituted or unsubstituted C2-C10

alkynyl group, a substituted or unsubstituted C1-C10 heteroalkyl group, a substituted or unsubstituted C2-C10 heteroalkenyl group, or a substituted or unsubstituted C2-C10 heteroalkynyl group.

In still another embodiment, the compound may be represented by Formula (VI):

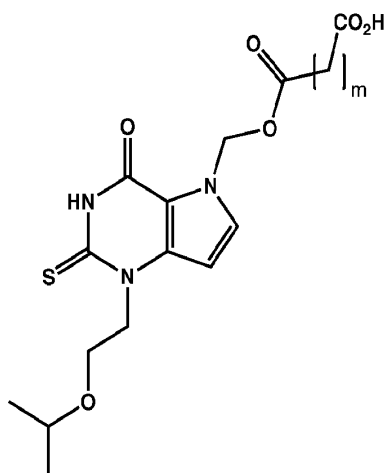


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(VI)

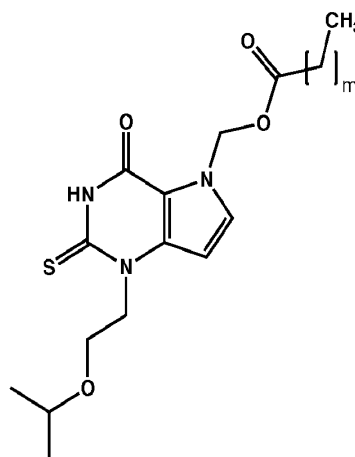
In Formula (VI), R_6 may be H or a side-chain group present in a natural amino acid. The compound may be an ester of the carboxylic acid represented by Formula (VI).

In still another embodiment, the compound may be represented by Formulae (VII), (VIII), (IX), or (X):

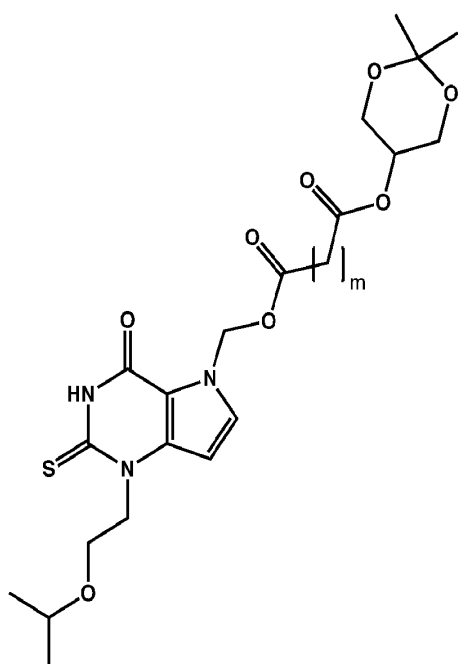


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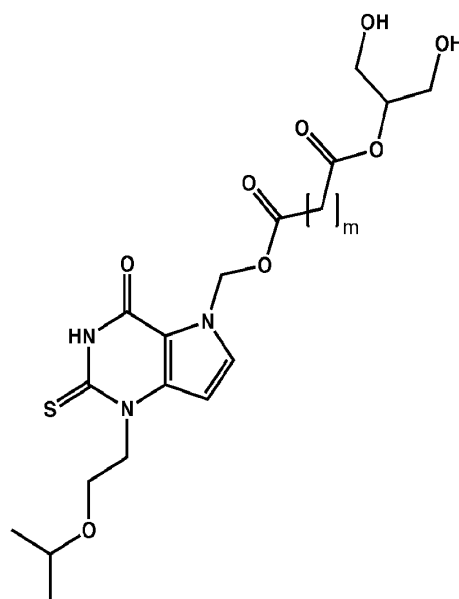
(VII)



(VIII)



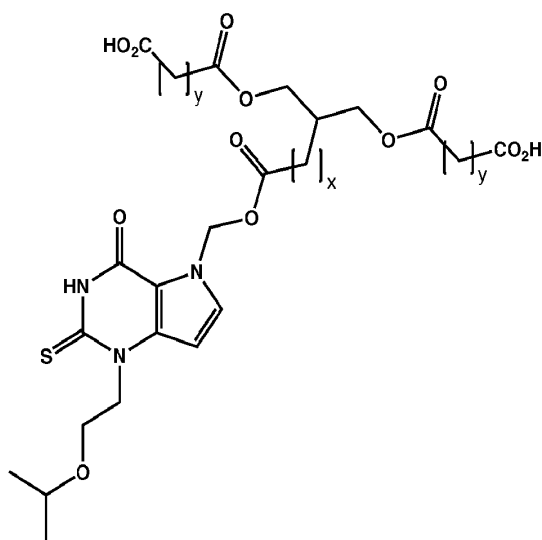
(IX)



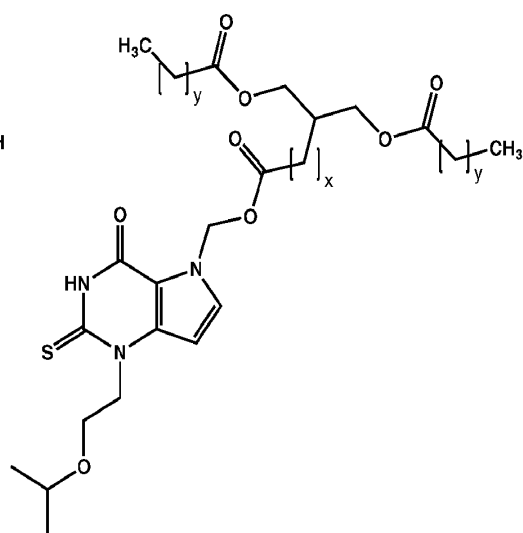
(X)

In Formulae (VII), (VIII), (IX), or (X), n may be an integer of 1 to 25. The compound may be an ester of the carboxylic acid represented by Formula (VII).

5 In still another embodiment, the compound may be represented by Formulae (XI) or (XII):



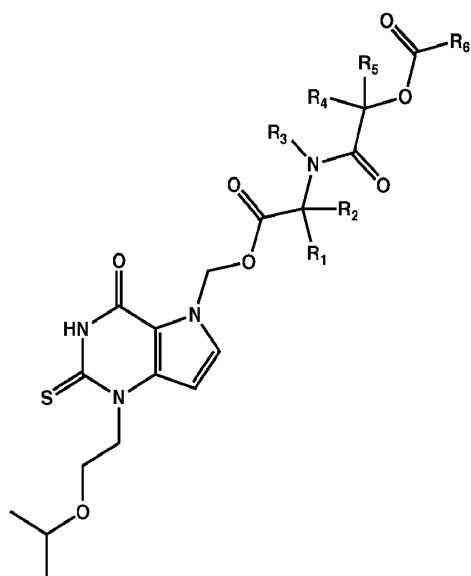
(XI)



(XII)

In Formulae (XI) and (XII), x and each y may independently be an integer of 1 to 25. The compound may be a mono- or di-ester of the carboxylic acid represented by Formula (XI).

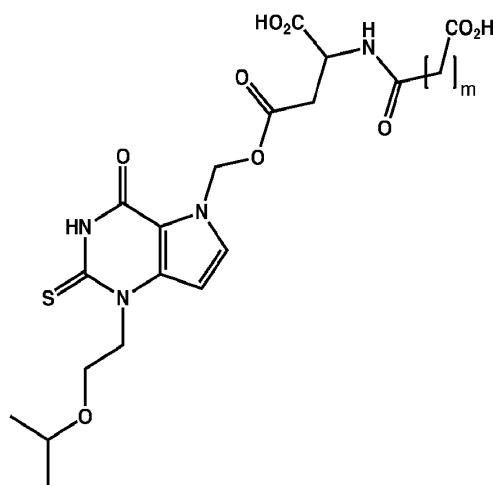
In still another embodiment, the compound may be represented by Formula (XIII):



(XIII)

In Formula (XIII), R_1 to R_5 may each independently be hydrogen or C1-C10 alkyl, and R_6 may be hydrogen, C1-C10 alkyl, or C6-C10 aryl, wherein any of groups R_1 to R_5 may be optionally connected to form a ring.

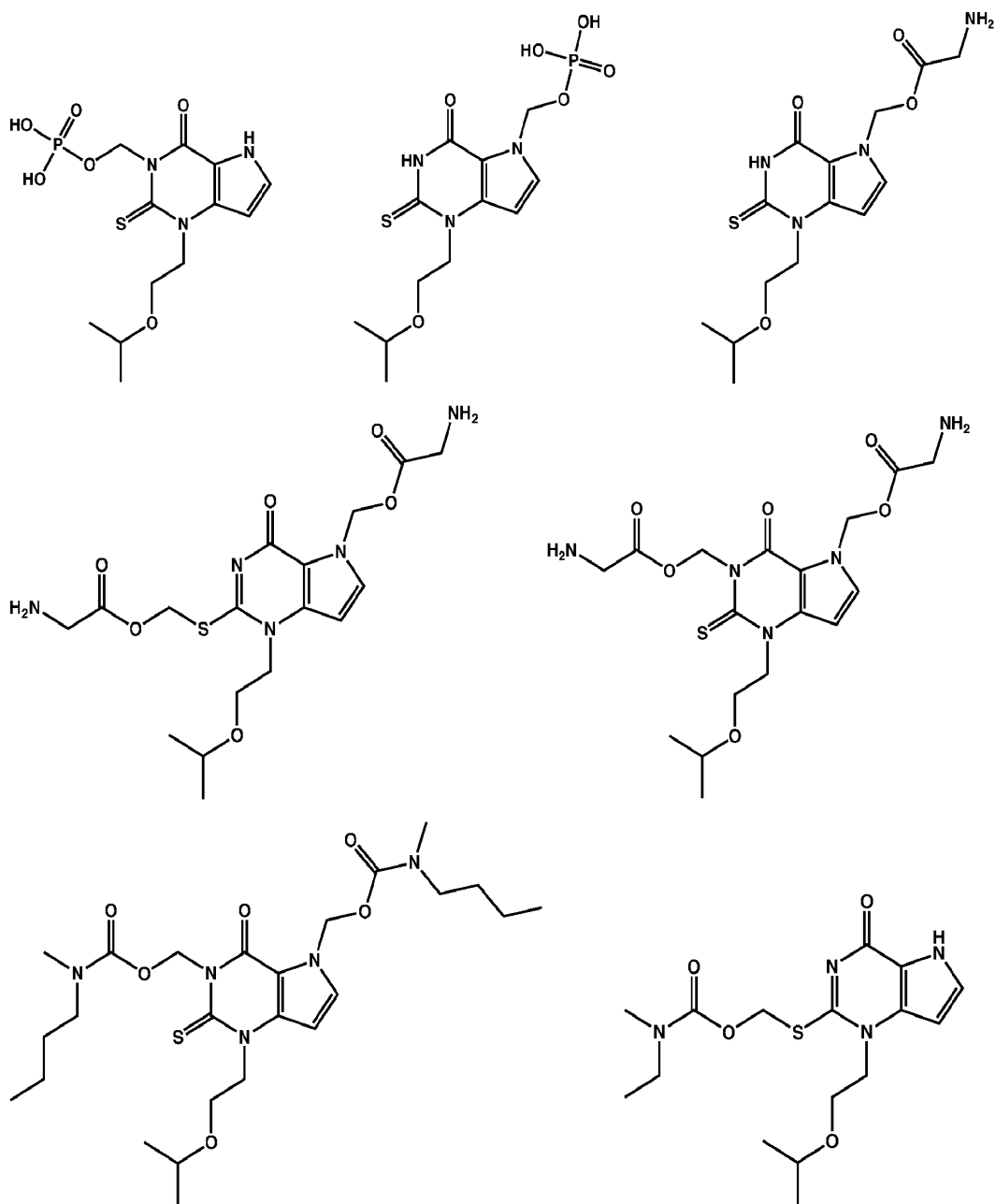
In yet another embodiment, the compound may be represented by Formula (XIV):

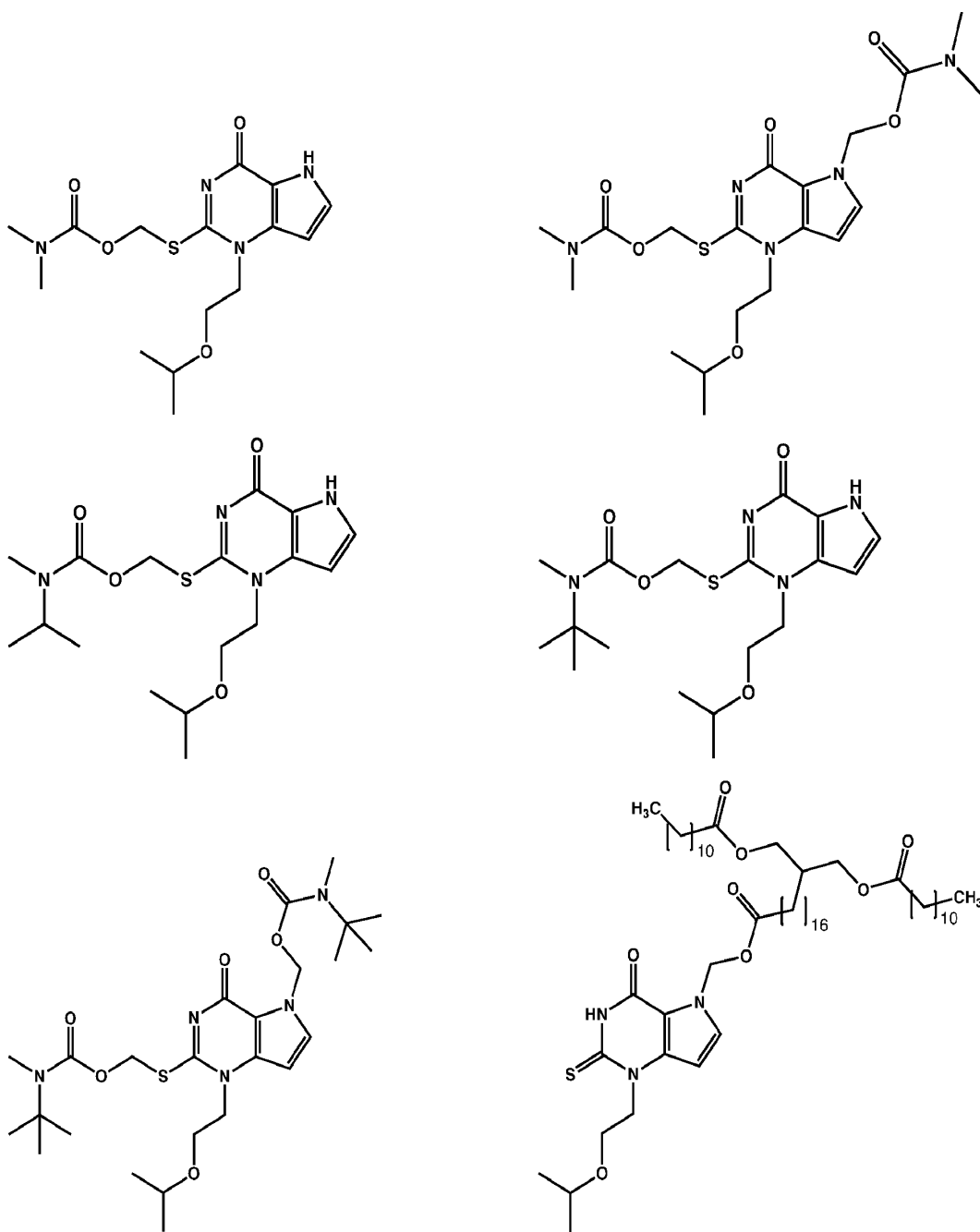


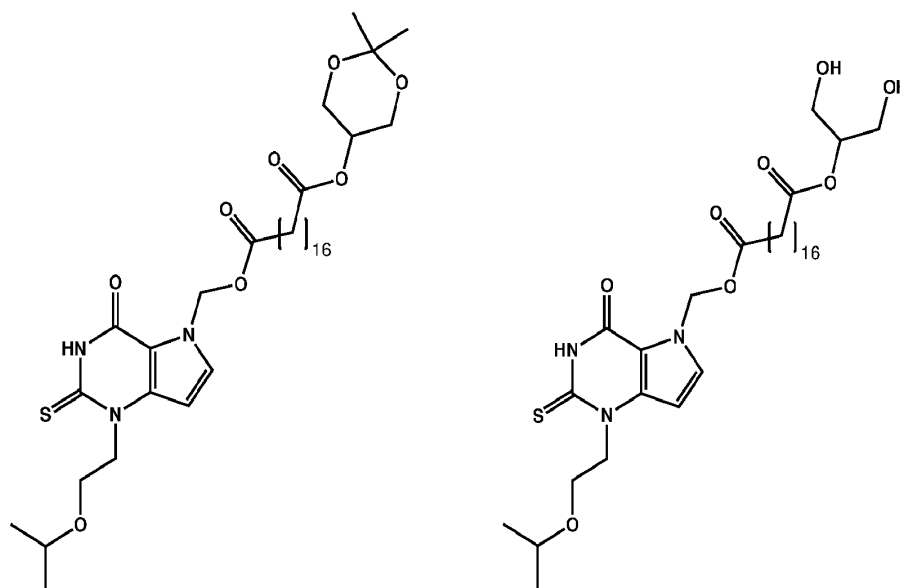
(XIV)

In Formula (XIV), m may be an integer of 1 to 25. The compound may be a mono- or di-ester of the carboxylic acid represented by Formula (XIV).

Non-limiting examples of the compounds according to the present invention may be:





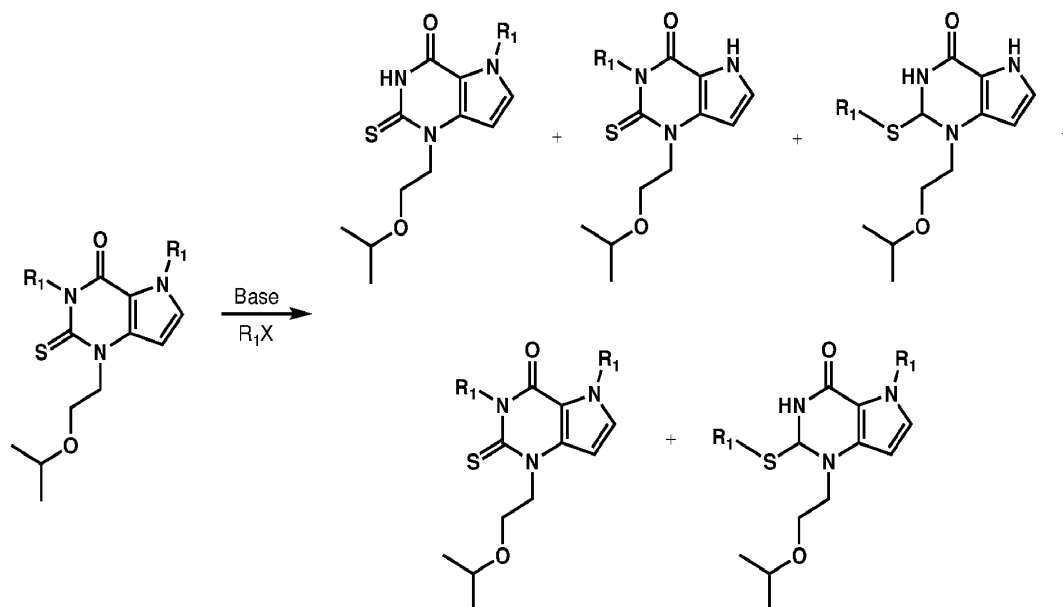


The compounds of the invention may be made in the form of pharmaceutically acceptable salts.

A person of ordinary skill in the art would readily understand how to make compounds of the present invention based on the available synthetic methods. For example, some of the compounds of

5 the invention may be prepared according to Reaction Scheme 1:

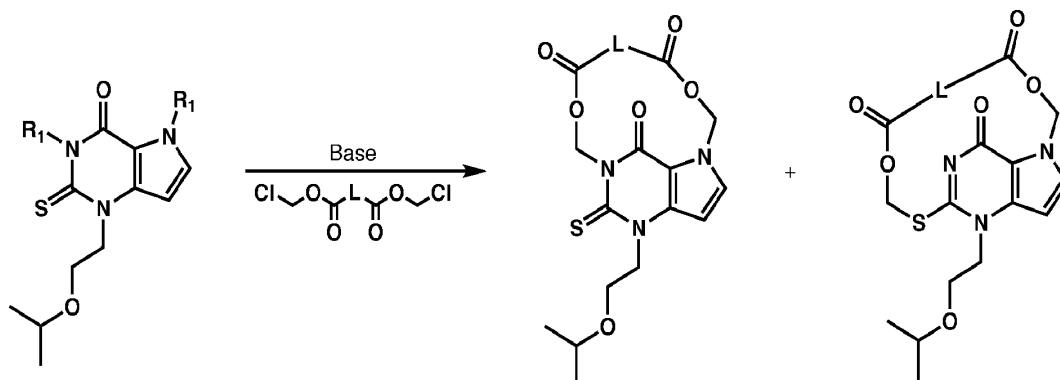
Reaction Scheme 1



In Reaction Scheme 1, "Base" may be lithium hexamethyldisilyl amide or sodium hydride and "R₁X" may be alkyl halide or sulfonyl chloride, wherein R₁ is as described in the present application.

Other compounds of the invention may be prepared according to Reaction Scheme 2:

Reaction Scheme 2



In Reaction Scheme 2, "Base" may be lithium hexamethyldisilyl amide or sodium hydride and L is
 5 as described in the present application.

The present invention is further directed to a pharmaceutical composition comprising a therapeutically effective amount of a compound. The pharmaceutical compositions of the present invention can be prepared in any suitable dosage form, but are typically prepared as tablets, capsules, powders, granules, or solutions.

10 The pharmaceutical compositions of the present invention comprising the compounds of the invention typically also include other pharmaceutically acceptable carriers and/or excipients such as, for example, binders, lubricants, diluents, coatings, disintegrants, barrier layer components, glidants, coloring agents, solubility enhancers, gelling agents, fillers, proteins, co-factors, emulsifiers, solubilizing agents, suspending agents, flavorants, preservatives and mixtures thereof. A skilled artisan in the art
 15 would know what other pharmaceutically acceptable carriers and/or excipients could be included in the formulations according to the invention. The choice of excipients would depend on the characteristics of the compositions and on the nature of other pharmacologically active compounds in the formulation. Appropriate excipients are known to those skilled in the art (see *Handbook of Pharmaceutical Excipients*, fifth edition, 2005 edited by Rowe et al., McGraw Hill) and have been utilized to yield a novel
 20 formulation with unexpected properties.

Examples of pharmaceutically acceptable carriers that may be used in preparing the pharmaceutical compositions of the present invention may include, but are not limited to, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropyl

methyl-cellulose, sodium carboxymethylcellulose, polyvinyl-pyrrolidone (PVP), talc, calcium sulphate, vegetable oils, synthetic oils, polyols, alginic acid, phosphate buffered solutions, emulsifiers, isotonic saline, pyrogen-free water and combinations thereof. If desired, disintegrating agents may be combined as well, and exemplary disintegrating agents may be, but not limited to, cross-linked polyvinyl

5 pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. In an embodiment, the flavoring agent may be selected from mint, peppermint, berries, cherries, menthol and sodium chloride flavoring agents, and combinations thereof. In an embodiment, the sweetener may be selected from sugar, sucralose, aspartame, acesulfame, neotame, and combinations thereof.

Typical routes of administering the pharmaceutical compositions of the invention include,
10 without limitation, oral administration. The compositions may also be administered by parenteral (*e.g.*, intramuscular, intraperitoneal, intravenous, intracerebroventricular, intracisternal injection or infusion, subcutaneous injection, or implant), by inhalation spray, nasal, vaginal, rectal, sublingual, or topical routes of administration and may be formulated, alone or together, in suitable dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers,
15 adjuvants and vehicles appropriate for each route of administration. In addition to the treatment of warm-blooded animals the compounds of the invention are effective for use in humans.

Pharmaceutical compositions according to certain embodiments of the present invention are formulated so as to allow the active ingredients contained therein to be bioavailable upon administration of the composition to a patient. Compositions that will be administered to a subject
20 or patient may take the form of one or more dosage units. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see *Remington: The Science and Practice of Pharmacy*, 20th Edition (Philadelphia College of Pharmacy and Science, 2000).

The present invention is further directed to a method for the manufacture of a medicament for
25 inhibition of MPO activity in humans and animals comprising combining a prodrug compound of the present invention with a pharmaceutical carrier or diluent. In general, the pharmaceutical compositions of the present invention may be manufactured in conventional methods known in the art, for example, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, lyophilizing processes and the like.

30 All methods include the step of bringing the active ingredient (or prodrug thereof) into association with the carrier which constitutes one or more accessory ingredients. In general, the

pharmaceutical compositions are prepared by uniformly and intimately bringing the active ingredient (or prodrug thereof) into association with a liquid carrier or a finely divided solid carrier or both, and then, if necessary, shaping the product into the desired formulation. In the pharmaceutical composition, the active compound (or prodrug thereof) is included in an amount
5 sufficient to produce the desired effect upon the process or condition of diseases. As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts. Such term in relation to pharmaceutical composition, is intended to encompass a product comprising the prodrug of the invention, and the
10 inert ingredient(s) that make up the carrier, as well as any product which results, directly or indirectly, from combination, complexation or aggregation of any two or more ingredients, or from dissociation of one or more ingredients, or from other types of reactions or interactions of one or more of the ingredients. Accordingly, the pharmaceutical compositions of the present invention encompass any composition made by admixing a compound of the present invention and a
15 pharmaceutically acceptable carrier. By "pharmaceutically acceptable" it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

Preferably, the pharmaceutical compositions containing the active ingredient (or prodrug thereof) may be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous
20 or oily suspensions, dispersible powders or granules, emulsions, solutions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and
25 palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients which are suitable for the manufacture of tablets. These excipients may be for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatin or acacia; and
30 lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to delay disintegration and absorption in the

gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate may be employed. They may also be coated by the techniques described in the U.S. Patent 4,256,108 published March 17, 1981; U.S. Patent 4,160,452 published July 10, 1979; and U.S. Patent 4,265,874 published May 5, 1981; to form osmotic therapeutic tablets for control release. Oral tablets may also be formulated for immediate release, such as fast melt tablets or wafers, rapid dissolve tablets or fast dissolve films.

Formulations for oral use may also be presented as hard gelatin capsules wherein the active ingredient (or prodrug thereof) is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient (or prodrug thereof) is mixed with water or an oil medium, for example peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions contain the active materials (or prodrugs thereof) in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethylcellulose, sodium alginate, polyvinyl-pyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents may be a naturally-occurring phosphatide, for example lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n-propyl, p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose or saccharin.

Oily suspensions may be formulated by suspending the active ingredient (or prodrug thereof) in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient (or prodrug thereof) in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional
5 excipients, for example sweetening, flavoring and coloring agents, may also be present.

The pharmaceutical compositions of the invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, for example olive oil or arachis oil, or a mineral oil, for example liquid paraffin or mixtures of these. Suitable emulsifying agents may be naturally-occurring gums, for example gum acacia or gum tragacanth, naturally-occurring phosphatides, for
10 example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening and flavoring agents.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol,
15 propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative and flavoring and coloring agents.

The compounds of the present invention may also be administered in the form of suppositories for rectal administration of the drug. These compositions can be prepared by mixing the drug with a suitable non-irritating excipient which is solid at ordinary temperatures but liquid at
20 the rectal temperature and will therefore melt in the rectum to release the drug. Such materials are cocoa butter and polyethylene glycols.

For topical use, creams, ointments, jellies, solutions or suspensions and the like, containing the compounds of the present invention are used. Similarly, transdermal patches may also be used for topical administration.

25 The pharmaceutical composition and method of the present invention may further include other therapeutically active compounds (or prodrug thereof) as noted herein which are usually applied in the treatment of the above mentioned pathological conditions.

In another embodiment, the invention is directed to a sterile injectable aqueous or oleagenous suspension. This suspension may be formulated according to the known art using
30 those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a

non-toxic parenterally-acceptable diluent or solvent, for example as a solution in 1,3-butane diol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose, any bland fixed oil may be employed including
5 synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

The invention is also directed to a therapeutically effective intravenous formulation of the compounds of the invention, which is solution stable and isotonic with human blood. The intravenous formulation preferably can be packaged in plastic or glass, and meets government and
10 compendial (USP in the US) particulate standards, and can be used as effective therapeutic agents.

The intravenous formulation may contain a buffer which can maintain the pH of the intravenous formulation within a desirable range. The buffering agent may maintain the intravenous formulation in an acceptable particulate profile for storage and subsequent use.

Pharmaceutical injectable formulations (such as subcutaneous formulations) will generally
15 include a therapeutically effective amount of a compound of the invention, in addition to one or more pharmaceutically acceptable excipients. The compositions are advantageously prepared together with liquid inert carriers, such as water. Suitable liquid excipients/carriers are Water for Injection (US Pharmacopeia) and saline solution. The solution should be pyrogen- free, and also should be absent of particulate matter. Limits for the amount of particulate matter (*i.e.*,
20 extraneous, mobile undissolved substances, other than gas bubbles) which may be found in IV fluids are defined in the US Pharmacopeia.

Other suitable excipients and other additives include solvents such as ethanol, glycerol, propylene glycol, and mixtures thereof; stabilizers such as EDTA (ethylene diamine tetraacetic acid), citric acid, and mixtures thereof; antimicrobial preservatives, such as benzyl alcohol, methyl
25 paraben, propyl paraben, and mixtures thereof; buffering agents, such as citric acid/sodium citrate, potassium hydrogen tartrate, sodium hydrogen tartrate, acetic acid/sodium acetate, maleic acid/sodium maleate, sodium hydrogen phthalate, phosphoric acid/potassium dihydrogen phosphate, phosphoric acid/disodium hydrogen phosphate, and mixtures thereof; tonicity modifiers, such as sodium chloride, mannitol, dextrose, and mixtures thereof; fluid and nutrient
30 replenishes such as synthetic amino acids, dextrose, sodium chloride, sodium lactate, Ringer's solution, and other electrolyte solutions.

The buffer system is generally a mixture of a weak acid and a soluble salt thereof, *e.g.*, sodium citrate/citric acid; or the monocation or dication salt of a dibasic acid, *e.g.*, potassium hydrogen tartrate; sodium hydrogen tartrate, phosphoric acid/potassium dihydrogen phosphate, and phosphoric acid/disodium hydrogen phosphate. The amount of buffer system used is
5 dependent on the desired pH and the amount of the compound of the invention. The choice of appropriate buffer and pH of a formulation, depending on solubility of the drug to be administered, is readily made by a person having ordinary skill in the art.

In an embodiment, the injectable formulation may be suitable for use with a needle-free injection device. Solid compositions are normally formulated in dosage units providing from about 1 to
10 about 1000 mg of the active ingredient per dose. Some examples of solid dosage units are 0.1 mg, 1 mg, 10 mg, 37.5 mg, 75 mg, 100 mg, 150 mg, 300 mg, 500 mg, 600 mg and 1000 mg. Typical dose ranges in accordance with the present invention include from about 10-600 mg, 25-300 mg, 25-150 mg, 50-100 mg, 60-90 mg, and 70-80 mg. Liquid compositions are generally in a unit dosage range of 1-100 mg/mL. Some examples of liquid dosage units are 0.1 mg/mL, 1 mg/mL, 10 mg/mL, 25 mg/mL, 50 mg/mL, and
15 100 mg/mL.

It will be understood, however, that the specific dose level and frequency of dosage for any particular patient may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug
20 combination, the severity of the particular condition, and the host undergoing therapy.

In some embodiments, a method may comprise administering to a subject one or more additional agent(s) simultaneously or sequentially with the compounds of the invention. The above combinations include combinations of a compound of the present invention not only with one other active compound (or prodrug thereof), but also with two or more other active compounds (or
25 prodrugs thereof). Likewise, compounds of the present invention may be used in combination with other drugs (or prodrugs thereof) that are used in the prevention, treatment, control, amelioration, or reduction of risk of the diseases or conditions for which compounds of the present invention are useful. Such other drugs may be administered, by a route and in an amount commonly used therefor, contemporaneously or sequentially with a compound of the present invention. When a compound of
30 the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition containing such other drugs in addition to the compound of the present invention is

preferred. Accordingly, the pharmaceutical compositions of the present invention include those that also contain one or more other active ingredients (or prodrug thereof), in addition to a compound of the present invention. The weight ratio of the compound of the compound of the present invention to the other active ingredient(s) (or prodrugs thereof) may be varied and will depend upon the effective dose of each ingredient. Generally, an effective dose of each will be used. Thus, for example, when a compound of the present invention is combined with another agent, the weight ratio of the compound of the present invention to the other agent will generally range from about 1000:1 to about 1:1000, or from about 200:1 to about 1:200. Combinations of a compound of the present invention and other active ingredients (or prodrugs thereof) will generally also be within the aforementioned range, but in each case, an effective dose of each active ingredient should be used. In such combinations the compound of the present invention and other active agents may be administered separately or in conjunction. In addition, the administration of one element may be prior to, concurrent to, or subsequent to the administration of other agent(s), *via* the same or different routes of administration.

In some embodiments, a therapeutic effect may be greater as compared to use of a compound of the invention or one or more additional agent(s) alone. Accordingly, a synergistic effect between a compound of the invention and the one or more additional agents may be achieved. In some embodiments, the one or more additional agent(s) may be taken by a subject prophylactically.

In an aspect, the invention also provides kits for use in the instant methods. Kits can include one or more containers comprising a pharmaceutical composition described herein and instructions for use in accordance with any of the methods described herein. Generally, these instructions comprise a description of administration of the pharmaceutical composition to treat, ameliorate or prevent multiple system atrophy, Huntington's disease, or other MPO disorder, according to any of the methods described herein. The kit may, for example, comprise a description of selecting an individual suitable for treatment based on identifying whether that individual has the disease or whether the individual is at risk of having the disease. The instructions are typically provided in the form of a package insert, or label, in accordance with the requirements of the regulatory having authority over the jurisdiction where the pharmaceutical composition is to be provided to patients.

EXAMPLES

The following examples illustrate the invention and are not intended to limit the scope of the invention. In some examples, abbreviations are used which are known to those skilled in the art or are readily accessible from the documents cited in the examples.

5

GENERAL EXPERIMENTALS

1. Analytical Methods

Method A: LC/MS data were determined with a Waters Alliance 2695 HPLC/MS (Waters Symmetry C18, 4.6 × 75 mm, 3.5 μm) with a 2996 diode array detector from 210–400 nm. The solvent system was 5–95% acetonitrile in water (with 0.1% TFA) over nine minutes using a linear gradient, and retention times are in minutes. Mass spectrometry was performed on a Waters ZQ using electrospray in positive mode.

Method A-2: LC/MS data were determined with a Waters Alliance 2695 HPLC/MS (Waters Symmetry C18, 4.6 × 75 mm, 3.5 μm) with a 2996 diode array detector from 210–400 nm; the solvent system is 40–95% acetonitrile in water (with 0.1% TFA) over nine minutes using a linear gradient, and retention times are in minutes. Mass spectrometry was performed on a Waters ZQ using electrospray in positive mode.

Method A-3: LC/MS data were determined with a Waters Alliance 2695 HPLC/MS (Waters Symmetry C18, 4.6 × 75 mm, 3.5 μm) with a 2996 diode array detector from 210–400 nm; the solvent system is 40–95% acetonitrile in water (with 0.1% TFA) over nine minutes using a linear gradient, then holding at 95% acetonitrile in water (with 0.1% TFA) for 10 minutes. Retention times are in minutes. Mass spectrometry was performed on a Waters ZQ using electrospray in positive mode.

Method B: Preparative reversed phase HPLC was performed on a Phenomenex LUNA column (19 × 100 mm, C18, 5 μm) with a 10 min mobile phase gradient of 10% acetonitrile/water to 90% acetonitrile/ water with 0.1% TFA as buffer using 214 and 254 nm as detection wavelengths. Injection and fraction collection were performed with a Gilson 215 liquid handling apparatus using Trilution LC software.

Method C: Preparative reversed phase HPLC was performed on a Waters Sunfire column (19 × 50 mm, C18, 5 μm) with a 10 min mobile phase gradient of 10% acetonitrile/water to 90% acetonitrile/ water with 0.1% TFA as buffer using 214 and 254 nm as detection wavelengths. Injection and fraction collection were performed with a Gilson 215 liquid handling apparatus using Trilution LC software.

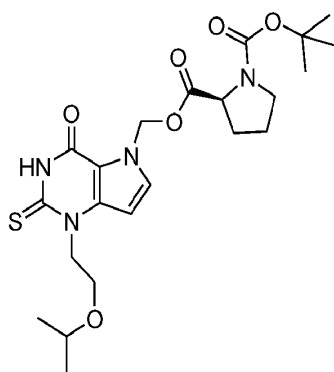
Method D: Preparative reversed phase HPLC was performed on a Waters Sunfire column (30 × 150 mm, C18, 10 μm) with a 15 min mobile phase gradient of with 0.1% TFA as buffer using 214 and 254 nm as detection wavelengths. Injection and fraction collection were performed with a Gilson 215 liquid handling apparatus using Trilution LC software.

5 ¹H-NMR spectra were taken on a Varian 300 MHz NMR using tetramethylsilane (TMS) as internal standard (δ = 0.00) with peaks reported downfield from TMS.

2. Experimental Procedures and Data

EXAMPLE 1:

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(S)-tert-Butyl (1,2,3,4-tetrahydro-1-(2-isopropoxyethyl)-4-oxo-2-thioxopyrrolo[3,2-d]pyrimidin-5-yl)methyl pyrrolidine-1,2-dicarboxylate. A solution of 2,3-dihydro-1-(2-isopropoxyethyl)-2-thioxo-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (100 mg, 400 μmol) in THF (2.0 mL) was treated with lithium hexamethyldisilylamide (1.0 M in THF, 440 μL, 440 μmol) and stirred for 20 mins. (S)-tert-Butyl chloromethyl pyrrolidine-1,2-dicarboxylate (133 mg, 480 μmol) was added and the mixture was stirred overnight. The reaction was quenched by the addition of methanol and the solvent was removed *in vacuo*. Crude product was purified by normal phase chromatography (12 g column, 0-70% MeOH/DCM) where the product fractions were combined and concentrated *in vacuo* to provide the pure product as a solid (60 mg, 31%). ¹H NMR (300 MHz, DMSO) δ 7.41-7.65 (m, 1H), 6.32-6.48 (m, 1H), 5.99-6.32 (m, 2H), 4.47 (t, J=6.15 Hz, 2H), 4.06-4.24 (m, 1H), 3.63-3.81 (m, 2H), 3.47-3.63 (m, 1H), 3.17-3.37 (m, 3H), 2.06-2.34 (m, 1H), 1.66-1.93 (m, 3H), 1.18-1.45 (m, 9H), 0.92-1.10 (m, 6H). LC/MS method A: R_t = 5.5 mins., (M+H)⁺ = 481, purity > 95%. Caco-2 P_{app} = 371 nm/s, SGF = 99% remaining at 1 h, SIF = 94% remaining at 1 h, hPlasma stability = 92% remaining at 1 h.

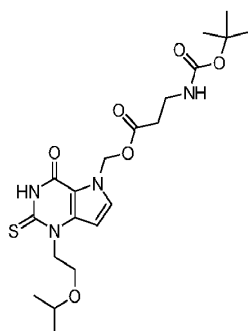
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Additional compounds prepared according to EXAMPLE 1:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
2	trifluoroacetic acid 1-tert-butyl 2-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-pyrrolidine-1,2-dicarboxylate	5.3	481	A	¹ H NMR (300 MHz, dmsO) δ 12.45 (s, 1H), 7.50-7.74 (m, 1H), 6.41-6.55 (m, 1H), 6.12-6.40 (m, 2H), 4.47-4.60 (m, 2H), 4.10-4.33 (m, 1H), 3.78 (q, J=5.66 Hz, 2H), 3.53-3.70 (m, 1H), 3.18-3.51 (m, 2H), 2.08-2.36 (m, 1H), 1.73-1.98 (m, 3H), 1.19-1.50 (m, 9H), 1.07 (d, J=6.44 Hz, 6H)				73% remaining at 1 h
3	1-tert-butyl 2-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-pyrrolidine-1,2-dicarboxylate	5.3	481	A	¹ H NMR (300 MHz, dmsO) δ 7.45-7.70 (m, 1H), 6.40 (d, J=2.93 Hz, 1H), 5.95-6.34 (m, 2H), 4.36-4.59 (m, 2H), 4.04-4.25 (m, 1H), 3.62-3.82 (m, 2H), 3.43-3.62 (m, 1H), 3.23-3.39 (m, 4H), 2.03-2.31 (m, 1H), 1.67-1.93 (m, 3H), 1.14-1.42 (m, 9H), 0.83-1.09 (m, 6H)	419	84% remaining at 1 h	89% remaining at 1 h	99% remaining at 1 h
4	1-benzyl 2-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-5-oxopyrrolidine-1,2-dicarboxylate	5.1	529	A	¹ H NMR (300 MHz, dmsO) δ 12.39 (s, 1H), 7.51 (d, J=2.93 Hz, 1H), 7.22-7.41 (m, 5H), 6.33-6.45 (m, 1H), 6.14-6.32 (m, 2H), 4.98-5.27 (m, 2H), 4.72 (dd, J=3.22, 9.08 Hz, 1H), 4.46 (t, J=6.15 Hz, 2H), 3.69 (t, J=5.86 Hz, 2H), 3.45-3.62 (m, 1H), 2.18-2.39 (m, 1H), 1.81-2.02 (m, 1H), 0.84-1.09 (m, 6H)	134	97% remaining at 1 h	94% remaining at 1 h	40% remaining at 1 h
5	1-(9H-fluoren-9-yl)methyl 2-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-pyrrolidine-1,2-dicarboxylate	6	603	A	¹ H NMR (300 MHz, dmsO) δ 12.04-12.39 (m, 1H), 7.76-8.02 (m, 2H), 7.13-7.70 (m, 6H), 5.96-6.40 (m, 3H), 5.81-5.83 (m, 1H), 3.76-4.56 (m, 6H), 3.32-3.81 (m, 5H), 3.20-3.20 (m, 1H), 2.96-3.20 (m, 1H), 1.72-1.98 (m, 3H), 0.72-1.04 (m, 5H)	140	90% remaining at 1 h	76% remaining at 1 h	97% remaining at 1 h

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EXAMPLE 6:



{4-Oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-(((tert-butoxy)carbonyl)amino)propanoate. A solution of 2,3-dihydro-1-(2-

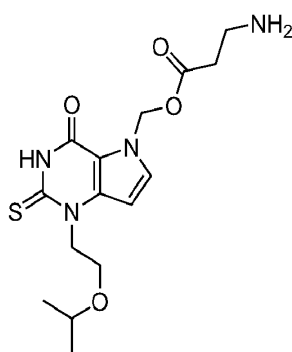
- isopropoxyethyl)-2-thioxo-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (100 mg, 400 μ mol) in THF (2.0 mL) was treated with lithium hexamethyldisilylamide (1.0 M in THF, 840 μ L, 840 μ mol) and stirred for 20 mins. tert-butyl 2-((chloromethoxy)carbonyl)ethylcarbamate (190 mg, 800 μ mol) was added and the mixture was stirred overnight. The reaction was quenched by the addition of water and extracted with EtOAc.
- 5 The organic layer was washed with brine and the solvent was removed *in vacuo*. Crude product was purified by normal phase chromatography (12 g column, 0-60% EtOAc/DCM) where the product fractions were combined and concentrated *in vacuo* to provide the pure product as a solid (120 mg, 66%). ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 9.34-9.57 (m, 1H), 7.20-7.32 (m, 1H), 6.13-6.30 (m, 3H), 4.44-4.59 (m, 2H), 3.84 (s, 2H), 3.49-3.63 (m, 1H), 3.16-3.45 (m, 2H), 2.55 (t, $J=6.15$ Hz, 2H), 1.42 (s, 9H),
- 10 0.86-1.14 (m, 6H). LC/MS method A: $R_t = 5.0$ mins ($M+H$) $^+ = 455$, purity > 95%. Caco-2 $P_{app} = 179$ nm/s, SGF = 82% remaining at 1 h, SIF = 67% remaining at 1 h, *h*Plasma stability = 59% remaining at 1 h.

Additional compounds prepared according to EXAMPLE 6:

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Example	Name	LCMS retention time	$M+H^+$	LCMS method	NMR	Caco-2 P_{app} (nm/s)	SGF	SIF	human Plasma stability
7	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[[[tert-butoxy)carbonyl]amino]pentanoate	5.2	483	A	^1H NMR (300 MHz, cdCl_3) δ 7.14-7.32 (m, 2H), 6.16-6.30 (m, 3H), 4.42-4.67 (m, 3H), 3.77-3.94 (m, 2H), 3.45-3.68 (m, 1H), 3.09 (q, $J=6.44$ Hz, 2H), 2.26-2.46 (m, 2H), 1.46-1.71 (m, 5H), 0.97-1.18 (m, 6H)	147	66% remaining at 1h	40% remaining at 1h	4% remaining at 1h

EXAMPLE 8:

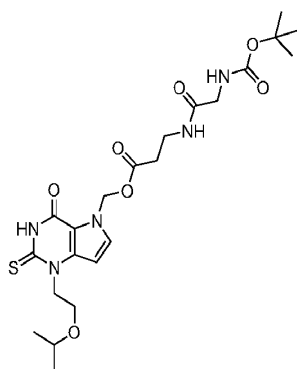


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Trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-aminopropanoate. To a solution of {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[[[tert-

butoxy)carbonyl]amino}propanoate (50 mg, 110 μ mol) in 2.0 mL DCM was added 1.0 mL TFA. The reaction was stirred for 1 hour. The solvent was removed *in vacuo* and crude product was purified by RP-HPLC (method D) where the product fractions were combined and lyophilized to provide the pure product as a white solid (45 mg, 87%). ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 8.15-8.40 (m, 2H), 7.19-7.30 (m, 2H), 6.10-6.38 (m, 3H), 4.45-4.61 (m, 2H), 3.84 (t, $J=5.57$ Hz, 2H), 3.48-3.65 (m, 1H), 3.31 (br. s., 2H), 2.73-2.95 (m, 2H), 0.98-1.18 (m, 6H). LC/MS method A: R_t = 3.3 mins ($M+H$) $^+$ = 355, purity > 95%. Caco-2 P_{app} = 4.6 nm/s, SGF = 97% remaining at 1 h, SIF = 68% remaining at 1 h, *h*Plasma stability = 45% remaining at 1 h.

EXAMPLE 9:

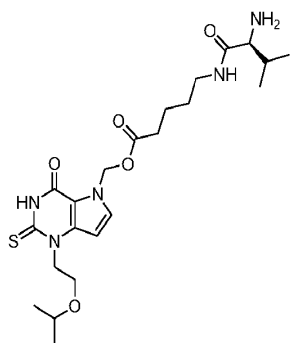


{4-Oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-({[(tert-butoxy)carbonyl]amino}acetamido)propanoate. To a solution of trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-aminopropanoate (36 mg, 80 μ mol) in 300 μ L DMF was added HATU (60 mg, 160 μ mol), N-Boc-glycine (26 mg, 160 μ mol), and DIPEA (56 μ L, 320 μ mol). The reaction stirred at room temperature overnight. 200 μ L H₂O was added and the crude product was purified by RP-HPLC (method D) where the product fractions were combined and lyophilized to provide the pure product as a white solid (32 mg, 78%). ^1H NMR (300 MHz, METHANOL-*d*₄) δ 7.54-7.71 (m, 1H), 6.51-6.62 (m, 1H), 6.44 (s, 2H), 4.69-4.86 (m, 2H), 3.97-4.11 (m, 2H), 3.59-3.90 (m, 5H), 3.45-3.53 (m, 1H), 2.65-2.83 (m, 2H), 1.55-1.68 (m, 9H), 1.18-1.31 (m, 6H). LC/MS method A: R_t = 4.5 mins ($M+H$) $^+$ = 512, purity > 95%. Caco-2 P_{app} = 15.3 nm/s, SGF = 100% remaining at 1 h, SIF = 61% remaining at 1 h, *h*Plasma stability = 52% remaining at 1 h.

Additional compounds prepared according to EXAMPLE 9:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
10	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[[[tert-butoxy]carbonyl]amino]-3-methylbutanamido]pentanoate	5.2	582	A	¹ H NMR (300 MHz, cdcl ₃) δ 7.25 (d, J=3.51 Hz, 1H), 6.13-6.33 (m, 4H), 4.41-4.63 (m, 2H), 3.95 (dd, J=6.74, 9.67 Hz, 1H), 3.74-3.90 (m, 2H), 3.51-3.65 (m, 1H), 3.08-3.35 (m, 2H), 2.28-2.46 (m, 2H), 1.49-1.73 (m, 4H), 1.46 (s, 9H), 1.00-1.14 (m, 6H), 0.86-1.00 (m, 6H)	48.7	81% remaining at 1h	76% remaining at 1h	72% remaining at 1h
11	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[[[tert-butoxy]carbonyl]amino]-3-methylbutanamido]propanoate	5.1	554	A	¹ H NMR (300 MHz, dmsol-d ₆) δ 7.78 (d, J=2.93 Hz, 1H), 6.67 (d, J=2.93 Hz, 1H), 6.45 (s, 2H), 4.75 (t, J=6.15 Hz, 2H), 3.74-4.09 (m, 4H), 3.38-3.69 (m, 4H), 2.65-2.86 (m, 9H), 2.00-2.24 (m, 1H), 1.54-1.74 (m, 9H), 1.19-1.39 (m, 6H), 0.96-1.15 (m, 6H)	14.4	74% remaining at 1h	69% remaining at 1h	99% remaining at 1h

EXAMPLE 12:



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Trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-amino-3-methylbutanamido]pentanoate. To a solution of {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[[[tert-butoxy]carbonyl]amino]-3-methylbutanamido]pentanoate (17 mg, 29 μmol) in 1.0 mL DCM was added 300 μL TFA. The reaction was stirred for 1 hour. The solvent was removed *in vacuo* and crude product was purified by RP-HPLC (method D) where the product fractions were combined and lyophilized to provide the pure product as a white solid (15 mg, 86%). ¹H NMR (300 MHz, METHANOL-*d*₄) δ 7.53-7.73 (m, 1H), 6.51-6.60 (m, 1H), 6.36-6.47 (m, 2H), 4.64-4.85 (m, 2H), 3.98-4.12 (m, 2H), 3.66-3.85 (m, 2H), 3.25-3.47 (m, 2H), 2.45-2.65 (m, 2H), 2.27-2.42 (m, 1H), 1.63-1.93 (m, 4H), 1.11-1.29 (m, 12H). LC/MS method A: R_t = 3.7 mins (M+H)⁺ = 482, purity > 95%. Caco-2 P_{app} = 4.0 nm/s, SGF = 100% remaining at 1 h, SIF = 94% remaining at 1 h, hPlasma stability = 76% remaining at 1 h.

Additional compounds prepared according to EXAMPLE 12:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
13	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(2-[(tert-butoxy)carbonyl]amino)acetamido} pentanoate	4.7	540	A	1H NMR (300 MHz, cd3od) δ 7.19-7.30 (m, 1H), 6.17 (d, J=2.34 Hz, 1H), 6.05 (s, 2H), 4.38 (s, 2H), 3.55-3.75 (m, 2H), 3.34-3.53 (m, 3H), 2.98 (t, J=6.74 Hz, 2H), 2.17 (t, J=7.03 Hz, 2H), 1.28-1.53 (m, 4H), 1.22-1.28 (m, 9H), 0.78-0.94 (m, 6H)	18.8	96% remaining at 1h	94% remaining at 1h	1% remaining at 1h
14	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-3-methylbutanamido]propanoate	3.5	454	A	1H NMR (300 MHz, cd3od) δ 7.48-7.62 (m, 1H), 6.44-6.55 (m, 1H), 6.37 (s, 2H), 4.69 (t, J=5.57 Hz, 2H), 3.87-4.07 (m, 2H), 3.47-3.77 (m, 4H), 2.63-2.82 (m, 2H), 2.11-2.35 (m, 1H), 0.98-1.23 (m, 12H)	<2.03	95% remaining at 1h	84% remaining at 1h	55% remaining at 1h
15	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(2-aminoacetamido)pentanoate	3.3	440	A	1H NMR (300 MHz, cd3od) δ 7.45-7.59 (m, 1H), 6.44 (s, 1H), 6.33 (s, 2H), 4.60-4.70 (m, 2H), 3.88-4.01 (m, 2H), 3.74 (s, 3H), 3.30 (t, J=6.44 Hz, 2H), 2.34-2.52 (m, 2H), 1.56-1.79 (m, 4H), 1.04-1.21 (m, 6H)	>5.67	100% remaining at 1h	4% remaining at 1h	9% remaining at 1h
16	trifluoroacetic acid benzyl (5S)-2-oxo-5-[(5-oxo-5-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]pentyl)carbamoyl]pyrrolidine-1-carboxylate	4.8	628	A	1H NMR (300 MHz, cd3od) δ 7.48 (br. s., 1H), 7.30-7.43 (m, 5H), 6.36-6.47 (m, 1H), 6.23-6.34 (m, 2H), 5.13-5.38 (m, 2H), 4.51-4.72 (m, 3H), 3.89 (t, J=5.57 Hz, 2H), 3.48-3.76 (m, 4H), 3.15 (t, J=6.44 Hz, 2H), 2.20-2.81 (m, 5H), 1.84-2.07 (m, 1H), 1.37-1.69 (m, 4H), 1.04-1.18 (m, 6H)	9.03	96% remaining at 1h	93% remaining at 1h	21% remaining at 1h
17	trifluoroacetic acid benzyl (5S)-2-oxo-5-[(3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl)carbamoyl]pyrrolidine-1-carboxylate	4.6	600	A	1H NMR (300 MHz, cd3od) δ 7.48-7.59 (m, 1H), 7.30-7.44 (m, 5H), 6.44 (d, J=2.93 Hz, 1H), 6.31 (d, J=1.17 Hz, 2H), 5.26-5.41 (m, 1H), 5.11-5.25 (m, 1H), 4.58-4.78 (m, 3H), 3.93 (t, J=5.57 Hz, 2H), 3.67 (t, J=5.86 Hz, 1H), 3.45 (cd, J=1.76, 6.44 Hz, 2H), 2.29-2.80 (m, 6H), 1.91-2.09 (m, 1H), 1.14 (d, J=5.86 Hz, 6H)	3.68	99% remaining at 1h	3% remaining at 1h	38% remaining at 1h
18	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-4-phenylbutanamido]pentanoate	5.7	644	A	1H NMR (300 MHz, cd3od) δ 7.42 (d, J=2.93 Hz, 1H), 7.08-7.33 (m, 6H), 6.29-6.41 (m, 1H), 6.20-6.29 (m, 2H), 4.73-4.80 (m, 1H), 4.57 (t, J=5.57 Hz, 2H), 3.91-4.08 (m, 1H), 3.79-3.91 (m, 2H), 3.52-3.67 (m, 1H), 3.08-3.29 (m, 3H), 2.49-2.82 (m, 2H), 2.29-2.43 (m, 2H), 1.74-2.15 (m, 2H), 1.49-1.73 (m, 4H), 1.46 (s, 9H), 1.00-1.12 (m, 6H)	75.9	100% remaining at 1h	65% remaining at 1h	86% remaining at 1h

19	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[[[tert-butoxycarbonyl]amino]-4-phenylbutanamido]propanoate	5.6	616	A	¹ H NMR (300 MHz, cd3od) δ 7.42-7.48 (m, 1H), 7.25-7.35 (m, 2H), 7.17-7.25 (m, 3H), 6.31-6.38 (m, 1H), 6.26-6.31 (m, 2H), 4.58 (t, J=5.86 Hz, 2H), 3.80-4.11 (m, 3H), 3.41-3.71 (m, 3H), 2.55-2.77 (m, 4H), 1.77-2.19 (m, 2H), 1.41-1.58 (m, 9H), 1.10 (d, J=5.86 Hz, 6H)	117	82% remaining at 1h	57% remaining at 1h	42% remaining at 1h
20	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[[[9H-fluoren-9-ylmethoxy]carbonyl]amino]-4-(methylsulfanyl)butanamido]pentanoate	5.9	736	A	¹ H NMR (300 MHz, cd3od) δ 7.87-7.98 (m, 1H), 7.75-7.87 (m, 2H), 7.62-7.73 (m, 2H), 7.21-7.46 (m, 6H), 6.28-6.40 (m, 1H), 6.15-6.26 (m, 2H), 4.31-4.62 (m, 4H), 4.11-4.30 (m, 2H), 3.77-3.95 (m, 2H), 3.45-3.67 (m, 1H), 3.08-3.25 (m, 2H), 2.29-2.62 (m, 4H), 1.74-2.15 (m, 6H), 1.36-1.70 (m, 4H), 0.94-1.17 (m, 6H)	9.85	80% remaining at 1h	76% remaining at 1h	64% remaining at 1h
21	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[[[9H-fluoren-9-ylmethoxy]carbonyl]amino]-4-(methylsulfanyl)butanamido]propanoate	5.9	708	A	¹ H NMR (300 MHz, cd3od) δ 7.94-8.13 (m, 1H), 7.81 (d, J=7.03 Hz, 2H), 7.61-7.73 (m, 2H), 7.21-7.48 (m, 5H), 6.33 (d, J=2.93 Hz, 1H), 6.22 (s, 2H), 4.49-4.63 (m, 2H), 4.39-4.49 (m, 2H), 4.14-4.30 (m, 2H), 3.79-3.91 (m, 2H), 3.38-3.66 (m, 3H), 2.36-2.67 (m, 4H), 2.09 (s, 3H), 1.78-2.03 (m, 2H), 1.07 (d, J=5.86 Hz, 6H)	57.9	88% remaining at 1h	75% remaining at 1h	91% remaining at 1h
22	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[[[9H-fluoren-9-ylmethoxy]carbonyl]amino]-3-phenylpropanamido]pentanoate	6.1	752	A	¹ H NMR (300 MHz, dmsod) δ 7.94 (d, J=7.62 Hz, 3H), 7.07-7.80 (m, 14H), 6.38-6.50 (m, 1H), 6.23 (s, 2H), 4.47-4.63 (m, 2H), 4.14-4.36 (m, 4H), 3.69-3.89 (m, 2H), 3.60 (t, J=5.86 Hz, 1H), 2.80-3.21 (m, 4H), 2.28-2.44 (m, 2H), 1.36-1.62 (m, 4H), 1.06 (d, J=6.44 Hz, 6H)	6.47	87% remaining at 1h	90% remaining at 1h	74% remaining at 1h
23	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[[[9H-fluoren-9-ylmethoxy]carbonyl]amino]-3-phenylpropanamido]propanoate	6	724	A	¹ H NMR (300 MHz, dmsod) δ 12.43 (s, 1H), 8.15 (s, 1H), 7.93 (d, J=7.03 Hz, 2H), 7.52-7.75 (m, 4H), 7.19-7.52 (m, 10H), 6.37-6.46 (m, 1H), 6.23-6.29 (m, 2H), 4.36-4.59 (m, 2H), 4.12-4.33 (m, 4H), 3.71-3.80 (m, 3H), 3.49-3.69 (m, 1H), 3.23-3.47 (m, 2H), 2.73-3.02 (m, 2H), 2.49 (t, J=6.74 Hz, 2H), 0.98-1.13 (m, 6H)	19.4	93% remaining at 1h	84% remaining at 1h	92% remaining at 1h
24	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-amino-4-phenylbutanamido]pentanoate	4	544	A	¹ H NMR (300 MHz, cd3od) δ 7.19 (d, J=2.93 Hz, 1H), 6.91-7.14 (m, 5H), 6.10-6.16 (m, 1H), 5.97-6.06 (m, 2H), 4.34 (t, J=5.57 Hz, 2H), 3.57-3.71 (m, 3H), 3.37 (td, J=6.30, 12.01 Hz, 1H), 2.92-3.06 (m, 2H), 2.41-2.54 (m, 2H), 2.09-2.24 (m, 2H), 1.82-2.03 (m, 2H), 1.30-1.56 (m, 4H), 0.85 (d, J=5.86 Hz, 6H)	3.02	99% remaining at 1h	76% remaining at 1h	1% remaining at 1h
25	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-4-phenylbutanamido]propanoate	4	516	A	¹ H NMR (300 MHz, cd3od) δ 7.48 (d, J=2.93 Hz, 1H), 7.21-7.43 (m, 5H), 6.34-6.39 (m, 1H), 6.30-6.34 (m, 2H), 4.60 (t, J=5.57 Hz, 2H), 3.84-4.03 (m, 3H), 3.43-3.77 (m, 3H), 2.63-2.84 (m, 4H), 2.05-2.29 (m, 2H), 1.03-1.22 (m, 6H)	2.87	99% remaining at 1h	43% remaining at 1h	96% remaining at 1h

26	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-4-methylpentanamido]pentanoate	5.5	596	A	1H NMR (300 MHz, cd3od) δ 7.45-7.59 (m, 1H), 6.46 (d, $J=2.93$ Hz, 1H), 6.34 (s, 2H), 4.67 (s, 2H), 4.02-4.22 (m, 1H), 3.96 (s, 2H), 3.56-3.80 (m, 2H), 3.12-3.37 (m, 2H), 2.39-2.56 (m, 2H), 1.48-1.85 (m, 16H), 1.10-1.22 (m, 6H), 1.03 (t, $J=6.44$ Hz, 6H)	127	99% remaining at 1 h	66% remaining at 1 h	32% remaining at 1 h
27	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[(tert-butoxy)carbonyl]amino]-4-methylpentanamido]propanoate	5.3	568	A	1H NMR (300 MHz, cd3od) δ 7.41-7.52 (m, 1H), 6.39 (d, $J=2.93$ Hz, 1H), 6.27 (d, $J=2.93$ Hz, 2H), 4.50-4.66 (m, 2H), 3.94-4.13 (m, 1H), 3.79-3.94 (m, 2H), 3.37-3.74 (m, 4H), 2.57 (t, $J=6.74$ Hz, 2H), 1.61-1.80 (m, 1H), 1.46 (s, 11H), 1.09 (d, $J=5.86$ Hz, 6H), 0.95 (t, $J=5.86$ Hz, 6H)	86.1	92% remaining at 1 h	61% remaining at 1 h	91% remaining at 1 h
28	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-4-(methylsulfanyl)butanamido]pentanoate	5.3	614	A	1H NMR (300 MHz, cd3od) δ 7.42-7.57 (m, 1H), 6.41 (d, $J=2.93$ Hz, 1H), 6.30 (s, 2H), 4.63 (s, 2H), 4.05-4.25 (m, 1H), 3.92 (s, 2H), 3.55-3.80 (m, 1H), 3.14-3.30 (m, 2H), 2.42 (s, 4H), 2.13 (s, 3H), 1.79-2.08 (m, 2H), 1.51-1.73 (m, 4H), 1.49 (s, 9H), 1.12 (d, $J=6.44$ Hz, 6H)	67	99% remaining at 1 h	75% remaining at 1 h	62% remaining at 1 h
29	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[(tert-butoxy)carbonyl]amino]-4-(methylsulfanyl)butanamido]propanoate	5.1	586	A	1H NMR (300 MHz, cd3od) δ 7.43-7.57 (m, 1H), 6.40 (d, $J=3.51$ Hz, 1H), 6.28 (s, 2H), 4.60 (s, 2H), 4.05-4.21 (m, 1H), 3.89 (s, 2H), 3.39-3.70 (m, 3H), 2.59 (s, 4H), 2.10 (s, 3H), 1.75-2.04 (m, 2H), 1.75-2.04 (m, 2H), 1.47 (s, 9H), 1.10 (d, $J=5.86$ Hz, 6H)	54.1	92% remaining at 1 h	62% remaining at 1 h	98% remaining at 1 h
30	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-4-methylpentanamido]propanoate	3.8	468	A	1H NMR (300 MHz, cd3od) δ 7.38-7.52 (m, 1H), 6.39 (d, $J=3.51$ Hz, 1H), 6.27 (s, 2H), 4.59 (t, $J=5.86$ Hz, 2H), 3.77-3.92 (m, 3H), 3.39-3.72 (m, 4H), 2.61 (t, $J=6.44$ Hz, 2H), 1.59-1.76 (m, 3H), 1.08 (d, $J=6.44$ Hz, 6H), 0.99 (d, $J=4.69$ Hz, 6H)	<2.69	93% remaining at 1 h	67% remaining at 1 h	40% remaining at 1 h
31	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-amino-4-(methylsulfanyl)butanamido]pentanoate	3.8	514	A	1H NMR (300 MHz, cd3od) δ 7.42-7.56 (m, 1H), 6.42 (d, $J=2.93$ Hz, 1H), 6.30 (s, 2H), 4.63 (t, $J=5.86$ Hz, 2H), 3.92 (t, $J=5.57$ Hz, 3H), 3.53-3.77 (m, 1H), 3.21-3.35 (m, 2H), 2.62 (s, 2H), 2.44 (s, 2H), 2.17 (s, 5H), 1.50-1.80 (m, 5H), 1.12 (d, $J=5.86$ Hz, 6H)	3.25	94% remaining at 1 h	85% remaining at 1 h	1% remaining at 1 h
32	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-4-(methylsulfanyl)butanamido]propanoate	3.5	486	A	1H NMR (300 MHz, cd3od) δ 7.35-7.55 (m, 1H), 6.35-6.47 (m, 1H), 6.21-6.34 (m, 2H), 4.61 (t, $J=5.86$ Hz, 2H), 3.80-4.04 (m, 3H), 3.63 (s, 3H), 2.46-2.71 (m, 4H), 1.98-2.22 (m, 5H), 1.69 (d, $J=19.92$ Hz, 1H), 1.10 (d, $J=6.44$ Hz, 6H)	1.57	97% remaining at 1 h	33% remaining at 1 h	17% remaining at 1 h
33	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S,3S)-2-[(tert-butoxy)carbonyl]amino]-3-methylpentanamido]pentanoate	5.4	596	A	1H NMR (300 MHz, cd3od) δ 7.97-8.11 (m, 1H), 7.42-7.63 (m, 1H), 6.41-6.51 (m, 1H), 6.23-6.39 (m, 2H), 4.59-4.76 (m, 2H), 3.82-4.03 (m, 3H), 3.55-3.76 (m, 1H), 3.13-3.35 (m, 2H), 2.36-2.54 (m, 2H), 1.45-1.90 (m, 16H), 1.07-1.24 (m, 7H), 0.92-1.06 (m, 6H)	54.7	90% remaining at 1 h	78% remaining at 1 h	53% remaining at 1 h

34	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S,3S)-2-[(tert-butoxy)carbonyl]amino]-3-methylpentanamido]propanoate	5.4	568	A	¹ H NMR (300 MHz, cd3od) δ 7.38-7.59 (m, 1H), 6.38-6.50 (m, 1H), 6.24-6.35 (m, 2H), 4.55-4.66 (m, 2H), 3.73-3.99 (m, 3H), 3.41-3.74 (m, 3H), 2.49-2.77 (m, 2H), 1.65-1.89 (m, 2H), 1.43-1.59 (m, 10H), 1.06-1.26 (m, 7H), 0.84-1.00 (m, 6H)	107	85% remaining at 1 h	90% remaining at 1 h	93% remaining at 1 h
35	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S,3R)-2-[(tert-butoxy)carbonyl]amino]-3-hydroxybutanamido]pentanoate	4.7	584	A	¹ H NMR (300 MHz, cd3od) δ 7.38-7.61 (m, 1H), 6.42 (d, J=2.93 Hz, 1H), 6.30 (s, 2H), 4.63 (t, J=5.57 Hz, 2H), 4.05-4.29 (m, 1H), 3.88-4.03 (m, 3H), 3.65 (t, J=5.86 Hz, 1H), 3.25 (dd, J=6.74, 13.18 Hz, 2H), 2.42 (t, J=7.03 Hz, 2H), 1.43-1.81 (m, 13H), 1.20-1.30 (m, 3H), 1.04-1.16 (m, 6H)	19.1	91% remaining at 1 h	99% remaining at 1 h	30% remaining at 1 h
36	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S,3R)-2-[(tert-butoxy)carbonyl]amino]-3-hydroxybutanamido]propanoate	4.6	556	A	¹ H NMR (300 MHz, cd3od) δ 7.45-7.57 (m, 1H), 6.43 (dd, J=1.17, 2.93 Hz, 1H), 6.32 (s, 2H), 4.64 (t, J=5.57 Hz, 2H), 4.07-4.28 (m, 1H), 3.84-4.05 (m, 3H), 3.42-3.77 (m, 3H), 2.64 (t, J=6.15 Hz, 2H), 1.52 (s, 9H), 1.21 (d, J=5.86 Hz, 3H), 1.07-1.17 (m, 6H)	8.35	95% remaining at 1 h	88% remaining at 1 h	79% remaining at 1 h
37	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S,3S)-2-amino-3-methylpentanamido]pentanoate	3.9	496	A	¹ H NMR (300 MHz, cd3od) δ 7.44-7.56 (m, 1H), 6.44 (d, J=2.93 Hz, 1H), 6.32 (s, 2H), 4.65 (t, J=5.86 Hz, 2H), 3.94 (t, J=5.57 Hz, 2H), 3.56-3.77 (m, 2H), 3.18-3.34 (m, 2H), 2.30-2.55 (m, 2H), 1.87-2.10 (m, 1H), 1.45-1.84 (m, 6H), 1.24-1.45 (m, 1H), 0.97-1.19 (m, 13H)	10.9	88% remaining at 1 h	89% remaining at 1 h	1% remaining at 1 h
38	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S,3S)-2-amino-3-methylpentanamido]propanoate	3.7	468	A	¹ H NMR (300 MHz, cd3od) δ 7.53 (d, J=2.93 Hz, 1H), 6.45 (d, J=2.93 Hz, 1H), 6.33 (s, 2H), 4.65 (t, J=5.57 Hz, 2H), 3.94 (t, J=5.57 Hz, 2H), 3.43-3.79 (m, 4H), 2.68 (t, J=6.44 Hz, 2H), 1.81-2.07 (m, 1H), 1.72-1.78 (m, 1H), 1.48-1.71 (m, 1H), 0.94-1.43 (m, 14H)	3.1	92% remaining at 1 h	84% remaining at 1 h	65% remaining at 1 h
39	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S,3R)-2-amino-3-hydroxybutanamido]pentanoate	3.4	484	A	¹ H NMR (300 MHz, cd3od) δ 7.36-7.59 (m, 1H), 6.43 (d, J=2.93 Hz, 1H), 6.31 (s, 2H), 4.64 (t, J=5.57 Hz, 2H), 4.00-4.15 (m, 1H), 3.85-3.98 (m, 2H), 3.56-3.74 (m, 2H), 3.13-3.34 (m, 2H), 2.32-2.53 (m, 2H), 1.50-1.81 (m, 6H), 1.24-1.42 (m, 3H), 0.96-1.19 (m, 6H)	<1.96	91% remaining at 1 h	91% remaining at 1 h	5% remaining at 1 h
40	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S,3R)-2-amino-3-hydroxybutanamido]propanoate	3.2	456	A	¹ H NMR (300 MHz, cd3od) δ 7.29 (d, J=3.51 Hz, 1H), 6.22 (d, J=3.51 Hz, 1H), 6.09 (s, 2H), 4.42 (t, J=5.57 Hz, 2H), 3.60-3.94 (m, 3H), 3.23-3.53 (m, 4H), 2.32-2.57 (m, 2H), 1.53 (s, 1H), 1.01-1.24 (m, 4H), 0.80-0.96 (m, 6H)	<2.35	100% remaining at 1 h	86% remaining at 1 h	88% remaining at 1 h
41	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-hydroxypropanamido]pentanoate	4.5	570	A	¹ H NMR (300 MHz, cd3od) δ 7.52-7.68 (m, 1H), 6.52 (d, J=3.51 Hz, 1H), 6.40 (s, 2H), 4.73 (t, J=5.57 Hz, 2H), 4.14-4.30 (m, 1H), 3.66-4.08 (m, 6H), 3.22-3.44 (m, 2H), 2.39-2.60 (m, 2H), 1.50-1.92 (m, 13H), 1.11-1.30 (m, 6H)	11.5	78% remaining at 1 h	87% remaining at 1 h	21% remaining at 1 h

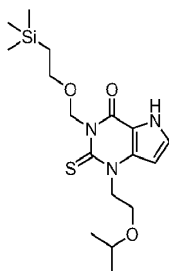
42	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-hydroxypropanamido]propanoate	4.4	542	A	¹ H NMR (300 MHz, cd3od) δ 7.47-7.57 (m, 1H), 6.44 (d, J=3.51 Hz, 1H), 6.32 (s, 2H), 4.65 (t, J=5.86 Hz, 2H), 4.06-4.20 (m, 1H), 3.86-4.03 (m, 3H), 3.45-3.84 (m, 5H), 2.59-2.74 (m, 2H), 1.52 (s, 9H), 1.14 (d, J=6.44 Hz, 6H)	5.07	86% remaining at 1 h	75% remaining at 1 h	51% remaining at 1 h
43	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-amino-3-hydroxypropanamido]pentanoate	3.4	470	A	¹ H NMR (300 MHz, cd3od) δ 7.39-7.58 (m, 1H), 6.43 (d, J=2.93 Hz, 1H), 6.30 (s, 2H), 4.64 (t, J=5.57 Hz, 2H), 3.75-4.02 (m, 5H), 3.65 (td, J=5.93, 12.16 Hz, 1H), 3.21-3.32 (m, 2H), 2.32-2.52 (m, 2H), 1.45-1.87 (m, 5H), 1.05-1.21 (m, 6H)	1.47	92% remaining at 1 h	87% remaining at 1 h	16% remaining at 1 h
44	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-3-hydroxypropanamido]propanoate	3.2	442	A	¹ H NMR (300 MHz, cd3od) δ 7.41-7.58 (m, 1H), 6.36-6.47 (m, 1H), 6.25-6.36 (m, 2H), 4.52-4.69 (m, 2H), 3.44-4.02 (m, 8H), 2.57-2.76 (m, 2H), 0.97-1.17 (m, 6H)	<2.22	96% remaining at 1 h	1% remaining at 1 h	5% remaining at 1 h
45	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-(4-hydroxyphenyl)propanamido]pentanoate	4.9	646	A	¹ H NMR (300 MHz, cd3od) δ 7.39-7.51 (m, 1H), 7.03 (d, J=8.79 Hz, 2H), 6.70 (d, J=8.20 Hz, 2H), 6.37 (d, J=2.93 Hz, 1H), 6.26 (s, 2H), 4.58 (t, J=5.86 Hz, 2H), 4.03-4.27 (m, 1H), 3.79-3.96 (m, 2H), 3.51-3.72 (m, 1H), 2.66-3.28 (m, 5H), 2.25-2.45 (m, 2H), 1.31-1.62 (m, 14H), 0.98-1.19 (m, 6H)	22.8	100% remaining at 1h	89% remaining at 1h	66% remaining at 1h
46	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-(4-hydroxyphenyl)propanamido]propanoate	4.8	618	A	¹ H NMR (300 MHz, cd3od) δ 7.41-7.59 (m, 1H), 6.98-7.17 (m, 2H), 6.75 (d, J=7.03 Hz, 2H), 6.36-6.44 (m, 1H), 6.30 (s, 2H), 4.51-4.65 (m, 2H), 4.11-4.29 (m, 1H), 3.78-3.95 (m, 2H), 3.45-3.73 (m, 2H), 2.66-3.00 (m, 2H), 2.53 (br. s., 2H), 1.29-1.53 (m, 9H), 1.12 (dd, J=2.34, 5.86 Hz, 6H)	11.2	98% remaining at 1h	100% remaining at 1h	63% remaining at 1h
47	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-(1H-indol-3-yl)propanamido]pentanoate	5.4	669	A	¹ H NMR (300 MHz, cd3od) δ 7.65 (d, J=7.62 Hz, 1H), 7.50 (d, J=3.51 Hz, 1H), 7.38 (d, J=8.20 Hz, 1H), 6.99-7.22 (m, 3H), 6.42 (d, J=2.93 Hz, 1H), 6.30 (s, 2H), 4.63 (t, J=5.86 Hz, 2H), 4.36 (s, 1H), 3.92 (t, J=5.57 Hz, 2H), 3.65 (t, J=5.86 Hz, 1H), 2.83-3.33 (m, 4H), 2.20-2.46 (m, 2H), 1.20-1.56 (m, 13H), 1.01-1.19 (m, 6H)	81.5	99% remaining at 1h	46% remaining at 1h	78% remaining at 1h
48	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-(1H-indol-3-yl)propanamido]propanoate	5.3	641	A	¹ H NMR (300 MHz, cd3od) δ 7.56-7.69 (m, 1H), 7.44-7.56 (m, 1H), 7.36-7.44 (m, 1H), 7.00-7.21 (m, 3H), 6.20-6.42 (m, 3H), 4.42-4.61 (m, 2H), 4.26-4.42 (m, 1H), 3.80-3.95 (m, 2H), 3.41-3.71 (m, 2H), 3.41-3.71 (m, 1H), 2.94-3.31 (m, 3H), 2.36-2.58 (m, 2H), 1.20-1.58 (m, 9H), 1.13 (dd, J=3.22, 6.15 Hz, 6H)	59.3	90% remaining at 1h	89% remaining at 1h	74% remaining at 1h

49	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-amino-3-(4-hydroxyphenyl)propanamido]pentanoate	3.7	546	A	¹ H NMR (300 MHz, cd3od) δ 7.47 (d, J=2.34 Hz, 1H), 7.09 (d, J=8.20 Hz, 2H), 6.79 (d, J=7.62 Hz, 2H), 6.32-6.43 (m, 1H), 6.28 (s, 2H), 4.60 (t, J=5.57 Hz, 2H), 3.78-4.04 (m, 3H), 3.49-3.71 (m, 1H), 3.17-3.29 (m, 1H), 2.91-3.15 (m, 3H), 2.27-2.41 (m, 2H), 1.34-1.55 (m, 4H), 1.01-1.16 (m, 6H)	1.54	99% remaining at 1 h	92% remaining at 1 h	1% remaining at 1 h
50	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-3-(4-hydroxyphenyl)propanamido]propanoate	3.5	518	A	¹ H NMR (300 MHz, cd3od) δ 7.41-7.57 (m, 1H), 6.98-7.14 (m, 2H), 6.71-6.90 (m, 2H), 6.32-6.43 (m, 1H), 6.24-6.32 (m, 2H), 4.44-4.65 (m, 2H), 3.80-4.08 (m, 3H), 3.42-3.68 (m, 2H), 2.85-3.10 (m, 2H), 2.47-2.65 (m, 2H), 1.01-1.19 (m, 6H)	2.15	99% remaining at 1 h	75% remaining at 1 h	25% remaining at 1 h
51	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-amino-3-(1H-indol-3-yl)propanamido]pentanoate	4	569	A	¹ H NMR (300 MHz, cd3od) δ 7.62 (d, J=8.20 Hz, 1H), 7.29-7.54 (m, 2H), 6.93-7.29 (m, 3H), 6.33-6.48 (m, 1H), 6.18-6.32 (m, 2H), 4.44-4.66 (m, 2H), 3.96-4.18 (m, 1H), 3.76-3.95 (m, 2H), 3.60 (s, 1H), 2.90-3.30 (m, 4H), 2.10-2.37 (m, 2H), 1.14-1.48 (m, 5H), 0.97-1.14 (m, 6H)	5.19	94% remaining at 1 h	83% remaining at 1 h	2% remaining at 1 h
52	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[(2S)-2-amino-3-(1H-indol-3-yl)propanamido]propanoate	3.8	541	A	¹ H NMR (300 MHz, cd3od) δ 7.55-7.68 (m, 1H), 7.34-7.51 (m, 2H), 7.00-7.26 (m, 3H), 6.10-6.39 (m, 3H), 4.18-4.54 (m, 2H), 3.95-4.12 (m, 1H), 3.70-3.88 (m, 2H), 3.44-3.65 (m, 2H), 3.02-3.30 (m, 2H), 2.36-2.61 (m, 2H), 1.07 (d, J=5.86 Hz, 6H)	2.5	95% remaining at 1 h	81% remaining at 1 h	61% remaining at 1 h
53	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(2-[[tert-butoxy]carbonyl](methyl)amino]acetamido)pentanoate	4.9	554	A	¹ H NMR (300 MHz, cd3od) δ 7.37-7.60 (m, 1H), 6.36-6.48 (m, 1H), 6.30 (d, J=1.76 Hz, 2H), 4.56-4.70 (m, 2H), 3.82-4.03 (m, 4H), 3.65 (s, 1H), 3.16-3.31 (m, 2H), 2.97 (d, J=1.76 Hz, 3H), 2.43 (dt, J=1.76, 7.03 Hz, 2H), 1.37-1.81 (m, 14H), 1.12 (dd, J=2.05, 6.15 Hz, 6H)	34.3	92% remaining at 1 h	98% remaining at 1 h	0% remaining at 1 h
54	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-(2-[[tert-butoxy]carbonyl](methyl)amino]acetamido)propanoate	4.7	526	A	¹ H NMR (300 MHz, cd3od) δ 7.51 (d, J=2.93 Hz, 1H), 6.43 (d, J=2.93 Hz, 1H), 6.31 (s, 2H), 6.23-6.35 (m, 1H), 4.55-4.72 (m, 2H), 3.92 (s, 4H), 3.44-3.72 (m, 3H), 2.94 (s, 3H), 2.63 (t, J=6.44 Hz, 2H), 1.38-1.62 (m, 9H), 1.13 (d, J=6.44 Hz, 6H)	31.4	93% remaining at 1 h	87% remaining at 1 h	74% remaining at 1 h
55	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[2-(methylamino)acetamido]pentanoate	3.3	454	A	¹ H NMR (300 MHz, cd3od) δ 7.49-7.68 (m, 1H), 6.62 (d, J=2.93 Hz, 1H), 6.39 (s, 2H), 4.73 (t, J=5.57 Hz, 2H), 4.02 (t, J=5.86 Hz, 2H), 3.91 (s, 2H), 3.75 (td, J=5.93, 12.16 Hz, 1H), 3.33-3.43 (m, 2H), 2.88 (s, 3H), 2.43-2.63 (m, 2H), 1.53-1.90 (m, 5H), 1.09-1.29 (m, 6H)	2.44	100% remaining at 1 h	98% remaining at 1 h	1% remaining at 1 h

56	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[2-(methylamino)acetamido]propanoate	3.2	426	A	¹ H NMR (300 MHz, cd3od) δ 7.18-7.40 (m, 1H), 6.25 (d, J=1.17 Hz, 1H), 6.11 (br. s., 2H), 4.35-4.53 (m, 2H), 3.74 (d, J=1.17 Hz, 2H), 3.54-3.67 (m, 2H), 3.46-3.69 (m, 3H), 3.32-3.54 (m, 3H), 3.23-3.23 (m, 1H), 2.55-2.65 (m, 3H), 2.39-2.54 (m, 2H), 0.89-1.01 (m, 6H)	1.44	64% remaining at 1 h	1% remaining at 1 h	0% remaining at 1 h
57	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[2-(2-[[[tert-butoxy]carbonyl]amino]-N-methylacetamido]acetamido]pentanoate	4.7	611	A	¹ H NMR (300 MHz, cd3od) δ 7.43 (d, J=2.93 Hz, 1H), 6.56-6.68 (m, 1H), 6.50-6.50 (m, 1H), 6.30-6.44 (m, 1H), 6.23 (s, 2H), 4.56 (t, J=5.57 Hz, 2H), 3.91-4.11 (m, 2H), 3.78-3.91 (m, 2H), 3.58 (quin, J=6.15 Hz, 1H), 3.13-3.27 (m, 1H), 2.88-3.11 (m, 2H), 2.27-2.47 (m, 2H), 2.08-2.08 (m, 1H), 1.32-1.71 (m, 12H), 1.00-1.16 (m, 6H)	2.8	81% remaining at 1 h	96% remaining at 1 h	0% remaining at 1 h
58	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[2-(2-[[[tert-butoxy]carbonyl]amino]-N-methylacetamido]acetamido]propanoate	4.5	583	A	¹ H NMR (300 MHz, cd3od) δ 7.82-7.95 (m, 2H), 7.28-7.45 (m, 4H), 6.54 (d, J=3.51 Hz, 2H), 6.09-6.25 (m, 2H), 3.21-3.28 (m, 4H), 2.87-3.03 (m, 4H), 2.38 (d, J=1.17 Hz, 6H), 2.18 (s, 6H)	2.87	77% remaining at 1 h	84% remaining at 1 h	49% remaining at 1 h
59	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[2-(2-amino-N-methylacetamido]acetamido]pentanoate	3.4	511	A	¹ H NMR (300 MHz, cd3od) δ 7.33-7.48 (m, 1H), 6.36 (d, J=2.93 Hz, 1H), 6.24 (s, 2H), 4.51-4.61 (m, 2H), 3.79-4.13 (m, 7H), 3.50-3.68 (m, 1H), 3.12-3.26 (m, 3H), 3.03 (s, 2H), 2.28-2.43 (m, 2H), 1.41-1.70 (m, 4H), 1.00-1.09 (m, 6H)	<2.54	95% remaining at 1 h	98% remaining at 1 h	11% remaining at 1 h
60	trifluoroacetic acid methyl 2-[[[3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl]carbonyl]pyrrolidine-1-carboxylate	4.1	510	A	¹ H NMR (300 MHz, cd3od) δ 8.07 (br. s., 1H), 7.45 (d, J=2.93 Hz, 1H), 6.36 (d, J=2.93 Hz, 1H), 6.24 (s, 2H), 4.49-4.62 (m, 2H), 4.16 (dd, J=2.93, 8.20 Hz, 1H), 3.85 (t, J=5.57 Hz, 2H), 3.35-3.72 (m, 9H), 2.43-2.65 (m, 2H), 1.74-2.25 (m, 4H), 0.95-1.17 (m, 6H)	6.11	99% remaining at 1 h	88% remaining at 1 h	37% remaining at 1 h
61	trifluoroacetic acid methyl 2-[[[5-oxo-5-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]pentyl]carbonyl]pyrrolidine-1-carboxylate	4.3	538	A	¹ H NMR (300 MHz, cd3od) δ 7.36-7.55 (m, 1H), 6.35 (d, J=2.93 Hz, 1H), 6.24 (s, 2H), 4.56 (t, J=5.86 Hz, 2H), 4.10-4.23 (m, 1H), 3.85 (t, J=5.57 Hz, 2H), 3.34-3.72 (m, 6H), 3.16 (s, 2H), 2.26-2.43 (m, 2H), 1.80-2.00 (m, 3H), 1.40-1.71 (m, 5H), 0.99-1.11 (m, 6H)	9.71	98% remaining at 1 h	92% remaining at 1 h	0% remaining at 1 h
62	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[[[(2S)-1-carbamoylpyrrolidin-2-yl]formamido]propanoate	3.6	495	A	¹ H NMR (300 MHz, cd3od) δ 7.45 (d, J=2.93 Hz, 1H), 6.36 (d, J=3.51 Hz, 1H), 6.24 (d, J=2.93 Hz, 2H), 4.57 (t, J=5.57 Hz, 2H), 4.21-4.34 (m, 1H), 3.85 (t, J=5.86 Hz, 2H), 3.33-3.71 (m, 5H), 2.43-2.61 (m, 2H), 2.03-2.22 (m, 1H), 1.86-2.01 (m, 3H), 1.06 (d, J=5.86 Hz, 6H)	1.62	99% remaining at 1 h	99% remaining at 1 h	91% remaining at 1 h

63	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[[[(2S)-1-methyl-5-oxopyrrolidin-2-yl]formamido]pentanoate	4	508	A	1H NMR (300 MHz, cd3od) δ 7.43 (d, $J=2.93$ Hz, 1H), 6.35 (d, $J=2.93$ Hz, 1H), 6.24 (s, 2H), 4.57 (t, $J=5.86$ Hz, 2H), 4.00-4.18 (m, 1H), 3.85 (t, $J=5.86$ Hz, 2H), 3.58 (quin, $J=6.00$ Hz, 1H), 3.11-3.25 (m, 3H), 2.67-2.81 (m, 3H), 2.17-2.54 (m, 6H), 1.84-2.07 (m, 1H), 1.33-1.70 (m, 5H), 0.96-1.13 (m, 6H)	2	97% remaining at 1h	98% remaining at 1h	0% remaining at 1h
64	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-[[[(2S)-1-methyl-5-oxopyrrolidin-2-yl]formamido]propanoate	3.7	480	A	1H NMR (300 MHz, cdcl3) δ 8.67 (d, $J=4.69$ Hz, 4H), 7.89 (d, $J=8.20$ Hz, 2H), 7.69 (s, 2H), 7.47-7.61 (m, 6H), 6.52 (d, $J=2.93$ Hz, 2H), 6.14 (d, $J=2.34$ Hz, 2H), 3.15-3.47 (m, 4H), 2.98 (t, $J=7.62$ Hz, 4H), 2.41 (s, 6H), 2.11-2.27 (m, 6H)	<1.90	98% remaining at 1h	97% remaining at 1h	76% remaining at 1h
65	trifluoroacetic acid ethyl 2-[(5-oxo-5-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]pentyl)carbamoyl]pyrrolidine-1-carboxylate	4.5	552	A	1H NMR (300 MHz, cd3od) δ 7.38-7.51 (m, 1H), 6.32-6.39 (m, 1H), 6.19-6.29 (m, 2H), 4.49-4.59 (m, 2H), 3.96-4.25 (m, 3H), 3.75-3.92 (m, 2H), 3.35-3.74 (m, 3H), 3.04-3.21 (m, 2H), 2.03-2.41 (m, 4H), 1.81-2.01 (m, 3H), 1.42-1.72 (m, 5H), 1.10-1.31 (m, 3H), 0.99-1.09 (m, 6H)	18.6	87% remaining at 1h	89% remaining at 1h	20% remaining at 1h
66	trifluoroacetic acid ethyl 2-[(3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl)carbamoyl]pyrrolidine-1-carboxylate	4.3	524	A	1H NMR (300 MHz, cd3od) δ 7.45 (d, $J=2.93$ Hz, 1H), 6.36 (d, $J=2.93$ Hz, 1H), 6.24 (s, 2H), 4.44-4.63 (m, 2H), 3.92-4.23 (m, 3H), 3.76-3.92 (m, 2H), 3.35-3.69 (m, 6H), 2.42-2.61 (m, 2H), 2.03-2.28 (m, 1H), 1.71-1.97 (m, 3H), 1.09-1.36 (m, 3H), 0.99-1.09 (m, 6H)	7.36	96% remaining at 1h	80% remaining at 1h	75% remaining at 1h
67	trifluoroacetic acid propan-2-yl 2-[(5-oxo-5-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]pentyl)carbamoyl]pyrrolidine-1-carboxylate	4.7	566	A	1H NMR (300 MHz, cd3od) δ 7.38-7.51 (m, 1H), 6.30-6.42 (m, 1H), 6.17-6.30 (m, 2H), 4.75-4.83 (m, 1H), 4.48-4.64 (m, 2H), 4.08-4.26 (m, 1H), 3.73-3.94 (m, 3H), 3.35-3.70 (m, 4H), 3.10-3.25 (m, 3H), 2.05-2.43 (m, 4H), 1.77-2.00 (m, 4H), 1.36-1.71 (m, 6H), 1.10-1.33 (m, 8H), 0.90-1.10 (m, 8H)	28.4	92% remaining at 1h	93% remaining at 1h	57% remaining at 1h
68	trifluoroacetic acid propan-2-yl 2-[(3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl)carbamoyl]pyrrolidine-1-carboxylate	4.6	538	A	1H NMR (300 MHz, cd3od) δ 7.35-7.58 (m, 1H), 6.36 (d, $J=2.93$ Hz, 1H), 6.20-6.30 (m, 2H), 4.78-4.84 (m, 1H), 4.40-4.65 (m, 2H), 4.07-4.25 (m, 1H), 3.75-3.93 (m, 2H), 3.35-3.69 (m, 6H), 2.43-2.63 (m, 2H), 2.00-2.31 (m, 1H), 1.71-1.96 (m, 4H), 1.10-1.31 (m, 7H), 1.01-1.08 (m, 6H)	22.6	76% remaining at 1h	69% remaining at 1h	100% remaining at 1h
69	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[[[(2S)-1-carbamoylpyrrolidin-2-yl]formamido]pentanoate	3.8	523	A	1H NMR (300 MHz, cd3od) δ 7.43 (d, $J=3.51$ Hz, 1H), 6.35 (d, $J=2.93$ Hz, 1H), 6.23 (s, 2H), 6.22-6.32 (m, 2H), 4.49-4.67 (m, 2H), 4.15-4.38 (m, 1H), 3.79-3.92 (m, 2H), 3.33-3.72 (m, 3H), 3.08-3.22 (m, 2H), 2.27-2.42 (m, 2H), 1.85-2.27 (m, 4H), 1.35-1.70 (m, 4H), 0.91-1.15 (m, 6H)	2.17	84% remaining at 1h	94% remaining at 1h	7% remaining at 1h

EXAMPLE 70:

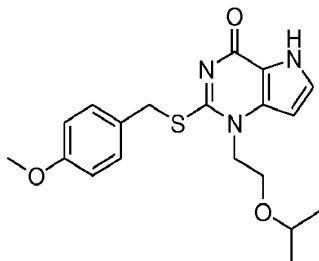


1-[2-(Propan-2-yloxy)ethyl]-2-sulfanylidene-3-[[2-(trimethylsilyl)ethoxy]methyl]-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one. To a solution of 2,3-dihydro-1-(2-isopropoxyethyl)-2-thioxo-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (250 mg, 1.0 mmol) in 5.0 mL DMF was added DIPEA (365 μ L, 2.1 mmol) and (2-(chloromethoxy)ethyl)trimethylsilane (195 μ L, 1.1 mmol). The reaction was stirred overnight at room temperature. The reaction was quenched by the addition of water and extracted with EtOAc. The organic layer was washed with brine and the solvent was removed *in vacuo*. Crude product was purified by normal phase chromatography (12 g column, 0-70% MeOH/DCM) where the product fractions were combined and concentrated *in vacuo* to provide the pure product as a solid (58 mg, 15%). ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 11.00-11.30 (m, 1H), 7.10-7.33 (m, 1H), 6.25 (t, $J=2.34$ Hz, 1H), 6.12 (s, 2H), 4.68 (t, $J=5.86$ Hz, 2H), 3.71-3.97 (m, 4H), 3.48-3.67 (m, 1H), 0.94-1.19 (m, 7H), -0.16-0.10 (m, 7H). LC/MS method A: R_t = 6.2 mins ($M+H$) $^+$ = 384, purity > 95%. Caco-2 P_{app} = 232, SGF = 96% remaining at 1h, SIF = 99% remaining at 1h, *h*Plasma 99% remaining at 1h.

Additional compounds prepared according to EXAMPLE 70:

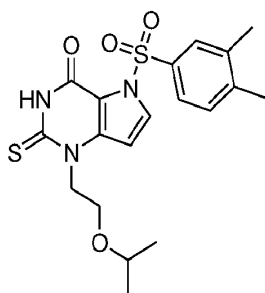
Example	Name	LCMS retention time	$M+H^+$	LCMS method	NMR	Caco-2 P_{app} (nm/s)	SGF	SIF	human Plasma stability
71	1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-3,5-bis-[[2-(trimethylsilyl)ethoxy]methyl]-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	7.8	514	A	^1H NMR (300 MHz, cdCl_3) δ 7.09-7.23 (m, 1H), 6.25 (d, $J=2.93$ Hz, 1H), 6.05 (s, 2H), 5.74 (s, 2H), 4.58-4.74 (m, 2H), 3.70-3.93 (m, 5H), 3.45-3.68 (m, 4H), 0.80-1.12 (m, 11H), -0.12-0.12 (m, 18H)	1.78	98% remaining at 1h	88% remaining at 1h	58% remaining at 1h
72	1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-5-[[2-(trimethylsilyl)ethoxy]methyl]-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	5.8	384	A	^1H NMR (300 MHz, cdCl_3) δ 9.19-9.38 (m, 1H), 7.20 (s, 1H), 6.27 (d, $J=3.52$ Hz, 1H), 5.70 (s, 2H), 4.55 (t, $J=5.57$ Hz, 2H), 3.86 (t, $J=5.86$ Hz, 2H), 3.44-3.68 (m, 3H), 1.07 (d, $J=5.86$ Hz, 6H), 0.82-0.99 (m, 2H), -0.11-0.04 (m, 9H)	264	97% remaining at 1h	98% remaining at 1h	78% remaining at 1h
73	1-[2-(propan-2-yloxy)ethyl]-5-[[2-(trimethylsilyl)ethoxy]methyl]-2-[[2-(trimethylsilyl)ethoxy]methyl]sulfanylidene-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	5.8	514	A	^1H NMR (300 MHz, cdCl_3) δ 7.12-7.21 (m, 1H), 6.21 (s, 1H), 5.89 (s, 2H), 5.61 (s, 2H), 4.21-4.34 (m, 2H), 3.76 (s, 8H), 1.02-1.17 (m, 6H), 0.92 (td, $J=8.20$, 17.57 Hz, 4H), -0.13-0.08 (m, 18H)	<7.17	35% remaining at 1h	55% remaining at 1h	99% remaining at 1h

EXAMPLE 74:



- 2-[[[4-Methoxyphenyl)methyl]sulfanyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one.** A solution of 2,3-dihydro-1-(2-isopropoxyethyl)-2-thioxo-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (100 mg, 400 μ mol) in THF (2.0 mL) was treated with lithium hexamethyldisilylamide (1.0 M in THF, 840 μ L, 840 μ mol) and stirred for 20 mins. 1-(chloromethyl)-4-methoxybenzene (114 μ L, 840 μ mol) was added and the mixture was stirred overnight. The reaction was quenched by the addition of water and extracted with EtOAc. The organic layer was washed with
- brine and the solvent was removed *in vacuo*. Crude product was purified by normal phase chromatography (12 g column, 20-100% EtOAc/hexanes) but the material did not elute. The column was flushed with 10% MeOH/DCM where the product fractions were combined and concentrated *in vacuo* to provide the pure product as a solid (34 mg, 23%). ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 7.30-7.48 (m, 3H), 6.76-6.96 (m, 2H), 6.09-6.27 (m, 1H), 4.59 (s, 2H), 4.27 (t, $J=6.15$ Hz, 2H), 3.67-3.83 (m, 5H), 3.51 (td, $J=5.93, 12.16$ Hz, 1H), 1.06 (d, $J=6.44$ Hz, 6H). LC/MS method A: $R_t = 4.4$ mins ($M+H$) $^+ = 374$, purity > 95%. SGF = 37% remaining at 1 h, SIF = 97% remaining at 1 h, *h*Plasma stability = 97% remaining at 1 h.

EXAMPLE 75:



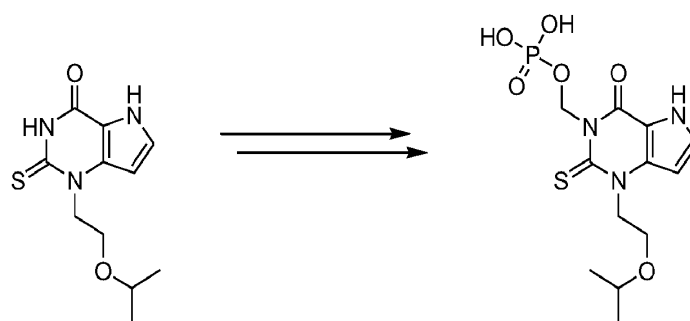
20

5-(3,4-Dimethylbenzenesulfonyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanyl-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one. A solution of 2,3-dihydro-1-(2-isopropoxyethyl)-2-thioxo-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (100 mg, 400 μ mol) in THF (2.0 mL) was treated with lithium hexamethyldisilylamide (1.0 M in THF, 840 μ L, 840 μ mol) and stirred for 20 mins. 3,4-Dimethylbenzene-1-sulfonyl chloride (171 mg, 840 μ mol) was added and the mixture was stirred overnight. The reaction was quenched by the addition of water and extracted with EtOAc. The organic layer was washed with brine and the solvent was removed *in vacuo*. Crude product was purified by normal phase chromatography (12 g column, 15-65% EtOAc/hexanes) where the product fractions were combined and concentrated *in vacuo* to provide the pure product as a solid (28 mg, 17%). ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 9.12-9.29 (m, 1H), 7.67-7.95 (m, 3H), 7.30 (s, 1H), 6.44 (dd, $J=1.17, 3.51$ Hz, 1H), 4.35-4.58 (m, 2H), 3.70-3.88 (m, 2H), 3.40-3.62 (m, 1H), 2.18-2.41 (m, 7H), 1.47-1.64 (m, 2H), 0.96-1.07 (m, 6H). LC/MS method A: $R_t = 5.4$ mins ($M+H$) $^+ = 422$, purity > 95%. SGF = 99% remaining at 1 h, SIF = 91% remaining at 1 h, *h*Plasma stability = 100% remaining at 1 h.

Additional compounds prepared according to EXAMPLE 75:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
76	5-methanesulfonyl-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	4.1	332	A	¹ H NMR (300 MHz, cdcl ₃) δ 9.59-9.87 (m, 1H), 7.65 (d, J=3.51 Hz, 1H), 6.46 (d, J=3.51 Hz, 1H), 4.55 (t, J=5.27 Hz, 2H), 3.66-3.96 (m, 5H), 3.55 (td, J=5.93, 12.16 Hz, 1H), 1.25 (s, 2H), 0.97-1.16 (m, 6H)		96% remaining at 1 h	91% remaining at 1 h	98% remaining at 1 h
77	5-(ethanesulfonyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	4.4	346	A	¹ H NMR (300 MHz, cdcl ₃) δ 7.55-7.71 (m, 1H), 6.46 (d, J=3.52 Hz, 1H), 4.55 (t, J=4.98 Hz, 2H), 4.01 (q, J=7.62 Hz, 2H), 3.85 (t, J=5.27 Hz, 2H), 3.45-3.64 (m, 1H), 1.25-1.51 (m, 5H), 1.06 (d, J=5.86 Hz, 6H)		99% remaining at 1 h	96% remaining at 1 h	98% remaining at 1 h
78	5-(benzenesulfonyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	4.9	394	A	¹ H NMR (300 MHz, cdcl ₃) δ 9.50-9.78 (m, 1H), 8.16 (d, J=7.62 Hz, 2H), 7.82 (d, J=3.52 Hz, 1H), 7.43-7.71 (m, 3H), 6.47 (d, J=3.52 Hz, 1H), 4.41-4.60 (m, 2H), 3.73-3.88 (m, 2H), 3.37-3.62 (m, 1H), 1.04 (d, J=5.86 Hz, 6H)		100% remaining at 1 h	80% remaining at 1 h	96% remaining at 1 h
79	5-(2-fluorobenzenesulfonyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	5	412	A	¹ H NMR (300 MHz, cdcl ₃) δ 9.42 (br. s., 1H), 8.34-8.56 (m, 1H), 7.81-7.98 (m, 1H), 7.58-7.76 (m, 1H), 7.32-7.49 (m, 1H), 7.02-7.21 (m, 1H), 6.36-6.56 (m, 1H), 4.41-4.60 (m, 2H), 3.82 (t, J=5.27 Hz, 2H), 3.34-3.66 (m, 1H), 0.95-1.12 (m, 6H)		92% remaining at 1 h	82% remaining at 1 h	98% remaining at 1 h
80	5-(2-methylbenzenesulfonyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	5.2	408	A	¹ H NMR (300 MHz, cdcl ₃) δ 9.15-9.35 (m, 1H), 8.34-8.49 (m, 1H), 7.90 (dd, J=2.05, 3.81 Hz, 1H), 7.28-7.65 (m, 3H), 6.39-6.57 (m, 1H), 4.41-4.60 (m, 2H), 3.82 (dt, J=2.34, 5.27 Hz, 2H), 3.45-3.64 (m, 1H), 2.42 (s, 3H), 1.05 (dd, J=2.05, 6.15 Hz, 6H)		90% remaining at 1 h	87% remaining at 1 h	99% remaining at 1 h

EXAMPLE 81:



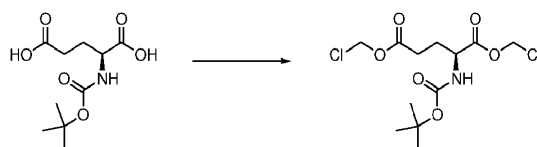
5 **{{4-Oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-3-yl)methoxy}phosphonic acid:**

A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (506 mg, 2.0 mmol) in DMF (8 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 1.8 mL, 1.8 mmol) and stirred for 15 mins.

Di-tert-butyl chloromethyl phosphate (520 mg, 2.0 mmol) was added *via* syringe with continued stirring of the reaction mixture overnight, followed by purification with RP-HPLC (Method D). The later fractions of similar retention time containing the desired product were combined and lyophilized to provide the di-tert-butyl protected intermediate (130 mg, 13.7%). Deprotection of tert-butyl protecting groups was carried out with glacial acetic acid and water (4:1 v/v) at 75° C for 30 mins. followed by stirring at room temperature overnight. The reaction mixture was purified by RP-HPLC (Method D), and similar fractions were lyophilized to provide the title compound as a white solid (54 mg). ¹H NMR (300 MHz, DMSO-*d*₆) δ = 12.50 (br s, 1H), 7.43 (t, *J*=2.9 Hz, 1H), 6.34 (t, *J*=2.6 Hz, 1H), 6.23 (d, *J*=4.7 Hz, 2H), 4.58 (t, *J*=6.4 Hz, 2H), 3.74 (t, *J*=6.2 Hz, 2H), 3.62 - 3.49 (m, 1H), 1.01 (d, *J*=6.1 Hz, 6H). LC/MS method A: *R*_t = 3.02 mins., (M+H)⁺ = 364, purity = 99%.

Additional compounds prepared according to EXAMPLE 81:

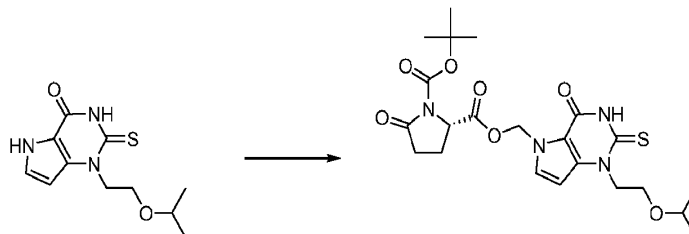
Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
83	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)phosphonic acid	2.82 mins	364		¹ H NMR (300 MHz, dmsO) δ 12.26 (s, 1H), 7.50 (d, <i>J</i> = 3.1 Hz, 1H), 6.31 (d, <i>J</i> = 3.1 Hz, 1H), 5.84 (d, <i>J</i> = 10.5 Hz, 2H), 4.48 (dd, <i>J</i> = 23.0, 16.8 Hz, 2H), 3.69 (dd, <i>J</i> = 12.2, 6.2 Hz, 2H), 3.54 (dt, <i>J</i> = 12.3, 6.2 Hz, 1H), 1.00 (dd, <i>J</i> = 6.1, 1.3 Hz, 6H).	<10.7	91% @ 1h	100% @ 1h	95% @ 1h



1,5-Dichloromethyl (2S)-2-(((tert-butoxy)carbonyl)amino)pentanedioate: A solution of (2S)-2-(((tert-butoxy)carbonyl)amino)pentanedioic acid (2.5 g, 10.11 mmol), tetrabutylammonium hydrogen sulfate (679 mg, 2.0 mmol), and sodium carbonate (4.54 g, 54 mmol) was dissolved in dichloromethane and water (50:50 v/v, 52 mL) and cooled at 0° C on an ice bath. Chloromethyl chlorosulfonate (2.42 mL, 24.3 mmol) was added dropwise and the reaction was warmed to room temperature with stirring overnight. The reaction was poured into a separatory funnel and separated. The aqueous layer was extracted one more time with dichloromethane and the combined organic fractions were washed with water and dried over magnesium sulfate and concentrated. The was purified by flash chromatography providing the titled compound (400 mg, 11.5%). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 5.84 – 5.59 (m,

4H), 5.07 (br d, $J = 7.6$ Hz, 1H), 4.45 – 4.31 (m, 1H), 2.62 – 2.41 (m, 2H), 2.33 – 2.17 (m, 1H), 2.11 – 1.90 (m, 1H), 1.44 (s, 9H).

EXAMPLE 85:

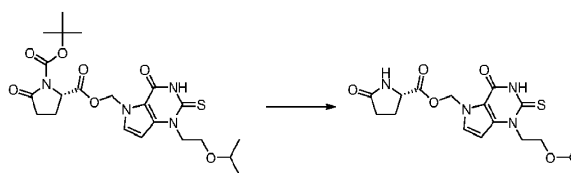


5

1-tert-Butyl 2-{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl (2S)-5-oxopyrrolidine-1,2-dicarboxylate: A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (25 mg, 98.7 μ mol) in DMF (1.5 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 197 μ L, 197 μ mol) and stirred for 15 mins. 1,5-Dichloromethyl (2S)-2-[(tert-butoxy)carbonyl]amino}pentanedioate (34 mg, 197 μ mol) in DMF (1.0 mL) was added *via* syringe with continued stirring of the reaction mixture overnight, followed by purification with RP-HPLC (Method D). Fractions containing the rearrangement product were freeze-dried and analysis determined the structure as the title compound, an orange solid (36.8 mg, 75.4%). ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ = 12.40 (s, 1H), 7.56 (d, $J = 3.0$ Hz, 1H), 6.41 (d, $J = 3.1$ Hz, 1H), 6.26 (d, $J = 5.5$ Hz, 2H), 4.64 - 4.54 (m, 1H), 4.46 (br t, $J = 5.9$ Hz, 2H), 3.69 (br t, $J = 6.0$ Hz, 2H), 3.63 - 3.32 (m, 1H), 2.44 - 2.32 (m, 2H), 2.25 (br s, 1H), 1.89 (br s, 1H), 1.40 (br d, $J = 5.6$ Hz, 1H), 1.28 (s, 9H), 0.99 (d, $J = 6.1$ Hz, 6H). LC/MS: R_t = 4.34 mins., $(\text{M} + \text{H})^+ = 395$, minus t-Boc, purity = 100%. Caco-2 P_{app} = 65.4 nm/s, SGF = 78% remaining at 1 h, SIF = 90% remaining at 1 h, hPlasma stability = 30% remaining at 1 h.

20

EXAMPLE 86:

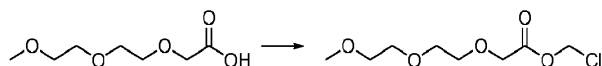


{4-Oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl(2S)-5-oxopyrrolidine-2-carboxylate: Trifluoroacetic acid in dichloromethane (30% v/v, 1 mL) was added to 1-tert-butyl 2-{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-

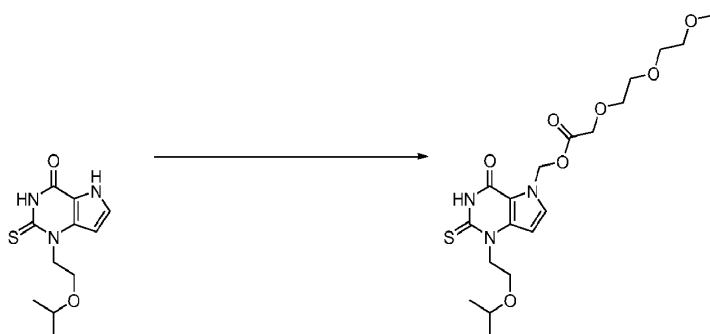
25

pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-5-oxopyrrolidine-1,2-dicarboxylate (15.5 mg, 31.4 μ mol) and stirred at room temperature for 20 minutes. The reaction was concentrated and purified by RP-HPLC (Method B), with fractions containing product freeze-dried giving the titled compound as a white solid (5.3 mg, 42.9%). ^1H NMR (300 MHz, DMSO- d_6) δ 12.39 (s, 1H), 8.00 (s, 1H), 7.55 (d, J = 3.1 Hz, 1H), 6.40 (d, J = 3.2 Hz, 1H), 6.27 – 6.12 (m, 2H), 4.46 (t, J = 6.0 Hz, 2H), 4.28 – 4.05 (m, 1H), 3.70 (t, J = 6.0 Hz, 2H), 3.51 (tt, J = 12.5, 6.3 Hz, 1H), 2.43 – 2.22 (m, 1H), 2.07 (dd, J = 10.0, 6.2 Hz, 2H), 1.91 (ddd, J = 11.7, 9.4, 5.8 Hz, 1H), 0.98 (d, J = 6.0 Hz, 6H). LC/MS method A: R_t = 3.45 mins., $(\text{M}+\text{H})^+$ = 395, purity > 95%. Caco-2 P_{app} = 2.4 nm/s, SGF = 98% remaining at 1 h, SIF = 17% remaining at 1 h, h Plasma stability = 0% remaining at 1 h.

EXAMPLE 87:



Chloromethyl 2-[2-(2-methoxyethoxy)ethoxy]acetate: A solution of 2-[2-(2-methoxyethoxy)ethoxy]acetic acid (2.08 mL, 13.5 mmol), tetrabutylammonium hydrogen sulfate (458 mg, 1.35 mmol), and sodium carbonate (4.54 g, 54 mmol) was dissolved in dichloromethane and water (50:50 v/v, 57 mL) and cooled at 0°C on an ice bath. Chloromethyl chlorosulfonate (1.62 mL, 16.2 mmol) was added dropwise and the reaction was warmed to room temperature with stirring overnight. The reaction was poured into a separatory funnel and separated. The aqueous layer was extracted one more time with dichloromethane and the combined organic fractions were washed with water and dried over magnesium sulfate and concentrated to provide the crude product (1.67 g), which was purified by flash chromatography eluting with a gradient of hexane to 50% ethyl acetate in hexane. The product, chloromethyl 2-[2-(2-methoxyethoxy)ethoxy]acetate, was isolated as a clear oil in appearance (990 mg, 32.4%). ^1H NMR (300 MHz, CHLOROFORM- d) δ 5.77 (s, 2H), 4.25 (s, 2H), 3.77 (m, 2H), 3.73 – 3.68 (m, 2H), 3.68 – 3.61 (m, 2H), 3.60 – 3.50 (m, 2H), 3.39 (s, 3H). LC/MS method A: R_t = 3.11 mins., $(\text{M}+\text{H})^+$ = 249 with sodium +23, purity = 100%.

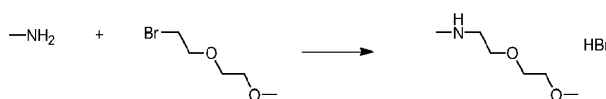


{{4-Oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-3-yl}methoxy)phosphonic acid: A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-

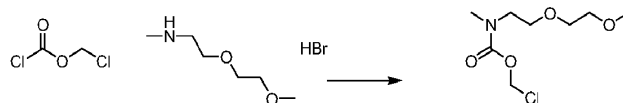
5 1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (150 mg, 592 μ mol) in DMF (1 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 1.18 mL, 1.18 mmol) and stirred for 10 mins. Chloromethyl 2-[2-(2-methoxyethoxy)ethoxy]acetate (267 mg, 1.18 mmol) dissolved in DMF (1 mL) was added *via* syringe with continued stirring of the reaction mixture overnight, followed by purification with RP-HPLC (Method D). For further purification RP-HPLC (Method B) provided 130 mg, with pure fractions
 10 yielding the desired product for testing (10 mg). ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 7.31 – 7.28 (m, 1H), 6.30 (s, 2H), 6.26 (d, J = 3.2 Hz, 1H), 4.53 (t, J = 5.6 Hz, 2H), 4.18 (s, 2H), 3.84 (t, J = 5.6 Hz, 2H), 3.77 – 3.50 (m, 9H), 3.37 (s, 3H), 1.07 (d, J = 6.1 Hz, 6H). LC/MS method A: R_t = 3.92 mins., $(\text{M}+\text{H})^+ = 444$, purity = 98%. Caco-2 P_{app} = 70.5 nm/s, SGF = 97% remaining at 1 h, SIF = 28% remaining at 1 h, *h*Plasma stability = 0% remaining at 1 h.

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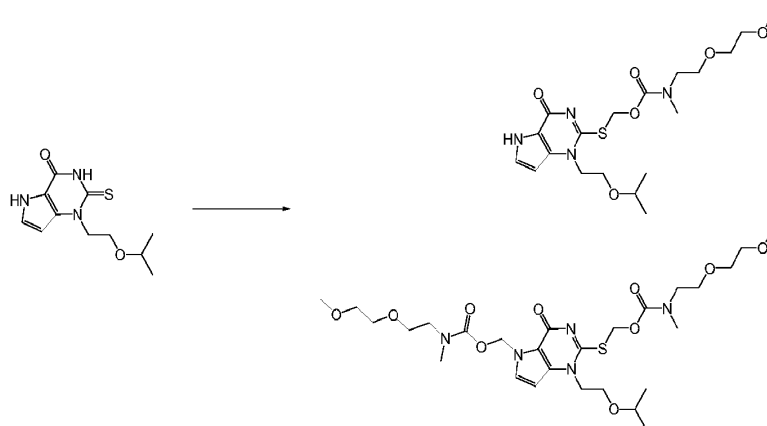
EXAMPLES 88 and 89:



[2-(2-Methoxyethoxy)ethyl](methyl)amine hydrobromide: 1-Bromo-2-(2-methoxyethoxy)ethane (942 μ L, 7 mmol) was dissolved in methyl ammonia in ethanol (10 mL, 33% by
 20 weight) and heated at 80 $^{\circ}\text{C}$ in a sealed tube overnight. The reaction was cooled to room temperature and concentrated to provide the desired product, in quantitative yield. ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 6.02 (s, 1H), 3.90 – 3.83 (m, 2H), 3.73 – 3.65 (m, 2H), 3.63 – 3.54 (m, 2H), 3.40 (s, 3H), 3.17 – 3.10 (m, 2H), 2.71 (s, 3H).



- Chloromethyl N-[2-(2-methoxyethoxy)ethyl]-N-methylcarbamate:** Di-isopropyl ethylamine (1.43 mL, 8.4 mmol) was added to [2-(2-Methoxyethoxy)ethyl](methyl)amine hydrobromide (642 mg, 3 mmol) in dichloromethane (10 mL) and cooled on an ice bath. Chloromethyl chloroformate was added dropwise and the reaction was warmed to room temperature overnight. The reaction was partitioned, separated, and the aqueous phase was extracted with dichloromethane (1x). The combined organic fractions were dried over magnesium sulfate and concentrated to provide 550 mg of crude product, which was purified using with flash chromatography eluting with a gradient of 10% ethyl acetate in hexane to 50% ethyl acetate in hexane. The titled compound was isolated as a clear oil (330 mg, 48.9%).
- ¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 5.79 (d, *J*=1.6 Hz, 2H), 3.82 - 3.42 (m, 8H), 3.38 (s, 3H), 3.02 (d, *J*=6.9 Hz, 3H).



- ({4-Oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl}sulfanyl)methyl N-[2-(2-methoxyethoxy)ethyl]-N-methylcarbamate and 2-[[[2-(2-methoxyethoxy)ethyl](methyl)carbamoyl]oxy]methyl sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl methyl N-[2-(2-methoxyethoxy)ethyl]-N-methylcarbamate:** A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (76 mg, 300 μ mol) in DMF (0.5 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 300 μ L, 300 μ mol) and stirred for 10 mins. Chloromethyl N-[2-(2-methoxyethoxy)ethyl]-N-

methylcarbamate (67.5 mg, 300 μ mol) in DMF (0.5 mL) was added slowly and the reaction was stirred overnight, followed by purification with RP-HPLC (Method D).

Spectra for EXAMPLE 88: **(4-Oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-[2-(2-methoxyethoxy)ethyl]-N-methylcarbamate**. ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 12.44 (s, 1H), 7.39 (t, *J* = 2.9 Hz, 1H), 6.23 – 6.21 (m, 1H), 6.06 (d, *J* = 2.1 Hz, 2H), 4.31 (t, *J* = 6.0 Hz, 2H), 3.75 (t, *J* = 6.0 Hz, 2H), 3.61 (m, 2H), 3.56 – 3.47 (m, 5H), 3.43 (m, 2H), 3.33 (d, *J* = 18.5 Hz, 3H), 2.97 (d, *J* = 17.8 Hz, 3H), 1.08 – 1.05 (m, 6H). LC/MS method A: *R*_t = 3.49 mins., (M+H)⁺ = 443, purity = 93%. Caco-2 *P*_{app} = 7.51 nm/s, SGF = 99% remaining at 1 h, SIF = 64% remaining at 1 h, *h*Plasma stability = 100% remaining at 1 h.

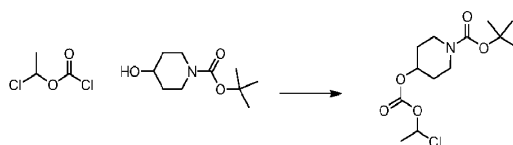
Spectra for EXAMPLE 89: **(2-[[[2-(2-methoxyethoxy)ethyl](methyl)carbamoyl]oxy)methyl]sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-[2-(2-methoxyethoxy)ethyl]-N-methylcarbamate**. ^1H NMR (300 MHz, CHLOROFORM-*d*) δ 7.37 (t, *J* = 3.2 Hz, 1H), 6.42 (d, *J* = 5.0 Hz, 2H), 6.17 (d, *J* = 3.2 Hz, 1H), 6.01 (s, 2H), 4.22 (t, *J* = 6.0 Hz, 2H), 3.75 – 3.67 (m, 2H), 3.66 – 3.41 (m, 17H), 3.40 – 3.33 (m, 6H), 2.96 (dd, *J* = 13.8, 9.1 Hz, 6H), 1.07 (d, *J* = 6.1 Hz, 6H). LC/MS method A: *R*_t = 3.87 mins., (M+H)⁺ = 632, purity = 100%. Caco-2 *P*_{app} = 4.88 nm/s, SGF = 99% remaining at 1 h, SIF = 65% remaining at 1 h, *h*Plasma stability = 100% remaining at 1 h.

Additional compounds prepared according to EXAMPLES 87-89:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
90	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl propan-2-yl carbonate	4.57 mins.	370		¹ H NMR (300 MHz, CDCl ₃) δ 9.14 (s, 1H), 7.38 – 7.19 (m, 1H), 6.26 (m, 3H), 4.89 (dd, J = 12.6, 6.3 Hz, 1H), 4.53 (t, J = 5.6 Hz, 2H), 3.84 (t, J = 5.6 Hz, 2H), 3.55 (dd, J = 12.3, 6.2 Hz, 1H), 1.28 (d, J = 6.2 Hz, 6H), 1.07 (d, J = 6.1 Hz, 6H).	180	77% remaining At 1h	56% remaining At 1h	0% remaining @ 1h
91	{4-oxo-2-[[[(propan-2-yloxy)carbonyloxy)methyl)sulfanyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl propan-2-yl carbonate	4.82 mins.	486		¹ H NMR (300 MHz, CDCl ₃) δ 7.43 – 7.11 (m, 1H), 6.44 (s, 2H), 6.29 – 6.14 (m, 1H), 6.00 (s, 2H), 5.09 – 4.73 (m, 2H), 4.33 – 4.07 (m, 2H), 3.71 (t, J = 5.9 Hz, 2H), 3.51 (hept, J = 6.1 Hz, 1H), 1.42 – 1.18 (m, 12H), 1.18 – 0.95 (m, 6H).	142	98% remaining At 1h	99% remaining At 1h	1% remaining @ 1h
92	1-{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)ethyl propan-2-yl carbonate	4.77 mins	384		¹ H NMR (300 MHz, CDCl ₃) δ 9.14 (s, 1H), 7.40 (q, J = 6.2 Hz, 1H), 7.30 (d, J = 3.2 Hz, 1H), 6.29 (d, J = 3.3 Hz, 1H), 4.95 – 4.79 (m, 1H), 4.52 (t, J = 5.8 Hz, 2H), 3.84 (t, J = 5.6 Hz, 2H), 3.55 (dd, J = 17.4, 11.8, 5.7 Hz, 1H), 1.81 (d, J = 6.2 Hz, 3H), 1.28 (d, J = 6.2 Hz, 3H), 1.26 – 1.23 (m, 3H), 1.08 (d, J = 6.1 Hz, 6H).	unstable	1% remaining At 1h	74% remaining At 1h	0% remaining @ 1h
93	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 3-(2-methoxyethoxy)propanoate	3.98 mins.	414		¹ H NMR (300 MHz, CDCl ₃) δ 9.16 (s, 1H), 7.29 – 7.27 (m, 1H), 6.26 (s, 2H), 6.25 (d, J = 3.2 Hz, 1H), 4.53 (t, J = 5.7 Hz, 2H), 3.84 (t, J = 5.7 Hz, 2H), 3.73 (t, J = 6.3 Hz, 2H), 3.63 – 3.52 (m, 4H), 3.51 – 3.46 (m, 3H), 3.35 (s, 3H), 2.64 (t, J = 6.3 Hz, 2H), 1.07 (d, J = 6.1 Hz, 6H).	168	99	38	0% remaining at 1 h
94	{(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(2,2,2-trifluoroethyl)carbamate	4.05 mins.	423		¹ H NMR (300 MHz, CDCl ₃) δ 12.01 (s, 1H), 7.42 (t, J = 3.1 Hz, 1H), 6.32 (m, 1H), 6.06 (d, J = 2.2 Hz, 2H), 4.37 (dd, J = 5.6, 3.7 Hz, 2H), 3.98 – 3.82 (m, 2H), 3.78 (dd, J = 9.5, 5.7 Hz, 2H), 3.57 – 3.45 (m, 1H), 3.04 (d, J = 14.2 Hz, 3H), 1.05 (d, J = 6.1 Hz, 6H).	151	99	95	99% remaining at 1 h
95	{2-[[[(methyl(2,2,2-trifluoroethyl)carbamoyloxy)methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(2,2,2-trifluoroethyl)carbamate	4.87 mins.	592		¹ H NMR (300 MHz, CDCl ₃) δ 7.45 (dd, J = 13.0, 3.3 Hz, 1H), 6.42 (d, J = 5.3 Hz, 2H), 6.31 – 6.27 (m, 1H), 5.98 (d, J = 7.0 Hz, 2H), 4.32 – 4.24 (m, 2H), 3.96 – 3.81 (m, 4H), 3.74 (d, J = 3.7 Hz, 2H), 3.55 – 3.45 (m, 1H), 3.03 (d, J = 9.5 Hz, 6H), 1.04 (dt, J = 7.7, 2.3 Hz, 6H).	188	100	95	99% remaining at 1 h
96	{(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N,N-bis(2,2,2-trifluoroethyl)carbamate	4.38 mins.	491		¹ H NMR (300 MHz, CDCl ₃) δ 7.45 (t, J = 3.8 Hz, 1H), 6.37 (t, J = 2.7 Hz, 1H), 6.09 (s, 2H), 4.39 (t, J = 5.4 Hz, 2H), 4.03 (dq, J = 16.9, 8.5 Hz, 4H), 3.78 (t, J = 5.6 Hz, 2H), 3.49 (dt, J = 12.3, 6.1 Hz, 1H), 1.24 – 0.82 (m, 6H).	203	98	97	98% remaining at 1 h

97	{2-([bis(2,2,2-trifluoroethyl)carbamoyloxy)methyl)sulfany]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N,N-bis(2,2,2-trifluoroethyl)carbamate	5.22 mins.	728	1H NMR (300 MHz, CDCl ₃) δ 7.33 (d, J = 3.3 Hz, 1H), 6.49 (s, 2H), 6.26 (d, J = 3.3 Hz, 1H), 6.06 (s, 2H), 4.24 (t, J = 5.6 Hz, 2H), 4.11 – 3.93 (m, 8H), 3.72 (t, J = 5.6 Hz, 2H), 3.53 – 3.41 (m, 1H), 1.03 – 1.00 (m, 6H).	308	98	96	99% remaining at 1 h
98	[3-([bis(2,2,2-trifluoroethyl)carbamoyloxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N,N-bis(2,2,2-trifluoroethyl)carbamate	5.76 mins.	728	1H NMR (300 MHz, CDCl ₃) δ 7.32 (d, J = 3.2 Hz, 1H), 6.69 (s, 2H), 6.33 (s, 2H), 6.26 (d, J = 3.2 Hz, 1H), 4.62 (t, J = 5.5 Hz, 2H), 4.15 – 3.91 (m, 8H), 3.86 (t, J = 5.5 Hz, 2H), 3.57 – 3.45 (m, 1H), 1.02 (d, J = 6.1 Hz, 6H).	65.3	95	80	99% remaining at 1 h

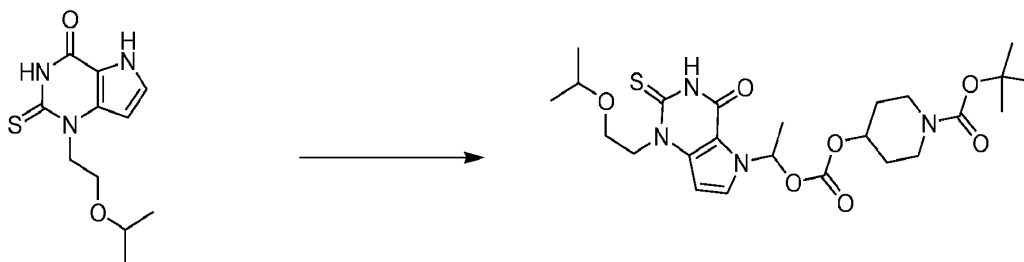
EXAMPLE 99:



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tert-Butyl 4-[[[1-(chloroethoxy)carbonyl]oxy]piperidine-1-carboxylate: Pyridine (647 μL, 8 mmol) was added to tert-butyl 4-hydroxypiperidine-1-carboxylate (1.61 g, 8 mmol) in dichloromethane (10 mL) and cooled on an ice bath. Chloroethyl chloroformate (826 μL, 8 mmol) was added dropwise and the reaction was warmed to room temperature overnight. Additional dichloromethane was added (20 mL) and washed with water (4 x 5 mL) and brine. After drying over magnesium sulfate and concentration under vacuum, purification *via* flash chromatography using a gradient of hexane to 40% ethyl acetate in hexane yielded the titled compound isolated as a clear oil (2.44 g, 99.1%). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 6.42 (q, *J* = 5.8 Hz, 1H), 4.85 (tt, *J* = 7.9, 3.8 Hz, 1H), 3.75 – 3.65 (m, 2H), 3.31 – 3.17 (m, 2H), 2.0 – 1.85 (m, 2H), 1.83 (d, *J* = 5.8 Hz, 3H), 1.80 – 1.60 (m, 2H), 1.45 (s, 9H).

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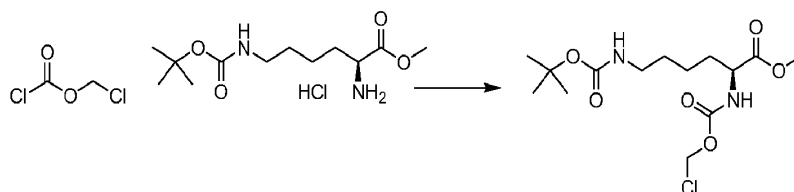
tert-Butyl 4-[[[1-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)ethoxy]carbonyl]oxy]piperidine-1-carboxylate: A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (101 mg, 400

μmol) in DMF (4.0 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 800 μL, 800 μmol) and stirred for 10 mins. tert-Butyl 4-[[[(1-chloroethoxy)carbonyl]oxy]piperidine-1-carboxylate (246 mg, 800 μmol) in DMF (1.0 mL) was added and the reaction was stirred overnight, followed by purification with RP-HPLC (Method B). Freeze-drying provided the titled compound as a white solid (15 mg, 7.1%). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 9.13 (s, 1H), 7.40 (q, *J* = 6.1 Hz, 1H), 7.30 (d, *J* = 3.2 Hz, 1H), 6.29 (d, *J* = 3.2 Hz, 1H), 4.75 (dt, *J* = 12.2, 4.2 Hz, 1H), 4.52 (t, *J* = 5.7 Hz, 2H), 3.83 (t, *J* = 5.9 Hz, 2H), 3.76 – 3.63 (m, 2H), 3.56 (dt, *J* = 12.2, 6.1 Hz, 1H), 3.26 – 3.06 (m, 2H), 1.95 – 1.85 (m, 2H), 1.82 (d, *J* = 6.2 Hz, 3H), 1.70 – 1.53 (m, 2H), 1.44 (s, 9H), 1.08 – 1.06 (m, 6H). LC/MS method A: *R*_t = 5.10 mins., (M+H)⁺ = 525, purity > 95%. Caco-2 *P*_{app} = 1.11 nm/s, SGF = 0% remaining at 1 h, SIF = 0% remaining at 1 h, hPlasma stability = 5% remaining at 1 h.

Additional compounds prepared according to EXAMPLE 99:

100	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(2,2,2-trifluoroethyl)carbamate	4.23 mins.	409	1H NMR (300 MHz, CDCl ₃) δ 9.18 (s, 1H), 7.33 (d, <i>J</i> = 3.2 Hz, 1H), 6.26 – 6.22 (m, 3H), 5.21 – 5.17 (m, 1H), 4.53 (t, <i>J</i> = 5.6 Hz, 2H), 3.84 (t, <i>J</i> = 5.6 Hz, 2H), 3.82 – 3.73 (m, 2H), 3.61 – 3.45 (m, 1H), 1.06 (d, <i>J</i> = 6.1 Hz, 6H).	277	99% remaining at 1 h	97% remaining at 1 h	97% remaining at 1 h
101	methyl (2S)-6-[[[(tert-butoxy)carbonyl]amino]-2-[[[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]carbonyl]amino]hexanoate	4.68 mins.	570	1H NMR (300 MHz, DMSO- <i>d</i> ₆) δ 12.35 (s, 1H), 7.90 (d, <i>J</i> = 7.4 Hz, 1H), 7.46 (d, <i>J</i> = 3.2 Hz, 1H), 6.77 – 6.71 (m, 1H), 6.36 (d, <i>J</i> = 3.2 Hz, 1H), 6.10 (d, <i>J</i> = 1.8 Hz, 2H), 4.45 (t, <i>J</i> = 6.0 Hz, 2H), 3.93 (dd, <i>J</i> = 12.7, 8.8 Hz, 1H), 3.68 (t, <i>J</i> = 6.0 Hz, 2H), 3.58 (s, 3H), 3.56 – 3.47 (m, 1H), 2.86 – 2.77 (m, 2H), 1.65 – 1.42 (m, 2H), 1.32 (s, 9H), 1.31 – 1.15 (m, 4H), 0.97 (d, <i>J</i> = 6.1 Hz, 6H).	14.6	75% remaining at 1 h	96% remaining at 1 h	97% remaining at 1 h

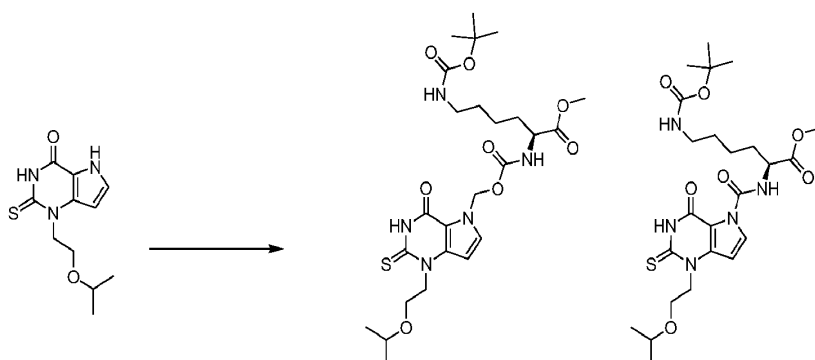
15 EXAMPLES 102 and 103:

**Methyl (2S)-6-[[[(tert-butoxy)carbonyl]amino]-2-[[[(chloromethoxy)carbonyl]amino]hexanoate:**

Pyridine (1.29 mL, 16 mmol) was added to methyl (2S)-2-amino-6-[[[(tert-butoxy)carbonyl]amino]hexanoate hydrogen chloride (2.37 g, 8 mmol) in dichloromethane (10 mL) and cooled on an ice bath. Chloromethyl chloroformate (711 μL, 8 mmol) was added dropwise and the

reaction was warmed to room temperature overnight. Additional dichloromethane was added (20 mL) and washed with water (4 x 5 mL) and brine. After drying over magnesium sulfate and concentration under vacuum, the titled compound was isolated (2.33 g, 82.6%), without need of further purification.

¹H NMR (300 MHz, DMSO-*d*₆) δ 8.16 (d, *J* = 7.7 Hz, 1H), 6.75 (t, *J* = 5.7 Hz, 1H), 5.82 (q, *J* = 6.1 Hz, 2H), 4.04 – 3.94 (m, 1H), 3.61 (s, 3H), 2.84 (q, *J* = 6.2 Hz, 2H), 1.71 – 1.45 (m, 2H), 1.33 (s, 10H), 1.28 – 1.20 (m, 3H).



Methyl (2S)-6-[[[(tert-butoxy)carbonyl]amino]-2-[[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]carbonyl]amino]hexanoate and

Methyl (2S)-6-[[[(tert-butoxy)carbonyl]amino]-2-[[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carbonyl]amino]hexanoate: A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (101 mg, 400 μmol) in DMF (2.0 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 800 μL, 800 μmol) and stirred for 10 mins. Methyl (2S)-6-[[[(tert-butoxy)carbonyl]amino]-2-[[[chloromethoxy]carbonyl]amino]hexanoate (141 mg, 400 μmol) in DMF (1.0 mL) was added and the reaction was stirred overnight, followed by purification with RP-HPLC (Method D).

Spectra for EXAMPLE 102: **Methyl (2S)-6-[[[(tert-butoxy)carbonyl]amino]-2-[[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]carbonyl]amino]hexanoate.** ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.35 (s, 1H), 7.90 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 3.2 Hz, 1H), 6.77 – 6.71 (m, 1H), 6.36 (d, *J* = 3.2 Hz, 1H), 6.10 (d, *J* = 1.8 Hz, 2H), 4.45 (t, *J* = 6.0 Hz, 2H), 3.93 (dd, *J* = 12.7, 8.8 Hz, 1H), 3.68 (t, *J* = 6.0 Hz, 2H), 3.58 (s, 3H), 3.56 – 3.47 (m, 1H), 2.86 – 2.77 (m, 2H), 1.65 – 1.42 (m, 2H), 1.32 (s, 9H), 1.31 – 1.15 (m, 4H), 0.97 (d, *J* = 6.1 Hz, 6H). LC/MS

method A: $R_t = 4.68$ mins., $(M+H)^+ = 570$, purity > 95%. Caco-2 $P_{app} = 14.6$ nm/s, SGF = 75% remaining at 1 h, SIF = 96% remaining at 1 h, hPlasma stability = 97% remaining at 1 h.

Spectra for EXAMPLE 103: **Methyl (2S)-6-([[(tert-butoxy)carbonyl]amino]-2-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-**

carbonyl]amino)hexanoate. 1H NMR (300 MHz, CHLOROFORM- d) δ 9.22 (s, 1H), 7.32 (s, 1H), 6.23 (d, $J = 3.1$ Hz, 1H), 6.21 – 6.20 (m, 1H), 5.52 (s, 1H), 4.53 (dd, $J = 6.6, 5.1$ Hz, 2H), 4.28 (s, 1H), 3.83 (t, $J = 5.7$ Hz, 2H), 3.72 (s, 3H), 3.63 – 3.50 (m, 1H), 3.10 – 3.00 (m, 2H), 1.95 – 1.55 (m, 3H), 1.43 (s, 10H), 1.38 – 1.26 (m, 2H), 1.07 (d, $J = 6.1$ Hz, 6H). LC/MS method A: $R_t = 5.03$ mins., $(M+H)^+ = 540$, purity > 95%. Caco-2 $P_{app} = 135$ nm/s, SGF = 96% remaining at 1 h, SIF = 96% remaining at 1 h, hPlasma stability = 92% remaining at 1 h.

Additional compounds prepared according to EXAMPLES 102-103:

104	(2-([[(2-(methoxyethoxy)ethoxy)carbonyl]oxy)methyl]sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-(2-methoxyethoxy)ethyl carbonate	4.00 mins.	606	1H NMR (300 MHz, CDCl $_3$) δ 7.37 (d, $J = 3.3$ Hz, 1H), 6.41 (s, 2H), 6.29 (d, $J = 3.3$ Hz, 1H), 5.98 (s, 2H), 4.35 – 4.23 (m, 6H), 3.77 – 3.67 (m, 6H), 3.66 – 3.58 (m, 4H), 3.56 – 3.46 (m, 5H), 3.36 (s, 3H), 3.35 (s, 3H), 1.08 – 1.03 (m, 6H).	2.76	96% remaining at 1 h	70% remaining at 1 h	18% remaining at 1 h
105	2-(2-methoxyethoxy)ethyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	3.97 mins.	430	1H NMR (300 MHz, CDCl $_3$) δ 9.18 (s, 1H), 7.31 – 7.27 (m, 1H), 6.28 – 6.25 (m, 3H), 4.52 (t, $J = 5.7$ Hz, 2H), 4.33 – 4.26 (m, 2H), 3.83 (t, $J = 5.7$ Hz, 2H), 3.73 – 3.67 (m, 2H), 3.64 – 3.59 (m, 2H), 3.57 (dd, $J = 9.8, 3.7$ Hz, 1H), 3.53 – 3.49 (m, 2H), 3.36 (s, 3H), 1.09 – 1.04 (m, 6H).	243	95% remaining at 1 h	84% remaining at 1 h	14% remaining at 1 h
106	{3-([[(2-(methoxyethoxy)ethoxy)carbonyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-(2-methoxyethoxy)ethyl carbonate	4.71 mins.	606	1H NMR (300 MHz, CDCl $_3$) δ 7.30 (d, $J = 3.2$ Hz, 1H), 6.63 (s, 2H), 6.27 (s, 2H), 6.25 (d, $J = 3.2$ Hz, 1H), 4.60 (t, $J = 5.7$ Hz, 2H), 4.36 – 4.27 (m, 4H), 3.83 (t, $J = 5.7$ Hz, 2H), 3.75 – 3.66 (m, 4H), 3.66 – 3.57 (m, 4H), 3.56 – 3.48 (m, 5H), 3.36 (s, 3H), 3.35 (s, 3H), 1.09 – 1.06 (m, 6H).	139	100% remaining at 1 h	1% remaining at 1 h	2% remaining at 1 h
107	tert-butyl (2S)-3-methyl-2-([[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]carbonyl]amino)butanoate	5.03 mins.	483	1H NMR (300 MHz, DMSO- d_6) δ 12.35 (s, 1H), 7.73 (d, $J = 8.2$ Hz, 1H), 7.47 (d, $J = 3.2$ Hz, 1H), 6.36 (d, $J = 3.1$ Hz, 1H), 6.11 (s, 2H), 4.45 (t, $J = 5.8$ Hz, 2H), 3.72 (dd, $J = 8.2, 6.1$ Hz, 1H), 3.68 (t, $J = 5.9$ Hz, 2H), 3.57 – 3.46 (m, 1H), 1.34 (s, 9H), 0.97 (d, $J = 6.1$ Hz, 6H), 0.81 (dd, $J = 6.8, 3.5$ Hz, 6H).	115	93% remaining at 1 h	92% remaining at 1 h	86% remaining at 1 h

EXAMPLE 109:



- (2S)-3-methyl-2-{{{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methoxy)carbonyl}amino}butanoic acid: tert-Butyl (2S)-3-methyl-2-{{{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methoxy)carbonyl}amino}butanoate (33.2 mg, 69 μ mol) was dissolved in trifluoroacetic acid in dichloromethane (30% v/v, 1.5 mL) and stirred for 1 hour. The reaction was concentrated and purified by RP-HPLC (Method B). Fractions containing the desired product were combined and freeze-dried to provide the titled compound (14.5 mg, 49.4%). ^1H NMR (300 MHz, DMSO- d_6) δ 12.58 (s, 1H), 12.36 (s, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.47 (d, J = 3.1 Hz, 1H), 6.36 (d, J = 3.2 Hz, 1H), 6.16 – 6.07 (m, 2H), 4.45 (t, J = 6.0 Hz, 2H), 3.80 (dd, J = 8.4, 5.9 Hz, 1H), 3.68 (t, J = 6.0 Hz, 2H), 3.56 – 3.47 (m, 1H), 1.98 (dd, J = 13.0, 6.7 Hz, 1H), 0.97 (dd, J = 6.1, 1.6 Hz, 6H), 0.81 (t, J = 7.0 Hz, 6H). LC/MS method A: R_t = 3.89 mins., $(\text{M}+\text{H})^+ = 427$, purity > 95%. Caco-2 P_{app} = 0.94 nm/s, SGF = 94% remaining at 1 h, SIF = 96% remaining at 1 h, h Plasma stability = 100% remaining at 1 h.

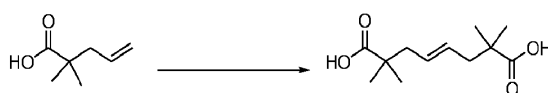
Additional compounds prepared according to EXAMPLE 109:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
110	trifluoroacetic acid methyl (2S)-6-amino-2-[[[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]carbonyl]amino]hexanoate	3.20 mins.	470		¹ H NMR (300 MHz, DMSO-d ₆) δ 7.92 (d, J = 7.6 Hz, 1H), 7.55 (br s, 2H), 7.46 (d, J = 3.1 Hz, 1H), 6.37 (d, J = 3.2 Hz, 1H), 6.10 (q, J = 10.4 Hz, 2H), 4.45 (t, J = 6.1 Hz, 2H), 4.00 – 3.92 (m, 1H), 3.69 (t, J = 6.0 Hz, 2H), 3.59 (s, 3H), 3.52 (dt, J = 12.1, 6.0 Hz, 1H), 2.75 – 2.65 (m, 2H), 1.67 – 1.38 (m, 4H), 1.33 – 1.23 (m, 2H), 0.98 – 0.96 (m, 6H).	1.42	81% remaining at 1h	45% remaining at 1h	62% remaining at 1h
111	methyl (2S)-6-[[[(2S)-2-[[[(tert-butoxy)carbonyl]amino]-3-methylbutanamido]-2-[[[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]carbonyl]amino]hexanoate	4.69 mins.	669		¹ H NMR (300 MHz, CDCl ₃) δ 7.32 – 7.30 (m, 1H), 6.28 – 6.10 (m, 3H), 5.81 – 5.75 (m, 1H), 5.28 – 5.22 (m, 1H), 4.57 – 4.47 (m, 2H), 4.28 – 4.18 (m, 1H), 3.86 – 3.77 (m, 3H), 3.71 (s, 3H), 3.57 (dt, J = 12.2, 6.1 Hz, 1H), 3.33 (dd, J = 14.0, 6.9 Hz, 1H), 3.17 (dd, J = 13.4, 5.8 Hz, 1H), 2.15 – 2.00 (m, 1H), 1.57 – 1.43 (m, 3H), 1.41 (s, 9H), 1.35 – 1.28 (m, 3H), 1.03 (d, J = 6.1 Hz, 6H), 0.93 (d, J = 6.7 Hz, 6H).	5.75	87% remaining at 1h	74% remaining at 1h	85% remaining at 1h
112	1-[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]ethyl N,N-bis(2,2,2-trifluoroethyl)carbamate	4.53 mins.	505		¹ H NMR (300 MHz, CDCl ₃) δ 12.07 – 11.90 (m, 1H), 7.40 – 7.35 (m, 1H), 7.08 – 6.96 (m, 1H), 6.30 – 6.25 (m, 1H), 4.47 – 3.82 (m, 6H), 3.75 (t, J = 5.8 Hz, 2H), 3.49 (dt, J = 8.3, 6.0 Hz, 1H), 1.85 (d, J = 6.6 Hz, 3H), 1.05 (t, J = 5.7 Hz, 6H).	211	100% remaining at 1h	100% remaining at 1h	99% remaining at 1h
113	tert-butyl 2-[methyl[(1-[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]ethoxy)carbonyl]amino]acetate	4.35 mins.	469		¹ H NMR (300 MHz, CDCl ₃) δ 11.48 (s, 1H), 7.32 – 7.27 (m, 1H), 6.95 – 6.81 (m, 1H), 6.21 – 6.19 (m, 1H), 4.42 – 3.79 (m, 4H), 3.74 (t, J = 6.1 Hz, 2H), 3.57 – 3.45 (m, 1H), 2.93 (d, J = 7.1 Hz, 3H), 1.87 (dd, J = 11.2, 6.6 Hz, 3H), 1.44 (s, 9H), 1.07 (dd, J = 6.1, 2.0 Hz, 6H).	78.6	44% remaining at 1h	96% remaining at 1h	99% remaining at 1h

114	trifluoroacetic acid methyl (2S)-6- [(2S)-2-amino-3- methylbutanamido]-2-[[[(4-oxo-1-[2- (propan-2-yloxy)ethyl]-2- sulfanylidene-1H,2H,3H,4H,5H- pyrrolo[3,2-d]pyrimidin-5- yl)methoxy]carbonyl]amino]hexano- ate	3.33 mins.	569	1H NMR (300 MHz, DMSO-d ₆) δ 12.36 (s, 1H), 8.35 – 8.28 (m, 1H), 8.01 (br s, 3H), 7.92 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 3.1 Hz, 1H), 6.37 (d, J = 3.2 Hz, 1H), 6.10 (q, J = 10.4 Hz, 2H), 4.45 (t, J = 6.0 Hz, 2H), 3.98 – 3.88 (m, 1H), 3.74 – 3.64 (m, 3H), 3.58 (s, 3H), 3.56 – 3.48 (m, 1H), 3.22 – 3.10 (m, 1H), 3.02 – 2.90 (m, 1H), 2.05 – 1.92 (m, 1H), 1.61 – 1.25 (m, 6H), 0.99 – 0.96 (m, 6H), 0.90 – 0.82 (m, 6H).	1.02	98% remaining at 1h	89% remaining at 1h	93% remaining at 1h
115	1-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)ethyl benzoate	4.88 mins.	402	1H NMR (300 MHz, CDCl ₃) δ 9.21 (s, 1H), 8.04 – 7.99 (m, 2H), 7.68 – 7.53 (m, 2H), 7.47 – 7.39 (m, 2H), 7.36 (d, J = 3.2 Hz, 1H), 6.27 (d, J = 3.2 Hz, 1H), 4.52 (td, J = 5.8, 2.8 Hz, 2H), 3.83 (dt, J = 5.9, 3.1 Hz, 2H), 3.56 (dq, J = 12.2, 6.1 Hz, 1H), 1.93 (d, J = 6.2 Hz, 3H), 1.08 – 1.05 (m, 6H).	60.5	63% remaining at 1h	67% remaining at 1h	59% remaining at 1h
116	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl benzoate	4.78 mins.	388	1H NMR (300 MHz, CDCl ₃) δ 9.21 (s, 1H), 8.04 (dt, J = 8.5, 1.6 Hz, 2H), 7.63 – 7.50 (m, 1H), 7.47 – 7.36 (m, 3H), 6.49 (s, 2H), 6.25 (d, J = 3.2 Hz, 1H), 4.52 (t, J = 5.7 Hz, 2H), 3.83 (t, J = 5.7 Hz, 2H), 3.53 (tt, J = 7.6, 3.8 Hz, 1H), 1.06 (d, J = 6.1 Hz, 6H).	64.1	99% remaining at 1h	46% remaining at 1h	1% remaining at 1h
117	{3-[(benzoyloxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl benzoate	5.21 mins.	522	1H NMR (300 MHz, CDCl ₃) δ 8.06 (ddd, J = 6.9, 3.2, 1.7 Hz, 4H), 7.61 – 7.52 (m, 2H), 7.47 – 7.37 (m, 5H), 6.68 (s, 2H), 6.25 (d, J = 3.3 Hz, 1H), 6.21 (s, 2H), 4.24 (t, J = 5.8 Hz, 2H), 3.70 (t, J = 5.8 Hz, 2H), 3.54 – 3.39 (m, 1H), 1.01 (d, J = 6.1 Hz, 6H).	57.6	100% remaining at 1h	79% remaining at 1h	20% remaining at 1h

EXAMPLES 118 and 119:

5

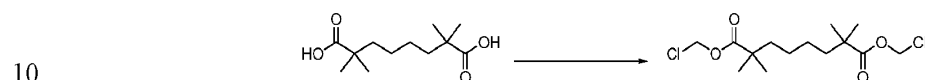


10

(4E)-2,2,7,7-Tetramethyloct-4-enedioic acid: 2,2-Dimethyl-4-pentenoic acid (7.7 g, 60 mmol) in dichloromethane (90 mL) with Grubbs 2nd generation catalyst (600 mg, 2.12 mmol) was purged with nitrogen for 10 minutes. The reaction was heated for 3 days at 41 °C then cooled to room temp. The dichloromethane was treated with saturated sodium bicarbonate. The dichloromethane layer was set aside and the aqueous layer was acidified to pH 1 with addition of 1 N HCl. This was extracted twice with ethyl acetate. The combined fractions were washed with brine and dried over magnesium sulfate, providing the title compound (4.28 g, 62.5%). ¹H NMR (300 MHz, CHLOROFORM-d) δ 5.53 – 5.47 (m, 2H), 2.21 (dd, J = 4.2, 1.8 Hz, 4H), 1.18 (s, 12H).

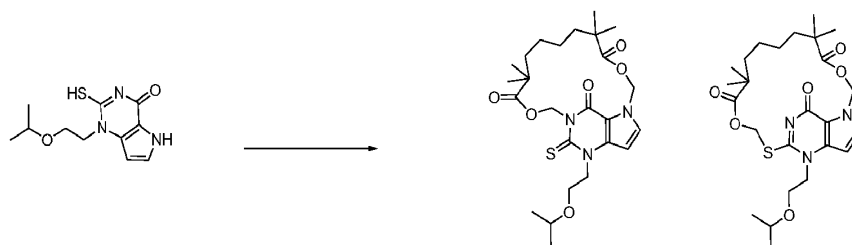


2,2,7,7-Tetramethyloctanedioic acid: A round-bottom flask containing a solution of (4E)-2,2,7,7-tetramethyloct-4-enedioic acid (4.26 g, 18.66 mmol) in methanol (130 mL) with palladium on carbon (5%, wet, 50 mg), was equipped with a balloon filled with hydrogen. The flask was quickly
 5 purged under vacuum and filled with hydrogen (3x), and stirred overnight. The palladium was removed by filtration and solvent removed to provide the titled compound (4.24 g, 98.7%). ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.00 (s, 2H), 1.49 – 1.24 (m, 4H), 1.15 – 1.07 (m, 4H), 1.02 (s, 12H).



10

1,8-Dichloromethyl 2,2,7,7-tetramethyloctanedioate: A solution of 2,2,7,7-tetramethyloctanedioic acid (4.62 g, 20.06 mmol), tetrabutylammonium hydrogen sulfate (681 mg, 2.0 mmol), and sodium carbonate (11.8 g, 140.4 mmol) was dissolved in dichloromethane and water (50:50
 15 v/v, 90 mL) and cooled at 0 °C on an ice bath. Chloromethyl chlorosulfonate (4.81 mL, 48.1 mmol) was added dropwise and the reaction was warmed to room temperature with stirring overnight. The reaction was poured into a separatory funnel and separated. The aqueous layer was extracted one more time with dichloromethane and the combined organic fractions were washed with brine and dried over magnesium sulfate and concentrated to provide the crude product (4.5 g), which was purified by flash
 20 chromatography eluting with a gradient of hexane to 10% ethyl acetate in hexane. The titled compound was isolated as a pale oil in appearance (3.1 g, 47.2%). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 5.70 (s, 4H), 1.54 – 1.49 (m, 4H), 1.24 – 1.18 (m, 4H), 1.18 (s, 12H).



5,5,10,10-Tetramethyl-16-[2-(propan-2-yloxy)ethyl]-15-sulfanylidene-3,12-dioxo-1,14,16-triazatricyclo[12.5.2.0^{17,20}]]henicosa-17(20),18-diene-4,11,21-trione and 8,8,13,13-Tetramethyl-22-[2-(propan-2-yloxy)ethyl]-6,15-dioxo-17-thia-4,19,22-triazatricyclo[16.3.1.0^{4,21}]]docosa-1(21),2,18-triene-7,14,20-trione: A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (50.6 mg, 200 μ mol) in DMF (9.0 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 200 μ L, 200 μ mol) and stirred for 10 mins at 0 °C. 1,8-Dichloromethyl 2,2,7,7-tetramethyloctanedioate (65.5 mg, 200 μ mol) in DMF (1.0 mL) was added and the reaction was warmed to room temperature over 2 hours. Next, the reaction was cooled to 0 °C and lithium hexamethyldisilylamide (1.0 M in THF, 200 μ L, 200 μ mol) was added and warmed to room temperature overnight. The reaction was quenched by the addition of water and partitioned between ethyl acetate and water (25 mL each). After separation, the aqueous layer was extracted an additional time with ethyl acetate. The combined organic fractions were washed with brine and dried over magnesium sulfate. After concentration, the crude was purified by RP-HPLC (Method B).

Spectra for EXAMPLE 118: **5,5,10,10-Tetramethyl-16-[2-(propan-2-yloxy)ethyl]-15-sulfanylidene-3,12-dioxo-1,14,16-triazatricyclo[12.5.2.0^{17,20}]]henicosa-17(20),18-diene-4,11,21-trione.** ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 7.30 – 7.29 (m, 1H), 6.73 (s, 2H), 6.21 (d, *J* = 3.1 Hz, 1H), 6.02 (s, 2H), 4.68 – 4.64 (m, 2H), 3.89 (t, *J* = 5.7 Hz, 2H), 3.53 (td, *J* = 11.8, 5.7 Hz, 1H), 1.40 – 1.20 (m, 6H), 1.19 – 1.10 (m, 2H), 1.13 (d, *J* = 12.1 Hz, 12H), 1.06 – 1.02 (m, 6H). LC/MS method A: *R*_t = 6.13 mins., (M+H)⁺ = 508, purity > 95%. Caco-2 *P*_{app} = 66 nm/s, SGF = 94% remaining at 1 h, SIF = 76% remaining at 1 h, *h*Plasma stability = 73% remaining at 1 h.

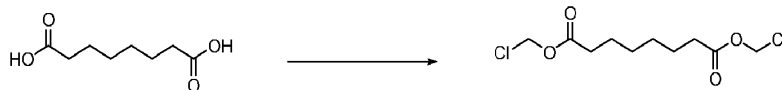
Spectra for EXAMPLE 119: **8,8,13,13-Tetramethyl-22-[2-(propan-2-yloxy)ethyl]-6,15-dioxo-17-thia-4,19,22-triazatricyclo[16.3.1.0^{4,21}]]docosa-1(21),2,18-triene-7,14,20-trione.** ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 7.32 (d, *J* = 3.2 Hz, 1H), 6.38 (d, *J* = 9.6 Hz, 1H), 6.25 (d, *J* = 11.0 Hz, 1H), 6.16 (d, *J* = 3.2 Hz, 1H), 6.02 (d, *J* = 10.0 Hz, 1H), 5.18 (d, *J* = 10.9 Hz, 1H), 4.60 – 4.44 (m, 1H), 4.20 – 4.08 (m, 1H), 3.75 – 3.67 (m, 2H), 3.55 – 3.45 (m, 1H), 1.70 – 1.60 (m, 1H), 1.33 – 0.94 (m, 25H). LC/MS method A: *R*_t = 5.04 mins., (M+H)⁺ = 508, purity > 95%. Caco-2 *P*_{app} = 317 nm/s, SGF = 94% remaining at 1 h, SIF = 98% remaining at 1 h, *h*Plasma stability = 90% remaining at 1 h.

Additional compounds prepared according to EXAMPLES 118-119:

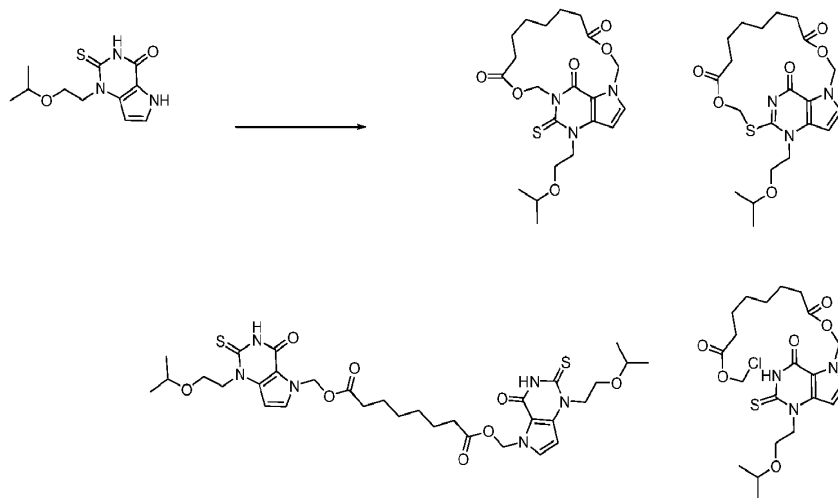
Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
120	5-([2-(2-((tert-butoxycarbonyl)amino)ethoxy)ethoxy]carbonyloxy)methyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	4.58 mins.	515		¹ H NMR (300 MHz, DMSO-d ₆) δ 12.40 (s, 1H), 7.52 (d, J = 3.2 Hz, 1H), 6.78 – 6.72 (m, 1H), 6.39 (d, J = 3.2 Hz, 1H), 6.17 (s, 2H), 4.45 (t, J = 6.1 Hz, 2H), 4.20 – 4.12 (m, 2H), 3.68 (t, J = 6.1 Hz, 2H), 3.57 – 3.47 (m, 3H), 3.35 – 3.25 (m, 2H), 3.00 (q, J = 5.9 Hz, 2H), 1.32 (s, 9H), 0.97 (d, J = 6.1 Hz, 6H).	149	83% remaining at 1 h	64% remaining at 1 h	30% remaining at 1 h
121	5-([2-(2-((tert-butoxycarbonyl)amino)ethoxy)ethoxy]carbonyloxy)methyl]-2-([2-(2-((tert-butoxycarbonyl)amino)ethoxy)ethoxy]carbonyloxy)methyl]sulfanyl)-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	4.82 mins.	776		¹ H NMR (300 MHz, DMSO-d ₆) δ 7.49 (d, J = 3.3 Hz, 1H), 6.75 (br s, 2H), 6.50 (d, J = 3.3 Hz, 1H), 6.29 (s, 2H), 5.84 (s, 2H), 4.25 (t, J = 5.2 Hz, 2H), 4.21 – 4.14 (m, 4H), 3.66 – 3.61 (m, 2H), 3.58 – 3.51 (m, 4H), 3.5 – 3.35 (m, 5H), 3.01 – 2.99 (m, 4H), 1.31 (s, 18H), 0.95 – 0.92 (m, 6H).	11.9	69% remaining at 1 h	56% remaining at 1 h	34% remaining at 1 h
122	3,5-bis([2-(2-((tert-butoxycarbonyl)amino)ethoxy)ethoxy]carbonyloxy)methyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	5.34 mins.	776		¹ H NMR (300 MHz, CDCl ₃) δ 7.31 (d, J = 3.1 Hz, 1H), 6.65 (s, 2H), 6.28 (s, 2H), 6.27 (d, J = 3.2 Hz, 1H), 4.88 (br s, 1H), 4.60 (t, J = 5.6 Hz, 2H), 4.34 – 4.25 (m, 4H), 3.83 (t, J = 5.6 Hz, 2H), 3.66 (ddd, J = 6.3, 4.7, 3.1 Hz, 4H), 3.60 – 3.46 (m, 5H), 3.33 – 3.23 (m, 4H), 1.43 (s, 9H), 1.43 (s, 9H), 1.07 (d, J = 6.1 Hz, 6H).	193	85% remaining at 1 h	22% remaining at 1 h	50% remaining at 1 h
123	trifluoroacetic acid 2-(2-aminoethoxy)ethyl (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	3.12 mins.	415		¹ H NMR (300 MHz, DMSO-d ₆) δ 12.40 (s, 1H), 7.68 (br s, 2H), 7.53 (d, J = 3.2 Hz, 1H), 6.40 (d, J = 3.2 Hz, 1H), 6.17 (s, 2H), 4.46 (t, J = 5.9 Hz, 2H), 4.26 – 4.19 (m, 2H), 3.69 (t, J = 6.0 Hz, 2H), 3.65 – 3.59 (m, 2H), 3.57 – 3.48 (m, 3H), 2.93 (dd, J = 10.4, 5.2 Hz, 2H), 0.97 (d, J = 6.1 Hz, 6H).	24.4	97% remaining at 1 h	1% remaining at 1 h	65% remaining at 1 h
124	bis(trifluoroacetic acid) (2-([2-(2-aminoethoxy)ethoxy]carbonyloxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-(2-aminoethoxy)ethyl carbonate	2.70 mins.	576		¹ H NMR (300 MHz, DMSO-d ₆) δ 7.73 (br s, 4H), 7.52 (d, J = 3.3 Hz, 1H), 6.52 (d, J = 3.3 Hz, 1H), 6.29 (s, 2H), 5.85 (s, 2H), 4.30 – 4.19 (m, 6H), 3.68 – 3.59 (m, 6H), 3.55 (td, J = 5.2, 2.3 Hz, 4H), 3.50 – 3.41 (m, 1H), 2.98 – 2.89 (m, 4H), 0.94 (d, J = 6.1 Hz, 1H).	11.8	67% remaining at 1 h	57% remaining at 1 h	28% remaining at 1 h
125	tert-butyl 3-([4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]carbonyloxy)azetidine-1-carboxylate	4.71 mins	483		¹ H NMR (300 MHz, DMSO-d ₆) δ 12.41 (s, 1H), 7.52 (d, J = 3.2 Hz, 1H), 6.40 (d, J = 3.2 Hz, 1H), 6.18 (s, 2H), 5.05 (dt, J = 10.5, 3.4 Hz, 1H), 4.45 (t, J = 6.0 Hz, 2H), 4.17 – 4.07 (m, 2H), 3.78 – 3.72 (m, 2H), 3.69 (t, J = 6.0 Hz, 2H), 3.57 – 3.46 (m, 1H), 1.33 (s, 9H), 0.98 – 0.95 (m, 6H).	249	85% remaining at 1 h	17% remaining at 1 h	3% remaining at 1 h
126	1-tert-butyl 4-[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl]butanedicate	4.82 mins.	440		¹ H NMR (300 MHz, CDCl ₃) δ 9.27 (s, 1H), 7.27 (d, J = 3.2 Hz, 1H), 6.26 (s, 2H), 6.24 (d, J = 3.2 Hz, 1H), 4.52 (t, J = 5.7 Hz, 2H), 3.83 (t, J = 5.7 Hz, 2H), 3.62 – 3.50 (m, 1H), 2.63 – 2.55 (m, 2H), 2.55 – 2.48 (m, 2H), 1.40 (s, 9H), 1.09 – 1.05 (m, 6H).	135	100% remaining at 1 h	67% remaining at 1 h	2% remaining at 1 h

127	1-tert-butyl 3-[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl azetidine-1,3-dicarboxylate	4.65 mins.	467	1H NMR (300 MHz, DMSO-d ₆) δ 12.38 (s, 1H), 7.53 (d, J = 3.2 Hz, 1H), 6.38 (d, J = 3.2 Hz, 1H), 6.19 (s, 2H), 4.45 (t, J = 6.0 Hz, 2H), 3.95 (t, J = 8.4 Hz, 2H), 3.80 (t, J = 7.0 Hz, 2H), 3.68 (t, J = 6.0 Hz, 2H), 3.56 – 3.46 (m, 1H), 3.46 – 3.37 (m, 1H), 1.32 (s, 9H), 0.98 – 0.95 (m, 6H).	77.9	80% remaining at 1 h	6% remaining at 1 h	1% remaining at 1 h
128	1-tert-butyl 4-[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl piperidine-1,4-dicarboxylate	4.89 mins.	495	1H NMR (300 MHz, CDCl ₃) δ 7.25 – 7.23 (m, 1H), 6.27 – 6.23 (m, 1H), 6.24 (s, 2H), 4.52 (t, J = 5.6 Hz, 2H), 4.03 – 3.93 (m, 2H), 3.84 (t, J = 5.6 Hz, 2H), 3.61 – 3.50 (m, 1H), 2.85 – 2.71 (m, 2H), 2.52 – 2.42 (m, 1H), 1.87 – 1.77 (m, 2H), 1.65 – 1.48 (m, 2H), 1.43 (s, 9H), 1.07 – 1.05 (m, 6H).	119	78% remaining at 1 h	83% remaining at 1 h	31% remaining at 1 h
129	1-tert-butyl 3-[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl (3R)-pyrrolidine-1,3-dicarboxylate	4.73 mins.	481	1H NMR (300 MHz, DMSO-d ₆) δ 12.37 (s, 1H), 7.52 (d, J = 3.1 Hz, 1H), 6.38 (d, J = 3.2 Hz, 1H), 6.22 – 6.12 (m, 2H), 4.45 (t, J = 6.0 Hz, 2H), 3.69 (t, J = 6.0 Hz, 2H), 3.57 – 3.46 (m, 1H), 3.33 – 3.25 (m, 2H), 3.24 – 3.05 (m, 3H), 2.05 – 1.82 (m, 2H), 1.34 (s, 9H), 0.97 (d, J = 6.1 Hz, 6H).	121	84% remaining at 1 h	21% remaining at 1 h	1% remaining at 1 h
130	1-tert-butyl 3-[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl (3S)-pyrrolidine-1,3-dicarboxylate	4.77 mins.	481	1H NMR (300 MHz, DMSO-d ₆) δ 12.37 (s, 1H), 7.52 (d, J = 3.2 Hz, 1H), 6.38 (d, J = 3.2 Hz, 1H), 6.21 – 6.12 (m, 2H), 4.45 (t, J = 6.0 Hz, 2H), 3.69 (t, J = 6.0 Hz, 2H), 3.58 – 3.45 (m, 1H), 3.32 – 3.27 (m, 2H), 3.23 – 3.05 (m, 3H), 2.05 – 1.82 (m, 2H), 1.34 (s, 9H), 0.97 (d, J = 6.1 Hz, 6H).	176	61% remaining at 1 h	64% remaining at 1 h	4% remaining at 1 h
131	4-[[5-[[[4-(tert-butoxy)-4-oxobutanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfanylmethyl 1-tert-butyl piperidine-1,4-dicarboxylate	5.44 mins.	681	1H NMR (300 MHz, CDCl ₃) δ 7.36 (d, J = 3.3 Hz, 1H), 6.41 (s, 2H), 6.27 (d, J = 3.3 Hz, 1H), 5.92 (s, 2H), 4.25 (t, J = 5.7 Hz, 2H), 4.05 – 3.95 (m, 2H), 3.72 (t, J = 5.7 Hz, 2H), 3.56 – 3.44 (m, 0H), 2.81 (t, J = 11.1 Hz, 2H), 2.60 – 2.45 (m, 5H), 1.92 – 1.83 (m, 2H), 1.67 – 1.53 (m, 2H), 1.43 (s, 9H), 1.40 (s, 9H), 1.07 – 1.04 (m, 6H).	65.8	99% remaining at 1h	75% remaining at 1h	1% remaining at 1h
132	4-[[5-[[[4-(tert-butoxy)-4-oxobutanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-3-yl]methyl 1-tert-butyl piperidine-1,4-dicarboxylate	6.47 mins.	681	1H NMR (300 MHz, CDCl ₃) δ 8.09 – 8.05 (m, 1H), 7.33 (s, 2H), 7.05 (s, 2H), 7.04 – 6.98 (m, 1H), 5.40 – 5.35 (m, 2H), 4.73 (d, J = 12.6 Hz, 2H), 4.61 (t, J = 5.6 Hz, 2H), 4.41 – 4.28 (m, 1H), 3.60 (t, J = 11.5 Hz, 2H), 3.40 – 3.20 (m, 5H), 2.54 – 2.36 (m, 4H), 2.20 (s, 9H), 2.17 (s, 9H), 1.85 (d, J = 6.1 Hz, 6H).	42.9	9% remaining at 1h	71% remaining at 1h	11% remaining at 1h
133	4-oxo-4-[[4-oxo-2-[[[piperidine-4-carbonyloxy]methyl]sulfanyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]butanoic acid; trifluoroacetic acid	2.97 mins.	525	1H NMR (300 MHz, CDCl ₃) δ 7.24 – 7.22 (m, 1H), 6.33 (s, 2H), 6.30 (d, J = 3.2 Hz, 1H), 5.74 (s, 2H), 4.27 (t, J = 5.6 Hz, 2H), 3.77 (t, J = 5.7 Hz, 2H), 3.60 – 3.48 (m, 3H), 3.25 – 3.15 (m, 2H), 2.83 – 2.75 (m, 1H), 2.63 – 2.57 (m, 2H), 2.54 – 2.47 (m, 2H), 2.23 – 2.14 (m, 4H), 1.10 – 1.06 (m, 6H).	<1.98	82% remaining at 1h	97% remaining at 1h	7% remaining at 1h

EXAMPLES 134-137:



- 1,8-Dichloromethyl octanedioate:** A solution of suberic acid (3.49 g, 20.06 mmol),
 5 tetrabutylammonium hydrogen sulfate (681 mg, 2.0 mmol), and sodium carbonate (11.8 g, 140.4 mmol)
 was dissolved in dichloromethane and water (50:50 v/v, 90 mL) and cooled at 0 °C on an ice bath.
 Chloromethyl chlorosulfonate (4.81 mL, 48.1 mmol) was added dropwise and the reaction was warmed to
 room temperature with stirring overnight. The reaction was poured into a separatory funnel and
 separated. The aqueous layer was extracted one more time with dichloromethane and the combined
 10 organic fractions were washed with brine and dried over magnesium sulfate and concentrated to
 provide the crude product (4.5 g), which was purified by flash chromatography eluting with a gradient of
 hexane to 10% ethyl acetate in hexane. The titled compound was isolated as a pale oil in appearance
 (170 mg). ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.81 (s, 4H), 2.37 (t, *J* = 7.3 Hz, 4H), 1.56 – 1.43 (m, 4H), 1.29 –
 1.21 (m, 4H).



15

16-[2-(Propan-2-yloxy)ethyl]-15-sulfanylidene-3,12-dioxo-1,14,16-triazatricyclo[12.5.2.0^{17,20}]henicosa-17(20),18-diene-4,11,21-trione and **22-[2-(propan-2-yloxy)ethyl]-6,15-dioxo-17-thia-4,19,22-triazatricyclo[16.3.1.0^{4,21}]docosa-1(21),2,18-triene-**

7,14,20-trione and 1,8-bis({4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl) octanedioate and 1-chloromethyl 8-{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl octanedioate: A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (149 mg, 590 μ mol) in DMF (28.0 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 590 μ L, 590 μ mol) and stirred for 10 mins at 0 °C. 1,8-Dichloromethyl octanedioate (160 mg, 590 μ mol) in DMF (2.0 mL) was added and the reaction was warmed to room temperature overnight. The reaction was quenched by the addition of water and partitioned between ethyl acetate and water (100 mL each). After separation, the aqueous layer was extracted an additional time with ethyl acetate. The combined organic fractions were washed with water and brine and dried over magnesium sulfate. Purification with RP-HPLC (Method B) in 5 separate runs provided cyclic compounds JTL-2-121-1, 26 mg; JTL-2-121-2, 12 mg; JTL-2-121-3, 29 mg, JTL-2-121-5, 8 mg. Repurification provided the following batches for testing: FC-12108 (6.7 mg), FC-12109 (5 mg), FC-12110 (23 mg), and FC-12111 (4 mg).

Spectra for EXAMPLE 134: **16-[2-(Propan-2-yloxy)ethyl]-15-sulfanylidene-3,12-dioxo-1,14,16-triazatricyclo[12.5.2.0^{17,20}]]henicosa-17(20),18-diene-4,11,21-trione.** ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 7.22 (d, *J* = 3.2 Hz, 1H), 6.77 (s, 2H), 6.24 (d, *J* = 3.1 Hz, 1H), 6.10 (s, 2H), 4.64 (t, *J* = 5.7 Hz, 2H), 3.88 (t, *J* = 5.7 Hz, 2H), 3.61 – 3.51 (m, 1H), 2.32 (dd, *J* = 12.4, 5.2 Hz, 4H), 1.39 – 1.10 (m, 8H), 1.06 (d, *J* = 6.1 Hz, 6H). LC/MS method A: *R*_t = 5.08 mins., (M+H)⁺ = 452, purity > 95%. SGF = 99% remaining at 1 h, SIF = 1% remaining at 1 h, *h*Plasma stability = 1% remaining at 1 h.

Spectra for EXAMPLE 135: **22-[2-(Propan-2-yloxy)ethyl]-6,15-dioxo-17-thia-4,19,22-triazatricyclo[16.3.1.0^{4,21}]]docosa-1(21),2,18-triene-7,14,20-trione.** ¹H NMR (300 MHz, CHLOROFORM-*d*) δ 7.30 – 7.27 (m, 1H), 6.35 – 6.20 (m, 2H), 6.18 (d, *J* = 3.2 Hz, 1H), 5.96 – 5.53 (m, 2H), 4.35 – 4.20 (m, 2H), 3.71 (t, *J* = 5.5 Hz, 2H), 3.47 (hept, *J* = 6.1 Hz, 1H), 1.70 – 1.51 (m, 1H), 1.50 – 1.35 (m, 2H), 1.34 – 1.20 (m, 3H), 1.19 – 1.07 (m, 2H), 1.05 – 1.01 (m, 6H). LC/MS method A: *R*_t = 4.06 mins., (M+H)⁺ = 452, purity > 95%. SGF = 86% remaining at 1 h, SIF = 67% remaining at 1 h, *h*Plasma stability = 67% remaining at 1 h.

Spectra for EXAMPLE 136: **1,8-Bis({4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl) octanedioate.** ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.35 (s, 2H), 7.49 (d, *J* = 3.1 Hz, 2H), 6.36 (d, *J* = 3.2 Hz, 2H), 6.13 (s, 4H), 4.44 (t, *J* = 6.0 Hz, 4H), 3.68 (t, *J* = 6.1 Hz, 4H), 3.60 – 3.44 (m, 2H), 2.22 (t, *J* = 7.2 Hz, 4H), 1.42 – 1.32 (m, 4H), 1.24 (s, 2H), 1.10 (s, 2H),

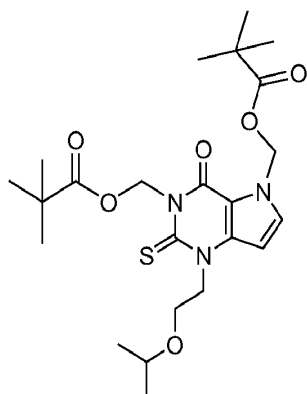
0.98 – 0.95 (m, 12H). LC/MS method A: R_t = 5.11 mins., $(M+H)^+$ = 705, purity > 95%. SGF = 77% remaining at 1 h, SIF = 2% remaining at 1 h, h Plasma stability = 2% remaining at 1 h.

Spectra for EXAMPLE 137: **1-Chloromethyl 8-{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl octanedioate**. 1H NMR (300 MHz, CHLOROFORM-
5 d) δ 9.23 (s, 1H), 6.24 (d, J = 3.2 Hz, 1H), 6.22 (s, 2H), 5.69 (s, 2H), 4.52 (t, J = 5.6 Hz, 2H), 3.83 (t, J = 5.6 Hz, 2H), 3.54 (tt, J = 9.3, 4.7 Hz, 1H), 2.33 (dt, J = 9.8, 7.4 Hz, 4H), 1.67 – 1.52 (m, 4H), 1.35 – 1.20 (m, 4H), 1.09 – 1.04 (m, 6H). LC/MS method A: R_t = 4.96 mins., $(M+H)^+$ = 488 and 490, purity > 95%, SGF = 74% remaining at 1 h, SIF = 56% remaining at 1 h, h Plasma stability = 1% remaining at 1 h.

10 Additional compounds prepared according to EXAMPLES 134-137:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
138	25-[2-(propan-2-yloxy)ethyl]-3,15-dioxo-5-thia-7,13,20,25-tetraazatetracyclo[18.2.2.1 ⁶ .10]0 ⁹ [9,13]pentacos-6,9,11-triene-2,8,16,19-tetrone	3.42 mins.	507		¹ H NMR (300 MHz, CDCl ₃) δ 7.34 (d, J = 3.4 Hz, 1H), 6.44 (br s, 1H), 6.29 (s, 2H), 6.17 (d, J = 3.2 Hz, 1H), 5.22 (br s, 1H), 4.48 – 4.37 (m, 1H), 4.14 (dt, J = 15.1, 5.0 Hz, 1H), 3.76 – 3.64 (m, 2H), 3.60 – 3.43 (m, 2H), 3.31 – 2.92 (m, 3H), 2.80 – 2.58 (m, 3H), 2.49 – 2.39 (m, 1H), 2.33 – 2.27 (m, 1H), 1.80 – 1.49 (m, 3H), 1.05 (dd, J = 6.1, 4.1 Hz, 6H).		100% remaining at 1 h	98% remaining at 1 h	66% remaining at 1 h
139	4-oxo-4-[(4-oxo-3-[(piperidine-4-carboxyloxy)methyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]butanoic acid; trifluoroacetic acid	3.23 mins.	525		¹ H NMR (300 MHz, DMSO-d ₆) δ 7.63 (d, J = 3.2 Hz, 1H), 6.47 (d, J = 3.2 Hz, 1H), 6.37 (s, 2H), 6.18 (s, 2H), 4.56 (t, J = 5.7 Hz, 2H), 3.72 (t, J = 5.9 Hz, 2H), 3.59 – 3.48 (m, 1H), 3.25 – 3.15 (m, 2H), 2.95 – 2.80 (m, 2H), 2.75 – 2.65 (m, 1H), 2.52 – 2.37 (m, 4H), 1.97 – 1.87 (m, 2H), 1.77 – 1.65 (m, 2H), 0.98 (d, J = 6.1 Hz, 6H).		99% remaining at 1 h	98% remaining at 1 h	8% remaining at 1 h
140	19-[2-(propan-2-yloxy)ethyl]-20-sulfanylidene-3,13-dioxo-1,8,15,19-tetraazatetracyclo[13.5.2.2 ⁴ (5,8).0 ⁴ (18,22)]tetracos-16,18(22)-diene-4,9,12,21-tetrone	4.38 mins.	507		¹ H NMR (300 MHz, CDCl ₃) δ 7.31 – 7.26 (m, 1H), 6.90 (br s, 2H), 6.28 (d, J = 10.4 Hz, 1H), 6.24 (d, J = 3.2 Hz, 1H), 6.18 (br s, 1H), 4.64 (br s, 2H), 3.87 (dt, J = 5.7, 2.3 Hz, 2H), 3.56 (dt, J = 12.2, 6.1 Hz, 1H), 3.50 – 3.05 (m, 4H), 2.85 – 2.75 (m, 2H), 2.48 (d, J = 14.9 Hz, 1H), 2.25 – 2.13 (m, 1H), 2.10 – 2.00 (m, 2H), 1.80 – 1.57 (m, 3H), 1.07 (dd, J = 6.1, 2.7 Hz, 6H).		99% remaining at 1 h	79% remaining at 1 h	10% remaining at 1 h
141	1-tert-butyl 4-[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-[12-(tert-butoxy)-12-oxododecanamido]butanedioate	6.31 mins.	723		¹ H NMR (300 MHz, DMSO-d ₆) δ 12.40 (s, 1H), 8.11 – 8.08 (m, 1H), 7.47 (d, J = 1.7 Hz, 1H), 6.37 (d, J = 3.2 Hz, 1H), 6.18 – 6.14 (m, 2H), 4.48 – 4.39 (m, 3H), 3.70 – 3.64 (m, 2H), 3.57 – 3.48 (m, 1H), 2.76 – 2.55 (m, 2H), 2.15 – 2.09 (m, 2H), 2.04 – 1.98 (m, 2H), 1.46 – 1.37 (m, 4H), 1.35 (s, 9H), 1.28 (s, 9H), 1.19 (s, 12H), 1.00 – 0.97 (m, 6H).				
142	11-[[[(1S)-1-carboxy-3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl]carbamoyl]undecanoic acid	4.28 mins.	611	A	¹ H NMR (300 MHz, DMSO-d ₆) δ 12.38 (s, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.46 (d, J = 3.2 Hz, 1H), 6.37 (d, J = 3.2 Hz, 1H), 6.15 (s, 2H), 4.51 – 4.40 (m, 3H), 3.67 (t, J = 6.0 Hz, 2H), 3.60 – 3.46 (m, 1H), 2.66 (ddd, J = 23.7, 16.4, 6.7 Hz, 2H), 2.14 (t, J = 7.3 Hz, 2H), 2.00 (t, J = 7.3 Hz, 2H), 1.51 – 1.31 (m, 4H), 1.18 (s, 12H), 0.98 (d, J = 6.1 Hz, 6H).	<1.9	100% remaining after 1 h	97% remaining after 1 h	97% remaining after 1 h

EXAMPLE 143:



2,2-Dimethyl-propionic acid 5-(2,2-dimethyl-propionyloxymethyl)-1-(2-isopropoxy-ethyl)-4-oxo-2-thioxo-1,2,4,5-tetrahydro-pyrrolo[3,2-d]pyrimidin-3-ylmethyl ester: Added potassium carbonate (0.120 g, 0.868 mmole) to a solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-5H-pyrrolo[3,2-d]pyrimidin-4-one (0.1 g, 0.394 mmole) and chloromethyl pivalate (0.125 mL, 0.868 mmole) at RT under N₂ and magnetically stirred in 5 mL of acetone. After 2 days, filtered off solids, and concentrated the filtrate *in vacuo*. Purified using a 20 g Agela silica gel column, eluting with 0-45% ethyl acetate in hexanes to yield **2,2-Dimethyl-propionic acid 5-(2,2-dimethyl-propionyloxymethyl)-1-(2-isopropoxy-ethyl)-4-oxo-2-thioxo-1,2,4,5-tetrahydro-pyrrolo[3,2-d]pyrimidin-3-ylmethyl ester:** (13 mg, 6.8%), ¹H NMR (CHLOROFORM-*d*) δ: 7.28 (d, J=3.1 Hz, 1H), 6.56 (s, 2H), 6.26 (s, 2H), 6.24 (d, J=3.2 Hz, 1H), 4.62 (t, J=5.7 Hz, 2H), 3.83-3.91 (m, 2H), 3.55 (quin, J=6.1 Hz, 1H), 1.20 (s, 9H), 1.15 (s, 9H), 1.05 (d, J=6.0 Hz, 6H). LC/MS method A: R_t = 6.47 mins., (M+H)⁺ = 482, purity = 95. Caco-2 P_{app} = 30 nm/s, SGF = 62% remaining at 1 h, SIF = 82% remaining at 1 h, hPlasma stability = 21% remaining at 1 h.

Additional compounds prepared similarly to EXAMPLE 143:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
144	[[5-[[[2,2-dimethylpropanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfonyl]methyl 2,2-dimethylpropanoate	5.38	482		¹ H NMR (CHLOROFORM-d) δ: 7.21 (d, J=3.3 Hz, 1H), 6.42 (s, 2H), 6.17 (d, J=3.3 Hz, 1H), 5.97 (s, 2H), 4.19 (t, J=5.9 Hz, 2H), 3.65-3.74 (m, 2H), 3.47 (quin, J=6.1 Hz, 1H), 1.14-1.20 (m, 9H), 1.12 (s, 9H), 1.01 (d, J=6.1 Hz, 6H)	51.1			
145	[[5-(hydroxymethyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfonyl]methyl 2,2-dimethylpropanoate	4.37	398		¹ H NMR (CHLOROFORM-d) δ: 7.26 (s, 2H), 7.09 (d, J=3.0 Hz, 1H), 6.70-6.85 (m, 1H), 6.14 (d, J=3.0 Hz, 1H), 5.99 (s, 2H), 5.56 (s, 2H), 4.26 (t, J=5.9 Hz, 2H), 3.73 (t, J=5.8 Hz, 2H), 3.51 (quin, J=5.9 Hz, 1H), 1.17-1.21 (m, 9H), 1.02-1.09 (m, 6H)				
146	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl 2,2-dimethylpropanoate	5.1 min	368		¹ H NMR (CHLOROFORM-d) δ: 9.39 (s, 1H), 7.25 (s, 1H), 6.24 (s, 3H), 4.53 (t, J=5.6 Hz, 2H), 3.85 (t, J=5.6 Hz, 2H), 3.54 (spt, J=6.1 Hz, 1H), 1.15 (s, 9H), 1.05 (d, J=6.0 Hz, 6H)				
147	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfonyl)methyl 2,2-dimethylpropanoate	4.37	368		¹ H NMR (CHLOROFORM-d) δ: 12.69 (s, 1H), 7.42 (t, J=3.0 Hz, 1H), 6.22 (dd, J=3.0, 1.9 Hz, 1H), 6.03 (s, 2H), 4.30 (t, J=6.0 Hz, 2H), 3.70-3.79 (m, 2H), 3.51 (quin, J=6.1 Hz, 1H), 1.18 (s, 9H), 1.06 (d, J=5.9 Hz, 6H)				
148	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl hexadecanoate	8.35 Method: 40-95% ACN with a hold for 10 min at 95% ACN	522		¹ H NMR (CHLOROFORM-d) δ: 9.69 (s, 1H), 7.30 (d, J=3.2 Hz, 1H), 6.20-6.29 (m, 3H), 4.53 (t, J=5.7 Hz, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.46-3.66 (m, 1H), 2.31 (t, J=7.5 Hz, 2H), 1.57-1.73 (br t, J=7.2 Hz, 2H), 1.19-1.31 (m, 24H), 1.04-1.10 (d, J=6.1 Hz, 6H), 0.83-0.93 (m, 3H)				
149	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl octadecanoate	9.9 Method: 40-95% ACN with a hold for 10 min at 95% ACN	550		¹ H NMR (CHLOROFORM-d) δ: 9.31 (s, 1H), 7.28 (d, J=3.2 Hz, 1H), 6.23-6.26 (m, 2H), 4.53 (t, J=5.7 Hz, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.56 (quin, J=6.1 Hz, 1H), 2.32 (t, J=7.5 Hz, 2H), 1.58 (s, 2H), 1.21-1.30 (m, 28H), 1.07 (d, J=6.0 Hz, 6H), 0.84-0.92 (m, 3H)				
150	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl nonadecanoate	10.88 Method: 40-95% ACN with a hold for 10 min at 95% ACN	565		¹ H NMR (CHLOROFORM-d) δ: 9.31 (s, 1H), 7.28 (d, J=3.2 Hz, 2H), 6.21-6.29 (m, 3H), 4.53 (t, J=5.7 Hz, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.56 (quin, J=6.1 Hz, 1H), 2.32 (t, J=7.5 Hz, 2H), 1.58 (m, 4H), 1.19-1.31 (m, 28H), 1.07 (d, J=5.9 Hz, 6H), 0.88 (s, 3H)				

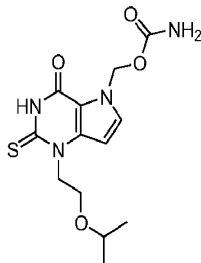
151	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl icosanoate	12.4 Method: 40-95% ACN with a hold for 10 min at 95% ACN	578	¹ H NMR (CHLOROFORM-d) δ: 9.40 (s, 1H), 7.28 (d, J=3.2 Hz, 1H), 6.18-6.42 (m, 3H), 4.53 (t, J=5.7 Hz, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.56 (spt, J=6.1 Hz, 1H), 2.32 (t, J=7.5 Hz, 2H), 1.51-1.70 (m, 4H), 1.25 (m, 30H), 1.07 (d, J=6.2 Hz, 6H), 0.84-0.92 (m, 3H)				
152	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl hencosanoate	Compound did not elute on the LCMS	Compound did not elute on the LCMS	¹ H NMR (CHLOROFORM-d) δ: 9.32 (s, 1H), 7.27-7.30 (m, 1H), 6.24 (s, 3H), 4.49-4.58 (m, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.56 (quin, J=6.1 Hz, 1H), 2.32 (t, J=7.9 Hz, 2H), 1.47-1.74 (m, 4H), 1.19-1.35 (m, 32H), 1.07 (d, J=6.1 Hz, 6H), 0.82-0.93 (m, 3H)				
153	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl docosanoate	Compound did not elute on the LCMS	Compound did not elute on the LCMS	¹ H NMR (CHLOROFORM-d) δ: 9.27 (s, 1H), 7.27-7.29 (m, 1H), 6.24 (s, 3H), 4.53 (t, J=5.6 Hz, 2H), 3.84 (t, J=5.6 Hz, 2H), 3.49-3.63 (m, 1H), 2.32 (t, J=7.5 Hz, 2H), 1.57 (s, 4H), 1.24 (br d, J=4.9 Hz, 36H), 1.03-1.11 (m, 6H), 0.83-0.92 (m, 3H)				
154	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl butanoate	4.58	354	¹ H NMR (CHLOROFORM-d) δ: 9.33 (s, 1H), 7.28 (d, J=3.2 Hz, 1H), 6.22-6.27 (m, 3H), 4.53 (t, J=5.6 Hz, 2H), 3.84 (t, J=5.6 Hz, 2H), 3.56 (dt, J=12.2, 6.1 Hz, 1H), 2.31 (t, J=7.4 Hz, 2H), 1.55-1.71 (m, 2H), 1.06 (d, J=6.2 Hz, 6H), 0.89 (t, J=7.4 Hz, 3H).	40.3	82% @ 1h	0% @ 1h	9% @ 1h
155	{[(5-[(butanoyloxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-c]pyrimidin-2-yl)sulfanylmethyl] butanoate	4.88	454	¹ H NMR (CHLOROFORM-d) δ: 7.25 (s, 1H), 6.44 (s, 2H), 6.19 (d, J=3.2 Hz, 1H), 5.98 (s, 2H), 4.21 (t, J=5.9 Hz, 2H), 3.69 (s, 2H), 3.51 (quin, J=6.1 Hz, 1H), 2.31 (q, J=7.6 Hz, 4H), 1.61-1.71 (m, 4H), 1.06 (d, J=6.1 Hz, 6H), 0.84-0.96 (m, 6H).	27.9	73% @ 1h	0% @ 1h	1% @ 1h
156	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl propanoate	4.25	340	¹ H NMR (CHLOROFORM-d) δ: 9.40 (s, 1H), 7.28 (d, J=3.2 Hz, 1H), 6.20-6.32 (m, 3H), 4.53 (t, J=5.7 Hz, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.56 (quin, J=6.1 Hz, 1H), 2.36 (q, J=7.5 Hz, 2H), 1.11 (t, J=7.6 Hz, 3H), 1.07 (d, J=6.2 Hz, 6H)	65.5	99% @ 1h	1% @ 1h	0% @ 1h
157	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl benzoate	5.67	388	¹ H NMR (CHLOROFORM-d) δ: 9.25 (s, 1H), 8.00-8.07 (m, 2H), 7.53-7.61 (m, 1H), 7.39-7.48 (m, 3H), 6.49 (s, 2H), 6.26 (d, J=3.1 Hz, 1H), 4.53 (t, J=5.7 Hz, 2H), 3.83 (t, J=5.7 Hz, 2H), 3.56 (quin, J=6.1 Hz, 1H), 1.06 (d, J=5.3 Hz, 6H)	73	96% @ 1h	20% @ 1h	0% @ 1h
158	trifluoroacetic acid {2-[[[benzoyloxy)methyl]sulfanylmethyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl benzoate	6.08	522	¹ H NMR (CHLOROFORM-d) δ: 8.01-8.15 (m, 4H), 7.52-7.64 (m, 2H), 7.34-7.50 (m, 4H), 6.69 (s, 2H), 6.25 (d, J=3.4 Hz, 1H), 6.22 (s, 2H), 4.24 (t, J=5.8 Hz, 2H), 3.71 (t, J=5.8 Hz, 2H), 3.48 (dt, J=12.1, 6.1 Hz, 1H), 1.02 (d, J=6.2 Hz, 6H)	53.7			

159	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl acetate	4.77	326	¹ H NMR (CHLOROFORM-d) δ: 9.23 (br s, 1H), 7.28 (d, J=3.2 Hz, 1H), 6.25 (d, J=3.4 Hz, 1H), 6.22-6.24 (m, 2H), 4.53 (t, J=5.7 Hz, 2H), 3.84 (t, J=5.7 Hz, 2H), 3.57 (dt, J=12.2, 6.1 Hz, 1H), 2.09 (s, 3H), 1.08 (d, J=6.4 Hz, 6H)	84.2	79% @ 1h	83% @ 1h	0% @ 1h
160	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-butyl-N-methylcarbamate	5.02	397	¹ H NMR (CHLOROFORM-d) δ: 12.52 (br s, 1H), 7.48 (t, J=3.0 Hz, 1H), 6.32-6.37 (m, 1H), 6.02 (d, J=1.2 Hz, 2H), 4.39 (t, J=5.7 Hz, 2H), 4.04-4.26 (m, 4H), 3.78 (t, J=5.6 Hz, 2H), 3.50 (quin, J=6.1 Hz, 1H), 3.24 (dt, J=19.2, 7.3 Hz, 2H), 2.88 (d, J=17.3 Hz, 3H), 1.36-1.57 (m, 2H), 1.12-1.35 (m, 2H), 1.04 (d, J=6.1 Hz, 6H), 0.74-0.96 (m, 3H)	158	92% @ 1h	95% @ 1h	99% @ 1h
161	{2-[[[(methyl(2-methylpropyl)carbamoyl)oxy)methyl]sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(2-methylpropyl)carbamate	6.07	540	¹ H NMR (CHLOROFORM-d) δ: 7.37 (d, J=3.2 Hz, 1H), 6.44 (s, 2H), 6.16 (d, J=3.2 Hz, 1H), 5.99-6.08 (m, 2H), 4.15-4.28 (m, 2H), 3.61-3.81 (m, 2H), 3.43-3.58 (m, 1H), 2.99-3.14 (m, 4H), 2.80-2.94 (m, 6H), 1.72-2.01 (m, 2H), 1.00-1.09 (m, 6H), 0.83-0.92 (m, 6H), 0.77 (dd, J=19.2, 6.7 Hz, 6H)	313	80% @ 1h	80% @ 1h	99% @ 1h
162	{2-[[[(butyl(methyl)carbamoyl)oxy)methyl]sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-butyl-N-methylcarbamate	6.93	540	¹ H NMR (CHLOROFORM-d) δ: 7.36 (m, 1H), 6.42 (d, 2H), 6.15 (m, 1H), 5.94-6.06 (m, 2H), 4.21 (m, 2H), 3.70 (m, 2H), 3.42-3.58 (m, 1H), 3.11-3.34 (m, 4H), 2.86 (m, 6H), 1.09-1.58 (m, 8H), 1.02-1.08 (m, 6H), 0.85-0.96 (m, 3H), 0.74-0.84 (m, 3H).	287	98% @ 1h	96% @ 1h	96% @ 1h
163	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-ethyl-N-methylcarbamate	5.2	369	¹ H NMR (CHLOROFORM-d) δ: 12.46 (br s, 1H), 7.40 (m, 1H), 6.22 (br s, 1H), 6.06 (s, 2H), 4.20-4.38 (m, 2H), 3.75 (m, 2H), 3.43-3.63 (m, 1H), 3.14-3.40 (m, 2H), 2.88 (d, 3H), 1.06 (d, 6H).	42	99% @ 1h	96% @ 1h	90% @ 1h
164	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N,N-dimethylcarbamate	5.22	355	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.64 (s, 1H), 7.52 (t, J=3.0 Hz, 1H), 6.48 - 6.25 (m, 1H), 6.00 (s, 2H), 4.39 (t, J=5.6 Hz, 2H), 3.78 (t, J=5.6 Hz, 2H), 3.60 - 3.39 (m, 1H), 2.90 (d, J=13.6 Hz, 6H), 1.03 (d, J=6.2 Hz, 6H).	42	100% @ 1h	99% @ 1h	98% @ 1h
165	trifluoroacetic acid [2-((((dimethylcarbamoyl)oxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N,N-dimethylcarbamate	5.28	455	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.51 (d, J=3.3 Hz, 1H), 6.37 (s, 2H), 6.29 - 6.22 (m, 1H), 5.95 (s, 2H), 4.28 (t, J=5.8 Hz, 2H), 3.74 (t, J=5.9 Hz, 2H), 3.60 - 3.44 (m, 1H), 2.90 (t, J=6.4 Hz, 11H), 1.06 (d, J=6.1 Hz, 6H).	25.6	84% @ 1h	99% @ 1h	97% @ 1h
166	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(propan-2-yl)carbamate	5.45	383	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.48 (s, 1H), 7.48 - 7.44 (m, 1H), 7.49 - 7.43 (m, 1H), 7.48 (t, J=3.0 Hz, 1H), 6.38 (t, J=2.5 Hz, 1H), 6.15 - 5.89 (m, 2H), 4.41 (t, J=5.5 Hz, 2H), 4.34 - 4.18 (m, 1H), 3.80 (t, J=5.6 Hz, 2H), 3.57 - 3.44 (m, 1H), 1.09 (dd, J=6.2, 11.7 Hz, 6H), 1.04 (d, J=6.1 Hz, 12H)	70.8	99% @ 1h	99% @ 1h	100% @ 1h

167	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-c]pyrimidin-2-yl)sulfanyl)methyl N-tert-butyl-N-methylcarbamate	5.92	397	1H NMR (300MHz, CHLOROFORM-d) δ = 12.76 - 12.39 (m, 1H), 7.60 - 7.41 (m, 1H), 6.35 (dd, J=1.9, 3.0 Hz, 2H), 5.99 (s, 2H), 4.39 (t, J=5.7 Hz, 2H), 3.89 - 3.67 (m, 2H), 3.50 (t, J=6.1 Hz, 1H), 2.89 (s, 3H), 1.37 (s, 9H), 1.04 (d, J=6.0 Hz, 6H)	178	99% @ 1h	99% @ 1h	98% @ 1h
168	trifluoroacetic acid {2-(((tert-butyl(methyl)carbamoyloxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-tert-butyl-N-methylcarbamate	7	540	1H NMR (300MHz, CHLOROFORM-d) δ = 7.48 (d, J=3.3 Hz, 1H), 6.36 (s, 2H), 6.24 (d, J=3.3 Hz, 1H), 5.94 (s, 2H), 4.27 (t, J=5.8 Hz, 2H), 3.74 (br t, J=5.6 Hz, 2H), 3.56 - 3.44 (m, 1H), 2.89 (s, 3H), 2.87 (s, 3H), 1.37 (s, 9H), 1.35 - 1.32 (m, 9H), 1.04 (d, J=6.0 Hz, 6H)	281	100% @ 1h	94% @ 1h	88% @ 1h
169	trifluoroacetic acid {2-(((ethyl(methyl)carbamoyloxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-ethyl-N-methylcarbamate	4.25	484	1H NMR (300MHz, CHLOROFORM-d) δ = 7.53 - 7.43 (m, 1H), 6.38 (s, 2H), 6.24 (d, J=3.2 Hz, 1H), 5.96 (d, J=2.3 Hz, 2H), 4.26 (t, J=5.8 Hz, 2H), 3.73 (t, J=5.8 Hz, 2H), 3.57 - 3.42 (m, 1H), 3.39 - 3.17 (m, 4H), 2.86 (dd, J=7.4, 11.5 Hz, 3H), 2.63 (t, J=5.6 Hz, 3H), 1.38 (d, J=6.6 Hz, 6H), 1.05 (d, J=6.1 Hz, 6H)	109	99% @ 1h	81% @ 1h	89% @ 1h
170	trifluoroacetic acid {2-(((methyl)propan-2-yl)carbamoyloxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-ethyl-N-methylcarbamate	4.45	498	1H NMR (300MHz, CHLOROFORM-d) δ = 7.51 (d, J=3.2 Hz, 1H), 6.46 - 6.34 (m, 2H), 6.26 (d, J=3.2 Hz, 1H), 6.06 - 5.94 (m, 2H), 4.28 (t, J=5.7 Hz, 2H), 3.79 - 3.69 (m, 2H), 3.59 - 3.43 (m, 1H), 3.38 - 3.20 (m, 3H), 2.97 - 2.66 (m, 6H), 1.18 - 0.98 (m, 15H)	141	99% @ 1h	92% @ 1h	99% @ 1h
171	trifluoroacetic acid {2-(((methyl)propan-2-yl)carbamoyloxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(propan-2-yl)carbamate	4.65	512	1H NMR (300MHz, CHLOROFORM-d) δ = 7.49 (d, J=3.2 Hz, 1H), 6.40 (d, J=6.3 Hz, 2H), 6.24 (d, J=3.2 Hz, 1H), 6.03 - 5.93 (m, 2H), 4.40 (ddd, J=6.9, 7.0, 13.6 Hz, 2H), 4.27 (t, J=5.8 Hz, 2H), 3.73 (t, J=5.8 Hz, 2H), 3.57 - 3.44 (m, 1H), 2.82 - 2.66 (m, 6H), 1.17 - 0.98 (m, 18H)	217	100% @ 1h	89% @ 1h	97% @ 1h
172	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(2-methylpropyl)carbamate	4.17	397	1H NMR (300MHz, CHLOROFORM-d) δ = 12.92 (s, 1H), 7.42 (t, J=3.0 Hz, 1H), 6.20 (dd, J=1.9, 3.0 Hz, 1H), 6.05 (s, 2H), 4.34 - 4.24 (m, 2H), 3.79 - 3.65 (m, 2H), 3.56 - 3.41 (m, 1H), 3.05 (dd, J=7.5, 17.5 Hz, 2H), 2.87 (d, J=19.9 Hz, 3H), 1.96 - 1.72 (m, 1H), 1.04 (d, J=6.1 Hz, 6H), 0.87 (d, J=6.8 Hz, 3H), 0.77 (d, J=6.7 Hz, 3H)	237	100% @ 1h	95% @ 1h	98% @ 1h
173	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-c]pyrimidin-2-yl)sulfanyl)methyl N-benzyl-N-methylcarbamate	4.23	431	1H NMR (300MHz, CHLOROFORM-d) δ = 12.68 (br d, J=14.7 Hz, 1H), 8.21 (s, 1H), 7.50 (q, J=3.4 Hz, 1H), 7.38 - 7.19 (m, 2H), 7.17 - 6.99 (m, 2H), 6.33 - 6.32 (m, 1H), 6.32 (q, J=2.6 Hz, 1H), 6.10 - 6.00 (m, 2H), 4.53 - 4.27 (m, 4H), 3.89 - 3.65 (m, 2H), 3.58 - 3.40 (m, 1H), 2.99 - 2.75 (m, 3H), 1.04 (dd, J=1.8, 5.9 Hz, 6H)	205	95% @ 1h	99% @ 1h	99% @ 1h

174	trifluoroacetic acid {2-[[[benzyl(methyl)carbamoyloxy]methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-benzyl-N-methylcarbamate	5.12	608	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.58 - 7.41 (m, 1H), 7.37 - 7.00 (m, 10H), 6.48 - 6.38 (m, 2H), 6.33 - 6.18 (m, 1H), 6.07 - 5.95 (m, 2H), 4.56 - 4.34 (m, 4H), 4.33 - 4.15 (m, 2H), 3.82 - 3.62 (m, 2H), 3.58 - 3.43 (m, 1H), 2.90 (dd, J=1.9, 12.3 Hz, 3H), 2.85 - 2.77 (m, 3H), 1.30 - 0.87 (m, 6H)	304	99% @ 1h	99% @ 1h	99% @ 1h
175	trifluoroacetic acid {(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(2-phenylethyl)carbamate	4.45	445	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.78 (br d, J=12.6 Hz, 1H), 7.49 (t, J=3.0 Hz, 1H), 7.37 - 6.94 (m, 5H), 6.29 (dd, J=1.8, 3.0 Hz, 1H), 6.06 - 5.95 (m, 2H), 4.35 (q, J=6.0 Hz, 2H), 3.86 - 3.68 (m, 2H), 3.57 - 3.37 (m, 3H), 2.88 - 2.64 (m, J=16.2 Hz, 5H), 1.08 - 1.00 (m, 6H)	309	99% @ 1h	92% @ 1h	95% @ 1h
176	trifluoroacetic acid {2-[[[methyl(2-phenylethyl)carbamoyloxy]methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(2-phenylethyl)carbamate	5.37	637	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.44 (dd, J=3.2, 7.1 Hz, 1H), 7.34 - 6.98 (m, 10H), 6.38 (d, J=4.8 Hz, 1H), 6.32 - 6.21 (m, 2H), 6.00 - 5.87 (m, 2H), 4.34 - 4.16 (m, 2H), 3.73 (q, J=5.9 Hz, 2H), 3.60 - 3.32 (m, 5H), 2.92 - 2.59 (m, 10H), 1.08 - 1.01 (m, 6H)	404	86% @ 1h	100% @ 1h	99% @ 1h
177	trifluoroacetic acid {(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(prop-2-en-1-yl)carbamate	3.85	381	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.68 (s, 1H), 7.47 (t, J=3.0 Hz, 1H), 6.28 (t, J=2.4 Hz, 1H), 6.03 (d, J=2.7 Hz, 2H), 5.84 - 5.57 (m, 1H), 5.20 - 4.95 (m, 2H), 4.43 - 4.27 (m, 2H), 3.94 - 3.69 (m, 4H), 3.56 - 3.42 (m, 1H), 2.86 (d, J=19.6 Hz, 3H), 1.09 - 1.00 (m, 6H)	152	99% @ 1h	89% @ 1h	99% @ 1h
178	trifluoroacetic acid {2-[[[methyl(prop-2-en-1-yl)carbamoyloxy]methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(prop-2-en-1-yl)carbamate	4.5	508	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.47 (t, J=3.5 Hz, 1H), 6.39 (d, J=3.6 Hz, 2H), 6.25 (br d, J=3.2 Hz, 1H), 5.98 (s, 2H), 5.85 - 5.54 (m, 2H), 5.25 - 4.96 (m, 4H), 4.26 (t, J=5.8 Hz, 2H), 3.94 - 3.77 (m, 4H), 3.73 (t, J=5.5 Hz, 2H), 3.59 - 3.42 (m, 1H), 2.85 (dd, J=6.9, 12.0 Hz, 6H), 1.05 (d, J=6.1 Hz, 6H).	194	99% @ 1h	75% @ 1h	86% @ 1h
179	trifluoroacetic acid {(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-(but-3-en-1-yl)-N-methylcarbamate	4.03	395	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.61 (br s, 1H), 7.49 (t, J=2.9 Hz, 1H), 6.33 (dd, J=1.5, 2.9 Hz, 1H), 6.02 (s, 2H), 5.86 - 5.57 (m, 1H), 5.20 - 4.88 (m, 2H), 4.45 - 4.31 (m, 2H), 3.78 (t, J=5.7 Hz, 2H), 3.56 - 3.43 (m, 1H), 3.40 - 3.20 (m, 2H), 2.89 (d, J=17.3 Hz, 3H), 2.38 - 2.10 (m, 2H), 1.04 (d, J=6.1 Hz, 6H)	145	95% @ 1h	91% @ 1h	99% @ 1h
180	trifluoroacetic acid {2-[[[but-3-en-1-yl)(methyl)carbamoyloxy]methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(but-3-en-1-yl)-N-methylcarbamate	4.77	536	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.49 (br t, J=4.0 Hz, 1H), 6.38 (s, 2H), 6.26 (d, J=3.2 Hz, 1H), 5.95 (s, 2H), 5.84 - 5.46 (m, 2H), 5.17 - 4.72 (m, 4H), 4.35 - 4.18 (m, 2H), 3.73 (br t, J=5.6 Hz, 2H), 3.58 - 3.41 (m, 1H), 3.30 (br t, J=8.2 Hz, 4H), 2.93 - 2.79 (m, 6H), 2.37 - 2.07 (m, 4H), 1.12 - 0.98 (m, 6H)	259	99% @ 1h	82% @ 1h	99% @ 1h

EXAMPLE 181



- 5-Hydroxymethyl-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one:** Dissolved 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (2.0 g, 7.9 mmole) in DMF (10 mL) and warmed to 130° C. After heating for 10 minutes, added the formaldehyde 37 % solution (1.9 mL, 24 mmole). Continued heating for 2 hours, then cooled to RT and concentrated *in vacuo*. Purified on a 120 g Silacel silica gel column, eluting with 0-4 % MeOH in CH₂Cl₂ to yield **5-hydroxymethyl-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one**: (2.1 g, 91 %), ¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 9.75 (br s, 1H), 7.13 (d, *J*=3.0 Hz, 1H), 6.18 (d, *J*=2.9 Hz, 1H), 5.61 - 5.48 (m, 2H), 5.43 - 5.30 (m, 1H), 4.55 (t, *J*=5.7 Hz, 2H), 3.85 (t, *J*=5.6 Hz, 2H), 3.62 - 3.45 (m, 1H), 1.07 (d, *J*=6.0 Hz, 6H). LC/MS Method A: *R*_t = 3.47 mins., (M+H)⁺ = 284, purity > 99%.
- Carbamic acid 1-(2-isopropoxy-ethyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrrolo[3,2-d]pyrimidin-5-ylmethyl ester:** At 23°C, added trichloroacetylisocyanate (0.073 mL, 0.12 g, 0.62 mmole) dropwise to a solution of **5-hydroxymethyl-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one** (0.07 g, 0.25 mmol) in CHCl₃ (3 mL). Let stir for 2 hours, then concentrated the reaction *in vacuo* and repeated by redissolving in CH₂Cl₂ and concentrating the reaction mixture down. Suspended the solid in 3 mL of the 10% H₂O/90% MeOH. Added Na₂CO₃, and let stir at 23°C for 18 hours, then filtered, washing first with H₂O, then with diethyl ether to yield **carbamic acid 1-(2-isopropoxy-ethyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrrolo[3,2-d]pyrimidin-5-ylmethyl ester**: (56 mg, 69 %). ¹H NMR (300 MHz, DMSO-*d*₆) δ = 12.33 (br s, 1H), 7.47 (d, *J*=3.1 Hz, 1H), 7.08 - 6.55 (m, 2H), 6.35 (d, *J*=3.1 Hz, 1H), 6.06 (s, 2H), 4.46 (br t, *J*=5.9 Hz, 2H), 3.69 (t, *J*=6.0 Hz, 2H), 3.59 - 3.48 (m, 1H), 0.99 (d, *J*=7.0 Hz, 6H). LC/MS Method A: *R*_t = 3.57 mins., (M+H)⁺ = 327, purity > 98%. Caco-2 *P*_{app} = 218 nm/s, SGF = 82% remaining at 1 h, SIF = 97% remaining at 1 h, *h*Plasma stability = 99% remaining at 1 h.

Additional compounds prepared similarly to EXAMPLE 181:

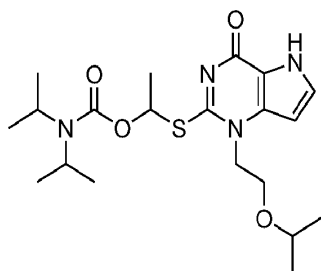
Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
182	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-propylcarbamate	4.28	369		¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.34 (s, 1 H), 7.48 (d, J=2.93 Hz, 1 H), 7.44 (t, J=5.57 Hz, 1 H), 6.36 (d, J=2.93 Hz, 1 H), 6.09 (s, 2 H), 4.46 (t, J=5.86 Hz, 2 H), 3.70 (t, J=5.86 Hz, 2 H), 3.49 - 3.58 (m, 1 H), 2.84 - 2.97 (m, 2 H), 1.28 - 1.42 (m, 2 H), 0.98 (d, J=6.45 Hz, 6 H), 0.68 - 0.84 (m, 3 H)		81% @ 1h	69% @ 1h	94% @ 1h
183	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-(((propylcarbamoyl)oxymethyl)sulfanyl)-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-propylcarbamate	4.32	484		¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.34 (d, J=3.2 Hz, 1H), 6.37 (s, 2H), 6.16 (d, J=3.2 Hz, 1H), 5.96 (s, 2H), 4.92 (q, J=5.9 Hz, 2H), 4.21 (t, J=5.9 Hz, 2H), 3.78 - 3.65 (m, 2H), 3.58 - 3.43 (m, 1H), 3.23 - 3.04 (m, 4H), 1.60 - 1.38 (m, 4H), 1.06 (d, J=6.1 Hz, 6H), 0.96 - 0.78 (m, 6H)	45.9	94% @ 1h	99% @ 1h	92% @ 1h
184	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-5-(propylcarbamoyl)-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-propylcarbamate	4.77	454		¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.18 (t, J=4.98 Hz, 1 H), 8.07 (d, J=3.52 Hz, 1 H), 7.55 (t, J=5.86 Hz, 1 H), 6.72 (d, J=3.52 Hz, 1 H), 5.78 (s, 2 H), 4.34 (t, J=4.98 Hz, 2 H), 3.67 (t, J=5.27 Hz, 2 H), 3.46 (t, J=5.86 Hz, 1 H), 3.21 - 3.30 (m, 2 H), 2.87 - 2.99 (m, 2 H), 1.50 - 1.65 (m, 2 H), 1.30 - 1.45 (m, 2 H), 0.89 - 1.00 (m, 9 H), 0.80 (t, J=7.33 Hz, 3 H)		99% @ 1h	86% @ 1h	95% @ 1h
185	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-butylcarbamate	5.28	482		¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.23 - 12.03 (m, 1H), 8.13 (d, J=3.6 Hz, 1H), 6.34 (d, J=3.6 Hz, 1H), 5.95 (s, 2H), 4.93 - 4.70 (m, 1H), 4.27 (t, J=5.6 Hz, 2H), 3.74 (t, J=5.6 Hz, 2H), 3.57 - 3.34 (m, 3H), 3.27 - 2.98 (m, 2H), 1.74 - 1.56 (m, 3H), 1.55 - 1.40 (m, 3H), 1.39 - 1.23 (m, 2H), 1.05 (d, J=6.0 Hz, 6H), 0.93 (td, J=7.6, 12.9 Hz, 6H)		78% @ 1h	67% @ 1h	96% @ 1h
186	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-(2-methylpropyl)carbamate	4.52	383		%. ¹ H NMR (300MHz, DMSO-d ₆) δ = 12.54 - 12.19 (m, 1H), 7.68 - 7.42 (m, 2H), 6.36 (d, J=3.3 Hz, 1H), 6.09 (s, 2H), 4.62 - 4.34 (m, 2H), 3.84 - 3.65 (m, 2H), 3.59 - 3.47 (m, 1H), 2.76 (t, J=6.4 Hz, 2H), 1.60 (ddd, J=6.7, 6.8, 13.5 Hz, 1H), 0.98 (d, J=6.1 Hz, 6H), 0.77 (d, J=6.7 Hz, 6H)	72.3	86% @ 1h	100% @ 1h	98% @ 1h
187	((5-[(2-methylpropyl)carbamoyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-(2-methylpropyl)carbamate	5.27	482		¹ H NMR (300MHz, DMSO-d ₆) δ = 12.20 (t, J=5.2 Hz, 1H), 8.08 (d, J=3.6 Hz, 1H), 7.59 (t, J=5.9 Hz, 1H), 6.72 (d, J=3.7 Hz, 1H), 5.79 (s, 2H), 4.33 (t, J=5.1 Hz, 2H), 3.67 (t, J=5.2 Hz, 2H), 3.52 - 3.40 (m, 1H), 3.15 (t, J=5.8 Hz, 2H), 2.79 (t, J=6.4 Hz, 2H), 1.83 (ddd, J=6.6, 6.7, 13.3 Hz, 1H), 1.63 (td, J=6.7, 13.4 Hz, 1H), 1.00 - 0.89 (m, 12H), 0.79 (d, J=6.7 Hz, 6H)	331	97% @ 1h	97% @ 1h	96% @ 1h

188	<chem>{2-}([([2-methylpropyl]carbamoyl)oxy)methyl]sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-c]pyrimidin-5-yl)methyl N-(2-methylpropyl)carbamate</chem>	4.68	512	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.33 (d, J=3.2 Hz, 1H), 6.37 (s, 2H), 6.15 (d, J=3.3 Hz, 1H), 5.96 (s, 2H), 5.10 - 4.89 (m, 2H), 4.20 (t, J=5.9 Hz, 2H), 3.77 - 3.65 (m, 2H), 3.59 - 3.41 (m, 1H), 3.12 - 2.88 (m, 4H), 1.87 - 1.59 (m, 2H), 1.05 (d, J=6.2 Hz, 6H), 0.88 (dd, J=6.7, 9.4 Hz, 12H)	117	98% @ 1h	97% @ 1h	99% @ 1h
189	<chem>{2-}([([ethyl](propan-2-yl)carbamoyl)oxy)methyl]sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-ethyl-N-(propan-2-yl)carbamate</chem>	4.98	540	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.52 (br s, 2H), 6.39 (s, 2H), 6.27 (d, J=3.2 Hz, 1H), 5.97 (s, 2H), 4.29 (t, J=5.6 Hz, 3H), 3.83 - 3.64 (m, 2H), 3.55 - 3.44 (m, 1H), 3.28 - 3.03 (m, 4H), 1.18 - 1.05 (m, 18H), 1.03 (d, J=6.1 Hz, 6H)	306	99% @ 1h	97% @ 1h	98% @ 1h
190	<chem>{([4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfanyl)methyl N-ethyl-N-(propan-2-yl)carbamate</chem>	4.1	397	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.69 (br s, 1H), 7.52 (t, J=3.1 Hz, 1H), 6.42 - 6.20 (m, 1H), 6.03 (s, 2H), 4.38 (t, J=5.6 Hz, 2H), 4.33 - 4.00 (m, 1H), 3.77 (t, J=5.6 Hz, 2H), 3.53 - 3.39 (m, 1H), 3.28 - 2.98 (m, 2H), 1.16 - 1.04 (m, 9H), 1.00 (d, J=6.2 Hz, 6H).	138	99% @ 1h	98% @ 1h	99% @ 1h
191	<chem>tert-butyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxylate</chem>	4.83	354	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.56 (s, 1H), 7.62 (d, J=3.6 Hz, 1H), 6.38 (d, J=3.6 Hz, 1H), 4.53 (t, J=5.4 Hz, 2H), 3.83 (t, J=5.4 Hz, 2H), 3.63 - 3.46 (m, 1H), 1.64 (s, 9H), 1.05 (d, J=6.0 Hz, 6H)	10.8	15% @ 1h	82% @ 1h	16% @ 1h
192	<chem>{([4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfanyl)methyl N-benzylcarbamate</chem>	4.58	417	¹ H NMR (300MHz, DMSO-d ₆) δ = 12.36 (s, 1H), 8.02 (t, J=6.2 Hz, 1H), 7.49 (d, J=3.1 Hz, 1H), 7.27 (br d, J=7.2 Hz, 2H), 7.24 - 7.15 (m, 3H), 6.37 (d, J=3.1 Hz, 1H), 6.12 (s, 2H), 4.56 - 4.39 (m, 2H), 4.15 (d, J=6.1 Hz, 2H), 3.70 (t, J=6.0 Hz, 2H), 3.59 - 3.44 (m, 1H), 0.99 (d, J=6.1 Hz, 6H)	38.4	100% remaining At 1h	50% remaining At 1h	97% remaining @ 1h
193	<chem>{([5-(benzylcarbamoyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-c]pyrimidin-2-yl]sulfanyl)methyl N-benzylcarbamate</chem>	5.28	550	¹ H NMR (300MHz, DMSO-d ₆) δ = 12.69 (t, J=5.4 Hz, 1H), 8.25 - 7.93 (m, 2H), 7.40 - 7.16 (m, 10H), 6.76 (d, J=3.7 Hz, 1H), 5.80 (s, 2H), 4.53 (d, J=5.3 Hz, 2H), 4.35 (t, J=5.3 Hz, 2H), 4.18 (d, J=6.1 Hz, 2H), 3.67 (t, J=5.2 Hz, 2H), 3.53 - 3.39 (m, 1H), 0.93 (d, J=6.0 Hz, 6H). LC/MS: Rt = 5.28 mins., (M+H) ⁺ = 550, purity > 95%.	316	98% remaining At 1h	57% remaining At 1h	95% remaining @ 1h
194	<chem>{([5-(butylcarbamoyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-c]pyrimidin-2-yl]sulfanyl)methyl N-butylcarbamate</chem>	5.28	482	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.23 - 12.03 (m, 1H), 8.13 (d, J=3.6 Hz, 1H), 6.34 (d, J=3.6 Hz, 1H), 5.95 (s, 2H), 4.93 - 4.70 (m, 1H), 4.27 (t, J=5.6 Hz, 2H), 3.74 (t, J=5.6 Hz, 2H), 3.57 - 3.34 (m, 3H), 3.27 - 2.98 (m, 2H), 1.74 - 1.56 (m, 3H), 1.55 - 1.40 (m, 3H), 1.39 - 1.23 (m, 2H), 1.05 (d, J=6.0 Hz, 6H), 0.93 (td, J=7.6, 12.9 Hz, 6H)	429	99% remaining At 1h	59% remaining At 1h	97% remaining @ 1h

195	((4-oxo-5-[(propan-2-yl)carbamoyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-(propan-2-yl)carbamate	4.7	454	¹ H NMR (300MHz, CHLOROFORM-d) δ = 12.13 (br d, J=6.6 Hz, 1H), 8.13 (d, J=3.7 Hz, 1H), 6.34 (d, J=3.6 Hz, 1H), 5.92 (s, 2H), 4.72 (br d, J=8.0 Hz, 1H), 4.28 (t, J=5.6 Hz, 2H), 4.13 - 3.94 (m, 1H), 3.89 - 3.78 (m, 1H), 3.74 (t, J=5.5 Hz, 2H), 3.55 - 3.42 (m, 1H), 1.33 (d, J=6.6 Hz, 6H), 1.15 (d, J=6.5 Hz, 6H), 1.05 (d, J=6.1 Hz, 6H)	300	100% remaining At 1h	99% remaining At 1h	97% remaining @ 1h
196	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-(propan-2-yl)carbamate	4.28	369	¹ H NMR (300MHz, DMSO-d ₆) δ = 12.34 (s, 1H), 7.48 (d, J=3.1 Hz, 1H), 7.37 (d, J=7.7 Hz, 1H), 6.36 (d, J=3.1 Hz, 1H), 6.08 (s, 2H), 4.46 (t, J=6.0 Hz, 2H), 3.70 (t, J=6.0 Hz, 2H), 3.62 - 3.42 (m, 2H), 0.99 (dd, J=4.2, 6.3 Hz, 12H)	195	99% remaining At 1h	98% remaining At 1h	99% remaining @ 1h
197	5-(hydroxymethyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	3.47	284	¹ H NMR (300MHz, CHLOROFORM-d) δ = 10.63-9.52 (bs, 1H), 7.13 (d, J=3.0 Hz, 1H), 5.54 (s, 2H), 4.55 (t, J=5.7 Hz, 2H), 3.85 (t, J=5.6 Hz, 2H), 3.64 - 3.49 (m, 1H), 1.07 (d, J=6.5 Hz, 6H)	unstable	98% remaining At 1h	55% remaining At 1h	86% remaining @ 1h
198	[2-(((methoxycarbonyl)oxy)methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl methyl carbonate	4.08	430	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.39 (d, J=3.3 Hz, 1H), 6.41 (s, 2H), 6.30 (d, J=3.3 Hz, 1H), 5.98 (s, 2H), 4.36 - 4.20 (m, 2H), 3.80 (d, J=6.1 Hz, 6H), 3.74 (t, J=5.6 Hz, 2H), 3.63 - 3.39 (m, 1H), 1.17 - 0.94 (m, 6H)	114	79% remaining At 1h	74% remaining At 1h	0% remaining @ 1h
199	methyl ((4-oxo-5-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl methyl carbonate	4.58	607	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.18 (s, 1H), 7.91 - 7.75 (m, 1H), 7.47 - 7.32 (m, 1H), 6.44 (s, 2H), 6.28 (d, J=3.3 Hz, 1H), 6.22 (s, 2H), 6.13 - 6.08 (m, 1H), 4.50 (t, J=5.9 Hz, 2H), 4.20 (t, J=5.5 Hz, 2H), 3.86 - 3.76 (m, 5H), 3.69 (t, J=5.5 Hz, 2H), 3.63 - 3.52 (m, 1H), 3.52 - 3.42 (m, 1H), 1.10 - 1.05 (m, 6H), 1.05 - 0.99 (m, 6H)	55.4	47% remaining At 1h	79% remaining At 1h	46% remaining @ 1h
200	methyl ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl methyl carbonate	4.25	342	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.32 (s, 1H), 7.30 (d, J=3.1 Hz, 1H), 6.26 (s, 3H), 4.53 (t, J=5.6 Hz, 2H), 3.84 (t, J=5.6 Hz, 2H), 3.80 (s, 3H), 3.63 - 3.48 (m, 1H), 1.07 (d, J=6.1 Hz, 6H)	97.6	100% remaining At 1h	75% remaining At 1h	2% remaining At 1h
201	ethyl ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl methyl carbonate	4.55	356	¹ H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.19 (br d, J=1.17 Hz, 1 H) 7.30 (d, J=2.93 Hz, 1 H) 6.20 - 6.34 (m, 3 H) 4.53 (t, J=5.57 Hz, 2 H) 4.22 (q, J=7.03 Hz, 2 H) 3.84 (t, J=5.57 Hz, 2 H) 3.45 - 3.62 (m, 1 H) 1.19 - 1.38 (t, J=5.9 Hz, 3 H) 1.07 (d, J=5.86 Hz, 6 H)		100% remaining At 1h	43% remaining At 1h	0% remaining At 1h

202	ethyl ((4-oxo-5-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl)-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl carbonate	4.82	621	¹ H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.16 (s, 1 H) 7.82 (d, J=2.93 Hz, 1 H) 7.34 (d, J=2.93 Hz, 1 H) 6.44 (s, 2 H) 6.27 (d, J=2.93 Hz, 1 H) 6.22 (s, 2 H) 6.10 (d, J=3.52 Hz, 1 H) 4.50 (t, J=5.86 Hz, 2 H) 4.12 - 4.31 (m, 4 H) 3.81 (t, J=5.86 Hz, 2 H) 3.69 (t, J=5.57 Hz, 2 H) 3.40 - 3.61 (m, 2 H) 1.29 (t, J=7.03 Hz, 3 H) 1.07 (d, J=5.86 Hz, 6 H) 1.02 (d, J=5.86 Hz, 6 H)		45% remaining At 1h	52% remaining At 1h	3% remaining At 1h
203	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl propan-2-yl carbonate	4.82	370	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.15 (s, 1H), 7.30 (d, J=3.1 Hz, 1H), 6.27 (d, J=3.2 Hz, 1H), 6.25 (s, 2H), 4.95 - 4.82 (m, 1H), 4.53 (t, J=5.6 Hz, 2H), 3.84 (t, J=5.6 Hz, 2H), 3.63 - 3.48 (m, 1H), 1.28 (d, J=6.3 Hz, 6H), 1.07 (d, J=6.1 Hz, 6H)	134	99% remaining At 1h	63% remaining At 1h	1% remaining At 1h
204	butyl ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl carbonate	5.15	384	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.44 (s, 1H), 7.30 (d, J=3.2 Hz, 1H), 6.26 (s, 3H), 4.53 (t, J=5.6 Hz, 2H), 4.15 (t, J=6.6 Hz, 2H), 3.84 (t, J=5.6 Hz, 2H), 3.65 - 3.43 (m, 1H), 1.65 - 1.56 (m, 2H), 1.43 - 1.28 (m, 2H), 1.07 (d, J=5.9 Hz, 6H), 0.95 - 0.86 (m, 3H)	63.5	85	2	1% remaining at 1 h
205	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl phenyl carbonate	5.07	404	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.23 (s, 1H), 7.43 - 7.34 (m, 2H), 7.35 - 7.34 (m, 1H), 7.34 - 7.27 (m, 1H), 7.24 - 7.12 (m, 2H), 6.37 (s, 2H), 6.30 (br d, J=3.2 Hz, 1H), 4.54 (s, 2H), 3.86 (t, J=5.5 Hz, 2H), 3.66 - 3.51 (m, 1H), 1.08 (d, J=6.2 Hz, 6H).		61	10	2% remaining at 1 h
206	octyl ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl carbonate	6.37	440	¹ H NMR (300MHz, CHLOROFORM-d) δ = 9.39 (s, 1H), 7.30 (d, J=3.2 Hz, 1H), 6.26 (s, 3H), 4.53 (s, 2H), 4.14 (t, J=6.7 Hz, 2H), 3.84 (t, J=5.6 Hz, 2H), 3.67 - 3.45 (m, 1H), 1.70 - 1.57 (m, 2H), 1.40 - 1.18 (m, 10H), 1.07 (d, J=6.0 Hz, 6H), 0.86 (t, J=7.0 Hz, 3H)	1.38	91	1	99% remaining at 1 h
207	octyl (2-(((octyloxy)carbonyloxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	7.47	626	¹ H NMR (300MHz, CHLOROFORM-d) δ = 7.30 (d, J=3.2 Hz, 1H), 6.43 (s, 2H), 6.23 (d, J=3.3 Hz, 1H), 6.03 (s, 2H), 4.25 (t, J=5.8 Hz, 2H), 4.18 - 4.08 (m, 4H), 3.76 - 3.68 (m, 2H), 3.57 - 3.44 (m, 1H), 1.72 - 1.56 (m, 4H), 1.42 - 1.19 (m, 20H), 1.06 (d, J=6.0 Hz, 6H), 0.86 (t, J=6.8 Hz, 6H)	2.67	90	29	92% remaining at 1 h

EXAMPLE 208:



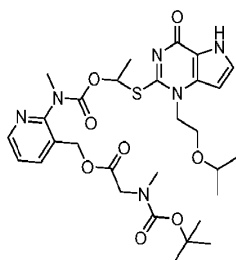
1-Chloroethyl N,N-bis(propan-2-yl)carbamate: Dissolved diisopropyl amine (0.12 g, 0.18 mL, 2.1 mmole) in 2 mL CH₂Cl₂, then added diisopropyl ethyl amine (0.73 mL, 2.5 mmole). Cooled in an ice bath, then added dropwise, over 1 min, 1-chloro-ethyl chloroformate (0.23 mL, 2.1 mmole). After 2 hours, partitioned between CH₂Cl₂ and H₂O. Separated layers and washed the org. layer with brine. Dried over H₂O filtered and concentrated *in vacuo* to yield **1-chloroethyl N,N-bis(propan-2-yl)carbamate**: ¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 6.78 - 6.49 (m, 1H), 4.10 (s, 1H), 3.74 (s, 1H), 1.82 (d, *J*=5.7 Hz, 3H), 1.22 (d, *J*=6.9 Hz, 12H). Took on as is. (0.35 g, 100%).

1-({4-Oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl}sulfanyl)ethyl N,N-bis(propan-2-yl)carbamate: Added sodium hydride (60 % dispersion in mineral oil (20 mg, 0.829 mmole) to a solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (0.10 g, 0.39 mmole) in THF (3 mL). After gas evolution had ceased, added **1-chloroethyl N,N-bis(propan-2-yl)carbamate** (0.35 g, 2.1 mmole) in 2 mL THF. After 18 hours, concentrated the reaction *in vacuo*, then purified on a 40 g Agela silica gel column, eluting with 0-5 % MeOH in CH₂Cl₂. Concentrated desired fractions *in vacuo*. Repeated purification using same conditions. To yield **1-({4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl}sulfanyl)ethyl N,N-bis(propan-2-yl)carbamate**: (55.4 mg, 33%). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 12.46 (s, 1H), 7.49 - 7.43 (m, 1H), 6.89 (d, *J*=6.5 Hz, 1H), 6.29 - 6.23 (m, 1H), 4.50 - 4.20 (m, 2H), 4.06 (s, 1H), 3.77 (t, *J*=5.9 Hz, 2H), 3.72 - 3.59 (m, 1H), 3.58 - 3.41 (m, 1H), 1.90 (d, *J*=6.5 Hz, 3H), 1.18 (dd, *J*=3.6, 6.8 Hz, 12H), 1.05 (dd, *J*=2.0, 6.1 Hz, 6H). LC/MS Method A: R_t = 4.52 mins., (M+H)⁺ = 425, purity 95 %. Caco-2 P_{app} = 183 nm/s, SGF = 1% remaining at 1 h, SIF = 93% remaining at 1 h, hPlasma stability = 98% remaining at 1 h.

Additional compounds prepared similarly to EXAMPLE 208:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
209	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-phenylcarbamate	4.18	417		¹ H NMR (300MHz, DMSO-d ₆) δ = 12.03 (s, 1H), 7.40 - 7.00 (m, 6H), 6.35 (s, 1H), 5.81 (d, J=2.2 Hz, 2H), 4.23 (q, J=5.7 Hz, 2H), 3.76 - 3.56 (m, 2H), 3.51 - 3.36 (m, 1H), 3.30 (s, 3H), 0.93 (dd, J=2.1, 6.0 Hz, 6H)	161	99% remaining at 1 h	99% remaining at 1 h	97% remaining at 1 h
210	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-(3-fluorophenyl)-N-methylcarbamate	4.3	435		¹ H NMR (300MHz, DMSO-d ₆) δ = 12.03 (br s, 1H), 7.34 - 7.24 (m, 2H), 7.20 - 7.07 (m, 2H), 7.05 - 6.93 (m, 1H), 6.35 (d, J=2.9 Hz, 1H), 5.84 (s, 2H), 4.24 (t, J=5.5 Hz, 2H), 3.65 (t, J=5.4 Hz, 2H), 3.52 - 3.38 (m, 1H), 3.20 (s, 3H), 0.98 - 0.88 (m, 6H)	183	100% remaining at 1 h	97% remaining at 1 h	97% remaining at 1 h
211	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-(4-fluorophenyl)-N-methylcarbamate	4.22	435		¹ H NMR (300MHz, DMSO-d ₆) δ = 12.08 (s, 1H), 7.30 (t, J=3.0 Hz, 2H), 7.26 (br d, J=6.3 Hz, 1H), 7.14 - 7.00 (m, 2H), 6.39 - 6.34 (m, 1H), 5.81 (s, 2H), 4.25 (t, J=5.4 Hz, 2H), 3.65 (t, J=5.4 Hz, 2H), 3.52 - 3.39 (m, 1H), 3.17 (s, 3H), 0.93 (d, J=6.1 Hz, 6H)	200	100% remaining at 1 h	96% remaining at 1 h	99% remaining at 1 h

EXAMPLE 212:



5 Step 1 -4-{[(1-chloroethoxy)carbonyl](methyl)amino}pyridin-3-yl)methyl 2-{[(tert-butoxy)carbonyl]-(methyl)amino}acetate was synthesized by following the procedure in J. Ohwada et al. *Bioorg. Med. Chem. Lett.* 13 (2003) 191–196.

(tert-Butoxycarbonyl-methyl-amino)-acetic acid 2-{[1-[2-isopropoxy-ethyl]-4-oxo-4,5-dihydro-1H-pyrrolo[3,2-d]pyrimidin-2-ylsulfanyl]-ethoxycarbonyl}-methyl-amino)-pyridin-3-ylmethyl ester: Added sodium hydride, 60 % dispersion in mineral oil (20 mg, 0.83 mmole) to a solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (0.10 g, 0.39 mmole) in THF (3 mL). After gas evolution had ceased, added (2-{[(1chloroethoxy)carbonyl](methyl)-amino}pyridin-3-yl)methyl 2-{[(tert-butoxy)carbonyl](methyl)amino}acetate (0.18 g, 0.434 mmole) in 2 mL THF. Monitored by LCMS and TLC. Let go for 18 hours while warming to 40° C. Added sodium
15 hydride (60 % dispersion in mineral oil (5 mg, 0.21 mmole) and warmed to 50 °C for 4 hours. Cooled to

RT and Concentrated *in vacuo*. Took up in CH₂Cl₂ and purified on the ISCO using a 20 g column eluting with 0-10 % MeOH in CH₂Cl₂. Concentrated desired fractions *in vacuo* to yield **(tert-Butoxycarbonyl-methyl-amino)-acetic acid 2-({1-[1-(2-isopropoxy-ethyl)-4-oxo-4,5-dihydro-1H-pyrrolo[3,2-d]pyrimidin-2-ylsulfanyl]-ethoxycarbonyl}-methyl-amino)-pyridin-3-ylmethyl ester**: (43 mg, 17 %). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 12.80 (br d, *J*=13.3 Hz, 1H), 8.37 (br s, 1H), 7.73 (br d, *J*=7.7 Hz, 1H), 7.37 (s, 1H), 7.24 - 7.13 (m, 1H), 7.10 - 6.77 (m, 1H), 6.60 - 6.60 (m, 1H), 6.16 (t, *J*=2.4 Hz, 1H), 5.11 (s, 2H), 4.46 - 4.10 (m, 2H), 3.97 - 3.79 (m, 2H), 3.72 (br t, *J*=5.7 Hz, 2H), 3.56 - 3.45 (m, 1H), 3.36 - 3.23 (m, 3H), 2.83 (s, 3H), 1.97 - 1.66 (m, 3H), 1.44 - 1.27 (m, 9H), 1.04 (dd, *J*=3.5, 6.1 Hz, 6H). LC/MS Method A:: *R*_t = 4.47 mins., (M+H)⁺ = 633.78. Caco-2 *P*_{app} = 8.7 nm/s, SGF = 89% remaining at 1 h, SIF = 97% remaining at 1 h, hPlasma stability = 97% remaining at 1 h.

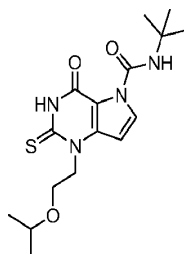
Additional compounds prepared similarly to EXAMPLE 212:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
213	hexyl {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfany-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	5.82	412		¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.26 - 12.61 (m, 1 H), 7.52 (d, J=3.52 Hz, 1 H), 6.39 (d, J=3.52 Hz, 1 H), 6.16 (s, 2 H), 4.45 (t, J=5.86 Hz, 2 H), 4.06 (t, J=6.74 Hz, 2 H), 3.69 (t, J=5.86 Hz, 2 H), 3.51 (dt, J=12.16, 5.93 Hz, 1 H), 1.45 - 1.62 (m, 2 H), 1.15 - 1.33 (m, 6 H), 0.97 (d, J=6.45 Hz, 6 H), 0.76 - 0.86 (m, 3 H)	30.3	76% remaining at 1h	1% remaining at 1h	44% remaining at 1h
214	hexyl 2-[[[(hexyloxy)carbonyloxy)methyl]sulfany]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	6.55	570		¹ H NMR (300MHz, DMSO-d ₆) δ = 7.49 (d, J=3.3 Hz, 1H), 6.50 (d, J=3.2 Hz, 1H), 6.28 (s, 2H), 5.83 (s, 2H), 4.25 (t, J=5.3 Hz, 2H), 4.13 - 4.01 (m, 4H), 3.67 - 3.61 (m, 2H), 3.50 - 3.38 (m, 1H), 1.62 - 1.44 (m, 4H), 1.30 - 1.15 (m, 12H), 0.93 (d, J=6.2 Hz, 6H), 0.81 (s, 6H)	16.3	80% remaining at 1h	2% remaining at 1h	77% remaining at 1h
215	hexyl [3-[[[(hexyloxy)carbonyloxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	7.22	570		¹ H NMR (300MHz, DMSO-d ₆) δ = 7.65 (d, J=3.2 Hz, 1H), 6.47 (d, J=3.2 Hz, 1H), 6.38 (s, 2H), 6.18 (s, 2H), 4.56 (t, J=5.8 Hz, 2H), 4.07 (q, J=6.4 Hz, 4H), 3.73 (t, J=5.8 Hz, 2H), 3.59 - 3.46 (m, 1H), 1.64 - 1.44 (m, 4H), 1.34 - 1.14 (m, 12H), 0.97 (d, J=6.1 Hz, 6H), 0.87 - 0.76 (m, 6H)	2.14	94% remaining at 1h	1% remaining at 1h	88% remaining at 1h
216	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfany-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl pentyl carbonate	5.48	398		¹ H NMR (300MHz, DMSO-d ₆) δ = 12.39 (s, 1H), 7.52 (d, J=3.1 Hz, 1H), 6.39 (d, J=3.2 Hz, 1H), 6.15 (s, 2H), 4.45 (t, J=6.0 Hz, 2H), 4.05 (t, J=6.6 Hz, 2H), 3.68 (t, J=6.0 Hz, 2H), 3.58 - 3.44 (m, 1H), 1.60 - 1.44 (m, 2H), 1.29 - 1.14 (m, 4H), 0.96 (d, J=6.0 Hz, 6H), 0.85 - 0.76 (m, 3H)	45.9	91% remaining at 1h	1% remaining at 1h	1% remaining at 1h

217	{4-oxo-2- [[[(pentylloxy)carbonyloxy)methyl] sulfanyl]-1-[2-(propan-2- yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2- d]pyrimidin-5-yl]methyl pentyl carbonate	6.13	542	1H NMR (300MHz, DMSO-d6) δ = 7.65 (d, J=3.1 Hz, 1H), 6.47 (d, J=3.2 Hz, 1H), 6.37 (s, 2H), 6.18 (s, 1H), 4.56 (br t, J=5.2 Hz, 2H), 4.07 (q, J=6.0 Hz, 3H), 3.72 (br t, J=5.5 Hz, 2H), 3.62 - 3.38 (m, 3H), 1.68 - 1.43 (m, 4H), 1.33 - 1.12 (m, 8H), 1.02 - 0.90 (m, 6H), 0.82 (q, J=5.9 Hz, 6H)	53.2	88% remaining at 1h	1% remaining at 1h	5% remaining at 1h
218	[4-oxo-3- (((pentylloxy)carbonyloxy)methyl)- 1-[2-(propan-2-yloxy)ethyl]-2- sulfanylidene-1H,2H,3H,4H,5H- pyrrolo[3,2-d]pyrimidin-5-yl]methyl pentyl carbonate	6.8	542	1H NMR (300MHz, DMSO-d6) δ = 7.49 (d, J=3.2 Hz, 1H), 6.50 (d, J=3.3 Hz, 1H), 6.28 (s, 2H), 5.83 (s, 2H), 4.25 (t, J=5.3 Hz, 2H), 4.13 - 3.98 (m, 4H), 3.64 (t, J=5.3 Hz, 2H), 3.52 - 3.35 (m, 1H), 1.62 - 1.42 (m, 4H), 1.32 - 1.10 (m, 8H), 0.93 (d, J=6.1 Hz, 6H), 0.86 - 0.73 (m, 6H)	6.5	100% remaining at 1h	2% remaining at 1h	74% remaining at 1h
219	heptyl {4-oxo-1-[2-(propan-2- yloxy)ethyl]-2-sulfanyl-1H,4H,5H- pyrrolo[3,2-d]pyrimidin-5-yl]methyl carbonate	6.07	426	1H NMR (300MHz, DMSO-d6) δ = 12.40 (s, 1H), 7.52 (d, J=3.1 Hz, 1H), 6.39 (d, J=3.1 Hz, 1H), 6.15 (s, 2H), 4.58 - 4.29 (m, 2H), 4.06 (t, J=6.5 Hz, 2H), 3.69 (t, J=5.9 Hz, 2H), 3.58 - 3.44 (m, 1H), 1.53 (br s, 2H), 1.20 (br d, J=4.7 Hz, 8H), 0.97 (d, J=6.2 Hz, 6H), 0.83 (br dd, J=9.4, 12.2 Hz, 3H)	8.47	98% remaining at 1h	23% remaining at 1h	21% remaining at 1h
220	heptyl {2- [[[(heptyloxy)carbonyloxy)methyl] sulfanyl]-4-oxo-1-[2-(propan-2- yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2- d]pyrimidin-5-yl]methyl carbonate	6.92	598	1H NMR (300MHz, DMSO-d6) δ = 7.49 (d, J=3.1 Hz, 1H), 6.50 (d, J=3.2 Hz, 1H), 6.28 (s, 2H), 5.83 (s, 2H), 4.25 (t, J=5.3 Hz, 2H), 4.13 - 4.00 (m, 4H), 3.64 (t, J=5.3 Hz, 2H), 3.50 - 3.41 (m, 1H), 1.54 (q, J=6.3 Hz, 4H), 1.30 - 1.13 (m, 16H), 0.93 (d, J=6.0 Hz, 6H), 0.80 (q, J=5.7 Hz, 6H)		77% remaining at 1h	5% remaining at 1h	55% remaining at 1h
221	(2-{methyl[[1-(4-oxo-1-[2-(propan-2- yloxy)ethyl]-2-sulfanyl-1H,4H,5H- pyrrolo[3,2-d]pyrimidin-5- yl]ethoxy)carbonyl]amino}phenyl)m ethyl acetate	4.33	503	1H NMR (300 MHz, DMSO-d6) δ ppm 12.03 (br s, 1 H) 7.19 - 7.49 (m, 4 H) 6.96 - 7.17 (m, 1 H) 6.49 - 6.67 (m, 1 H) 6.33 (d, J=2.34 Hz, 1 H) 4.84 - 5.06 (m, 2 H) 3.99 - 4.35 (m, 2 H) 3.36 - 3.75 (m, 3 H) 3.08 (d, J=8.21 Hz, 3 H) 2.01 (s, 2 H) 1.92 - 1.96 (m, 1 H) 1.68 - 1.82 (m, 1 H) 1.49 - 1.63 (m, 2 H) 0.86 - 1.02 (m, 6 H)	25.4	67% remaining at 1h	68% remaining at 1h	94% remaining at 1h
222	(2-{methyl[[1-(4-oxo-1-[2-(propan-2- yloxy)ethyl]-2-sulfanyl-1H,4H,5H- pyrrolo[3,2-d]pyrimidin-5- yl]methoxy)carbonyl]amino}phenyl) methyl acetate	4.07	489	1H NMR (300 MHz, DMSO-d6) δ ppm 11.77 - 12.39 (m, 1 H) 6.80 - 7.79 (m, 5 H) 6.34 (br d, J=2.93 Hz, 1 H) 5.71 (d, J=5.86 Hz, 2 H) 4.56 - 5.13 (m, 2 H) 4.03 - 4.42 (m, 2 H) 3.54 - 3.75 (m, 2 H) 3.46 (dt, J=11.87, 6.08 Hz, 1 H) 3.24 - 3.40 (m, 32 H) 3.01 - 3.17 (m, 3 H) 1.83 - 2.00 (m, 3 H) 0.86 - 1.02 (m, 6 H)	20.5	98% remaining at 1h	88% remaining at 1h	22% remaining at 1h
223	4-oxo-N-(propan-2-yl)-1-[2-(propan- 2-yloxy)ethyl]-2-sulfanylidene- 1H,2H,3H,4H,5H-pyrrolo[3,2- d]pyrimidin-5-carboxamide	5	339	1H NMR (300 MHz, DMSO-d6) δ ppm 12.93 (s, 1 H) 10.67 - 11.03 (m, 1 H) 8.05 (d, J=3.52 Hz, 1 H) 6.59 (d, J=3.52 Hz, 1 H) 4.51 (t, J=5.86 Hz, 2 H) 3.78 - 3.98 (m, 1 H) 3.70 (t, J=5.57 Hz, 2 H) 3.51 (quin, J=6.01 Hz, 1 H) 1.19 (d, J=6.45 Hz, 6 H) 0.96 (d, J=5.86 Hz, 6 H)	37.9	87% remaining at 1h	70% remaining at 1h	99% remaining at 1h

224	N-butyl-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-c]pyrimidine-5-carboxamide	5.37	353	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.94 (s, 1 H) 10.87 (t, J=5.28 Hz, 1 H) 8.05 (d, J=3.52 Hz, 1 H) 6.59 (d, J=3.52 Hz, 1 H) 4.51 (t, J=5.86 Hz, 2 H) 3.70 (t, J=5.86 Hz, 2 H) 3.51 (quin, J=6.01 Hz, 1 H) 3.24 - 3.31 (m, 2 H) 1.43 - 1.57 (m, 2 H) 1.27 - 1.42 (m, 2 H) 0.96 (d, J=5.86 Hz, 6 H) 0.82 - 0.92 (m, 3 H)	12.6	83% remaining at 1 h	100% remaining at 1 h	89% remaining at 1 h
225	4-oxo-1-[2-(propan-2-yloxy)ethyl]-N-propyl-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-c]pyrimidine-5-carboxamide	5	339	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.94 (s, 1 H) 10.88 (t, J=4.98 Hz, 1 H) 8.06 (d, J=3.52 Hz, 1 H) 6.59 (d, J=4.10 Hz, 1 H) 4.51 (t, J=5.86 Hz, 2 H) 3.65 - 3.76 (m, 2 H) 3.51 (quin, J=6.15 Hz, 1 H) 3.24 (td, J=6.74, 5.27 Hz, 2 H) 1.54 (q, J=7.03 Hz, 2 H) 0.96 (d, J=5.86 Hz, 6 H) 0.88 - 0.94 (m, 3 H)	24.3	98% remaining at 1 h	78% remaining at 1 h	99% remaining at 1 h
226	N-(butan-2-yl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-c]pyrimidine-5-carboxamide	5.25	353	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.93 (s, 1 H) 10.86 (br d, J=7.03 Hz, 1 H) 8.05 (d, J=3.52 Hz, 1 H) 6.59 (d, J=3.52 Hz, 1 H) 4.51 (t, J=5.86 Hz, 2 H) 3.70 (t, J=5.86 Hz, 3 H) 3.51 (quin, J=6.01 Hz, 1 H) 1.52 (t, J=7.33 Hz, 2 H) 1.15 (d, J=6.45 Hz, 3 H) 0.94 - 1.02 (m, 6 H) 0.88 (t, J=7.33 Hz, 3 H)	35.1	91% remaining at 1 h	83% remaining at 1 h	97% remaining at 1 h
227	4-oxo-N-phenyl-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-c]pyrimidine-5-carboxamide	5.62	373	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 13.08 - 13.32 (m, 1 H) 8.18 (d, J=3.52 Hz, 1 H) 7.53 - 7.62 (m, 2 H) 7.33 - 7.43 (m, 2 H) 7.22 - 7.29 (m, 1 H) 7.09 - 7.20 (m, 1 H) 6.69 (d, J=3.52 Hz, 1 H) 4.55 (t, J=5.86 Hz, 2 H) 3.73 (t, J=5.86 Hz, 2 H) 3.53 (quin, J=6.15 Hz, 1 H) 0.98 (d, J=6.45 Hz, 6 H)	16.7	100% remaining at 1 h	95% remaining at 1 h	99% remaining at 1 h
228	N-benzyl-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-c]pyrimidine-5-carboxamide	5.38	387	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.95 (s, 1 H) 11.36 (br s, 1 H) 8.09 (d, J=3.52 Hz, 1 H) 7.07 - 7.47 (m, 5 H) 6.62 (d, J=3.52 Hz, 1 H) 4.51 (d, J=5.86 Hz, 4 H) 3.65 - 3.75 (m, 2 H) 3.44 - 3.57 (m, 1 H) 0.96 (d, J=5.86 Hz, 6 H)	103	95% remaining at 1 h	100% remaining at 1 h	99% remaining at 1 h

EXAMPLE 229:



N-tert-butyl-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxamide: Added sodium hydride 60 % dispersion in mineral oil (12 mg, 0.49 mmole) to a solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (0.050 g, 0.39 mmole) in DMF (3 mL). After gas evolution had ceased, added t-butyl isocyanate (0.024 mL, 0.22 mmole). After 2 hours, partitioned reactions between ethyl acetate and H₂O. Washed the organic layer with H₂O, then washed the combined organic layers with brine. Dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purified on the ISCO, eluting with 0-70%, ethyl acetate in hexanes. Repurified on the RP HPLC Gilson, method B, eluting with 30-95 % instead of 5 to 95 %. Lyophilized desired fractions to **N-tert-butyl-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxamide:** (13.5 mg, 19.4 %). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ ppm 9.01 - 9.49 (m, 1 H) 7.68 (br s, 1 H) 6.44 (br s, 1 H) 4.25 - 4.65 (m, 3 H) 3.86 (br d, *J*=4.69 Hz, 2 H) 3.53 (quin, *J*=6.15 Hz, 1 H) 1.36 - 1.51 (m, 6 H) 1.05 (d, *J*=5.86 Hz, 9 H). LC/MS Method A : R_t = 5.43 mins., (M+H)⁺ = 353. Caco-2 P_{app} = 264 nm/s, SGF = 98% remaining at 1 h, SIF = 76% remaining at 1 h, hPlasma stability = 96% remaining at 1 h.

Additional compounds prepared similarly to EXAMPLE 229:

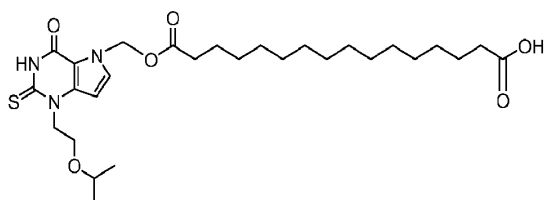
Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
230	ethyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxylate	4.32	326		¹ H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.01 - 9.49 (m, 1 H) 7.68 (br s, 1 H) 6.44 (br s, 1 H) 4.25 - 4.65 (m, 4 H) 3.86 (br d, J=4.69 Hz, 2 H) 3.53 (quin, J=6.15 Hz, 1 H) 1.36 - 1.51 (m, 3 H) 1.05 (d, J=5.86 Hz, 6 H)	4.56	99% remaining at 1 h	33% remaining at 1 h	2% remaining at 1 h
231	propan-2-yl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxylate	4.65	340		¹ H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.25 (br d, J=2.93 Hz, 1 H) 7.66 (br s, 1 H) 6.42 (br s, 1 H) 5.24 (quin, J=6.30 Hz, 1 H) 4.54 (br s, 2 H) 3.85 (br s, 2 H) 3.54 (quin, J=6.15 Hz, 1 H) 1.44 (d, J=6.45 Hz, 6 H) 0.88 - 1.20 (m, 6 H).	36.3	100% remaining at 1 h	40% remaining at 1 h	0% remaining at 1 h
232	2-methylpropyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxylate	5.05	354		¹ H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.27 (br s, 1 H) 7.68 (br d, J=2.93 Hz, 1 H) 6.44 (br d, J=1.76 Hz, 1 H) 4.54 (br s, 2 H) 4.22 (d, J=6.45 Hz, 2 H) 3.85 (t, J=5.27 Hz, 2 H) 3.54 (quin, J=6.01 Hz, 1 H) 2.14 (dt, J=13.33, 6.52 Hz, 1 H) 1.03 - 1.07 (m, 6 H) 1.02 (d, J=6.45 Hz, 6 H)	2.56	98% remaining at 1 h	3% remaining at 1 h	2% remaining at 1 h
233	methyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxylate	3.95	312		¹ H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.02 - 9.54 (m, 1 H) 7.68 (br s, 1 H) 6.45 (br s, 1 H) 4.55 (br s, 2 H) 4.06 (s, 3 H) 3.85 (br s, 2 H) 3.53 (dt, J=12.16, 5.93 Hz, 1 H) 1.04 (d, J=6.45 Hz, 6 H)	3.14	98% remaining at 1 h	70% remaining at 1 h	2% remaining at 1 h

234	3-fluorophenyl {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	5.12	422	1H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.27 (br s, 1 H) 7.28 - 7.41 (m, 3 H) 6.87 - 7.03 (m, 2 H) 6.36 (s, 2 H) 6.31 (br s, 1 H) 4.54 (br s, 2 H) 3.85 (br t, J=5.27 Hz, 2 H) 3.56 (dt, J=12.02, 6.30 Hz, 1 H) 0.94 - 1.19 (m, 6 H)	<3.30	34% remaining at 1h	8% remaining at 1h	2% remaining at 1h
235	4-fluorophenyl {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	5.1	422	1H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.25 (br s, 1 H) 7.30 (br s, 1 H) 6.99 - 7.18 (m, 4 H) 6.35 (s, 2 H) 6.30 (br s, 1 H) 4.54 (br s, 2 H) 3.86 (br d, J=4.69 Hz, 2 H) 3.56 (dt, J=12.16, 5.93 Hz, 1 H) 1.07 (d, J=5.86 Hz, 6 H)	<3.69	60% remaining at 1h	1% remaining at 1h	2% remaining at 1h
236	4-methylphenyl {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	5.3	418	1H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.23 (br s, 1 H) 7.31 (br d, J=2.34 Hz, 1 H) 7.16 (d, J=8.21 Hz, 2 H) 7.01 (d, J=8.79 Hz, 2 H) 6.35 (s, 2 H) 6.29 (br s, 1 H) 4.45 - 4.61 (m, 2 H) 3.85 (br t, J=5.27 Hz, 2 H) 3.56 (quin, J=6.15 Hz, 1 H) 2.33 (s, 3 H) 1.02 - 1.16 (m, 6 H)	5.9	53% remaining at 1h	1% remaining at 1h	1% remaining at 1h
237	3-methylphenyl {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	5.27	418	1H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.25 (br s, 1 H) 7.32 (br d, J=1.76 Hz, 1 H) 7.27 (m, J=1.17 Hz, 1 H) 7.06 (d, J=7.62 Hz, 1 H) 6.87 - 6.98 (m, 2 H) 6.35 (s, 2 H) 6.29 (br d, J=2.34 Hz, 1 H) 4.54 (br s, 2 H) 3.85 (br t, J=5.27 Hz, 2 H) 3.56 (quin, J=6.01 Hz, 1 H) 2.34 (s, 3 H) 1.07 (d, J=5.86 Hz, 6 H)	7.23	74% remaining at 1h	2% remaining at 1h	1% remaining at 1h
238	2-fluorophenyl {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	5.05	422	1H NMR (300 MHz, CHLOROFORM-d) δ ppm 9.24 (br s, 1 H) 7.32 (br s, 1 H) 7.07 - 7.24 (m, 4 H) 6.39 (s, 2 H) 6.31 (br s, 1 H) 4.54 (br s, 2 H) 3.86 (br t, J=4.98 Hz, 2 H) 3.36 - 3.69 (m, 1 H) 1.07 (d, J=5.86 Hz, 6 H)	<3.39	13% remaining at 1h	1% remaining at 1h	1% remaining at 1h
239	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-(2-fluorophenyl)-N-methylcarbamate	4.22	435	1H NMR (300 MHz, DMSO-d6) δ ppm 11.86 - 12.29 (m, 1 H) 7.19 - 7.45 (m, 3 H) 7.09 (br s, 2 H) 6.35 (d, J=2.93 Hz, 1 H) 5.58 - 6.04 (m, 2 H) 4.24 (br t, J=5.27 Hz, 2 H) 3.65 (br t, J=4.98 Hz, 2 H) 3.45 (dt, J=12.16, 5.93 Hz, 1 H) 3.13 (s, 3 H) 0.94 (d, J=5.86 Hz, 6 H)	117	99% remaining at 1h	96% remaining at 1h	85% remaining at 1h
240	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-(2-chlorophenyl)-N-methylcarbamate	4.33	451	1H NMR (300 MHz, DMSO-d6) δ ppm 12.06 (br s, 1 H) 7.15 - 7.61 (m, 5 H) 6.30 - 6.42 (m, 1 H) 5.65 - 6.04 (m, 2 H) 4.18 - 4.34 (m, 2 H) 3.57 - 3.77 (m, 2 H) 3.36 - 3.53 (m, 1 H) 3.01 - 3.14 (m, 3 H) 0.84 - 1.07 (m, 6 H)	154	99% remaining at 1h	97% remaining at 1h	83% remaining at 1h
241	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-(4-methoxyphenyl)-N-methylcarbamate	4.15	447	1H NMR (300 MHz, DMSO-d6) δ ppm 12.05 (br s, 1 H) 7.28 (d, J=2.34 Hz, 1 H) 7.10 (br s, 2 H) 6.78 (br s, 2 H) 6.35 (d, J=2.34 Hz, 1 H) 5.68 - 5.87 (m, 2 H) 4.24 (t, J=5.27 Hz, 2 H) 3.60 - 3.70 (m, 5 H) 3.45 (quin, J=6.15 Hz, 1 H) 3.13 (s, 3 H) 0.94 (d, J=5.86 Hz, 6 H)	105	57% remaining at 1h	97% remaining at 1h	100% remaining at 1h

242	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(2-methylphenyl)carbamate	4.28	431	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 11.89 - 12.14 (m, 1 H) 7.26 (br d, J=2.93 Hz, 1 H) 7.18 - 7.23 (m, 1 H) 7.08 - 7.17 (m, 3 H) 6.21 - 6.51 (m, 1 H) 5.73 (d, J=1.17 Hz, 2 H) 4.13 - 4.35 (m, 2 H) 3.55 - 3.79 (m, 2 H) 3.39 - 3.52 (m, 1 H) 3.04 - 3.13 (m, 3 H) 2.01 (s, 3 H) 0.83 - 1.04 (m, 6 H)	156	52% remaining at 1h	96% remaining at 1h	81% remaining at 1h
243	{2-[[([methyl(2-methylphenyl)carbamoyloxy)methyl]sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl N-methyl-N-(2-methylphenyl)carbamate	6.15	608	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 7.34 - 7.52 (m, 2 H) 7.01 - 7.32 (m, 8 H) 6.03 - 6.61 (m, 2 H) 5.71 (br d, J=11.14 Hz, 2 H) 4.13 - 4.31 (m, 2H) 3.55 - 3.73 (m, 2H) 3.36 - 3.53 (m, 1 H) 2.96 - 3.14 (m, 6 H) 1.78 - 2.19 (m, 6H) 0.84 - 0.99 (m, 6 H)	314	88% remaining at 1h	99% remaining at 1h	99% remaining at 1h
244	[3-[[([methyl(2-methylphenyl)carbamoyloxy)methyl]sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl N-methyl-N-(2-methylphenyl)carbamate	6.15	608	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 7.43 - 7.68 (m, 2 H) 6.99 - 7.35 (m, 8H) 5.91 - 6.55 (m, 6 H) 5.73 (s, 1 H) 4.34 - 4.71 (m, 2 H) 3.60 - 3.84 (m, 2 H) 3.36 - 3.57 (m, 1 H) 2.95 - 3.14 (m, 6 H) 2.13 (br s, 6 H) - 1.03 (m, 6 H)	74.7	98% remaining at 1h	99% remaining at 1h	52% remaining at 1h
245	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(3-methylphenyl)carbamate	4.37	431	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.04 (br s, 1 H) 7.28 (d, J=2.93 Hz, 1 H) 7.06 - 7.18 (m, 1 H) 6.90 - 7.04 (m, 3 H) 6.35 (d, J=2.93 Hz, 1 H) 5.80 (s, 2 H) 4.25 (t, J=5.57 Hz, 2 H) 3.66 (t, J=5.57 Hz, 2 H) 3.45 (dt, J=12.16, 5.93 Hz, 1 H) 3.16 (s, 3 H) 2.12 (s, 3 H) 0.94 (d, J=6.45 Hz, 6 H)	216	99% remaining at 1h	99% remaining at 1h	63% remaining at 1h
246	{2-[[([methyl(3-methylphenyl)carbamoyloxy)methyl]sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl N-methyl-N-(3-methylphenyl)carbamate	6.15	609	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 7.46 (d, J=2.93 Hz, 1 H) 7.07 - 7.22 (m, 3 H) 6.88 - 7.03 (m, 5 H) 6.45 (d, J=3.52 Hz, 1 H) 6.25 (s, 2 H) 5.79 (s, 2 H) 4.25 (t, J=5.27 Hz, 2 H) 3.64 (t, J=5.27 Hz, 2 H) 3.44 (dt, J=12.16, 5.93 Hz, 1 H) 3.15 (d, J=9.38 Hz, 6 H) 2.01 - 2.22 (m, 6 H) 0.92 (d, J=6.45 Hz, 6 H)	217	98% remaining at 1h	99% remaining at 1h	99% remaining at 1h
247	[3-[[([methyl(3-methylphenyl)carbamoyloxy)methyl]sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl N-methyl-N-(3-methylphenyl)carbamate	6.15	609	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 7.59 (d, J=3.52 Hz, 1 H) 7.02 - 7.22 (m, 4 H) 6.92 (br d, J=4.10 Hz, 4 H) 6.42 (d, J=2.93 Hz, 1 H) 6.34 (s, 2 H) 6.13 (s, 2 H) 4.56 (t, J=5.86 Hz, 2 H) 3.73 (t, J=5.86 Hz, 2 H) 3.49 (dt, J=12.16, 5.93 Hz, 1 H) 3.14 (d, J=11.72 Hz, 6 H) 2.10 - 2.25 (m, 6 H) 0.93 (d, J=5.86 Hz, 6 H)	39.9	64% remaining at 1h	81% remaining at 1h	31% remaining at 1h
248	((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-methyl-N-(4-methylphenyl)carbamate	4.22	431	¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 12.03 (br s, 1 H), 7.28 (d, J=2.93 Hz, 1 H), 6.97 - 7.17 (m, 4 H), 6.29 - 6.42 (m, 1 H), 5.80 (s, 2 H), 4.24 (t, J=5.57 Hz, 2 H), 3.65 (t, J=5.57 Hz, 2 H), 3.38 - 3.51 (m, 1 H), 3.15 (s, 3 H), 2.21 (s, 3 H), 0.94 (d, J=5.86 Hz, 6 H)	235	99% remaining at 1h	98% remaining at 1h	96% remaining at 1h

249	{2-(((2-chlorophenyl)(methyl)carbamoyl]oxymethyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(2-chlorophenyl)-N-methylcarbamate	5.38	648	1H NMR (300 MHz, DMSO-d ₆) δ ppm 7.05 - 7.74 (m, 9 H) 6.09 - 6.55 (m, 3 H) 5.61 - 5.96 (m, 2 H) 4.07 - 4.37 (m, 2 H) 3.52 - 3.78 (m, 2 H) 3.37 - 3.52 (m, 1 H) 3.00 - 3.11 (m, 6 H) 0.83 - 0.98 (m, 6 H)	284	89% remaining at 1 h	95% remaining at 1 h	98% remaining at 1 h
250	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(2-chlorophenyl)-N-methylcarbamate	5.07	M+Na ⁺ = 473	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.27 (br s, 1 H) 7.39 - 7.58 (m, 3H) 7.26 - 7.38 (m, 2 H) 6.29 - 6.42 (m, 1 H) 5.98 - 6.25 (m, 2 H) 4.35 - 4.55 (m, 2 H) 3.64 - 3.77 (m, 2 H) 3.49 (dt, J=12.16, 5.93 Hz, 1 H) 2.99 - 3.09 (m, 3 H) 0.86 - 1.02 (m, 6 H)		99% remaining at 1 h	93% remaining at 1 h	100% remaining at 1 h
251	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(2-methylphenyl)carbamate	5.05	431	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.29 (br s, 1 H) 7.43 (d, J=2.93 Hz, 1 H) 7.04 - 7.28 (m, 4 H) 6.29 - 6.44 (m, 1 H) 6.19 (s, 1 H) 5.83 - 6.26 (m, 2 H) 4.35 - 4.54 (m, 2 H) 3.62 - 3.77 (m, 2 H) 3.49 (dq, J=12.02, 5.96 Hz, 1 H) 2.97 - 3.09 (m, 3 H) 1.85 - 2.15 (m, 3 H) 0.94 (d, J=5.86 Hz, 6 H)		99% remaining at 1 h	100% remaining at 1 h	96% remaining at 1 h
252	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-methyl-N-(3-methylphenyl)carbamate	5.12	431	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.38 (s, 1 H) 7.49 (d, J=2.93 Hz, 1 H) 7.15 (t, J=7.62 Hz, 1 H) 6.97 (br d, J=8.21 Hz, 3 H) 6.29 - 6.42 (m, 1 H) 6.12 (s, 2 H) 4.45 (t, J=6.15 Hz, 2 H) 3.63 - 3.75 (m, 2 H) 3.50 (quin, J=6.15 Hz, 1 H) 3.13 (s, 3 H) 2.19 (s, 3 H) 0.95 (d, J=5.86 Hz, 6 H)		100% remaining at 1 h	80% remaining at 1 h	100% remaining at 1 h
253	{2-(((4-methoxyphenyl)(methyl)carbamoyl]oxymethyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(4-methoxyphenyl)-N-methylcarbamate	5.03	640	1H NMR (300 MHz, DMSO-d ₆) δ ppm 7.45 (d, J=2.93 Hz, 1 H) 7.10 (br s, 4 H) 6.80 (br s, 4 H) 6.45 (d, J=2.93 Hz, 1 H) 6.24 (br s, 2 H) 5.79 (br d, J=7.03 Hz, 2 H) 4.23 (br t, J=5.28 Hz, 2 H) 3.58 - 3.75 (m, 8 H) 3.39 - 3.52 (m, 1 H) 3.14 (s, 3 H) 3.10 (s, 3 H) 0.93 (d, J=5.86 Hz, 6 H)				
254	{(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-(4-methoxyphenyl)-N-methylcarbamate	4.13	447	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.05 (br s, 1 H) 7.28 (t, J=2.93 Hz, 1 H) 7.10 (br s, 2 H) 6.77 (br d, J=1.76 Hz, 2 H) 6.29 - 6.41 (m, 1 H) 5.80 (br d, J=8.21 Hz, 2 H) 4.12 - 4.37 (m, 2 H) 3.57 - 3.74 (m, 5 H) 3.45 (quin, J=6.15 Hz, 1 H) 3.13 (s, 3 H) 0.94 (d, J=6.45 Hz, 6 H)	85.3	95% remaining after 1 h	94% remaining after 1 h	88% remaining after 1 h

EXAMPLE 255:



5 Charged a 250 mL round bottom flask with hexanedioic acid (5 g, 17.4 mmole), t-butanol (43 mL, 272 mmole), EDC (2.71 g, 17.46 mmole) and DMAP (2.13 g, 17.46 mmole). Dissolved in 30 mL of CH₂Cl₂,
105

at ambient temperature. After 18 hours, partitioned between ethyl acetate 50 mL and 20 mL of 0.01 N HCl. Separated layers and washed the organic layer with brine. Dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purified on a 40 g silica gel column, eluting with 0-100% ethyl acetate in hexanes. Combined desired fractions *in vacuo* to yield 045b: (2.18 g, 40 %). ¹H NMR (300 MHz, DMSO-*d*₆) δ ppm 2.08 - 2.20 (m, 4 H) 1.37 - 1.51 (m, 4 H) 1.35 (s, 5 H) 1.20 (s, 21 H) 1.11 - 1.16 (m, 2 H) 1.07 (s, 9 H).

To a solution of MAM-6-386-045 (0.50 g, 1.6 mmol) in DCM:H₂O (12:8 mL) at RT was added NaHCO₃ (0.53 g, 6.3 mmole), then tetrabutylammonium hydrogen sulfate (0.054 g, 0.16 mmole). Cooled to 0°C and let stir for 15 minutes. then added chloromethylchlorosulfate (5.07 mmole, 0.513 mL). Let warm slowly to RT over the 3 days. Partitioned reaction between CH₂Cl₂ and H₂O. Separated layers and washed the aqueous layer with 2 x 20 mL of CH₂Cl₂. Product has some solubility issues. Added MeOH to help solubilize, and EtOAc and Hexanes. Washed the combined organic layers with brine. Dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purified on the ISCO using an 40 g SiliaSep column, eluting with 0-100 % EtOAc/hexanes. Concentrated the first spot *in vacuo* to yield 047 (212 mg, 36%), ¹H NMR (300 MHz, CHLOROFORM-*d*) δ ppm 5.69 (s, 2 H) 2.11 - 2.43 (m, 4H) 1.51 - 1.75 (m, 4 H) 1.43 (s, 9 H) 1.13 - 1.35 (m, 20 H).

Added sodium hydride 60 % dispersion in mineral oil (33 mg, 1.4 mmole) to a solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-*d*]pyrimidin-4-one (0.14 g, 0.55 mmole) in DMF (3 mL). After gas evolution had ceased, added mam-6-386-047 (0.135 g, 0.592 mmole) in 1 mL DMF. After 24 hours, partitioned between ethyl acetate (40 mL) and H₂O (20 mL). Separated layers and washed the aqueous layer with 20 mL of ethyl acetate. Washed the combined organic layers with 2 x 20 mL H₂O, then brine. Dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purified on a 40 g silica gel column, eluting with 0-100% EtOAc in hexanes to yield 067 (0.10 g, 30 %). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ ppm 9.52 (br s, 1 H) 7.27 (d, *J*=3.52 Hz, 1 H) 6.22 (s, 3 H) 4.52 (t, *J*=5.57 Hz, 2 H) 3.83 (t, *J*=5.57 Hz, 2 H) 3.54 (dq, *J*=12.09, 6.13 Hz, 3 H) 2.10 - 2.43 (m, 6 H) 1.49 - 1.74 (m, 6 H) 1.43 (s, 9 H) 1.14 - 1.29 (m, 35 H) 1.06 (d, *J*=5.86 Hz, 7 H). LC/MS Method A-2: R_t = 7.95 mins., (M+H)⁺ = 609, purity = 90%.

Added TFA (0.94 mmole, 0.63 mL) to a solution of MAM-6-386-067 (0.100 g, 0.395 mmole) in CH₂Cl₂, 4 mL. After 2 hours, partitioned between CH₂Cl₂ (40 mL) and H₂O 20 mL. Separated layers and washed the aqueous layer with 20 mL of CH₂Cl₂. Washed the combined organic layers with 1 x 20 mL H₂O, then brine. Dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purified on a 40 g silica gel

column, eluting with 0-100% EtOAc in hexanes, to give **16-oxo-16-({4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy}hexadecanoic acid**: (29 mg, 32 %), ^1H NMR (300 MHz, DMSO- d_6) δ ppm 11.63 - 12.77 (m, 2 H), 7.49 (d, $J=3.52$ Hz, 1 H), 6.36 (d, $J=2.93$ Hz, 1 H), 6.14 (s, 2 H), 4.45 (t, $J=6.15$ Hz, 2 H), 3.69 (t, $J=6.15$ Hz, 2 H), 3.52 (dt, $J=12.16, 5.93$ Hz, 1 H), 2.25 (t, $J=7.33$ Hz, 2 H), 2.14 (t, $J=7.33$ Hz, 2 H), 1.43 (br d, $J=3.52$ Hz, 4 H), 1.08 - 1.27 (m, 20 H), 0.97 (d, $J=5.86$ Hz, 6 H). LC/MS Method A: $R_t = 6.33$ mins., $(\text{M}+\text{H})^+ = 552$, purity >95 %. Caco-2 $P_{app} = 27.2$ nm/s, SGF = 95% remaining at 1 h, SIF = 2% remaining at 1 h, hPlasma stability = 76% remaining at 1 h.

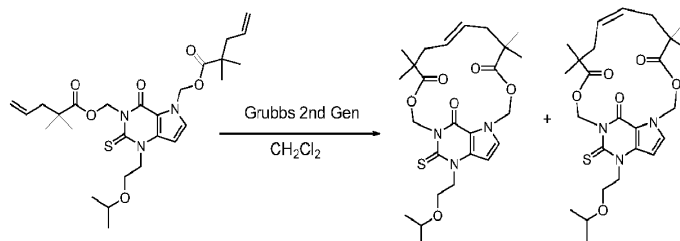
Additional compounds prepared similarly to EXAMPLE 255:

Example	Name	LCMS retention time	$\text{M}+\text{H}^+$	LCMS method	NMR	Caco-2 P_{app} (nm/s)	SGF	SIF	human Plasma stability
256	1-({4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 16-propan-2-yl hexadecanedioate	7.52	595		^1H NMR (300 MHz, DMSO- d_6) δ ppm 12.34 (br s, 1 H) 7.49 (d, $J=3.52$ Hz, 1 H) 6.36 (d, $J=3.52$ Hz, 1 H) 6.14 (s, 2 H) 4.68 - 4.99 (m, 1 H) 4.45 (t, $J=5.86$ Hz, 2 H) 3.68 (t, $J=5.86$ Hz, 2 H) 3.52 (quin, $J=6.15$ Hz, 1 H) 2.15 - 2.29 (m, 4H) 1.44 (br dd, $J=7.33, 2.05$ Hz, 4 H) 1.06 - 1.26 (m, 26 H) 0.90 - 1.02 (m, 6 H)	2.5	99% remaining after 1 h	9% remaining after 1 h	88% remaining after 1 h
257	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(4-methoxyphenyl)-N-methylcarbamate	4.85	447		^1H NMR (300 MHz, DMSO- d_6) δ ppm 12.34 (s, 1 H) 7.48 (br d, $J=2.93$ Hz, 1 H) 7.09 (br s, 2 H) 6.61 - 6.93 (m, 2 H) 6.35 (d, $J=2.93$ Hz, 1 H) 6.10 (br s, 2 H) 4.45 (t, $J=6.15$ Hz, 2 H) 3.65 - 3.74 (m, 5 H) 3.45 - 3.57 (m, 1 H) 3.10 (s, 3 H) 0.96 (d, $J=6.45$ Hz, 6 H)				
258	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(2-fluorophenyl)-N-methylcarbamate	4.87	435		^1H NMR (300 MHz, DMSO- d_6) δ ppm 12.29 (br s, 1 H) 7.44 (br s, 1 H) 7.06 - 7.37 (m, 4 H) 6.35 (br s, 1 H) 6.03 - 6.22 (m, 2 H) 4.44 (br t, $J=5.86$ Hz, 2 H) 3.69 (t, $J=6.15$ Hz, 2 H) 3.43 - 3.58 (m, 1 H) 3.10 (s, 3 H) 0.96 (d, $J=6.45$ Hz, 6 H)				
259	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(3-fluorophenyl)-N-methylcarbamate	4.95	435		^1H NMR (300 MHz, DMSO- d_6) δ ppm 12.36 (s, 1 H) 7.51 (d, $J=3.52$ Hz, 1 H) 7.26 - 7.39 (m, 1 H) 6.94 - 7.18 (m, 3 H) 6.36 (d, $J=3.52$ Hz, 1 H) 6.15 (s, 2 H) 4.45 (t, $J=5.86$ Hz, 2 H) 3.69 (t, $J=5.86$ Hz, 2 H) 3.45 - 3.56 (m, 1 H) 3.17 (s, 3 H) 0.92 - 1.00 (m, 6 H)				
260	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-(4-fluorophenyl)-N-methylcarbamate	4.95	435		^1H NMR (300 MHz, DMSO- d_6) δ ppm 12.34 (s, 1 H) 7.48 (d, $J=2.93$ Hz, 1 H) 7.23 (br s, 2 H) 7.06 - 7.17 (m, 2 H) 6.35 (d, $J=3.52$ Hz, 1 H) 6.07 - 6.16 (m, 2 H) 4.44 (t, $J=6.15$ Hz, 2 H) 3.69 (t, $J=6.15$ Hz, 2 H) 3.45 - 3.56 (m, 1 H) 3.13 (s, 3 H) 0.90 - 1.04 (m, 6 H)				

261	12-oxo-12-((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)dodecanoic acid	5.3	496	1H NMR (300 MHz, DMSO-d ₆) δ ppm 11.75 - 12.65 (m, 2 H) 7.49 (d, J=2.93 Hz, 1 H) 6.37 (d, J=2.93 Hz, 1 H) 6.14 (s, 2 H) 4.45 (t, J=6.15 Hz, 2 H) 3.68 (t, J=5.86 Hz, 2 H) 3.52 (quin, J=6.15 Hz, 1 H) 2.25 (t, J=7.33 Hz, 2 H) 2.14 (t, J=7.33 Hz, 2 H) 1.36 - 1.51 (m, 4 H) 1.06 - 1.22 (m, 12 H) 0.97 (d, J=6.45 Hz, 6 H)	117	99% remaining after 1 h	2% remaining after 1 h	94% remaining after 1 h
262	1-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 12-propan-2-yl dodecanedioate	6.53	538	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.34 (br s, 1 H) 7.49 (d, J=3.52 Hz, 1 H) 6.36 (d, J=3.52 Hz, 1 H) 6.14 (s, 2 H) 4.68 - 4.99 (m, 1 H) 4.45 (t, J=5.86 Hz, 2 H) 3.68 (t, J=5.86 Hz, 2 H) 3.52 (quin, J=6.15 Hz, 1 H) 2.15 - 2.29 (m, 4 H) 1.44 (br dd, J=7.33, 2.05 Hz, 4 H) 1.06 - 1.26 (m, 18 H) 0.90 - 1.02 (m, 6 H)	<2.14	92% remaining after 1 h	2% remaining after 1 h	41% remaining after 1 h
263	13-oxo-13-((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)tridecanoic acid	5.5	510	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.36 (br d, J=1.17 Hz, 2 H) 7.50 (d, J=2.93 Hz, 1 H) 6.38 (d, J=2.93 Hz, 1 H) 6.15 (s, 2 H) 4.45 (t, J=6.15 Hz, 2 H) 3.61 - 3.80 (m, 2 H) 3.52 (quin, J=6.15 Hz, 1 H) 2.26 (t, J=7.33 Hz, 2 H) 2.15 (t, J=7.33 Hz, 2 H) 1.37 - 1.57 (m, 4 H) 1.09 - 1.27 (m, 14 H) 0.98 (d, J=6.45 Hz, 6 H)				
264	15-oxo-15-((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)pentadecanoic acid	5.98	539	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.36 (br s, 2 H) 7.50 (d, J=3.52 Hz, 1 H) 6.38 (d, J=3.52 Hz, 1 H) 6.15 (s, 2 H) 4.45 (t, J=6.15 Hz, 2 H) 3.69 (t, J=6.15 Hz, 2 H) 3.52 (dt, J=12.02, 6.30 Hz, 1 H) 2.26 (t, J=7.03 Hz, 2 H) 2.15 (t, J=7.33 Hz, 2 H) 1.44 (br d, J=4.10 Hz, 4 H) 1.17 (br d, J=18.76 Hz, 18 H) 0.98 (d, J=6.45 Hz, 6 H)				
265	1-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 15-propan-2-yl pentadecanedioate	7.1	581	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.37 (s, 1 H) 7.50 (d, J=2.93 Hz, 1 H) 6.38 (d, J=2.93 Hz, 1 H) 6.15 (s, 2 H) 4.77 - 4.90 (m, 1 H) 4.45 (t, J=5.86 Hz, 2 H) 3.59 - 3.74 (m, 2 H) 3.52 (quin, J=6.01 Hz, 1 H) 2.26 (t, J=7.33 Hz, 2 H) 2.20 (t, J=7.33 Hz, 2 H) 1.45 (br dd, J=7.03, 2.34 Hz, 4 H) 1.10 - 1.24 (m, 24 H) 0.94 - 1.00 (m, 6 H)				
266	18-oxo-18-((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)octadecanoic acid	5.79 Method: 40-95% ACN	581	1H NMR (300 MHz, DMSO-d ₆) δ ppm 12.01 - 12.68 (m, 1 H) 7.50 (d, J=3.52 Hz, 1 H) 6.37 (d, J=2.93 Hz, 1 H) 6.27 (s, 1 H) 6.15 (s, 2 H) 4.45 (t, J=5.86 Hz, 2 H) 3.69 (t, J=6.15 Hz, 2 H) 3.46 - 3.58 (m, 1 H) 2.22 - 2.30 (m, 2 H) 2.15 (t, J=7.33 Hz, 2 H) 1.44 (br d, J=4.10 Hz, 4 H) 1.07 - 1.28 (m, 24 H) 0.98 (d, J=6.45 Hz, 6 H)				

267	18-[[2-([[(17-carboxyheptadecanoyl)oxy]methyl)sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]-18-oxooctadecanoic acid	7.97 Method: 40-95% CAN	907		¹ H NMR (300 MHz, DMSO-d ₆) δ ppm 7.45 (d, J=2.93 Hz, 1 H) 6.47 (d, J=3.52 Hz, 1 H) 6.27 (s, 2 H) 5.79 (s, 2 H) 4.22 (br t, J=4.98 Hz, 2 H) 3.64 (br t, J=5.27 Hz, 2 H) 2.03 - 2.35 (m, 8 H) 1.36 - 1.57 (m, 9 H) 1.03 - 1.31 (m, 48 H) 0.94 (d, J=6.45 Hz, 6 H) 0.77 - 0.87 (m, 2 H).				
268	[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl]methyl 2,2-dimethylpent-4-enoate								
269	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl 2,2-dimethylpent-4-enoate								
270	(3-[[[2,2-dimethylpent-4-enoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2,2-dimethylpent-4-enoate								
271	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-3-yl}methyl 2,2-dimethylpent-4-enoate								
272	[(5-[[[2,2-dimethylpent-4-enoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl]methyl 2,2-dimethylpent-4-enoate								

EXAMPLES 273 and 274:



- 5 A solution of diene (60 mg, 0.112 mmol) in dichloromethane (100 mL) was degassed with N₂ for 10 min, followed by quick addition of Grubbs 2nd Gen (48 mg, 0.056 mmol) and degassing for 15 min. The mixture was heated at 40 °C for 24 h. The reaction was concentrated and the crude product mixture was purified twice by PLC eluted with 20% EtOAc/hexanes to get two pure isomer products as white solid. EXAMPLE 273 (28 mg, 50%), EXAMPLE 274 (16 mg, 28%). ¹H NMR (300 MHz, CHLOROFORM-*d*)
- 10 δ 7.23 (d, J=2.93 Hz, 1 H), 6.71 (s, 2 H), 6.20 (d, J=2.93 Hz, 1 H), 6.07 (br s, 2 H), 5.16 - 5.33 (m, 1 H), 4.74 - 4.92 (m, 1 H), 4.60 - 4.67 (m, 2 H), 3.88 (t, J=5.57 Hz, 2 H), 3.48 - 3.59 (m, 1 H), 2.07 - 2.35 (m, 4 H), 1.19

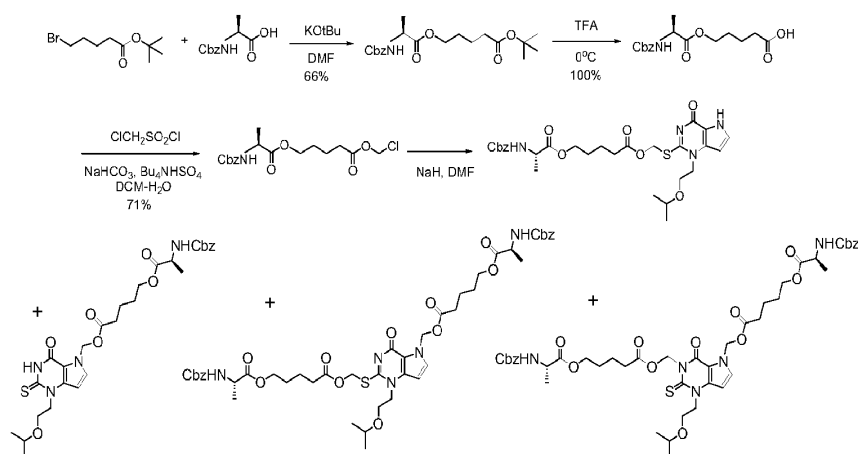
- 1.29 (m, 6 H), 1.08 - 1.19 (m, 6 H), 1.04 (d, J=6.45 Hz, 6 H). LC/MS Method A: R_t = 6.48 mins., $(M+H)^+$ = 507, purity >95 %.

Additional compounds prepared by the method of EXAMPLES 273 and 274:

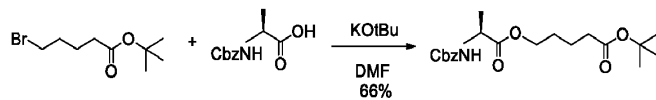
5

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
275	(10Z)-8,8,13,13-tetramethyl-22-[2-(propan-2-yloxy)ethyl]-6,15-dioxatriazatricyclo[16.3.1.0 ^{4,21}]docosa-1(21),2,10,18-tetraene-7,14,20-trione								
276	(10E)-8,8,13,13-tetramethyl-22-[2-(propan-2-yloxy)ethyl]-6,15-dioxatriazatricyclo[16.3.1.0 ^{4,21}]docosa-1(21),2,10,18-tetraene-7,14,20-trione								

Examples 277-280:

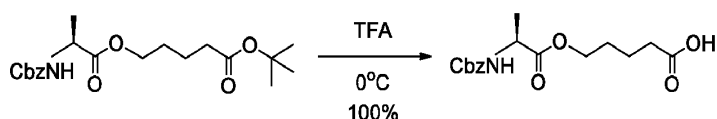


10

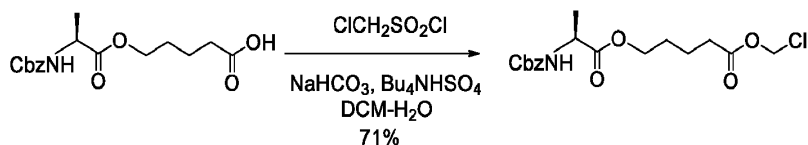


(S)-tert-Butyl 6-((2-(((benzyloxy)carbonyl)amino)-3-methylbutanoyloxy)pentanoate. To a solution of (S)-2-(((benzyloxy)carbonyl)amino)propanoic acid (1 g, 4.48 mmol) in DMF (15 mL) was

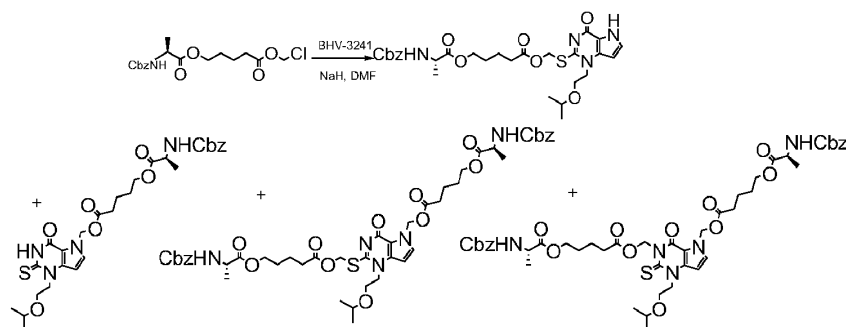
added potassium tert-butoxide (0.55 g, 4.93 mmol) and the mixture was stirred at room temperature for 10 minutes. Tert-butyl 6-bromopentanoate (1.17 g, 4.93 mmol) was added and the reaction mixture was heated at 65 °C for 6 hours. After cooled to room temperature, the mixture was poured into saturated sodium bicarbonate aqueous solution and extracted by ethyl acetate (3 x 20 mL). The combined extracts were dried (Na₂SO₄), filtered and purified by silica chromatography eluted with 20% EtOAc/hexanes to get the product as a white solid (1.24 g, 66%).



(S)-6-((2-((benzyloxycarbonyl)amino)-3-methylbutanoyl)oxy)pentanoic acid. (S)-tert-butyl 6-((2-((benzyloxycarbonyl)amino)-3-methylbutanoyl)oxy)pentanoate (1.24 g, 3.26 mmol) was added trifluoroacetic acid (5 mL) at 0 °C. The solution was kept stirring at 0 °C for 2 hour and concentrated to give 0.95 g of the crude product as thick oil.



(S)-chloromethyl 6-((2-((benzyloxycarbonyl)amino)-3-methylbutanoyl)oxy)pentanoate. To a solution of (S)-6-((2-((benzyloxycarbonyl)amino)-3-methylbutanoyl)oxy)pentanoic acid (0.85 g, 2.64 mmol) in dichloromethane (8 mL) and water (8 mL) was added sodium bicarbonate (0.89 g, 10.6 mmol) and Bu₄HSO₄ (90 mg, 0.264 mmol) followed by dropwise addition of chloromethylchlorosulfonate (650 mg, 3.93 mmol). The mixture was stirred for 20 h, diluted with water (30 mL) and extracted with dichloromethane (50 mL). The organic layer was separated and washed with water (25 mL), dried (MgSO₄) and evaporated. The product mixture was purified by silica chromatography eluted with 20% EtOAc/hexanes to get the product as a white solid (500 mg, 51%).



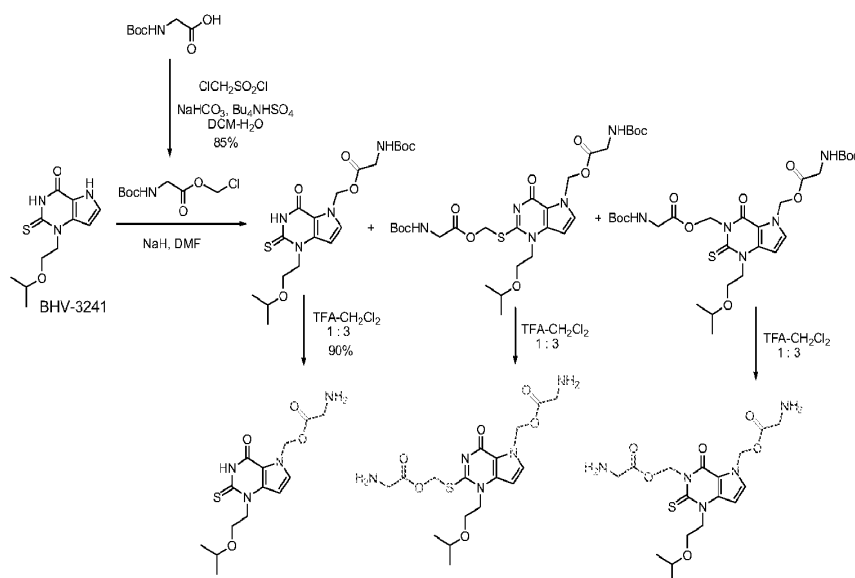
A suspension of BHV-3241, 1-(2-isopropoxyethyl)-2-thioxo-2,3-dihydro-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (100 mg, 0.395 mmol) in DMF (2 mL) was treated with sodium hydride (60% in mineral oil, 25.3 mg, 0.632 mmol) under N₂ and stirred for 30 minutes. (S)-Chloromethyl 6-(((2-(((benzyloxy)carbonyl)amino)-3-methylbutanoyl)oxy)pentanoate (234 mg, 0.632 mmol) in DMF (0.5 mL) was added *via* syringe and the mixture was stirred for 18 h. The reaction was quenched with a few drops of saturated NH₄Cl, filtered with a syringe filter (45 μm) and the crude product mixture was purified by RP-HPLC (method B) to get the pure product separated from other isomers as a white solid (25 mg, 11%).

10

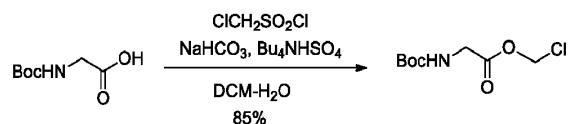
Additional compounds prepared similarly to EXAMPLES 277-280:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
281	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-[[[(tert-butoxy)carbonyl]amino]acetate					117	90% @ 1h	28% @ 1h	0% @ 1h
282	[[5-[[2-[[[(tert-butoxy)carbonyl]amino]acetyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl 2-[[[(tert-butoxy)carbonyl]amino]acetate								
283	(3-[[2-[[[(tert-butoxy)carbonyl]amino]acetyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-[[[(tert-butoxy)carbonyl]amino]acetate					57.8	82% @ 1h	1% @ 1h	26% @ 1h
284	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-aminoacetate					15.5	100% @ 1h	6% @ 1h	0% @ 1h

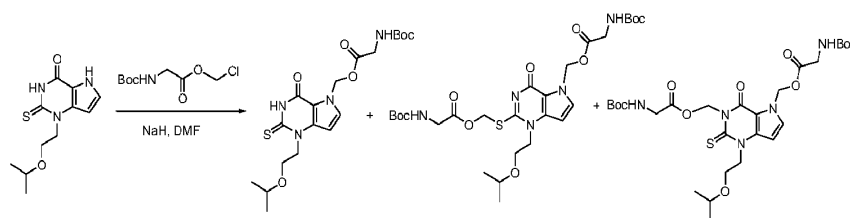
EXAMPLES 285-288:



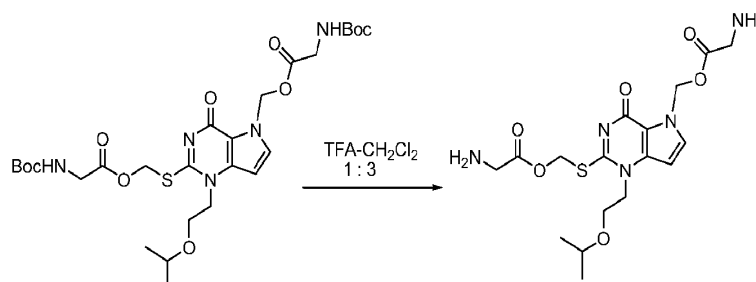
5



Chloromethyl 2-((tert-butoxycarbonyl)amino)acetate. To a solution of 2-((tert-butoxycarbonyl)amino)acetic acid (1.75 g, 10 mmol) in dichloromethane (20 mL) and water (20 mL) was added sodium bicarbonate (3.36 g, 40 mmol) and Bu₄NHSO₄ (340 mg, 1 mmol) followed by dropwise addition of chloromethylchlorosulfonate (1.2 mL, 12 mmol). The mixture was stirred for 20 h, diluted with water (30 mL) and extracted with dichloromethane (50 mL). The organic layer was separated and washed with water (25 mL), dried (MgSO₄) and evaporated. The product mixture was purified by silica chromatography eluted with 30% EtOAc/hexanes to get the product as a white solid (1.9 g, 85%).



1-(2-isopropoxyethyl)-2-thioxo-2,3-dihydro-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one, by the same procedure as EXAMPLE 2, on 250 mg scale purified by Method B as white solid.



- 5 To a solution of (20 mg, 0.032 mmol) in dichloromethane (1.5 mL) was added trifluoroacetic acid (0.55 mL). The reaction mixture was complete upon LC-MS monitoring after stirring for 30 min. The solution was concentrated and the residue was purified by RP-HPLC (method B) to get the pure product as a white solid (10 mg, 59%).

10 Additional compounds prepared similarly to EXAMPLES 285-288:

Example	Name	LCMS retention time	M+H ⁺	LCMS method	NMR	Caco-2 P _{app} (nm/s)	SGF	SIF	human Plasma stability
289	bis(trifluoroacetic acid) [3-(((2S)-2-aminopropanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-aminopropanoate					<3.66	100% @ 1h	97% @ 1h	39% @ 1h
290	trifluoroacetic acid [5-(hydroxymethyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-3-yl)methyl (2S)-2-aminopropanoate					unstable	98% @ 1h	10% @ 1h	
291	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-[[[tert-butoxy]carbonyl]amino]propanoate					219	66% @ 1h	30% @ 1h	0% @ 1h

292	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-3-methylbutanoate					<10.6	99% @ 1h	7% @ 1h	20% @ 1h
293	bis(trifluoroacetic acid) [3-(((2R)-2-aminopropanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-3-methylbutanoate					<10.6	100% @ 1h	29% @ 1h	25% @ 1h
294	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-(((tert-butoxy)carbonyl)amino)-3-methylbutanoate					268	98% @ 1h	3% @ 1h	98% @ 1h
295	{[5-(((2S)-2-(((tert-butoxy)carbonyl)amino)-3-methylbutanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2S)-2-(((tert-butoxy)carbonyl)amino)-3-methylbutanoate					170	58% @ 1h	0% @ 1h	81% @ 1h
296	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-amino-3-methylbutanoate					11.8	97% @ 1h	43% @ 1h	12% @ 1h
297	bis(trifluoroacetic acid) [3-(((2S)-2-amino-3-methylbutanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-amino-3-methylbutanoate					4.62	100% @ 1h	6% @ 1h	6% @ 1h
298	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-(((tert-butoxy)carbonyl)amino)-3-methylbutanoate					335	99% @ 1h	59% @ 1h	99% @ 1h
299	{[5-(((2R)-2-(((tert-butoxy)carbonyl)amino)-3-methylbutanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2R)-2-(((tert-butoxy)carbonyl)amino)-3-methylbutanoate					158	54% @ 1h	27% @ 1h	94% @ 1h
300	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-3-methylbutanoate					129	100% @ 1h	70% @ 1h	2% @ 1h
301	bis(trifluoroacetic acid) [3-(((2R)-2-amino-3-methylbutanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-3-methylbutanoate					17.2	97% @ 1h	10% @ 1h	5% @ 1h
302	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-(((tert-butoxy)carbonyl)amino)-3-phenylpropanoate					44.8	97% @ 1h	5% @ 1h	67% @ 1h

303	{[5-([[(2S)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2S)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoate				55.6	46% @ 1h	1% @ 1h	28% @ 1h
304	[3-([[(2S)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoate				3.4	44% @ 1h	67% @ 1h	99% @ 1h
305	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoate				38.4	73% @ 1h	1% @ 1h	39% @ 1h
306	{[5-([[(2R)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2R)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoate				38	41% @ 1h	1% @ 1h	72% @ 1h
307	[3-([[(2R)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-[(tert-butoxy)carbonyl]amino)-3-phenylpropanoate				3.34	26% @ 1h	43% @ 1h	99% @ 1h
308	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-amino-3-phenylpropanoate				<3.64	97% @ 1h	44% @ 1h	2.5% @ 1h
309	bis(trifluoroacetic acid) {[5-([[(2S)-2-amino-3-phenylpropanoyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2S)-2-amino-3-phenylpropanoate				<1.23	98% @ 1h	86% @ 1h	5% @ 1h
310	trifluoroacetic acid {[4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2S)-2-amino-3-phenylpropanoate					99% @ 1h	32% @ 1h	4% @ 1h
311	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-3-phenylpropanoate				54.4	98% @ 1h	7% @ 1h	4% @ 1h
312	bis(trifluoroacetic acid) {[5-([[(2R)-2-amino-3-phenylpropanoyl]oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2R)-2-amino-3-phenylpropanoate				>0.994	99% @ 1h	29% @ 1h	24% @ 1h

313	bis(trifluoroacetic acid) [3-(((2R)-2-amino-3-phenylpropanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-3-phenylpropanoate					4.9	88% @ 1h	51% @ 1h	99% @ 1h
314	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate								
315	{[5-(((2S)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2S)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate					141	78% @ 1h	5% @ 1h	7% @ 1h
316	[3-(((2S)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate					76	99% @ 1h	6% @ 1h	37% @ 1h
317	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate					0.93	56% @ 1h	30% @ 1h	99% @ 1h
318	{[5-(((2R)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2R)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate					254	81% @ 1h	2% @ 1h	85% @ 1h
319	[3-(((2R)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate					105	34% @ 1h	0% @ 1h	42% @ 1h
320	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-amino-4-methylpentanoate					<2.59	48% @ 1h	42% @ 1h	98% @ 1h
321	bis(trifluoroacetic acid) {[5-(((2S)-2-amino-4-methylpentanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2S)-2-amino-4-methylpentanoate					<3.65	92% @ 1h	2% @ 1h	1% @ 1h
322	bis(trifluoroacetic acid) [3-(((2S)-2-amino-4-methylpentanoyl]oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-amino-4-methylpentanoate					<1.06	56% @ 1h	61% @ 1h	64% @ 1h

323	trifluoroacetic acid [3-(hydroxymethyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2S)-2-amino-4-methylpentanoate					<3.55	95% @ 1h	52% @ 1h	12% @ 1h
324	trifluoroacetic acid [4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-4-methylpentanoate						98% @ 1h	24% @ 1h	1% @ 1h
325	bis(trifluoroacetic acid) [(5-(((2R)-2-amino-4-methylpentanoyl)oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl (2R)-2-amino-4-methylpentanoate					9.08	99% @ 1h	3% @ 1h	1% @ 1h
326	bis(trifluoroacetic acid) [3-(((2R)-2-amino-4-methylpentanoyl)oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-4-methylpentanoate					<3.38	97% @ 1h	9% @ 1h	17% @ 1h
327	trifluoroacetic acid [3-(hydroxymethyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-2-amino-4-methylpentanoate					<10.3	100% @ 1h	49% @ 1h	21% @ 1h
328	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2-[(tert-butoxy)carbonyl]amino)acetyl]oxy]pentanoate						97% @ 1h	6% @ 1h	11% @ 1h
329	{(5-[(5-[(2-[(tert-butoxy)carbonyl]amino)acetyl]oxy]pentanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl 5-[(2-[(tert-butoxy)carbonyl]amino)acetyl]oxy]pentanoate					59.6	95% @ 1h	35% @ 1h	1% @ 1h
330	trifluoroacetic acid [4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2-aminoacetyl)oxy]pentanoate					6.41	84% @ 1h	7% @ 1h	2% @ 1h
331	bis(trifluoroacetic acid) [(5-[(5-[(2-aminoacetyl)oxy]pentanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl 5-[(2-aminoacetyl)oxy]pentanoate					36.8	93% @ 1h	1% @ 1h	1% @ 1h
332	bis(trifluoroacetic acid) [3-[(5-[(2-aminoacetyl)oxy]pentanoyl)oxy)methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2-aminoacetyl)oxy]pentanoate					<0.73	91% @ 1h	4% @ 1h	4% @ 1h
333	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino]-3-methylbutanoyl]oxy]pentanoate					<0.72	98% @ 1h	4% @ 1h	5% @ 1h

334	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2S)-2-((tert-butoxy)carbonyl)amino)-3-phenylpropanoyl)oxy}pentanoate					62.6	90	2	58% remaining at 1 h
335	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2S)-2-amino-3-methylbutanoyl)oxy}pentanoate					33.2	99	9	3% remaining at 1 h
336	2-[(hydroxymethyl)sulfanyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one					18.2	93	6	73% remaining at 1 h
337	bis(trifluoroacetic acid) (3-(((5-(((2S)-2-amino-3-methylbutanoyl)oxy}pentanoyl)oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2S)-2-amino-3-methylbutanoyl)oxy}pentanoate					—	98	30	60% remaining at 1 h
338	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2R)-2-amino-3-methylbutanoyl)oxy}pentanoate						99	3	4% remaining at 1 h
339	bis(trifluoroacetic acid) (3-(((5-(((2R)-2-amino-3-methylbutanoyl)oxy}pentanoyl)oxy)methyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2R)-2-amino-3-methylbutanoyl)oxy}pentanoate					38.6	99	72	44% remaining at 1 h
340	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2S)-2-amino-3-phenylpropanoyl)oxy}pentanoate					6.44	100	99	4% remaining at 1 h
341	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-(((2R)-2-amino-3-phenylpropanoyl)oxy}pentanoate					2.59	99	33	1% remaining at 1 h
342	5-oxo-5-({4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy}pentyl (2S)-2-((tert-butoxy)carbonyl)amino)-4-methylpentanoate								
343	5-[[2-(((5-(((2S)-2-((tert-butoxy)carbonyl)amino)-4-methylpentanoyl)oxy}pentanoyl)oxymethyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]-5-oxopentyl (2S)-2-(((tert-butoxy)carbonyl)amino)-4-methylpentanoate					46.7	82% remaining at 1h	29% remaining at 1h	1% remaining at 1h

344	5-[(3-[(5-[(2S)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoyl]oxy]pentanoyl]oxymethyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]-5-oxopentyl (2S)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoate				24.6	100% remaining at 1h	26% remaining at 1h	28% remaining at 1h
345	trifluoroacetic acid 5-oxo-5-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)pentyl (2S)-2-amino-4-methylpentanoate				<0.662	71% remaining at 1h	2% remaining at 1h	77% remaining at 1h
346	bis(trifluoroacetic acid) 5-[(2-[(5-[(2S)-2-amino-4-methylpentanoyl]oxy]pentanoyl]oxymethyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]-5-oxopentyl (2S)-2-amino-4-methylpentanoate				<0.623	97% remaining at 1h	7% remaining at 1h	98% remaining at 1h
347	5-oxo-5-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)pentyl (2R)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoate				10.6	98% remaining at 1h	4% remaining at 1h	16% remaining at 1h
348	5-[(2-[(5-[(2R)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoyl]oxy]pentanoyl]oxymethyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]-5-oxopentyl (2R)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoate				<0.965	88% remaining at 1h	20% remaining at 1h	33% remaining at 1h
349	5-[(3-[(5-[(2R)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoyl]oxy]pentanoyl]oxymethyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]-5-oxopentyl (2R)-2-[(tert-butoxy)carbonyl]amino)-4-methylpentanoate				49.9	99% remaining at 1h	8% remaining at 1h	6% remaining at 1h
350	trifluoroacetic acid 5-oxo-5-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)pentyl (2R)-2-amino-4-methylpentanoate				0.782	29% remaining at 1h	52% remaining at 1h	44% remaining at 1h
351	bis(trifluoroacetic acid) 5-[(2-[(5-[(2R)-2-amino-4-methylpentanoyl]oxy]pentanoyl]oxymethyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]-5-oxopentyl (2R)-2-amino-4-methylpentanoate					69% remaining at 1h	14% remaining at 1h	99% remaining at 1h
352	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[(2S)-2-[(tert-butoxy)carbonyl]amino)-4-(methylsulfanyl)butanoyl]oxy}pentanoate				20.3	92% remaining at 1h	9% remaining at 1h	9% remaining at 1h

353	trifluoroacetic acid 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 5-[[[2S)-2-amino-4-(methylsulfanyl)butanoyl]oxy]penta noate					5.49	33% remaining at 1h	66% remaining at 1h	3% remaining at 1h
354	trifluoroacetic acid 2-(2-aminoethoxy)ethyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate						99% remaining at 1h	3% remaining at 1h	1% remaining at 1h
355	4-oxo-4-((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)butyl (2R)-2-[[[tert-butoxy]carbonyl]amino]-3-methylbutanoate					21.6	99% remaining at 1h	100% remaining at 1h	43% remaining at 1h
356	trifluoroacetic acid 4-oxo-4-[[4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]butyl (2R)-2-amino-3-methylbutanoate					113	99% remaining at 1h	25% remaining at 1h	5% remaining at 1h
357	4-[[[2-[[[4-[[[2R)-2-[[[tert-butoxy]carbonyl]amino]-3-methylbutanoyl]oxy]butanoyl]oxy]methyl]sulfanyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]-4-oxobutyl (2R)-2-[[[tert-butoxy]carbonyl]amino]-3-methylbutanoate					15	98% remaining at 1h	14% remaining at 1h	5% remaining at 1h
358	bis(trifluoroacetic acid) 4-(((5-(((4-((D-valyl)oxy)butanoyl)oxy)methyl)-1-(2-isopropoxyethyl)-4-oxo-4,5-dihydro-1H-pyrrolo[3,2-d]pyrimidin-2-yl)thio)methoxy)-4-oxobutyl D-valinate					17.8	80% remaining at 1h	48	12% remaining at 1h
359	(((1-(2-isopropoxyethyl)-4-oxo-2-thioxo-1,4-dihydro-3H-pyrrolo[3,2-d]pyrimidine-3,5(2H)-diyl)bis(methylene))bis(oxy))bis(4-oxobutane-4,1-diyl) (2R,2'R)-bis(2-((tert-butoxycarbonyl)amino)-3-methylbutanoate)					<2.97	99% remaining at 1h	41% remaining at 1h	8% remaining at 1h
360	bis(trifluoroacetic acid) 4-[[[3-[[[4-[[[2R)-2-amino-3-methylbutanoyl]oxy]butanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]-4-oxobutyl (2R)-2-amino-3-methylbutanoate					<6.28	46% remaining at 1h	56% remaining at 1h	3% remaining at 1h
361	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 4-[[[2R)-2-[[[tert-butoxy]carbonyl]amino]-3-phenylpropanoyl]oxy]butanoate					<3.10	95% remaining at 1h	9% remaining at 1h	8% remaining at 1h
362	trifluoroacetic acid 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 4-[[[2R)-2-amino-3-phenylpropanoyl]oxy]butanoate					51.2	90% remaining at 1h	2% remaining at 1h	3% remaining at 1h

363	[[5-[[[4-[[[2R)-2-[[[tert-butoxy)carbonyl]amino]-3-phenylpropanoyl]oxy]butanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfonyl]methyl 4-[[[2R)-2-[[[tert-butoxy)carbonyl]amino]-3-phenylpropanoyl]oxy]butanoate					16.3	97% remaining at 1h	18% remaining at 1h	42% remaining at 1h
364	bis(trifluoroacetic acid) [[5-[[[4-[[[2R)-2-amino-3-phenylpropanoyl]oxy]butanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl]sulfonyl]methyl 4-[[[2R)-2-amino-3-phenylpropanoyl]oxy]butanoate					2.77	47% remaining at 1h	1% remaining at 1h	31% remaining at 1h
365	(3-[[[4-[[[2R)-2-[[[tert-butoxy)carbonyl]amino]-3-phenylpropanoyl]oxy]butanoyl]oxy]methyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfonylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl 4-[[[2R)-2-[[[tert-butoxy)carbonyl]amino]-3-phenylpropanoyl]oxy]butanoate					<2.63	85% remaining at 1h	5% remaining at 1h	11% remaining at 1h
366	trifluoroacetic acid 3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfonylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl (2R)-2-amino-4-(methylsulfonyl)butanoate					<7.6	76% remaining at 1h	2% remaining at 1h	74% remaining at 1h
367	trifluoroacetic acid 3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfonylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl (2S)-2-amino-4-methylpentanoate					<1.08	100% remaining at 1h	0% remaining at 1h	1% remaining at 1h
368	trifluoroacetic acid 3-oxo-3-[(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfonylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy]propyl (2R)-2-amino-4-methylpentanoate					1.2	100% remaining at 1h	1% remaining at 1h	1% remaining at 1h
369	2-[[[2-[[[2-[[[tert-butoxy)carbonyl]amino]ethoxy]ethoxy]carbonyl]oxy]methyl]sulfonyl]-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one					<1.07	89% remaining at 1h	1% remaining at 1h	1% remaining at 1h
370	5-[[[2-[[[2-[[[tert-butoxy)carbonyl]amino]ethoxy]ethoxy]ethoxy]carbonyl]oxy]methyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfonylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	516			H NMR (300 MHz, CHLOROFORM-d6) δ 10.68 (br s, 1 H), 7.55 (t, J=3.13 Hz, 1 H), 6.28 - 6.42 (m, 1 H), 6.04 (s, 2 H), 4.38 - 4.49 (m, 2 H), 4.23 - 4.41 (m, 2 H), 3.70 - 3.83 (m, 2 H), 3.65 - 3.70 (m, 2 H), 3.45 - 3.65 (m, 3 H), 3.28 (br s, 2 H), 1.41 (s, 9 H), 0.91 - 1.16 (m, 6 H).	15.4	99% remaining at 1h	35% remaining at 1h	1% remaining at 1h
371	trifluoroacetic acid 2-[2-(2-aminoethoxy)ethoxy]ethyl 4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfonylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl carbonate	416			1H NMR (300 MHz, CHLOROFORM-d6) δ 10.68 (br s, 1 H), 8.11 (br s, 2 H), 7.15 - 7.34 (m, 2 H), 6.26 (d, J=3.52 Hz, 1 H), 6.20 (s, 2 H), 4.51 (t, J=5.57 Hz, 2 H), 4.23 - 4.41 (m, 2 H), 3.65 - 3.93 (m, 6 H), 3.45 - 3.65 (m, 1 H), 3.22 (br s, 2 H), 1.07 (d, J=6.45 Hz, 6 H).				

372	tert-butyl N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)amino)ethoxy)ethyl]carbamate		560	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 9.55 (br s, 1 H), 7.28 (d, <i>J</i> =2.93 Hz, 1 H), 6.15 - 6.34 (m, 3 H), 4.52 (t, <i>J</i> =5.57 Hz, 2 H), 4.21 - 4.35 (m, 2 H), 3.83 (t, <i>J</i> =5.57 Hz, 2 H), 3.64 - 3.76 (m, 2 H), 3.41 - 3.64 (m, 8 H), 3.28 (br s, 2 H), 1.42 (s, 9 H), 1.06 (d, <i>J</i> =5.86 Hz, 6 H).	117	85% remaining at 1h	60% remaining at 1h	0% remaining at 1h
373	trifluoroacetic acid (4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-[2-(2-aminoethoxy)ethyl]carbamate		459	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 10.78 (s, 1 H), 7.97 (br s, 2 H), 7.31 (d, <i>J</i> =2.93 Hz, 1 H), 6.24 (d, <i>J</i> =2.93 Hz, 1 H), 6.19 (s, 2 H), 4.50 (t, <i>J</i> =5.57 Hz, 2 H), 4.28 (dt, <i>J</i> =3.81, 2.20 Hz, 2 H), 3.44 - 3.83 (m, 11 H), 3.22 (br s, 2 H), 1.05 (d, <i>J</i> =5.86 Hz, 6 H).	1.23	90% remaining at 1h	72% remaining at 1h	68% remaining at 1h
374	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanylmethyl N-[2-(2-aminoethoxy)ethyl]carbamate		515	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 9.64 (br s, 1 H), 7.36 (d, <i>J</i> =2.93 Hz, 1 H), 6.13 - 6.28 (m, 3 H), 5.56 (br s, 1 H), 4.52 (t, <i>J</i> =5.86 Hz, 2 H), 3.82 (t, <i>J</i> =5.86 Hz, 2 H), 3.39 - 3.64 (m, 5 H), 3.11 - 3.39 (m, 4 H), 1.42 (s, 9 H), 0.96 - 1.18 (m, 6 H).	90.6	75% remaining at 1h	94% remaining at 1h	82% remaining at 1h
375	tert-butyl N-[2-(2-(((1-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)ethoxy)carbonyl)amino)ethoxy)ethyl]carbamate		415	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 7.33 (d, <i>J</i> =3.52 Hz, 1 H), 6.20 (d, <i>J</i> =2.93 Hz, 1 H), 6.09 (s, 2 H), 4.49 (t, <i>J</i> =5.86 Hz, 2 H), 3.79 (t, <i>J</i> =5.57 Hz, 2 H), 3.40 - 3.69 (m, 5 H), 3.29 (t, <i>J</i> =4.69 Hz, 2 H), 3.09 (t, <i>J</i> =4.69 Hz, 2 H), 1.04 (d, <i>J</i> =5.86 Hz, 6 H).	<1.75	89% remaining at 1h	99% remaining at 1h	99% remaining at 1h
376	N-[2-(2-aminoethoxy)ethyl]-4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carboxamide; trifluoroacetic acid		415	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 11.85 (br s, 1 H), 8.20 (brs, 2 H), 7.10 - 7.20 (m, 1 H), 6.08 - 6.20 (m, 1 H), 5.74 (s, 2 H), 4.22 (t, <i>J</i> =5.27 Hz, 2 H), 3.59 - 3.88 (m, 5 H), 3.44 - 3.59 (m, 2 H), 3.25 - 3.44 (m, 2 H), 2.96 - 3.24 (m, 2 H), 1.06 (d, <i>J</i> =5.86 Hz, 6 H).		98% remaining at 1h	99% remaining at 1h	95% remaining at 1h
377	(2R)-2-(((tert-butoxy)carbonyl)amino)-3-methyl-N-[2-(2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethoxy]ethyl]butanamide		528	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 10.99 (br s, 1 H), 8.15 (d, <i>J</i> =3.52 Hz, 1 H), 6.42 (d, <i>J</i> =3.52 Hz, 1 H), 6.18 (brs, 1 H), 4.57 (t, <i>J</i> =5.27 Hz, 2 H), 3.85 (t, <i>J</i> =5.27 Hz, 2 H), 3.46 - 3.72 (m, 7 H), 3.38 - 3.40 (m, 2 H), 1.50 (s, 9 H), 1.05 (d, <i>J</i> =5.86 Hz, 6 H).		83	11	8% remaining at 1h
378	tert-butyl N-[(1R)-2-methyl-1-((2-[2-(4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidine-5-carbonyl)amino)ethoxy)ethyl]carbamoyl)propyl]carbamate		385	1H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 12.00 (br s, 1 H), 11.03 (t, <i>J</i> =4.40 Hz, 1 H), 8.24 (br s, 3 H), 8.09 (d, <i>J</i> =3.52 Hz, 1 H), 6.29 (d, <i>J</i> =3.52 Hz, 1 H), 4.33 (t, <i>J</i> =5.28 Hz, 2 H), 3.58 - 3.91 (m, 8 H), 3.43 - 3.51 (m, 1 H), 3.22 - 3.31 (m, 2 H), 1.01 (d, <i>J</i> =5.86 Hz, 7 H).	0.903	98	96	93% remaining at 1h

379	tert-butyl N-[2-{2-[methoxy(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methoxycarbonyl)amino]ethoxy}ethyl)carbamate		659	1H NMR (300 MHz, CHLOROFORM- d6) δ 9.68 (br s, 1 H), 7.29 (d, J=2.93 Hz, 1 H), 6.15 - 6.33 (m, 3 H), 4.53 (t, J=5.86 Hz, 2 H), 4.22 - 4.37 (m, 2 H), 3.89 - 4.02 (m, 1 H), 3.83 (t, J=5.57 Hz, 2 H), 3.64 - 3.76 (m, 2 H), 3.26 - 3.64 (m, 9 H), 1.93 - 2.21 (m, 1 H), 1.43 (s, 9 H), 0.99 - 1.14 (m, 6 H), 0.72 - 0.99 (m, 6 H).		93% remaining at 1 h	69% remaining at 1 h	0% remaining at 1 h
380	trifluoroacetic acid ((4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl)sulfanyl)methyl N-[2-(2-aminoethoxy)ethyl]-N-methylcarbamate		584	1H NMR (300 MHz, CHLOROFORM- d6) δ 12.02 (s, 1 H), 11.00 (br s, 1 H), 8.16 (d, J=3.52 Hz, 1 H), 7.57 (br s, 1 H), 6.42 (d, J=4.10 Hz, 1 H), 5.38 (d, J=9.96 Hz, 1 H), 4.44 - 4.71 (m, 2 H), 4.04 - 4.31 (m, 2 H), 3.86 (t, J=5.27 Hz, 2 H), 3.41 - 3.80 (m, 5 H), 3.22 - 3.41 (m, 1 H), 2.93 (br s, 2 H), 1.91 (dt, J=6.65, 6.52 Hz, 1 H), 1.50 (s, 9 H), 1.05 (d, J=5.86 Hz, 6 H), 0.76 - 1.00 (m, 6 H).		100% remaining at 1 h	99% remaining at 1 h	85% remaining at 1 h
381	tert-butyl N-[2-{2-(((2-(((2-(((tert-butoxy)carbonyl)amino)ethoxy)ethyl)(methyl)carbamoyl)oxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxycarbonyl](methyl)amino]ethoxyethyl]carbamate		529	1H NMR (300 MHz, CHLOROFORM- d6) δ 12.58 - 12.78 (m, 1 H), 9.90 (br s, 1 H), 7.43 (t, J=2.64 Hz, 1 H), 6.12 - 6.33 (m, 1 H), 5.96 (d, J=7.62 Hz, 2 H), 4.31 (t, J=5.57 Hz, 2 H), 3.72 (t, J=5.86 Hz, 2 H), 3.27 - 3.60 (m, 7 H), 3.05 - 3.25 (m, 2 H), 2.90 (d, J=17.58 Hz, 3 H), 1.35 (d, J=2.34 Hz, 9 H), 0.98 (d, J=6.45 Hz, 6 H).		82% remaining at 1 h	97% remaining at 1 h	97% remaining at 1 h
382	bis(trifluoroacetic acid) (2-(((2-(2-aminoethoxy)ethyl)(methyl)carbamoyl)oxy)methyl)sulfanyl)-4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl N-[2-(2-aminoethoxy)ethyl]-N-methylcarbamate		429	1H NMR (300 MHz, CHLOROFORM- d6) δ 12.29 (br s, 1 H), 8.23 (br s, 2 H), 7.39 - 7.41 (m, 1 H), 6.28 - 6.30 (m, 1 H), 5.82 - 5.90 (m, 3 H), 4.34 (t, J=4.98 Hz, 2 H), 3.73 - 3.85 (m, 2 H), 3.26 - 3.60 (m, 7 H), 3.10 - 3.23 (m, 2 H), 2.73 - 2.98 (m, 3 H), 1.03 (d, J=6.45 Hz, 6 H).		100% remaining at 1 h	99% remaining at 1 h	98% remaining at 1 h
383	(2R)-2-(((tert-butoxy)carbonyl)amino)-3-methyl-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy]ethoxy)ethyl]butanamide		803	1H NMR (300 MHz, CHLOROFORM- d6) δ 7.82 (d, J=7.62 Hz, 1 H), 7.43 - 7.56 (m, 1 H), 6.36 (d, J=9.38 Hz, 2 H), 6.27 (d, J=2.93 Hz, 1 H), 5.85 - 6.02 (m, 2 H), 4.66 (br s, 2 H), 4.28 (t, J=5.57 Hz, 2 H), 3.67 - 3.81 (m, 2 H), 3.34 - 3.67 (m, 13 H), 3.09 - 3.34 (m, 4 H), 2.81 - 3.09 (m, 6 H), 1.28 - 1.50 (m, 18 H), 0.98 - 1.12 (m, 6 H).				
384	(2R)-2-amino-3-methyl-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy]ethoxy)ethyl]butanamide; trifluoroacetic acid		603	1H NMR (300 MHz, CHLOROFORM- d6) δ 7.30 - 7.42 (m, 1 H), 6.20 - 6.30 (m, 3 H), 5.82 (br s, 2 H), 4.28 (t, J=5.57 Hz, 2 H), 3.67 - 3.81 (m, 4 H), 3.45 - 3.67 (m, 15 H), 2.79 - 3.09 (m, 6 H), 1.08 (d, J=5.86 Hz, 6 H).				

385	(2R)-2-((tert-butoxycarbonyl)amino)-4-methyl-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethyl]pentanamide		637		¹ H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 9.84 (br s, 1 H), 7.20 - 7.33 (m, 1 H), 6.76 (br s, 1 H), 6.08 - 6.40 (m, 3 H), 4.53 (t, J=5.57 Hz, 2 H), 4.28 - 4.35 (m, 2 H), 3.95 (t, J=5.56 Hz, 1 H), 3.83 (t, J=5.57 Hz, 2 H), 3.61 - 3.77 (m, 2 H), 3.47 - 3.61 (m, 3 H), 2.87 - 2.98 (m, 2 H), 2.01 - 2.10 (m, 1 H), 1.42 (s, 9 H), 1.07 (d, J=6.45 Hz, 6 H), 0.75 - 0.99 (m, 6 H).	38.7	94% remaining after 1 h	84% remaining after 1 h	1% remaining after 1 h
386	(2R)-2-amino-4-methyl-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethyl]pentanamide; trifluoroacetic acid		515		¹ H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 10.75 (br s, 1 H), 7.99 (br s, 1 H), 7.31 (d, J=2.93 Hz, 1 H), 6.12 - 6.36 (m, 3 H), 4.51 (br t, J=5.57 Hz, 2 H), 4.19 - 4.38 (m, 2 H), 3.95 - 4.00 (m, 1 H), 3.81 (t, J=5.57 Hz, 2 H), 3.62 - 3.70 (m, 2 H), 3.48 - 3.62 (m, 3 H), 3.40 - 3.50 (m, 2 H), 2.05 - 2.34 (m, 1 H), 0.86 - 1.14 (m, 12 H).	0.77	93% remaining after 1 h	86% remaining after 1 h	23% remaining after 1 h
387	(2R)-2-((tert-butoxycarbonyl)amino)-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethyl]-3-phenylpropanamide		(M+Na) ⁺ = 651		¹ H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 9.80 (br s, 1 H), 7.26 - 7.33 (m, 1 H), 6.76 (br s, 1 H), 6.08 - 6.40 (m, 3 H), 4.53 (t, J=5.57 Hz, 2 H), 4.22 - 4.32 (m, 2 H), 3.83 (t, J=5.57 Hz, 2 H), 3.61 - 3.77 (m, 2 H), 3.47 - 3.61 (m, 3 H), 3.40 - 3.47 (m, 1 H), 3.01 - 3.23 (m, 2 H), 1.55 - 1.78 (m, 1 H), 1.31 - 1.55 (m, 11 H), 1.06 (d, J=5.86 Hz, 6 H), 0.81 - 0.98 (m, 6 H).	45	92% remaining after 1 h	75% remaining after 1 h	1% remaining after 1 h
388	(2R)-2-amino-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethyl]-3-phenylpropanamide; trifluoroacetic acid		529		¹ H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 10.84 (br s, 1 H), 8.11 (br s, 2 H), 7.30 (d, J=2.93 Hz, 1 H), 6.05 - 6.32 (m, 3 H), 4.37 - 4.61 (m, 2 H), 4.23 - 4.50 (m, 2 H), 4.05 - 4.18 (m, 1 H), 3.81 (t, J=5.57 Hz, 2 H), 3.62 - 3.70 (m, 2 H), 3.44 - 3.62 (m, 4 H), 3.31 - 3.44 (m, 1 H), 1.44 - 1.81 (m, 3 H), 1.06 (d, J=6.45 Hz, 6 H), 0.89 (br t, J=4.69 Hz, 6 H).	<19.9	97% remaining after 1 h	73% remaining after 1 h	1% remaining after 1 h
389	(2R)-2-((tert-butoxycarbonyl)amino)-4-(methylsulfanyl)-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethyl]butanamide		663		¹ H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 9.73 (br s, 1 H), 7.11 - 7.34 (m, 6 H), 6.15 - 6.35 (m, 3 H), 4.53 (t, J=5.57 Hz, 2 H), 4.23 (t, J=4.40 Hz, 2 H), 3.78 - 3.89 (m, 2 H), 3.49 - 3.63 (m, 2 H), 3.23 - 3.43 (m, 2 H), 2.98 - 3.05 (m, 2 H), 2.51 - 2.65 (m, 4 H), 1.39 (s, 9 H), 1.07 (d, J=6.45 Hz, 6 H).	59.4	98% remaining after 1 h	60% remaining after 1 h	1% remaining after 1 h
390	(2R)-2-amino-4-(methylsulfanyl)-N-[2-(2-(((4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methoxy)carbonyl)oxy)ethoxy)ethyl]butanamide; trifluoroacetic acid		563		¹ H NMR (300 MHz, CHLOROFORM- <i>d</i> ₆) δ 10.69 (br s, 1 H), 7.62 (br s, 1 H), 7.04 - 7.33 (m, 6 H), 6.24 (d, J=2.93 Hz, 1 H), 6.03 - 6.21 (m, 2 H), 4.50 (t, J=5.57 Hz, 2 H), 4.27 - 4.44 (m, 1 H), 4.18 - 4.21 (m, 2 H), 3.81 (t, J=5.57 Hz, 2 H), 3.41 - 3.69 (m, 4 H), 3.09 - 3.41 (m, 5 H), 1.06 (d, J=5.86 Hz, 6 H).	4.9	100% remaining after 1 h	64% remaining after 1 h	0% remaining after 1 h

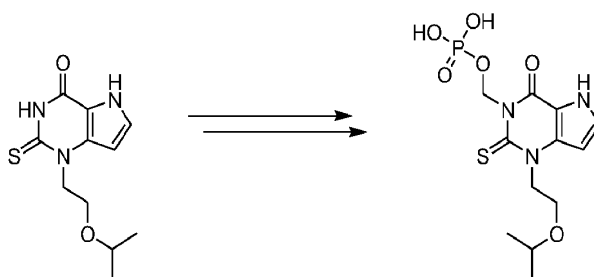
391	trifluoroacetic acid ({4-oxo-1-[2-(propan-2-yloxy)ethyl]-1H,4H,5H-pyrrolo[3,2-d]pyrimidin-2-yl}sulfanyl)methyl N-(2-{2-[(2R)-2-amino-3-methylbutanamido]ethoxy}ethyl)-N-methylcarbamate		647	1H NMR (300 MHz, CHLOROFORM-d6) δ 9.76 (br s, 1 H), 7.17 - 7.36 (m, 1 H), 6.73 (br s, 1 H), 6.15 - 6.35 (m, 3 H), 4.53 (t, J=5.57 Hz, 2 H), 4.27 - 4.32 (m, 3 H), 3.84 (t, J=5.57 Hz, 2 H), 3.66 (t, J=4.40 Hz, 2 H), 3.31 - 3.61 (m, 5 H), 2.50 - 2.60 (m, 2 H), 2.09 (s, 3 H), 1.80 - 1.98 (m, 2 H), 1.43 (s, 9 H), 0.97 - 1.19 (m, 6 H).	36.5	96% remaining after 1 h	70% remaining after 1 h	1% remaining after 1 h
392	tert-butyl 3-(2-[[{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]carbonyl]oxy)ethoxy)propanoate		547	1H NMR (300 MHz, CHLOROFORM-d6) δ 10.86 (br s, 1 H), 7.95 (br s, 1 H), 7.31 (d, J=2.93 Hz, 1 H), 6.08 - 6.33 (m, 3 H), 4.49 - 4.54 (m, 2 H), 4.24 - 4.32 (m, 3 H), 3.81 (t, J=5.57 Hz, 2 H), 3.61 - 3.74 (m, 2 H), 3.21 - 3.60 (m, 5 H), 2.45 - 2.70 (m, 2 H), 2.04 - 2.25 (m, 2 H), 2.02 (s, 3 H), 0.92 - 1.12 (m, 7 H).	1.2	95% remaining after 1 h	71% remaining after 1 h	1% remaining after 1 h
393	1-tert-butyl 2-({4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl (2R)-pyrrolidine-1,2-dicarboxylate		528	1H NMR (300 MHz, CHLOROFORM-d6) δ 12.00 (br s, 1 H), 8.52 (br s, 2 H), 8.17 (br s, 1 H), 7.40 (t, J=2.64 Hz, 1 H), 6.25 - 6.30 (m, 1 H), 6.13 (d, J=11.14 Hz, 1 H), 5.57 (d, J=11.14 Hz, 1 H), 4.30 - 4.40 (m, 2 H), 4.00 - 4.16 (m, 2 H), 3.77 (t, J=5.57 Hz, 2 H), 3.41 - 3.57 (m, 2 H), 3.02 - 3.42 (m, 6 H), 2.95 (s, 2 H), 2.84 (s, 1 H), 2.20 - 2.30 (m, 1 H), 0.92 - 1.15 (m, 12 H).	1.1	99% remaining after 1 h	94% remaining after 1 h	92% remaining after 1 h
394	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl (2R)-pyrrolidine-2-carboxylate			Ref Joe's first batch				
395	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl 2-[(tert-butoxy)carbonyl](methyl)amino}acetate		501	1H NMR (300 MHz, CHLOROFORM-d6) δ 7.28 (d, J=2.93 Hz, 1 H), 6.25 - 6.26 (m, 3 H), 4.51 (s, 2 H), 4.24 - 4.27 (m, 2 H), 3.82 (t, J=5.57 Hz, 2 H), 3.62 - 3.67 (m, 4 H), 3.55 (s, 1 H), 2.43 (t, J=6.01 Hz, 1 H), 1.42 (s, 9 H), 1.05 (d, J=5.86 Hz, 6 H).	144	97% remaining after 1 h	23% remaining after 1 h	1% remaining after 1 h
396	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methyl 2-(methylamino)acetate	(M+Na) ⁺ = 504		1H NMR (300 MHz, CHLOROFORM-d6) δ 9.13 - 9.34 (m, 1 H), 7.25 - 7.33 (m, 1 H), 6.08 - 6.43 (m, 3 H), 4.42 - 4.64 (m, 2 H), 4.15 - 4.36 (m, 1 H), 3.83 (t, J=5.57 Hz, 2 H), 3.30 - 3.59 (m, 3 H), 2.05 - 2.15 (m, 1 H), 1.69 - 1.99 (m, 3 H), 1.25 (s, 9 H), 1.05 (d, J=5.86 Hz, 6 H).				
397	3-(2-[[{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl]methoxy]carbonyl]oxy)ethoxy)propanoic acid		381	1H NMR (300 MHz, CHLOROFORM-d6) δ 10.82 (br s, 1 H), 7.13 - 7.43 (m, 1 H), 6.18 - 6.42 (m, 3 H), 4.45 - 4.60 (m, 3 H), 3.84 (t, J=5.57 Hz, 2 H), 3.33 - 3.60 (m, 2 H), 2.30 - 2.43 (m, 2 H), 1.94 - 2.26 (m, 3 H), 1.06 (d, J=5.86 Hz, 6 H).				

398	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-1-[2-(acetyloxy)acetyl]pyrrolidine-2-carboxylate	(M+Na) ⁺ = 478	1H NMR (300 MHz, CHLOROFORM-d) δ 9.48 (br d, J=13.48 Hz, 1 H), 7.21 - 7.36 (m, 1 H), 6.17 - 6.37 (m, 3 H), 4.52 (t, J=5.57 Hz, 2 H), 3.76 - 3.94 (m, 4 H), 3.50 - 3.60 (m, 1 H), 2.88 (d, J=4.69 Hz, 3 H), 1.43 (s, 9 H), 1.06 (d, J=5.86 Hz, 6 H).				
399	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-1-[(2S)-2-(benzoyloxy)-3-methylbutanoyl]pyrrolidine-2-carboxylate	356	1H NMR (300 MHz, CHLOROFORM-d) δ 11.21 (s, 1 H), 7.16 - 7.36 (m, 1 H), 6.18 - 6.42 (m, 3 H), 4.55 (t, J=5.57 Hz, 2 H), 3.95 (s, 2 H), 3.84 (t, J=5.27 Hz, 2 H), 3.25 - 3.60 (m, 1 H), 2.83 (s, 3 H), 1.06 (d, J=5.86 Hz, 6 H).				
400	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-[(2-acetyloxy)-N-methylacetamido]acetate	467	1H NMR (300 MHz, CHLOROFORM-d) δ 10.28 (s, 1 H), 7.30 (d, J=3.52 Hz, 1 H), 6.11 - 6.37 (m, 3 H), 4.53 (t, J=5.57 Hz, 2 H), 4.20 - 4.37 (m, 2 H), 3.52 - 3.93 (m, 7 H), 2.59 (t, J=6.15 Hz, 2 H), 0.99 - 1.16 (m, 6 H).	2.42	99% remaining after 1 h	26% remaining after 1 h	89% remaining after 1 h
401	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-[(2S)-2-(benzoyloxy)-N,3-dimethylbutanamido]acetate	482	1H NMR (300 MHz, CHLOROFORM-d) δ 9.32 (s, 1 H), 7.19 - 7.36 (m, 1 H), 6.24 - 6.38 (m, 3 H), 4.46 - 4.85 (m, 4 H), 3.72 - 3.92 (m, 2 H), 3.43 - 3.67 (m, 2 H), 2.03 - 2.24 (m, 5 H), 1.85 - 1.92 (m, 4 H), 1.06 (d, J=5.86 Hz, 6 H).	4.3	90% remaining after 1 h	8% remaining after 1 h	0% remaining after 1 h
402	5-[[[(2-[2-(carbamoyloxy)ethoxy]ethoxy)carboxyl]oxy]methyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	586	1H NMR (300 MHz, CHLOROFORM-d) δ 9.39 (s, 1 H), 7.97 - 8.14 (m, 2 H), 7.52 - 7.63 (m, 1 H), 7.41 - 7.52 (m, 2 H), 7.16 - 7.20 (m, 1 H), 6.12 - 6.30 (m, 2 H), 6.09 (d, J=2.93 Hz, 1 H), 5.05 - 5.13 (m, 1 H), 4.40 - 4.54 (m, 3 H), 4.01 - 4.10 (m, 1 H), 3.69 - 3.89 (m, 3 H), 3.40 - 3.62 (m, 2 H), 2.22 - 2.47 (m, 2 H), 1.84 - 2.14 (m, 2 H), 0.94 - 1.17 (m, 12 H).	246	99% remaining after 1 h	89% remaining after 1 h	99% remaining after 1 h
403	3-[[[(2-[2-(carbamoyloxy)ethoxy]ethoxy)carboxyl]oxy]methyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	457	1H NMR (300 MHz, CHLOROFORM-d) δ 9.24 (brs, 1 H), 7.13 - 7.23 (m, 1 H), 6.17 - 6.31 (m, 3 H), 4.82 (s, 2 H), 4.52 (t, J=5.57 Hz, 2 H), 4.18 (s, 2 H), 3.84 (t, J=5.57 Hz, 2 H), 3.44 - 3.63 (m, 1 H), 3.05 (s, 3 H), 2.23 (s, 3 H), 1.06 (d, J=5.86 Hz, 6 H).	4.77	98% remaining after 1 h	54% remaining after 1 h	0% remaining after 1 h
404	17-[2-(propan-2-yloxy)ethyl]-16-sulfanylidene-3,5,8,11,13-penta-1,1,5,17-triazatricyclo[13.5.2.0 ^{18,21}]docosa-18(21),19-diene-4,12,22-trione	560	1H NMR (300 MHz, CHLOROFORM-d) δ 9.46 (s, 1 H), 7.98 - 8.15 (m, 2 H), 7.51 - 7.69 (m, 1 H), 7.36 - 7.51 (m, 2 H), 7.18 - 7.34 (m, 1 H), 6.14 - 6.37 (m, 3 H), 5.27 (d, J=7.03 Hz, 2 H), 4.38 - 4.64 (m, 2 H), 3.70 - 3.92 (m, 3 H), 3.51 - 3.61 (m, 1 H), 3.25 (s, 3 H), 2.22 - 2.44 (m, 1 H), 0.94 - 1.18 (m, 12 H).	50.8	92% remaining after 1 h	86% remaining after 1 h	77% remaining after 1 h

405	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-1-[2-{2-[(tert-butoxy)carbonyl]amino}acetamido)acetyl]pyrrolidine-2-carboxylate		460	1H NMR (300 MHz, CHLOROFORM-d6) δ 9.43 (s, 1 H), 7.26 - 7.33 (m, 1 H), 6.18 - 6.35 (m, 3 H), 4.78 (brs, 2 H), 4.45 - 4.61 (m, 2 H), 4.24 - 4.42 (m, 2 H), 4.06 - 4.24 (m, 2 H), 3.76 - 3.87 (m, 2 H), 3.62 - 3.76 (m, 4 H), 3.41 - 3.62 (m, 1 H), 1.00 - 1.14 (m, 6 H).		83% remaining after 1 h	81% remaining after 1 h	1% remaining after 1 h
406	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl (2R)-1-[2-(2-aminoacetamido)acetyl]pyrrolidine-2-carboxylate		460	1H NMR (300 MHz, CHLOROFORM-d6) δ 10.67 (br s, 1 H), 7.18 - 7.26 (m, 2 H), 6.66 (s, 2 H), 6.25 (t, J=2.34 Hz, 1 H), 5.08 (br s, 2 H), 4.64 (t, J=5.86 Hz, 2 H), 4.27 - 4.43 (m, 2 H), 4.10 - 4.27 (m, 2 H), 3.87 (t, J=5.86 Hz, 2 H), 3.42 - 3.79 (m, 5 H), 0.95 - 1.15 (m, 6 H).	34.2	88% remaining after 1 h	71% remaining after 1 h	0% remaining after 1 h
407	{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-[2-(2-[(tert-butoxy)carbonyl]amino)acetamido)-N-methylacetamido]acetate		473	1H NMR (300 MHz, CHLOROFORM-d6) δ 7.12 (d, J=2.93 Hz, 1 H), 6.83 (s, 2 H), 6.25 (d, J=2.93 Hz, 1 H), 6.14 (s, 2 H), 4.61 (t, J=5.57 Hz, 2 H), 4.32 - 4.40 (m, 4 H), 3.76 - 3.90 (m, 2 H), 3.64 - 3.76 (m, 4 H), 3.57 (dt, J=12.02, 6.30 Hz, 1 H), 1.08 (d, J=5.86 Hz, 6 H).	146	98% remaining after 1 h	1% remaining after 1 h	0% remaining after 1 h
408	trifluoroacetic acid {4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-5-yl)methyl 2-[2-(2-aminoacetamido)-N-methylacetamido]acetate		596	1H NMR (300 MHz, CHLOROFORM-d6) δ 7.18 - 7.31 (m, 1 H), 6.07 - 6.41 (m, 3 H), 4.37 - 4.68 (m, 3 H), 4.08 (d, J=5.86 Hz, 2 H), 3.80 - 3.90 (m, 3 H), 3.41 - 3.63 (m, 2 H), 2.65 - 2.72 (s, 2 H), 1.87 - 2.25 (m, 4 H), 1.45 (s, 9 H), 0.96 - 1.19 (m, 6 H).				
409	15-[2-(propan-2-yloxy)ethyl]-14-sulfanylidene-3,5,9,11-tetraoxa-1,13,15-triazatricyclo[11.5.2.0 ^{16,19}]cosa-16(19),17-diene-4,10,20-trione		496	1H NMR (300 MHz, CHLOROFORM-d6) δ 11.01 (br s, 1 H), 8.57 (br s, 1 H), 8.11 (brs, 2 H), 7.25 - 7.34 (m, 1 H), 6.19 - 6.25 (m, 3 H), 4.40 - 4.68 (m, 3 H), 3.75 - 4.10 (m, 5 H), 3.41 - 3.63 (m, 2 H), 2.75 (s, 2 H), 2.01 - 2.15 (m, 2 H), 1.72 - 2.00 (m, 2 H), 1.05 (d, J=6.45 Hz, 6 H).	<1.07	94% remaining after 1 h	28% remaining after 1 h	4% remaining after 1 h
410	5-[[[3-(carbamoyloxy)propoxy]carbonyl]oxymethyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one		570	1H NMR (300 MHz, CHLOROFORM-d6) δ 9.94 (br s, 1 H), 7.20 - 7.35 (m, 1 H), 6.18 - 6.39 (m, 3 H), 5.32 (br s, 1 H), 4.53 (t, J=5.57 Hz, 2 H), 4.08 - 4.24 (m, 3 H), 3.71 - 3.94 (m, 4 H), 3.50 - 3.61 (m, 1 H), 3.05 (s, 3 H), 2.87 (br s, 2 H), 1.42 (s, 9 H), 1.07 (d, J=5.86 Hz, 6 H).				
411	5-[[[4-(carbamoyloxy)butoxy]carbonyl]oxymethyl]-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one		470	1H NMR (300 MHz, CHLOROFORM-d6) δ 11.06 (br s, 1 H), 8.33 - 8.67 (m, 1 H), 7.84 - 8.13 (m, 2 H), 7.26 - 7.30 (m, 1 H), 6.18 - 6.30 (m, 3 H), 4.34 - 4.49 (m, 2 H), 4.05 - 4.31 (m, 3 H), 3.65 - 3.85 (m, 3 H), 3.25 - 3.60 (m, 4 H), 3.09 (s, 3 H), 2.87 (br s, 2 H), 1.04 (d, J=5.27 Hz, 6 H).	<1.07	92% remaining after 1 h	22% remaining after 1 h	1% remaining after 1 h

412	3-(((4-(carbamoyloxy)butoxy)carbonyloxy)methyl)-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one	442	1H NMR (300 MHz, CHLOROFORM-d6) δ 7.12 (d, J=2.93 Hz, 1 H), 6.90 (br s, 2 H), 6.22 - 6.31 (m, 1 H), 6.13 (br s, 2 H), 4.61 (t, J=5.97 Hz, 2 H), 4.22 - 4.46 (m, 4 H), 3.84 (t, J=5.57 Hz, 2 H), 3.50 - 3.62 (m, 1 H), 2.07 - 2.27 (m, 2 H), 1.02 - 1.16 (m, 6 H).				
413	16-[2-(propan-2-yloxy)ethyl]-15-sulfanylidene-3,5,10,12-tetraoxa-1,14,16-triazatricyclo[12.5.2.0 ⁶ {17,20}]henicos-17(20),18-diene-4,11,21-trione	429	1H NMR (300 MHz, CHLOROFORM-d6) δ 9.32 (br s, 1 H), 7.28 - 7.35 (m, 2 H), 6.11 - 6.37 (m, 3 H), 4.64 (br s, 2 H), 4.53 (t, J=5.86 Hz, 2 H), 4.25 (t, J=6.45 Hz, 2 H), 4.03 - 4.19 (m, 2 H), 3.84 (t, J=5.57 Hz, 2 H), 3.50 - 3.60 (m, 1 H), 1.85 - 2.10 (m, 2 H), 1.07 (d, J=5.86 Hz, 6 H).				

EXAMPLE 414:

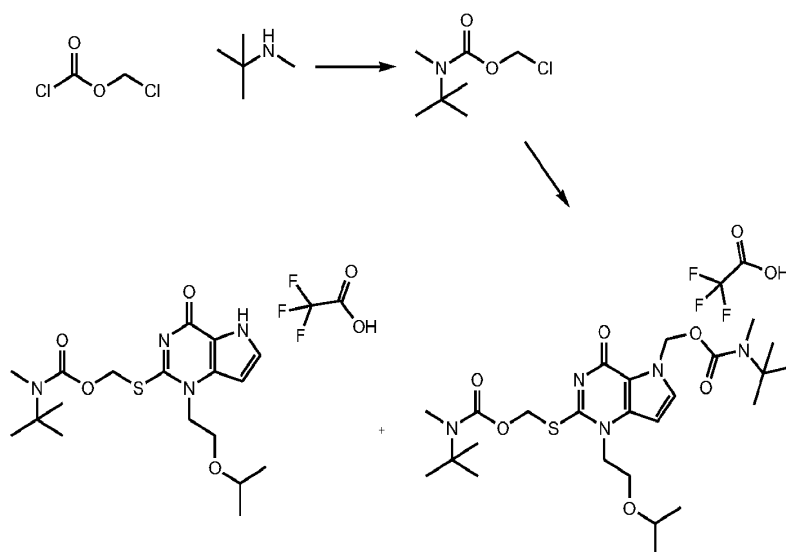


5 **{{4-oxo-1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-3-yl)methoxy}phosphonic acid.** A solution of 1-[2-(propan-2-yloxy)ethyl]-2-sulfanylidene-1H,2H,3H,4H,5H-pyrrolo[3,2-d]pyrimidin-4-one (506 mg, 2.0 mmol) in DMF (8 mL) under nitrogen was treated with lithium hexamethyldisilylamide (1.0 M in THF, 1.8 mL, 1.8 mmol), and the reaction mixture was stirred for 15 minutes. Di-tert-butyl chloromethyl phosphate (520 mg, 2.0 mmol) was added *via*

10 syringe with continued stirring of the reaction mixture overnight, followed by purification with RP-HPLC (Method D). The later fractions of similar retention time containing the desired product were combined and lyophilized to provide the di-tert-butyl protected intermediate (130 mg, 13.7%). Deprotection of tert-butyl protecting groups was carried out with glacial acetic acid and water (4:1 v/v) at 75° C for 30 minutes followed by stirring at room temperature overnight. The reaction mixture was purified by RP-

15 HPLC (Method D), and similar fractions were lyophilized to provide the title compound as a white solid (54 mg). ¹H NMR (300 MHz, DMSO-*d*₆) δ = 12.50 (br s, 1H), 7.43 (t, *J*=2.9 Hz, 1H), 6.34 (t, *J*=2.6 Hz, 1H), 6.23 (d, *J*=4.7 Hz, 2H), 4.58 (t, *J*=6.4 Hz, 2H), 3.74 (t, *J*=6.2 Hz, 2H), 3.62 - 3.49 (m, 1H), 1.01 (d, *J*=6.1 Hz, 6H). LC/MS method A: *R*_t = 3.02 mins. (M+H)⁺ = 364, purity = 99%.

EXAMPLE 415:

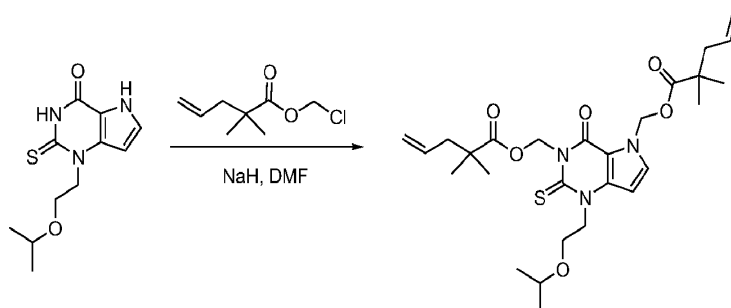


tert-Butyl-methyl-carbamic acid chloromethyl ester. To an ice cooled solution of t-butyl methyl amine (0.135 g, 1.55 mmole) in 2 mL of CH_2Cl_2 was added diisopropylethyl amine (0.67 mL, 2.36 mmole) and chloromethyl chloroformate (0.136 mL, 1.511 mmole) dropwise over 1 minute. After 18 hours, the reaction mixture was concentrated *in vacuo* and purified on a 40 g Agela column eluting with 0-60 % EtOAc in hexanes. The desired fractions were concentrated *in vacuo* to yield the titled product (0.188 g, 67 %). ^1H NMR (300MHz, $\text{CHLOROFORM-}d$) δ = 5.78 (s, 1H), 2.94 (s, 1H), 1.41 (s, 4H).

tert-Butyl-methyl-carbamic acid 1-(2-isopropoxy-ethyl)-4-oxo-4,5-dihydro-1H-pyrrolo[3,2-d]pyrimidin-2-ylsulfanylmethyl ester, trifluoroacetic acid salt. Sodium hydride (23 mg, 0.98 mmole) was added to a solution of 1-(2-Isopropoxy-ethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrrolo[3,2-d]pyrimidin-4-one (0.10 g, 0.39 mmole) in 5 mL of THF. After gas evolution had ceased, tert-butyl-methyl-carbamic acid chloromethyl ester (0.156 g, 0.86 mmole) in 1 mL of THF was added. After 18 hours, the reaction was quenched with saturated aqueous NH_4Cl . The aqueous layer was extracted with 2 x 20 mL of EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The product was purified by RP-HPLC 40-95% ACN in H_2O with 0.1% TFA. The desired fractions were lyophilized to yield tert-butyl-methyl-carbamic acid 1-(2-isopropoxy-ethyl)-4-oxo-4,5-dihydro-1H-pyrrolo[3,2-d]pyrimidin-2-ylsulfanylmethyl ester, trifluoroacetic acid salt (68.5 mg, 26 %). ^1H NMR

(300MHz, CHLOROFORM-*d*) δ = 12.76 - 12.39 (m, 1H), 7.60 - 7.41 (m, 1H), 6.35 (dd, J =1.9, 3.0 Hz, 1H), 5.99 (s, 2H), 4.39 (t, J =5.7 Hz, 3H), 3.89 - 3.67 (m, 2H), 3.50 (t, J =6.1 Hz, 1H), 2.89 (s, 3H), 1.37 (s, 9H), 1.04 (d, J =6.0 Hz, 6H). LC/MS: R_t = 5.92 mins. $(M+H)^+$ = 397, purity > 95% and tert-butyl-methyl-carbamic acid 2-[(tert-butyl-methyl-carbamoyloxy)-methylsulfanyl]-1-(2-isopropoxy-ethyl)-4-oxo-1,4-dihydro-pyrrolo[3,2-d]pyrimidin-5-ylmethyl ester; trifluoro-acetic acid salt (69.0 mg, 27%). ¹H NMR (300MHz, CHLOROFORM-*d*) δ = 7.48 (d, J =3.3 Hz, 1H), 6.36 (s, 2H), 6.24 (d, J =3.3 Hz, 1H), 5.94 (s, 2H), 4.27 (t, J =5.8 Hz, 2H), 3.74 (br t, J =5.6 Hz, 7H), 3.56 - 3.44 (m, 1H), 2.89 (s, 3H), 2.87 (s, 3H), 1.37 (s, 9H), 1.35 - 1.32 (m, 9H), 1.04 (d, J =6.0 Hz, 6H). LC/MS: R_t = 7.00 mins. $(M+H)^+$ = 540, purity > 95%.

10 EXAMPLE 416:



(1-(2-isopropoxyethyl)-4-oxo-2-thioxo-1H-pyrrolo[3,2-d]pyrimidine-3,5(2H,4H)-diyl)bis(methylene) bis(2,2-dimethylpent-4-enoate). A suspension of 1-(2-isopropoxyethyl)-2-thioxo-2,3-dihydro-1H-pyrrolo[3,2-d]pyrimidin-4(5H)-one (50 mg, 0.197 mmol) in DMF (1 mL) was treated with sodium hydride (60% in mineral oil, 12.6 mg, 0.315 mmol) under N₂ and stirred for 30 minutes. Chloromethyl 2,2-dimethylpent-4-enoate (69.5 mg, 0.394 mmol) in DMF (0.5 mL) was added *via* syringe and the mixture was stirred for 18 h. The reaction was quenched with a few drops of saturated aqueous NH₄Cl and purified by normal phase chromatography (20% EtOAc/hexanes) to get the pure product separated from other isomers as a white solid (12 mg, 15%). ¹H NMR (300MHz, CHLOROFORM-*d*) δ = 7.28 (d, J =3.3 Hz, 1H), 6.57 (s, 2H), 6.26 - 6.23 (m, 3H), 5.71 - 5.85 (m, 1H), 5.50 - 5.62 (m, 1H), 5.00 - 5.08 (m, 2H), 4.85 - 4.91 (m, 2H), 4.62 (t, J =5.6 Hz, 2H), 3.86 (t, J =5.6 Hz, 2H), 3.50 - 3.61 (m, 1H), 2.26 - 2.29 (m, 2H), 2.20 - 2.23 (m, 2H), 1.18 (s, 6H), 1.12 (s, 6H), 1.06 (d, J =6.4 Hz, 6H). LC/MS (method A) $(M+H)^+$ = 535, purity > 95%.

The above schemes and procedures are provided only to illustrate embodiments of the present invention. In some cases, the final product may be further modified, for example, by manipulation of substituents. These manipulations may include, but are not limited to, reduction, oxidation, alkylation, acylation, and hydrolysis reactions which are commonly known to those of ordinary skill in the art.

5 In some cases, the order of carrying out the reactions in the foregoing schemes may be varied to facilitate the reaction or to avoid unwanted reaction products. Additionally, various protecting group strategies may be employed to facilitate the reaction or to avoid unwanted reaction products. The following examples are provided so that the invention might be more fully understood. These examples are illustrative only and should not be construed as limiting the invention in any way.

10

COMPOUND SYNTHESIS AND CHARACTERIZATION

The compounds of the invention may be tested for biological activity as MPO inhibitors by methods known to those skilled in the art. In addition, methods such as, for example, a Caco-2 assay, may be used to test the bioavailability of the compounds of the invention. A description of a Caco-2 permeability assay is as follows:

15

CACO-2 PERMEABILITY ASSAY

- The Caco-2 monolayer is widely used across the pharmaceutical industry as an *in vitro* model of the human small intestinal mucosa to predict the absorption of orally administered drugs.¹⁻⁴
- 20 • The Caco-2 cell model mimics processes such as transcellular transport, paracellular transport, and some aspects of efflux and active transport.

Readout: P_{app} (A→B), P_{app} (B→A), Efflux ratio, % Recovery

Controls: with and without Pgp inhibitor; Atenolol, Propanolol, Taxel-1

25

Assay Description:

The Caco-2 cells are cultured to confluency, trypsinized and seeded onto a filter transwell insert at a density of ~32,000 cells/well in DMEM cell culture medium. Cells are grown in a humidified atmosphere of 5% CO₂ at 37 °C. Following an overnight attachment period (24 h after seeding), the cell medium is replaced with fresh medium in both the apical and basolateral compartments every other day. The cell monolayers are used for transport studies 21 days post seeding after measuring the TEER

30

values ($>600 \text{ Ohms/cm}^2$). The apical sides and basolateral sides are washed consecutively with HBSS 2.5% (v/v), HEPES (pH 7.4) or HBSS 2.5% (v/v), HEPES 10% (v/v), and Fetal Bovine Serum (pH 7.4) at 37°C in an incubator under an atmosphere of 5% CO_2 .

Donor working solution is prepared by dilution of DMSO stock of test article or positive control
5 with transport media to $10 \mu\text{M}$.

For A $\rightarrow$ B directional transport, the donor working solution (with test article or positive control, with or without Pgp inhibitor) is added to the apical (A) compartment and the transport media as receiver working solution is added to the basolateral (B) compartment. For B $\rightarrow$ A directional transport, the donor working solution (with positive control or test article, with or without Pgp inhibitor) is added
10 to the basolateral (B) compartment and transport media as receiver working solution is added to the apical (A) compartment.

The cells are incubated in a humidified atmosphere of 5% CO_2 at 37°C for 90 minutes.

At the end of the incubation, samples are taken from both donor and receiver compartments and transferred into 96-well assay plates containing internal standard solution (IS) in each well. After
15 centrifugation, the supernatant solutions are transferred to clean 96 well plates and analyzed by LC-MS/MS. The MS detection is performed using a Sciex API 4000 instrument. Each compound is analyzed by reversed phase HPLC.

Data Analysis:

20 The parameters P_{app} (apparent permeability) and efflux ratio are calculated as follows:

$$P_{\text{app}} = (dQ/dt) \times (1/C_0) \times (1/A)$$

$$\text{Efflux ratio} = P_{\text{app}} [\text{B} \rightarrow \text{A}] / P_{\text{app}} [\text{A} \rightarrow \text{B}]$$

where dQ/dt is the permeability rate, C_0 is the initial concentration in the donor compartment, and A is the surface area of the cell monolayer (0.33cm^2). The P_{app} value is a rate measured in cm/s .

25 Calculated P_{app} is ranked as low ($<1 \times 10^{-6} \text{ cm/s}$), moderate ($1-10 \times 10^{-6} \text{ cm/s}$), and high ($>10 \times 10^{-6} \text{ cm/s}$).

Comparing the efflux ratios generated in the presence and absence of a Pgp inhibitor identifies whether the test article is a Pgp substrate. A compound is considered to be a Pgp substrate when the efflux ratio in the absence of inhibitor is >1.99 and is significantly reduced (≤ 1) in the presence of an
30 inhibitor.

Recovery is calculated as follows:

%Recovery = (Total compound mass in donor and receiver compartments at the end of the incubation / Initial compound mass in the donor compartment) × 100.

STABILITY IN SIMULATED GASTRIC FLUID (SGF) AND SIMULATED INTESTINAL FLUID (SIF)

5 Simulated gastric fluid (SGF) and Simulated intestinal fluid (SIF) stability are *in vitro* metrics indicating the ability of a compound to pass through the gastrointestinal tract digested, partially digested or completely digested. An undigested or nearly undigested compound will usually survive gut transit long enough to be absorbed into the systemic circulation. Greater than 50% remaining intact compound at 1 hour indicates a relatively stable molecule that will likely be absorbed in the gut.

10 For each test compound, samples at a final concentration of 2 µg/mL are prepared in respective blank simulated gastric fluid with pepsin (pH 1.2) and simulated intestinal fluid with pancreatin (pH 6.8). All samples are incubated at 37 °C on a 150-rpm orbital shaker, and an aliquot is removed at predetermined time points (0 to 60 minutes). Samples are precipitated with three volumes of acetonitrile containing propranolol as internal standard, and centrifuged for 10 min at 2,000 g before LC-
15 MS/MS analysis of the supernatant solutions. Percent parent compound remaining is determined relative to 0-minute incubation samples. If a sufficient number of time points are available, the degradation half-life is calculated based on the natural log of % compound remaining vs. time plot.

 Plasma stability estimates the ability of a compound to remain intact in the blood. For prodrugs that are intended to be hydrolyzed by plasma enzymes a certain level of instability in plasma indicates
20 the compound is probably breaking down to the parent drug. A stability range of 25-75% remaining parent compound after 1 hour in plasma indicates the compound is likely breaking down to the parent drug molecule and a patient will be exposed to this parent molecule.

PLASMA STABILITY

25 Assessment of plasma stability was carried out by individual incubations of drug candidates in fresh human plasma at a concentration of 1 µM for 1 hour at 37 °C. After which, the samples were deproteinized by addition of 2 volumes of acetonitrile containing 0.1% formic acid and internal standard, vortex mixed for 2 minutes and centrifuged at 4,000 rpm for 10 minutes to pellet precipitated protein. The resulting supernatant containing the drug candidates was diluted 5-fold with water containing 0.1%
30 formic acid and submitted to LCMS/MS analysis. All determinations were done in triplicate. Plasma stability was expressed as percent of control remaining.

See Pelletier *et al.* *ACS Med. Chem. Lett.* **2018**, *9*, 752–756.

Abbreviations:

	ACN	Acetonitrile
5	DCM	Dichloromethane
	DMEM	Dulbecco's Modified Eagle Medium
	DMF	Dimethylformamide
	DMSO	Dimethylsulfoxide
	EtOAc	Ethyl acetate
10	HBSS	Hank's Buffered Salt Solution
	HEPES	4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid
	hPlasma	Human plasma
	HPLC	High-performance liquid chromatography
	MeOH	Methanol
15	MPO	Myeloperoxidase
	LC/MS	Liquid chromatography/mass spectrometry
	Pgp	P-glycoprotein 1, also known as multidrug resistance protein 1 (MDR1)
	LC	Liquid chromatography
	LiHMDS	Lithium bis(trimethylsilyl)amide
20	MS	Mass spectrometry
	NMR	Nuclear magnetic resonance
	RP-HPLC	Reversed phase high-performance liquid chromatography
	SIF	Simulated intestinal fluid
	SGF	Simulated gastric fluid
25	TEER	Transepithelial Resistance (in Ohm/cm ²)
	TFA	Trifluoroacetic acid
	THF	Tetrahydrofuran
	TMS	Tetramethylsilane
30	Literature:	

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Throughout this application, various publications are referenced by author name and date, or by patent number or patent publication number. The disclosures of these publications are hereby incorporated in their entireties by reference into this application in order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described and claimed
15 herein. However, the citation of a reference herein should not be construed as an acknowledgement that such reference is prior art to the present invention.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, numerous equivalents to the specific procedures described herein. Such equivalents are considered to be within the scope of this invention and are covered by the following claims. For
20 example, pharmaceutically acceptable salts other than those specifically disclosed in the description and Examples herein can be employed. Furthermore, it is intended that specific items within lists of items, or subset groups of items within larger groups of items, can be combined with other specific items, subset groups of items or larger groups of items whether or not there is a specific disclosure herein identifying such a combination.

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