

SULFUR COMPOUNDS AS INHIBITORS OF HEPATITIS C VIRUS NS3 SERINE PROTEASE

Field of the Invention

The present invention relates to novel hepatitis C virus ("HCV") protease inhibitors, pharmaceutical compositions containing one or more such inhibitors, methods of preparing such inhibitors and methods of using such inhibitors to treat hepatitis C and related disorders. This invention additionally
5 discloses novel compounds as inhibitors of the HCV NS3/NS4a serine protease. This application claims priority from U.S. provisional application Serial No. 60/548,670 filed February 27, 2004.

Background of the Invention

10 Hepatitis C virus (HCV) is a (+)-sense single-stranded RNA virus that has been implicated as the major causative agent in non-A, non-B hepatitis (NANBH), particularly in blood-associated NANBH (BB-NANBH) (see, International Patent Application Publication No. WO 89/04669 and European Patent Application Publication No. EP 381 216). NANBH is to be
15 distinguished from other types of viral-induced liver disease, such as hepatitis A virus (HAV), hepatitis B virus (HBV), delta hepatitis virus (HDV), cytomegalovirus (CMV) and Epstein-Barr virus (EBV), as well as from other forms of liver disease such as alcoholism and primary biliar cirrhosis.

20 Recently, an HCV protease necessary for polypeptide processing and viral replication has been identified, cloned and expressed. (See, e.g., U.S. Patent No. 5,712,145). This approximately 3000 amino acid polyprotein contains, from the amino terminus to the carboxy terminus, a nucleocapsid protein (C), envelope proteins (E1 and E2) and several non-structural proteins

(NS1, 2, 3, 4a, 5a and 5b). NS3 is an approximately 68 kda protein, encoded by approximately 1893 nucleotides of the HCV genome, and has two distinct domains: (a) a serine protease domain consisting of approximately 200 of the N-terminal amino acids; and (b) an RNA-dependent ATPase domain at the C-terminus of the protein. The NS3 protease is considered a member of the chymotrypsin family because of similarities in protein sequence, overall three-dimensional structure and mechanism of catalysis. Other chymotrypsin-like enzymes are elastase, factor Xa, thrombin, trypsin, plasmin, urokinase, tPA and PSA. The HCV NS3 serine protease is responsible for proteolysis of the polypeptide (polyprotein) at the NS3/NS4a, NS4a/NS4b, NS4b/NS5a and NS5a/NS5b junctions and is thus responsible for generating four viral proteins during viral replication. This has made the HCV NS3 serine protease an attractive target for antiviral chemotherapy. The inventive compounds can inhibit such protease. They also can modulate the processing of hepatitis C virus (HCV) polypeptide.

It has been determined that the NS4a protein, an approximately 6 kda polypeptide, is a co-factor for the serine protease activity of NS3. Autocleavage of the NS3/NS4a junction by the NS3/NS4a serine protease occurs intramolecularly (*i.e.*, *cis*) while the other cleavage sites are processed intermolecularly (*i.e.*, *trans*).

Analysis of the natural cleavage sites for HCV protease revealed the presence of cysteine at P1 and serine at P1' and that these residues are strictly conserved in the NS4a/NS4b, NS4b/NS5a and NS5a/NS5b junctions. The NS3/NS4a junction contains a threonine at P1 and a serine at P1'. The Cys→Thr substitution at NS3/NS4a is postulated to account for the requirement of *cis* rather than *trans* processing at this junction. See, *e.g.*, Pizzi *et al.* (1994) *Proc. Natl. Acad. Sci (USA)* 91:888-892, Failla *et al.* (1996) *Folding & Design* 1:35-42. The NS3/NS4a cleavage site is also more

tolerant of mutagenesis than the other sites. See, e.g., Kollykhalov et al. (1994) J. Virol. 68:7525-7533. It has also been found that acidic residues in the region upstream of the cleavage site are required for efficient cleavage. See, e.g., Komoda et al. (1994) J. Virol. 68:7351-7357.

5 Inhibitors of HCV protease that have been reported include antioxidants (see, International Patent Application Publication No. WO 98/14181), certain peptides and peptide analogs (see, International Patent Application Publication No. WO 98/17679, Landro et al. (1997) Biochem. 36:9340-9348, Ingallinella et al. (1998) Biochem. 37:8906-8914, Llinàs-
10 Brunet et al. (1998) Bioorg. Med. Chem. Lett. 8:1713-1718), inhibitors based on the 70-amino acid polypeptide eglin c (Martin et al. (1998) Biochem. 37:11459-11468, inhibitors affinity selected from human pancreatic secretory trypsin inhibitor (hPSTI-C3) and minibody repertoires (MBip) (Dimasi et al. (1997) J. Virol. 71:7461-7469), cV_HE2 (a "camelized" variable domain
15 antibody fragment) (Martin et al. (1997) Protein Eng. 10:607-614), and α 1-antichymotrypsin (ACT) (Elzouki et al. (1997) J. Hepat. 27:42-28). A ribozyme designed to selectively destroy hepatitis C virus RNA has recently been disclosed (see, *BioWorld Today* 9(217): 4 (November 10, 1998)).

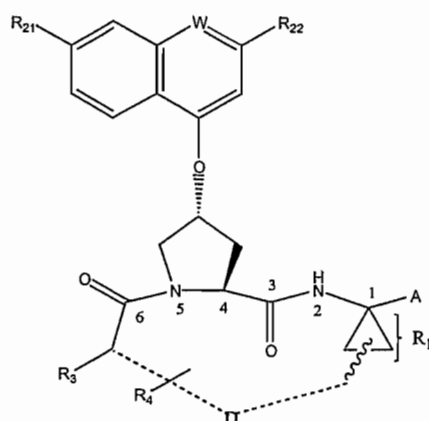
Reference is also made to the PCT Publications, No. WO 98/17679,
20 published April 30, 1998 (Vertex Pharmaceuticals Incorporated); WO 98/22496, published May 28, 1998 (F. Hoffmann-La Roche AG); and WO 99/07734, published February 18, 1999 (Boehringer Ingelheim Canada Ltd.).

HCV has been implicated in cirrhosis of the liver and in induction of hepatocellular carcinoma. The prognosis for patients suffering from HCV
25 infection is currently poor. HCV infection is more difficult to treat than other forms of hepatitis due to the lack of immunity or remission associated with HCV infection. Current data indicates a less than 50% survival rate at four years post cirrhosis diagnosis. Patients diagnosed with localized resectable

hepatocellular carcinoma have a five-year survival rate of 10-30%, whereas those with localized unresectable hepatocellular carcinoma have a five-year survival rate of less than 1%.

Reference is made to WO 00/59929 (US 6,608,027, Assignee:

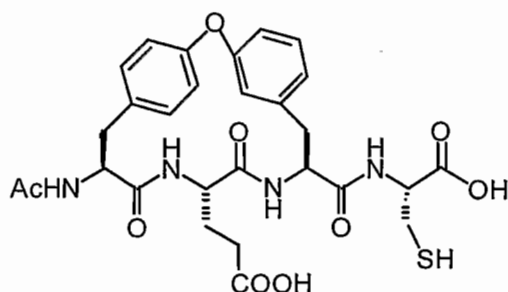
- 5 Boehringer Ingelheim (Canada) Ltd.; Published October 12, 2000) which discloses peptide derivatives of the formula:



Reference is made to A. Marchetti *et al*, *Synlett*, S1, 1000-1002 (1999)

describing the synthesis of bicyclic analogs of an inhibitor of HCV NS3

- 10 protease. A compound disclosed therein has the formula:



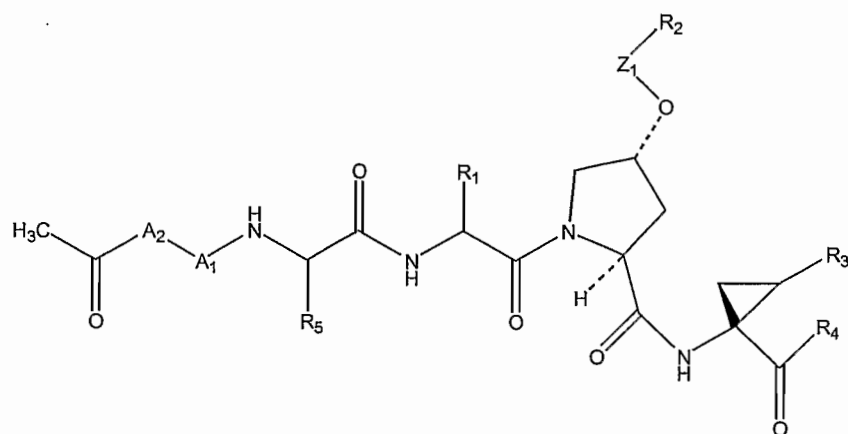
Reference is also made to W. Han *et al*, *Bioorganic & Medicinal Chem.*

Lett, (2000) 10, 711-713, which describes the preparation of certain α -

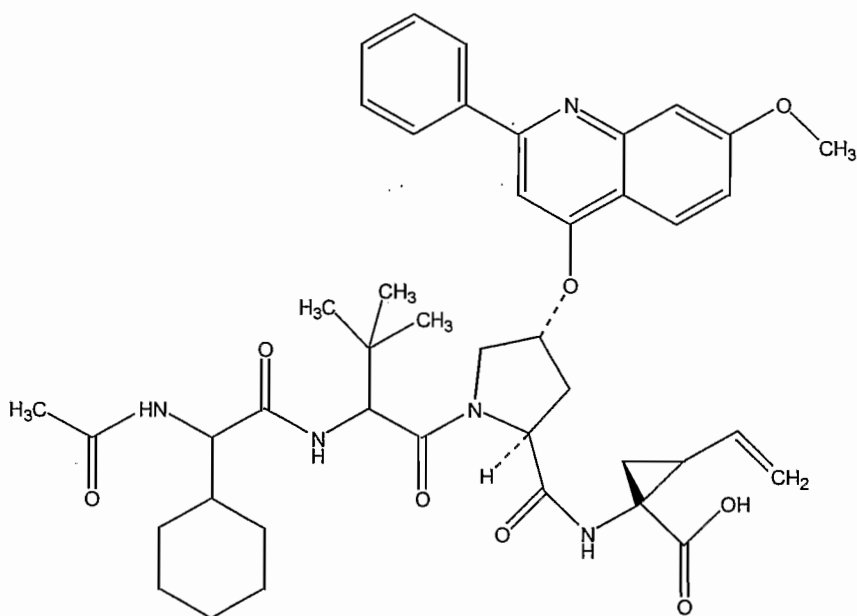
ketoamides, α -ketoesters and α -diketones containing allyl and ethyl

- 15 functionalities.

Reference is also made to WO 00/09558 (Assignee: Boehringer Ingelheim Limited; Published February 24, 2000) which discloses peptide derivatives of the formula:

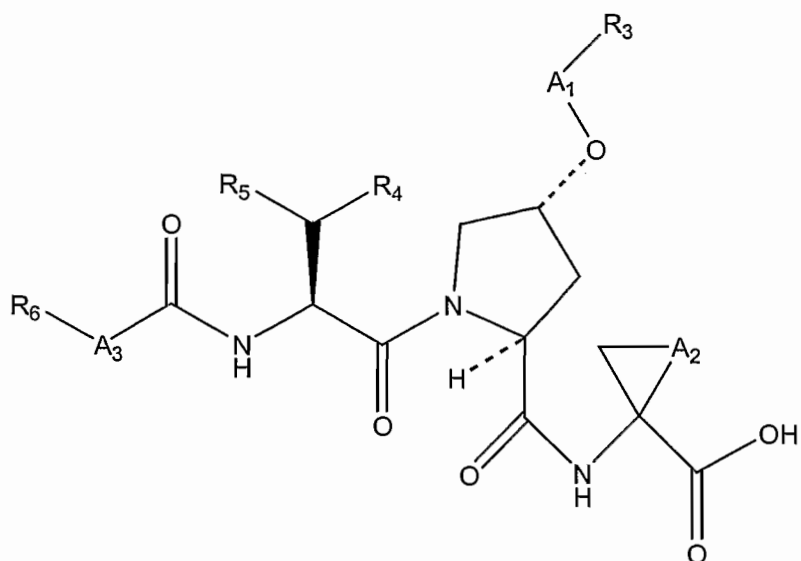


5 where the various elements are defined therein. An illustrative compound of that series is:

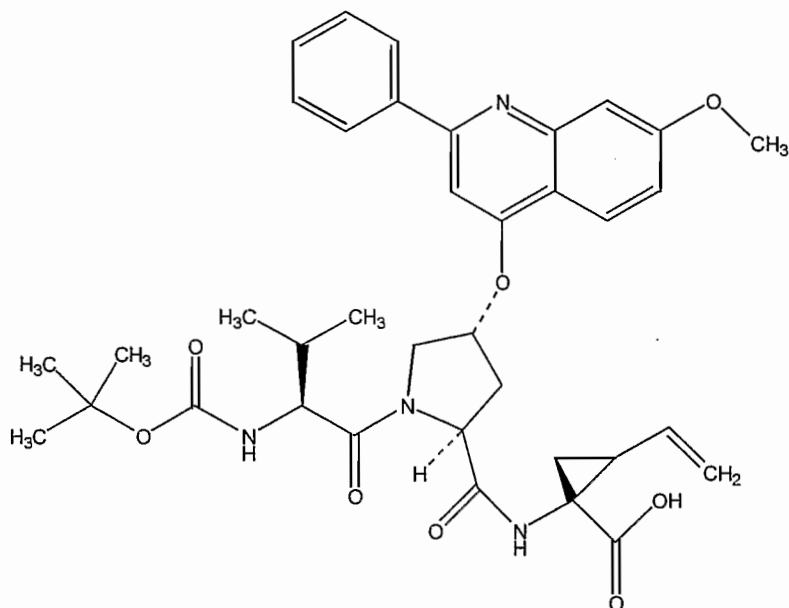


Reference is also made to WO 00/09543 (Assignee: Boehringer Ingelheim Limited; Published February 24, 2000) which discloses peptide

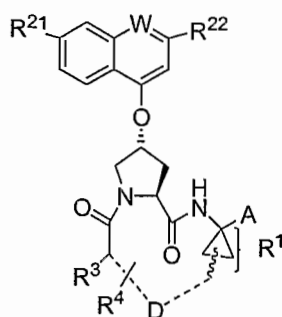
10 derivatives of the formula:



where the various elements are defined therein. An illustrative compound of that series is:



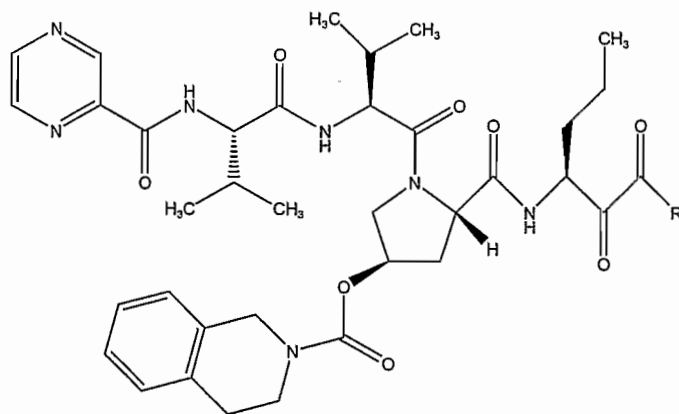
- 5 Reference is also made to U.S. 6,608,027 (Boehringer Ingelheim, Canada) which discloses NS3 protease inhibitors of the type:



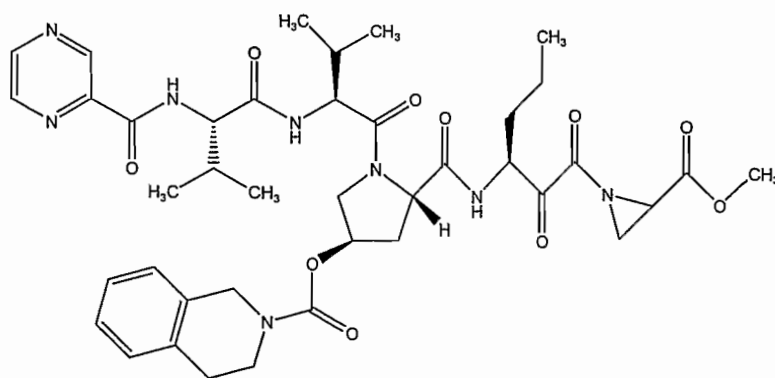
wherein the various moieties are defined therein.

Current therapies for hepatitis C include interferon- α (INF $_{\alpha}$) and combination therapy with ribavirin and interferon. See, e.g., Beremguer et al. (1998) Proc. Assoc. Am. Physicians 110(2):98-112. These therapies suffer from a low sustained response rate and frequent side effects. See, e.g., Hoofnagle et al. (1997) N. Engl. J. Med. 336:347. Currently, no vaccine is available for HCV infection.

Reference is further made to WO 01/74768 (Assignee: Vertex Pharmaceuticals Inc) published October 11, 2001, which discloses certain compounds of the following general formula (R is defined therein) as NS3-serine protease inhibitors of Hepatitis C virus:



A specific compound disclosed in the afore-mentioned WO 01/74768 has the following formula:



PCT Publications WO 01/77113; WO 01/081325; WO 02/08198; WO 02/08256; WO 02/08187; WO 02/08244; WO 02/48172; WO 02/08251; and
5 pending U.S. patent application, Serial No. 10/052,386, filed January 18, 2002, disclose various types of peptides and/or other compounds as NS-3 serine protease inhibitors of hepatitis C virus. The disclosures of those applications are incorporated herein by reference thereto.

There is a need for new treatments and therapies for HCV infection.

10 There is a need for compounds useful in the treatment or prevention or amelioration of one or more symptoms of hepatitis C.

There is a need for methods of treatment or prevention or amelioration of one or more symptoms of hepatitis C.

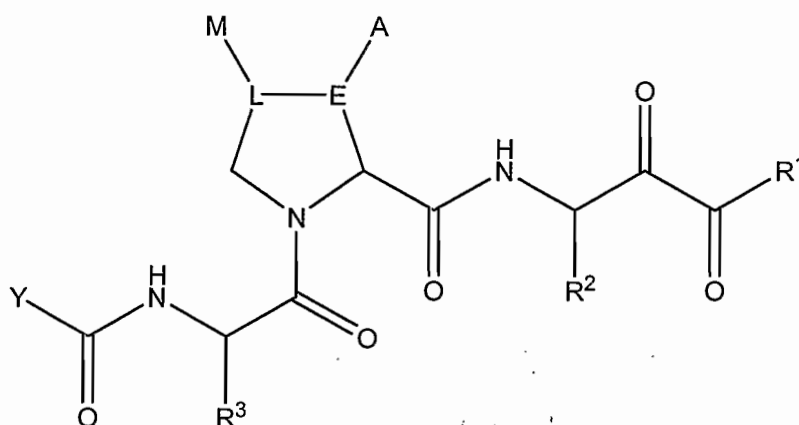
15 There is a need for methods for modulating the activity of serine proteases, particularly the HCV NS3/NS4a serine protease, using the compounds provided herein.

There is a need for methods of modulating the processing of the HCV polypeptide using the compounds provided herein.

Summary of the Invention

20 In its many embodiments, the present invention provides a novel class of inhibitors of the HCV protease, pharmaceutical compositions containing one or more of the compounds, methods of preparing pharmaceutical

formulations comprising one or more such compounds, and methods of treatment or prevention of HCV or amelioration of one or more of the symptoms of hepatitis C using one or more such compounds or one or more such formulations. Also provided are methods of modulating the interaction of an HCV polypeptide with HCV protease. Among the compounds provided herein, compounds that inhibit HCV NS3/NS4a serine protease activity are preferred. The present invention discloses compounds, as well as pharmaceutically acceptable salts, solvates or esters of said compounds, said compounds having the general structure shown in structural Formula I:



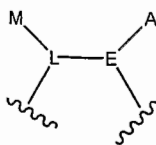
Formula I

wherein:

R^1 is H, OR^8 , NR^9R^{10} , or CHR^9R^{10} , wherein R^8 , R^9 and R^{10} can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, heteroalkyl-, heteroaryl-, cycloalkyl-, heterocyclyl-, arylalkyl-, and heteroarylalkyl;

A and M can be the same or different, each being independently selected from R, OR, NHR, NRR' , SR, SO_2R , and halo; or A and M are connected to each other such that the moiety:

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shown above in Formula I forms either a three, four, six, seven or eight-membered cycloalkyl, a four to eight-membered heterocyclyl, a six to ten-membered aryl, or a five to ten-membered heteroaryl;

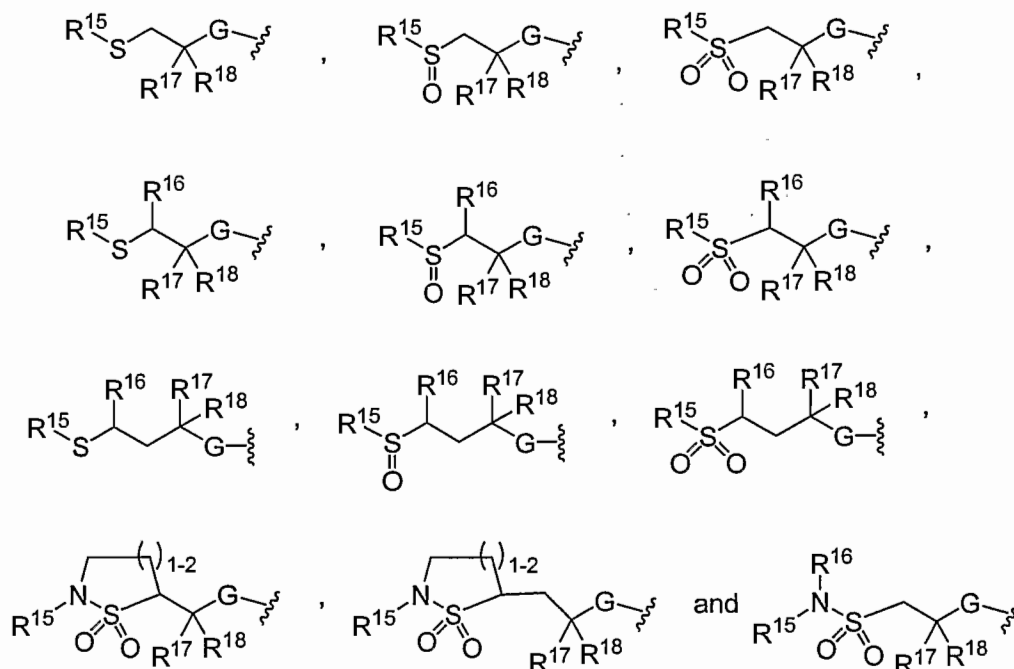
5 E is C(H) or C(R);

L is C(H), C(R), CH₂C(R), or C(R)CH₂;

R, R', R², and R³ can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, cycloalkyl-, heteroalkyl-, heterocyclyl-, aryl-, heteroaryl-,

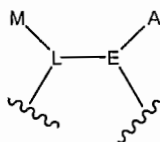
10 (cycloalkyl)alkyl-, (heterocyclyl)alkyl-, aryl-alkyl-, and heteroaryl-alkyl-; or alternately R and R' in NRR' are connected to each other such that NRR' forms a four to eight-membered heterocyclyl;

and Y is selected from the following moieties:

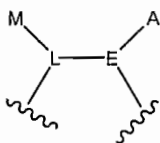


wherein G is NH or O; and R¹⁵, R¹⁶, R¹⁷ and R¹⁸ can be the same or different, each being independently selected from the group consisting of H, alkyl, heteroalkyl, alkenyl, heteroalkenyl, alkynyl, heteroalkynyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or alternately, (i) R¹⁵ and R¹⁶ are connected to each other to form a four to eight-membered cyclic structure, and (ii) likewise, independently R¹⁷ and R¹⁸ are connected to each other to form a three to eight-membered cycloalkyl or heterocyclyl; wherein each of said alkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl can be unsubstituted or optionally independently substituted with one or more moieties selected from the group consisting of: hydroxy, alkoxy, aryloxy, thio, alkylthio, arylthio, amino, amido, alkylamino, arylamino, alkylsulfonyl, arylsulfonyl, sulfonamido, alkylsulfonamido, arylsulfonamido, alkyl, aryl, heteroaryl, keto, carboxy, carbalkoxy, carboxamido, alkoxycarbonylamino, alkoxycarbonyloxy, alkylureido, arylureido, halo, cyano, and nitro.

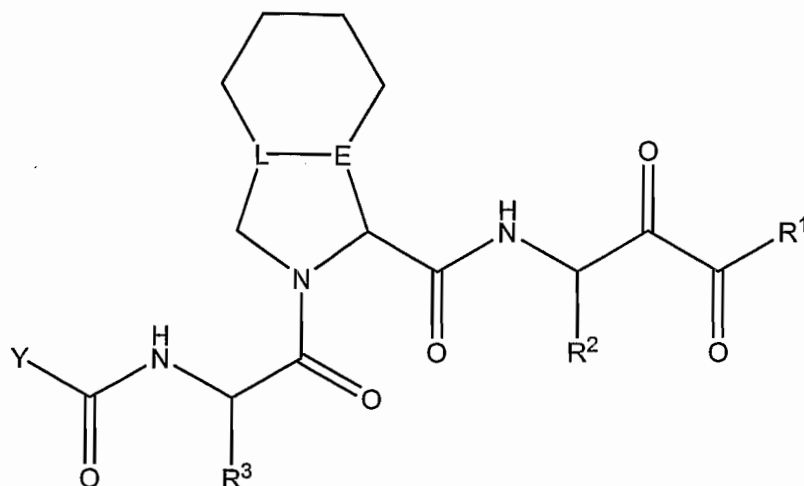
The above-noted statement "A and M are connected to each other such that the moiety:



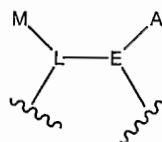
shown above in Formula I forms either a three, four, six, seven or eight-membered cycloalkyl, a four to eight-membered heterocyclyl, a six to ten-membered aryl, or a five to ten-membered heteroaryl" can be illustrated in a non-limiting manner as follows. Thus, for example, in the case where A and M are connected such that the moiety:



shown above in Formula I forms a six -membered cycloalkyl (cyclohexyl),
Formula I can be depicted as:



- 5 One with ordinary skill in the art will appreciate that similar depictions for
Formula I can be arrived at when A and M shown above in the moiety:



- (M-L-E-A taken together) are connected to form a three, four, seven or eight-
membered cycloalkyl, a four to eight-membered heterocyclyl, a six to ten-
10 membered aryl, or a five to ten-membered heteroaryl.

- The statement "alternately, (i) R^{15} and R^{16} are connected to each other
to form a four to eight-membered cyclic structure, and (ii) likewise,
independently R^{17} and R^{18} are connected to form a three to eight-membered
cycloalkyl or heterocyclyl" means the following possibilities: (i) R^{15} and R^{16} are
15 connected to form a cyclic structure while R^{17} and R^{18} are not; (ii) R^{17} and R^{18}
are connected to form a cyclic structure while R^{15} and R^{16} are not; and (iii) R^{15}
and R^{16} are connected to form a cyclic structure, *and* R^{17} and R^{18} are also

connected to form a cyclic structure. These possibilities can occur independent of one another.

In the above noted definitions of R, R', R² and R³, preferred alkyl is made of one to ten carbon atoms, preferred alkenyl or alkynyl is made of two to ten carbon atoms, preferred cycloalkyl is made of three to eight carbon atoms;, and preferred heteroalkyl, heteroaryl or heterocycloalkyl has one to six oxygen, nitrogen, sulfur, or phosphorus atoms.

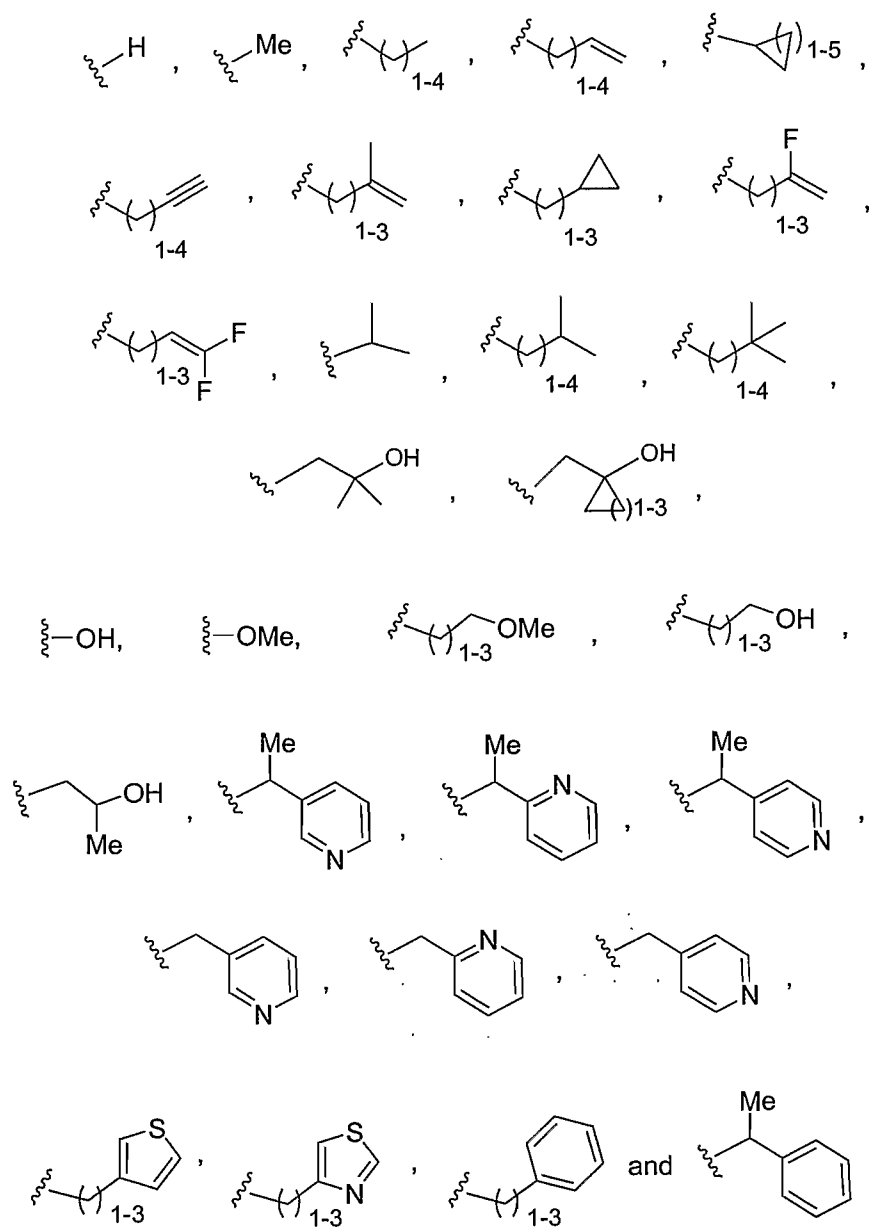
The compounds represented by Formula I, by themselves or in combination with one or more other suitable agents disclosed herein, can be useful for treating diseases such as, for example, HCV, HIV, (AIDS, Acquired Immune Deficiency Syndrome), and related disorders, as well as for modulating the activity of hepatitis C virus (HCV) protease, preventing HCV, or ameliorating one or more symptoms of hepatitis C. Such modulation, treatment, prevention or amelioration can be done with the inventive compounds as well as with pharmaceutical compositions or formulations comprising such compounds. Without being limited to theory, it is believed that the HCV protease may be the NS3 or NS4a protease. The inventive compounds can inhibit such protease. They can also modulate the processing of hepatitis C virus (HCV) polypeptide.

Detailed Description

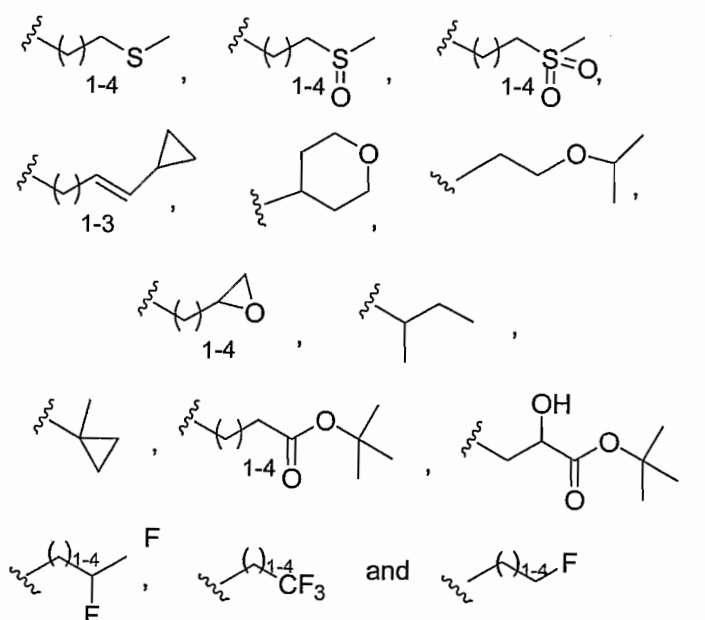
In an embodiment, the present invention discloses compounds which are represented by structural Formula I or a pharmaceutically acceptable salt or solvate or ester thereof, wherein the various moieties are as defined above.

In another embodiment, R¹ is NR⁹R¹⁰, and R⁹ is H, R¹⁰ is H, or R¹⁴ wherein R¹⁴ is H, alkyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, aryl-alkyl, alkenyl, alkynyl or heteroaryl-alkyl.

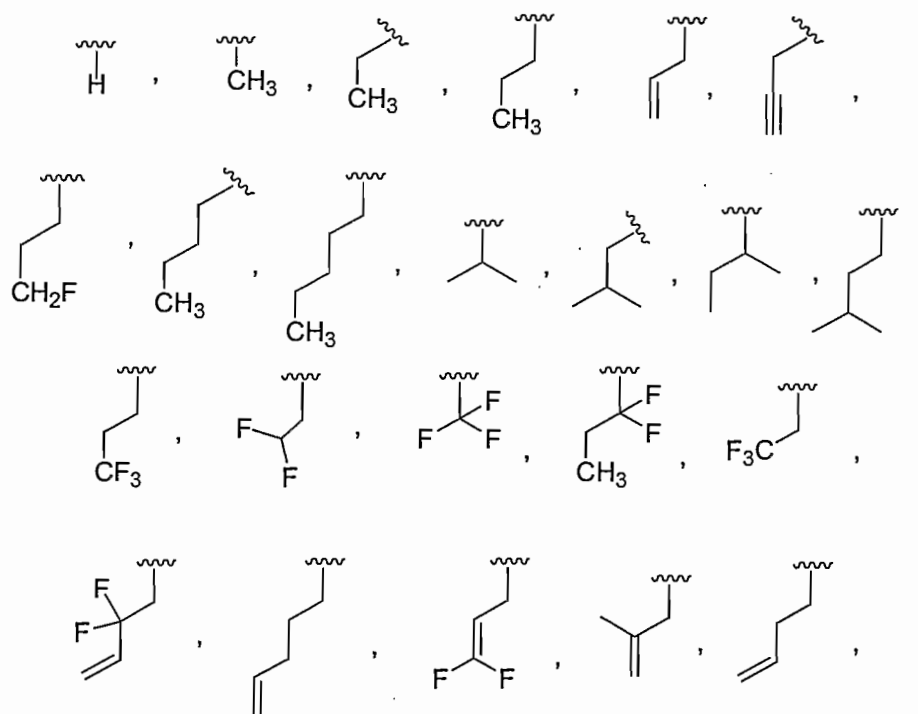
In another embodiment, R¹⁴ is selected from the group consisting of:

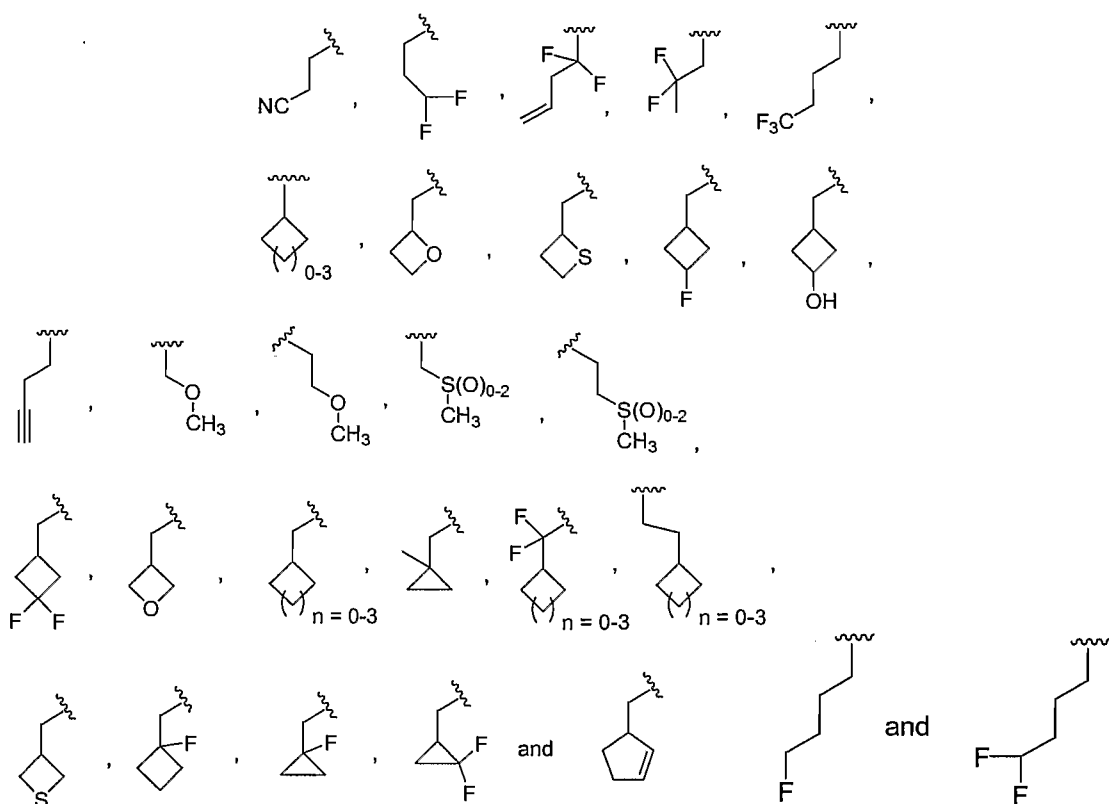


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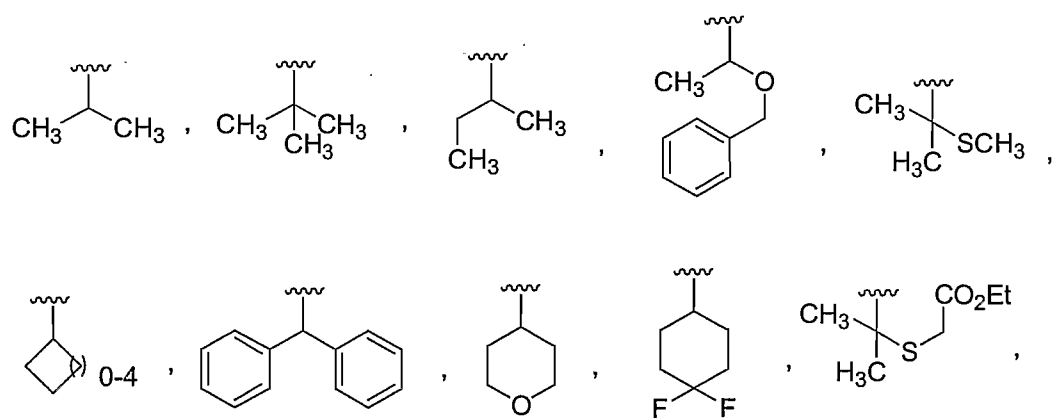


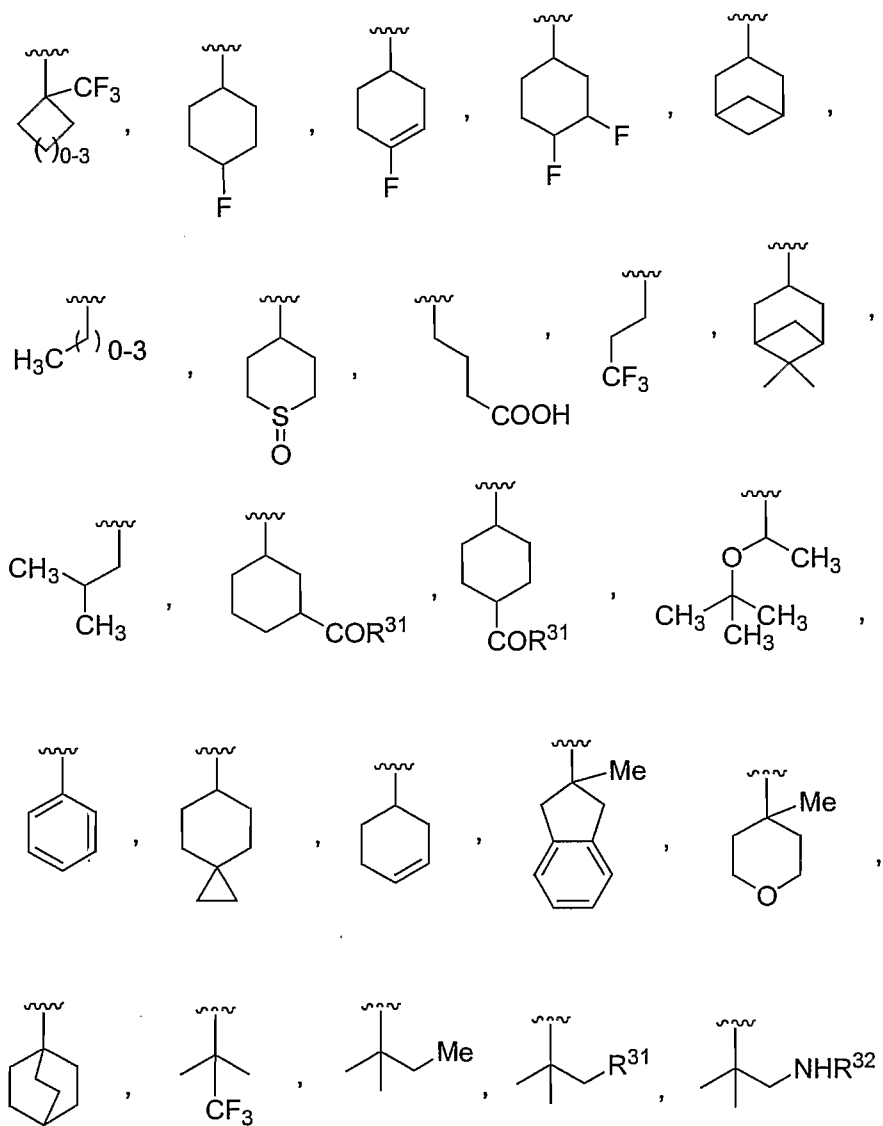
In another embodiment, R² is selected from the group consisting of the following moieties:

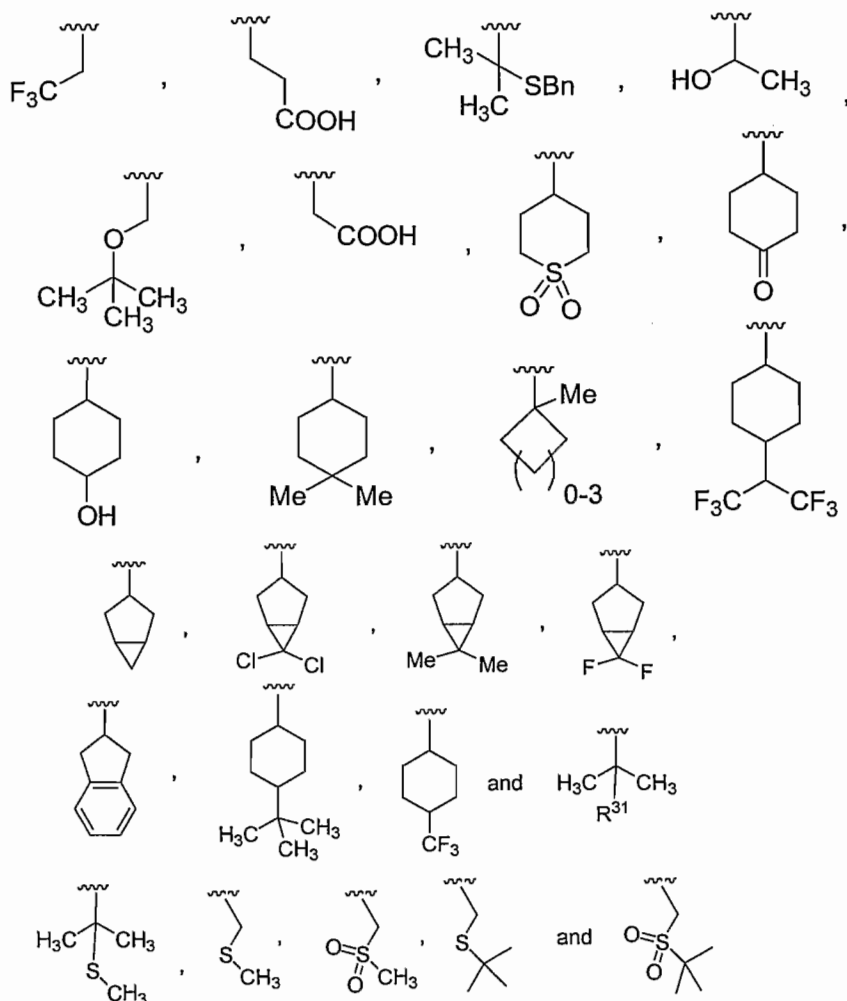




In another embodiment, R^3 is selected from the group consisting of:





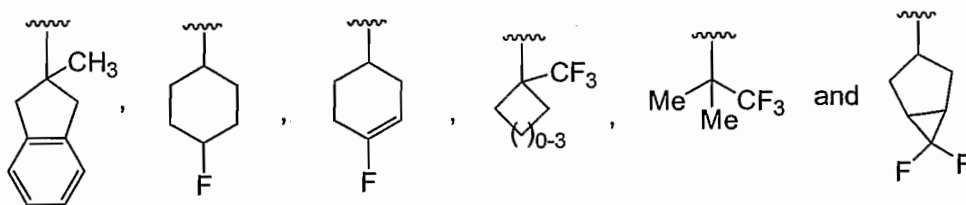
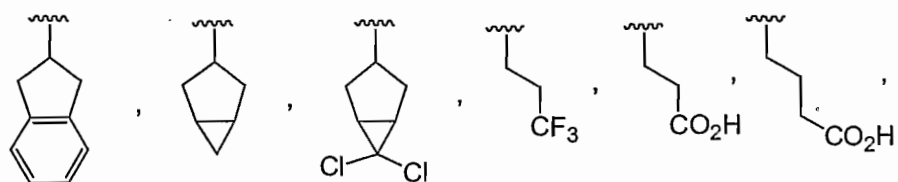
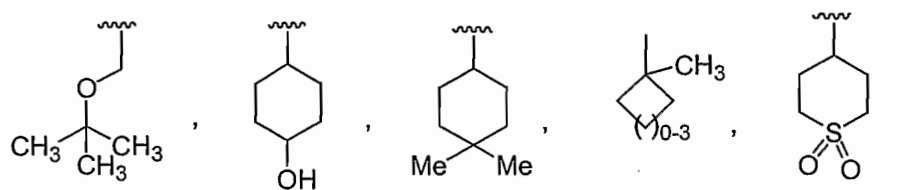
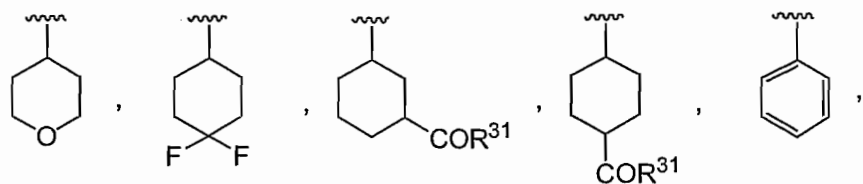
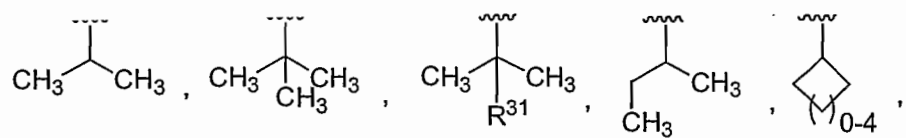


wherein R^{31} is OH or O-alkyl; and

5 R^{32} is H, C(O)CH₃, C(O)OtBu or C(O)N(H)tBu.

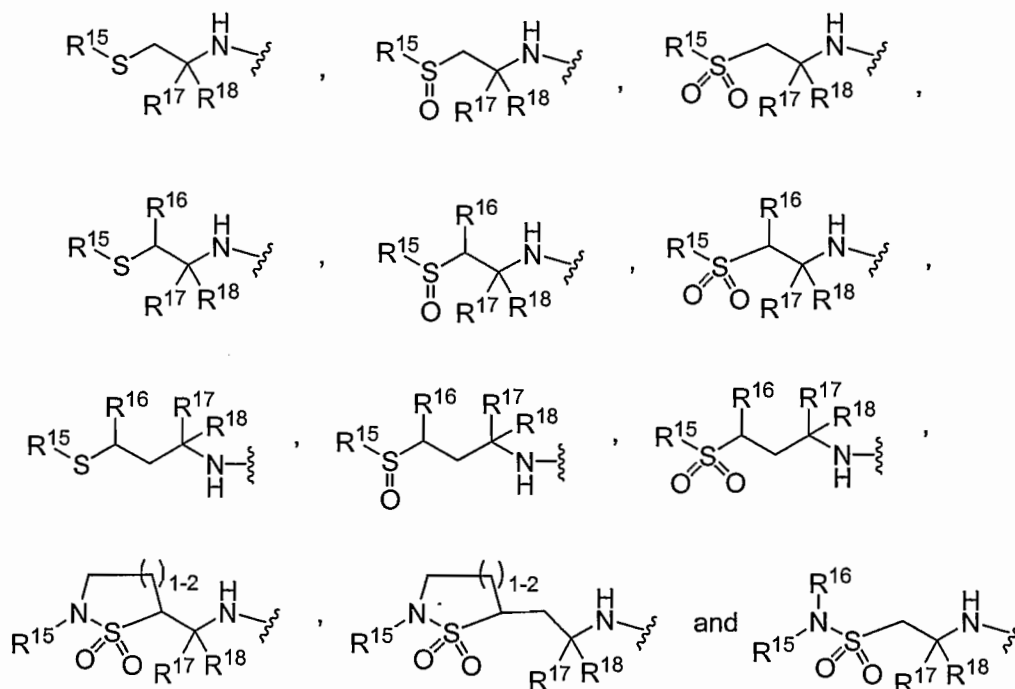
In an additional embodiment, R^3 is selected from the group consisting of the following moieties:

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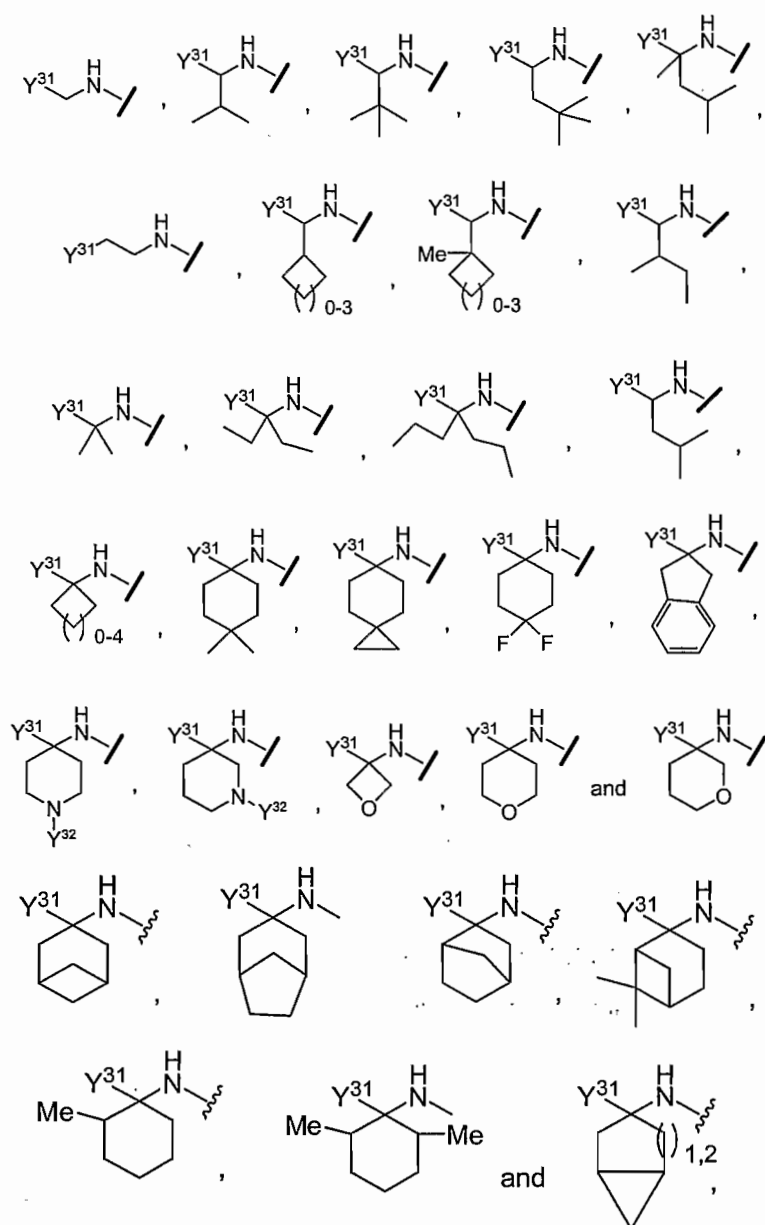
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In another embodiment, Y is selected from the following moieties:

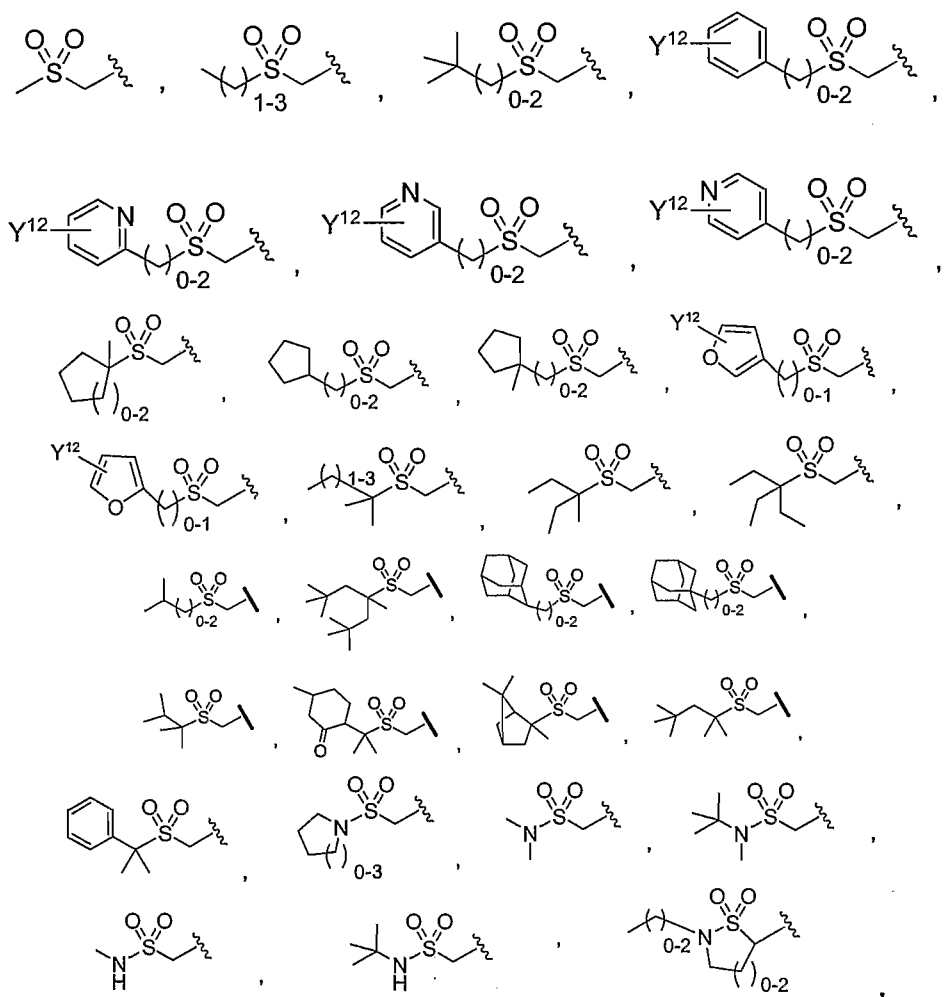


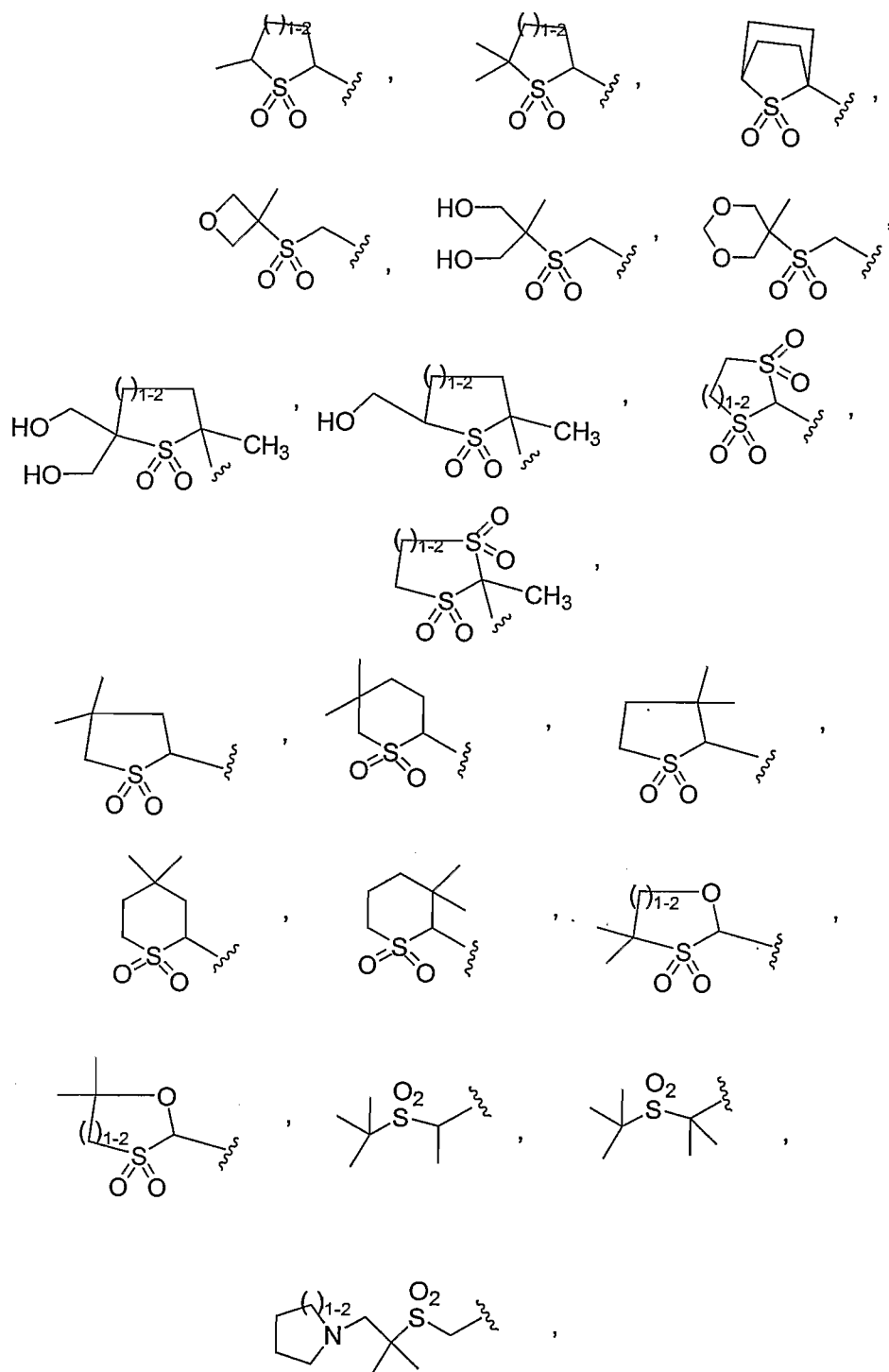
wherein R^{15} , R^{16} , R^{17} and R^{18} can be the same or different, each being independently selected from the group consisting of H, alkyl, heteroalkyl, alkenyl, heteroalkenyl, alkynyl, heteroalkynyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl, or alternately, R^{15} and R^{16} are connected to each other to form a four to eight-membered cycloalkyl or heterocyclic structure, and/or R^{17} and R^{18} are connected to each other to form a three to eight-membered cycloalkyl or heterocyclyl, wherein each of said aryl, heteroaryl, cycloalkyl or heterocyclyl can be unsubstituted or optionally independently substituted with one or more moieties selected from the group consisting of: hydroxy, alkoxy, aryloxy, thio, alkylthio, arylthio, amino, amido, alkylamino, arylamino, alkylsulfonyl, arylsulfonyl, sulfonamido, alkylsulfonamido, arylsulfonamido, carboxy, carbalkoxy, carboxamido, alkoxycarbonylamino, alkoxycarbonyloxy, alkylureido, arylureido, halo, cyano, and nitro.

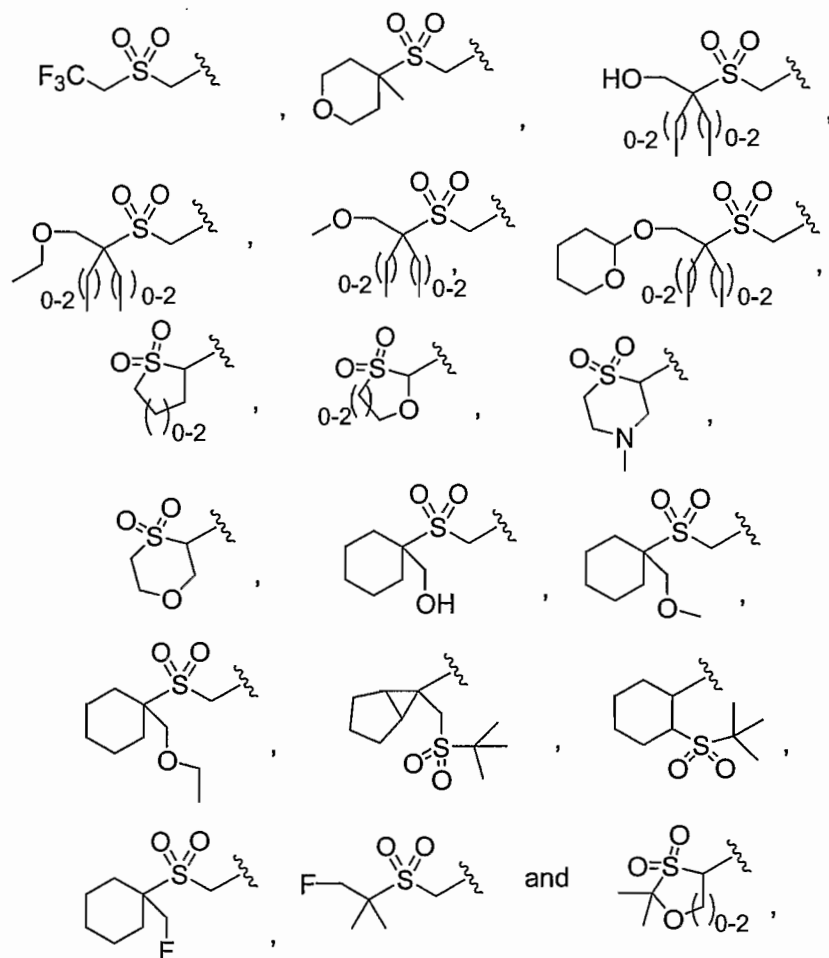
In an additional embodiment, Y is selected from the group consisting of:



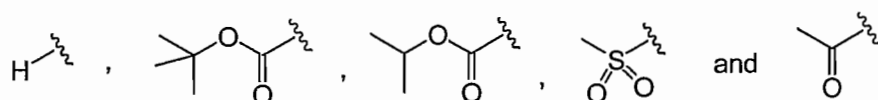
wherein Y³¹ is selected from the group consisting of:







Y^{32} is selected from the group consisting of:

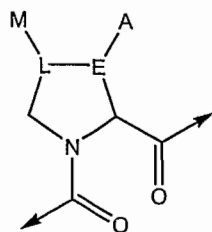


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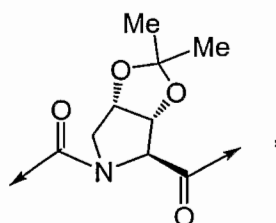
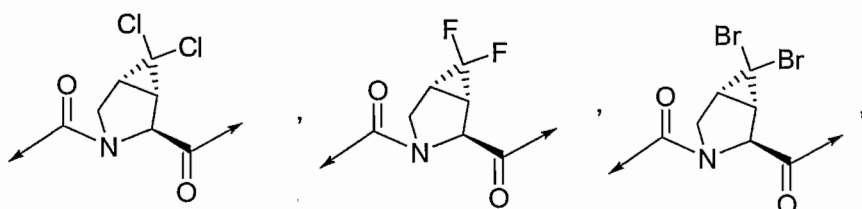
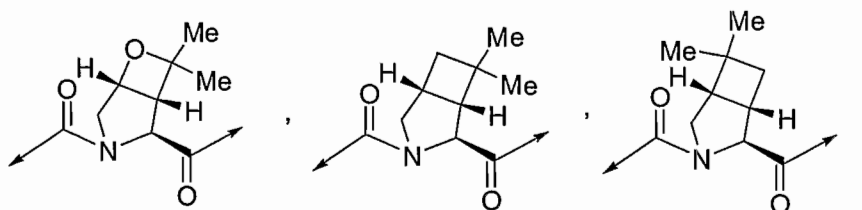
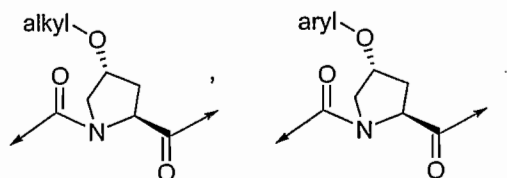
and Y¹² is selected from the group consisting of H, CO₂H, CO₂Me, OMe, F, Cl, Br, NH₂, N(H)S(O₂)CH₃, N(H)C(O)CH₃, NO₂, S(O₂)NH₂, CF₃, Me, OH, OCF₃, and C(O)NH₂.

In another embodiment, the moiety:

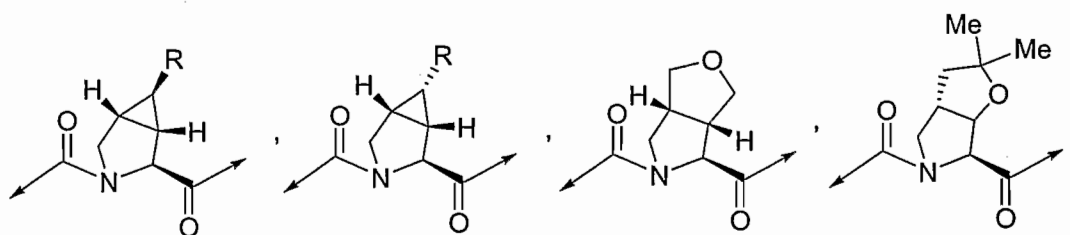
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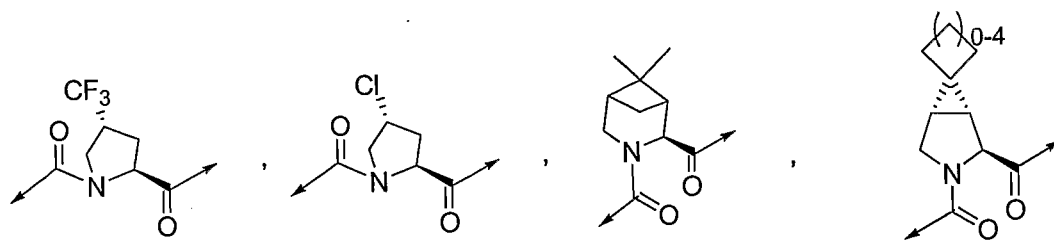


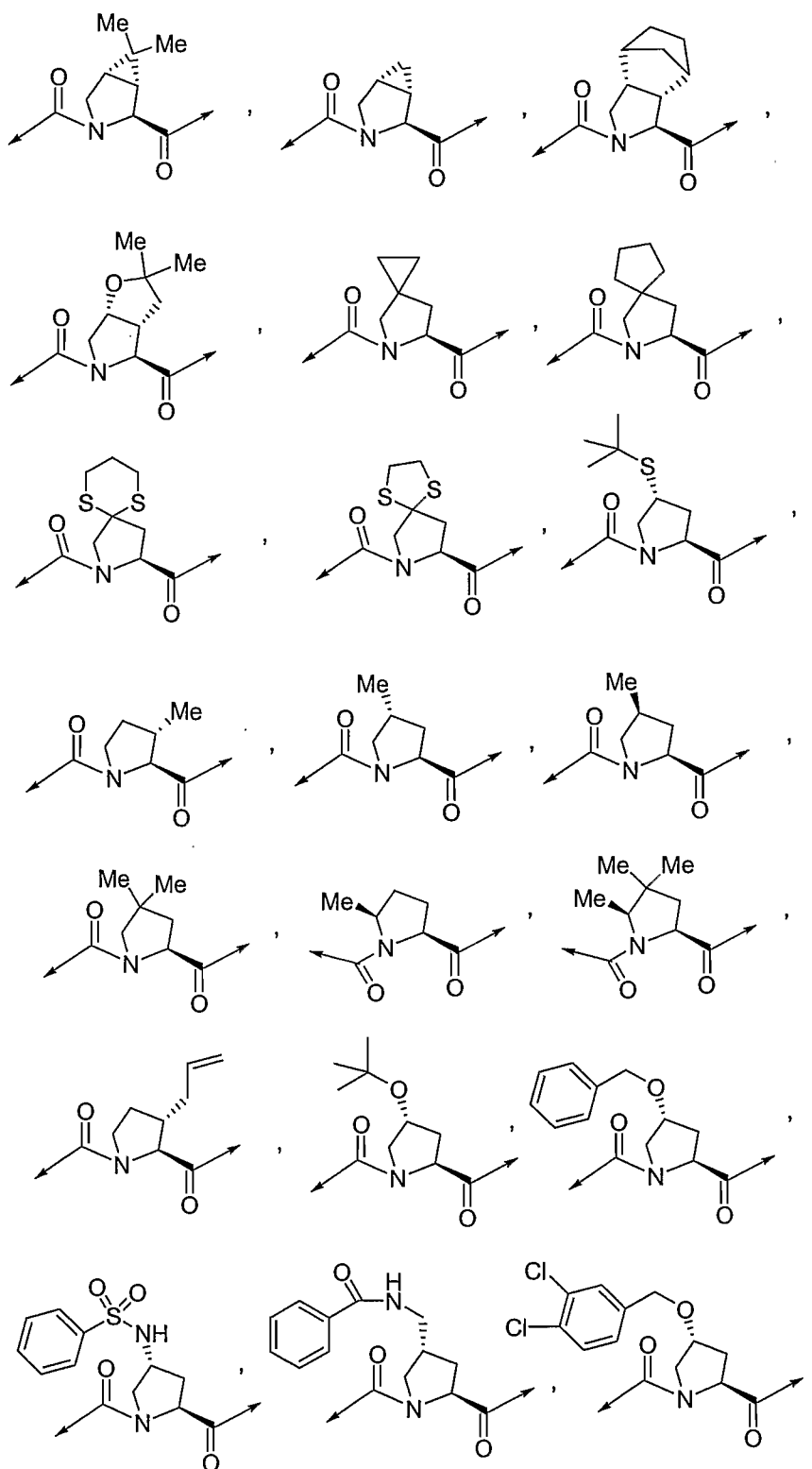
is selected from the following structures:

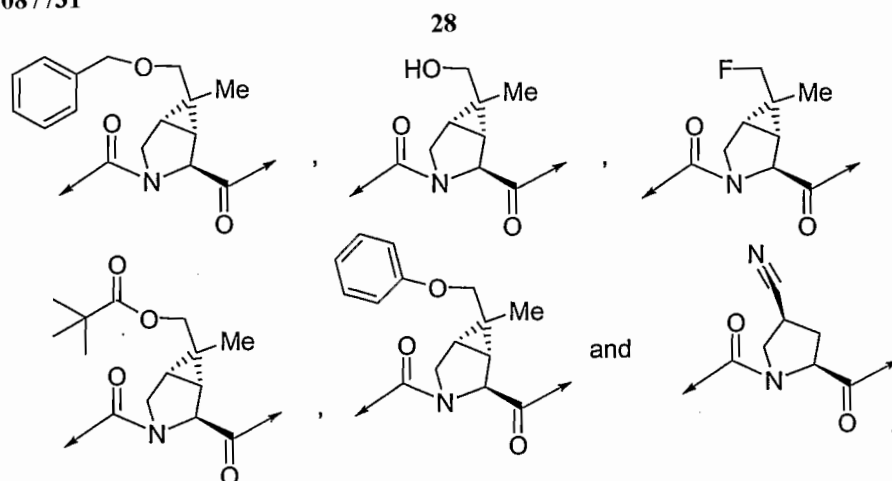


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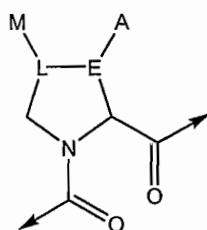




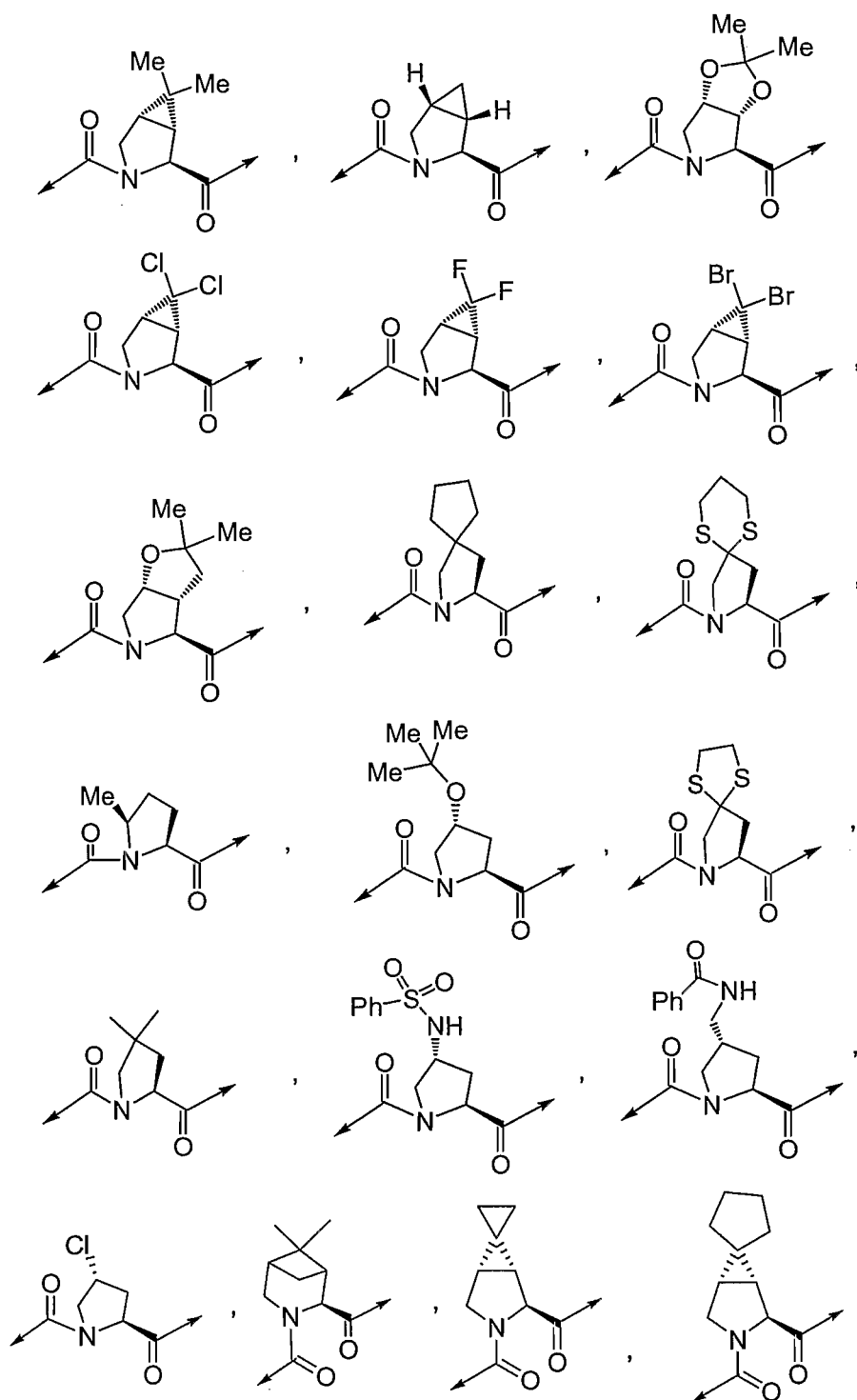


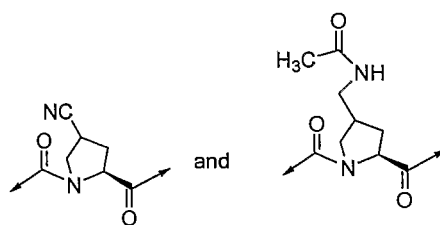


In an additional embodiment, the moiety:

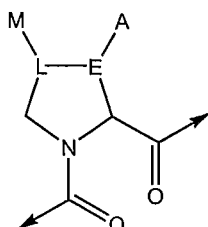


5 is selected from the following structures:

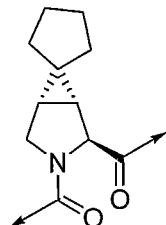
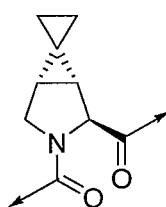
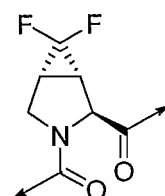
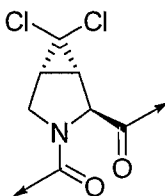
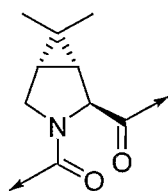




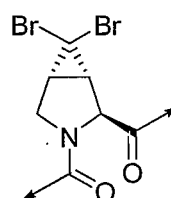
In an additional embodiment, the moiety:



is selected from the following structures:

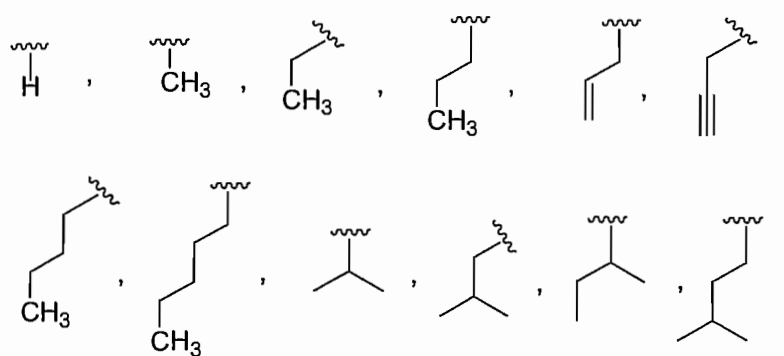
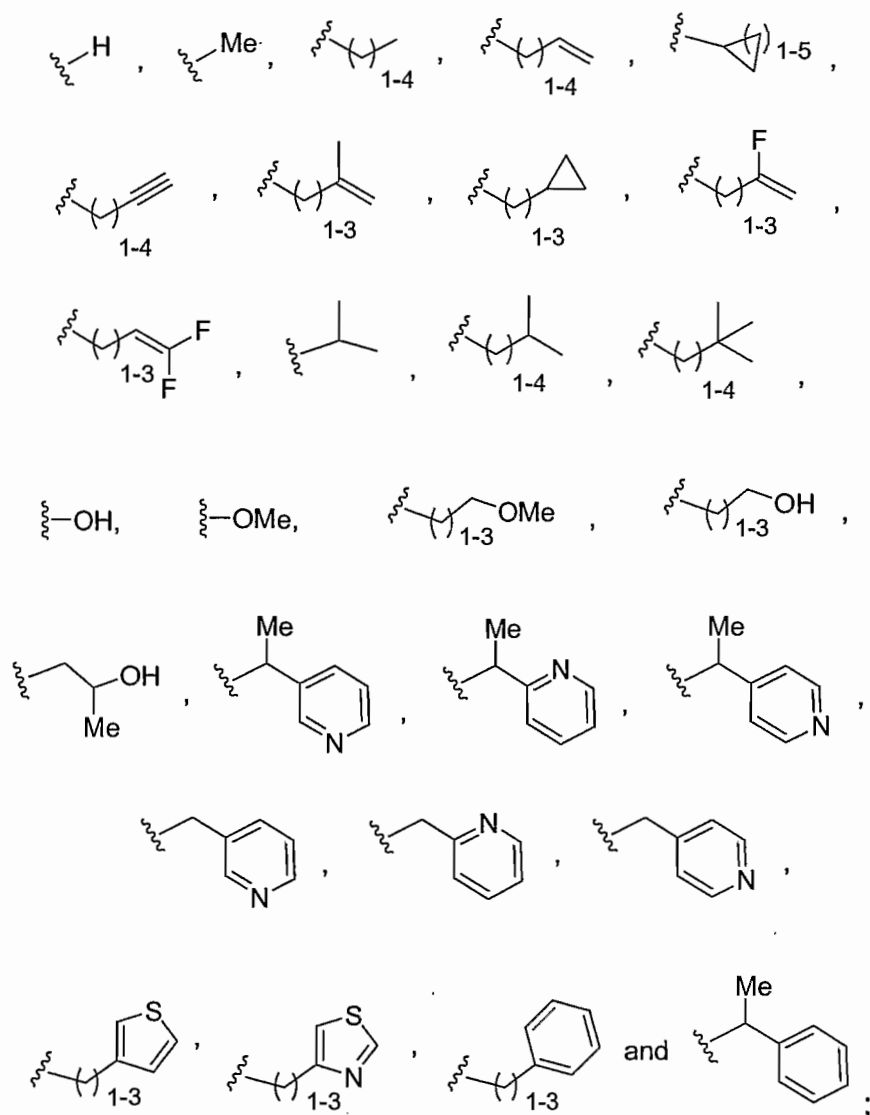


and

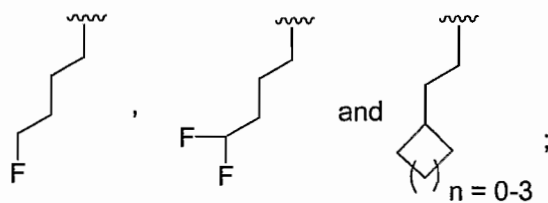


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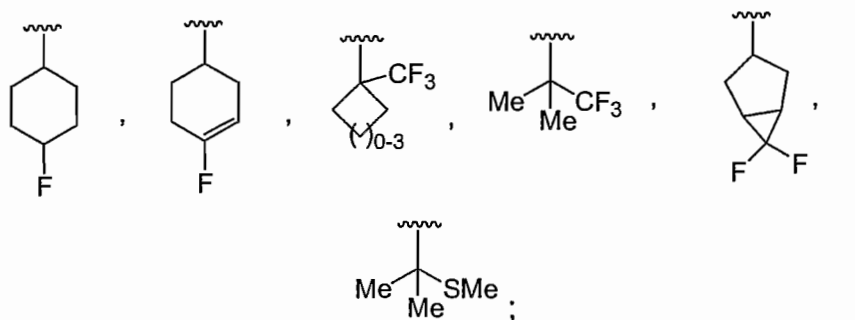
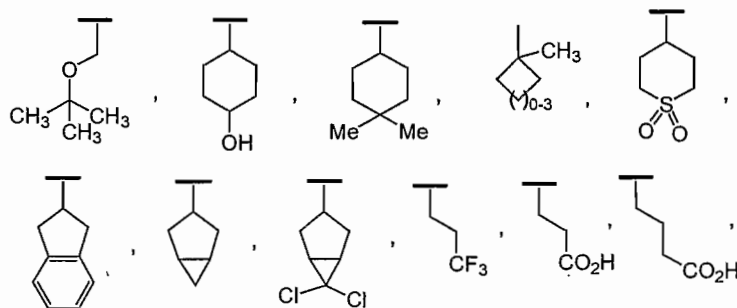
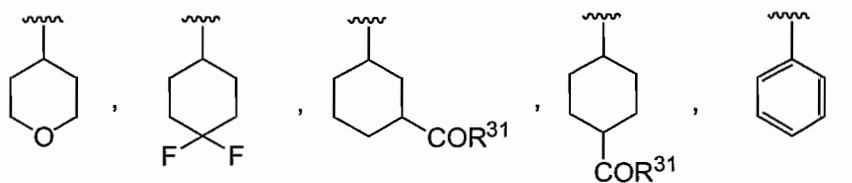
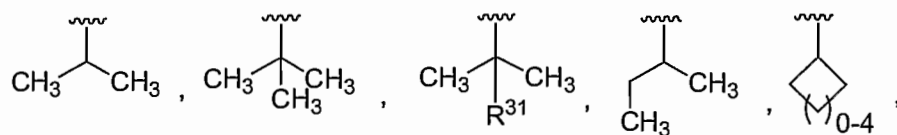
In a still additional embodiment, R^1 is NHR^{14} , where R^{14} is selected from the group consisting of:



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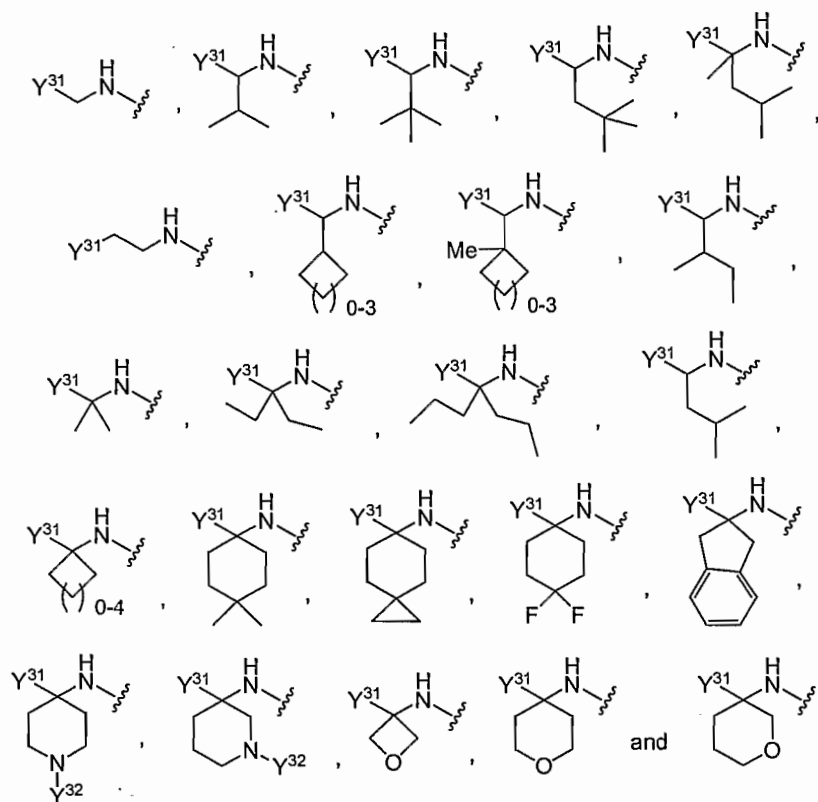


R^3 is selected from the group consisting of the following moieties:

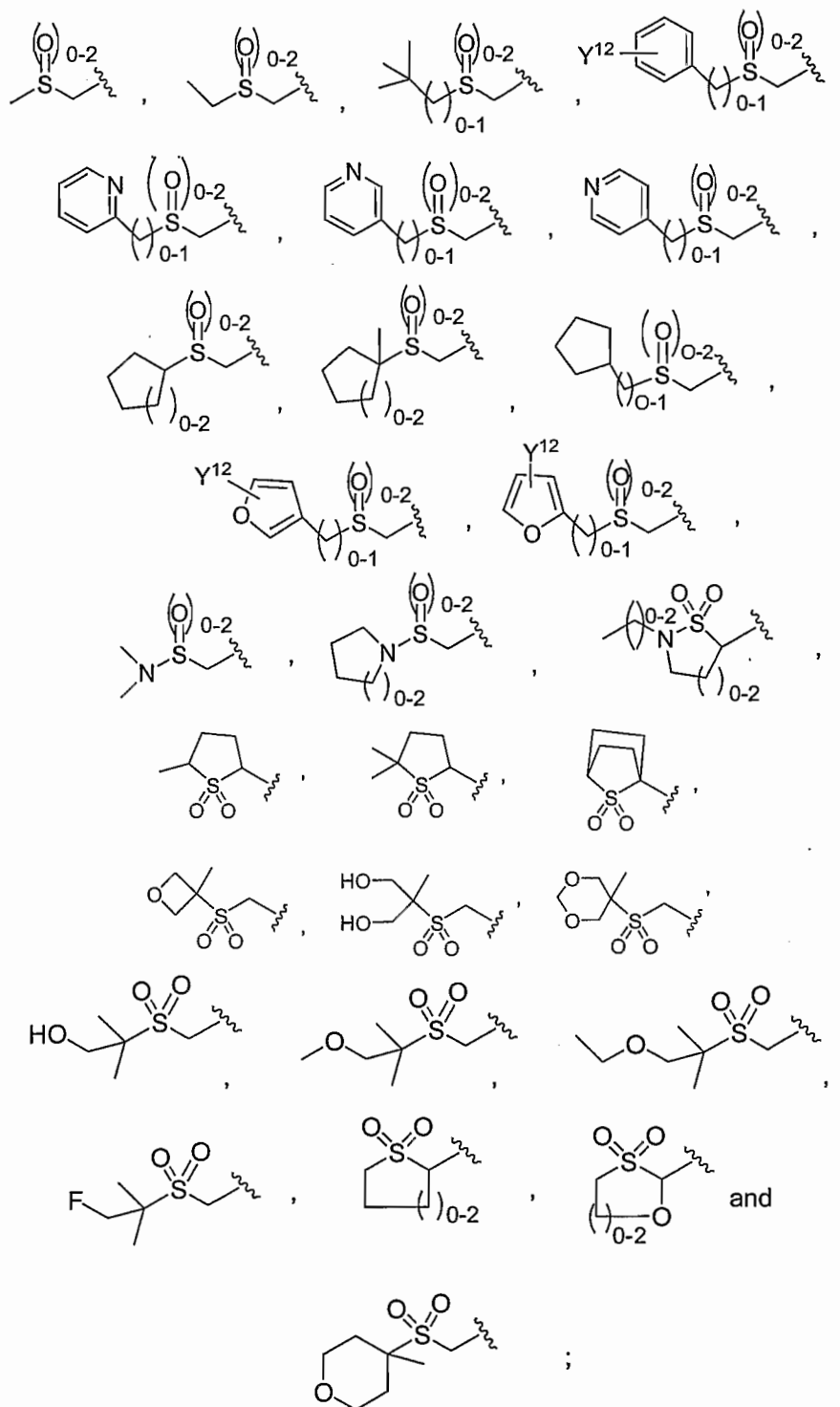


Y is selected from the group consisting of:

34

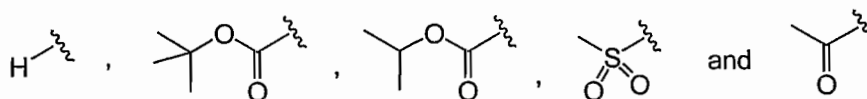


wherein Y³¹ is selected from the group consisting of:

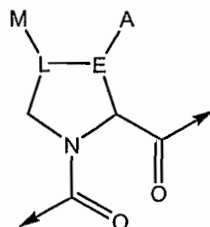


Y^{32} is selected from the group consisting of:

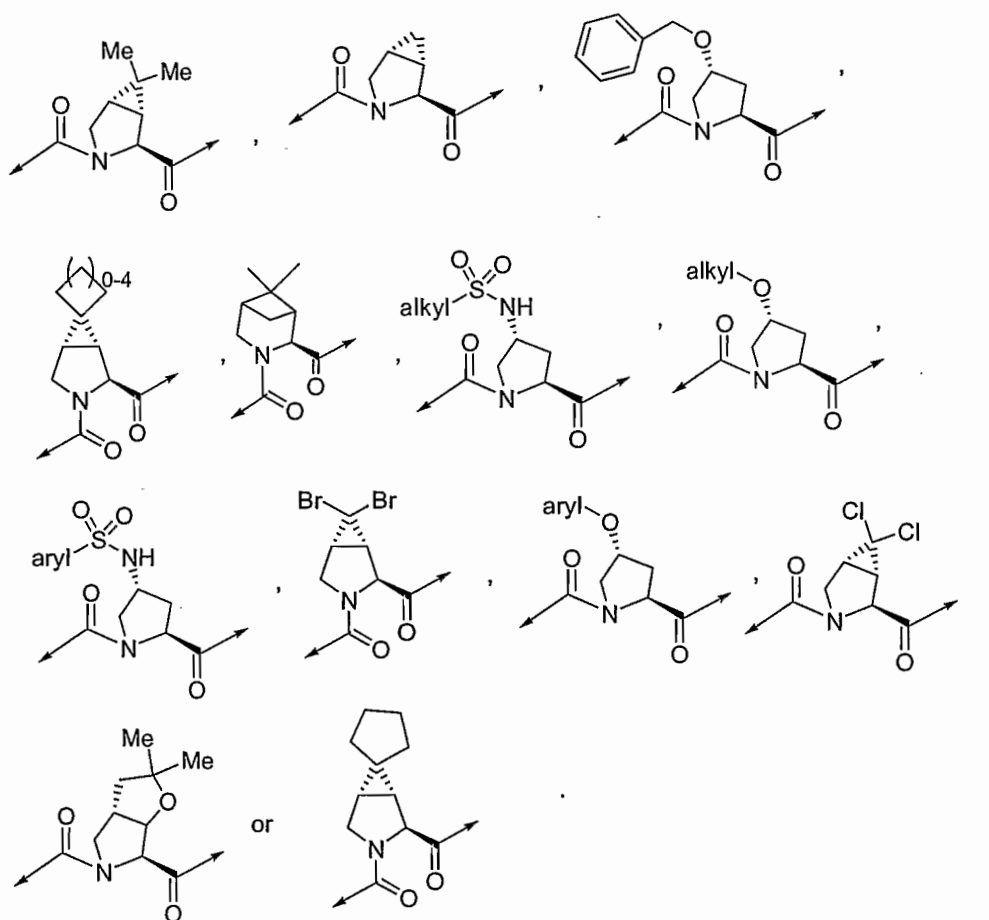
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and Y^{12} is selected from the group consisting of H , CO_2H , CO_2Me , OMe , F , Cl , Br , NH_2 , $N(H)S(O_2)CH_3$, $N(H)C(O)CH_3$, NO_2 , $S(O_2)NH_2$, CF_3 , Me ,
 5 OH , OCF_3 , and $C(O)NH_2$; and the moiety:

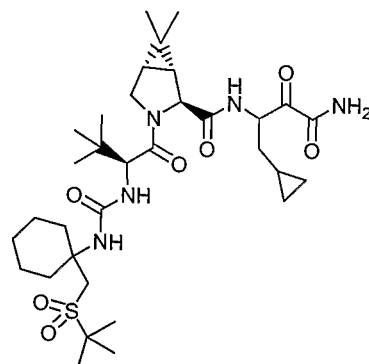
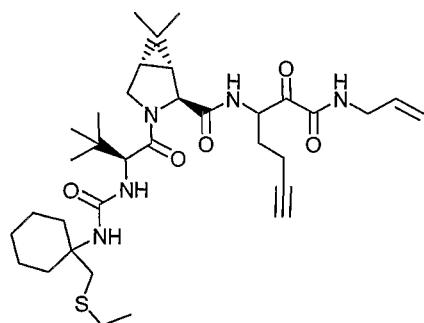
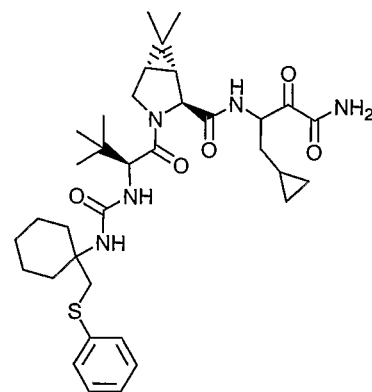
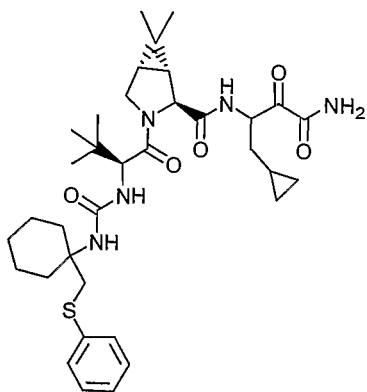
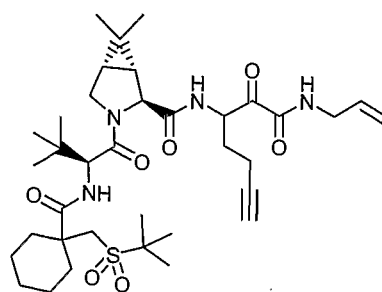
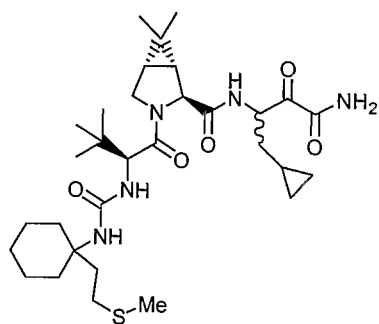


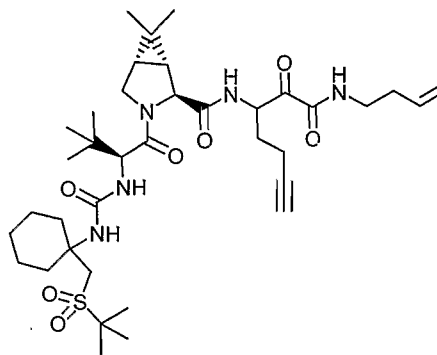
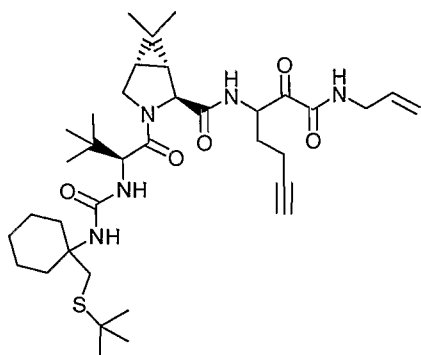
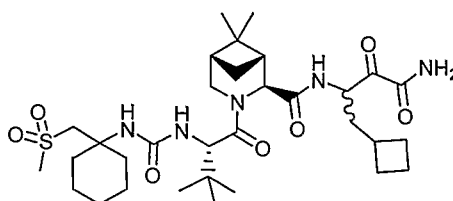
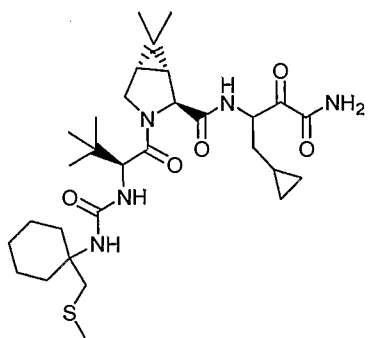
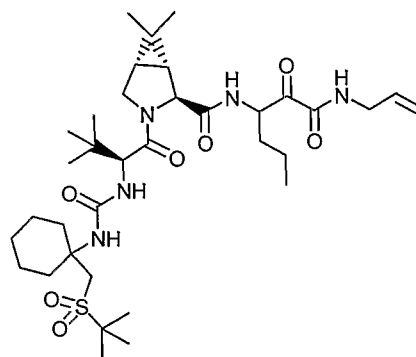
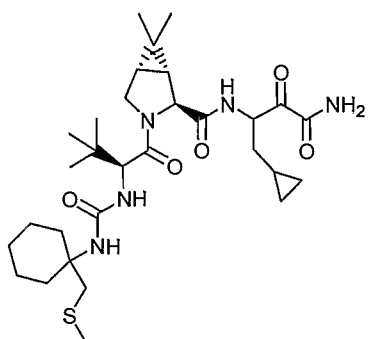
is:

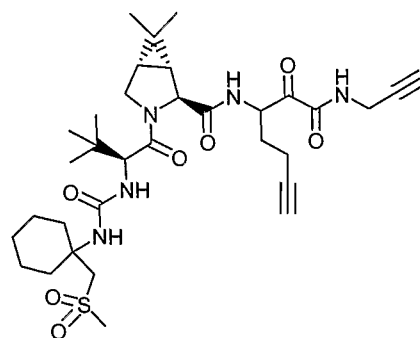
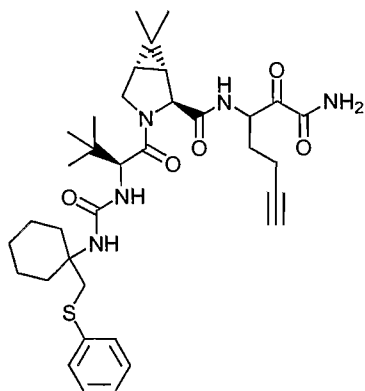
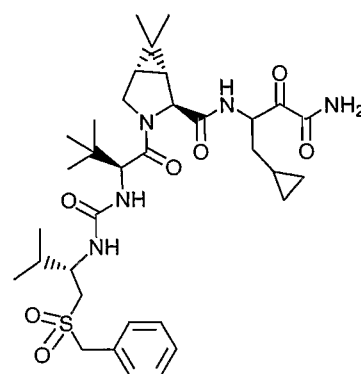
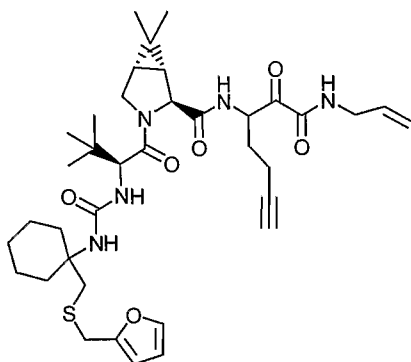
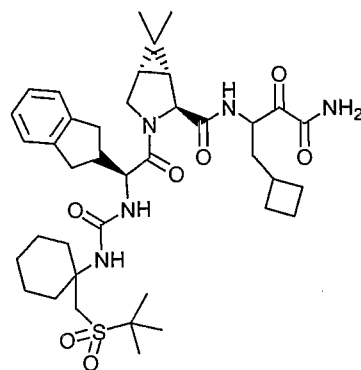
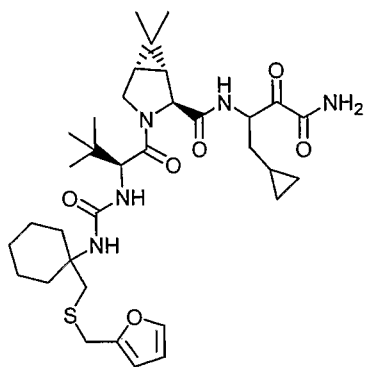


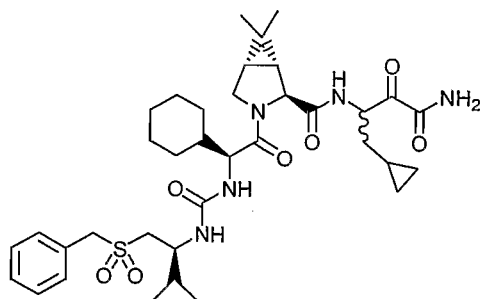
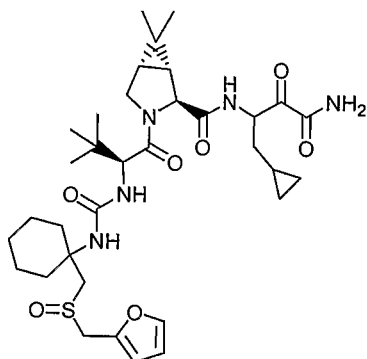
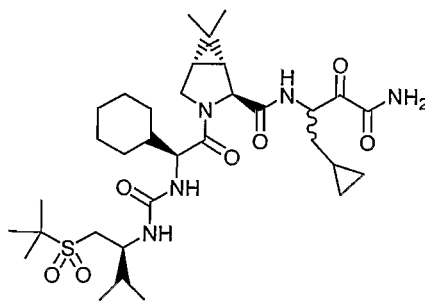
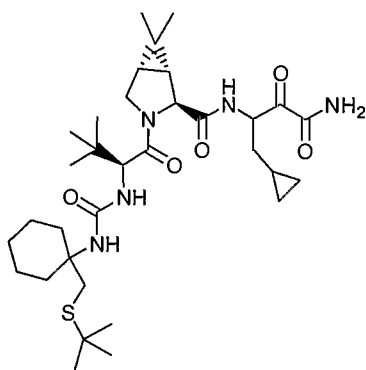
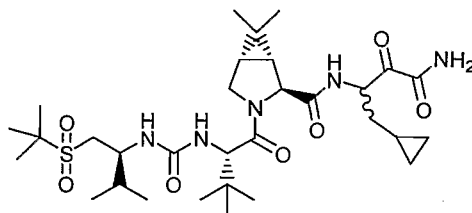
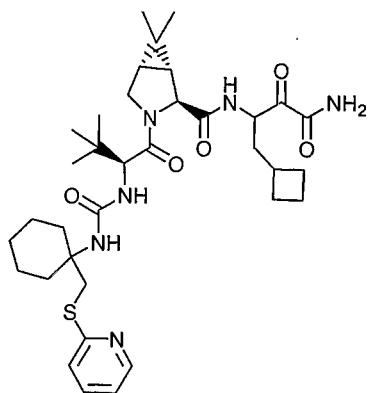
Yet another embodiment of the invention discloses compounds in **Table 1** below, as well as shown later in **Table 1**, **Table 3**, **Table 3A**, **Table 4**, **Table 4A** and **Table 5**:

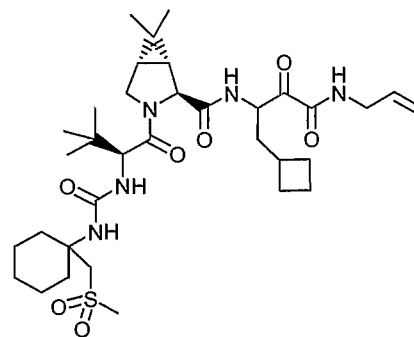
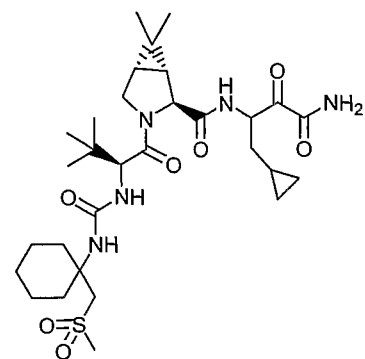
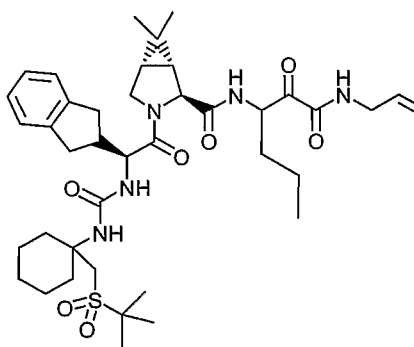
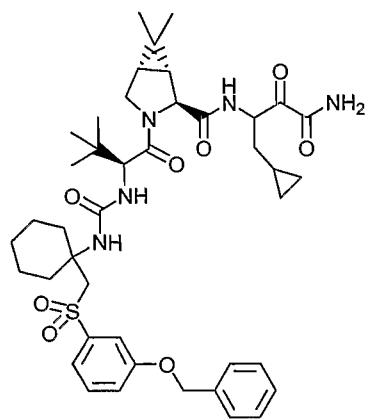
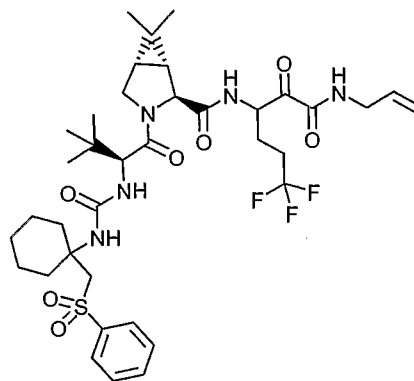
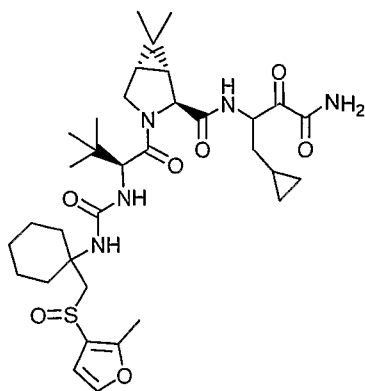
Table 1

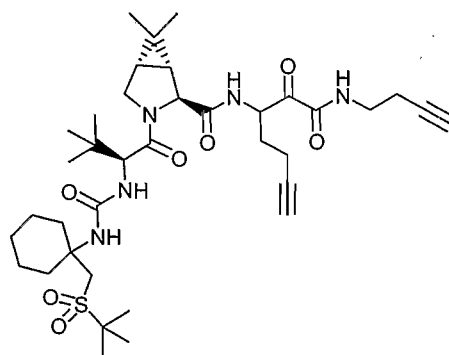
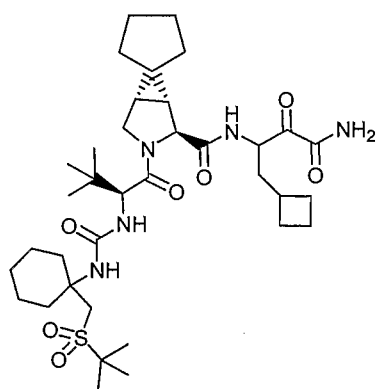
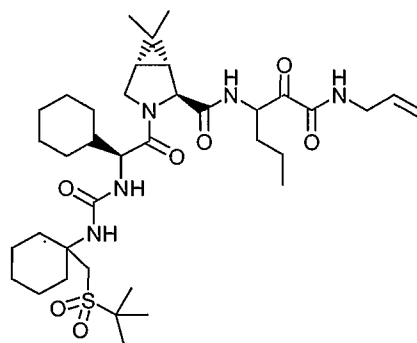
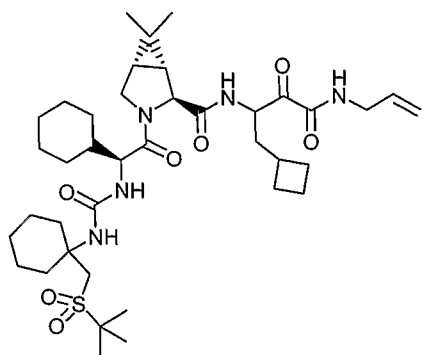
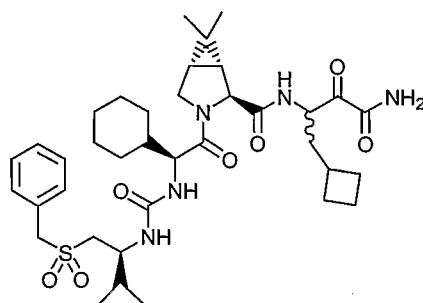
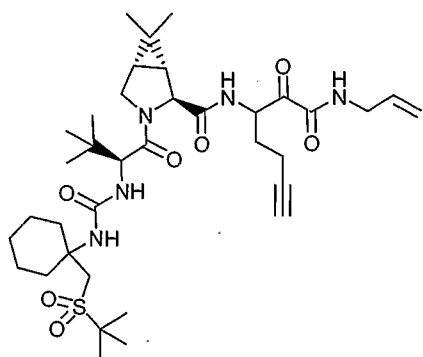


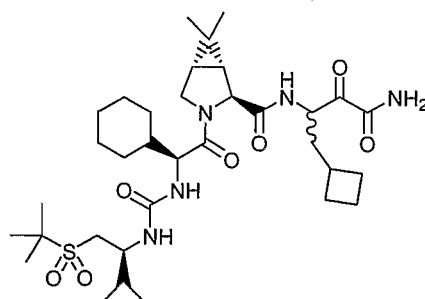
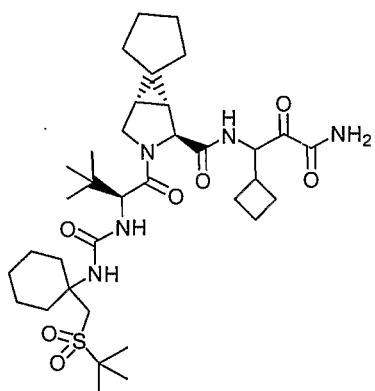
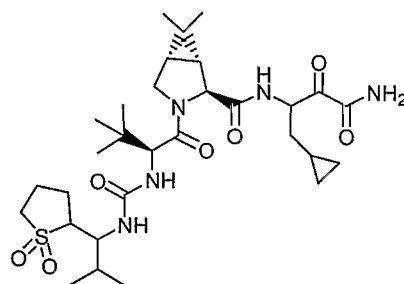
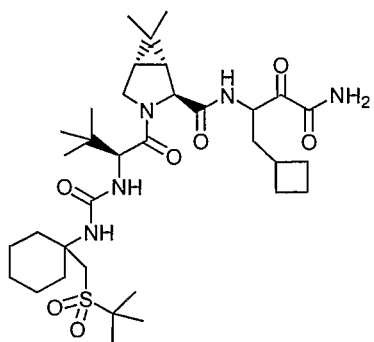
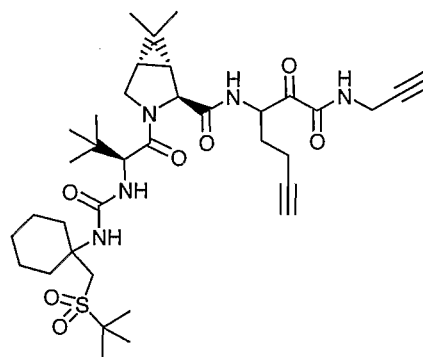
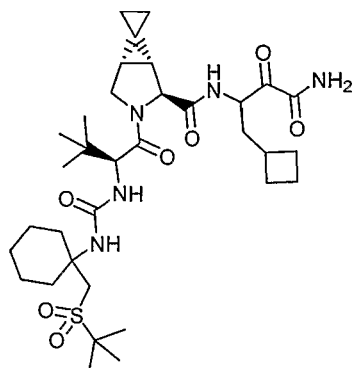


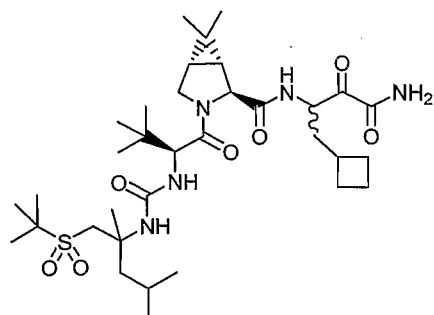
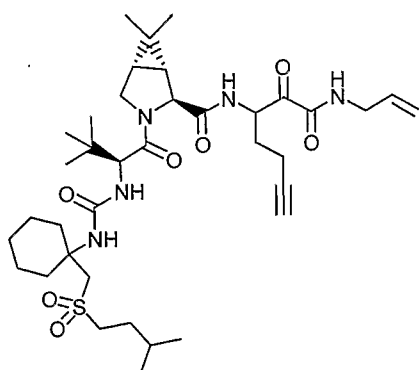
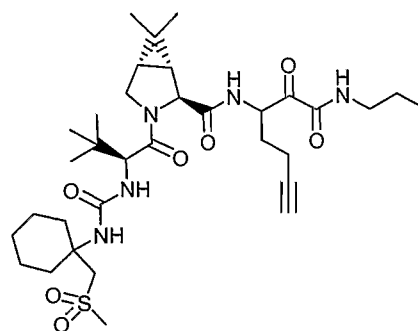
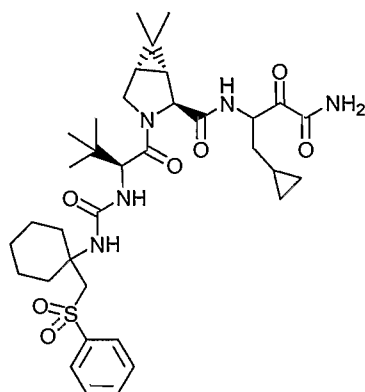
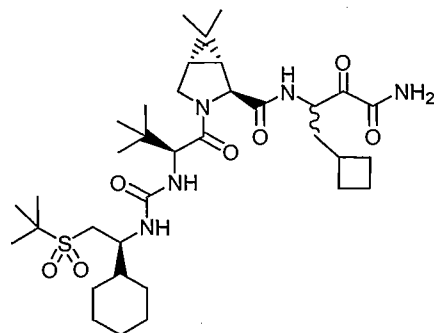
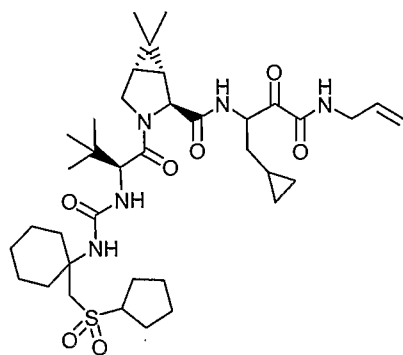


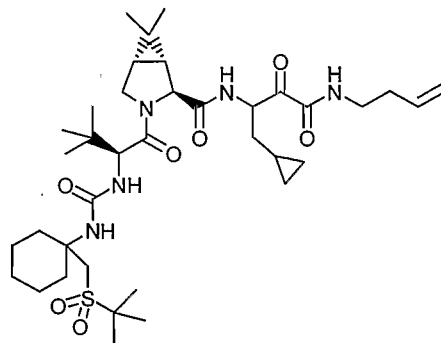
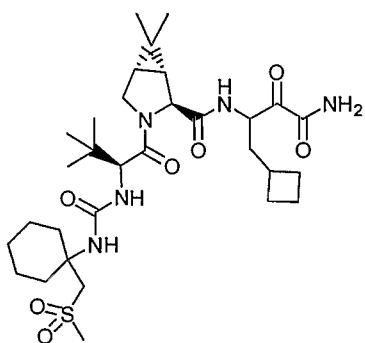
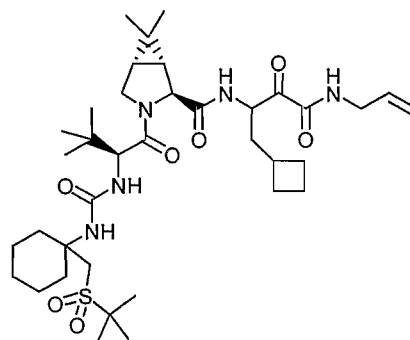
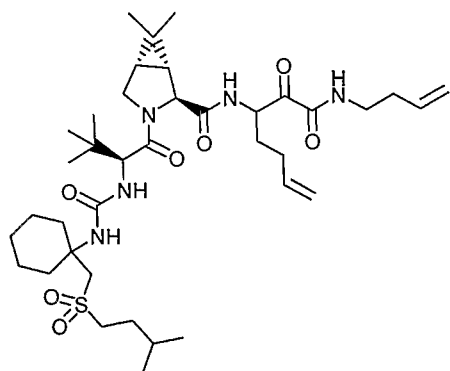
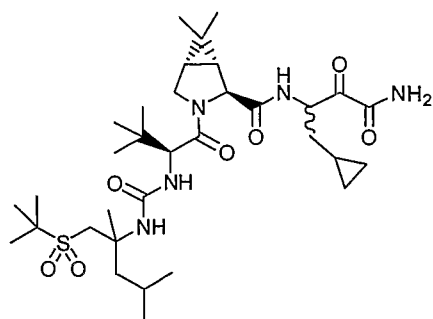
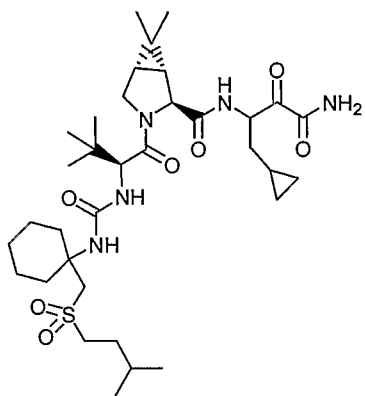


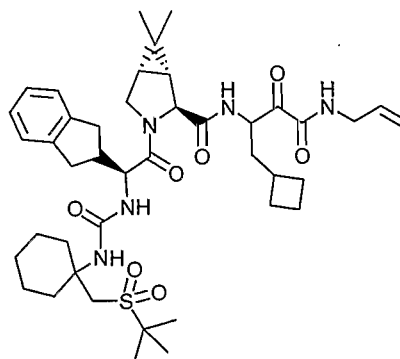
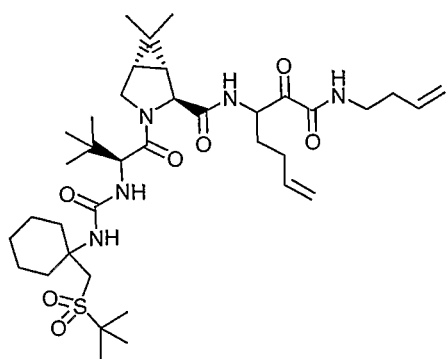
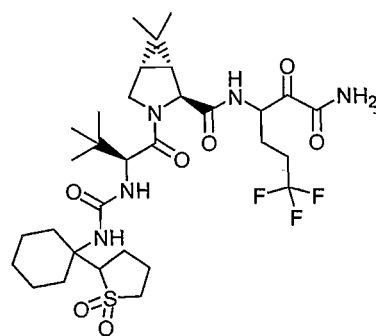
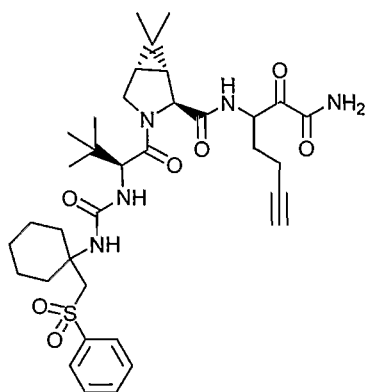
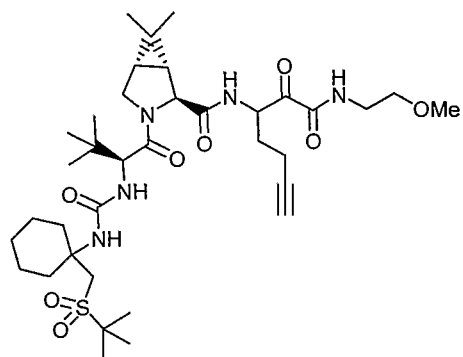
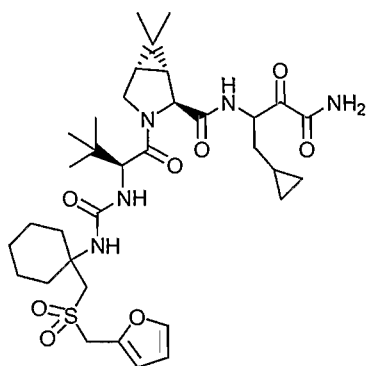


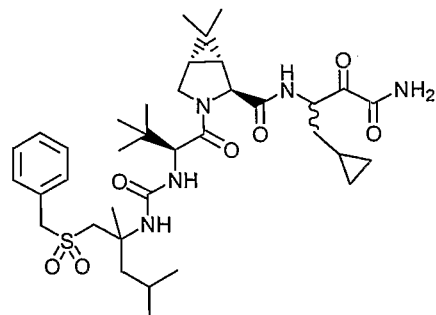
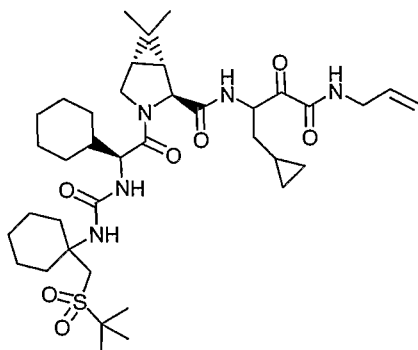
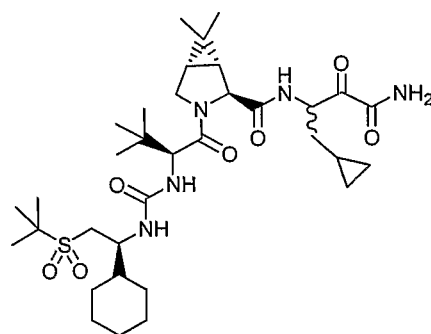
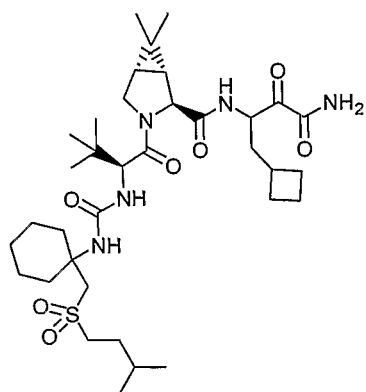
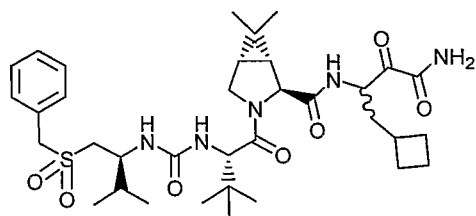
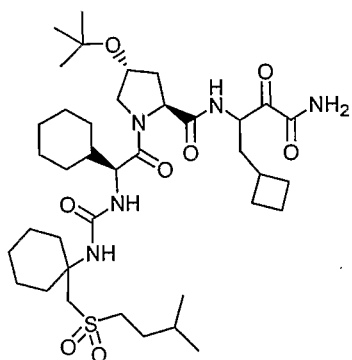


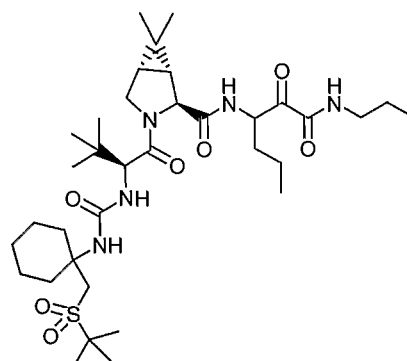
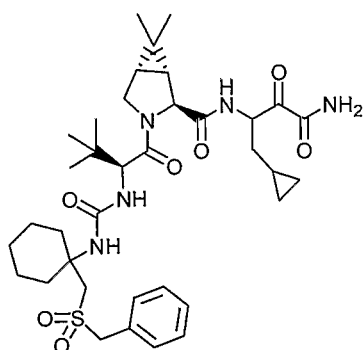
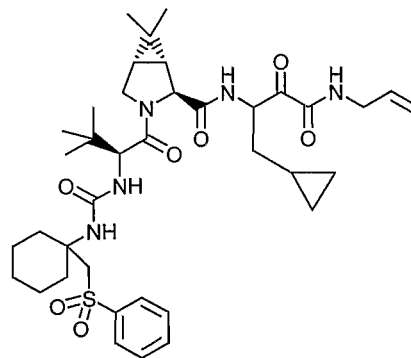
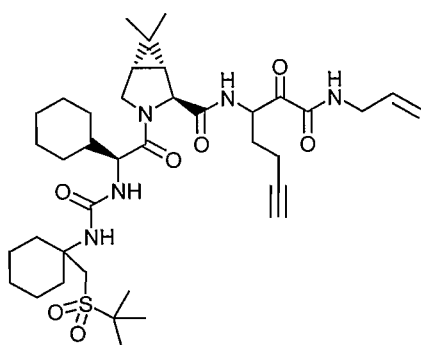
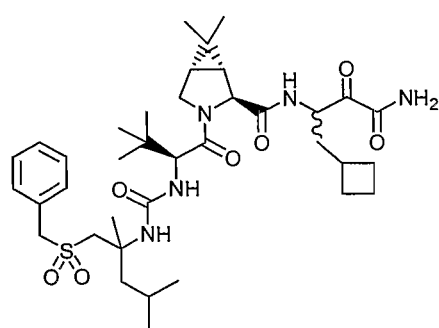
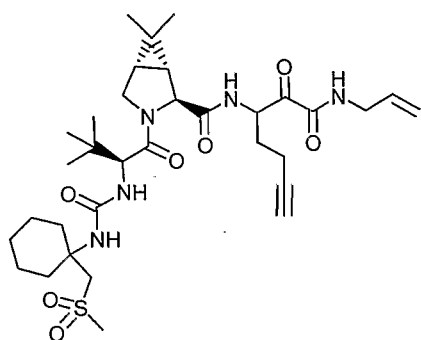


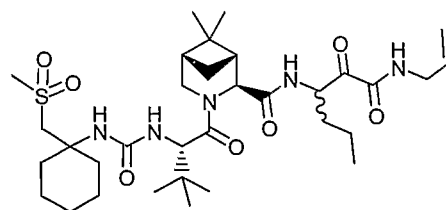
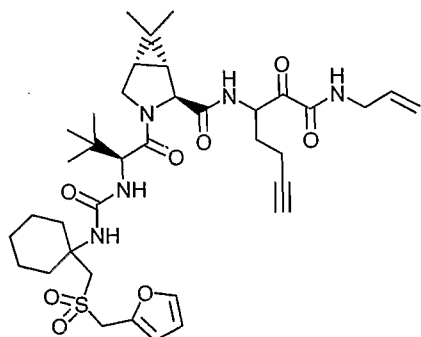
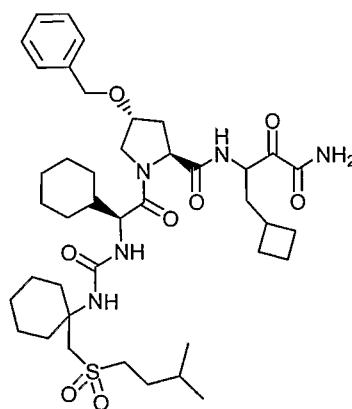
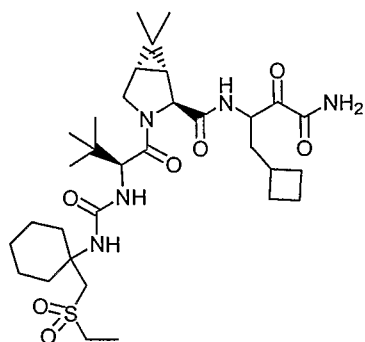
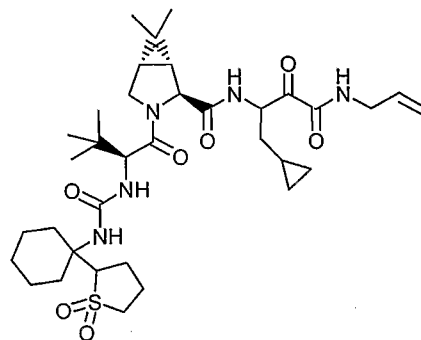
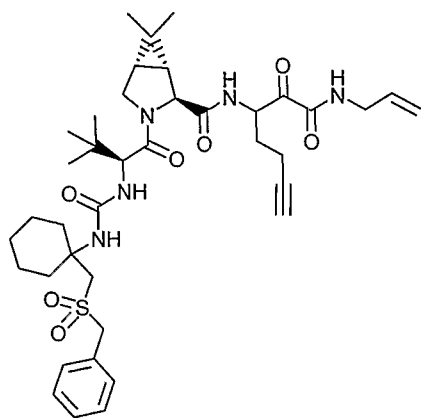


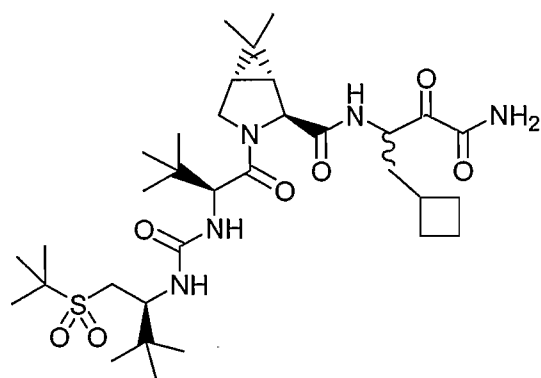
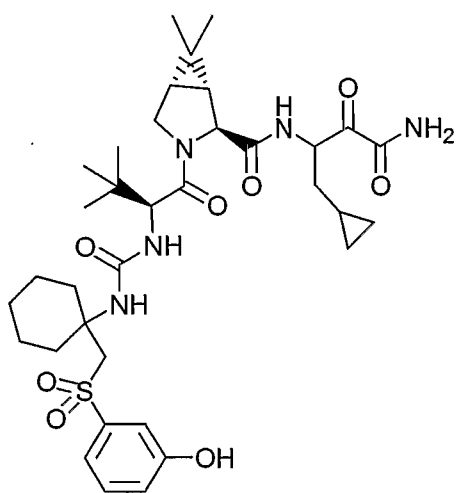
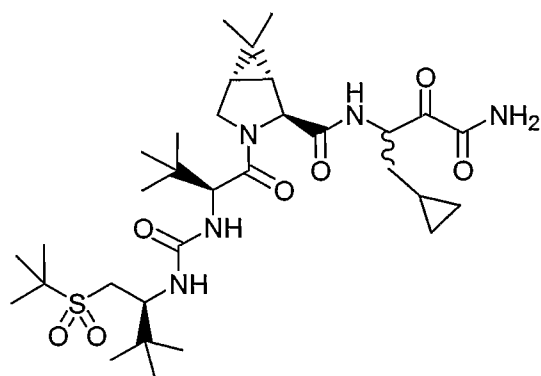
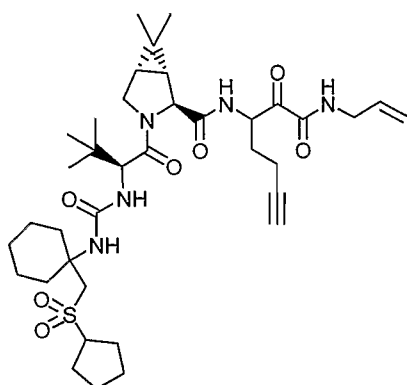
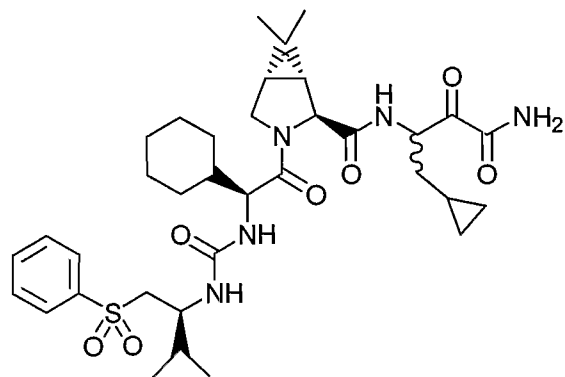
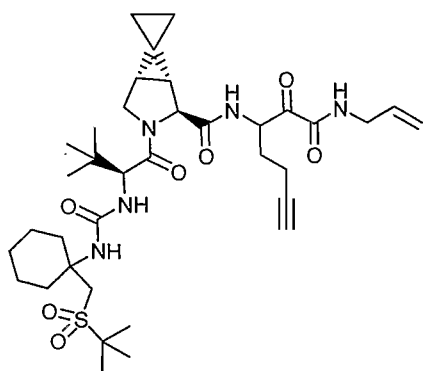


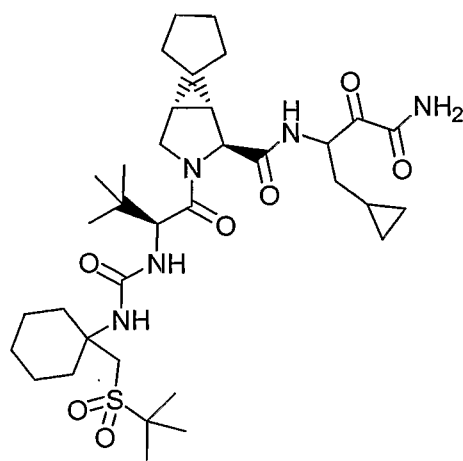
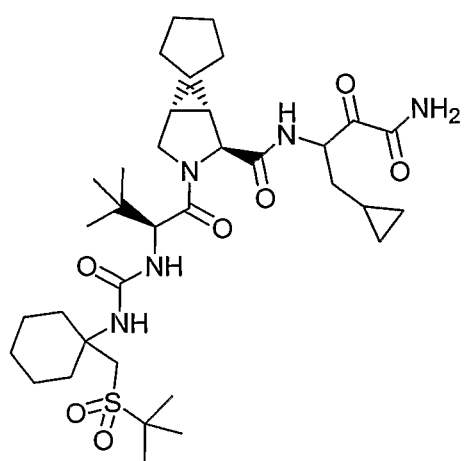
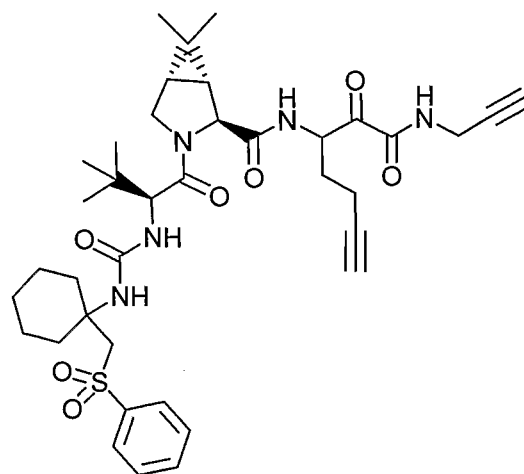
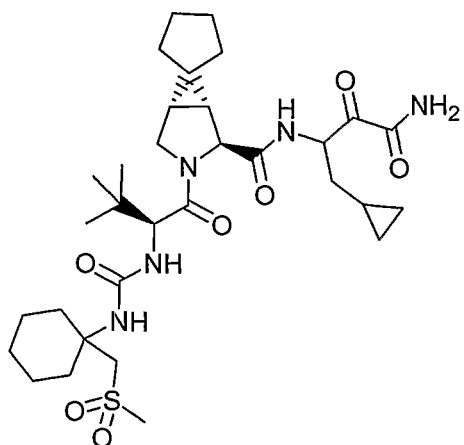


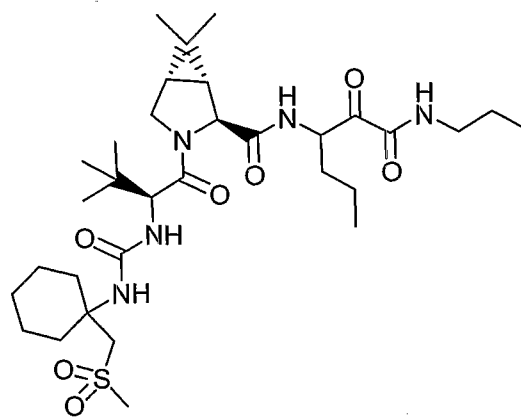
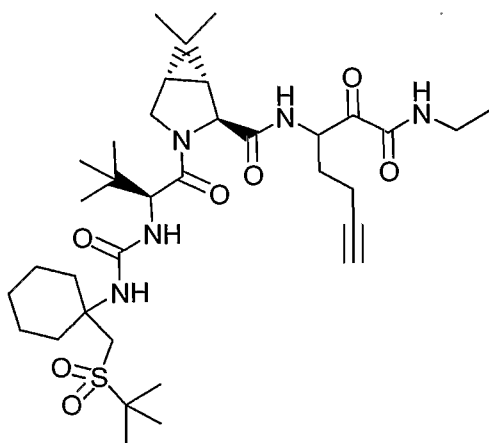
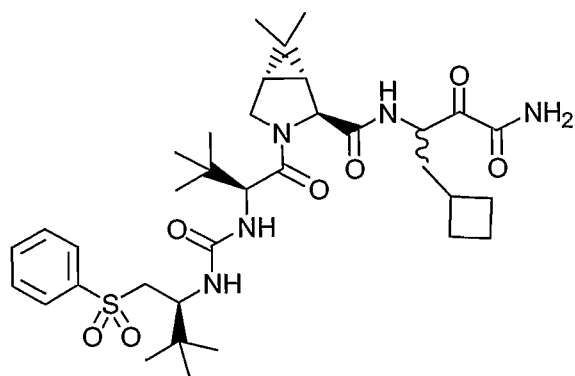
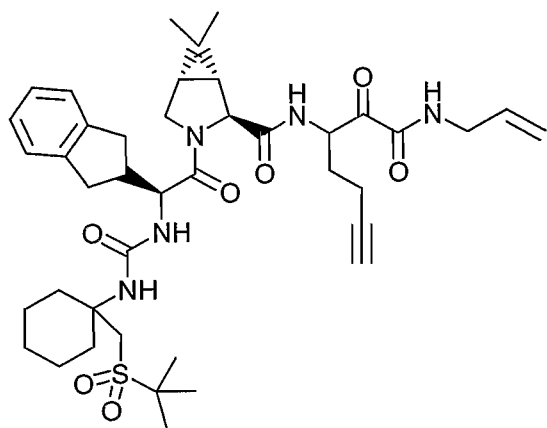
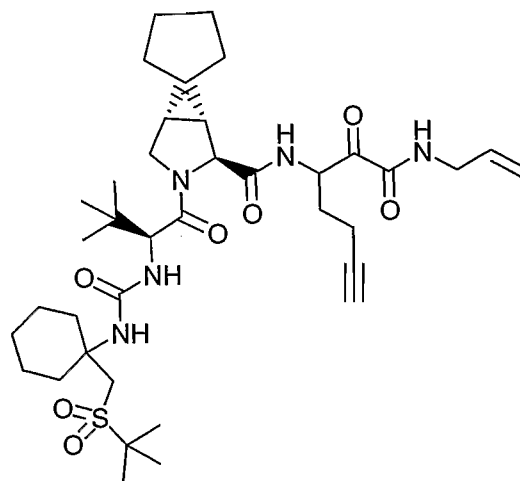
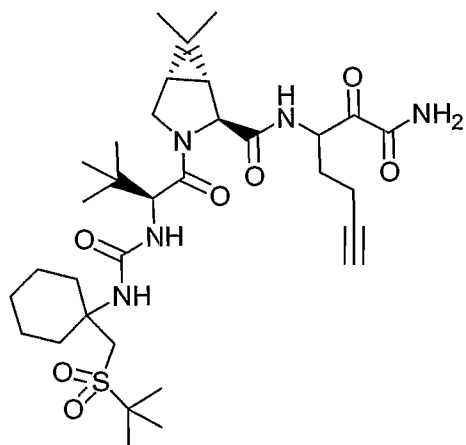


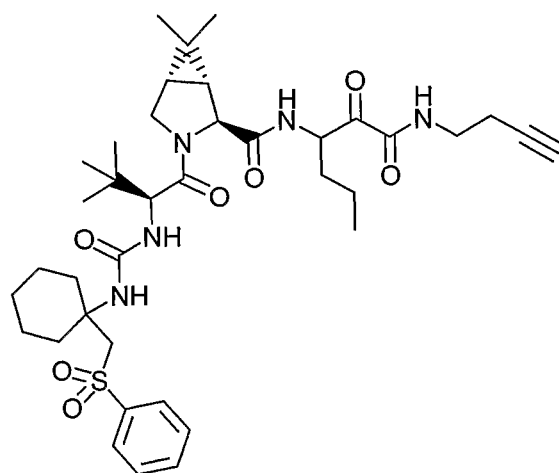
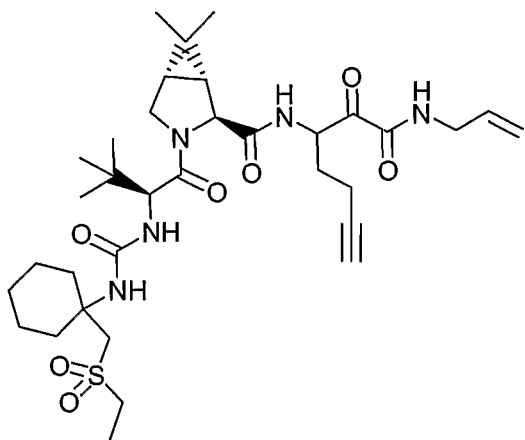
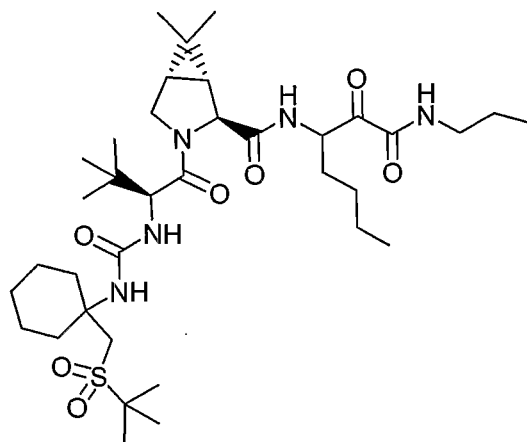
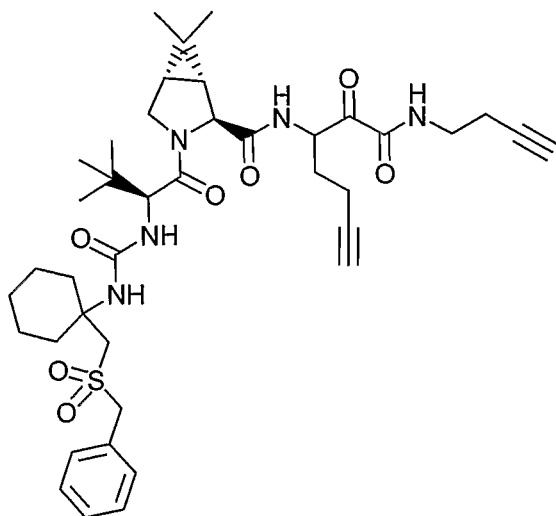


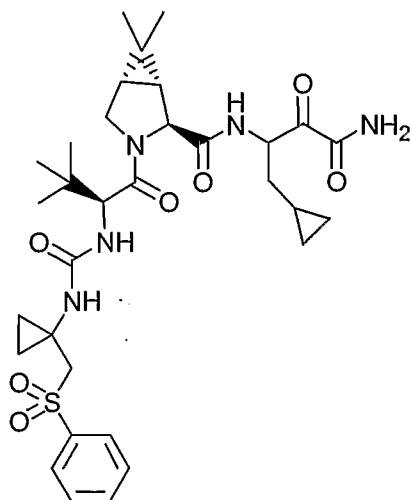
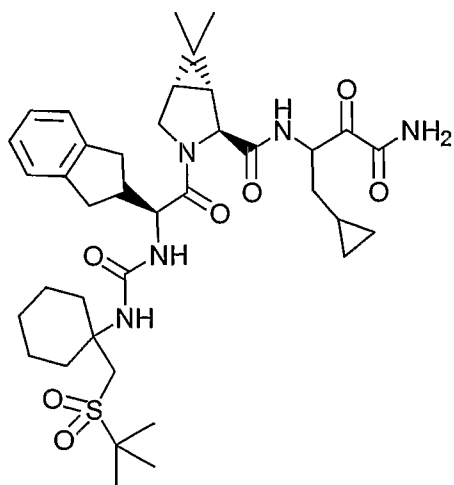
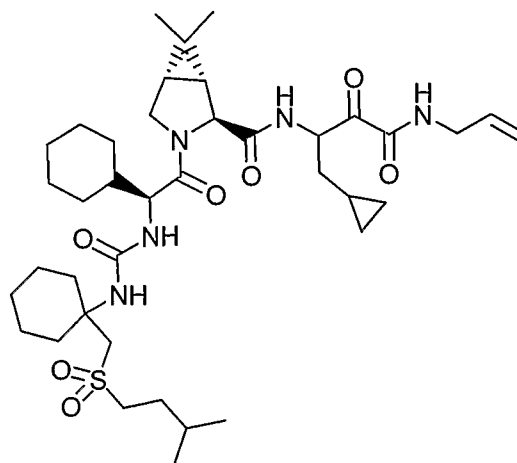
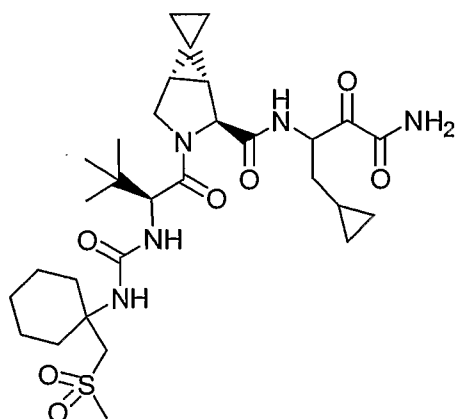


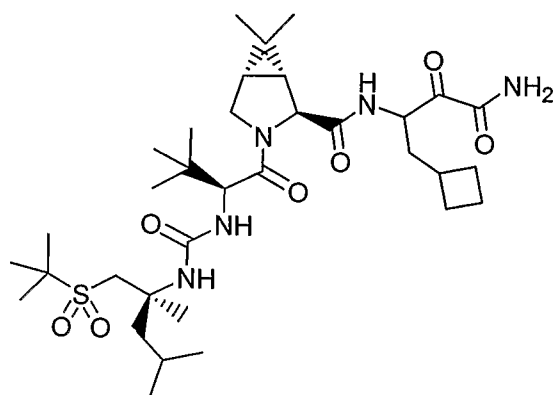
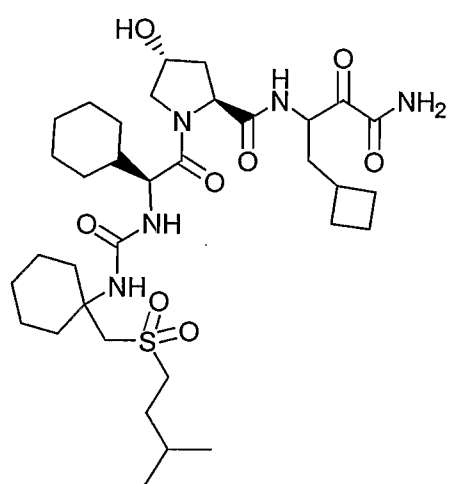
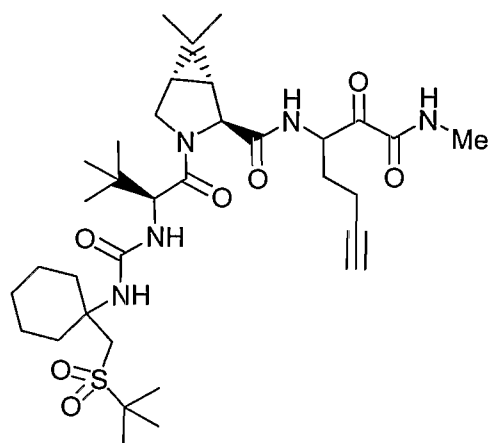
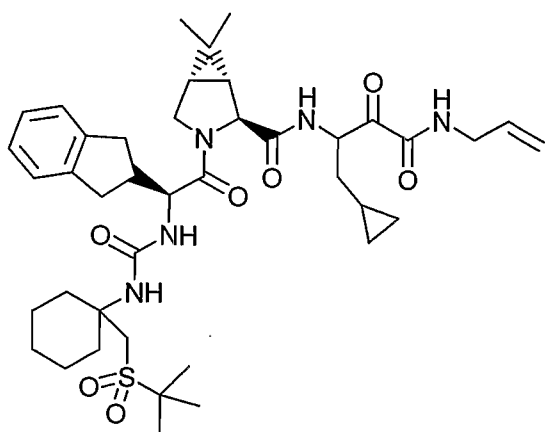


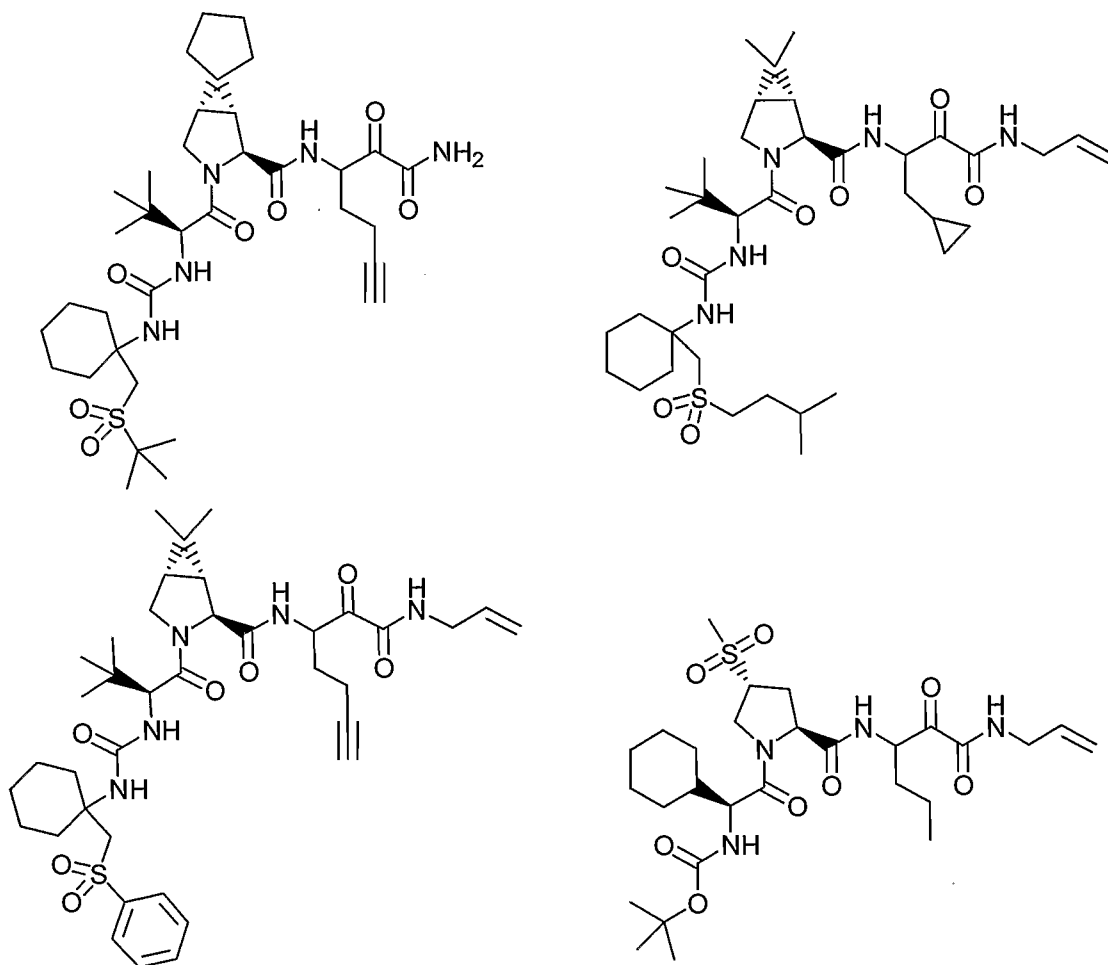


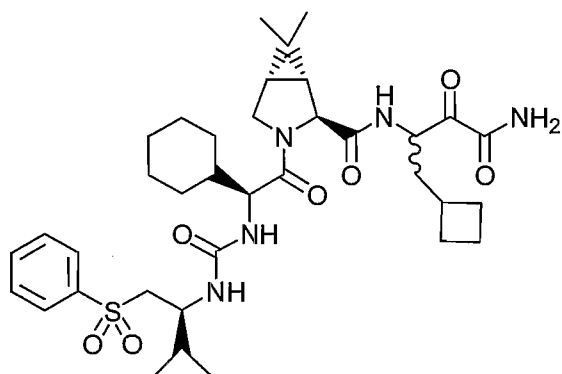
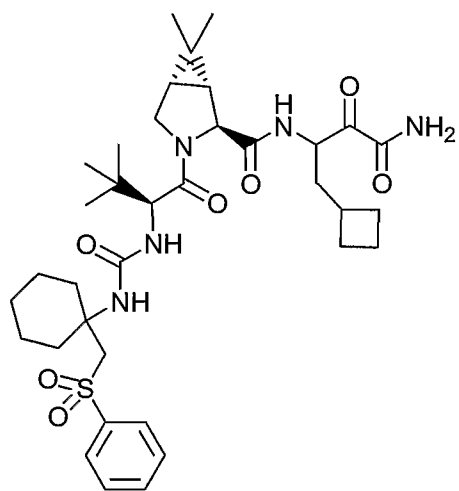
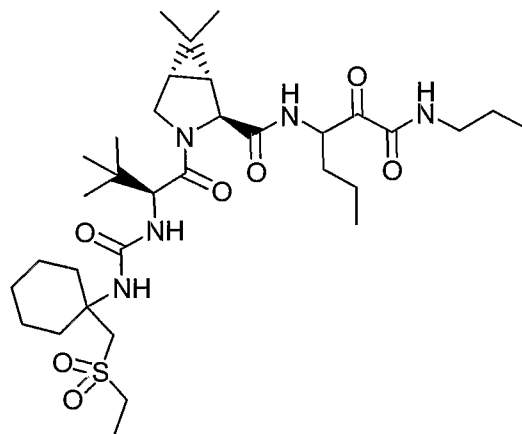
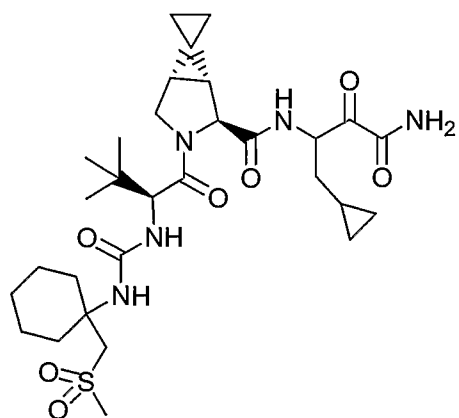
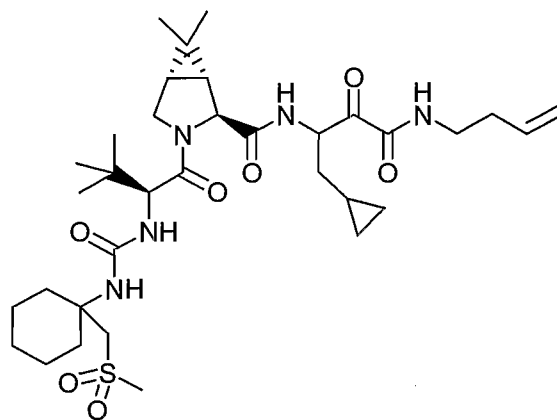
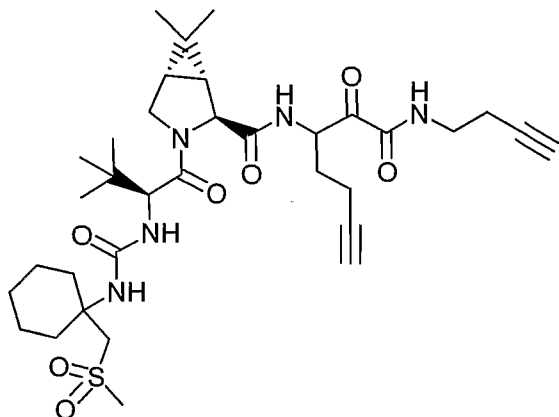


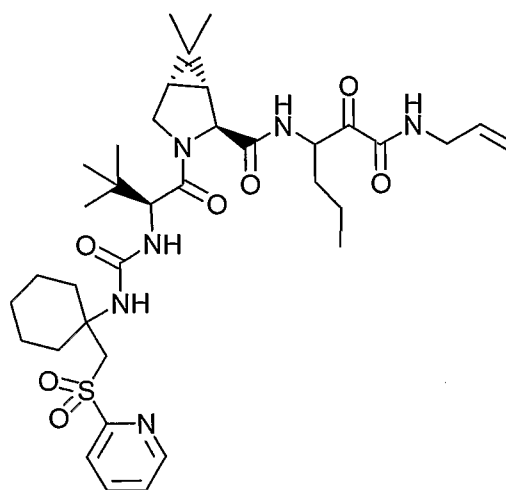
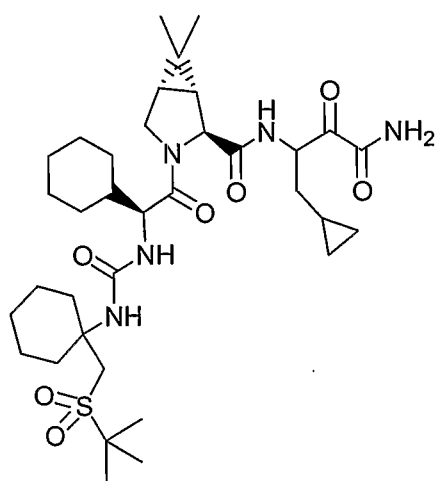
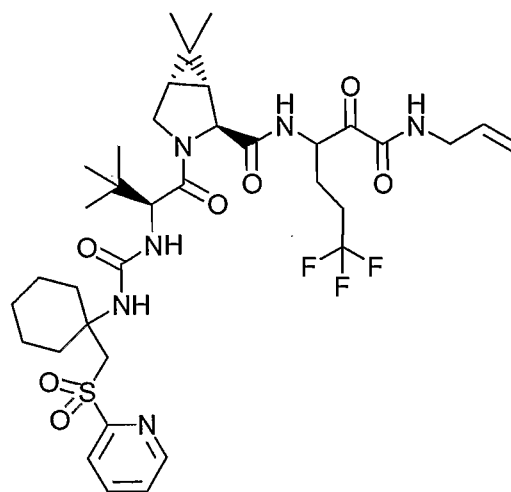
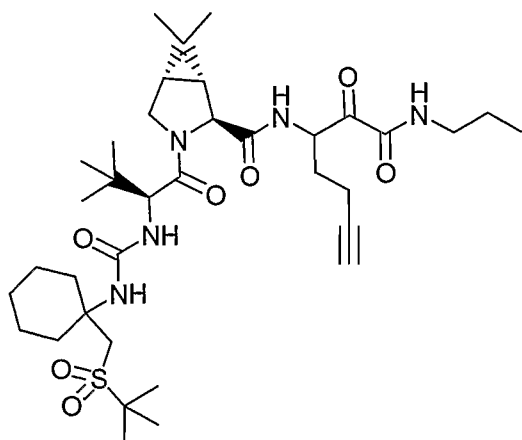


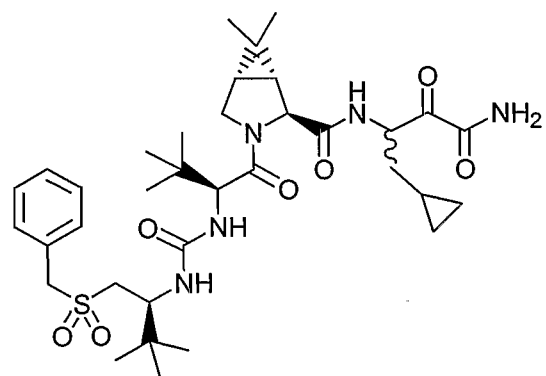
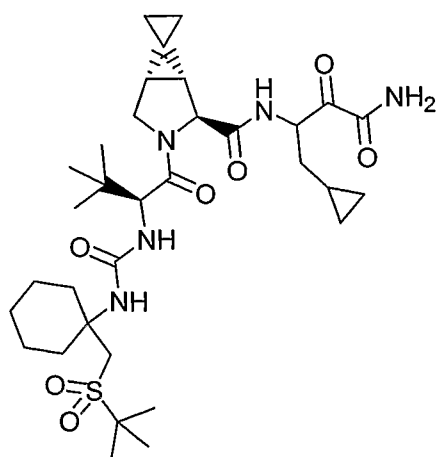
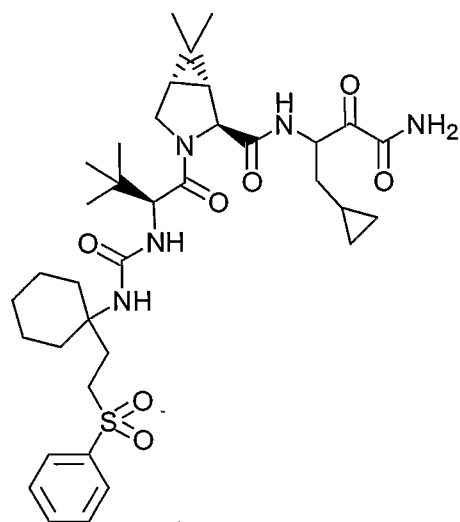
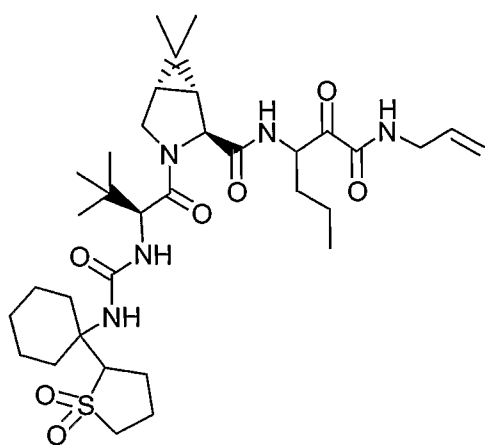
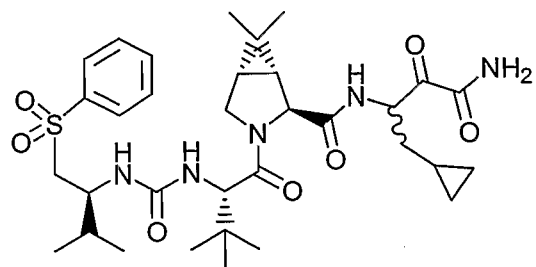
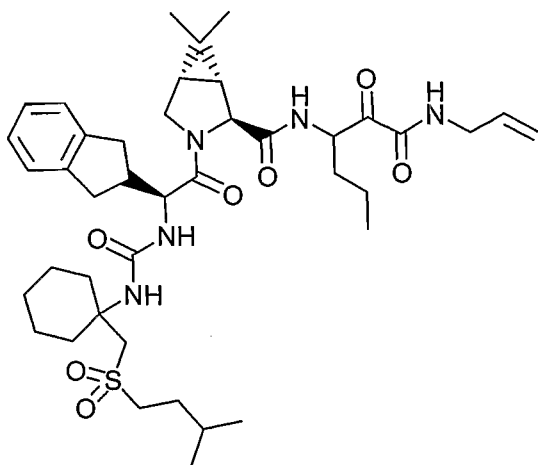


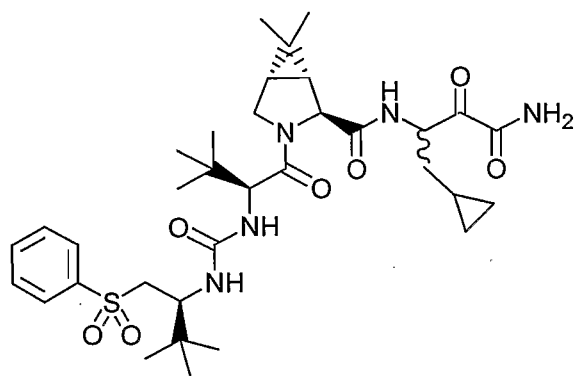
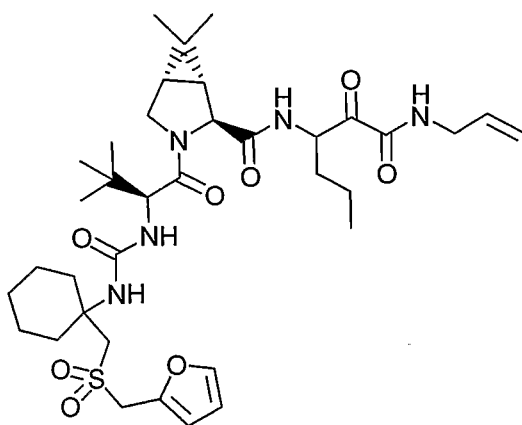
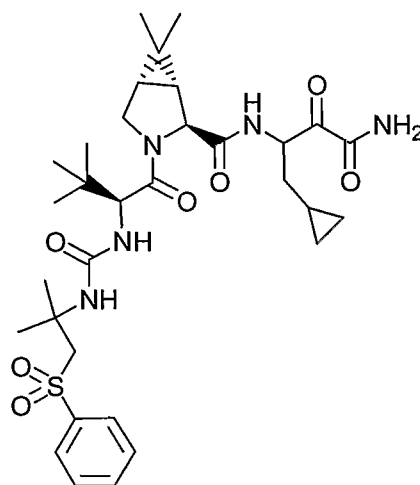
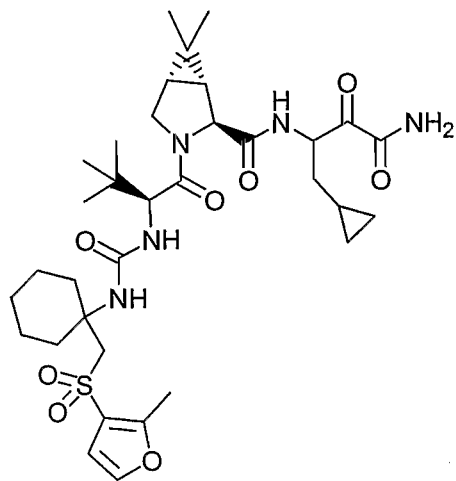
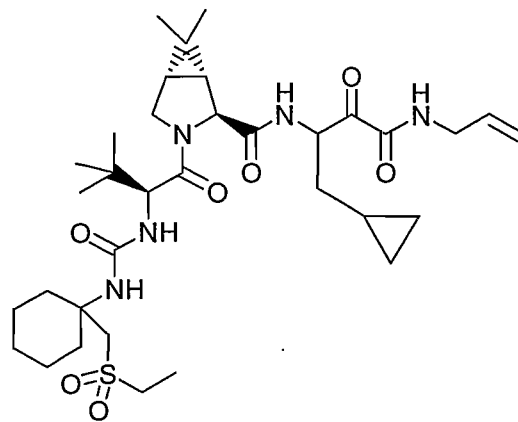
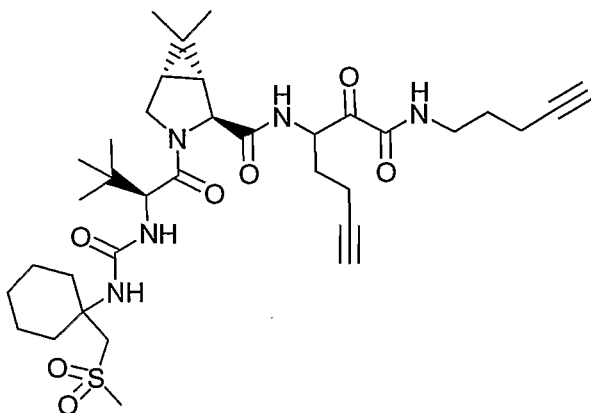


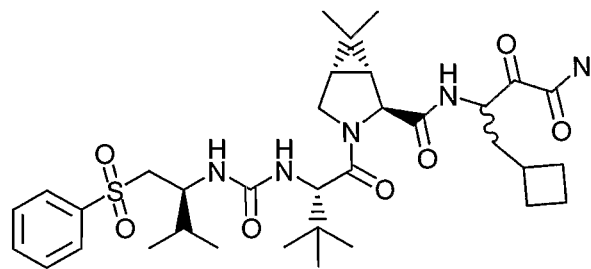
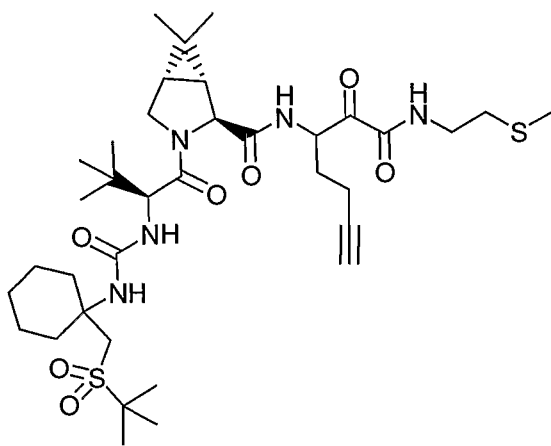
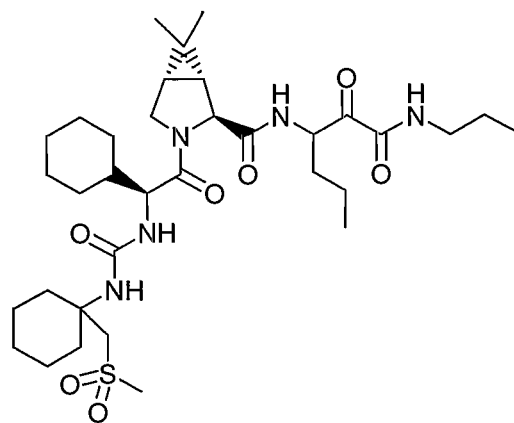
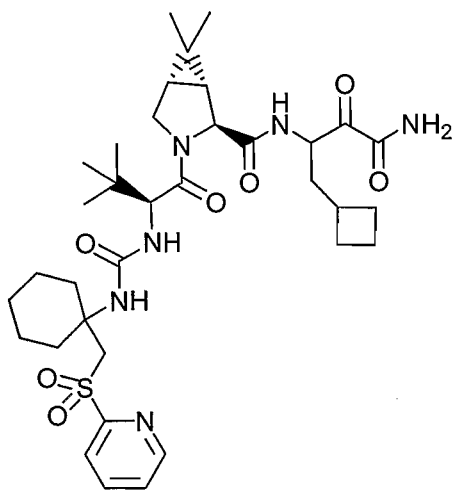
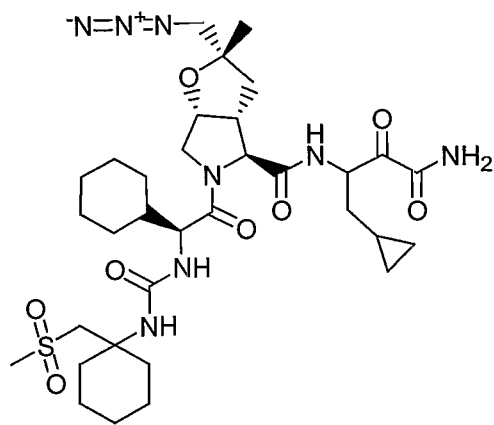
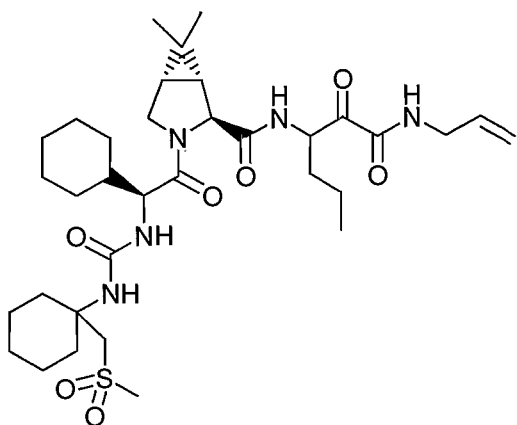


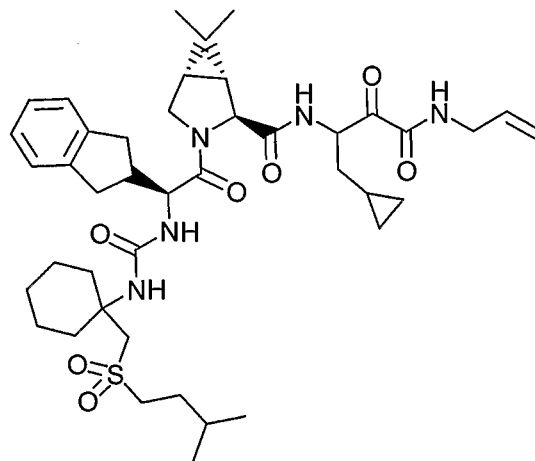
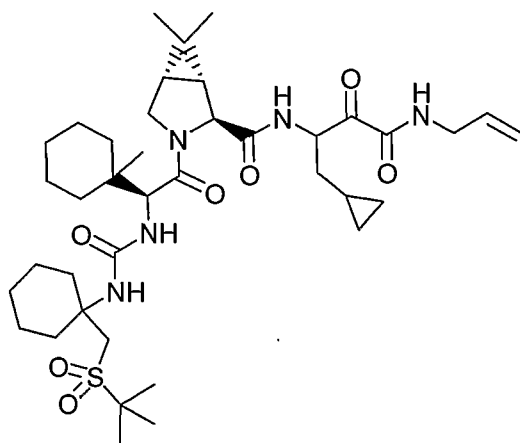
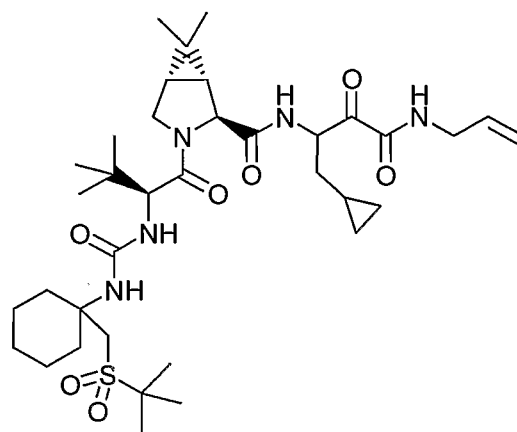
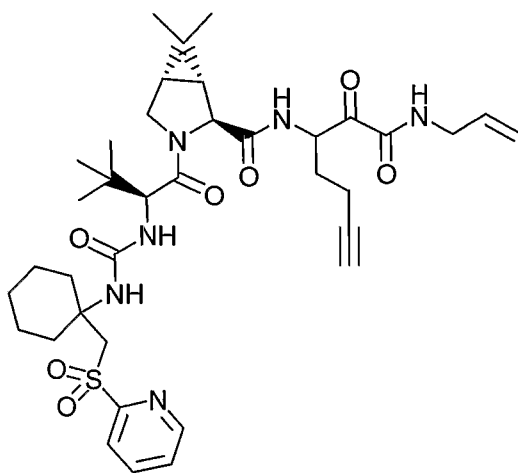
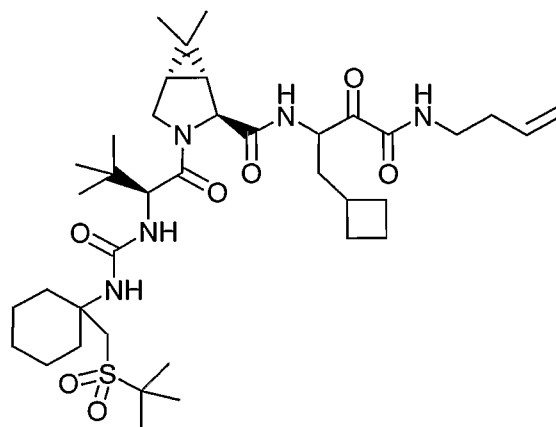
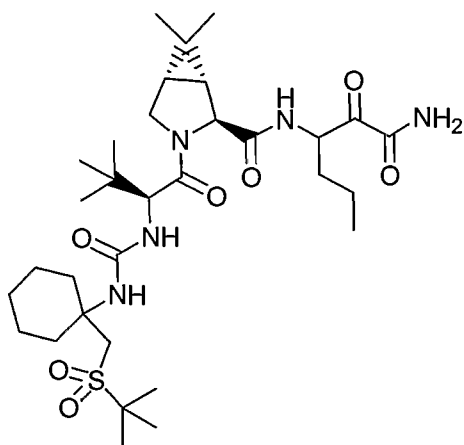


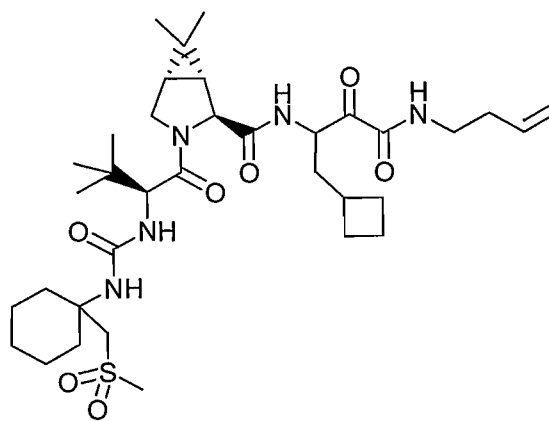
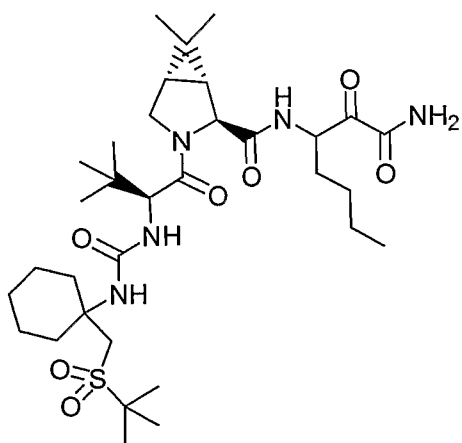
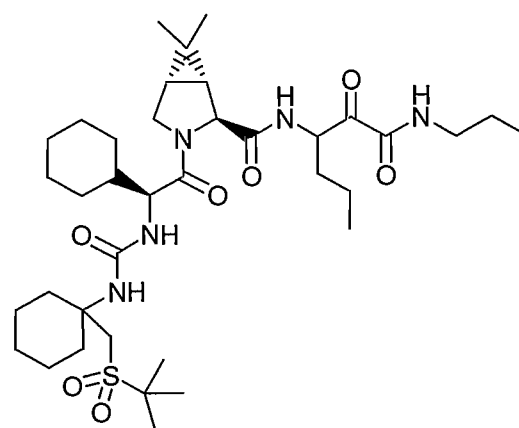
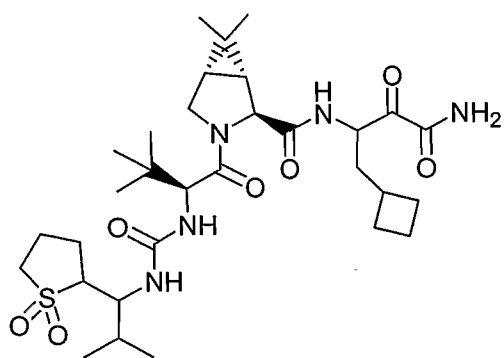
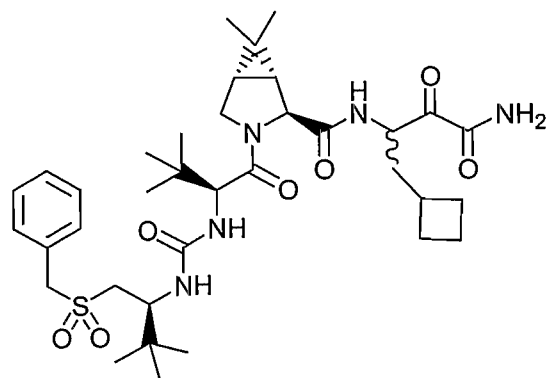
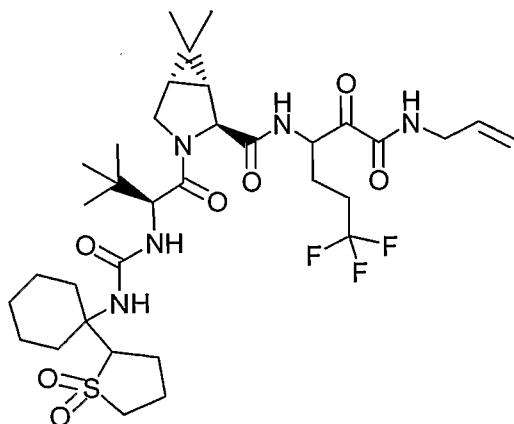


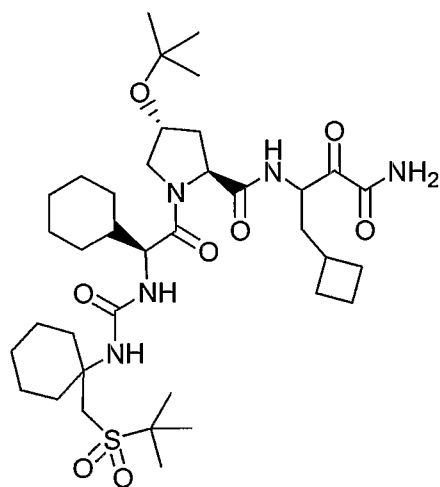
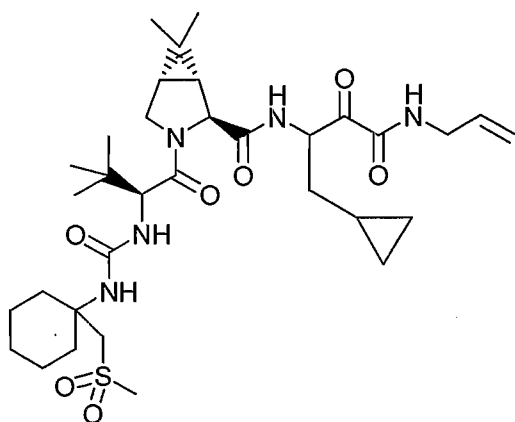
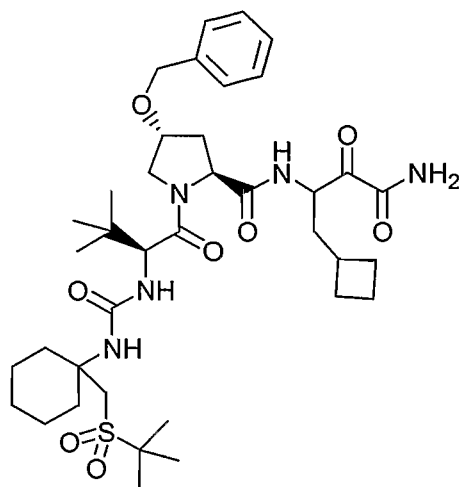
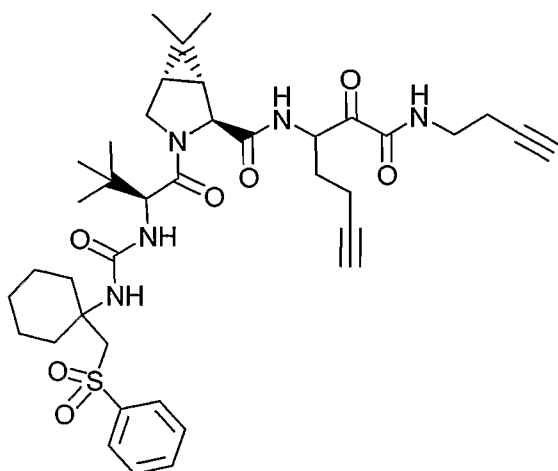


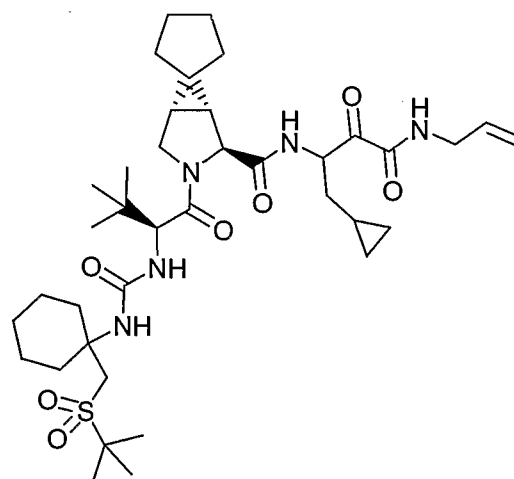
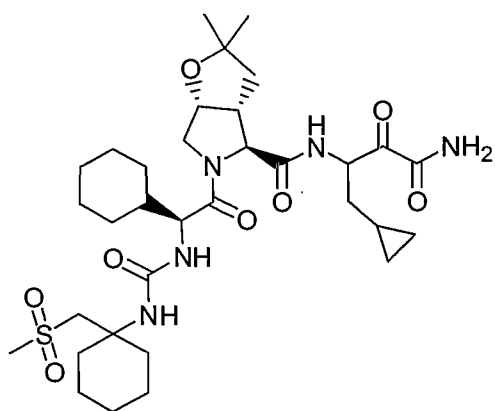
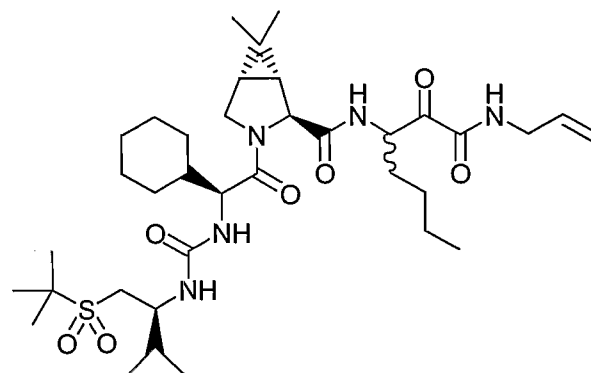
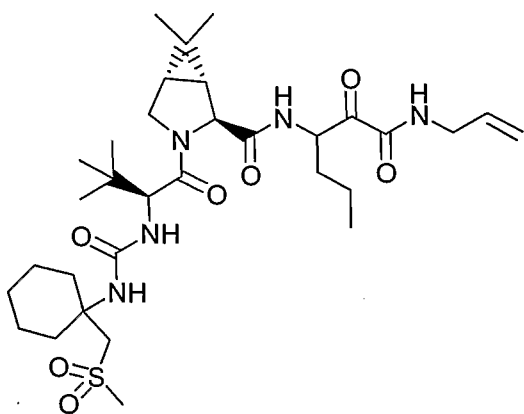
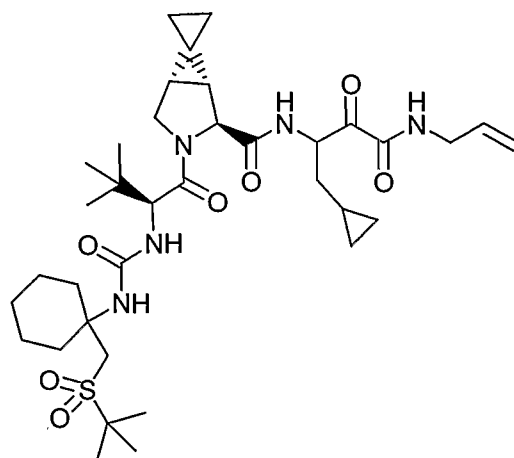
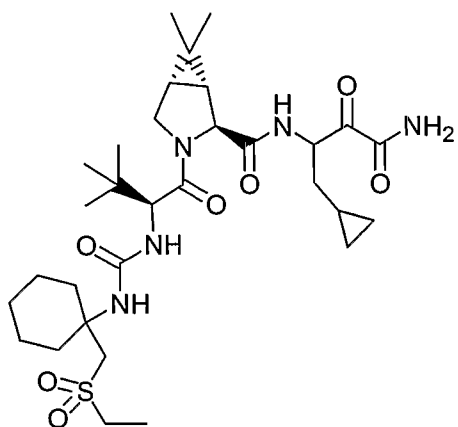


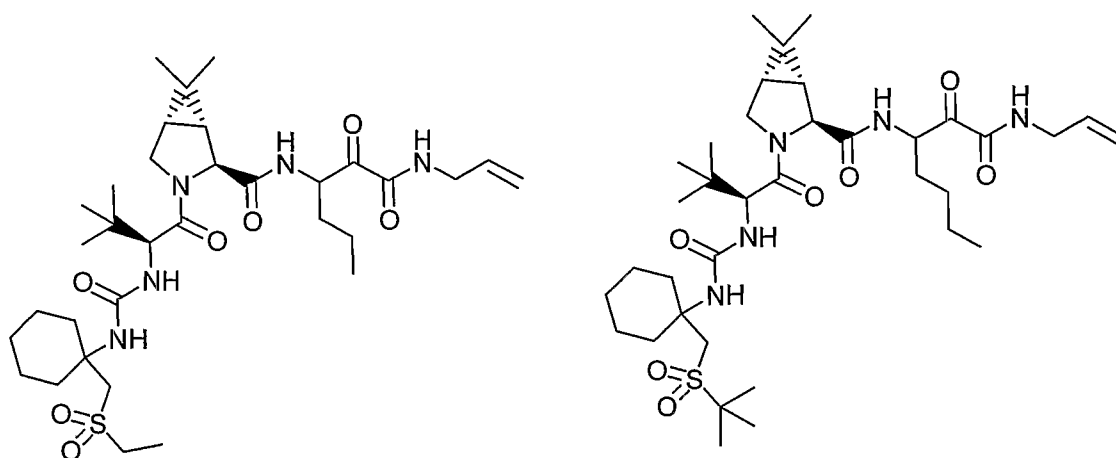






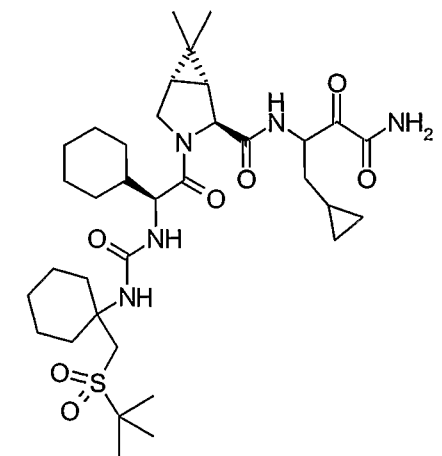
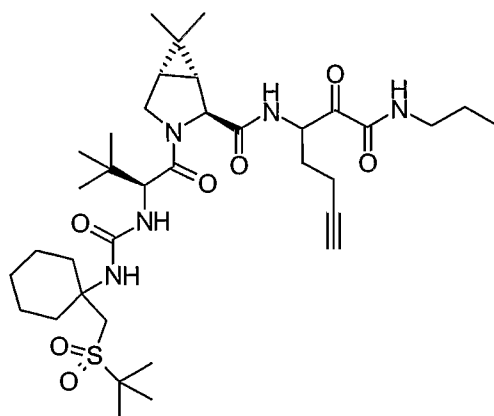
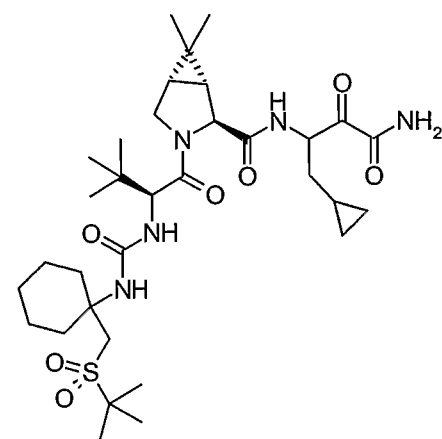
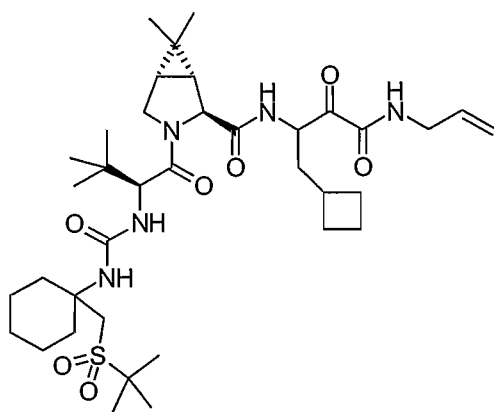
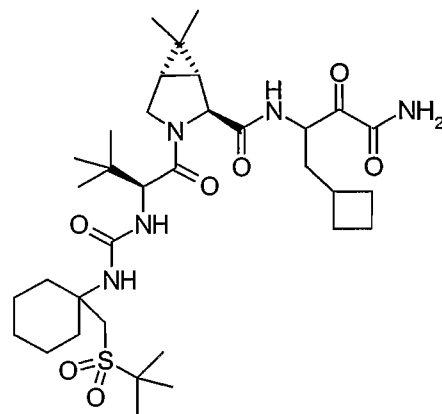
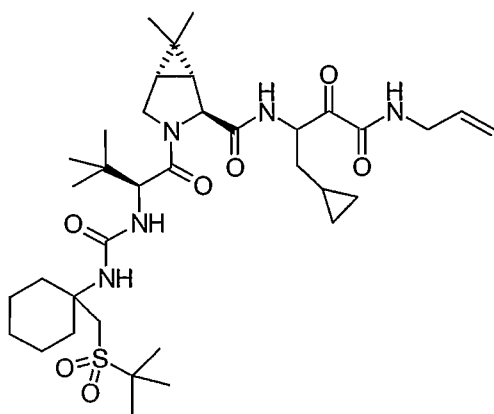


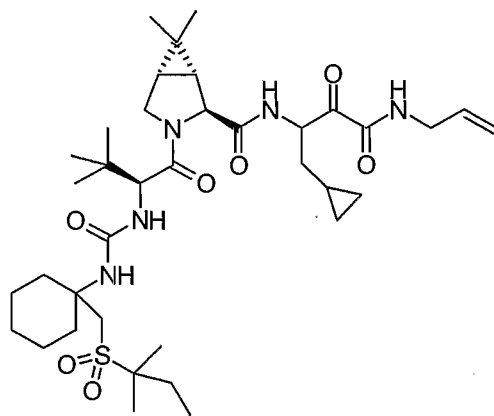
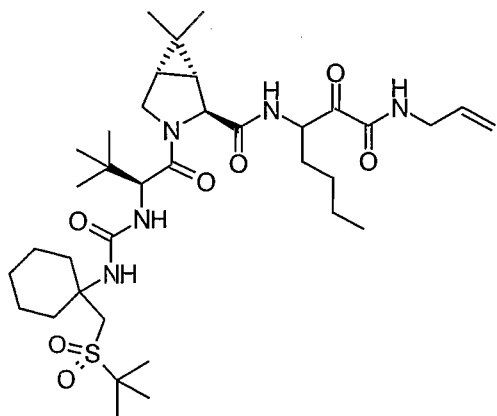
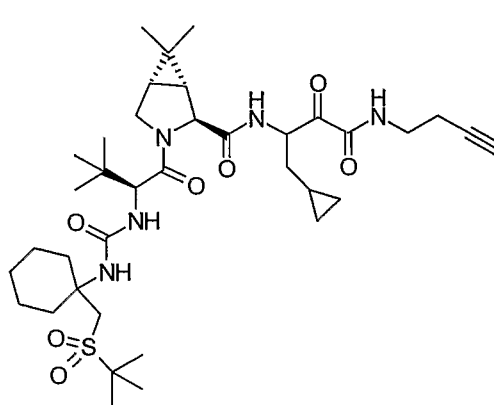
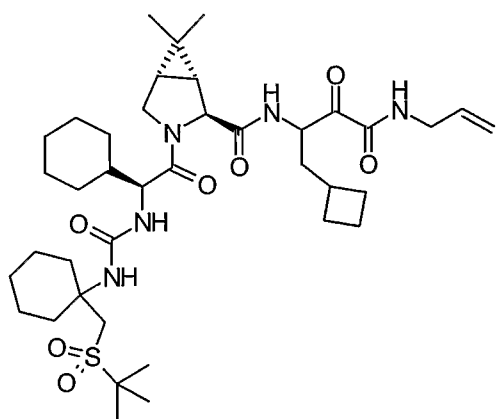
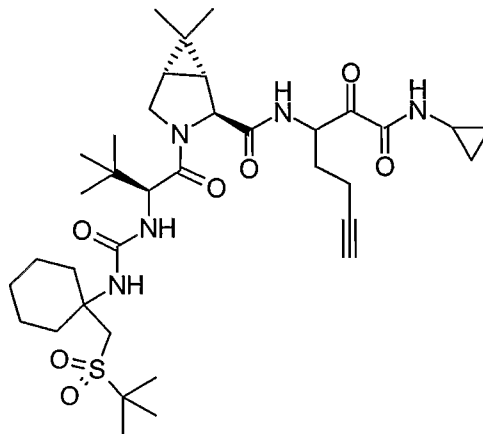
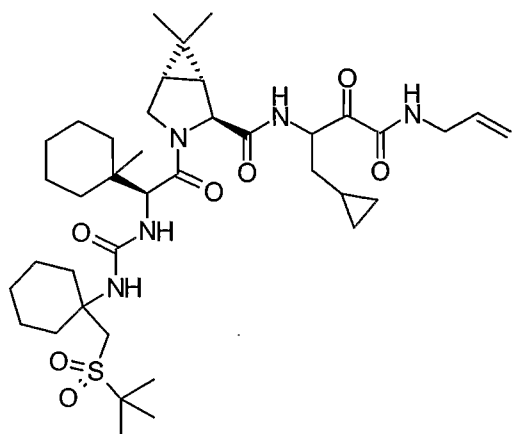


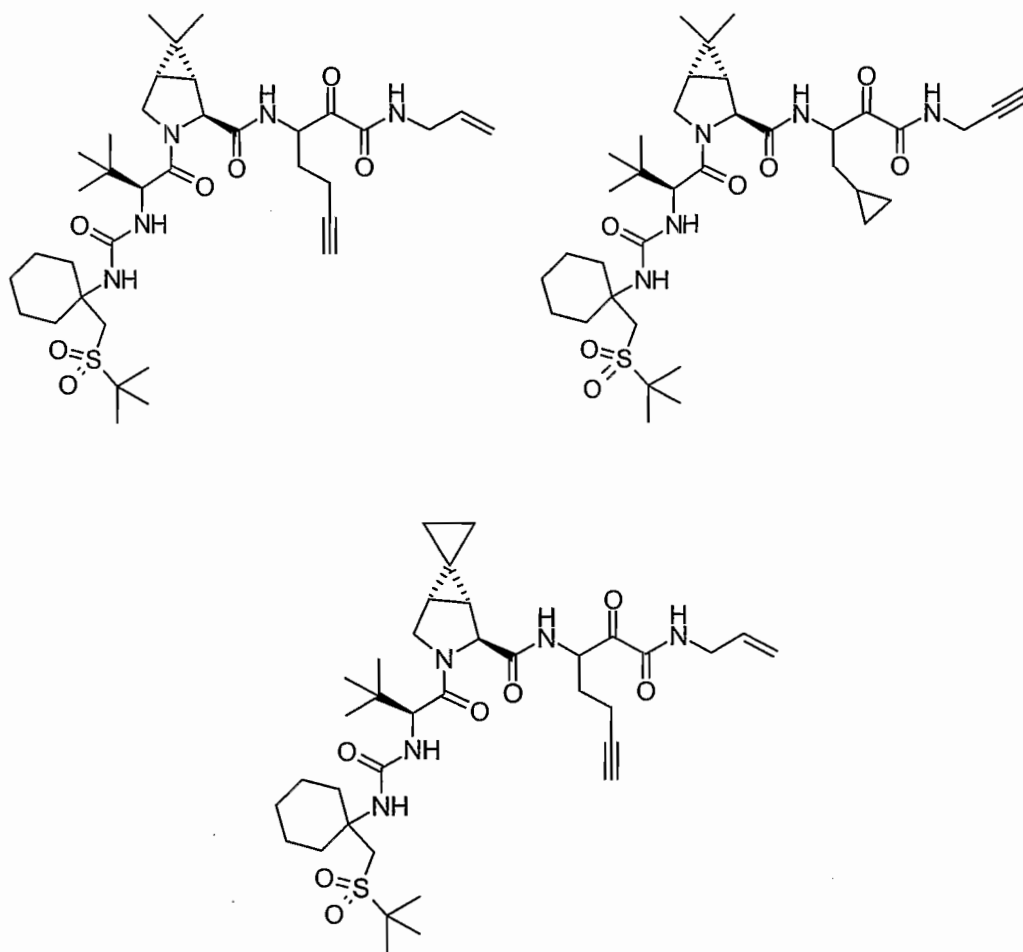


In an additional embodiment, this invention discloses the following compounds in **Table 2**:

Table 2







As used above, and throughout this disclosure, the following terms, unless otherwise indicated, shall be understood to have the following

5 meanings:

"Patient" includes both human and animals.

"Mammal" means humans and other mammalian animals.

"Alkyl" means an aliphatic hydrocarbon group which may be straight or branched and comprising about 1 to about 20 carbon atoms in the chain.

10 Preferred alkyl groups contain about 1 to about 12 carbon atoms in the chain. More preferred alkyl groups contain about 1 to about 6 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl,

ethyl or propyl, are attached to a linear alkyl chain. "Lower alkyl" means a group having about 1 to about 6 carbon atoms in the chain which may be straight or branched. The term "substituted alkyl" means that the alkyl group may be substituted by one or more substituents which may be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, aryl, cycloalkyl, cyano, hydroxy, alkoxy, alkylthio, amino, -NH(alkyl), -NH(cycloalkyl), -N(alkyl)₂, -N(cycloalkyl)₂, carboxy and -C(O)O-alkyl. Non-limiting examples of suitable alkyl groups include methyl, ethyl, n-propyl, isopropyl and t-butyl.

"Alkenyl" means an aliphatic hydrocarbon group containing at least one carbon-carbon double bond and which may be straight or branched and comprising about 2 to about 15 carbon atoms in the chain. Preferred alkenyl groups have about 2 to about 12 carbon atoms in the chain; and more preferably about 2 to about 6 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl, are attached to a linear alkenyl chain. "Lower alkenyl" means about 2 to about 6 carbon atoms in the chain which may be straight or branched. The term "substituted alkenyl" means that the alkenyl group may be substituted by one or more substituents which may be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, aryl, cycloalkyl, cyano, alkoxy and -S(alkyl). Non-limiting examples of suitable alkenyl groups include ethenyl, propenyl, n-butenyl, 3-methylbut-2-enyl, n-pentenyl, octenyl and decenyl.

"Alkynyl" means an aliphatic hydrocarbon group containing at least one carbon-carbon triple bond and which may be straight or branched and comprising about 2 to about 15 carbon atoms in the chain. Preferred alkynyl groups have about 2 to about 12 carbon atoms in the chain; and more preferably about 2 to about 4 carbon atoms in the chain. Branched means that

one or more lower alkyl groups such as methyl, ethyl or propyl, are attached to a linear alkynyl chain. "Lower alkynyl" means about 2 to about 6 carbon atoms in the chain which may be straight or branched. Non-limiting examples of suitable alkynyl groups include ethynyl, propynyl, 2-butynyl and 3-methylbutynyl. The term "substituted alkynyl" means that the alkynyl group may be substituted by one or more substituents which may be the same or different, each substituent being independently selected from the group consisting of alkyl, aryl and cycloalkyl.

"Aryl" means an aromatic monocyclic or multicyclic ring system comprising about 6 to about 14 carbon atoms, preferably about 6 to about 10 carbon atoms. The aryl group can be optionally substituted with one or more "ring system substituents" which may be the same or different, and are as defined herein. Non-limiting examples of suitable aryl groups include phenyl and naphthyl.

"Heteroaryl" means an aromatic monocyclic or multicyclic ring system comprising about 5 to about 14 ring atoms, preferably about 5 to about 10 ring atoms, in which one or more of the ring atoms is an element other than carbon, for example nitrogen, oxygen or sulfur, alone or in combination. Preferred heteroaryls contain about 5 to about 6 ring atoms. The "heteroaryl" can be optionally substituted by one or more "ring system substituents" which may be the same or different, and are as defined herein. The prefix aza, oxa or thia before the heteroaryl root name means that at least a nitrogen, oxygen or sulfur atom respectively, is present as a ring atom. A nitrogen atom of a heteroaryl can be optionally oxidized to the corresponding N-oxide. Non-limiting examples of suitable heteroaryls include pyridyl, pyrazinyl, furanyl, thienyl, pyrimidinyl, pyridone (including N-substituted pyridones), isoxazolyl, isothiazolyl, oxazolyl, thiazolyl, pyrazolyl, furazanyl, pyrrolyl, pyrazolyl, triazolyl, 1,2,4-thiadiazolyl, pyrazinyl, pyridazinyl, quinoxaliny, phthalazinyl,

oxindolyl, imidazo[1,2-a]pyridinyl, imidazo[2,1-b]thiazolyl, benzofurazanyl, indolyl, azaindolyl, benzimidazolyl, benzothienyl, quinolinyl, imidazolyl, thienopyridyl, quinazolinyl, thienopyrimidyl, pyrrolopyridyl, imidazopyridyl, isoquinolinyl, benzoazaindolyl, 1,2,4-triazinyl, benzothiazolyl and the like. The
5 term "heteroaryl" also refers to partially saturated heteroaryl moieties such as, for example, tetrahydroisoquinolyl, tetrahydroquinolyl and the like.

"Aralkyl" or "arylalkyl" means an aryl-alkyl- group in which the aryl and alkyl are as previously described. Preferred aralkyls comprise a lower alkyl group. Non-limiting examples of suitable aralkyl groups include benzyl, 2-
10 phenethyl and naphthalenylmethyl. The bond to the parent moiety is through the alkyl.

"Alkylaryl" means an alkyl-aryl- group in which the alkyl and aryl are as previously described. Preferred alkylaryls comprise a lower alkyl group. Non-limiting example of a suitable alkylaryl group is tolyl. The bond to the parent
15 moiety is through the aryl.

"Cycloalkyl" means a non-aromatic mono- or multicyclic ring system comprising about 3 to about 10 carbon atoms, preferably about 5 to about 10 carbon atoms. Preferred cycloalkyl rings contain about 5 to about 7 ring atoms. The cycloalkyl can be optionally substituted with one or more "ring
20 system substituents" which may be the same or different, and are as defined above. Non-limiting examples of suitable monocyclic cycloalkyls include cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl and the like. Non-limiting examples of suitable multicyclic cycloalkyls include 1-decalinyl, norbornyl, adamantyl and the like, as well as partially saturated species such as, for
25 example, indanyl, tetrahydronaphthyl and the like.

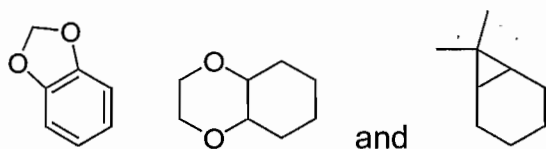
"Halogen" or "halo" means fluorine, chlorine, bromine, or iodine. Preferred are fluorine, chlorine and bromine.

"Ring system substituent" means a substituent attached to an aromatic or non-aromatic ring system which, for example, replaces an available hydrogen on the ring system. Ring system substituents may be the same or different, each being independently selected from the group consisting of

5 alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, alkylaryl, heteroaralkyl, heteroarylalkenyl, heteroarylalkynyl, alkylheteroaryl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylthio, arylthio, heteroarylthio, aralkylthio,

10 heteroaralkylthio, cycloalkyl, heterocyclyl, $-C(=N-CN)-NH_2$, $-C(=NH)-NH_2$, $-C(=NH)-NH(alkyl)$, Y_1Y_2N- , $Y_1Y_2N-alkyl-$, $Y_1Y_2NC(O)-$, $Y_1Y_2NSO_2-$ and $-SO_2NY_1Y_2$, wherein Y_1 and Y_2 can be the same or different and are independently selected from the group consisting of hydrogen, alkyl, aryl, cycloalkyl, and aralkyl. "Ring system substituent" may also mean a single

15 moiety which simultaneously replaces two available hydrogens on two adjacent carbon atoms (one H on each carbon) on a ring system. Examples of such moiety are methylene dioxy, ethylenedioxy, $-C(CH_3)_2-$ and the like which form moieties such as, for example:



20 "Heterocyclyl" means a non-aromatic saturated monocyclic or multicyclic ring system comprising about 3 to about 10 ring atoms, preferably about 5 to about 10 ring atoms, in which one or more of the atoms in the ring system is an element other than carbon, for example nitrogen, oxygen or sulfur, alone or in combination. There are no adjacent oxygen and/or sulfur

25 atoms present in the ring system. Preferred heterocyclyls contain about 5 to about 6 ring atoms. The prefix aza, oxa or thia before the heterocyclyl root

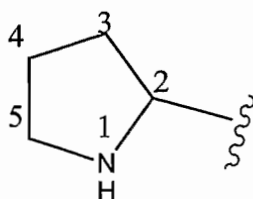
name means that at least a nitrogen, oxygen or sulfur atom respectively is present as a ring atom. Any -NH in a heterocyclyl ring may exist protected such as, for example, as an -N(Boc), -N(CBz), -N(Tos) group and the like; such protections are also considered part of this invention. The heterocyclyl

5 can be optionally substituted by one or more "ring system substituents" which may be the same or different, and are as defined herein. The nitrogen or sulfur atom of the heterocyclyl can be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide. Non-limiting examples of suitable monocyclic heterocyclyl rings include piperidyl, pyrrolidinyl, piperazinyl, morpholinyl,

10 thiomorpholinyl, thiazolidinyl, 1,4-dioxanyl, tetrahydrofuranyl, tetrahydrothiophenyl, lactam, lactone, and the like.

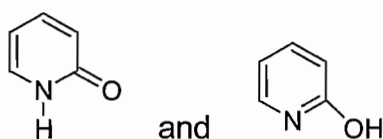
It should be noted that in hetero-atom containing ring systems of this invention, there are no hydroxyl groups on carbon atoms adjacent to a N, O or S, as well as there are no N or S groups on carbon adjacent to another

15 heteroatom. Thus, for example, in the ring:



there is no -OH attached directly to carbons marked 2 and 5.

It should also be noted that tautomeric forms such as, for example, the moieties:



are considered equivalent in certain embodiments of this invention.

"Alkynylalkyl" means an alkynyl-alkyl- group in which the alkynyl and alkyl are as previously described. Preferred alkynylalkyls contain a lower

alkynyl and a lower alkyl group. The bond to the parent moiety is through the alkyl. Non-limiting examples of suitable alkynylalkyl groups include propargylmethyl.

5 "Heteroaralkyl" means a heteroaryl-alkyl- group in which the heteroaryl and alkyl are as previously described. Preferred heteroaralkyls contain a lower alkyl group. Non-limiting examples of suitable aralkyl groups include pyridylmethyl, and quinolin-3-ylmethyl. The bond to the parent moiety is through the alkyl.

10 "Hydroxyalkyl" means a HO-alkyl- group in which alkyl is as previously defined. Preferred hydroxyalkyls contain lower alkyl. Non-limiting examples of suitable hydroxyalkyl groups include hydroxymethyl and 2-hydroxyethyl.

"Acyl" means an H-C(O)-, alkyl-C(O)- or cycloalkyl-C(O)-, group in which the various groups are as previously described. The bond to the parent moiety is through the carbonyl. Preferred acyls contain a lower alkyl. Non-limiting examples of suitable acyl groups include formyl, acetyl and propanoyl.

"Aroyl" means an aryl-C(O)- group in which the aryl group is as previously described. The bond to the parent moiety is through the carbonyl. Non-limiting examples of suitable groups include benzoyl and 1-naphthoyl.

20 "Alkoxy" means an alkyl-O- group in which the alkyl group is as previously described. Non-limiting examples of suitable alkoxy groups include methoxy, ethoxy, n-propoxy, isopropoxy and n-butoxy. The bond to the parent moiety is through the ether oxygen.

"Aryloxy" means an aryl-O- group in which the aryl group is as previously described. Non-limiting examples of suitable aryloxy groups include phenoxy and naphthoxy. The bond to the parent moiety is through the ether oxygen.

"Aralkyloxy" means an aralkyl-O- group in which the aralkyl group is as previously described. Non-limiting examples of suitable aralkyloxy groups

include benzyloxy and 1- or 2-naphthalenemethoxy. The bond to the parent moiety is through the ether oxygen.

"Alkylthio" means an alkyl-S- group in which the alkyl group is as previously described. Non-limiting examples of suitable alkylthio groups
5 include methylthio and ethylthio. The bond to the parent moiety is through the sulfur.

"Arylthio" means an aryl-S- group in which the aryl group is as previously described. Non-limiting examples of suitable arylthio groups include phenylthio and naphthylthio. The bond to the parent moiety is through
10 the sulfur.

"Aralkylthio" means an aralkyl-S- group in which the aralkyl group is as previously described. Non-limiting example of a suitable aralkylthio group is benzylthio. The bond to the parent moiety is through the sulfur.

"Alkoxy carbonyl" means an alkyl-O-CO- group. Non-limiting examples
15 of suitable alkoxy carbonyl groups include methoxy carbonyl and ethoxy carbonyl. The bond to the parent moiety is through the carbonyl.

"Aryloxy carbonyl" means an aryl-O-C(O)- group. Non-limiting examples of suitable aryloxy carbonyl groups include phenoxy carbonyl and naphthoxy carbonyl. The bond to the parent moiety is through the carbonyl.

"Aralkoxy carbonyl" means an aralkyl-O-C(O)- group. Non-limiting
20 example of a suitable aralkoxy carbonyl group is benzyloxy carbonyl. The bond to the parent moiety is through the carbonyl.

"Alkylsulfonyl" means an alkyl-S(O₂)- group. Preferred groups are those in which the alkyl group is lower alkyl. The bond to the parent moiety is
25 through the sulfonyl.

"Arylsulfonyl" means an aryl-S(O₂)- group. The bond to the parent moiety is through the sulfonyl.

The term "substituted" means that one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency under the existing circumstances is not exceeded, and that the substitution results in a stable compound. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. By "stable compound" or "stable structure" is meant a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

The term "one or more" or "at least one", when indicating the number of substituents, compounds, combination agents and the like, refers to at least one, and up to the maximum number of chemically and physically permissible, substituents, compounds, combination agents and the like, that are present or added, depending on the context. Such techniques and knowledge are well known within the skills of the concerned artisan.

The term "optionally substituted" means optional substitution with the specified groups, radicals or moieties.

The term "isolated" or "in isolated form" for a compound refers to the physical state of said compound after being isolated from a synthetic process or natural source or combination thereof. The term "purified" or "in purified form" for a compound refers to the physical state of said compound after being obtained from a purification process or processes described herein or well known to the skilled artisan, in sufficient purity to be characterizable by standard analytical techniques described herein or well known to the skilled artisan.

It should also be noted that any heteroatom with unsatisfied valences in the text, schemes, examples and Tables herein is assumed to have the hydrogen atom(s) to satisfy the valences.

When a functional group in a compound is termed "protected", this means that the group is in modified form to preclude undesired side reactions at the protected site when the compound is subjected to a reaction. Suitable protecting groups will be recognized by those with ordinary skill in the art as well as by reference to standard textbooks such as, for example, T. W. Greene *et al*, *Protective Groups in organic Synthesis* (1991), Wiley, New York.

When any variable (e.g., aryl, heterocycle, R^2 , etc.) occurs more than one time in any constituent or in Formula I, its definition on each occurrence is independent of its definition at every other occurrence.

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.

Prodrugs and solvates of the compounds of the invention are also contemplated herein. The term "prodrug", as employed herein, denotes a compound that is a drug precursor which, upon administration to a subject, undergoes chemical conversion by metabolic or chemical processes to yield a compound of Formula I or a salt and/or solvate thereof. A discussion of prodrugs is provided in T. Higuchi and V. Stella, *Pro-drugs as Novel Delivery Systems* (1987) 14 of the A.C.S. Symposium Series, and in *Bioreversible Carriers in Drug Design*, (1987) Edward B. Roche, ed., American Pharmaceutical Association and Pergamon Press, both of which are incorporated herein by reference thereto.

"Solvate" means a physical association of a compound of this invention with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when

one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. "Solvate" encompasses both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include ethanolates, methanolates, and the like. "Hydrate" is a solvate wherein the solvent molecule is H₂O.

"Effective amount" or "therapeutically effective amount" is meant to describe an amount of compound or a composition of the present invention effective in inhibiting the CDK(s) and thus producing the desired therapeutic, ameliorative, inhibitory or preventative effect.

The compounds of Formula I can form salts which are also within the scope of this invention. Reference to a compound of Formula I herein is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. In addition, when a compound of Formula I contains both a basic moiety, such as, but not limited to a pyridine or imidazole, and an acidic moiety, such as, but not limited to a carboxylic acid, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein. Pharmaceutically acceptable (i.e., non-toxic, physiologically acceptable) salts are preferred, although other salts are also useful. Salts of the compounds of the Formula I may be formed, for example, by reacting a compound of Formula I with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

Exemplary acid addition salts include acetates, ascorbates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, fumarates, hydrochlorides, hydrobromides, hydroiodides, lactates, maleates, methanesulfonates, naphthalenesulfonates, nitrates,

oxalates, phosphates, propionates, salicylates, succinates, sulfates, tartarates, thiocyanates, toluenesulfonates (also known as tosylates,) and the like. Additionally, acids which are generally considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use*. (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19; P. Gould, *International J. of Pharmaceutics* (1986) 33 201-217; Anderson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; and in *The Orange Book* (Food & Drug Administration, Washington, D.C. on their website). These disclosures are incorporated herein by reference thereto.

Exemplary basic salts include ammonium salts, alkali metal salts such as sodium, lithium, and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases (for example, organic amines) such as dicyclohexylamines, t-butyl amines, and salts with amino acids such as arginine, lysine and the like. Basic nitrogen-containing groups may be quarternized with agents such as lower alkyl halides (e.g. methyl, ethyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (e.g. dimethyl, diethyl, and dibutyl sulfates), long chain halides (e.g. decyl, lauryl, and stearyl chlorides, bromides and iodides), aralkyl halides (e.g. benzyl and phenethyl bromides), and others.

All such acid salts and base salts are intended to be pharmaceutically acceptable salts within the scope of the invention and all acid and base salts are considered equivalent to the free forms of the corresponding compounds for purposes of the invention.

Pharmaceutically acceptable esters of the present compounds include the following groups: (1) carboxylic acid esters obtained by esterification of

the hydroxy groups, in which the non-carbonyl moiety of the carboxylic acid portion of the ester grouping is selected from straight or branched chain alkyl (for example, acetyl, n-propyl, t-butyl, or n-butyl), alkoxyalkyl (for example, methoxymethyl), aralkyl (for example, benzyl), aryloxyalkyl (for example, phenoxymethyl), aryl (for example, phenyl optionally substituted with, for example, halogen, C₁₋₄alkyl, or C₁₋₄alkoxy or amino); (2) sulfonate esters, such as alkyl- or aralkylsulfonyl (for example, methanesulfonyl); (3) amino acid esters (for example, L-valyl or L-isoleucyl); (4) phosphonate esters and (5) mono-, di- or triphosphate esters. The phosphate esters may be further esterified by, for example, a C₁₋₂₀ alcohol or reactive derivative thereof, or by a 2,3-di (C₆₋₂₄)acyl glycerol.

Compounds of Formula I, and salts, solvates, esters and prodrugs thereof, may exist in their tautomeric form (for example, as an amide or imino ether). All such tautomeric forms are contemplated herein as part of the present invention.

All stereoisomers (for example, geometric isomers; optical isomers and the like) of the present compounds (including those of the salts, solvates, esters and prodrugs of the compounds as well as the salts and solvates of the prodrugs), such as those which may exist due to asymmetric carbons on various substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons), rotameric forms, atropisomers, and diastereomeric forms, are contemplated within the scope of this invention, as are positional isomers (such as, for example, 4-pyridyl and 3-pyridyl).

Individual stereoisomers of the compounds of the invention may, for example, be substantially free of other isomers, or may be admixed, for example, as racemates or with all other, or other selected, stereoisomers. The chiral centers of the present invention can have the S or R configuration as defined by the IUPAC 1974 Recommendations. The use of the terms "salt", "solvate"

"prodrug" and the like, is intended to equally apply to the salt, solvate and prodrug of enantiomers, stereoisomers, rotamers, tautomers, positional isomers, racemates or prodrugs of the inventive compounds.

Polymorphic forms of the compounds of Formula I, and of the salts,
5 solvates, esters and prodrugs of the compounds of Formula I, are intended to be included in the present invention.

It is to be understood that the utility of the compounds of Formula I for the therapeutic applications discussed herein is applicable to each compound by itself or to the combination or combinations of one or more compounds of
10 Formula I as illustrated, for example, in the next immediate paragraph. The same understanding also applies to pharmaceutical composition(s) comprising such compound or compounds and method(s) of treatment involving such compound or compounds.

The compounds according to the invention can have pharmacological
15 properties; in particular, the compounds of Formula I can be inhibitors of HCV protease, each compound by itself or one or more compounds of Formula I can be combined with one or more compounds selected from within Formula I. The compound(s) can be useful for treating diseases such as, for example, HCV, HIV, (AIDS, Acquired Immune Deficiency Syndrome), and related
20 disorders, as well as for modulating the activity of hepatitis C virus (HCV) protease, preventing HCV, or ameliorating one or more symptoms of hepatitis C.

The compounds of Formula I may be used for the manufacture of a medicament to treat disorders associated with the HCV protease, for
25 example, the method comprising bringing into intimate contact a compound of Formula I a pharmaceutically acceptable carrier.

In another embodiment, this invention provides pharmaceutical compositions comprising the inventive compound or compounds as an active

ingredient. The pharmaceutical compositions generally additionally comprise at least one pharmaceutically acceptable carrier diluent, excipient or carrier (collectively referred to herein as carrier materials). Because of their HCV inhibitory activity, such pharmaceutical compositions possess utility in treating hepatitis C and related disorders.

In yet another embodiment, the present invention discloses methods for preparing pharmaceutical compositions comprising the inventive compounds as an active ingredient. In the pharmaceutical compositions and methods of the present invention, the active ingredients will typically be administered in admixture with suitable carrier materials suitably selected with respect to the intended form of administration, i.e. oral tablets, capsules (either solid-filled, semi-solid filled or liquid filled), powders for constitution, oral gels, elixirs, dispersible granules, syrups, suspensions, and the like, and consistent with conventional pharmaceutical practices. For example, for oral administration in the form of tablets or capsules, the active drug component may be combined with any oral non-toxic pharmaceutically acceptable inert carrier, such as lactose, starch, sucrose, cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, talc, mannitol, ethyl alcohol (liquid forms) and the like. Moreover, when desired or needed, suitable binders, lubricants, disintegrating agents and coloring agents may also be incorporated in the mixture. Powders and tablets may be comprised of from about 5 to about 95 percent inventive composition.

Suitable binders include starch, gelatin, natural sugars, corn sweeteners, natural and synthetic gums such as acacia, sodium alginate, carboxymethylcellulose, polyethylene glycol and waxes. Among the lubricants there may be mentioned for use in these dosage forms, boric acid, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrants include starch, methylcellulose, guar gum and the like.

Sweetening and flavoring agents and preservatives may also be included where appropriate. Some of the terms noted above, namely disintegrants, diluents, lubricants, binders and the like, are discussed in more detail below.

5 Additionally, the compositions of the present invention may be formulated in sustained release form to provide the rate controlled release of any one or more of the components or active ingredients to optimize the therapeutic effects, i.e. HCV inhibitory activity and the like. Suitable dosage forms for sustained release include layered tablets containing layers of
10 varying disintegration rates or controlled release polymeric matrices impregnated with the active components and shaped in tablet form or capsules containing such impregnated or encapsulated porous polymeric matrices.

 Liquid form preparations include solutions, suspensions and emulsions.
15 As an example may be mentioned water or water-propylene glycol solutions for parenteral injections or addition of sweeteners and pacifiers for oral solutions, suspensions and emulsions. Liquid form preparations may also include solutions for intranasal administration.

 Aerosol preparations suitable for inhalation may include solutions and
20 solids in powder form, which may be in combination with a pharmaceutically acceptable carrier such as inert compressed gas, e.g. nitrogen.

 For preparing suppositories, a low melting wax such as a mixture of fatty acid glycerides such as cocoa butter is first melted, and the active ingredient is dispersed homogeneously therein by stirring or similar mixing.
25 The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool and thereby solidify.

 Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for either oral or

parenteral administration. Such liquid forms include solutions, suspensions and emulsions.

The compounds of the invention may also be deliverable transdermally. The transdermal compositions may take the form of creams, lotions, aerosols and/or emulsions and can be included in a transdermal patch of the matrix or reservoir type as are conventional in the art for this purpose.

The compounds of the invention may also be administered orally, intravenously, intranasally or subcutaneously.

The compounds of the invention may also comprise preparations which are in a unit dosage form. In such form, the preparation is subdivided into suitably sized unit doses containing appropriate quantities of the active components, e.g., an effective amount to achieve the desired purpose.

The quantity of the inventive active composition in a unit dose of preparation may be generally varied or adjusted from about 1.0 milligram to about 1,000 milligrams, preferably from about 1.0 to about 950 milligrams, more preferably from about 1.0 to about 500 milligrams, and typically from about 1 to about 250 milligrams, according to the particular application. The actual dosage employed may be varied depending upon the patient's age, sex, weight and severity of the condition being treated. Such techniques are well known to those skilled in the art.

Generally, the human oral dosage form containing the active ingredients can be administered 1 or 2 times per day. The amount and frequency of the administration will be regulated according to the judgment of the attending clinician. A generally recommended daily dosage regimen for oral administration may range from about 1.0 milligram to about 1,000 milligrams per day, in single or divided doses.

Some useful terms are described below:

Capsule - refers to a special container or enclosure made of methyl cellulose, polyvinyl alcohols, or denatured gelatins or starch for holding or containing compositions comprising the active ingredients. Hard shell capsules are typically made of blends of relatively high gel strength bone and pork skin gelatins. The capsule itself may contain small amounts of dyes, opaquing agents, plasticizers and preservatives.

Tablet- refers to a compressed or molded solid dosage form containing the active ingredients with suitable diluents. The tablet can be prepared by compression of mixtures or granulations obtained by wet granulation, dry granulation or by compaction.

Oral gel- refers to the active ingredients dispersed or solubilized in a hydrophilic semi-solid matrix.

Powder for constitution refers to powder blends containing the active ingredients and suitable diluents which can be suspended in water or juices.

Diluent - refers to substances that usually make up the major portion of the composition or dosage form. Suitable diluents include sugars such as lactose, sucrose, mannitol and sorbitol; starches derived from wheat, corn, rice and potato; and celluloses such as microcrystalline cellulose. The amount of diluent in the composition can range from about 10 to about 90% by weight of the total composition, preferably from about 25 to about 75%, more preferably from about 30 to about 60% by weight, even more preferably from about 12 to about 60%.

Disintegrant - refers to materials added to the composition to help it break apart (disintegrate) and release the medicaments. Suitable disintegrants include starches; "cold water soluble" modified starches such as sodium carboxymethyl starch; natural and synthetic gums such as locust bean, karaya, guar, tragacanth and agar; cellulose derivatives such as methylcellulose and sodium carboxymethylcellulose; microcrystalline

celluloses and cross-linked microcrystalline celluloses such as sodium croscarmellose; alginates such as alginic acid and sodium alginate; clays such as bentonites; and effervescent mixtures. The amount of disintegrant in the composition can range from about 2 to about 15% by weight of the composition, more preferably from about 4 to about 10% by weight.

Binder - refers to substances that bind or "glue" powders together and make them cohesive by forming granules, thus serving as the "adhesive" in the formulation. Binders add cohesive strength already available in the diluent or bulking agent. Suitable binders include sugars such as sucrose; starches derived from wheat, corn rice and potato; natural gums such as acacia, gelatin and tragacanth; derivatives of seaweed such as alginic acid, sodium alginate and ammonium calcium alginate; cellulosic materials such as methylcellulose and sodium carboxymethylcellulose and hydroxypropylmethylcellulose; polyvinylpyrrolidone; and inorganics such as magnesium aluminum silicate. The amount of binder in the composition can range from about 2 to about 20% by weight of the composition, more preferably from about 3 to about 10% by weight, even more preferably from about 3 to about 6% by weight.

Lubricant - refers to a substance added to the dosage form to enable the tablet, granules, etc. after it has been compressed, to release from the mold or die by reducing friction or wear. Suitable lubricants include metallic stearates such as magnesium stearate, calcium stearate or potassium stearate; stearic acid; high melting point waxes; and water soluble lubricants such as sodium chloride, sodium benzoate, sodium acetate, sodium oleate, polyethylene glycols and d,l-leucine. Lubricants are usually added at the very last step before compression, since they must be present on the surfaces of the granules and in between them and the parts of the tablet press. The amount of lubricant in the composition can range from about 0.2 to about 5%

by weight of the composition, preferably from about 0.5 to about 2%, more preferably from about 0.3 to about 1.5% by weight.

Glident - material that prevents caking and improve the flow characteristics of granulations, so that flow is smooth and uniform. Suitable
5 glidents include silicon dioxide and talc. The amount of glident in the composition can range from about 0.1% to about 5% by weight of the total composition, preferably from about 0.5 to about 2% by weight.

Coloring agents - excipients that provide coloration to the composition or the dosage form. Such excipients can include food grade dyes and food
10 grade dyes adsorbed onto a suitable adsorbent such as clay or aluminum oxide. The amount of the coloring agent can vary from about 0.1 to about 5% by weight of the composition, preferably from about 0.1 to about 1%.

Bioavailability - refers to the rate and extent to which the active drug ingredient or therapeutic moiety is absorbed into the systemic circulation from
15 an administered dosage form as compared to a standard or control.

Conventional methods for preparing tablets are known. Such methods include dry methods such as direct compression and compression of granulation produced by compaction, or wet methods or other special procedures. Conventional methods for making other forms for administration
20 such as, for example, capsules, suppositories and the like are also well known.

Another embodiment of the invention discloses the use of the inventive compounds or pharmaceutical compositions disclosed above for treatment of diseases such as, for example, hepatitis C and the like. The method
25 comprises administering a therapeutically effective amount of the inventive compound or pharmaceutical composition to a patient having such a disease or diseases and in need of such a treatment.

In yet another embodiment, the compounds of the invention may be used for the treatment of HCV in humans in monotherapy mode or in a combination therapy (e.g., dual combination, triple combination etc.) mode such as, for example, in combination with antiviral and/or immunomodulatory agents. Examples of such antiviral and/or immunomodulatory agents include Ribavirin (from Schering-Plough Corporation, Madison, New Jersey) and LevovirinTM (from ICN Pharmaceuticals, Costa Mesa, California), VP 50406TM (from Viropharma, Incorporated, Exton, Pennsylvania), ISIS 14803TM (from ISIS Pharmaceuticals, Carlsbad, California), HeptazymeTM (from Ribozyne Pharmaceuticals, Boulder, Colorado), VX 497TM (from Vertex Pharmaceuticals, Cambridge, Massachusetts), ThymosinTM (from SciClone Pharmaceuticals, San Mateo, California), MaxamineTM (Maxim Pharmaceuticals, San Diego, California), mycophenolate mofetil (from Hoffman-LaRoche, Nutley, New Jersey), interferon (such as, for example, interferon-alpha, PEG-interferon alpha conjugates) and the like. "PEG-interferon alpha conjugates" are interferon alpha molecules covalently attached to a PEG molecule. Illustrative PEG-interferon alpha conjugates include interferon alpha-2a (RoferonTM, from Hoffman La-Roche, Nutley, New Jersey) in the form of pegylated interferon alpha-2a (e.g., as sold under the trade name PegasysTM), interferon alpha-2b (IntronTM, from Schering-Plough Corporation) in the form of pegylated interferon alpha-2b (e.g., as sold under the trade name PEG-IntronTM), interferon alpha-2c (Berofer AlphaTM, from Boehringer Ingelheim, Ingelheim, Germany) or consensus interferon as defined by determination of a consensus sequence of naturally occurring interferon alphas (InfergenTM, from Amgen, Thousand Oaks, California).

As stated earlier, the invention includes tautomers, rotamers, enantiomers and other stereoisomers of the inventive compounds also. Thus, as one skilled in the art appreciates, some of the inventive compounds may

exist in suitable isomeric forms. Such variations are contemplated to be within the scope of the invention.

Another embodiment of the invention discloses a method of making the compounds disclosed herein. The compounds may be prepared by several techniques known in the art. Illustrative procedures are outlined in the following reaction schemes. The illustrations should not be construed to limit the scope of the invention which is defined in the appended claims. Alternative mechanistic pathways and analogous structures will be apparent to those skilled in the art.

It is to be understood that while the following illustrative schemes describe the preparation of a few representative inventive compounds, suitable substitution of any of both the natural and unnatural amino acids will result in the formation of the desired compounds based on such substitution. Such variations are contemplated to be within the scope of the invention.

For the procedures described below, the following abbreviations are used:

THF: Tetrahydrofuran
DMF: N,N-Dimethylformamide
EtOAc: Ethyl acetate
AcOH: Acetic acid
HOObt: 3-Hydroxy-1,2,3-benzotriazin-4(3H)-one
EDCI: 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
NMM: N-Methylmorpholine
ADDP: 1,1'-(Azodicarbonyl)dipiperidine
DEAD: Diethylazodicarboxylate
MeOH: Methanol
EtOH: Ethanol
Et₂O: Diethyl ether

DMSO: Dimethylsulfoxide

HOBt: N-Hydroxybenzotriazole

PyBrOP: Bromo-tris-pyrrolidinophosphonium hexafluorophosphate

DCM: Dichloromethane

5 DCC: 1,3-Dicyclohexylcarbodiimide

TEMPO: 2,2,6,6-Tetramethyl-1-piperidinyloxy

Phg: Phenylglycine

Chg: Cyclohexylglycine

Bn: Benzyl

10 Bzl: Benzyl

Et: Ethyl

Ph: Phenyl

DMF-DMA: N,N-Dimethylformamide-dimethylacetal

iBoc: isobutoxycarbonyl

15 iPr: isopropyl

^tBu or Bu^t: tert-Butyl

Boc: tert-Butyloxycarbonyl

Cbz: Benzyloxycarbonyl

Cp: Cyclopentylidienyl

20 Ts: p-toluenesulfonyl

Me: Methyl

HATU: O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium
hexafluorophosphate

DMAP: 4-N,N-Dimethylaminopyridine

25 BOP : Benzotriazol-1-yl-oxy-tris(dimethylamino)hexafluorophosphate

PCC: Pyridiniumchlorochromate

KHMDS: Potassium Hexamethyldisilazide or Potassium
bis(trimethylsilylamide)

NaHMDS: Sodium Hexamethyldisilazide or Sodium bis(trimethylsilylamide)

LiHMDS: Lithium Hexamethyldisilazide or Lithium bis(trimethylsilylamide)

10% Pd/C: 10% Palladium on carbon (by weight).

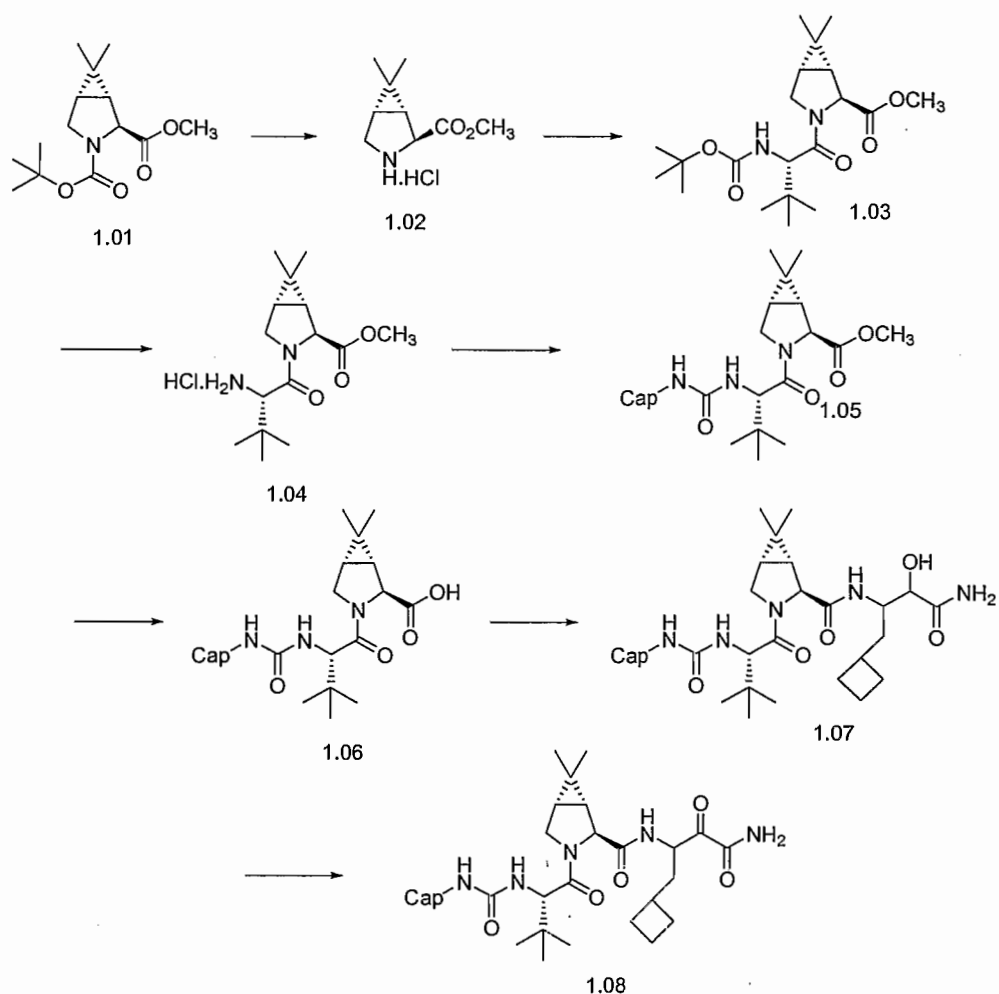
TG: Thioglycerol

5 **General Schemes for Preparation of Target Compounds**

Compounds of the present invention were synthesized using the general schemes (Methods A-E) described below.

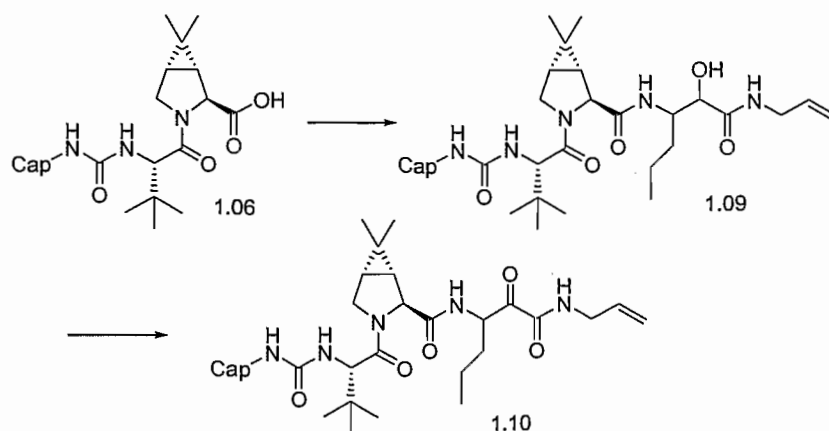
Method A

Deprotection of the N-Boc functionality of 1.01 under acidic conditions
10 provided the hydrochloride salt 1.02 which was subsequently coupled with N-Boc-tert-leucine under peptide coupling methodology to afford 1.03. N-Boc deprotection followed by treatment with appropriate isocyanate gave the urea 1.05. Hydrolysis of the methyl ester provided the acid 1.06. Peptide coupling
15 of the acid 1.06 with the appropriate P₁-P' primary amide moiety afforded the hydroxyl amide 1.07. Oxidation (Moffatt oxidation or related process – see, T. T. Tidwell, *Synthesis*, 1990, 857), or Dess-Martin Periodinane – *J. Org. Chem.*, (1983) 48, 4155) resulted in the target compound 1.08.



Method B

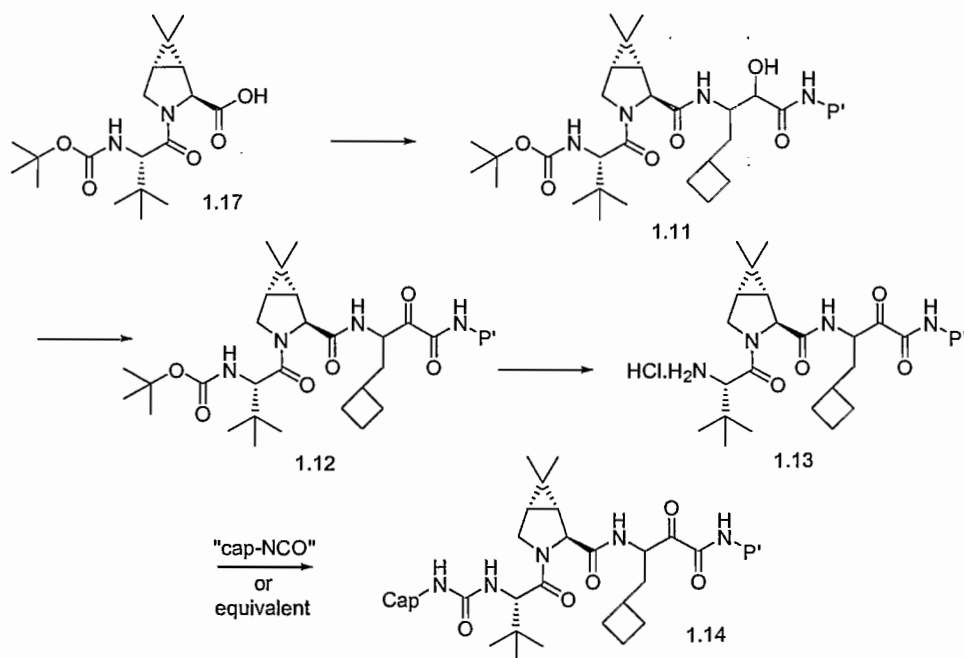
Peptide coupling of the acid 1.06 with the appropriate P₁-P' secondary
5 amide moiety afforded the hydroxyl amide 1.09. Oxidation (Moffatt or Dess-
Martin's) resulted in the target compound 1.10.



Method C

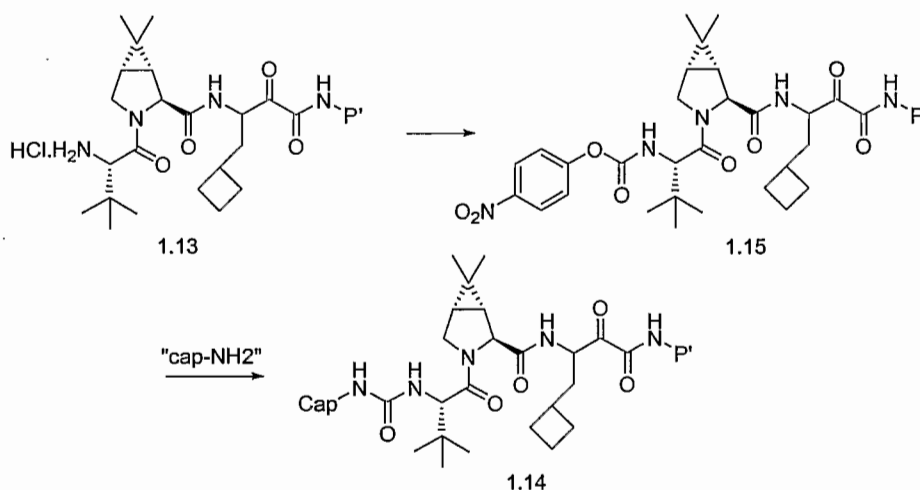
In another variation, peptide coupling of the N-Boc-P₂-P₃-acid 1.17 with the appropriate P₁-P' amide moiety afforded the hydroxyl amide 1.11.

- 5 Oxidation (Moffatt or Dess-Martin Periodinane) resulted in the keto amide 1.12. Deprotection of the N-Boc functionality gave the hydrochloride salt 1.13. Treatment with a suitable isocyanate (or isocyanate equivalent) resulted in the target compound 1.14.



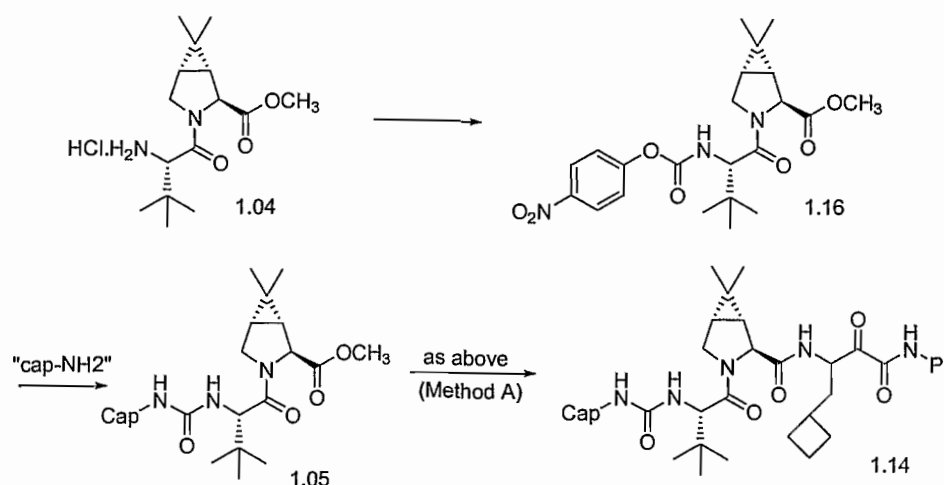
Method D

In yet another variation, the hydrochloride salt 1.13 was converted to the 4-nitrophenyl carbamate 1.15 by reaction with 4-nitrophenyl chloroformate. Subsequent treatment with an amine (or amine hydrochloride salt) of choice provided the target compound 1.14.



Method E

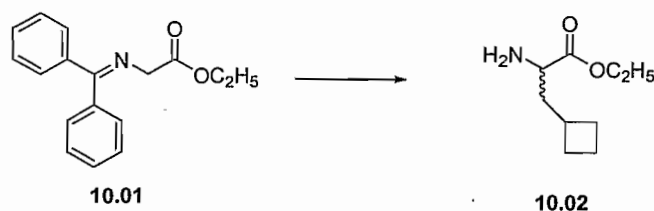
In yet another variation, the dipeptide hydrochloride salt 1.03 was converted to the 4-nitrophenyl carbamate as described above. Treatment with an amine (or amine hydrochloride salt) of choice provided the urea derivative 1.05. Hydrolysis and further elaboration as described in Methods A/B provided the target compounds 1.14.



Preparation of P1-P' moieties

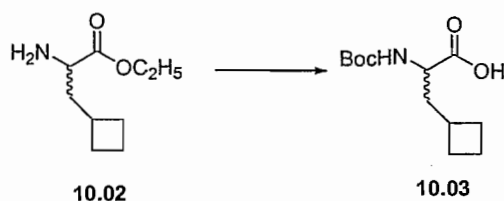
Preparation of Intermediates **10.11** and **10.12**

Step 1.



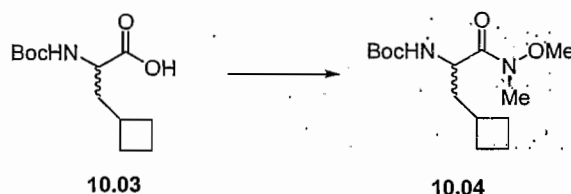
A stirred solution of ketimine **10.01** (50 g, 187.1 mmol) under N₂ in dry THF (400 mL) was cooled to -78 °C and treated with 1 M solution of K^tBuO (220 mL, 1.15 equiv.) in THF. The reaction mixture was warmed to 0 °C and stirred for 1 h and treated with bromomethyl cyclobutane (28 mL, 249 mmol). The reaction mixture was stirred at room temperature for 48 h and concentrated *in vacuo*. The residue was dissolved in Et₂O (300 mL) and treated with aq. HCl (2 M, 300 mL). The resulting solution was stirred at room temperature for 5 h and extracted with Et₂O (1 L). The aqueous layer was made basic to pH ~12-14 with NaOH (50 % aq.) and extracted with CH₂Cl₂ (3x300 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated to give the pure amine (**10.02**, 18 g) as a colorless oil.

Step 2.

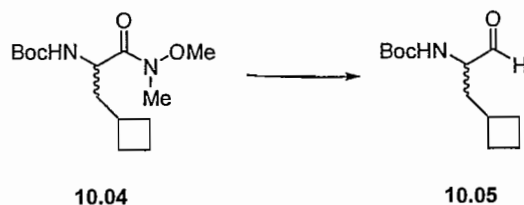


A solution of the amine **10.02** (18g, 105.2 mmol) at 0 °C in CH₂Cl₂ (350 mL) was treated with di-*tert*-butyldicarbonate (23 g, 105.4 mmol) and stirred at rt. for 12 h. After the completion of the reaction (TLC), the reaction mixture was concentrated in *vacuo* and the residue was dissolved in THF/H₂O (200 ml, 1:1) and treated with LiOH•H₂O (6.5 g, 158.5 mmol) and stirred at room temperature for 3 h. The reaction mixture was concentrated and the basic aqueous layer was extracted with Et₂O. The aqueous layer was acidified with conc. HCl to pH~1-2 and extracted with CH₂Cl₂. The combined organic layers were dried (MgSO₄), filtered, and concentrated *in vacuo* to yield **10.03** as a colorless viscous oil which was used for the next step without any further purification.

Step 3.

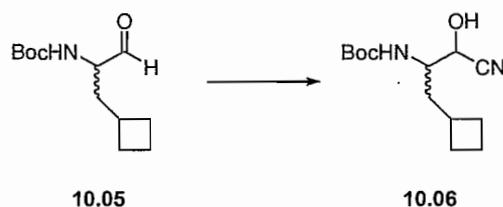


A solution of the acid **10.03** (15.0 g, 62 mmol) in CH₂Cl₂ (250 mL) was treated with BOP reagent (41.1 g, 93 mmol), N-methyl morpholine (27 mL), N,O-dimethyl hydroxylamine hydrochloride (9.07 g, 93 mmol) and stirred overnight at rt. The reaction mixture was diluted with 1 N aq. HCl (250 mL), and the layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3x300 ml). The combined organic layers were dried (MgSO₄), filtered and concentrated *in vacuo* and purified by chromatography (SiO₂, EtOAc/Hex 2:3) to yield the amide **10.04** (15.0 g) as a colorless solid.

Step 4.

A solution of the amide **10.04** (15 g, 52.1 mmol) in dry THF (200 mL) was treated dropwise with a solution of LiAlH₄ (1M, 93 mL, 93 mmol) at 0 °C.

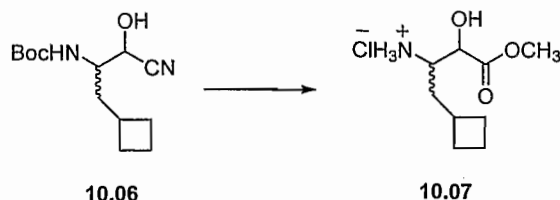
- 5 The reaction mixture was stirred at room temperature for 1 h and carefully quenched at 0 °C with a solution of KHSO₄ (10% aq.) and stirred for 0.5 h. The reaction mixture was diluted with aq. HCl (1 M, 150 mL) and extracted with CH₂Cl₂ (3x200 mL). The combined organic layers were washed with aq. HCl (1 M), saturated NaHCO₃, brine, and dried (MgSO₄). The mixture was
- 10 filtered and concentrated *in vacuo* to yield **10.05** as a viscous colorless oil (14 g).

Step 5:

- A solution of the aldehyde **10.05** (14 g, 61.6 mmol) in CH₂Cl₂ (50 mL),
- 15 was treated with Et₃N (10.73 mL, 74.4 mmol), and acetone cyanohydrin (10.86 g, 127.57 mmol) and stirred at room temperature for 24 hrs. The reaction mixture was concentrated *in vacuo* and diluted with aq. HCl (1 M, 200 mL) and extracted into CH₂Cl₂ (3x200 mL). The combined organic layer were washed with H₂O, brine, dried (MgSO₄), filtered, concentrated *in vacuo* and
- 20 purified by chromatography (SiO₂, EtOAc/Hex 1:4) to yield **10.06** (10.3 g) as a colorless liquid

Step 6.

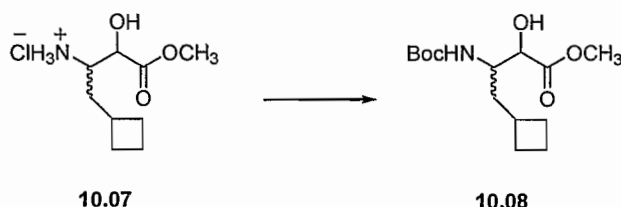
101



Methanol saturated with HCl*, prepared by bubbling HCl gas through CH₃OH (700 ml) at 0 °C, was treated with the cyanohydrin **10.06** and heated to reflux for 24 h. The reaction was concentrated *in vacuo* to yield **10.07**, which was used in the next step without purification.

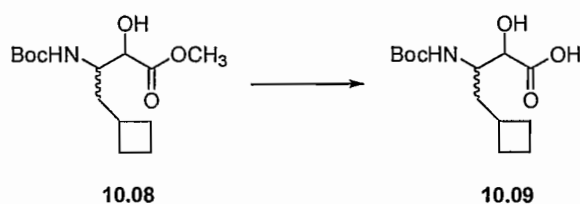
* Alternatively 6M HCl prepared by addition of AcCl to dry methanol can also be used.

Step 7.



A solution of the amine hydrochloride **10.07** in CH₂Cl₂ (200 mL) was treated with Et₃N (45.0 mL, 315 mmol) and Boc₂O (45.7g, 209 mmol) at -78 °C. The reaction mixture was then stirred at room temperature overnight and diluted with HCl (2 M, 200 mL) and extracted into CH₂Cl₂. The combined organic layers were dried (MgSO₄) filtered, concentrated *in vacuo* and purified by chromatography (EtOAc/Hex 1:4) to yield hydroxy ester **10.08**.

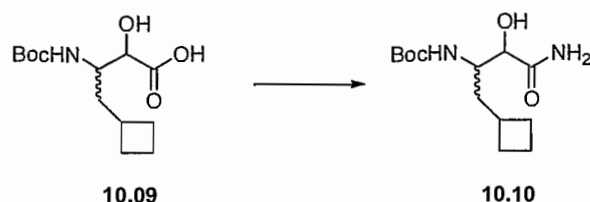
Step 8.



A solution of methyl ester **10.08** (3g, 10.5 mmol) in THF/H₂O (1:1) was treated with LiOH•H₂O (645 mg, 15.75 mmol) and stirred at rt. for 2 h. The

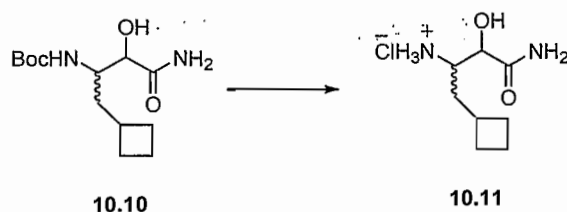
reaction mixture was acidified with aq HCl (1 M, 15 mL) and concentrated *in vacuo*. The residue was dried in vacuum to afford **10.09** in quantitative yield.

Step 9



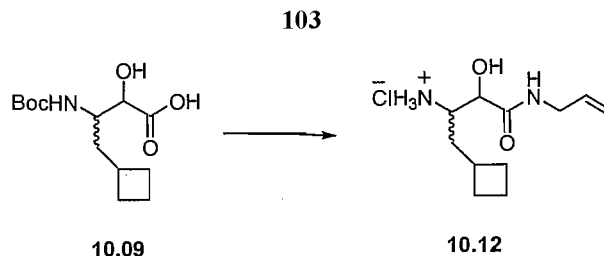
- 5 A solution of the acid **10.09** (from above) in CH₂Cl₂ (50 mL) and DMF (25 mL) was treated with NH₄Cl (2.94 g, 55.5 mmol), EDCI (3.15 g, 16.5 mmol), HOObt (2.69 g, 16.5 mmol), and NMM (4.4 g, 44 mmol). The reaction mixture was stirred at room temperature for 3 d. The solvents were removed under *vacuo* and the residue was diluted with aq. HCl (250 mL) and extracted
- 10 with CH₂Cl₂. The combined organic layers were washed with aq. saturated NaHCO₃, dried (MgSO₄) filtered concentrated in *vacuo* to obtain **10.10**, which was used as it was in the following steps. (Alternatively **10.10** can also be obtained directly by the reaction of **10.06** (4.5 g, 17.7 mmol) with aq. H₂O₂ (10 mL), LiOH•H₂O (820 mg, 20.8 mmol) at 0 °C in 50 mL of CH₃OH for 0.5 h.).

15 Step 10.



- A solution of **10.10** obtained in the previous step was dissolved in 4 N HCl in dioxane and stirred at rt. for 2 h. The reaction mixture was concentrated in *vacuo* to give the intermediate **10.11** as a solid, which was
- 20 used without further purification.

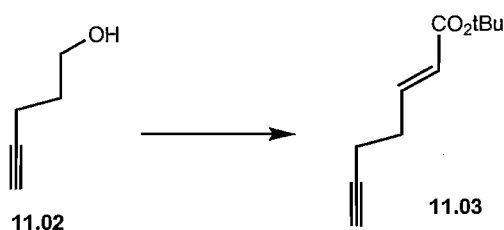
Step 11.



The required intermediate **10.12** was obtained from compound **10.09** using essentially the procedures described above in Steps 9, 10 with appropriate reagents.

5 Preparation of Intermediate 11.01

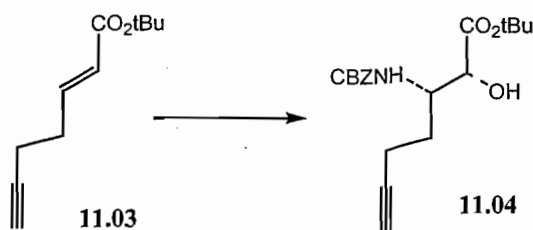
Step 1



To a solution of 4-pentyn-1-ol, **11.02** (4.15g; Aldrich) was added Dess-Martin Periodinane (30.25g; Aldrich) and the resulting mixture was stirred for 45min. before the addition of (tert-

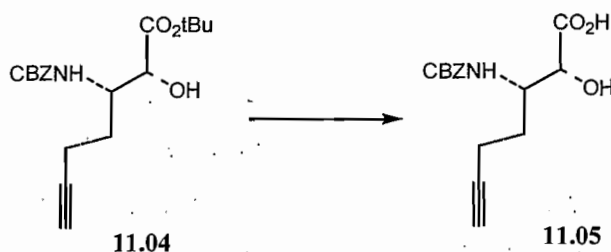
Butoxycarbonylmethylene)triphenylphosphorane (26.75g; Aldrich). The resulting dark reaction was stirred overnight, diluted with EtOAc), washed with aq. sodium sulfite. sat. aq. NaHCO₃, water, brine and dried. The volatiles were removed under reduced pressure and the residue was purified by silica gel column chromatography using 1% EtOAc in hexanes as eluent to give the desired compound, **11.03** (3.92g). Some impure fractions were also obtained but set aside at this time.

Step 2



Using the alkene **11.03** (1.9g) in n-propanol (20ml; Aldrich)), benzyl carbamate (4.95g; Aldrich) in n-propanol (40ml), NaOH (1.29g) in water (79ml), tert-butyl hypochlorite (3.7ml), (DHQ)2PHAL (0.423g; Aldrich)) in n-propanol (37.5ml), and potassium osmate:dehydrate (0.1544g; Aldrich) and the procedure set forth in *Angew. Chem. Int. Ed. Engl* (1998), 35, (23/24), pp. 2813-7, gave a crude product which was purified by silica gel column chromatography using EtOAc:Hexanes (1:5) to give the desired amino alcohol **11.04** (1.37g, 37%) as a white solid.

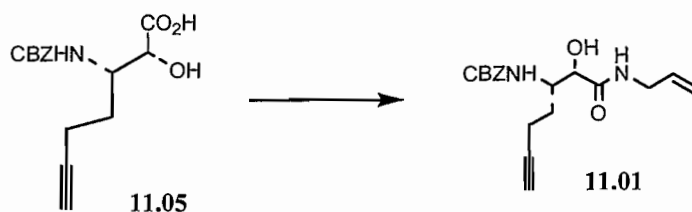
10 **Step 3**



To the ester **11.04** (0.700g) was added 4M HCl in dioxane (20ml; Aldrich) and the resulting mixture was allowed to stand at room temperature overnight. The volatiles were removed under reduced pressure to give the acid **11.05** (0.621g) as a white solid.

15

Step 4



BOP reagent (3.65g; Sigma) followed by triethylamine (3.45ml) were added to a dichloromethane (20ml) solution of the carboxylic acid **11.05** (2.00g) and allyl amine (0.616ml) at room temperature and the resulting mixture was stirred overnight. The reaction mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (magnesium sulfate). The crude reaction product was purified by silica gel column chromatography using (EtOAc:Hexanes; 70:30) as eluent to provide the desired amide **11.01** (1.73g) as a viscous yellow oil.

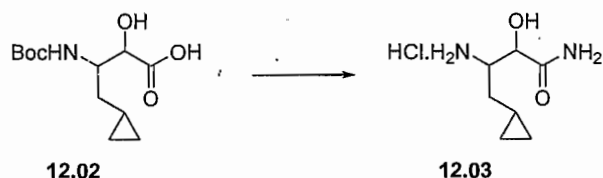
10 Preparation of Intermediates **12.03** and **12.04**

Step 1



Compound **12.01** was converted to the required material **12.02** using essentially the procedures described for Intermediate **10.11**, Steps 3-8.

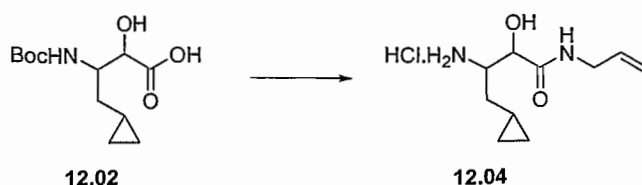
15 Step 2



Compound **12.02** was converted to the required intermediate **12.03** using essentially the procedures described for Intermediate **10.11**, Steps 9, 10.

20 Step 3

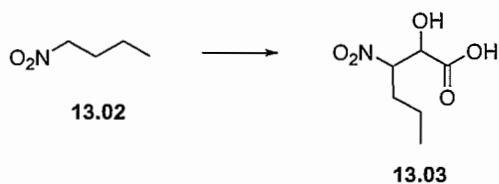
106



Compound **12.02** was converted to the required intermediate **12.03** using essentially the procedures described for Intermediate **10.12**, Step 11.

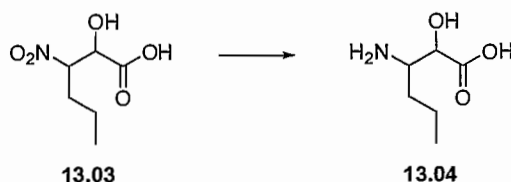
Preparation of Intermediate 13.01

5 Step 1



To a stirred solution of 1-nitrobutane, **13.02** (16.5 g, 0.16 mol) and glyoxylic acid in H₂O (28.1 g, 0.305 mol) and MeOH (122 mL) at 0°C-5°C, was added dropwise triethylamine (93 mL, 0.667 mol) over 2 hrs. The solution was warmed to room temperature, stirred overnight and concentrated to dryness to give an oil. The oil was then dissolved in H₂O and acidified to pH =1 with 10% HCl, followed by extraction with EtOAc. The combined organic solution was washed with brine, dried over Na₂SO₄, filtered and concentrated to dryness to give the product **13.03** (28.1 g, 99% yield).

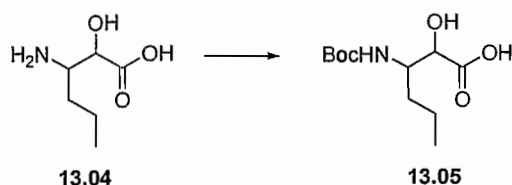
15 Step 2



To a stirred solution of compound **13.03** (240 g, 1.35 mol) in acetic acid (1.25 L) was added 10% Pd/C (37 g). The resulting solution was hydrogenated at 59 psi for 3 hrs and then at 60 psi overnight. The acetic acid was then evaporated and azeotroped 3 times with toluene, then triturated with

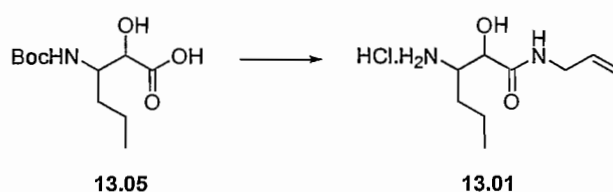
MeOH and ether. The solution was then filtered and azeotroped twice with toluene to afford **13.04** as an off white solid (131 g, 0.891 mol, 66%).

Step 3



- 5 To a stirred solution of the amino acid **13.04** (2.0 g, 13.6 mmol) in dioxane (10 mL) and H₂O (5mL) at 0°C, was added 1N NaOH solution (4.3 mL, 14.0 mmol). The resulting solution was stirred for 10 minutes, followed by addition of di-*t*-butyldicarbonate (0.110 g, 14.0 mmol) and stirred at 0°C for 15 minutes. The solution was then warmed to room temperature, stirred for 45
- 10 minutes and kept at refrigerator overnight and concentrated to dryness to give a crude material. To the solution of this crude material in EtOAc (100 mL) and ice, was added KHSO₄ (3.36 g) and H₂O (32 mL) and stirred for 4-6 minutes. The organic layer was then separated and the aqueous layer was extracted twice with EtOAc and the combined organic layer was washed with water,
- 15 brine, dried over Na₂SO₄, filtered and concentrated to dryness to give the product **13.05** as a clear gum (3.0 g, 89% yield).

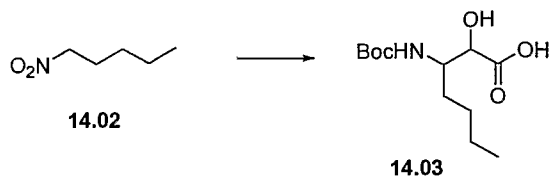
Step 4



- Compound **13.05** was converted to the required intermediate **13.01**
- 20 using essentially the procedures described for Intermediate **10.12**, Step 11.

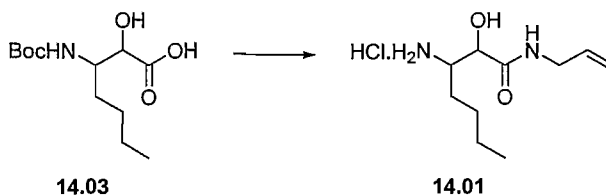
Preparation of Intermediate **14.01**

Step 1



Compound **14.02** was converted to the required material **14.03** using essentially the procedures described for Intermediate **13.01**, Steps 1-3.

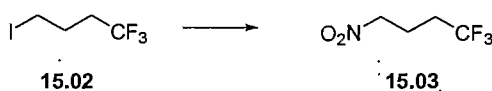
Step 2



Compound **14.03** was converted to the required intermediate **14.01** using essentially the procedures described for Intermediate **10.12**, Step 11.

Preparation of Intermediate 15.01

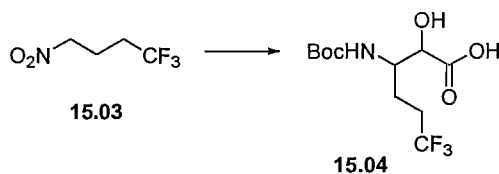
Step 1



To a suspension of silver nitrite (9 g, 58.5 mmol) in diethyl ether (25 mL) at 0°C was added a solution of 4-iodo-1,1,1-trifluorobutane, **15.02** (10 g, 42.0 mmol) in diethyl ether (25 mL) slowly through an addition funnel (approx. 15 min). The resulting mixture was vigorously stirred at 0°C and warmed to rt.

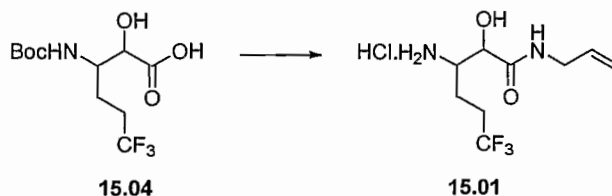
After 50 h, the solid material was filtered off through a celite pad. The resulting diethyl ether solution was concentrated *in vacuo* to give **15.03** as colorless oil, which was used without further purification.

Step 2



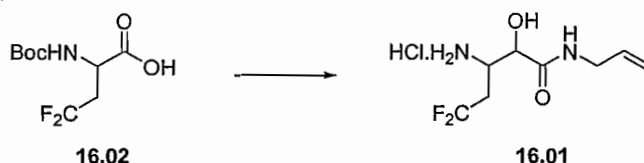
Compound **15.03** was converted to the required material **15.04** using essentially the procedures described for Intermediate **13.01**, Steps 1-3.

Step 3



Compound **15.04** was converted to the required intermediate **15.01** using essentially the procedures described for Intermediate **10.12**, Step 11.

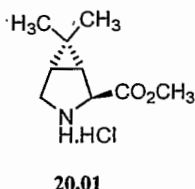
Preparation of Intermediate **16.01**



The acid **16.02** (Winkler, D.; Burger, K., *Synthesis*, **1996**, 1419) is processed as described above (preparation of Intermediate **10.12**) to give the expected intermediate **16.01**

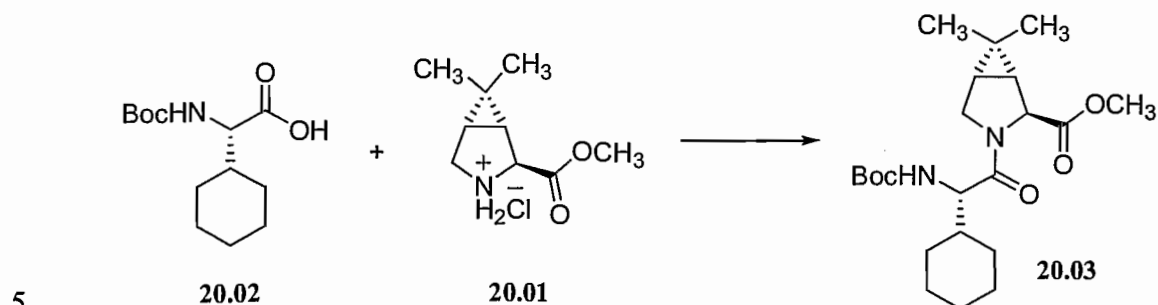
PREPARATION OF P2 / P3-P2 MOIETIES

Preparation of Intermediate **20.01**



The amino ester **20.01** was prepared following the method of R. Zhang and J. S. Madalenoitia (*J. Org. Chem.* **1999**, 64, 330), with the exception that the Boc group was cleaved by the reaction of the Boc-protected amino acid with methanolic HCl.

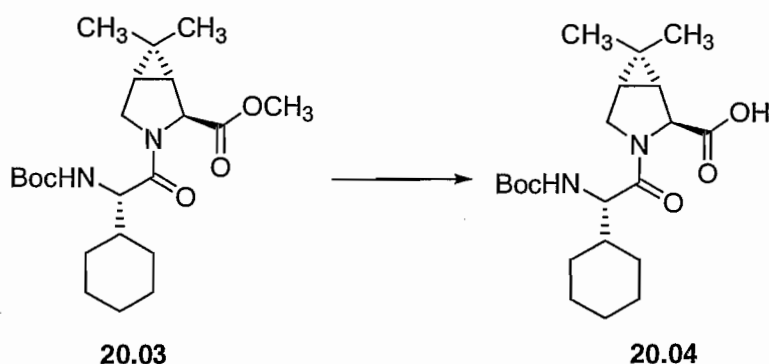
(Note: In a variation of the reported synthesis, the sulfonium ylide was replaced with the corresponding phosphonium ylide).

Preparation of Intermediate 20.04Step 1

A solution of commercial amino acid Boc-Chg-OH, **20.02** (Senn chemicals, 6.64 g, 24.1 mmol) and amine hydrochloride **20.01** (4.5 g, 22 mmol) in CH_2Cl_2 (100 mL) at 0 °C was treated with BOP reagent and stirred at rt. for 15 h. The reaction mixture was concentrated *in vacuo*, then it was
10 diluted with aq. 1 M HCl and extracted into EtOAc (3x200 mL). The combined organic layers were washed with saturated NaHCO_3 (200 mL), dried (MgSO_4), filtered and concentrated *in vacuo*, and chromatographed (SiO_2 , EtOAc/Hex 3:7) to obtain **20.03** (6.0 g) as a colorless solid.

Step 2

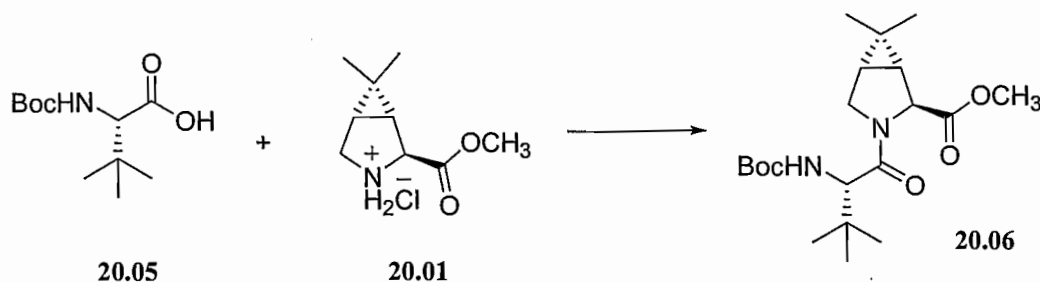
15



A solution of methyl ester **20.03** (4.0 g, 9.79 mmol) in THF/H₂O (1:1) was treated with LiOH•H₂O (401 mg, 9.79 mmol) and stirred at rt. for 3 h. The reaction mixture was acidified with aq. HCl and concentrated *in vacuo* to obtain the required intermediate, free acid **20.04**.

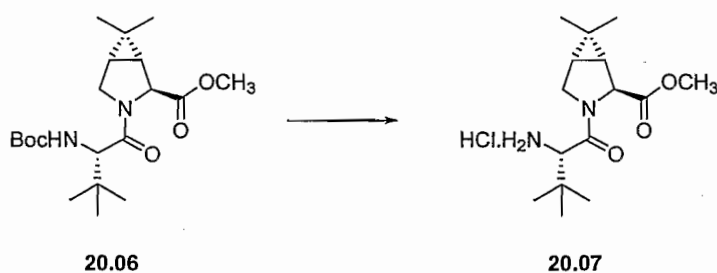
5 Preparation of Intermediate **20.07**

Step 1



- 10 A solution of Boc-tert-Leu **20.05** (Fluka, 5.0 g 21.6 mmol) in dry CH₂Cl₂/DMF (50 mL, 1:1) was cooled to 0 °C and treated with the amine salt **20.01** (5.3 g, 25.7 mmol), NMM (6.5 g, 64.8 mmol) and BOP reagent (11.6 g, 25.7 mmol). The reaction was stirred at rt. for 24h, diluted with aq. HCl (1 M) and extracted with CH₂Cl₂. The combined organic layers were washed with
- 15 HCl (aq, 1 M), saturated NaHCO₃, brine, dried (MgSO₄), filtered and concentrated *in vacuo* and purified by chromatography (SiO₂, Acetone/Hexane 1:5) to yield **20.06** as a colorless solid.

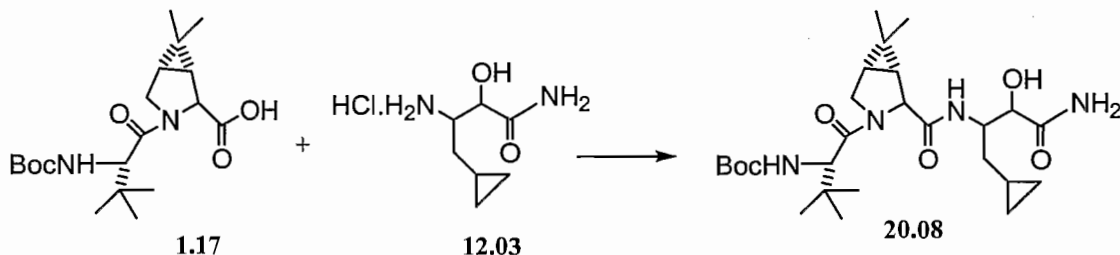
Step 2



A solution of methyl ester **20.06** (4.0 g, 10.46 mmol) was dissolved in 4M HCl in dioxane and stirred at rt. for 3 h. The reaction mixture was concentrated in *vacuo* to obtain the amine hydrochloride salt, **20.07** which was used without purification.

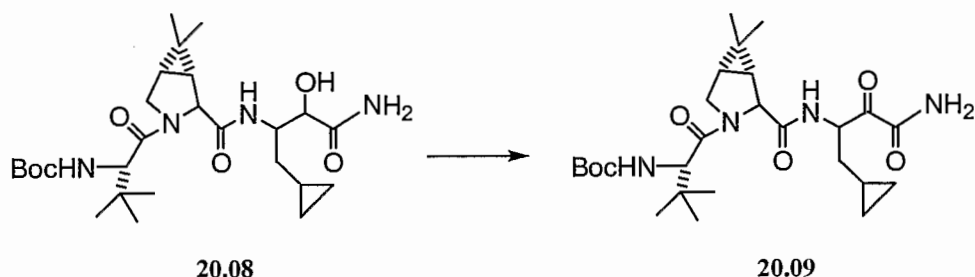
5 Preparation of Intermediate 20.10

Step 1

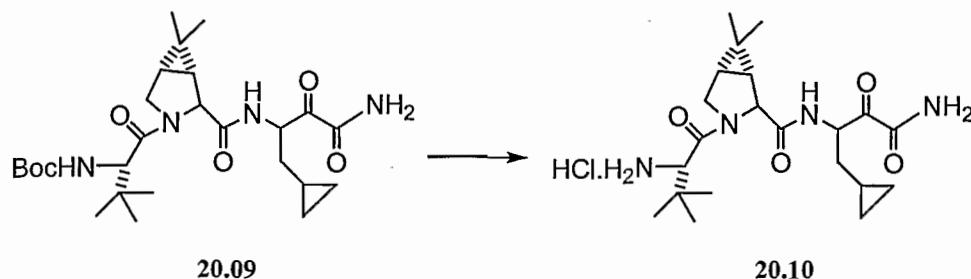


To a -20°C solution **1.17** (10.4 g, 28 mmol) in DCM (300 mL) was added HATU (1.05 equiv, 29.4mmol, 11.2g), amine salt, Intermediate **12.03** (1.0 equiv, 28 mmol, 5.48 g). After 10 min at -20°C, DIPEA (3.6 equiv, 100 mmol, 17.4 mL) was added. Reaction was stirred at this temp for 16 hr. After 16 hr, the reaction was diluted with EtOAc and washed successively with NaHCO₃, citric acid (10% w/w) and brine. Organic layer was dried over
15 MgSO₄, filtered and concentrated *in vacuo* to yield 14 g of the required intermediate **20.08**.

Step 2



The hydroxyamide **20.08** was oxidized to the required ketoamide **20.09**
20 in a manner described for Example **198 (Step 8)**. LC-MS = 507 (M+H)⁺.

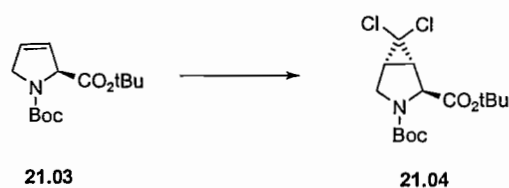
Step 3

Deprotection of the t-Boc functionality of **20.09** to give the required material **20.10** was carried out as described for the transformation of **20.06** to **20.07**.

Preparation of Intermediate **21.01**:

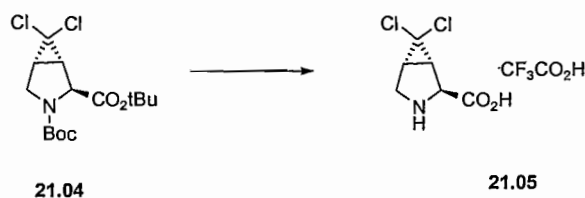
Step 1:

To a stirred solution of *N*-Boc-3,4-dehydroproline **21.02** (5.0 g, 23.5 mmol), di-*tert*-butyl dicarbonate (7.5 g, 34.4 mmol), and 4-*N,N*-dimethylaminopyridine (0.40 g, 3.33 mmol) in acetonitrile (100 mL) at room temperature was added triethylamine (5.0 mL, 35.6 mmol). The resulting solution was stirred at this temperature for 18 h before it was concentrated *in vacuo*. The dark brown residue was purified by flash column chromatography eluting with 10-25% EtOAc/hexane to give the product **21.03** as a pale yellow oil (5.29 g, 84%).

Step 2:

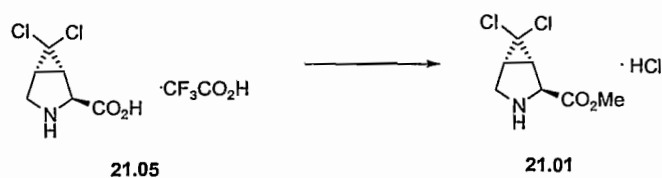
To a stirred solution of the dehydropyrroline derivative **21.03** (10.1 g, 37.4 mmol), benzyltriethylammonium chloride (1.60 g, 7.02 mmol) in chloroform (120 mL) at room temperature was added 50% aqueous sodium hydroxide (120 g). After vigorously stirred at this temperature for 24 h, the dark mixture was diluted with CH₂Cl₂ (200 mL) and diethyl ether (600 mL). After the layers were separated, the aqueous solution was extracted with CH₂Cl₂/Et₂O (1:2, 3x600 mL). The organic solution was dried (MgSO₄) and concentrated. The residue was purified by flash column chromatography using 5-20% EtOAc/hexane to afford 9.34 g (71%) of **21.04** as an off-white solid.

Step 3:



The solution of **21.04** (9.34 g, 26.5 mmol) in CH₂Cl₂ (25 mL) and CF₃CO₂H (50 mL) was stirred at room temperature for 4.5 h before it was concentrated *in vacuo* to give a brown residue, **21.05** which was used in Step 4 without further purification.

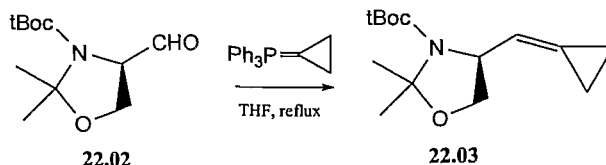
Step 4



Concentrated hydrochloric acid (4.5 mL) was added to a solution of the residue **21.05** from Step 3 in methanol (70 mL) and the resulting mixture was warmed to 65°C in an oil bath. After 18 h, the mixture was concentrated *in vacuo* to give a brown oil **21.01**, which was used further without purification.

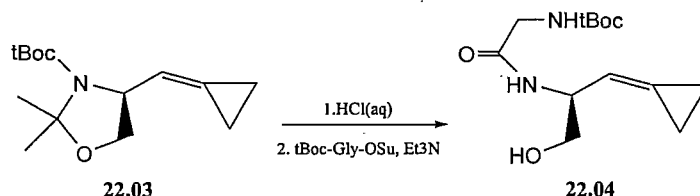
Preparation of Intermediate **22.01**

Step 1



- Potassium bis(trimethylsilyl)amide (158ml of a 0.5M solution in toluene; 79mmol) was added to a stirred suspension of cyclopropyltriphenylphosphonium bromide (33.12g; 86.4mmol) in anhydrous tetrahydrofuran (130ml) and the resulting orange mixture was stirred under an atmosphere of nitrogen at room temperature for a period of 1h., before the addition of the aldehyde **22.02** (9.68g; 42.2mmol) in THF (8ml). The reaction was then refluxed under an atmosphere of nitrogen for a period of 2h. After cooling, methanol, diethyl ether and Rochelles salt were added. The organic phase was separated, washed with brine, dried and concentrated under reduced pressure. The crude reaction product was purified by silica gel column chromatography using EtOAc-hexane (1:99) to EtOAc-hexane (5:95) to provide the alkene **22.03** (8.47g) as a yellow oil.

Step 2



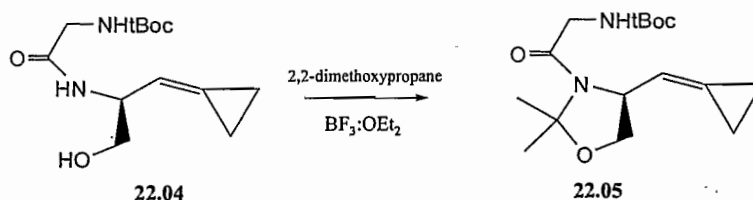
- A solution of 1M HCl in MeOH/MeOAc was prepared by adding 14.2ml of acetyl chloride dropwise into cold methanol and diluting the resulting solution to 200ml at room temperature.

The carbamate **22.03** (9.49g; 37.5mmol) was dissolved in methanol (12ml) and added to 1M HCl in MeOH/MeOAc (150ml) while cooled in an ice bath. The resulting mixture was maintained at this temperature for 1h., then

the ice bath was removed and stirring continued overnight at room temperature. The volatiles were removed under reduced pressure to yield a yellow oil which was used in the next step without purification.

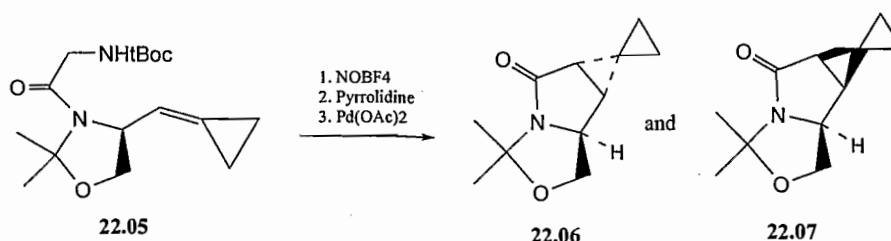
The yellow oil was dissolved in a mixture of THF (30ml) and MeOH (20ml) and treated with triethylamine (15ml; 108mmol) until the solution was pH=9-10. After placing in an ice bath, the mixture was treated with N-Boc-Gly-OSu (11.22g; 41mmol). The ice bath was withdrawn and the reaction stirred at room temp. for 1h. The volatiles were removed under reduced pressure and the residue was purified by silica gel column chromatography using methanol (1-3%) in dichloromethane providing the desired amide **22.04** (9.09g).

Step 3



The alcohol **22.04** (9.09g; 33.6mmol) was dissolved in acetone (118.5ml) and treated with 2,2-dimethoxypropane (37.4ml; 304mmol) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (0.32ml; 2.6mmol) and the resulting mixture was stirred at room temperature for a period of 5.5h. The reaction solution was treated with a few drops of triethylamine and the volatiles were removed under reduced pressure. The residue was purified by silica gel column chromatography using 5-25% EtOAc in hexanes to provide the N,O-acetal **22.05** (8.85g).

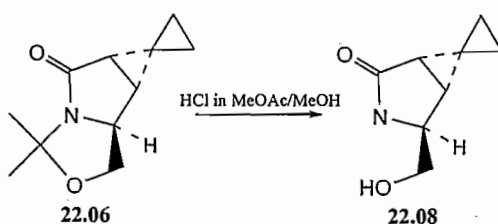
Step 4



The carbamate **22.05** (8.81g; 28.4mmol) was dissolved in acetonitrile (45ml) and the solution was cooled to -40°C under an atmosphere of nitrogen. Pyridine (6.9ml; 85.3mmol) followed by nitrosium tetrafluoroborate (6.63g; 56.8mmol) were added and the resulting reaction mixture maintained below 0°C until TLC indicated that no starting material remained (approx. 2.25h.). Pyrrolidine (20ml; 240mmol) was added and the cooling bath was withdrawn and stirring was continued at room temperature for 1h. and then the volatiles were removed under reduced pressure. The residue was quickly passed through a pad of silica gel to provide a yellow oil.

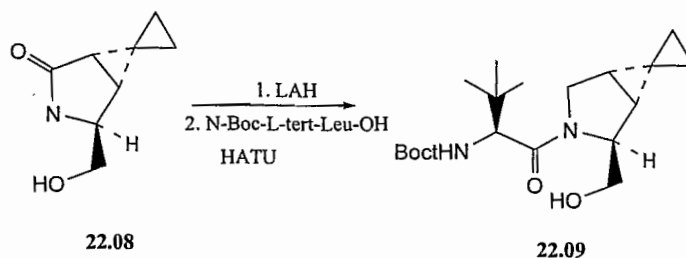
The yellow oil was dissolved in anhydrous benzene (220ml) and palladium acetate (0.317g; 1.41mmol) was added before heating the resulting mixture to reflux, under an atmosphere of nitrogen for a period of 1.5h. After cooling, the volatiles were removed under reduced pressure and the dark residue was purified by silica gel column chromatography using EtOAc-hexane (1:4) to provide the i) the trans- pyrrolidinone **22.06** (1.94g) followed by ii) the cis-pyrrolidinone **22.07** (1.97g).

Step 5



Freshly prepared 1M HCl in MeOAc/MeOH (10ml; as described above) was added to the N,O-acetal **22.06** and stirred at room temperature for 1h. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography using 0-4%MeOH in dichloromethane as eluent to provide the desired alcohol **22.08** (1.42g), a yellow oil.

Step 6

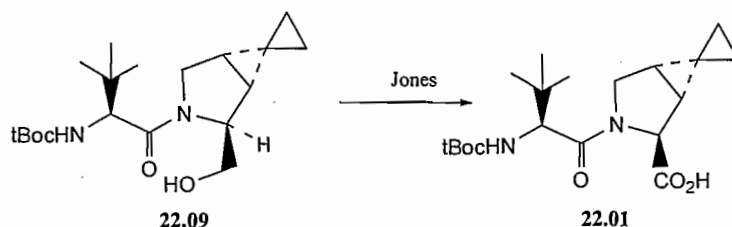


To a solution of the lactam **22.08** (1.29g; 8.44mmol) in anhydrous tetrahydrofuran (55ml) was added lithium aluminum hydride (2.40g; 63.2mmol) and the resulting mixture was refluxed for 8h. After cooling, water, followed by 15% aq. NaOH were added and the resulting mixture was filtered through celite and the solid was washed thoroughly with THF and MeOH. The solvent was removed under reduced pressure and the residue redissolved in dichloromethane, dried and concentrated under reduced pressure to provide the pyrrolidine, used without purification.

Hunigs base (4.5ml; 25.8mmol) was added to a mixture of N-Boc-L-tert-Leu-OH (1.76g; 7.6mmol), The crude pyrrolidine and HATU (2.89g; 7.6mmol) in anhydrous dichloromethane (50ml) at -60°C , under an atmosphere of nitrogen. The resulting reaction was allowed to come to room temperature slowly, overnight. EtOAc was added and the yellow solution was washed with dil. aq. HCl, sat. aq. sodium bicarbonate, water, brine. The organic layer was dried and concentrated under reduced pressure. The

residue was purified by silica gel column chromatography using EtOAc:hexanes (1:3) to give the desired amide **22.09** (2.00g).

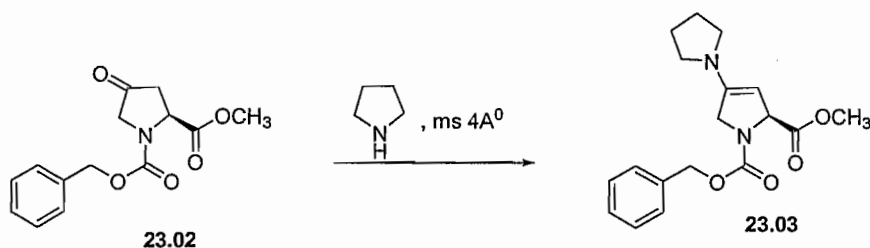
Step 7



- 5 The alcohol **22.09** (2.00g; 5.67mmol) was dissolved in acetone (116ml) and cooled in an ice bath for 10min. This solution was then added to a cooled Jones reagent (14.2ml; approx 2mmol/ml) and the resulting mixture was stirred at 5°C for 0.5h and the cooling bath was removed. The reaction was stirred for a further 2h. at room temp., before adding to sodium sulfate
- 10 (28.54g), celite (15g) in EtOAc (100ml). Isopropanol (15ml) was added after 1min and then stirred for a further 10min. and filtered. The filtrate was concentrated under reduced pressure, providing a brown oil which was dissolved in EtOAc. This solution was washed with water, 3% aq. citric acid, brine, dried and concentrated to provide the desired carboxylic acid **22.01**
- 15 (1.64g) as a white solid.

Preparation of Intermediate **23.01**

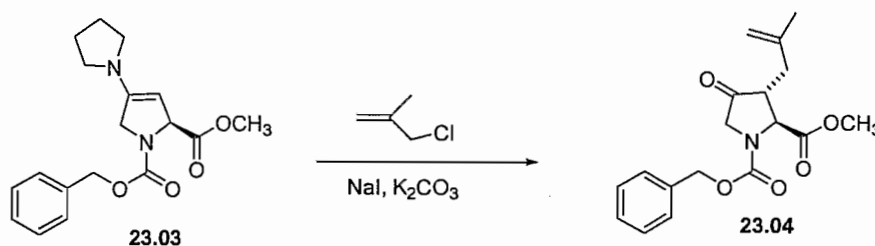
Step 1:



- 20 To the mixture of ester **23.02** (6.0g) and molecular sieve (5.2g) in anhydrous methylene chloride (35 mL) was added pyrrolidine (5.7 mL, 66.36 mmol). The resulting brown slurry was stirred at room temperature under N₂

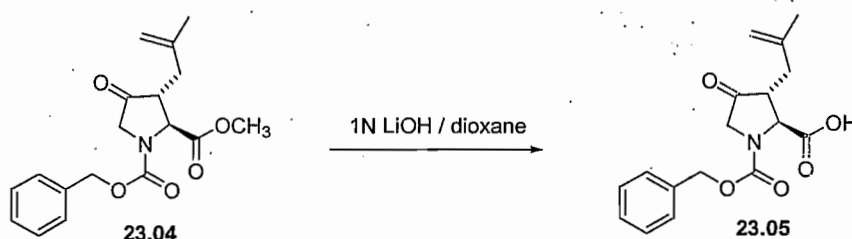
for 24 h, filtered and washed with anhydrous CH_3CN . The combined filtrate was concentrated to yield the desired product, **23.03**.

Step 2:

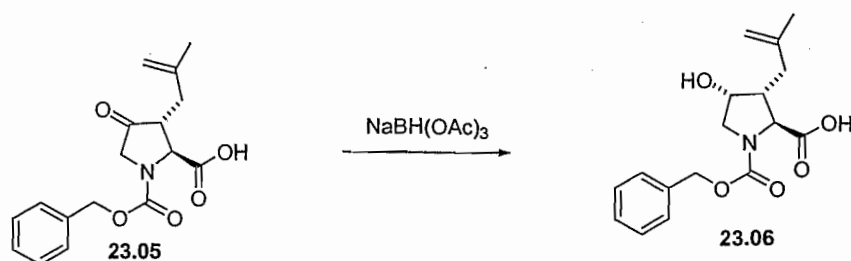


To a solution of the product **23.03** from proceeding step in CH_3CN (35 mL) was added anhydrous K_2CO_3 , methallyl chloride (2.77g, 30.5 mmol), NaI (1.07g, 6.7 mmol). The resulting slurry was stirred at ambient temperature under N_2 for 24 h. 50 mL of ice-cold water was added followed by 2N KHSO_4 solution until pH was 1. EtOAc (100 mL) was added and the mixture was stirred for 0.75h. Combined organic layer was collected and washed with brine, dried over MgSO_4 , and evaporated to yield the desired product, **23.04**.

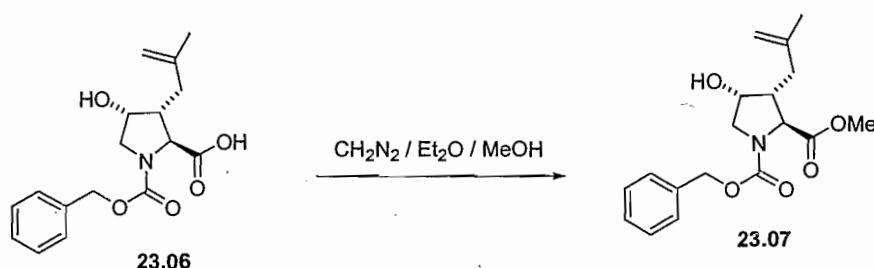
Step 3:



The product **23.04** from the preceding step (2.7 g, 8.16 mmol) was dissolved in dioxane (20 mL) and treated with freshly prepared 1N LiOH (9 mL). The reaction mixture was stirred at ambient temperature under N_2 for 20 h. The reaction mixture was taken in EtOAc and washed with H_2O . The combined aqueous phase was cooled to 0°C and acidified to pH 1.65 using 1N HCl. The turbid mixture was extracted with EtOAc (2 x 100 mL). Combined organic layer was washed with brine, dried over MgSO_4 , and concentrated to give the desired acid, **23.05** (3.40 g).

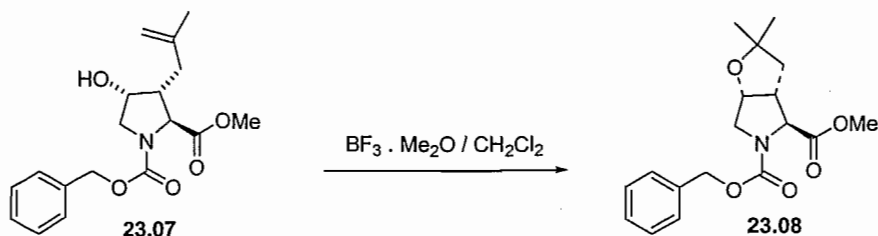
Step 4:

To a suspension of $\text{NaBH}(\text{OAc})_3$ (3.93g, 18.5 mmol) in CH_2Cl_2 (55 mL) was added a solution of product **23.05** from preceding step in anhydrous CH_2Cl_2 (20 mL) and acetic acid (2 mL). The slurry was stirred at ambient temperature for 20 h. Ice cold water (100 mL) was added to the slurry and stirred for 1/2 hr. Organic layer was separated, filtered, dried and evaporated to yield the desired product, **23.06**.

Step 5:

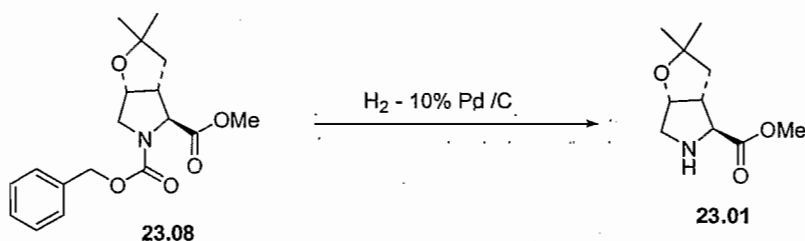
To a solution of the product **23.06** from preceding step (1.9g) in MeOH (40 mL) was treated with excess of CH_2N_2 / Et_2O solution and stirred for overnight. The reaction mixture was concentrated to dryness to yield a crude residue. The residue was chromatographed on silica gel, eluting with a gradient of EtOAc / hexane to afford 1.07 g of the pure desired product, **23.07**.

Step 6:



To a solution of product **23.07** from preceding step (1.36 g) in anhydrous CH_2Cl_2 (40 mL) was treated with $\text{BF}_3 \cdot \text{Me}_2\text{O}$ (0.7 mL). The reaction mixture was stirred at ambient temperature for 20 h and quenched with sat. NaHCO_3 (30 mL) and stirred for 1/2 hr. Organic layer was separated and combined organic layer was washed with brine, dried over MgSO_4 , concentrated to give crude residue. The residue was chromatographed on silica gel eluting with a gradient of EtOAc / hexane to afford 0.88 g of the desired compound, **23.08**.

10 Step 7:



To a solution of the product **23.08** (0.92 g) from preceding step in MeOH (30 mL) was added 10 % Pd/C (0.16 g) at room temperature and hydrogenated at ambient temperature under 1 atm. Pressure. The reaction mixture was stirred for 4 h and concentrated to dryness to yield the desired compound, **23.01**.

PREPARATION OF P3 MOIETIES

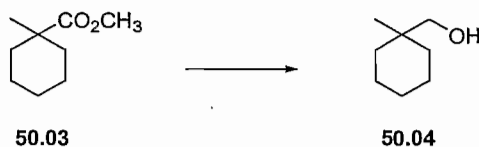
Preparation of Intermediate 50.01

Step 1



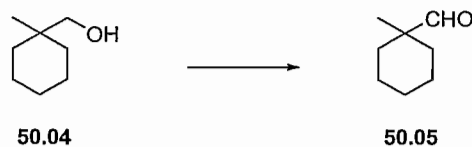
To a solution of **50.02** (15 g) in MeOH (150 mL) was added conc HCl (3-4 mL) and the mixture was refluxed for 16 h. The reaction mixture was cooled to room temperature and concentrated. The residue was taken in diethyl ether (250 mL) and washed with cold saturated sodium bicarbonate solution, and brine. The organic layer was dried (Na_2SO_4) and concentrated to afford the methyl ester **50.03** (12.98 g) which was carried forward without further purification.

Step 2



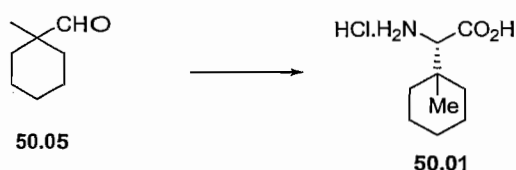
The methyl ester **50.03** from above was dissolved in methylene chloride (100 mL) and cooled to -78°C , under nitrogen atmosphere. DIBAL (1.0 M solution in methylene chloride, 200 mL) was added dropwise over 2 h period. The reaction mixture was warmed to room temperature over 16 h. The reaction mixture was cooled to 0°C and MeOH (5-8 mL) was added dropwise. A solution of aqueous 10% sodium potassium tartarate (200 mL) was slowly added with stirring. Diluted with methylene chloride (100 mL) and separated the organic layer (along with some white precipitate). The organic layer was washed with 1 N HCl (250 mL), brine (200 mL), dried (Na_2SO_4) and concentrated to provide the alcohol **50.04** (11.00 g) as a clear oil.

Step 3



The alcohol **50.04** from above was dissolved in methylene chloride (400 mL) and cooled to 0°C under nitrogen atmosphere. PCC (22.2 g) was added in portions and the reaction mixture was slowly warmed to room temperature over 16 h. The reaction mixture was diluted with diethyl ether (500 mL) and filtered through a pad of celite. The filtrate was concentrated and the residue was taken in diethyl ether (500 mL). This was passed through a pad of silica gel and the filtrate was concentrated to provide the aldehyde **50.05** which was carried forward without further purification.

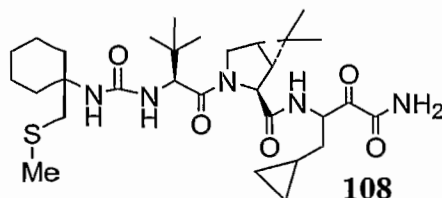
Step 4



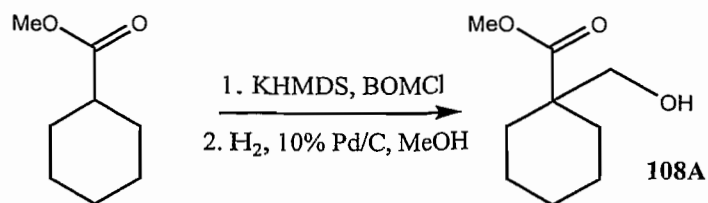
The aldehyde **50.05** from above was converted to the desired material **50.01** using essentially the method of Chakraborty *et. al* (Tetrahedron, **1995**, 51(33), 9179-90).

PREPARATION OF SPECIFIC EXAMPLES

Example 108:



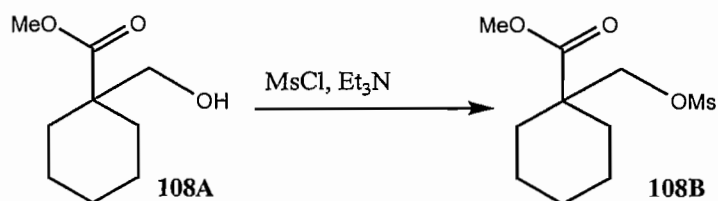
Steps 1 and 2:

**Step1:**

KHMDS (200ml of a 0.5M solution in toluene) was added, dropwise to a stirred solution of Methyl cyclohexanecarboxylate (11.1g; 78mmol) in anhydrous THF (200ml), at -78°C under an atmosphere of nitrogen. When the addition was complete the reaction was maintained at this temperature for a further 0.5h. before the addition of Benzyl Chloromethyl Ether (18.6ml; 134mmol). The reaction was allowed to warm to room temperature overnight and water (100ml) was added. Aqueous work-up provided a residue which was purified by silica gel column chromatography using EtOAc; hexanes (1:10) as eluent to give the desired, impure, intermediate ether (14.98g) as a colorless oil.

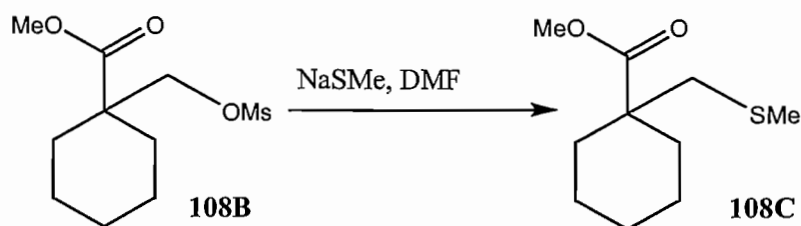
Step2:

A black suspension of 10% Pd/C (0.5g) and the aforementioned crude ether (4.1g) in MeOH (80ml) was exposed to an atmosphere of nitrogen (balloon) at room temp., overnight. The reaction was filtered through a pad of celite and the solid was washed thoroughly with methanol. The combined filtrate was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography using EtOAc; hexanes (1:5) to give the primary alcohol (**108A**; 0.62g), a colorless oil.

Step 3:

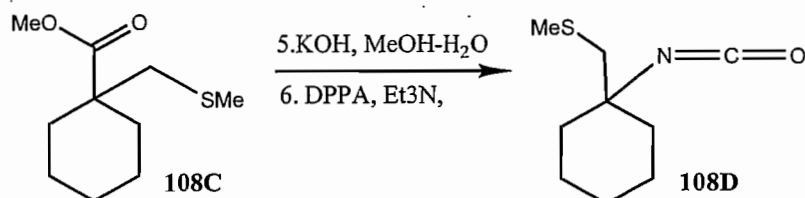
Methanesulfonyl Chloride (0.31ml) followed by triethylamine (0.75ml) were added to a stirred solution of the primary alcohol (**108A**; 0.62g) at 0C, under an atmosphere of nitrogen. The resulting mixture was stirred at this temperature for 0.5h. The reaction mixture was extracted into EtOAc and washed with aqueous 1M HCl, sat. aq. NaHCO₃, water, dried (MgSO₄) and concentrated. The residue (mesylate **108B**; 0.74g), was obtained as a yellow oil, which was used in subsequent steps without purification.

Step 4:



Sodium Methanethiolate (0.236g; 2eq.) was added to a DMF (2ml) solution of the mesylate (**108B**; 0.42g) and the mixture was heated to 100C for 1h. Aqueous work-up and purification of the crude reaction product by silica gel column chromatography using EtOAc; hexanes (1:20) gave the sulfide (**108C**; 0.089g).

Steps 5 and 6:



Step 5:

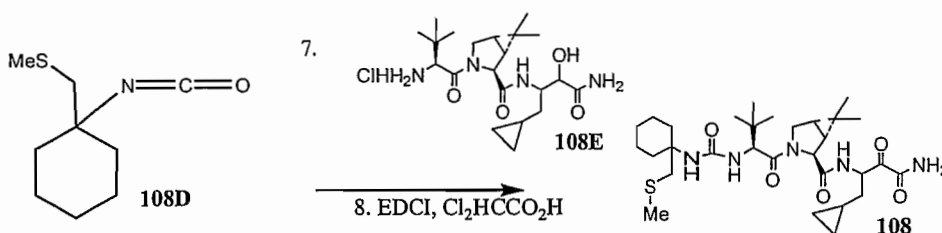
Potassium hydroxide (0.25g) was dissolved in a mixture of water (1ml) and ethanol (5ml) and added to the methyl ester (**108C**; 0.089g) and the resulting mixture was heated to reflux, under an atmosphere of nitrogen over a week-end (approx. 72h.). After cooling, the reaction was partitioned between EtOAc and dilute aq. HCl. The organic phase was separated,

washed with brine, dried and concentrated to yield the crude intermediate carboxylic acid, used without purification.

Step 6:

Triethylamine (61ul) followed by DPPA (95ul) were added to a toluene solution of the carboxylic acid from the previous step and the reaction was heated to 100C overnight. After cooling, the reaction mixture was partitioned between EtOAc and sat. aq. sodium bicarbonate. The organic phase was separated, dried and concentrated to yield the isocyanate (**108D**; 50mgs), used without purification.

Steps 7 and 8:



Step 7:

The isocyanate (**108D**; 50mg) in dichloromethane (1ml) was added to a mixture of the hydrochloride salt (**108E**; prepared from 20.08 in a manner described for the transformation of 20.06 to 20.07; 100mg) and triethylamine (111ul) in dichloromethane (2ml) and the resulting mixture was stirred at room temperature for 4 hours. The reaction mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (magnesium sulfate) and concentrated to yield a residue which was used in step 8 without purification.

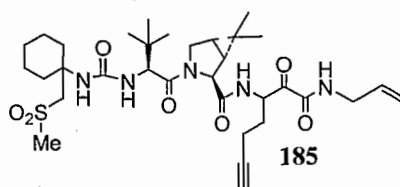
Step 8:

The residue in the aforementioned step was dissolved in a mixture of toluene (3ml) and dimethylsulfoxide (3ml) and EDCI (647 mg) followed by dichloroacetic acid (140ul) were added and the resulting reaction mixture was

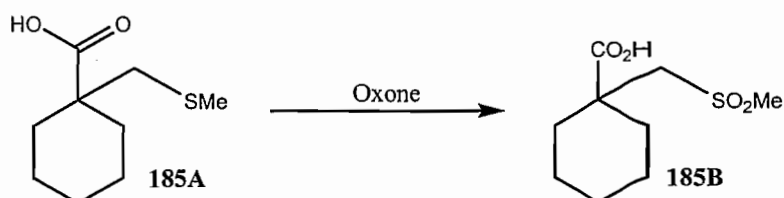
stirred at room temperature for a period of 4h. The reaction mixture was partitioned between EtOAc and 5% aq. sodium sulfite. The organic phase was separated, washed with 10% aq. HCl, sat. aq. sodium bicarbonate, water, dried (magnesium sulfate) and concentrated to yield a residue which was

5 purified by silica gel column chromatography using acetone: hexanes (40:60) as eluent to provide the desired keto-amide (**108**; 11.5mgs). MS: MH⁺, 592.1.

Example 185:



Step 1:

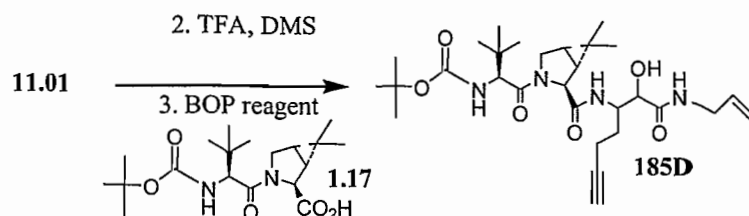


10

Oxone (5.68g) was dissolved in water (5ml) and added to the carboxylic acid **185A** (1.25g) in methanol (5ml) while cooled in an ice bath. The reaction mixture was allowed to warm to room temp., overnight. The volatiles were removed under reduced pressure and the residue was

15 partitioned between methylene chloride and water. The aqueous phase was separated and extracted with methylene chloride (X2). The combined organic phases were dried and concentrated to yield the sulfone (**185B**; 1.10g) as a white solid, used in subsequent procedures without purification.

Steps 2 and 3:



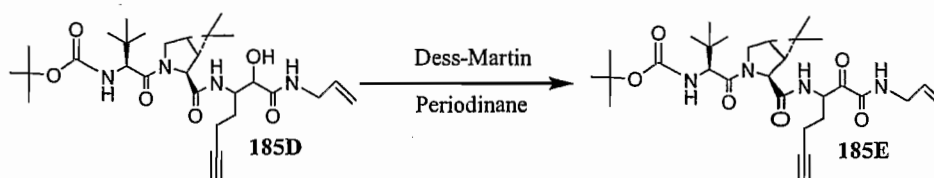
Step 2:

The benzyl carbamate (**11.01**; 0.16g) was dissolved in TFA (7ml) and dimethyl sulfide (1.78ml) was added and the resulting mixture was allowed to stand at room temperature for a period of 3h., before removing the volatiles under reduced pressure. This gave a residue which was used in step 3 below.

Step3:

Triethylamine (111ul) was added to a mixture of the residue from step 2, the carboxylic acid (**1.17**; 0.180g) and BOP reagent (0.236g) in dichloromethane (5ml) and the reaction mixture was stirred at room temperature overnight. The reaction was partitioned between ethyl acetate and aq. 10% HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (magnesium sulfate) and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc: Hexanes (70:30) as eluent to give the desired hydroxy-amide (**185D**; 0.165g) as a white solid.

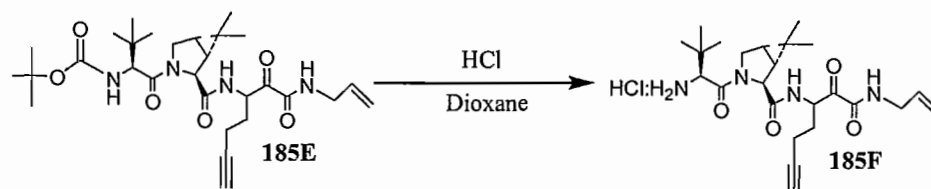
Step 4:



The periodinane (0.236g) was added to a stirred solution of the alcohol (**185D**; 0.152g) in dichloromethane (5ml) and the resulting white suspension was stirred for a period of 2h. before being added to a mixture of EtOAc and 5% aq. sodium sulfite. The organic phase was separated washed with sat. aq.

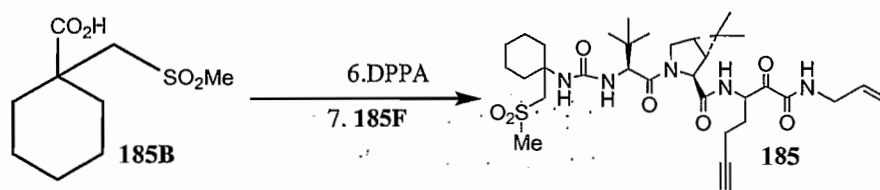
sodium bicarbonate, water, dried and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc: Hexanes (40:60) as eluent to give the desired keto-amide (**185E**; 0.147g) as a white solid. MS: MH⁺, 545.5.

5 Step 5;



A solution of HCl in dioxane (4M; 5ml; Aldrich) was added to the carbamate (**185E**; 0.14g) and allowed to stand at room temperature for a period of 3h. The volatiles were removed under reduced pressure to provide the hydrochloride salt (**185F**; 0.126g; contains a small quantity of dioxane).

Steps 6 and 7:



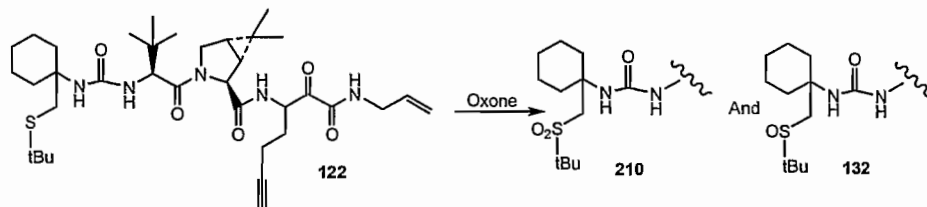
Step 6:

DPPA (19ul) was added to a mixture of the carboxylic acid (**185B**; 20mgs) and triethylamine (13ul) in toluene (1ml) and the resulting reaction mixture was heated to reflux for a period of 1h. After cooling, the reaction was partitioned between EtOAc and sat. aq. sodium bicarbonate. The organic phase was separated, dried and the volatiles removed under reduced pressure. Gave the crude intermediate isocyanate which was used in step 7, below without purification.

Step 7:

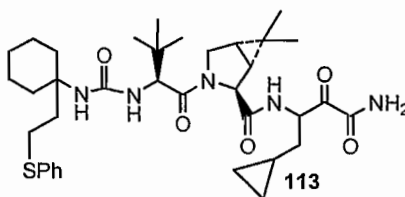
The product from step 6 was dissolved in dichloromethane (1mL) and added to a mixture of the hydrochloride salt (**185F**; 20mgs) and triethylamine (60ul) in dichloromethane (1ml) and the resulting mixture was stirred at room temperature for a period of 1h. The reaction was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried and the volatiles were removed under reduced pressure. The resulting residue was purified by silica gel plate chromatography using EtOAc: Hexanes (1:1) as eluent to provide the keto-amide (**185**; 16.3mgs) as a white solid. MS: MH⁺, 662.5.

Preparation of Compounds of Formulas **132** and **210** Directly From a Compound of Formula **122**

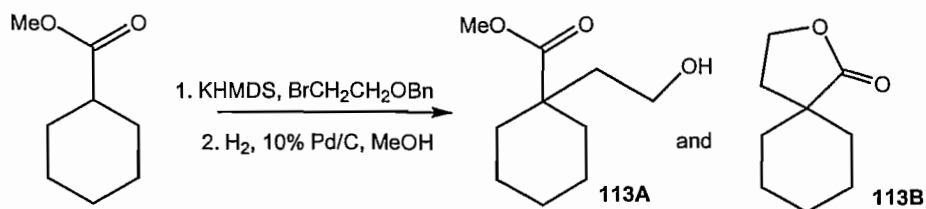


Using the sulfide **122** (prepared in a similar manner as 108 using methyl ester 210A rather than 108C; 20mg), oxone (27mg; 1.5eq.), water (1ml), methanol (1ml) and the procedure set forth previously (**185A** to **185B**) gave a crude reaction product which was purified by silica gel plate chromatography using EtOAc as eluent. Gave the sulfone (**210**; MH⁺ = 704.4; 5.6mg) as a white solid followed by a mixture of sulfoxides (**132**; MH⁺ = 688.5; 6.3mg), also a white solid.

Preparation of Compound **113**



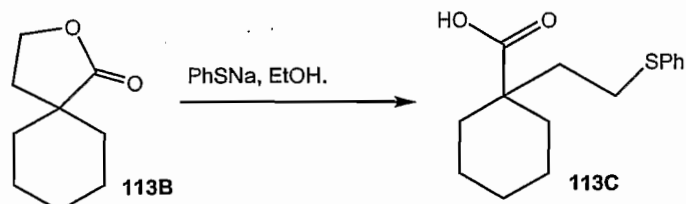
Steps 1 and 2:

**Step 1:**

Using Methyl cyclohexanecarboxylate (5.55g), KHMDS (100ml of a 0.5M solution in toluene), anhydrous THF (100ml) and benzyl 2-bromoethyl ether (10.09g) and the procedure set forth previously (Example 108, Step1), the desired intermediate benzyl ether (6.83g) was obtained after silica gel column chromatography (EtOAc:Hexanes:15:85).

Step 2:

Using the aforementioned benzyl ether (5.00g), 10% Pd/C (1.00g), methanol (20ml) and the procedure set forth previously (Example 108; Step2) the lactone (113B; 0.87g), followed by the alcohol (113A; 2.01g) were obtained following column chromatography on silica gel (EtOAc; Hexanes; 1:10).

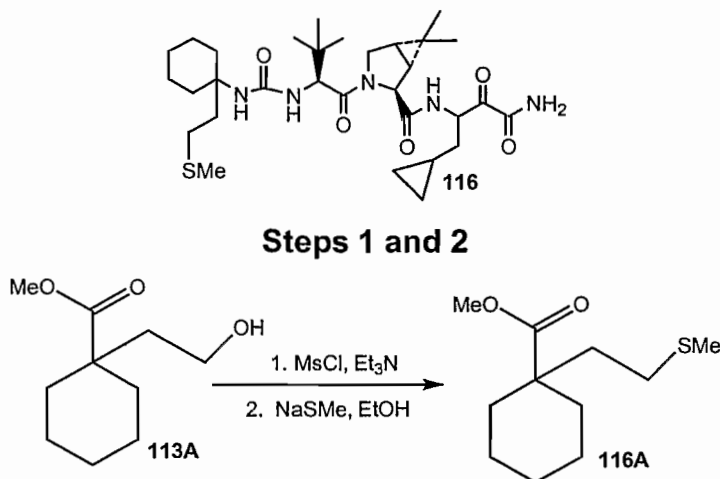
Step 3:**Step 3:**

Sodium thiophenoxide (0.68g) was added to a solution of the lactone (113B; 0.84g) in ethanol (15ml) and the resulting mixture was heated to reflux, under an atmosphere of nitrogen overnight. After cooling, aqueous work-up and purification of the crude reaction product by silica gel column

chromatography (EtOAc-Hexanes; 30:70) gave the carboxylic acid (**113C**; 0.32g), as a yellow solid.

Using previously described chemistry for the conversion of **108C** to **108**, **113C** was converted to **113** in a similar manner. MS, MH⁺, 668.3.

5 Preparation of Compound 116:



Step 1:

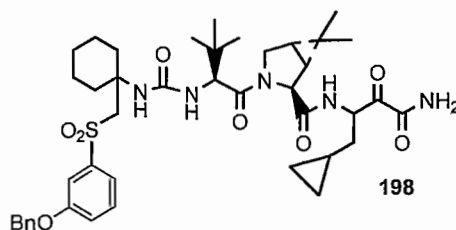
10 Using the alcohol (**113A**; 1.00g), methane sulfonylchloride (1.12g), triethylamine (0.82g), methylene chloride (10ml) and the procedure set forth previously (**108A** to **108B**), the desired, intermediate mesylate was obtained and was used in the next step, without purification.

Step 2:

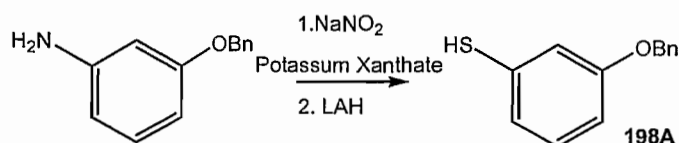
15 Using the aforementioned mesylate, sodium methanethiolate (0.75g), ethanol (10ml) and the procedure set forth previously (**108B** to **108C**) at room temperature, the desired sulfide (**116A**; 0.78g) was obtained after silica gel column chromatography (EtOAc-Hexanes; 1:10). Using the procedures set forth previously (**108C** to **108D**) and (**108D** to **108**), intermediate **116A** was

20 transformed into **116**. MS; MH⁺, 606.1.

Preparation of Compound 198



Steps 1 and 2"



Steps 1 and 2:

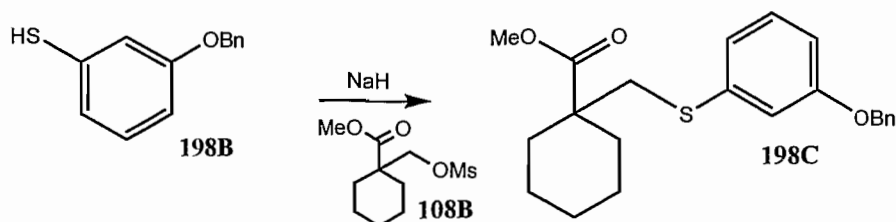
5 Step 1:

3-Benzyloxylaniline (5.00g; Aldrich) was dissolved in a mixture of conc. HCl (10ml) and ice (10.00g) was added. Sodium nitrite (1.85g) in water (10ml) was added while cooled in an ice bath. When the addition was complete, Potassium O-Ethylxanthate was added and stirred at this temperature until the evolution of nitrogen gas ceased, then heated at 40-45C for a period of 1.5h. After cooling, aqueous work-up and purification by silica gel column chromatography (2-5% EtOAc in hexanes) to give the intermediate xanthate (3.60g).

Step 2:

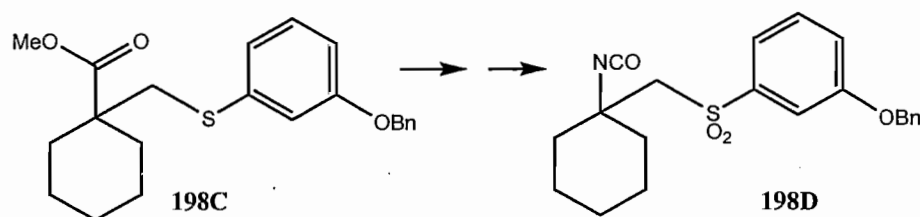
15 Lithium Aluminum Hydride (6.4ml of a 1M solution in THF) was added dropwise to a stirred solution of the aforementioned xanthate (1.49g) in THF (10ml) and stirred at R.T. for a period of 0.5h. The reaction was quenched with excess acetone and partitioned between EtOAc and aq. 1M HCl. The organic phase was separated, dried and concentrated. The crude reaction product was purified by silica gel column chromatography (1-2% EtOAc in hexanes) to give the thiophenol (**198A**; 0.84g), a white solid.

Step 3:



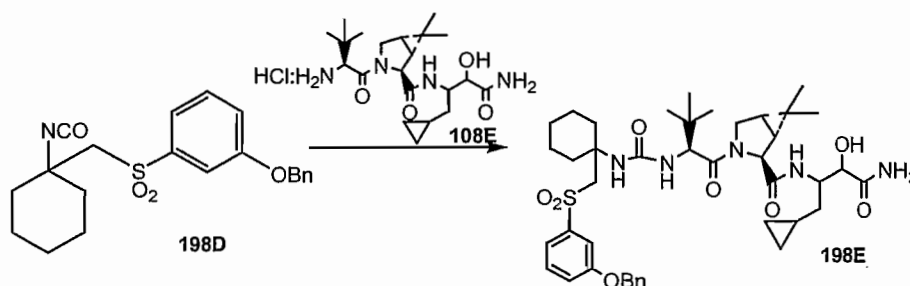
The mercaptan (**198B**; 0.72g) was added to a suspension of NaH (0.08g of a 60% dispersion in mineral oil) in anhydrous DMF, while cooled in an ice bath under an atmosphere of nitrogen. The resulting mixture was stirred for 1h. and the mesylate (**108B**; 0.417g) was added and the reaction was allowed to warm to R.T., overnight. Aqueous work-up and purification of the crude reaction product by silica gel column chromatography (3% EtOAc in hexanes) gave the sulfide (**198C**; 0.313g).

Steps 4-6:



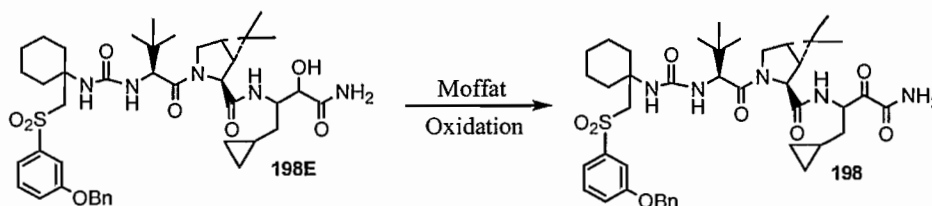
Using the sulfide (**198C**) generated in the previous step, the isocyanate (**198D**) is produced using procedures set forth in (**108C** to **108D**) and **185A** to **185D**). The isocyanate (**198D**) is used in subsequent procedures without purification.

Step 7:



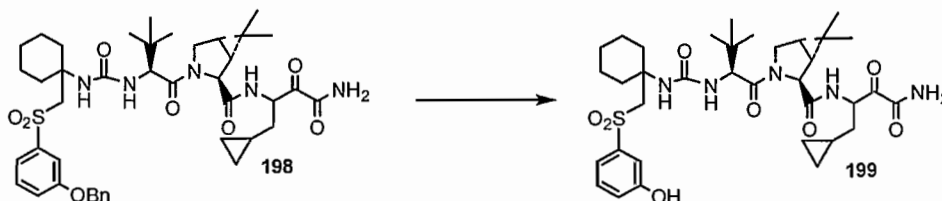
The isocyanate (**198D**; 0.139g) in a minimal amount of dichloromethane (approx. 1ml) was added to a mixture of the hydrochloride salt (**108E**; 0.080g) and triethylamine (0.126ml) and the resulting mixture was stirred at room temperature for a period of 4 hours. The reaction mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried and concentrated. The crude reaction product (**198E**) was used crude in the next step.

Step 8:



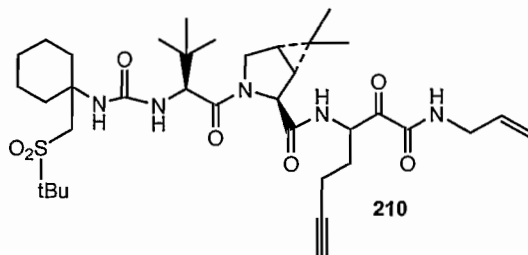
The crude product from the previous step (**198E**) was dissolved in DMSO (3ml) and toluene (3ml) and EDCI (0.346g) followed by dichloroacetic acid (0.074ml) was added and the resulting mixture was stirred at room temperature for a period of 4 hours. The reaction was partitioned between EtOAc and 5% aq. sodium sulfite. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried and concentrated. The crude reaction product was purified by silica gel column chromatography using acetone:hexane (30:70) as eluent to give the keto-amide (**198**; $MH^+ = 792.2$; 55mgs).

Preparation of the Phenol **199** from Benzyl Ether **198**:

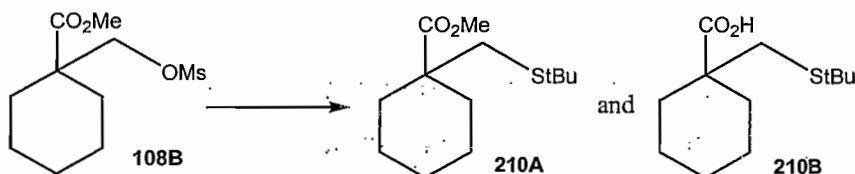


10% Pd-C (25mg) followed by formic acid (0.125ml) were added to a solution of the benzyl ether (**198**; 50mg) in ethanol (4ml) and the resulting black suspension was refluxed for a period of 1 hour. After cooling, the reaction was filtered through a pad of celite and the solid was washed with methanol. The combined filtrate was concentrated under reduced pressure to give the desired phenol (**199**; $MH^+ = 702.2$; 23mg).

Alternative Preparation of Compound of Formula **210**:



Step1:

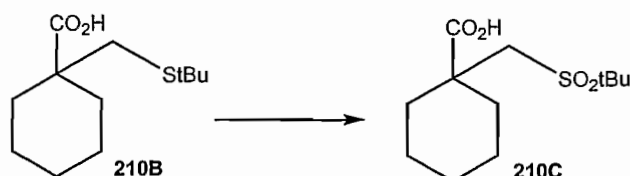


Dimethylformamide (20ml; anhydrous; Aldrich) was added to sodium hydride (0.56g; Aldrich) and tert-butyl mercaptan was added to the suspension while cooled in an ice bath under an atmosphere of nitrogen.

Once the addition was complete the mesylate (**108B**; prepared as above from 2.00g of alcohol; **108A**) was added and the resulting mixture was stirred overnight at room temperature. The reaction was partitioned between EtOAc and water and the organic phase was separated, dried ($MgSO_4$), column chromatography on silica gel using EtOAc-Hexanes (2:98) to provide the methyl ester-sulfide (**210A**; 1.75g).

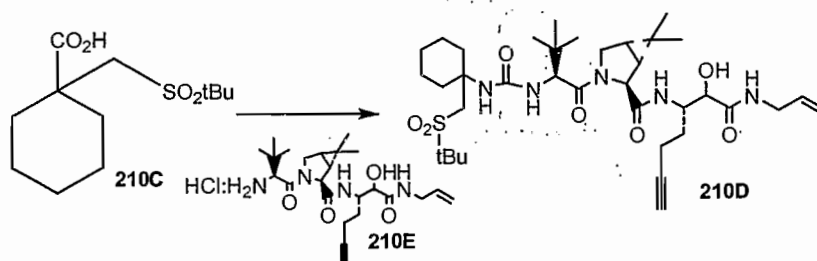
EtOAc was added to the aqueous phase and 10% aq. HCl was added until the water layer pH=1. The organic layer was separated, washed with water, dried and concentrated under reduced pressure to give the sulfide-carboxylic acid (**210B**; 0.747g) as a white solid.

5 Step 2:



To the sulfide (**210B**; 2.287g) in methanol (75ml) was added a solution of oxone (18.00g; Aldrich) and the resulting white suspension was stirred overnight at room temperature. The volatiles were removed under reduced pressure and the white solid partitioned between EtOAc and water. The organic phase was separated, dried and concentrated to provide the sulfone (**210C**; 2.52g; contains some solvent).

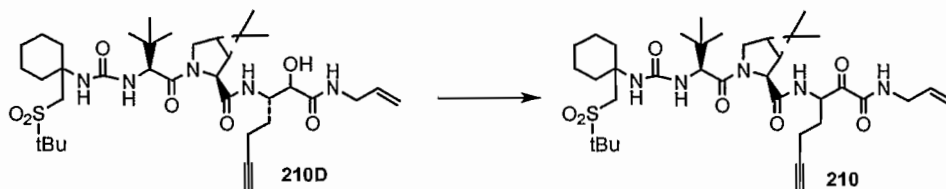
Step 3:



Triethylamine (0.173ml), followed by DPPA (0.268ml) were added to a solution of the carboxylic acid (**210E**; 0.325g) in toluene (3ml) and the resulting mixture was heated to 110C (oil bath) for a period of 1 hour. After cooling the reaction mixture was partitioned between EtOAc and sat. aq. sodium bicarbonate. The organic phase was separated, dried and concentrated. The residue was dissolved in dichloromethane (1ml) and added to a mixture of the hydrochloride salt (**185F**; 0.300g) and triethylamine

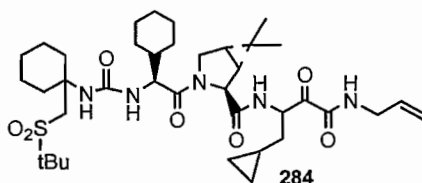
(0.044ml) in dichloromethane (3ml) and the resulting reaction mixture was stirred at room temperature overnight. The reaction was partitioned between EtOAc and 10% aq. HCl, The organic phase was separated, washed with saturated aq. sodium bicarbonate, water, dried and concentrated to yield a crude product which was used in the next step without purification.

Step 4:

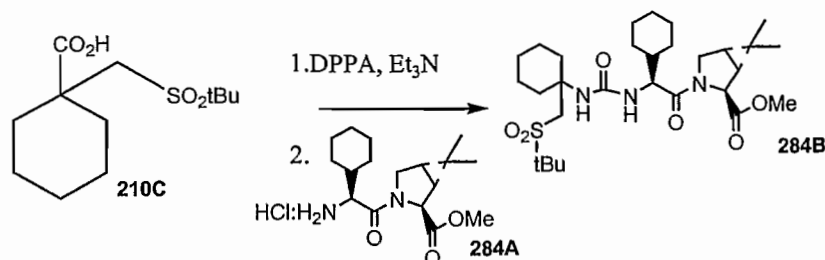


The residue from the previous step (**210D**) was dissolved in dichloromethane (5ml) and Dess-Martin periodinane (0.527g) was added and the reaction mixture was stirred at room temperature for 3 hours. The reaction was partitioned between EtOAc and 5% aq. sodium sulfite. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc-Hexanes (70:30) as eluent to give the desired keto-amide (**210**; 0.310g).

Preparation of Compound of Formula **284**:



Steps 1 and 2:



Step 1:

Using the carboxylic acid (**210C**; 2.52g), DPPA (2.07ml), triethylamine (1.34ml) in toluene (10ml) and the procedure set above the crude isocyanate was formed.

Step 2:

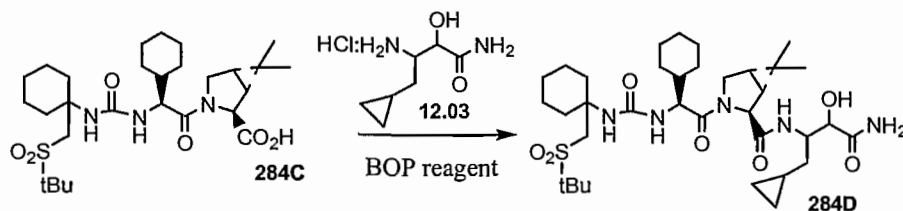
The intermediate isocyanate was dissolved in dichloromethane (2ml) and added to a mixture of the hydrochloride salt **284A** (prepared from 20.04 using the transformation described for 20.06 to 20.07; 1.66g) and triethylamine (3.4ml) and the mixture stirred at room temperature overnight. Aqueous work-up and purification of the residue on silica gel using EtOAc-Hexanes (3:97) gave the desired urea (**284B**).

Step 3:



The methyl Ester (**284B**) was dissolved in a mixture of dioxane (90ml) and water (30ml) and lithium hydroxide: monohydrate (0.402g; 2eq) was added and the reaction was allowed to stir at room temperature for 3 hours. The reaction mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, dried and concentrated to yield the carboxylic acid (**284C**; 2.65g).

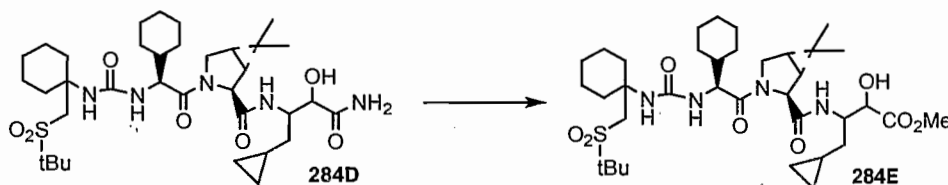
Step 4:



BOP reagent (2.54g) followed by triethylamine (2.4ml) were added to a solution of the carboxylic acid (**284C**; 2.65g) and the hydrochloride salt (**12.03**; 0.933g) in dichloromethane (20ml) and stirred at room temperature overnight.

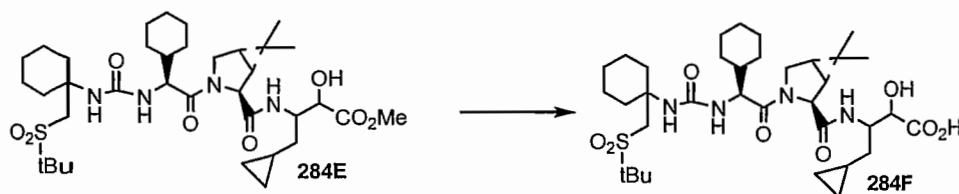
- 5 The reaction was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried and concentrated. The residue was purified by silica gel column chromatography using 2-10% MeOH in dichloromethane as eluent to give the desired amide (**284D**; 2.92g).

10 Step 5:



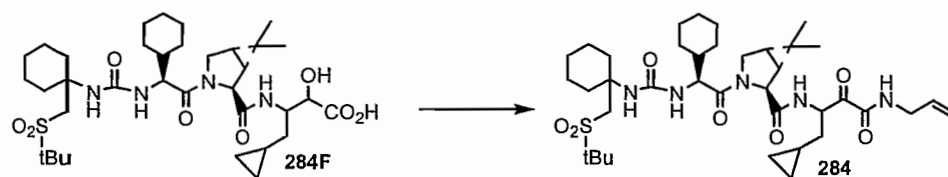
To a solution of the carboxamide (**284D**; 2.92g) in methanol (30ml) was added DMF-DMA (1.12ml) and the resulting mixture was stirred at room temperature for 3 hours and then refluxed for 1.5 hours until T.L.C. indicated that no starting material was left. After cooling, the reaction was partitioned between diethyl ether and 1N aq. HCl. The organic phase was separated, dried and concentrated. Silica gel column chromatography of the residue gave the methyl ester (**284E**), which was treated as shown in Step 6, below.

Step 6:



The methyl ester (**284E**) was dissolved in a mixture of dioxane (30ml) and water (10ml) and lithium hydroxide: monohydrate (0.354g) was added and the resulting mixture was stirred for 3 hours. The reaction was partitioned
 5 between EtOAc and 10% aq. HCl. The organic phase was separated, dried and concentrated to provide the carboxylic acid (**284F**; 2.80g).

Steps 7 and 8:



Step 7:

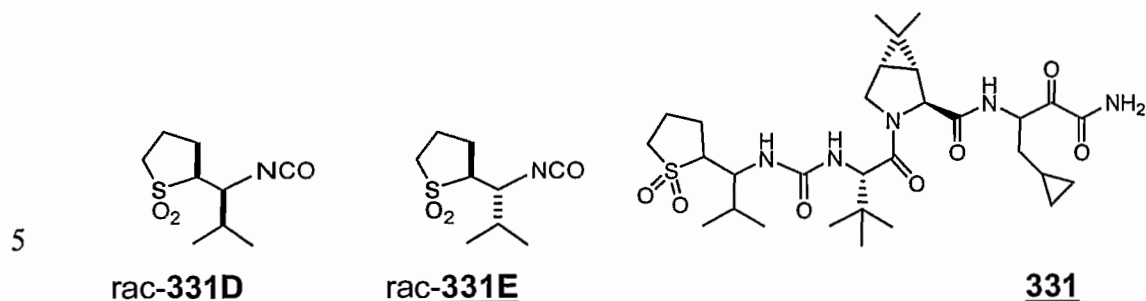
10 Allyl amine (0.045ml), BOP reagent (0.266g) and triethylamine (0.25ml) were added to a mixture of a solution of the hydroxy-acid (**284F**; 0.348g) in dichloromethane (5ml) and the resulting mixture was stirred at room temperature overnight. The reaction was partitioned between EtOAc and 10%
 15 aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried and concentrated to provide a residue, used without purification in Step 8, below..

Step 8:

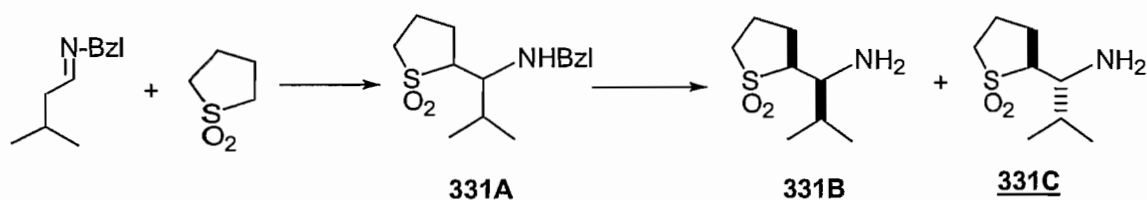
The residue was dissolved in dichloromethane (5ml) and Dess-Martin periodinane (0.424g) was added and the reaction mixture was stirred at room
 20 temperature for 3 hours. The reaction was partitioned between EtOAc and 5% aq. sodium sulfite. The organic phase was separated, washed with sat. aq, sodium bicarbonate, water, dried and concentrated. The crude reaction

product was purified by silica gel column chromatography to yield the desired keto-amide (**284**; 0.296g). MH⁺, 732.2.

Preparative Example 331. Preparation of Intermediates of Formulas **331D** and **331E** for the Compound of Formula **331**:



Step 1. Preparation of Compounds of Formulas **331B** and **331C**:

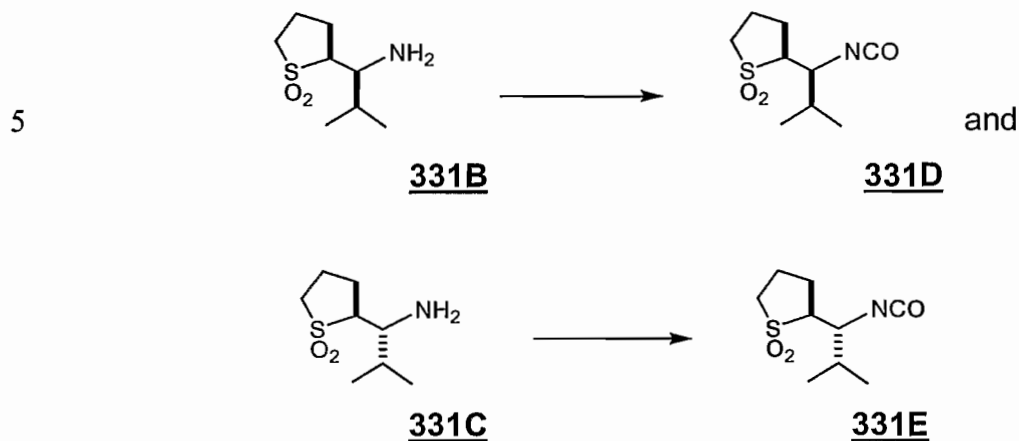


N-benzyl-4-methylbutanimine (prepared as described: *Synthesis*, **1985**, 679) and tetrahydrothiophene 1,1-dioxide were reacted in the manner described in Example 336, except at -78° C, to afford compound **331A**, which was hydrogenolyzed in the manner described in

15 Example 336, except at a pressure of 1 atm. The crude product was chromatographed on silica gel, eluting with a gradient of EtOAc to 1:1 acetone-EtOAc to obtain first one racemic diastereomer: H¹-NMR (CDCl₃) δ 3.2 (m, 1H), 3.1-2.9 (m, 3H), 2.3-2.1 (m, 2H), 2.1-1.9 (m, 1H), 1.9-1.7 (m, 2H), 1.02 (d, 3H), 0.85 (d, 3H).

Further elution afforded the other racemic diastereomer: ^1H -NMR (CDCl_3) δ 3.2 (m, 1H), 3.2-2.9 (m, 4H), 2.3-2.1 (m, 3H), 2.1-2.0 (m, 1H), 1.78 (sex., 1H), 0.96 (m, 6H).

Step 2. Preparation of Compounds of Formulas **331D** and **331E**.



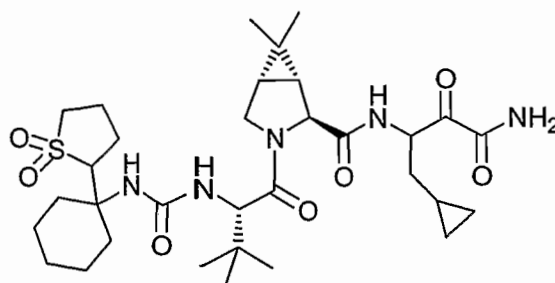
10

Compounds **331B** and **331C** were separately reacted with phosgene in the manner described in Example 336 to afford two diastereomeric isocyanates:

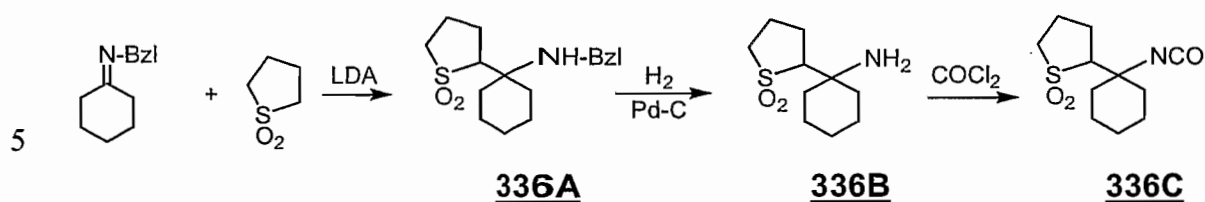
15 the one, from the higher R_f amine: ^1H -NMR (CDCl_3) δ 3.79 (dd, $J_1 = 9.9$ Hz, $J_2 = 3.0$ Hz, 1H), 3.25 (m, 1H), 3.1-3.0 (m, 2H), 2.25 (m, 2H), 2.2-2.0 (m, 1H), 2.0-1.7 (m, 2H), 1.09 (d, $J = 6.9$ Hz, 3H), 0.93 (d, $J = 6.9$ Hz, 3H).

the other, from the lower R_f amine: ^1H -NMR (CDCl_3) δ 3.92 (dd, $J_1 = 6.6$ Hz, $J_2 = 4.8$ Hz, 1H), 3.3-2.9 (m, 3H), 2.4 (m, 1H), 2.3 (m, 1H), 2.2-2.0 (m, 3H), 1.03 (t, $\Delta v = 6.3$, 6H).

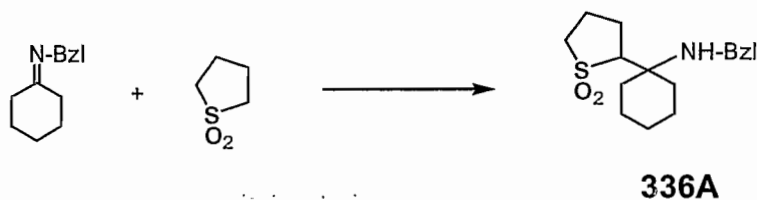
20 Preparative Example 336. Preparation of Compound of Formula 336.

**336**

SCHEME 336-1



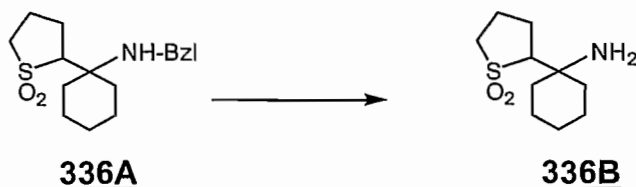
Step 1. Preparation of Compound of Formula **336A**.



- 10 A solution of 20 mL of 2N LDA in hexane-THF was added to 60 mL THF and the solution was cooled to -30° C. Then 4.80 g of tetrahydrothiophene 1,1-dioxide (Aldrich Chemical Co.) was added slowly between -30° C and -10° C, and the stirred at -10° C for an additional 10 min. At -10° C, 7.5 g of N-benzylcyclohexylimine (prepared as described:
- 15 *Synthesis, 1998, 1609.*) was added at once. After 0.5 h at ambient temperature the mixture was quenched with saturated aqueous NaHCO₃, and extracted with CH₂Cl₂. The extracts are dried over anhydrous MgSO₄, filtered, and the filtrate evaporated. The residue was chromatographed on silica gel, eluting with EtOAc-hexane (3:7) to afford 1.3 g of compound **336A**:

^1H -NMR (CDCl_3): δ 7.5-7.2 (m, 5H), 3.76 (ABq, $\Delta\nu = 230$ Hz, $J = 12$, 2H), 3.41 (m, 1H), 3.13 (m, 1H), 2.94 (m, 1H), 2.4-1.3 (m, 14H).

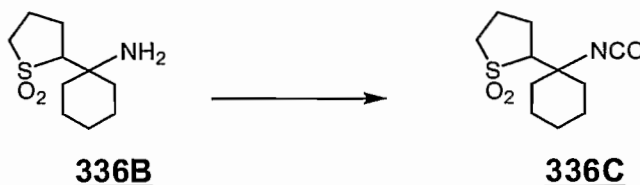
Step 2. Preparation of Compound of Formula **336B**.



A solution of 1.3 g of compound **336A**, 30 mL EtOH, 1.2 mL of 4n HCl/dioxane solution, and 0.35 g of 10% Pd-C was hydrogenated at 3 atm for 1.5 h. The mixture was filtered, and the filtrate evaporated. The residue was treated with 2 n NaOH and extracted with CH_2Cl_2 , the extract was dried and

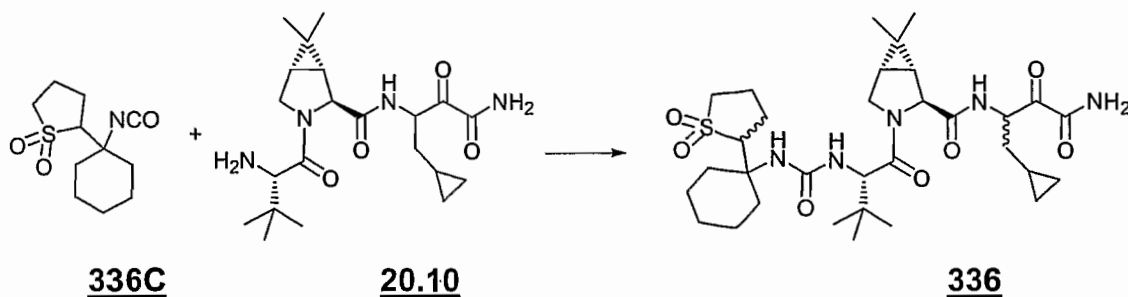
10 evaporated to leave 0.51 g of compound **336B**, which solidified on standing: ^1H -NMR (CDCl_3) δ 3.2-2.9 (m, 3H), 2.4-1.8 (m, 6H), 1.7-1.2 (m, 8H).

Step 3. Preparation of Compound of Formula **336C**



15 To a solution of 0.75 g phosgene in 30 mL toluene at 0° C was slowly a solution of 0.5 g of compound **336B** and 0.80 mL diisopropylethylamine in 10 mL CH_2Cl_2 . The mixture was stirred at room temperature for 5 h, concentrated to 15 mL, filtered, then diluted with fresh toluene to 18 mL to produce a 0.12 M solution of compound **336C**, which was used for

20 subsequent reactions. .

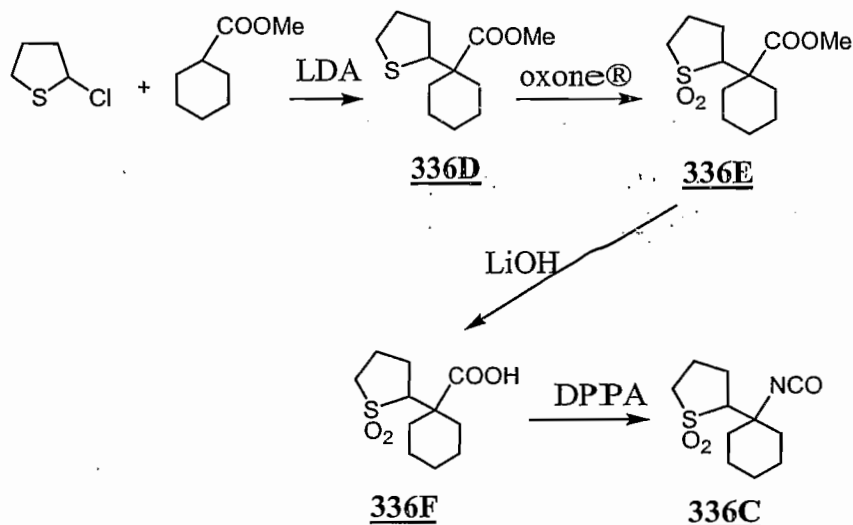
Step 4. Preparation of Compound of Formula **336**

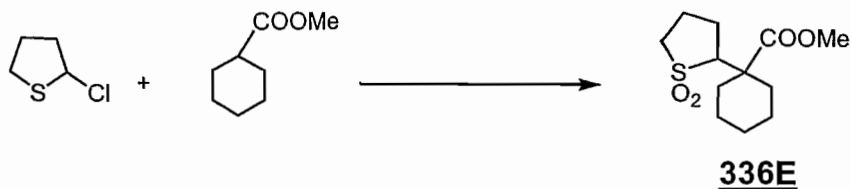
Compound **336C** was reacted with compound **20.10** in the manner

- 5 described in preparative example 108 to produce compound **336** as a mixture of diastereomers ^1H -NMR (DMSO- d_6) δ 8.40(m), 8.33 (m), 8.00 (d), 7.75 (s), 6.25 (m), 6.10 (s), 6.01 (s), 4.18 (m), 3.92(m), 3.83 (m), 3.78 (m), 3.13 (m), 2.90 (m) 2.47 (m), 2.1-0.8 (m; Me_A : 1.01; Me_B : 0.82; Bu^t : 0.91), 0.40 (m), 0.19 (m).

- 10 Example **336C**. Alternate synthesis of compound **336C**.

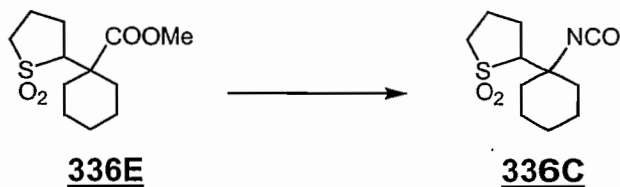
SCHEME 336-2



Step 1. Preparation of Compound of Formula **336E**.

2-Chlorotetrahydrothiophene (prepared as described: *Chem. Pharm.*

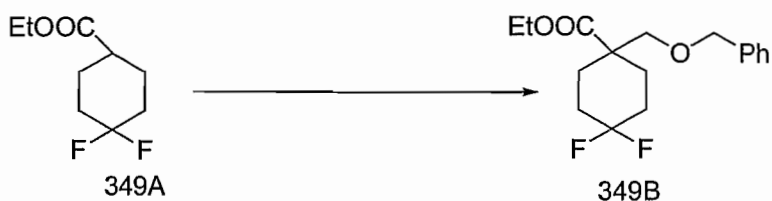
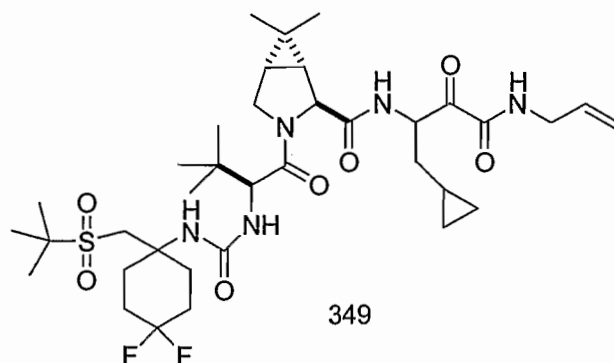
- 5 *Bull.*, **1986**, 34(9), 3644) was reacted with α -lithiocyclohexanecarboxylic acid in the manner described in preceding examples to afford sulfide ester compound **336D** in 39% yield. Compound **336D** was oxidized with oxone[®] in the manner described in preceding examples to afford sulfone ester compound **336E**: ^1H NMR(CDCl_3) δ 3.73 (s, 3H) 3.3-3.0 (m, 2H), 3.0-2.9 (m, 1H), 2.6-2.4 (m, 1H), 2.4-1.3 (m, 13H).
- 10

Step 2. Preparation of Compound of Formula **336C**.

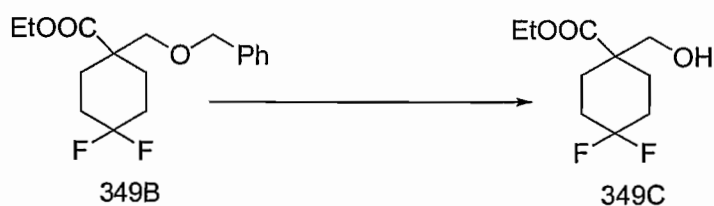
Compound **336E** was hydrolyzed with LiOH in water-dioxane at 100° C in the manner described in preceding examples to afford sulfone carboxylic acid compound **336F**: ^1H NMR(CDCl_3) δ 3.4-3.2(m, 1H), 3.2-3.1 (m, 1H), 3.1-2.9 (m, 1H), 2.3-2.1 (m, 3H), 2.1-1.8 (m, 3H), 1.8-1.3 (m, 7H). Compound **336F** was reacted with diphenylphosphoryl azide in the manner described in preceding examples to afford compound **336C** as a colorless solid:

- 20 ^1H NMR(CDCl_3) δ 3.2 (m, 1H), 3.1-2.9 (m, 2H), 2.45 (d, 1H), 2.4-1.9 (m, 4H), 1.85-1.5 (m, 7H), 1.5-1.2 (m, 2H).

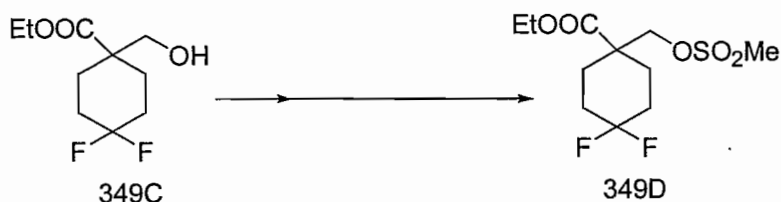
Synthesis of Compound 349:



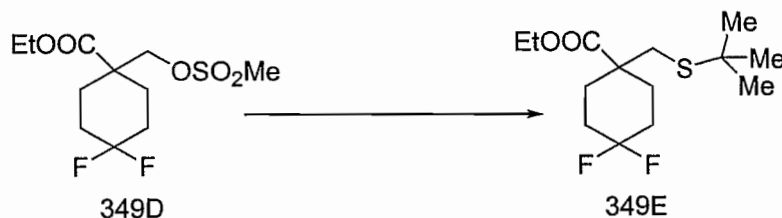
To a solution of the ethyl ester (**349A**; 10 g; 0.052 mol.) in diethyl ether (50 ml) at -78°C (bath temp.) was added KHMDS (0.5 M in toluene; 156.087 ml; 1.5 equiv.). The resulting solution was stirred for 30 minutes, then benzyl chloromethyl ether (11.89 ml; density 1.13; 1.65 equiv.) was added. The reaction mixture was stirred at -78°C to R.T. for 24 h. Reaction was stopped by addition of saturated aq. NH_4Cl . It was then diluted with ethyl acetate and the combined organic phase was washed with brine, dried over Na_2SO_4 and evaporated to dryness *in vacuo* to provide a light brown oil (24.2 g). It was chromatographed over silica gel (300 g). The column was eluted with 1% - 4% ethyl acetate in n-hexane providing in some of the fractions pure **349B** (6.54 g).



A solution of the benzyl ether (**239B**; 2.8316 g; 0.0091 mol.) in CHCl_3 (49.5 ml) was treated with methane sulfonic acid (22.65 ml) and the reaction mixture stirred at room temperature for ~70 minutes. Ice was added to the reaction mixture and it was diluted with ethyl acetate. The organic phase was washed with saturated NaHCO_3 , dried over Na_2SO_4 and evaporated to dryness *in vacuo* to provide yellowish oil (2.86 g). It was chromatographed over SiO_2 (65 g). The column was eluted with 15% - 25% ethyl acetate in n-hexane providing in some of the fractions pure **349C** (1.5913 g).

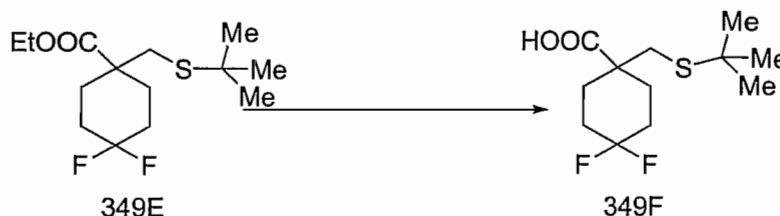


A stirred solution of the alcohol (**349C**; 1.14 g; 0.0051 mol.) in methylene chloride (6.4 ml) was cooled in ice bath and treated with Et_3N (0.7857 ml; density 0.726; 1.1 equiv.) and methanesulfonyl chloride (0.4168 ml; density 1.48; 1.05 equiv.). After ~2 hrs the reaction mixture was diluted with methylene chloride and it was washed with 6N HCl followed by saturated NaHCO_3 . The organic phase was dried over Na_2SO_4 and evaporated to dryness *in vacuo* to provide the mesylate **349D** (1.5447 g) as a light yellow oil.

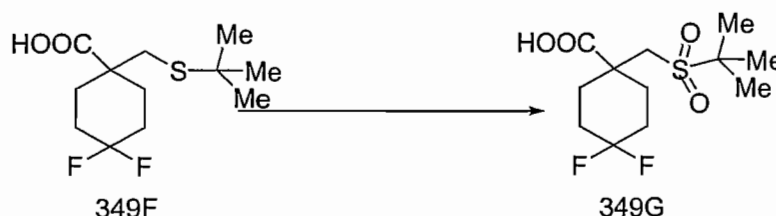


A stirred suspension of NaH (0.4114 g; 60% dispersion in mineral oil; 2 equiv.) in dry DMF was treated with tert.-butyl thiol (1.16 ml; density 0.8; 2 equiv.) with ice bath cooling. The reaction mixture was stirred for 30 minutes after which the mesylate (**349D**; 1.5447 g; 1 equiv.) was added in dry DMF (8+2 ml). Ice bath was removed and the reaction mixture was stirred at room

temperature overnight. The reaction mixture was acidified with 6N HCl and extracted with ethyl acetate. The ethyl acetate extract was dried over Na₂SO₄ and evaporated to dryness *in vacuo* to provide crude 349D (2.87 g) which was chromatographed over SiO₂ (60 g). The column was eluted with 3% ethyl acetate providing in some of the fractions pure **349E** (1.38 g) as a colorless oil.

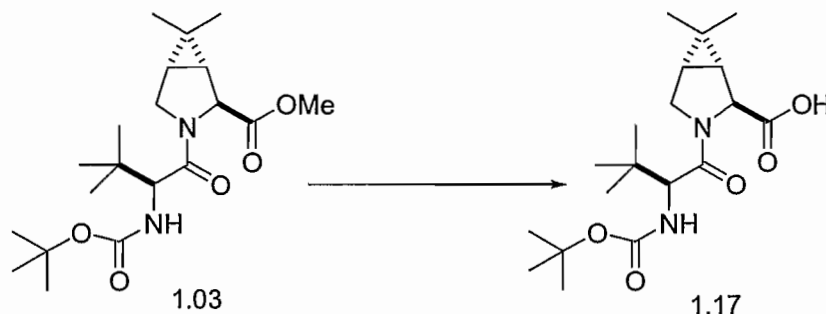


A solution of the ethyl ester (**349E**; 1.38 g; 0.00468 mol.) in ethanol (16 ml) and water (4.13 ml) was treated with KOH pellets (2.63 g; 10 equiv.). The resulting solution was refluxed for 7 h and then allowed to cool to room temperature overnight. Ethanol was evaporated *in vacuo* and the residue partitioned between CH₂Cl₂/water, acidified with 6N HCl to pH 1. The organic phase was separated and the aqueous phase extracted three times with CH₂Cl₂. The combined organic phase was dried over Na₂SO₄ and evaporated to dryness *in vacuo* to provide **349F** (1.19 g) as a off white solid, m.p. 93-95⁰ C.

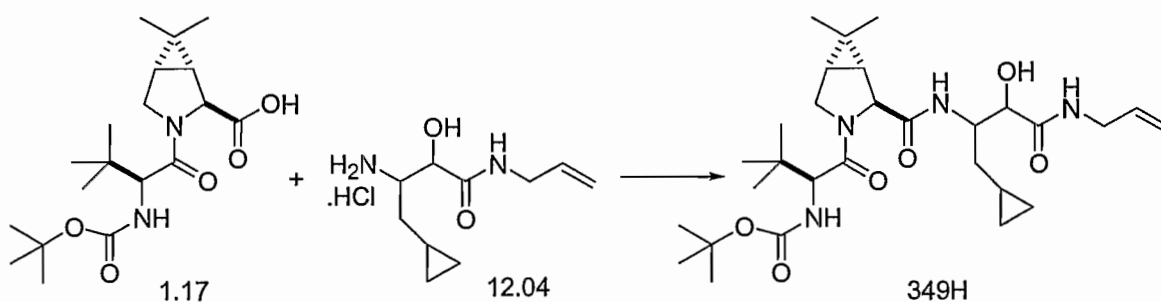


The oxone (8.24 g; 3 equiv.) dissolved in water (31 ml) was added to a stirred solution of the sulfide (**349F**; 1.19 g; 1 equiv.) in methanol (31 ml) at 0⁰ C (bath temp). The reaction was stirred at 0⁰ C to R.T. over the weekend. Solvents were evaporated in-vacuo and the residue partitioned between

CH₂Cl₂/water. The organic layer was separated and the aqueous layer extracted twice with CH₂Cl₂. The combined organic phase was dried over Na₂SO₄ and evaporated to dryness *in vacuo* to provide **349G** (1.29 g) as a crystalline solid, m.p. 212⁰ C.

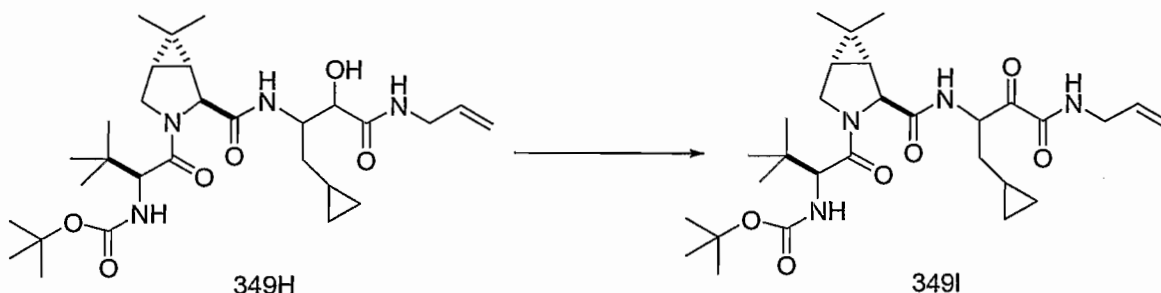


To a cooled (ice bath) solution of the ester (**1.03**; 4.56 g; 0.0119 mol.) in dioxane (18.23 ml) was added with stirring 1.0 N LiOH (18.23 ml). The reaction mixture was stirred for 2 hrs. TLC indicated some starting material still remaining, so added 2+1 ml 1.0 N LiOH and stirred overnight. Reaction complete by TLC. 6N HCl was added to acidify the reaction mixture to pH 1 and ethyl acetate (150 ml) added. After shaking, the ethyl acetate phase was separated and the aqueous phase extracted with ethyl acetate. The combined ethyl acetate phase was washed once with brine, dried (Na₂SO₄) and evaporated to dryness *in vacuo* to provide **1.17** as a amorphous solid (4.7805 g; occluded solvent).

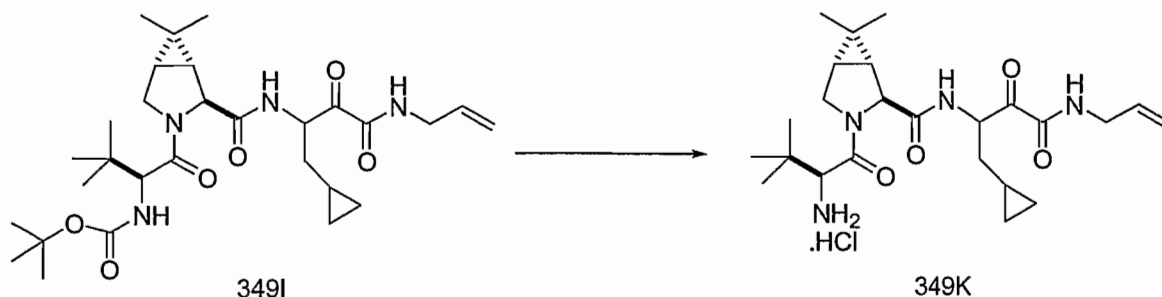


To a -20⁰ C solution of the acid **1.17** (0.7079 g; 0.00192 mol.) and the amine salt (**12.04**; 0.5231 g; 1.16 equiv.) in CH₂Cl₂ (10 ml) was added HATU

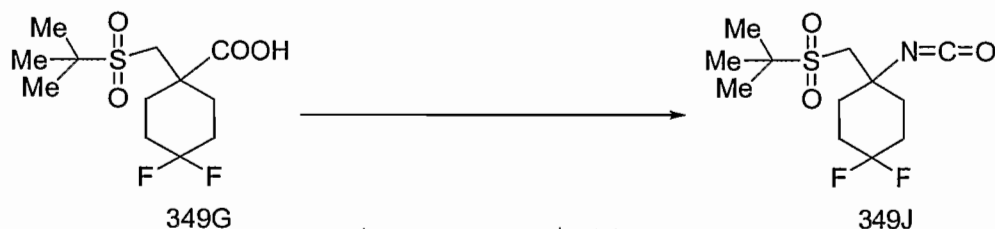
(0.77 g; 1.05 equiv.) followed by diisopropylethylamine (0.8913 g; 1.2 ml; 3.59 equiv.). The reaction mixture was stirred at -20°C for ~16 hrs. It was then diluted with EtOAc (~150 ml) and washed successively with satd. NaHCO_3 , 10% citric acid and dried over Na_2SO_4 . Evaporation of the solvent *in vacuo* provided a amorphous solid which was chromatographed over SiO_2 (42 g). Elution of the column with 50%-60% EtOAc in n-hexane provided in some of the fractions pure **349H** (0.7835 g).



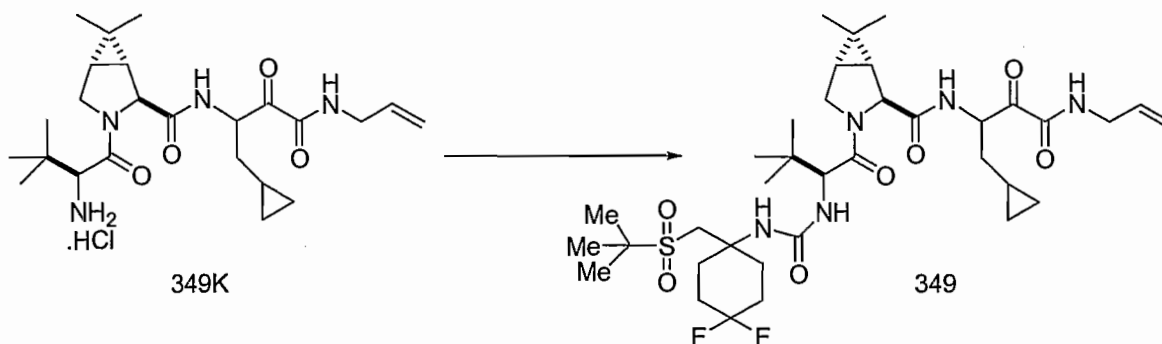
A solution of the hydroxyamide **349H** (0.7835 g; 0.00142 mol.) in dry methylene chloride (32 ml) was treated with stirring and cooling (ice bath) with Dess-Martin reagent (1.5134 g; 2.5 equiv.). Ice bath was removed and the reaction mixture was allowed to stir at room temperature for 2.5 hrs. Saturated $\text{Na}_2\text{S}_2\text{O}_3$ (32 ml) was added to destroy excess oxidant and stirring continued until the cloudy solution turned clear two-phase system. The reaction mixture was then diluted with CH_2Cl_2 (~100 ml), the organic phase separated and washed once with satd. NaHCO_3 , water then dried. Evaporation to dryness *in vacuo* provided **349I** (0.7466 g) as an amorphous solid.



The tert.-butylcarbamate **349I** (0.7466 g) was treated with 4M HCl/dioxane (20 ml) and left in a stoppered flask for 45 minutes. Most of the dioxane was evaporated in-vacuo and the residue evaporated with n-hexane twice; the remaining residue was triturated with ether leaving **349K** (0.6341 g) as a free flowing solid.

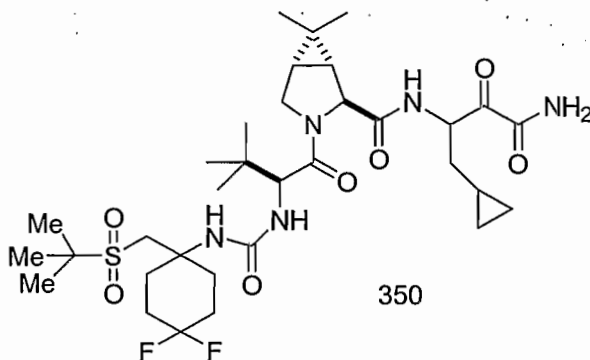


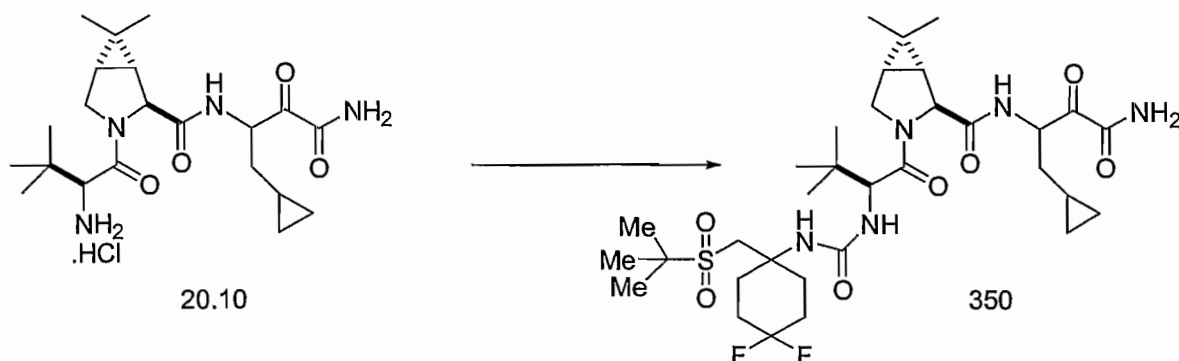
To a toluene solution (7.5 ml) of the acid **349G** (0.1 g; 0.0003351 mol.) were added Et₃N (0.0467 ml; 46.7 μl; 1 equiv.) followed by diphenylphosphoryl azide (0.072; 72 μl; 1equiv.). The reaction mixture was refluxed for 1 h. After cooling down, it was treated with ethyl acetate (~50 ml), the organic phase washed with saturated NaHCO₃ and concentrated *in vacuo* to provide **349J** (0.1 g).



To a stirred suspension of the amine hydrochloride **349K** (0.1 g; 0.000207 mol.) in methylene chloride (5 ml) was added diisopropylethylamine (0.135 g; 5 equiv.). After 1 minute was added the isocyanate **349J** (0.1 g; 0.0003385 mol.). The reaction mixture was stirred at room temperature for 2 hrs. It was then diluted with EtOAc and washed with 1N HCl, satd. NaHCO₃, dried over Na₂SO₄ and finally evaporated to dryness in-vacuo to provide an amorphous solid. It was subjected to preparatory TLC on silica gel plates using 40% acetone in n-hexane as eluent. The uv positive band was extracted with 60% acetone in methylene chloride to provide **349** (0.122 g) as an amorphous solid.

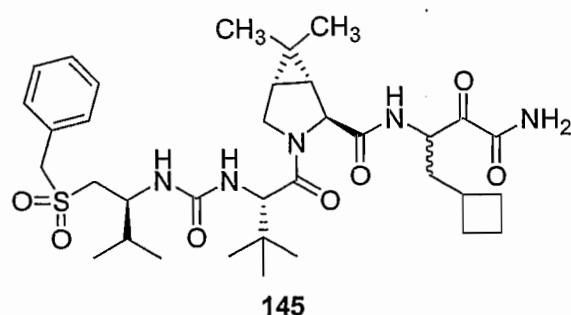
Synthesis of Compound 350:



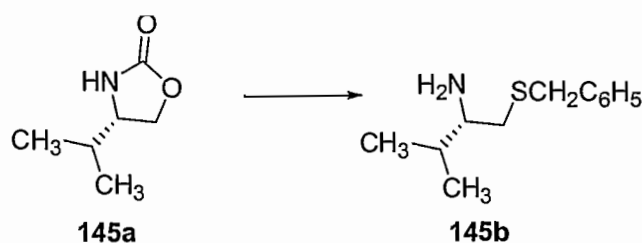


To a stirred suspension of the amine hydrochloride **20.10** (0.0966 g; 0.000223 mol.) in methylene chloride (5 ml) was added diisopropylethylamine (0.144 g; 5 equiv.). After 1 minute was added the isocyanate **349H** (0.1 g; 0.0003385 mol.). The reaction mixture was stirred at room temperature for 2 hrs. It was then diluted with EtOAc (~100 ml), then washed with 1N HCl, satd. NaHCO₃, dried over Na₂SO₄ and finally evaporated to dryness *in vacuo* to provide an amorphous white solid (0.1731 g). It was subjected to preparatory TLC on silica gel using 40% acetone in n-hexane as eluent. The uv positive band was extracted with 60% acetone in methylene chloride to provide **350** (0.0671 g) as an amorphous solid.

Example 145 Preparation of compound of formula 145:

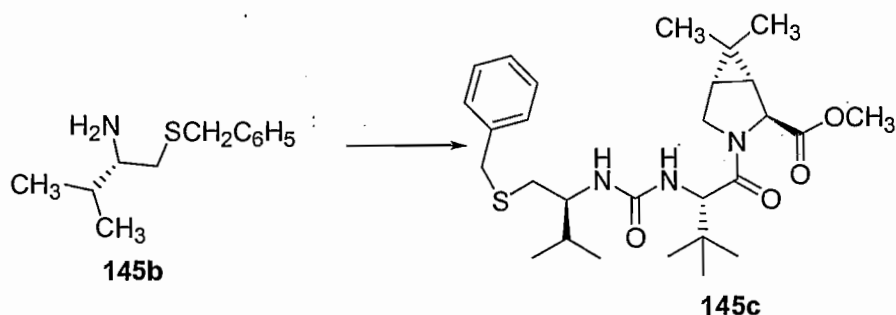


Step 1



1-Propanol was treated with metallic sodium (361 mg, 15.7 mmol) and stirred at RT for 1 h. After complete dissolution of sodium, benzylthiol (2.74 mL, 23.2 mmol) was added and the reaction mixture was stirred at RT for 0.5 h. (S)-4-isopropyl-oxazolidinone (Aldrich, 1g, 7.74 mmol) was added and the reaction mixture was heated at reflux for 16 h. The reaction mixture was concentrated in *vacuo* and the crude mixture was diluted with cold water and extracted with ether (3x150 mL). The combined organic layers were dried, filtered concentrated in *vacuo* to yield amine **145b**. It was converted to the hydrochloride salt with 4 M HCl and dried in high vacuum to yield **145b.HCl** (1.9 g).

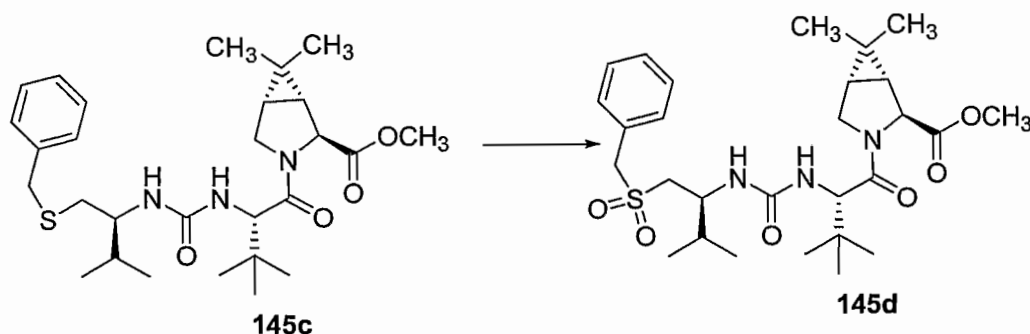
Step 2



A solution of **145b.HCl** (1 g, 4.07 mmol) in CH_2Cl_2 (50 mL) and satd. NaHCO_3 (70 mL) at 0°C was treated with phosgene (15% in toluene 10 mL) and stirred at 0°C for 3 h. The reaction mixture was poured into a separatory funnel and the organic layer was separated. The organic layer was washed with cold NaHCO_3 , brine and dried (MgSO_4). It was concentrated and used as it is in next step.

Amine hydrochloride salt (**1.04**; 865 mg, 2.7 mmol) was dissolved in $\text{CH}_2\text{Cl}_2/\text{DMF}$ 1:1 and cooled to 0°C . The mixture was treated with $(\text{C}_2\text{H}_5)_3\text{N}$ (682 mg, 6.75 mmol) and isocyanate prepared as above (950 mg, 4.07 mmol) and stirred at RT overnight. The solvent was evaporated and the residue was dissolved in EtOAc. The organic layer was washed with aq. HCl, aq NaHCO_3 , brine. The reaction mixture was dried, filtered and concentrated in *vacuo*. The residue was purified by chromatography (SiO_2 , EtOAc/Hexanes 1:3) to yield **145c** (880 mg).

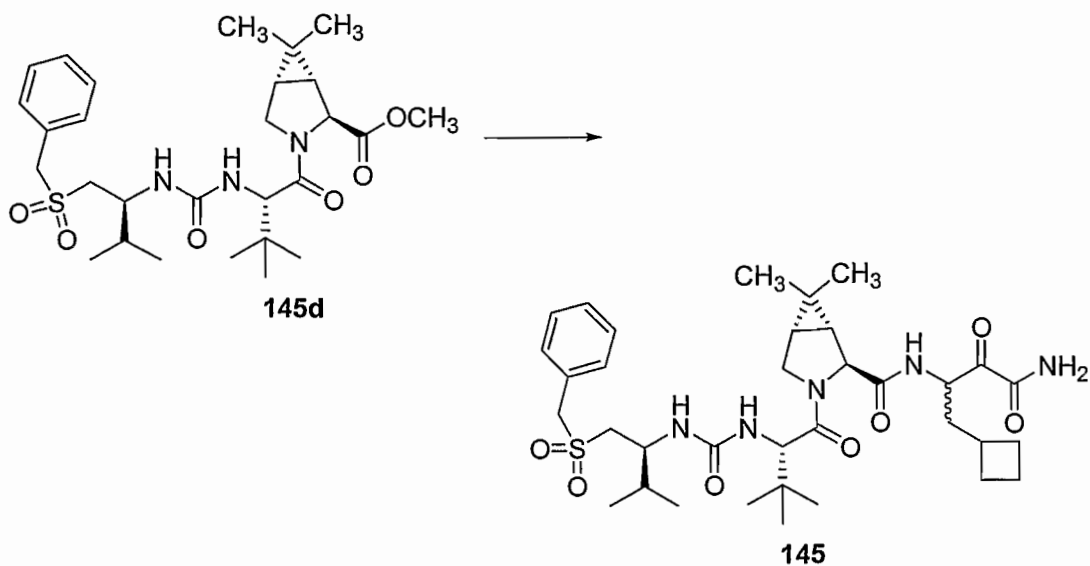
Step 3



A solution of **145c** (500 mg, 0.9 mmol) in 1,2 dichloroethane (10 mL) was treated with MCPBA (70%, 500 mg,) and 0°C and diluted with ether and aq. solution of $\text{Na}_2\text{S}_2\text{O}_3$. The organic layer was separated and washed extensively with aq. saturated NaHCO_3 and brine. The reaction mixture was dried (MgSO_4) filtered concentrated in *vacuo* and purified by chromatography (SiO_2 , EtOAc/Hexane 2:3) to yield **145d** (530 mg). MS (ESI) 550 $[(\text{M}+1)^+]$, 100], 381 (95), 353 (20).

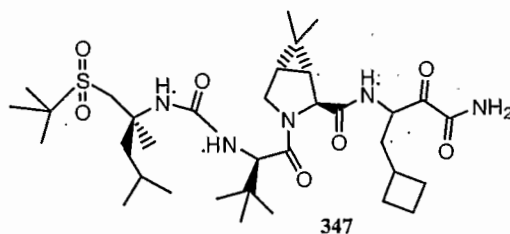
15

Step 4

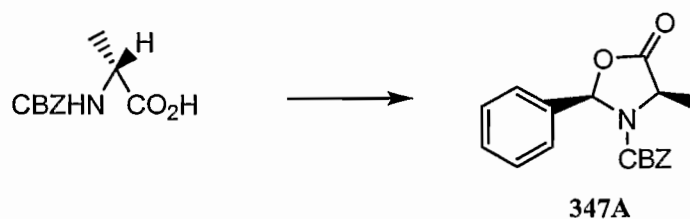


The conversion of **145d** to **145** was identical to the procedure described in the conversion of **284B** to **284D** and **108D** to **108 MS** (ESI) 690 [(M+1)⁺, 100), 381 (30).

Preparation of Intermediate of Formula 347:



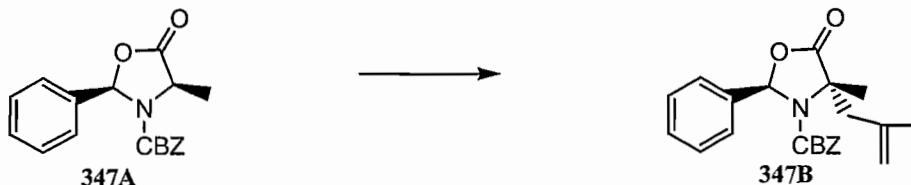
Step1:



Dimethyl benzaldehyde acetal (10.0 mL, 67.2 mmol) was added to a cooled solution of CBZ-*D*-alanine (15.0 g, 67.2 mmol) in Et₂O (180 mL), followed by BF₃·Et₂O (50.6 mL, 403.2 mmol) over 15 min. The reaction

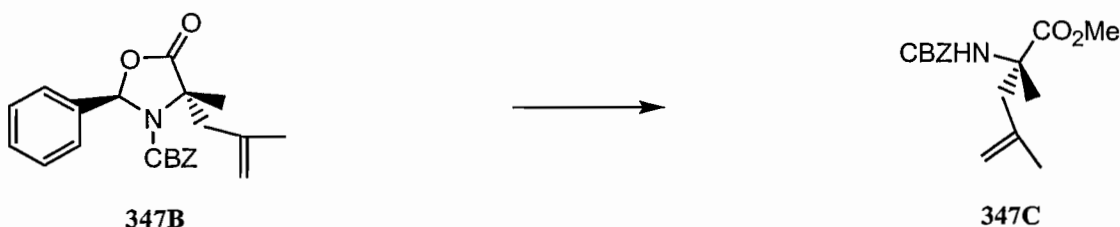
mixture was stirred at -20 °C for 4 days and quenched by addition of ice cold saturated NaHCO₃ (350.0 mL). The organic layer was diluted with Et₂O (500 mL), separated, washed with NaHCO₃ (5% aqueous solution), brine, dried over MgSO₄, filtered and concentrated. The crude was recrystallized using Et₂O/hexane to yield **347A** (13.6 g, 65%).

Step 2



THF(48.0 mL) was added to a flame dried flask and cooled to -35 °C. KHDMS(0.5 M solution in PhMe, 42.0 mL, 21 mmol) was added to it, followed by dropwise addition of a mixture of **347A** (6.22g, 20.0 mol) and 3-bromo-2-propene (2.02 mL, 20 mmol) maintaining the internal temperature between -30 and -35 °C. The reaction mixture was stirred at -35 °C for 2 h, then allowed to warm up over 2.5 h, quenched by addition of ice cold saturated NaHCO₃ (400.0 mL). The organic layer was diluted with Et₂O (600 mL), separated, washed with brine, dried over MgSO₄, filtered and concentrated. The crude was purified over SiO₂ using CH₂Cl₂ to yield **347B** (14.2 g, 90%).

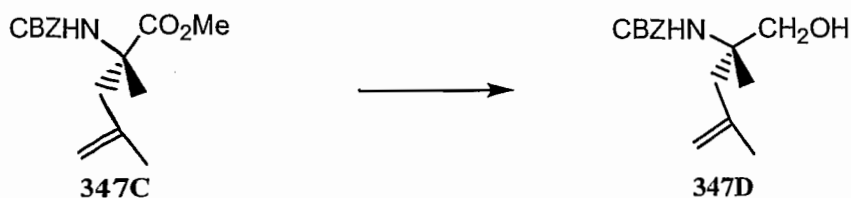
Step 3



To a solution of **347B** (10.7 g, 29.4 mmol) in MeOH (200 mL) was added LiOH (4N, 15 mL) and stirred at RT for 30 min, diluted with H₂O (500 mL), extracted with EtOAc (4 x 400 mL), washed with brine, dried over

MgSO₄, filtered and concentrated. The crude was purified over SiO₂ using CH₂Cl₂ to yield **347C** (8.65 g, 88%).

Step 4



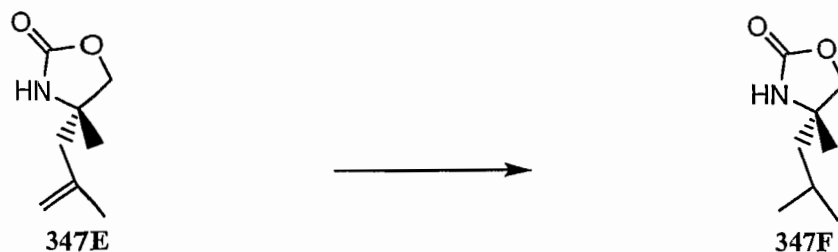
- 5 To a ice-cold solution of **347C** (8.56 g, 29.4 mmol) in EtOH (100 mL) was added LiBH₄ (960 mg, 44.1 mmol) and stirred at RT for 12h, another portion of LiBH₄ (960 mg) was added to it at 5 °C and stirred at RT for 4h, diluted with H₂O (100 mL) and MeOH(100 mL), evaporated to dryness, dissolved in H₂O (100 ml), extracted with EtOAc (500 mL), washed with brine,
- 10 dried over MgSO₄, filtered and concentrated. The crude was purified over SiO₂ using EtOAc (1-8%) in CH₂Cl₂ to yield **347D** (4.7 g, 60%).

Step 5



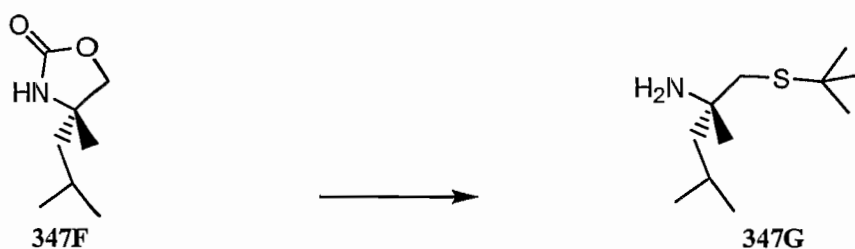
- 15 *t*-BuOK (1M in THF, 3.85 mL) was added to a cooled (-5 °C) solution of **347D** (4.06 g, 15.4 mmol) in THF (20 mL) and stirred at that temperature for 2h. The reaction mixture was concentrated, redissolved in EtOAc (250 mL) and NaOH (2N, 50 mL). The organic layer was diluted with EtOAc (600 mL), separated, washed with brine, dried over MgSO₄, filtered and concentrated. The crude was purified over SiO₂ using 10% CH₂Cl₂ in EtOAc to yield **347E**
- 20 (1.4 g).

Step 6



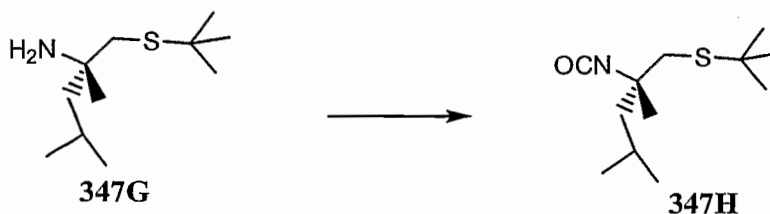
347E (1.37 g, 8.82mmol) was dissolved in EtOH (25 mL) and Pd-C (10% by weight, 275.0 mg) was added to it. The reaction mixture was stirred under a hydrogen atmosphere for 12h, filtered, concentrated and purified over SiO₂ using 10% CH₂Cl₂ in EtOAc to yield **347F** (1.04g, 75%).

Step 7



347F (2.58 g, 16.4mmol) was dissolved in PrOH (40 mL) and NaSBu-t (10.2 g, 82 mmol) was added to it. The reaction mixture was refluxed for 136 h, cooled, evaporated and redissolved in EtOAc, washed with H₂O and the organic layer dried over MgSO₄, filtered and concentrated. The crude was purified over SiO₂ using 30% acetone in CH₂Cl₂ to yield **347G** (0.6 g, 19%) and **347F** (1.1g).

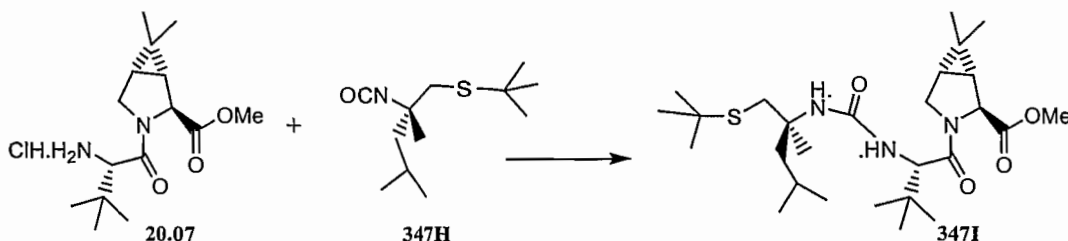
Step 8



Saturated NaHCO₃ was added to an ice-cold solution of **347G** (0.6 g, 3.0 mmol) in CH₂Cl₂ (30 mL). The reaction mixture was stirred vigorously for

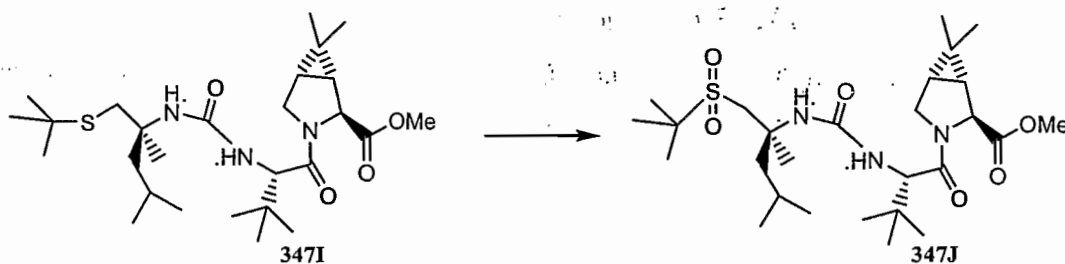
10 min. and COCl_2 (1.85 M solution in PhMe, 4.51 mL) was added to it and stirring was continued at room temperature for 1h. The organic layer was dried over MgSO_4 , filtered and concentrated to half the volume to yield **347H** as a solution in CH_2Cl_2 .

5 Step 9



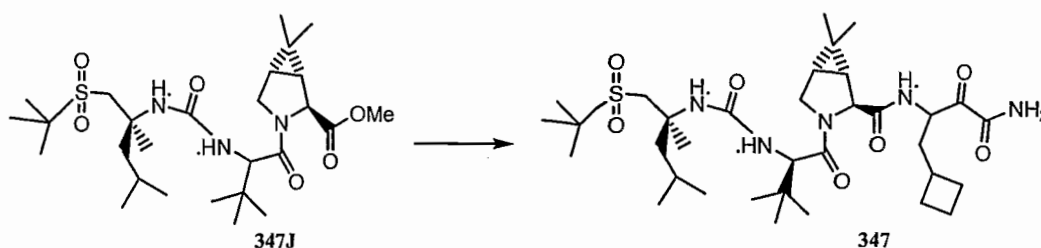
To a cooled solution (0°C) of **347H** (685 mg, 3.0 mmol) in DMF (10.0 mL) was added **20.07** (1.05 g, 3.34 mmol), followed by DIPEA (1.45 mL, 8.35 mmol). The reaction mixture was stirred at room temperature for 1.2 h, diluted with ethyl acetate, washed with 3% citric acid, brine, dried over MgSO_4 , filtered, concentrated and purified over SiO_2 using acetone/ CH_2Cl_2 (1:9) to yield **347I** (1.57g).

Step 10



To a cooled solution (0°C) of the **347I** (1.5 g, 3.34 mmol) in CH_2Cl_2 (100.0 mL) was added *m*-CPBA (2.51g, 10.02 mmol). The reaction mixture was warmed to room temperature over 12 h, diluted with CH_2Cl_2 (300.0 mL), washed with brine, dried over MgSO_4 , filtered, concentrated and purified over SiO_2 using acetone/ CH_2Cl_2 (1:9) to yield **347J** (1.57g).

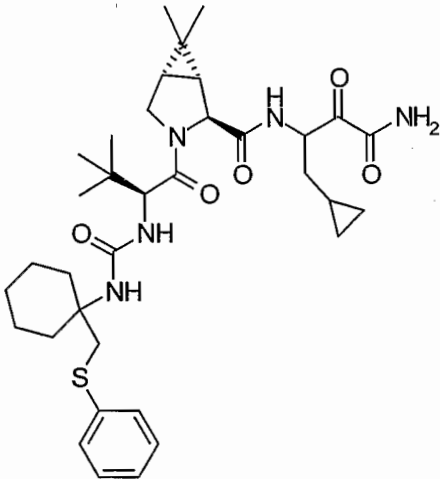
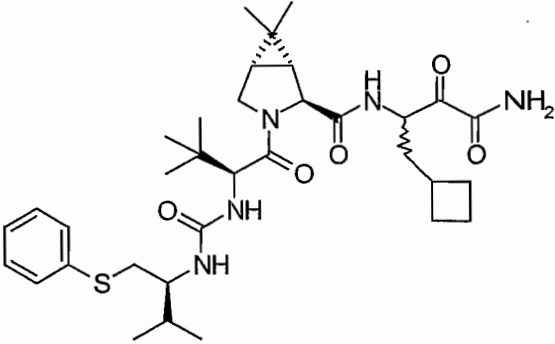
Step 11

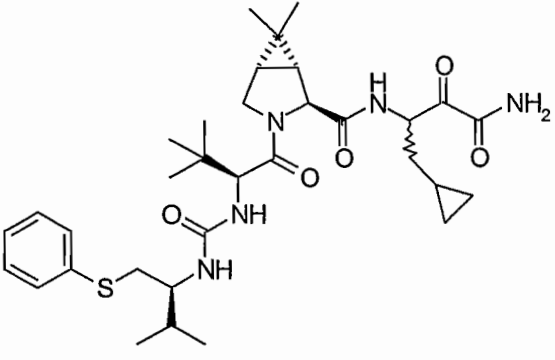
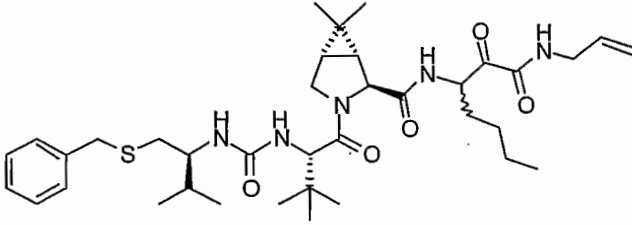
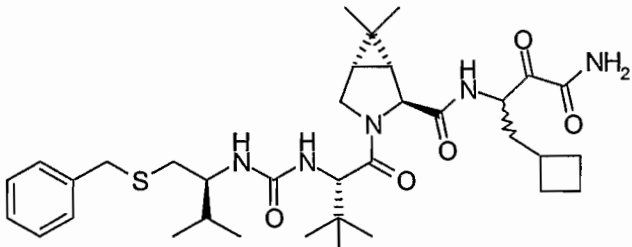


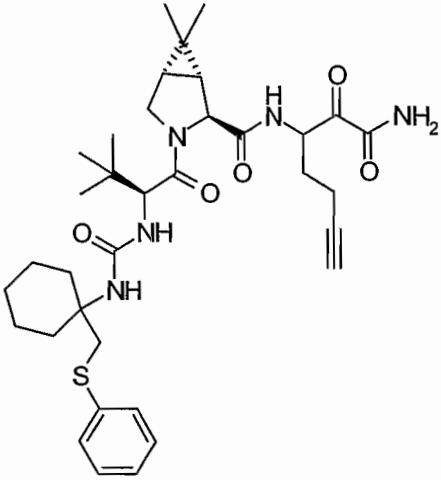
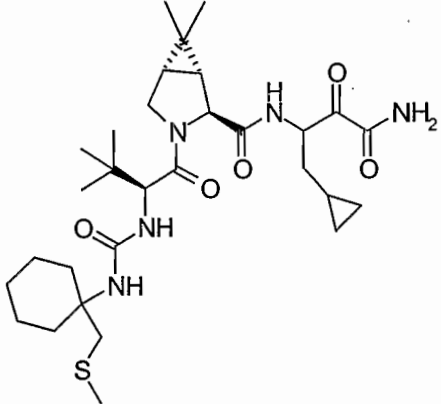
The conversion of **347J** to **347** was similar in procedure to those described in the conversion of **284B** to **284D** and **108D** to **108 MS**(LCMS) calcd. 681.94, found (MH^+) 683.2.

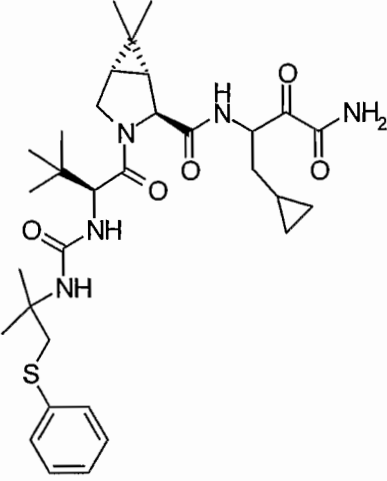
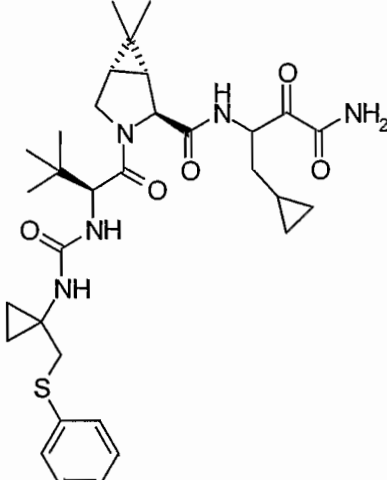
- 5 **Table 3** lists some of the inventive compounds and their HCV serine protease inhibitory activity ranges, as determined by the assay described later. The activity is shown as K_i^* ranges (nanoMolar), which are: A = <75 nM; B = 75 - 250 nM; and C = >250 nM.

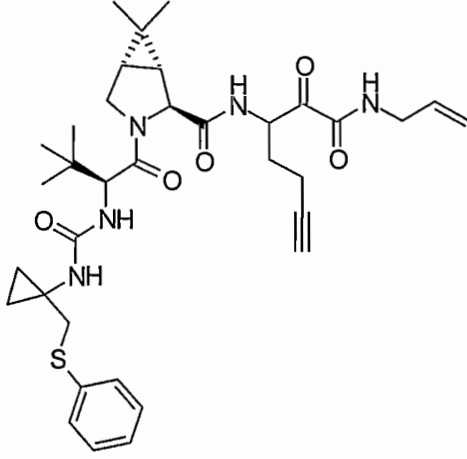
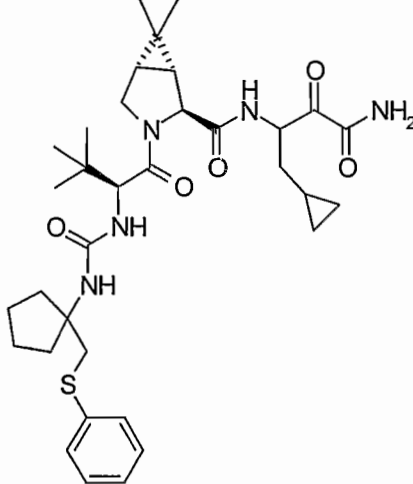
Table 3
Sulfide Compounds

Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
	[Ki* ranges are: A = <75 nM; B = 75 - 250 nM; C = >250 nM]		
102		LCMS; MH ⁺ , 654.1	A
103			B

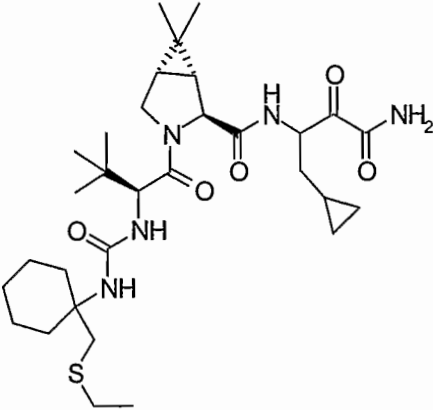
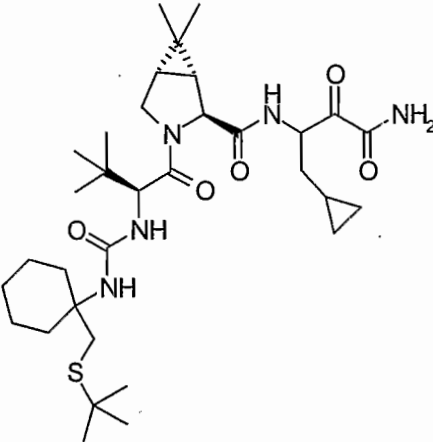
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
104			A
105			C
106			B

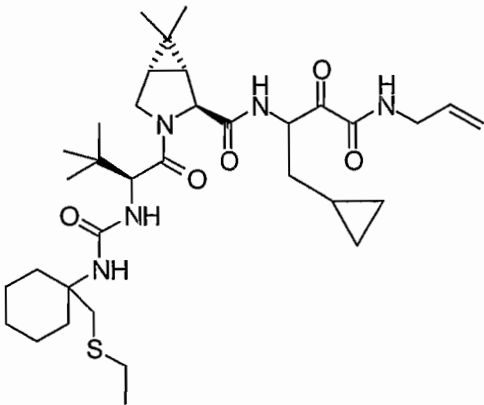
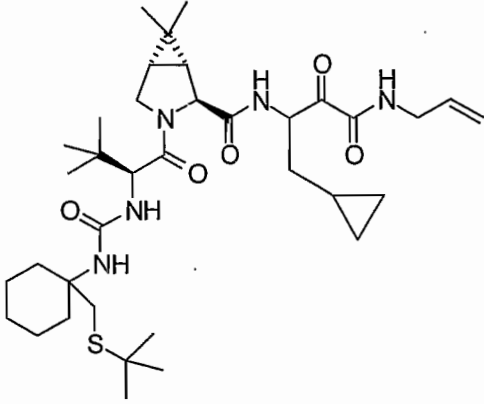
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
107		FABMS, (M+TG) ⁺ , 760.5. TG= thioglycerol	A
108			A

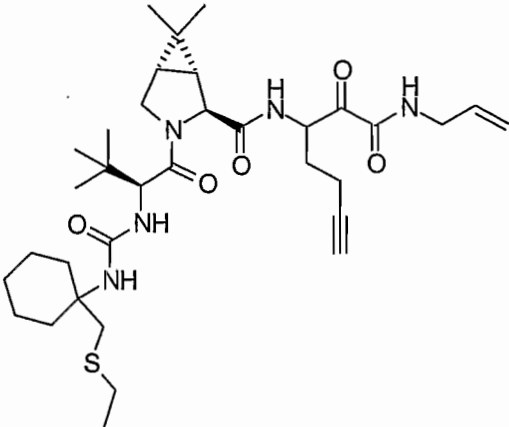
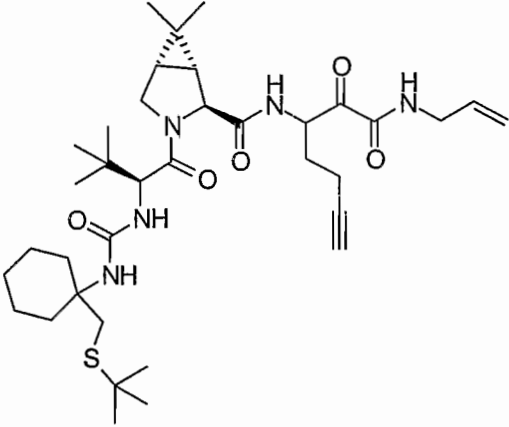
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
109	 Chemical structure of compound 109: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a cyclopropylmethyl group, which is further substituted with a primary amide group (-NH₂). The pyrrolidine ring is also linked via a carbonyl group to a chiral center (indicated by a wedge bond) that is part of a side chain. This side chain includes a secondary amide group (-NH-) and a thioether group (-S-) connected to a phenyl ring.		A
110	 Chemical structure of compound 110: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a cyclopropylmethyl group, which is further substituted with a primary amide group (-NH₂). The pyrrolidine ring is also linked via a carbonyl group to a chiral center (indicated by a wedge bond) that is part of a side chain. This side chain includes a secondary amide group (-NH-) and a thioether group (-S-) connected to a phenyl ring.		A

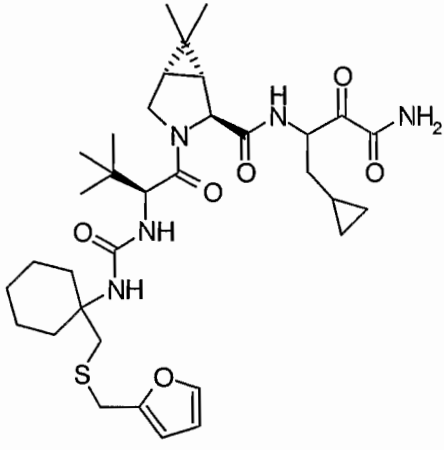
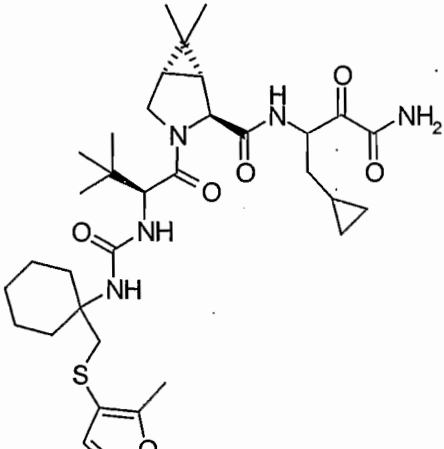
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
111		FABMS: (MH) ⁺ , 650.3.	B
112			A

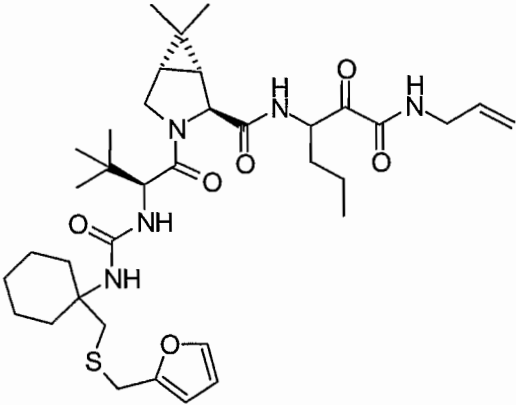
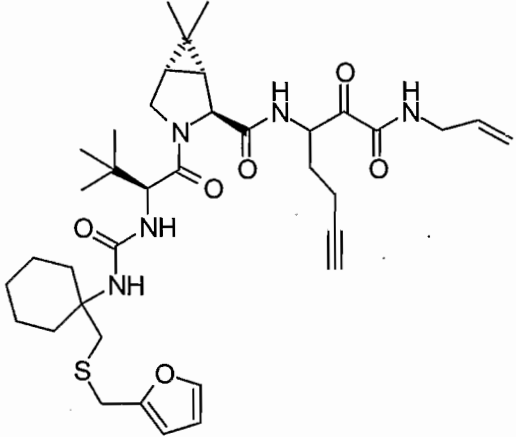
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
113	 <chem>CC(C)(C)C(=O)N1C(=O)C(=O)N1C(=O)NCC2CC2C(=O)NCC3CCCCC3SC4=CC=CC=C4</chem>	FABMS: (MH) ⁺ ,668.3	A
114	 <chem>CC(C)(C)C(=O)N1C(=O)C(=O)N1C(=O)NCC2CC2C(=O)NCC(C)(C)CSC</chem>		A

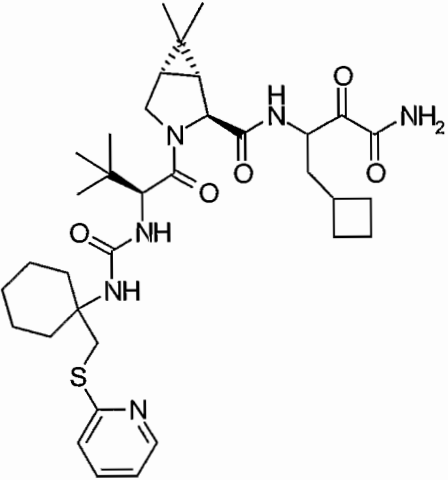
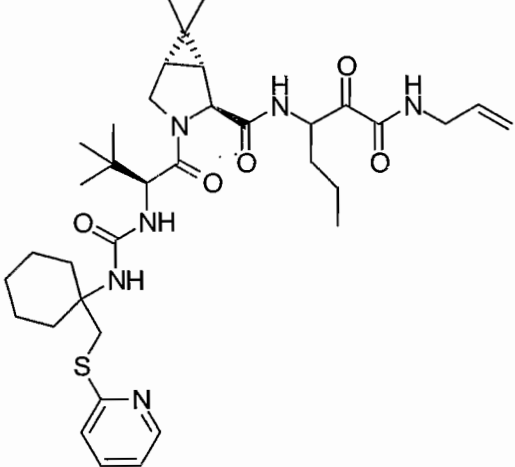
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
117	 Chemical structure of compound 117: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position (indicated by a dashed bond), a carbonyl group at the 3-position, and an amide group at the 4-position. The amide group is connected to a cyclopropylmethyl chain, which is further substituted with a carboxamide group. The carbonyl group at the 3-position is connected to a chiral center (indicated by a wedged bond) that is also substituted with a tert-butyl group and an amide group. This amide group is connected to a cyclohexyl ring, which is further substituted with a thioether group (indicated by a dashed bond) and a methyl group.		A
118	 Chemical structure of compound 118: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position (indicated by a dashed bond), a carbonyl group at the 3-position, and an amide group at the 4-position. The amide group is connected to a cyclopropylmethyl chain, which is further substituted with a carboxamide group. The carbonyl group at the 3-position is connected to a chiral center (indicated by a wedged bond) that is also substituted with a tert-butyl group and an amide group. This amide group is connected to a cyclohexyl ring, which is further substituted with a thioether group (indicated by a dashed bond) and a methyl group.		A

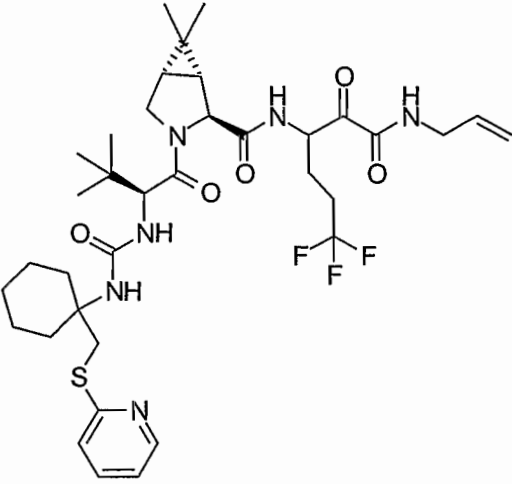
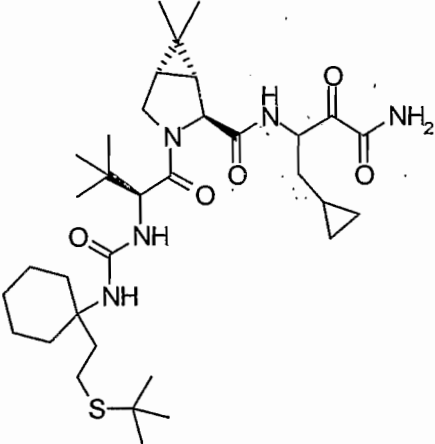
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
119	 Chemical structure of compound 119: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a cyclopropylmethyl group attached to a carbonyl group, which is further linked to an amide group with a vinyl group. Additionally, the pyrrolidine ring is linked to a cyclohexyl ring via a carbonyl group, which is also part of an amide linkage to a side chain. The side chain consists of a cyclopropylmethyl group attached to a carbonyl group, which is further linked to an amide group with a vinyl group.		B
120	 Chemical structure of compound 120: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a cyclopropylmethyl group attached to a carbonyl group, which is further linked to an amide group with a vinyl group. Additionally, the pyrrolidine ring is linked to a cyclohexyl ring via a carbonyl group, which is also part of an amide linkage to a side chain. The side chain consists of a cyclopropylmethyl group attached to a carbonyl group, which is further linked to an amide group with a vinyl group.		C

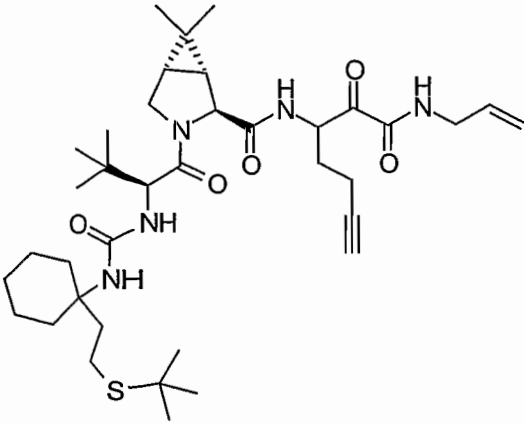
Prep. Ex.	COMPOUND	Select Mass Spectra Data	K ⁱ rang e
121		FABMS; MH ⁺ , 644.2	A
122		FABMS; MH ⁺ , 672.5.	A

Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
123	 Chemical structure of compound 123: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group, a dimethylamino group, and a carbonyl group. This carbonyl is part of an amide linkage to a side chain containing a cyclopropyl group and a primary amide. Another amide branch connects the central carbonyl to a cyclohexane ring, which is further substituted with a thiomethyl group linked to a furan ring.		A
124	 Chemical structure of compound 124: Similar to compound 123, but the furan ring is substituted with a methyl group at the 2-position.		B

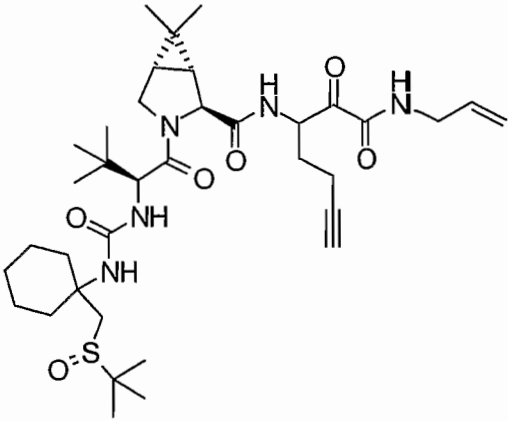
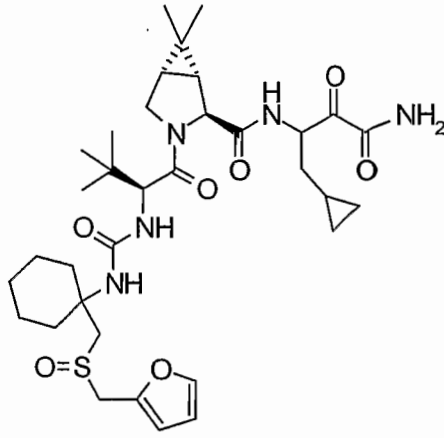
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
125	 Chemical structure of compound 125: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a side chain containing a propyl group and a terminal vinyl group. The carbonyl at the 4-position is part of an amide linkage to a side chain containing a propyl group and a terminal vinyl group. The pyrrolidine ring is also substituted with a tert-butyl group at the 2-position. The side chain at the 3-position is a 2-allyl-3-oxopropyl group. The side chain at the 4-position is a 2-allyl-3-oxopropyl group. The pyrrolidine ring is also substituted with a tert-butyl group at the 2-position. The side chain at the 3-position is a 2-allyl-3-oxopropyl group. The side chain at the 4-position is a 2-allyl-3-oxopropyl group.		B
126	 Chemical structure of compound 126: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a side chain containing a propyl group and a terminal vinyl group. The carbonyl at the 4-position is part of an amide linkage to a side chain containing a propyl group and a terminal vinyl group. The pyrrolidine ring is also substituted with a tert-butyl group at the 2-position. The side chain at the 3-position is a 2-allyl-3-oxopropyl group. The side chain at the 4-position is a 2-allyl-3-oxopropyl group. The pyrrolidine ring is also substituted with a tert-butyl group at the 2-position. The side chain at the 3-position is a 2-allyl-3-oxopropyl group. The side chain at the 4-position is a 2-allyl-3-oxopropyl group.		A

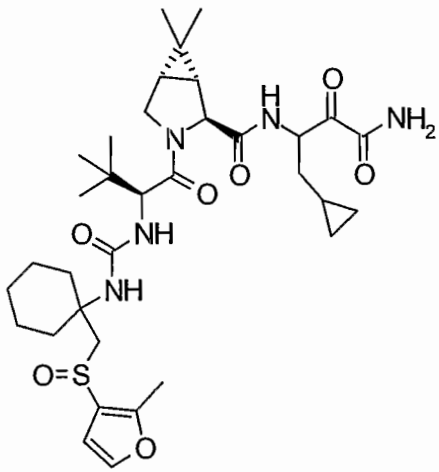
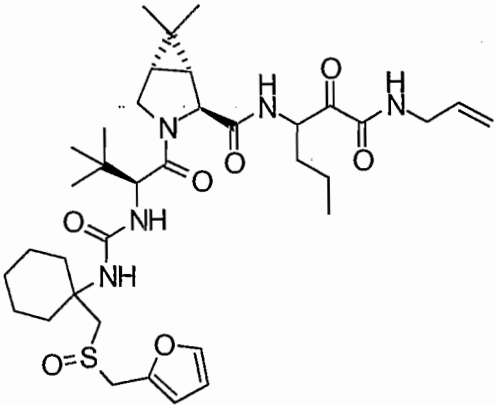
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
127	 Chemical structure of compound 127: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group, a dimethylamino group, and a carbonyl group. This carbonyl is part of an amide linkage to a cyclobutane ring, which is further substituted with an amide group and a carboxamide group. The molecule also includes a cyclohexane ring and a pyridine ring connected via a sulfur atom.		A
128	 Chemical structure of compound 128: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group, a dimethylamino group, and a carbonyl group. This carbonyl is part of an amide linkage to a propyl chain, which is further substituted with an amide group and a vinyl group. The molecule also includes a cyclohexane ring and a pyridine ring connected via a sulfur atom.		B

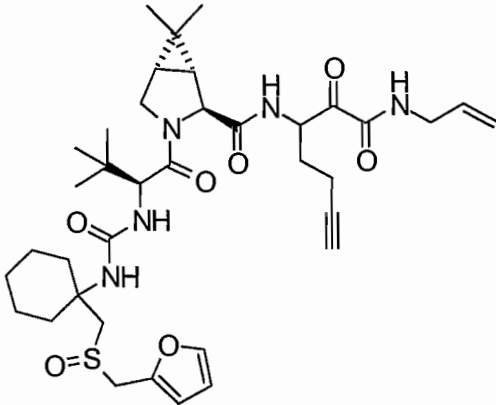
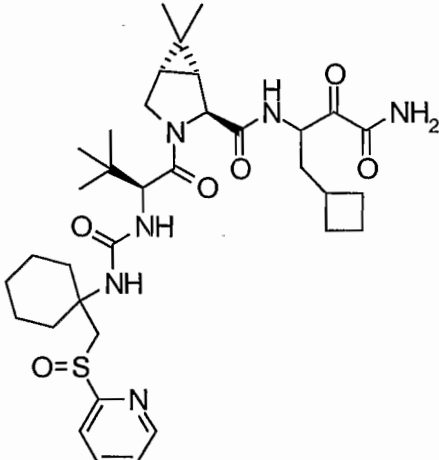
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
129	 Chemical structure of compound 129: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a side chain containing a trifluoromethyl group and a terminal vinyl group. The carbonyl at the 4-position is part of an amide linkage to a side chain containing a cyclohexyl group and a pyridine ring. The pyridine ring is substituted with a methyl group at the 2-position.		C
130	 Chemical structure of compound 130: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a side chain containing a cyclopropyl group and a terminal amino group. The carbonyl at the 4-position is part of an amide linkage to a side chain containing a cyclohexyl group and a thioether group. The thioether group is substituted with a tert-butyl group.		B

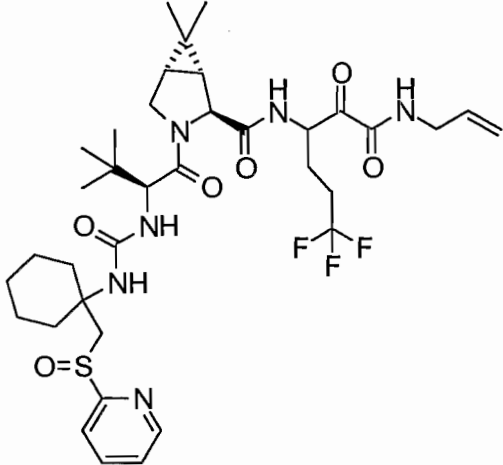
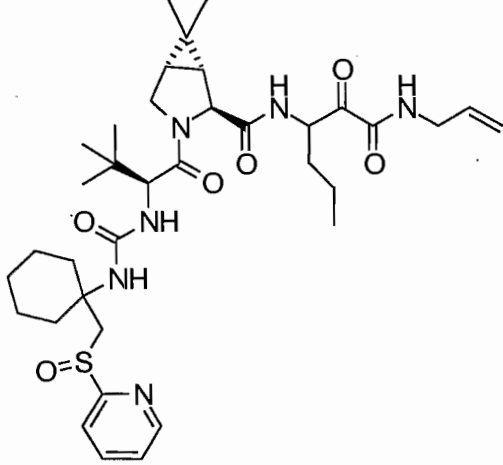
Prep. Ex.	COMPOUND	Select Mass Spectra Data	Ki* rang e
131	 <chem>CC(C)(C)SCC1CCCCC1NC(=O)C[C@H](C)C(=O)N2CC[C@H](C(C)(C)C)C2C(=O)NCC(=O)C[C@H](C#C)C(=O)NCC=C</chem>		B

Sulfoxide Compounds

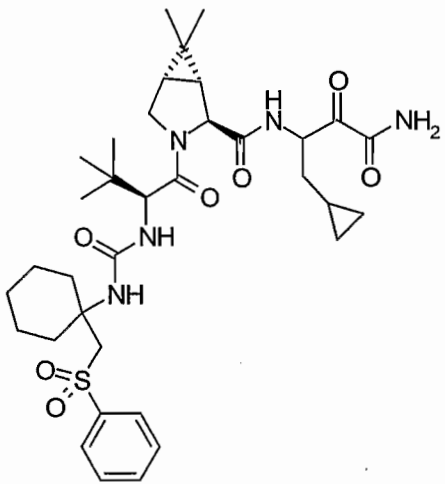
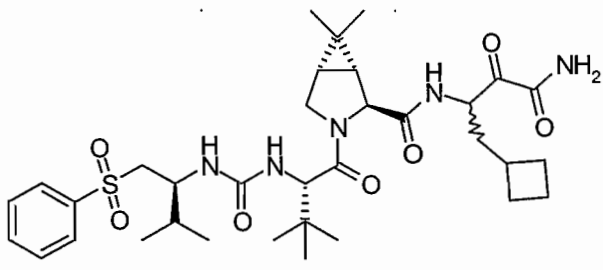
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
	[Ki* ranges are: A = <75 nM; B = 75 - 250 nM; C = >250 nM]		
132		FABMS; MH ⁺ , 688.5.	A
133			A

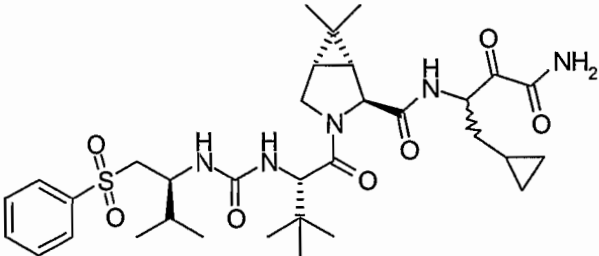
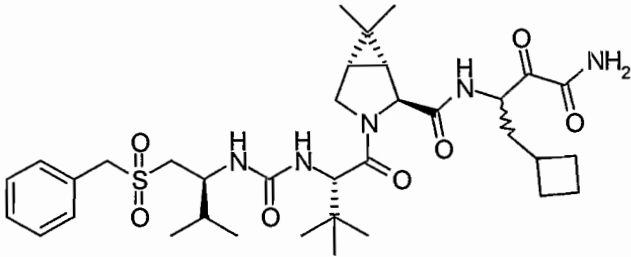
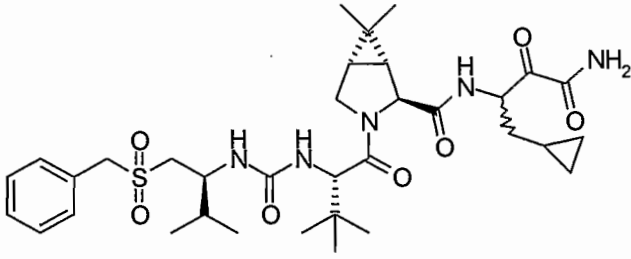
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
134	 Chemical structure of compound 134: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group, and a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group. The pyrrolidine ring is also substituted with a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group. The pyrrolidine ring is also substituted with a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group. The pyrrolidine ring is also substituted with a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group.		A
135	 Chemical structure of compound 135: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group, and a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group. The pyrrolidine ring is also substituted with a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group. The pyrrolidine ring is also substituted with a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group. The pyrrolidine ring is also substituted with a (2-oxo-2-(cyclopropylmethyl)ethyl)carbamoyl group.		A

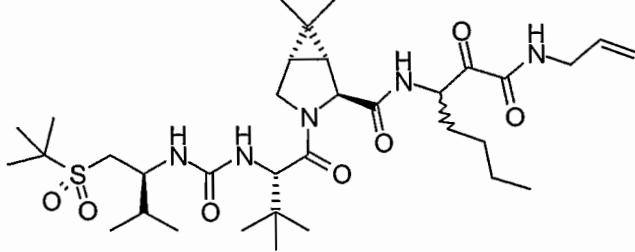
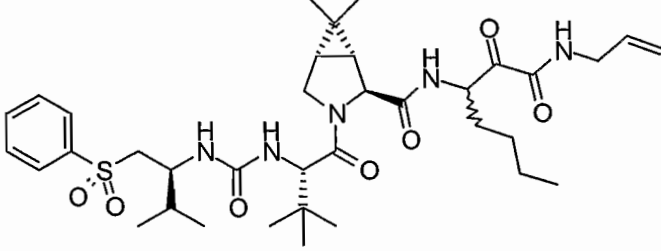
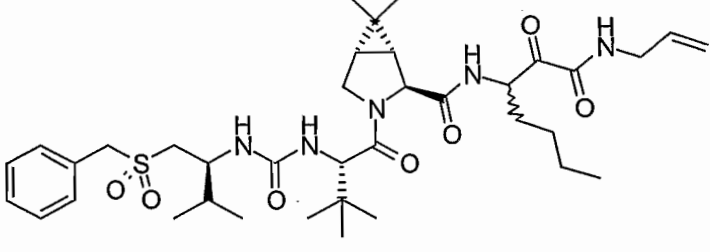
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
136	 Chemical structure of compound 136: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a dimethylamino group, and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a propargyl group (alkyne), a carbonyl group, and a terminal vinyl group. Additionally, the pyrrolidine ring is linked to a cyclohexane ring via a carbonyl group, which is further substituted with a sulfonamide group (SO₂CH₂Ph).		A
137	 Chemical structure of compound 137: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a dimethylamino group, and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclobutyl group, a carbonyl group, and a terminal amino group (NH₂). Additionally, the pyrrolidine ring is linked to a cyclohexane ring via a carbonyl group, which is further substituted with a sulfonamide group (SO₂CH₂Ph).		A

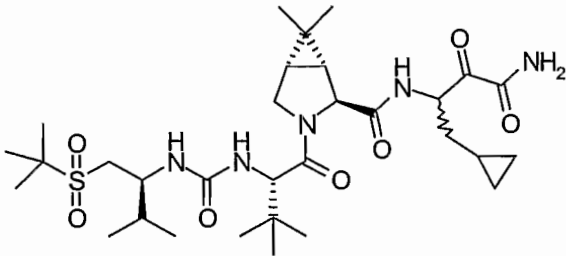
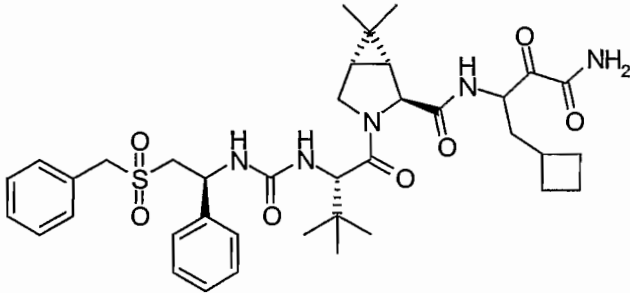
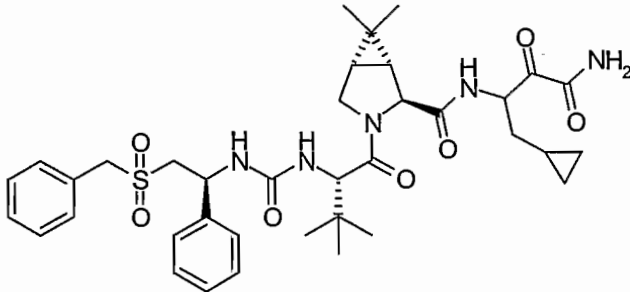
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
138	 Chemical structure of compound 138: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group, a dimethylamino group, and a side chain containing a carbonyl, a trifluoromethyl group, and a vinyl amide. This side chain is linked via a carbonyl to a cyclohexane ring, which is also substituted with a sulfonamide group (O=S(=O)N) and a pyridine ring.		B
139	 Chemical structure of compound 139: Similar to compound 138, but the side chain contains an ethyl group instead of a trifluoromethyl group.		A

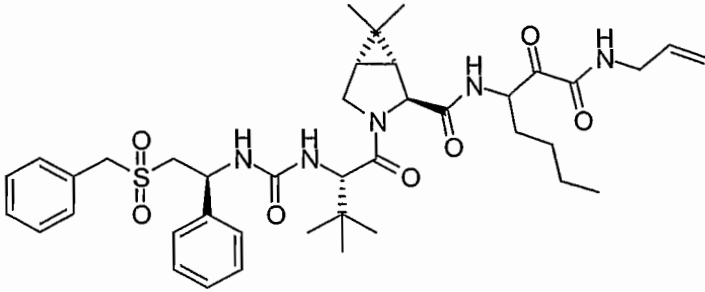
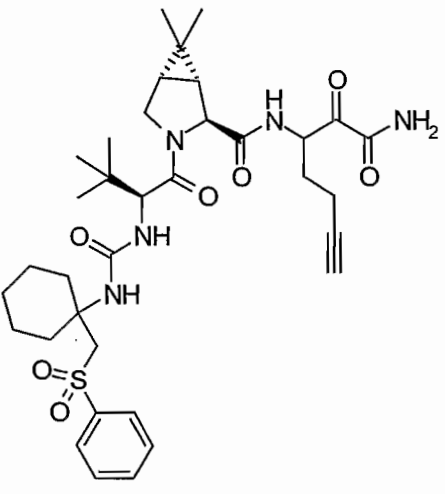
Sulfone Compounds

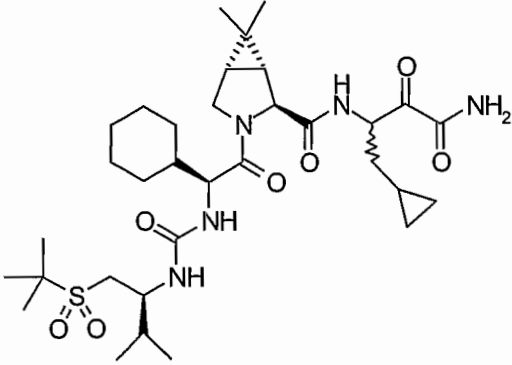
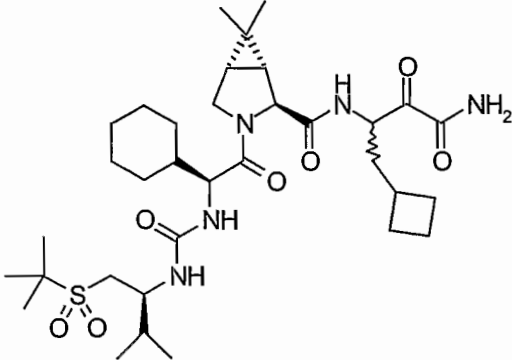
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
	[Ki* ranges are: A = <75 nM; B = 75 - 250 nM; C = >250 nM]		
142		LCMS: MH ⁺ , 686.1.	A
143			A

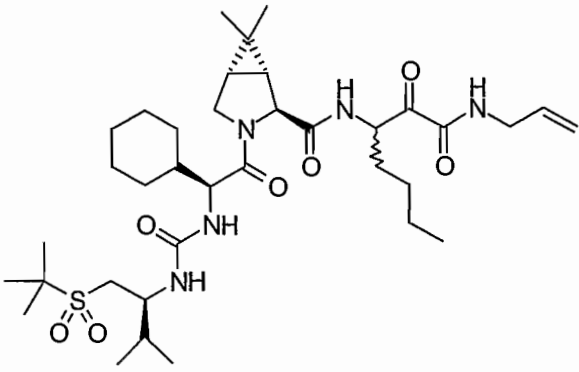
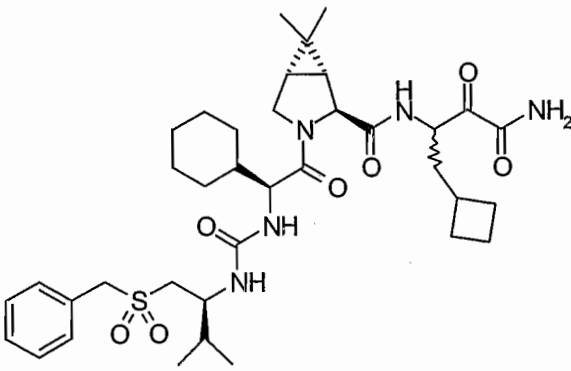
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
144			A
145			A
146			A

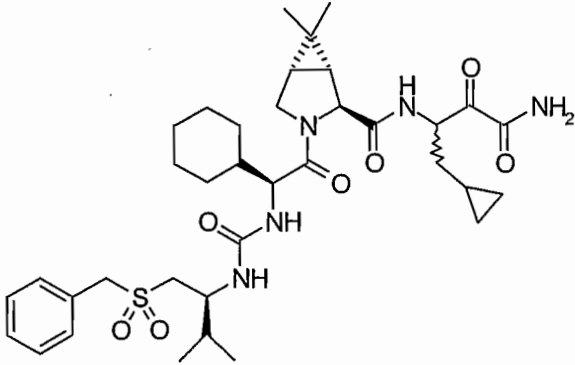
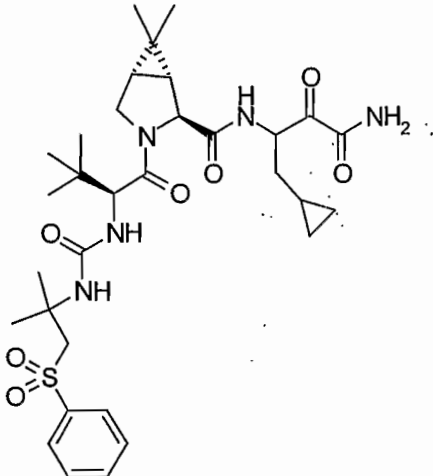
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i * range
147			B
148			B
149			B

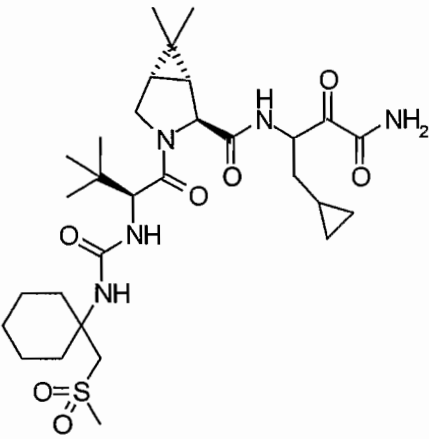
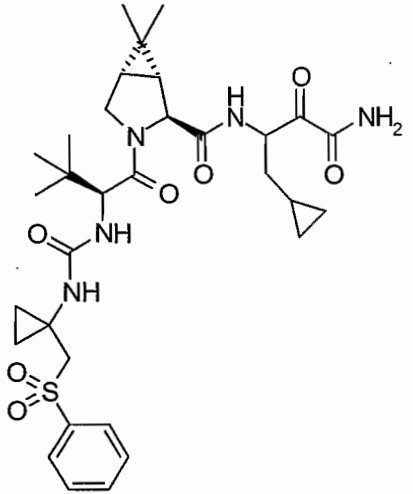
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
150			A
151			B
152			B

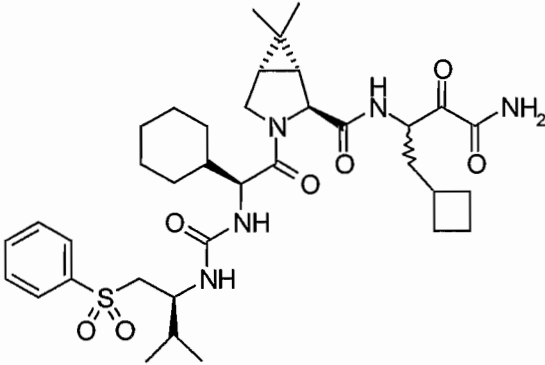
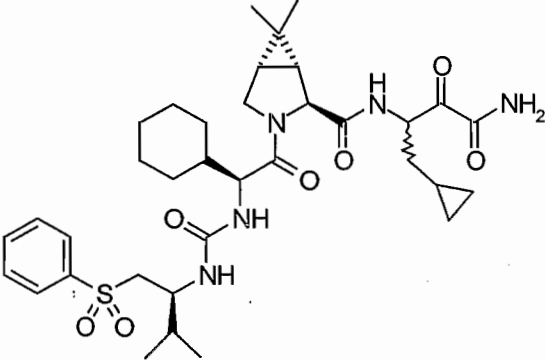
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
153			C
154		FABMS; MH ⁺ , 684.2.	A

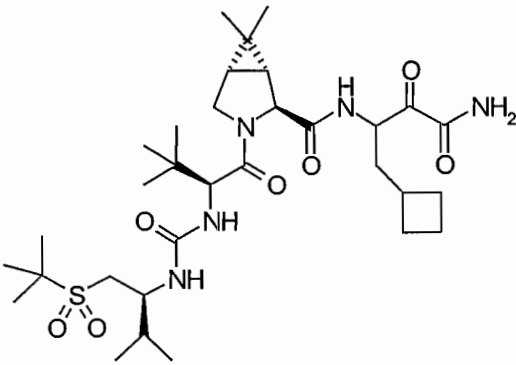
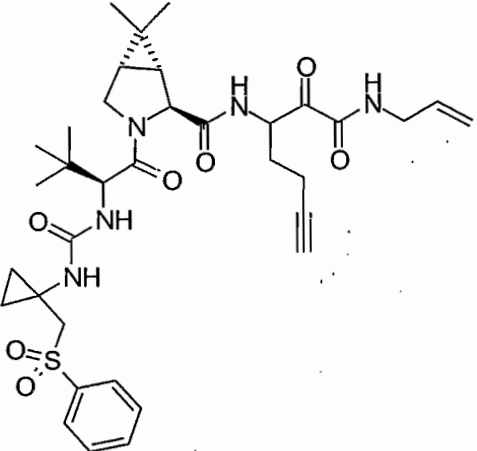
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
155	 Chemical structure of compound 155: A complex molecule featuring a central cyclohexane ring. Attached to the cyclohexane ring is a side chain containing a carbonyl group, an amide group, and a sulfonamide group. The sulfonamide group is further substituted with a tert-butyl group. The amide group is linked to a side chain that includes a carbonyl group, an amide group, and a cyclopropyl group. The cyclopropyl group is further substituted with a carbonyl group and an amide group.		A
156	 Chemical structure of compound 156: A complex molecule featuring a central cyclohexane ring. Attached to the cyclohexane ring is a side chain containing a carbonyl group, an amide group, and a sulfonamide group. The sulfonamide group is further substituted with a tert-butyl group. The amide group is linked to a side chain that includes a carbonyl group, an amide group, and a cyclobutyl group. The cyclobutyl group is further substituted with a carbonyl group and an amide group.		A

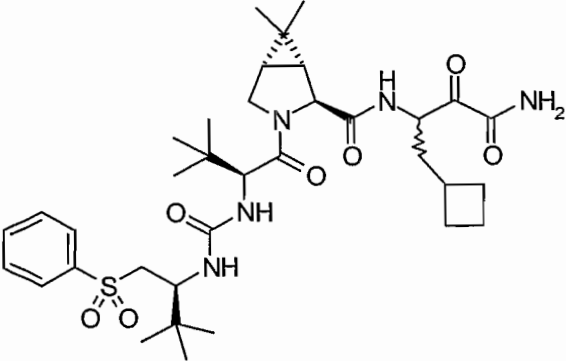
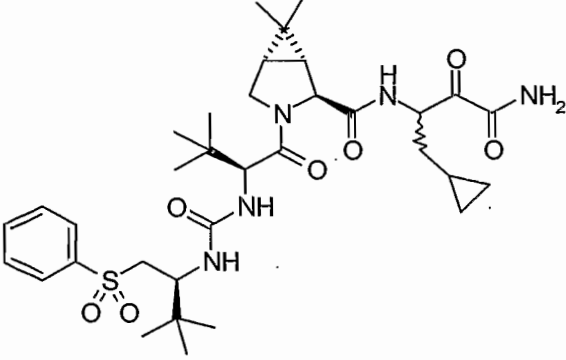
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K ⁱ * range
157	 Chemical structure of compound 157: A complex molecule featuring a central cyclohexane ring. Attached to the cyclohexane ring is a side chain containing a carbonyl group, an amide group, and a sulfonamide group. The sulfonamide group is further substituted with a tert-butyl group. The amide group is linked to a side chain containing a carbonyl group, an amide group, and a vinyl group.		A
158	 Chemical structure of compound 158: A complex molecule featuring a central cyclohexane ring. Attached to the cyclohexane ring is a side chain containing a carbonyl group, an amide group, and a sulfonamide group. The sulfonamide group is further substituted with a benzyl group. The amide group is linked to a side chain containing a carbonyl group, an amide group, and a cyclobutyl group.		A

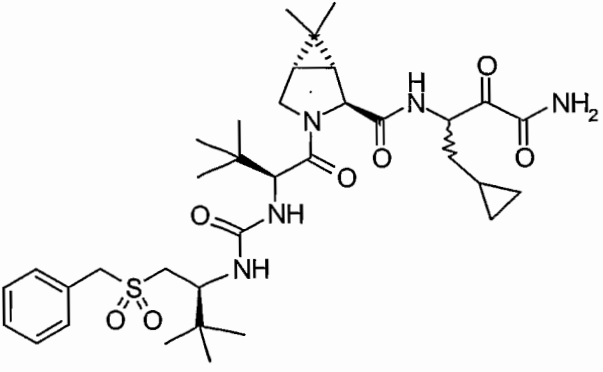
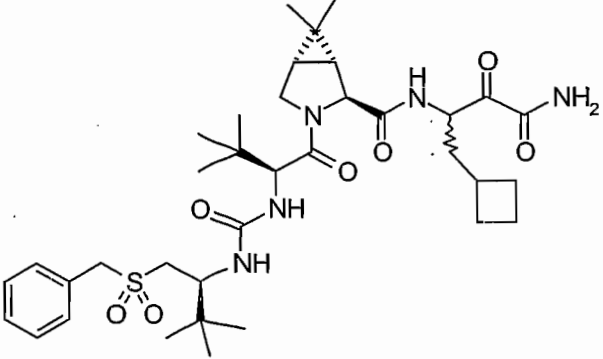
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i * range
159	 Chemical structure of compound 159: A complex molecule featuring a central pyrrolidine ring substituted with a cyclohexyl group, a tert-butyl group, and a side chain containing a carbamate and a cyclopropyl group. It is also linked to a sulfonamide moiety via an amide bond.		A
160	 Chemical structure of compound 160: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a side chain containing a carbamate and a cyclopropyl group. It is also linked to a sulfonamide moiety via an amide bond.		A

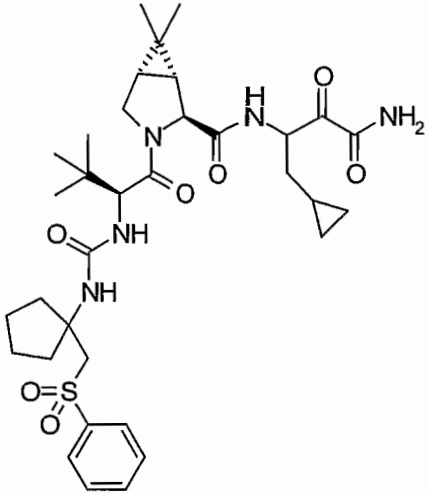
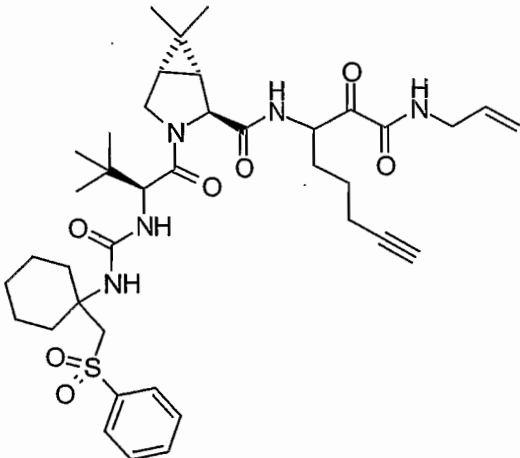
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
161	 Chemical structure of compound 161: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a methyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. This side chain includes a cyclopropylmethyl group, a carbonyl group, and a primary amide group (NH₂). The pyrrolidine ring is also linked to a cyclohexylmethyl group via a carbonyl group, which is further linked to a sulfonamide group (SO₂Me).		A
162	 Chemical structure of compound 162: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a methyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. This side chain includes a cyclopropylmethyl group, a carbonyl group, and a primary amide group (NH₂). The pyrrolidine ring is also linked to a cyclopropylmethyl group via a carbonyl group, which is further linked to a sulfonamide group (SO₂Ph).		A

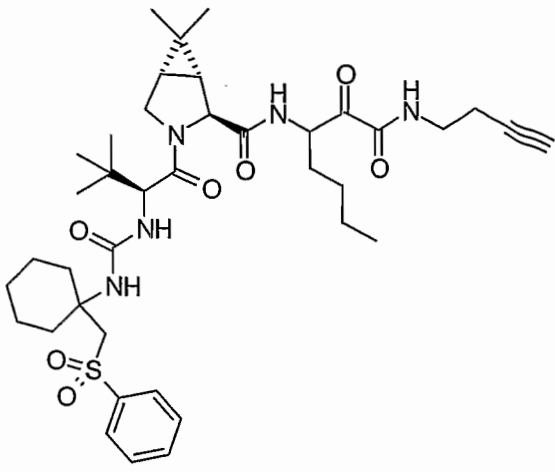
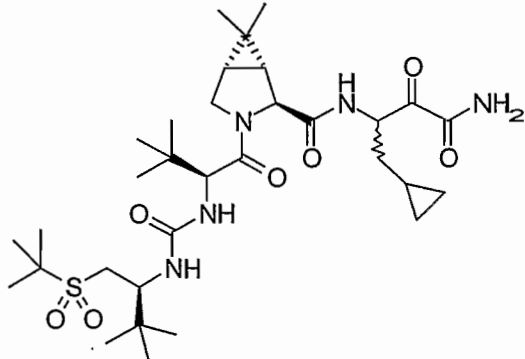
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
163	 Chemical structure of compound 163: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-((2-((benzenesulfonyl)amino)propan-2-yl)amino)cyclohexyl group, and a 2-((2-aminopropanamido)methyl)cyclobutyl group.		A
164	 Chemical structure of compound 164: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-((2-((benzenesulfonyl)amino)propan-2-yl)amino)cyclohexyl group, and a 2-((2-aminopropanamido)methyl)cyclopropyl group.		A

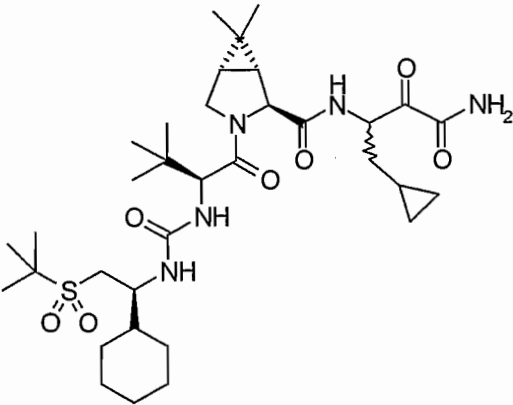
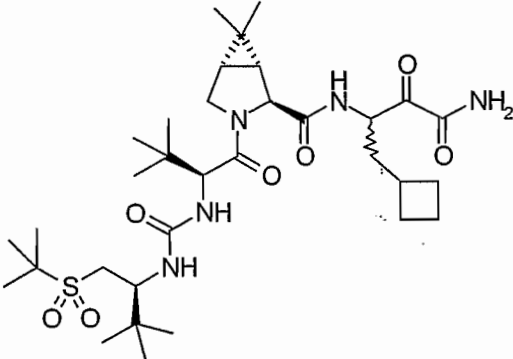
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
165	 <chem>CC(C)(C)S(=O)(=O)CC(C)NC(=O)N[C@@H](C(C)C)C(=O)N[C@@H](C1CC[C@H]1)C(=O)NC(=O)N</chem>		A
166	 <chem>CC(C)(C)S(=O)(=O)C1CC1NC(=O)N[C@@H](C(C)C)C(=O)N[C@@H](CC#CC)C(=O)NCC=C</chem>	FABMS; MH ⁺ , 682.3.	B

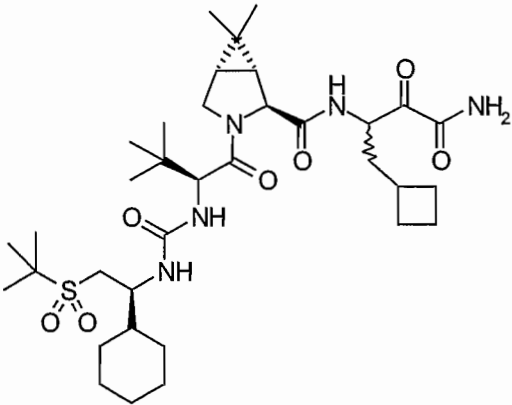
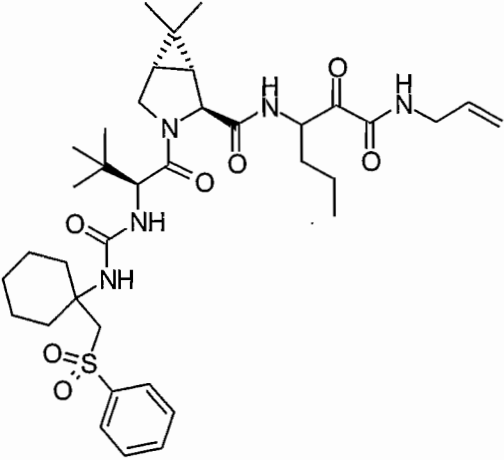
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
167	 Chemical structure of compound 167: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a carbamate group. The carbamate is linked to a cyclobutane ring, which is further connected to a chain containing a sulfonamide group and a phenyl ring.		A
168	 Chemical structure of compound 168: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a carbamate group. The carbamate is linked to a cyclopropyl ring, which is further connected to a chain containing a sulfonamide group and a phenyl ring.		A

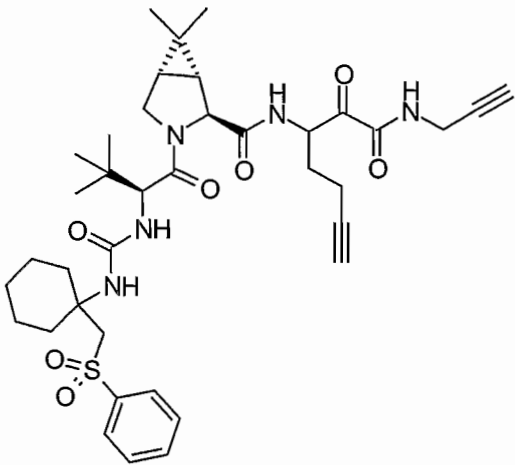
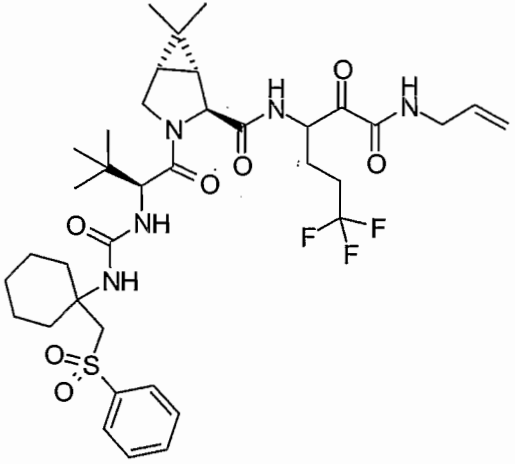
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
169	 Chemical structure of compound 169: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a dimethylamino group (dashed bond), and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclopropylmethyl group, a carbonyl group, and a primary amide group (NH₂). Additionally, there is a tert-butyl group and a benzylsulfonyl group (SO₂CH₂Ph) attached to the side chain.		A
170	 Chemical structure of compound 170: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a dimethylamino group (dashed bond), and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclobutylmethyl group, a carbonyl group, and a primary amide group (NH₂). Additionally, there is a tert-butyl group and a benzylsulfonyl group (SO₂CH₂Ph) attached to the side chain.		A

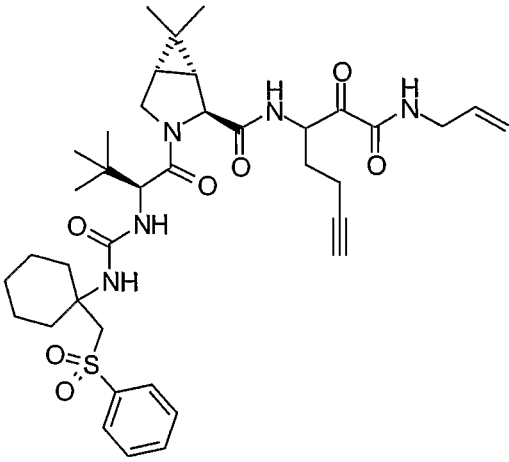
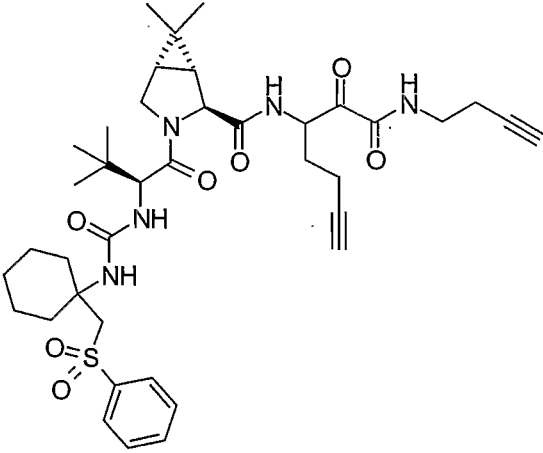
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K ⁱ * range
171	 Chemical structure of compound 171: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a carbonyl group, and a side chain containing a cyclopropylmethyl group and a primary amide. The side chain is further substituted with a cyclopentylmethyl group and a sulfonamide group (SO₂Ph).		A
172	 Chemical structure of compound 172: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a carbonyl group, and a side chain containing a propyl group and a primary amide. The side chain is further substituted with a cyclohexylmethyl group and a sulfonamide group (SO₂Ph).	LCMS; MH ⁺ , 738.2.	B

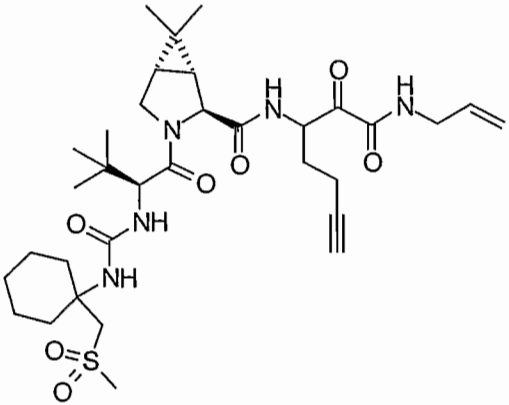
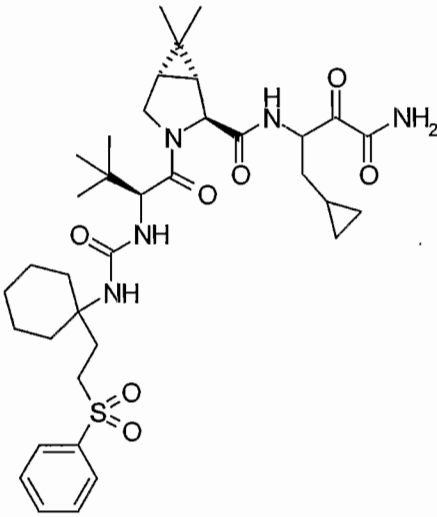
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
173	 Chemical structure of compound 173: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a carbonyl group (dash bond), and a carbonyl group (wedge bond). The carbonyl group (wedge bond) is part of an amide linkage to a side chain containing a propyl group and a terminal alkyne group. The carbonyl group (dash bond) is part of an amide linkage to a side chain containing a cyclohexyl group and a sulfonamide group (SO₂Ph).		A
174	 Chemical structure of compound 174: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a carbonyl group (dash bond), and a carbonyl group (wedge bond). The carbonyl group (wedge bond) is part of an amide linkage to a side chain containing a cyclopropyl group and a terminal amide group (NH₂). The carbonyl group (dash bond) is part of an amide linkage to a side chain containing a tert-butyl group and a sulfonamide group (SO₂Ph).		A

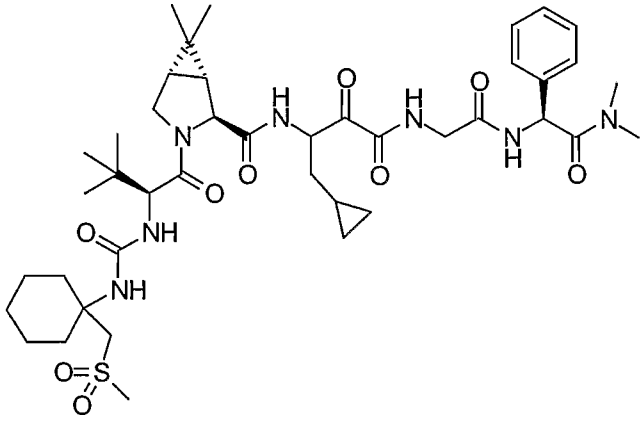
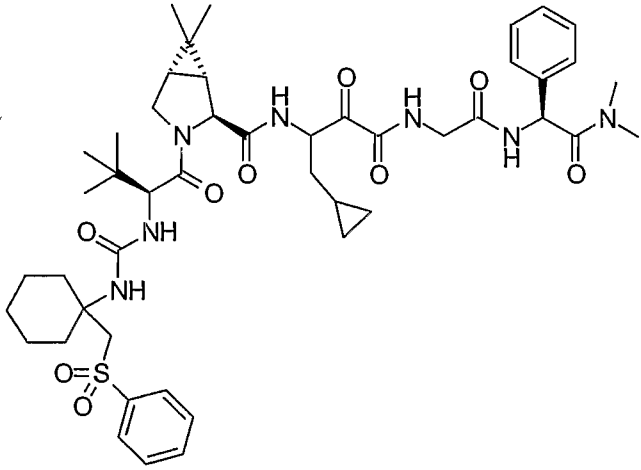
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
175	 Chemical structure of compound 175: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a cyclopropylmethyl group. The carbonyl at the 4-position is part of an amide linkage to a cyclohexylmethyl group. The cyclohexylmethyl group is further substituted with a tert-butylsulfonyl group and a carbonyl group. The cyclopropylmethyl group is further substituted with a carbonyl group and an amide linkage to a cyclohexylmethyl group.		A
176	 Chemical structure of compound 176: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a cyclobutylmethyl group. The carbonyl at the 4-position is part of an amide linkage to a cyclohexylmethyl group. The cyclohexylmethyl group is further substituted with a tert-butylsulfonyl group and a carbonyl group. The cyclobutylmethyl group is further substituted with a carbonyl group and an amide linkage to a cyclohexylmethyl group.		A

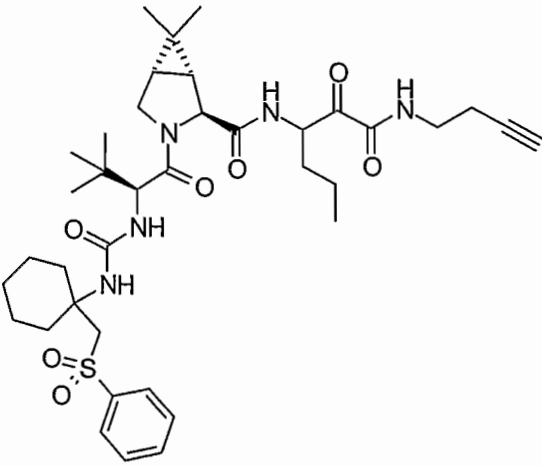
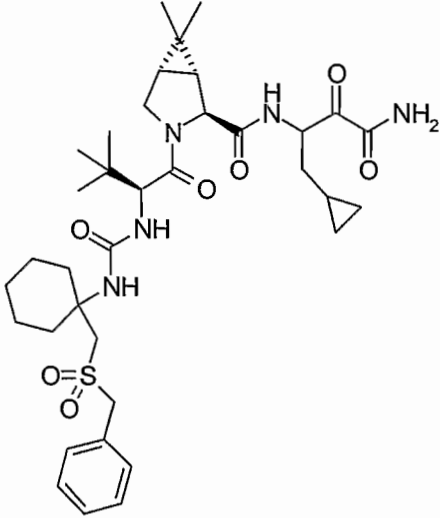
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
177	 Chemical structure of compound 177: A complex molecule featuring a cyclohexane ring substituted with a tert-butylsulfonyl group and an amide linkage to a pyrrolidine ring. The pyrrolidine ring is further substituted with a tert-butyl group and an amide linkage to a chain containing a cyclobutane ring and a terminal amide group.		A
178	 Chemical structure of compound 178: A complex molecule featuring a cyclohexane ring substituted with a tert-butylsulfonyl group and an amide linkage to a pyrrolidine ring. The pyrrolidine ring is further substituted with a tert-butyl group and an amide linkage to a chain containing an amide group and a terminal vinyl group.	LCMS; MH ⁺ , 714.1.	A

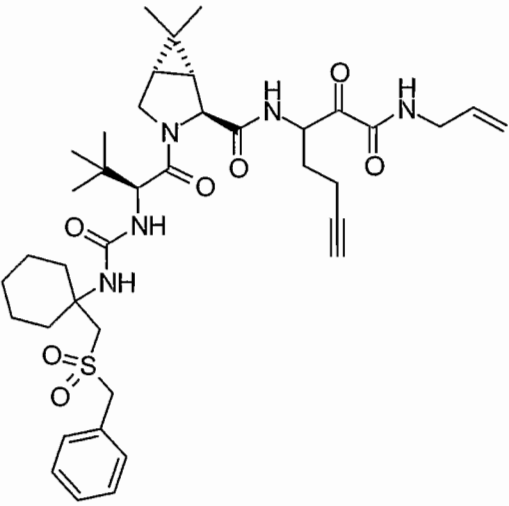
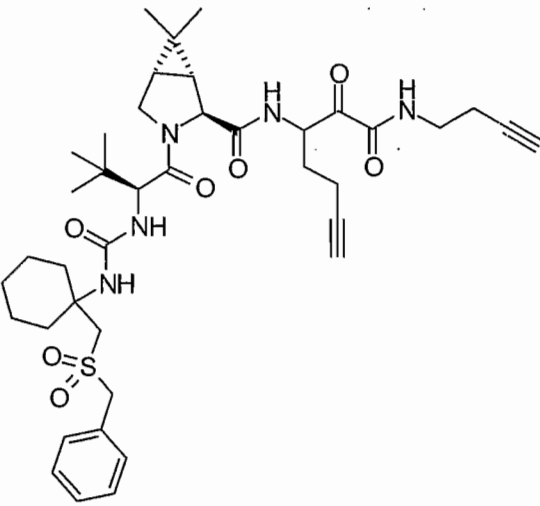
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
179	 Chemical structure of compound 179: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂Ph) and a carbamate group. The carbamate is linked to a chain containing a pyrrolidine ring, a carbonyl group, and a terminal alkyne group.		A
180	 Chemical structure of compound 180: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂Ph) and a carbamate group. The carbamate is linked to a chain containing a pyrrolidine ring, a carbonyl group, and a terminal alkene group.		A

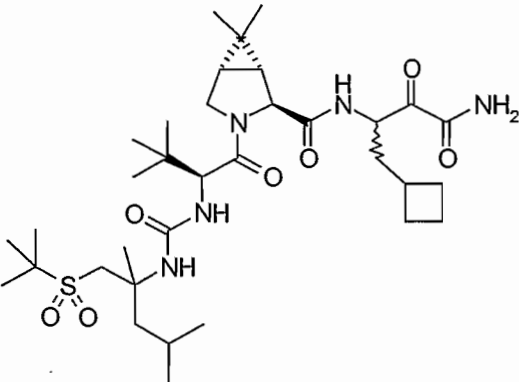
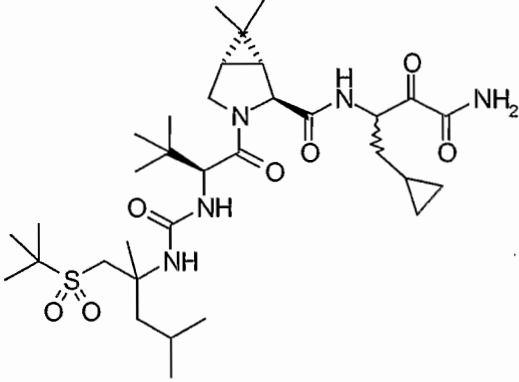
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
181	 Chemical structure of compound 181: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂Ph) and a carbamate group. The carbamate is linked to a pyrrolidine ring, which is further substituted with a tert-butyl group and a carbonyl group. This carbonyl is part of a chain that includes an amide linkage to a propargyl group, which is then linked to another amide group with a vinyl substituent.	FABMS; MH ⁺ , 724.6.	A
182	 Chemical structure of compound 182: Similar to compound 181, but the terminal vinyl group is replaced by a propargyl group (a three-carbon chain ending in a triple bond).	FABMS; MH ⁺ , 736.5.	A

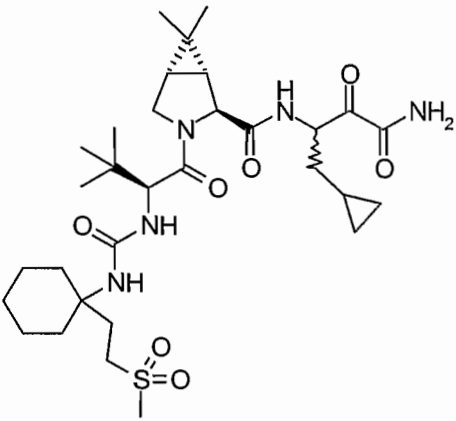
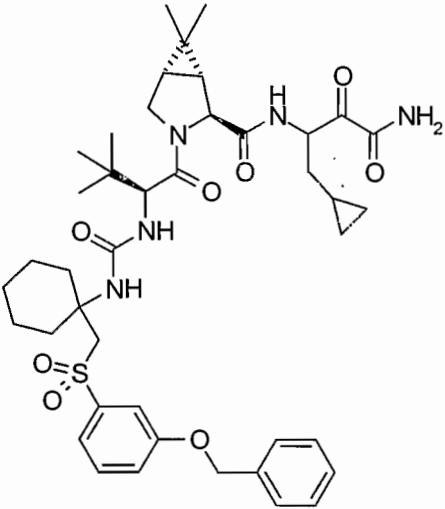
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
185	 Chemical structure of compound 185: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a methyl group (dash bond), and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a propargyl group (alkyne), a carbonyl group, and a terminal allyl group (alkene). Another amide linkage connects the pyrrolidine ring to a cyclohexane ring, which is further substituted with a methanesulfonyl group (SO₂CH₃).	FABMS; MH ⁺ , 662.5.	A
186	 Chemical structure of compound 186: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a methyl group (dash bond), and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclopropyl group, a carbonyl group, and a terminal amide group (NH₂). Another amide linkage connects the pyrrolidine ring to a cyclohexane ring, which is further substituted with a benzenesulfonyl group (SO₂Ph).	FABMS; MH ⁺ , 700.3.	A

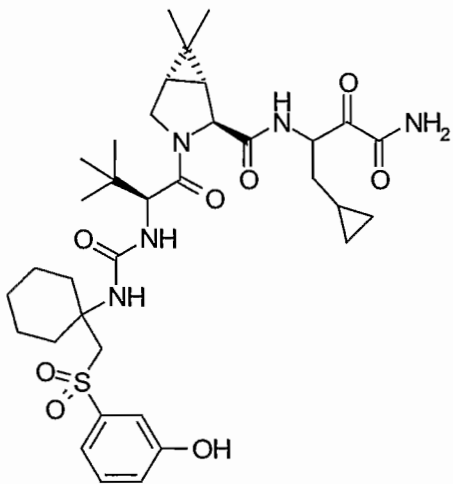
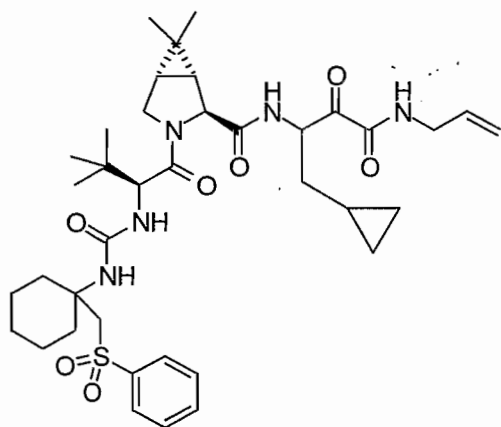
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
187	 Chemical structure of compound 187: A complex molecule featuring a central chain of amide and ester linkages. It includes a cyclohexane ring with a sulfonamide group, a pyrrolidine ring, a cyclopropyl group, and a dimethylamino group.		A
188	 Chemical structure of compound 188: A complex molecule featuring a central chain of amide and ester linkages. It includes a cyclohexane ring with a sulfonamide group, a pyrrolidine ring, a cyclopropyl group, and a dimethylamino group. The sulfonamide group is substituted with a phenyl ring.		A

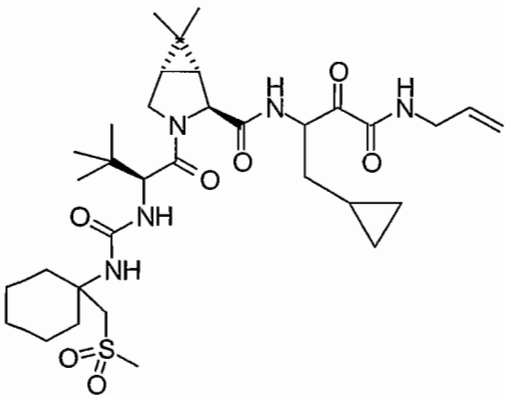
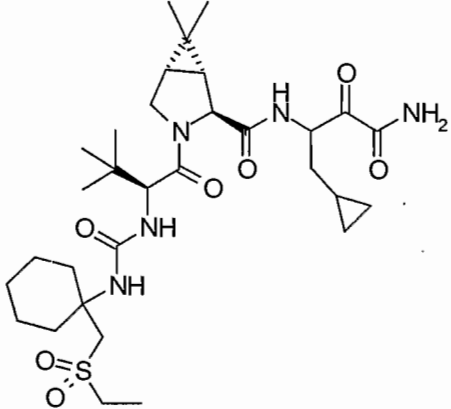
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
189	 Chemical structure of compound 189: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a carbonyl group, and a side chain containing a carbonyl group, an amide group, and a terminal alkyne group. The side chain also includes a cyclohexyl ring and a sulfonamide group.		A
190	 Chemical structure of compound 190: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a carbonyl group, and a side chain containing a carbonyl group, an amide group, and a terminal amine group. The side chain also includes a cyclohexyl ring and a sulfonamide group.		A

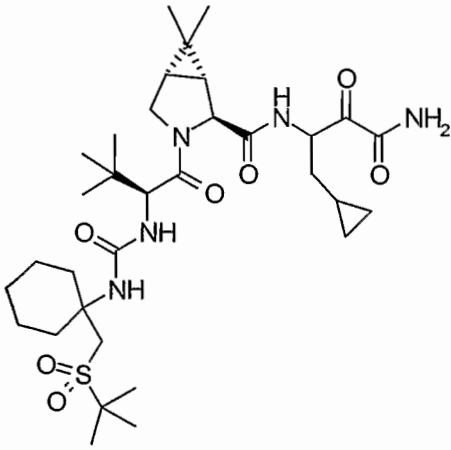
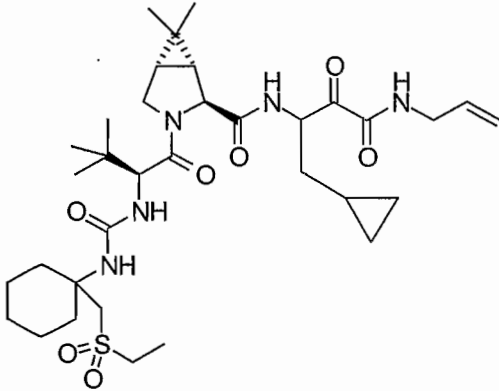
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
191	 Chemical structure of compound 191: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂Ph) and a carbamate group (NH-C(=O)-CH(CH₃)-). The carbamate is linked to a pyrrolidine ring, which is further substituted with a tert-butyl group and a carbonyl group. This carbonyl is part of a chain that includes an amide linkage to a propargyl group (CH₂CH₂C≡CH) and a terminal amide group (NH-CH₂-CH=CH₂).	FABMS; MH ⁺ , 738.4.	A
192	 Chemical structure of compound 192: Similar to compound 191, but the terminal amide group is replaced by a propargyl group (NH-CH₂-CH₂-C≡CH).		A

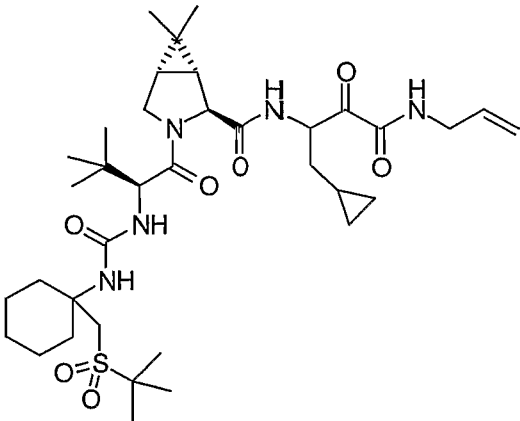
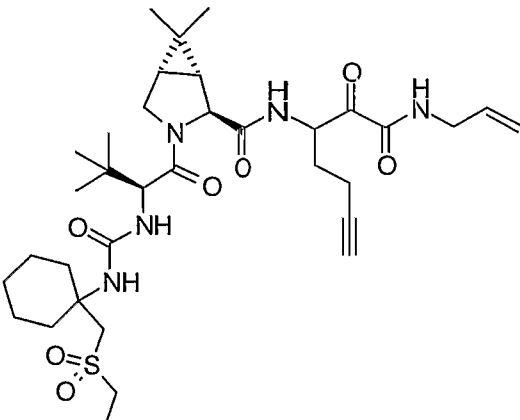
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
193	 Chemical structure of compound 193: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (dashed bond), a carbonyl group (solid bond), and a side chain. The side chain consists of a carbonyl group linked to a cyclobutane ring, which is further substituted with an amide group (NH₂) and a carbonyl group. The pyrrolidine ring is also linked to a carbonyl group, which is further substituted with a tert-butyl group (dashed bond) and a side chain. The side chain consists of a carbonyl group linked to a cyclobutane ring, which is further substituted with an amide group (NH₂) and a carbonyl group. The pyrrolidine ring is also linked to a carbonyl group, which is further substituted with a tert-butyl group (dashed bond) and a side chain. The side chain consists of a carbonyl group linked to a cyclobutane ring, which is further substituted with an amide group (NH₂) and a carbonyl group.		A
194	 Chemical structure of compound 194: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (dashed bond), a carbonyl group (solid bond), and a side chain. The side chain consists of a carbonyl group linked to a cyclopropane ring, which is further substituted with an amide group (NH₂) and a carbonyl group. The pyrrolidine ring is also linked to a carbonyl group, which is further substituted with a tert-butyl group (dashed bond) and a side chain. The side chain consists of a carbonyl group linked to a cyclopropane ring, which is further substituted with an amide group (NH₂) and a carbonyl group. The pyrrolidine ring is also linked to a carbonyl group, which is further substituted with a tert-butyl group (dashed bond) and a side chain. The side chain consists of a carbonyl group linked to a cyclopropane ring, which is further substituted with an amide group (NH₂) and a carbonyl group.		A

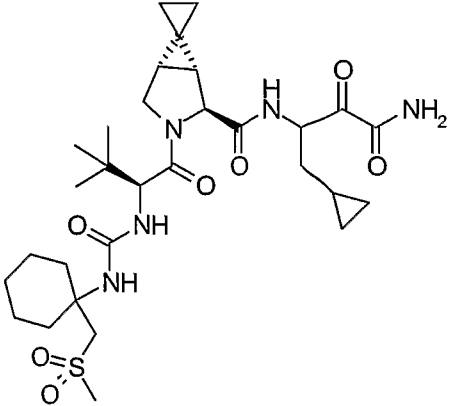
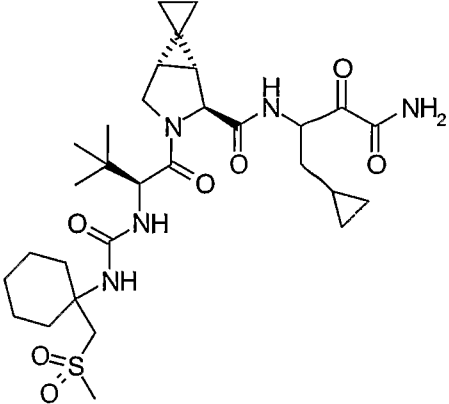
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
197	 Chemical structure of compound 197: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (-SO₂CH₂NH-) and a carbamate group (-NHCOO-). The carbamate is linked to a pyrrolidine ring, which is further substituted with a cyclopropyl group and a carboxamide group (-CONH₂).	FABMS; MH ⁺ , 638.3.	A
198	 Chemical structure of compound 198: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (-SO₂CH₂NH-) and a carbamate group (-NHCOO-). The carbamate is linked to a pyrrolidine ring, which is further substituted with a cyclopropyl group and a carboxamide group (-CONH₂). The sulfonamide group is further substituted with a benzyl group (-CH₂Ph).	LCMS; MH ⁺ , 792.2.	A

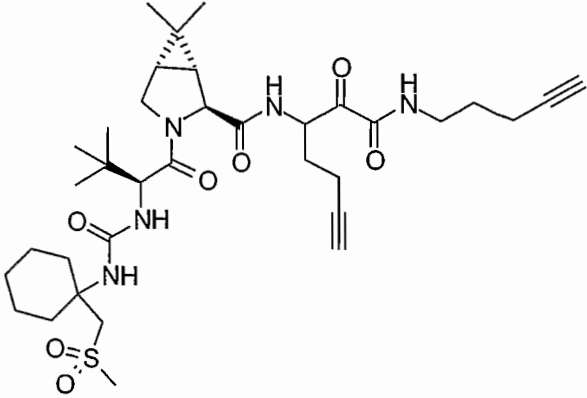
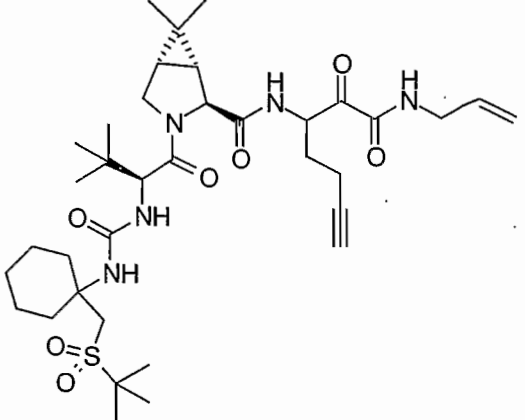
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
199		LCMS: MH ⁺ , 702.2.	A
200		FABMS; MH ⁺ , 726.5.	A

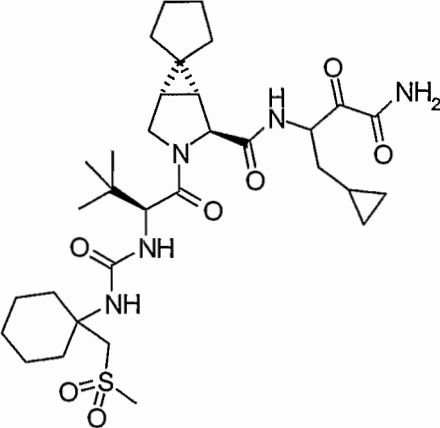
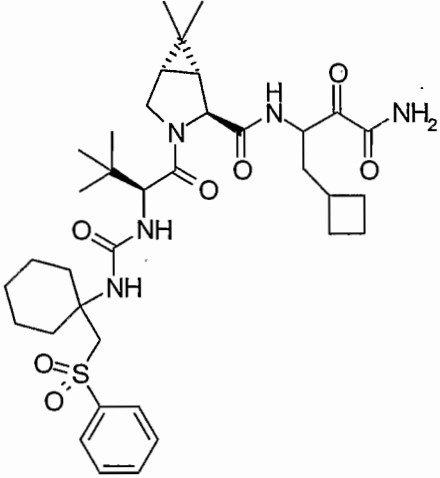
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
201	 Chemical structure of compound 201: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂NH-) and an amide group (-NH-C(=O)-). This amide is linked to a side chain containing a pyrrolidine ring, a carbonyl group, and a cyclopropylmethyl group. The side chain also includes a terminal amide group (-NH-C(=O)-NH-CH₂-CH=CH₂).		A
202	 Chemical structure of compound 202: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂NH-) and an amide group (-NH-C(=O)-). This amide is linked to a side chain containing a pyrrolidine ring, a carbonyl group, and a cyclopropylmethyl group. The side chain also includes a terminal amide group (-NH-C(=O)-NH₂).		A

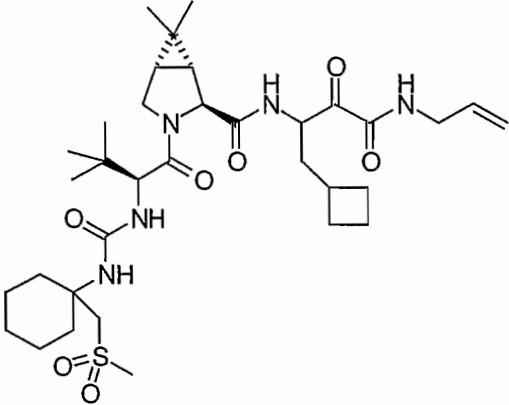
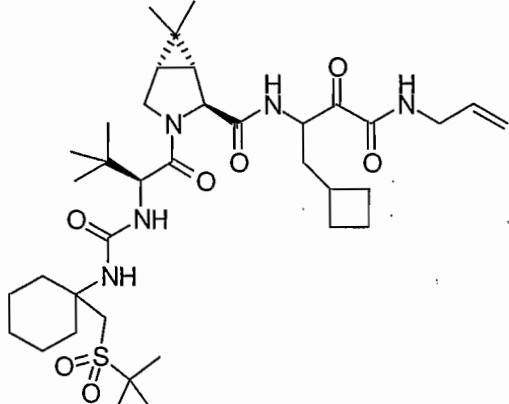
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
203	 Chemical structure of compound 203: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group (-CH₂-SO₂-C(CH₃)₃) and a carbamate group (-NH-CO-NH-). The carbamate is linked to a chiral center (a carbon with a methyl group and a hydrogen atom) which is part of a five-membered ring containing a nitrogen atom. This five-membered ring is further substituted with a cyclopropylmethyl group and a carbamate group (-NH-CO-NH-) which is linked to a chiral center (a carbon with a methyl group and a hydrogen atom) which is part of a five-membered ring containing a nitrogen atom. This five-membered ring is further substituted with a cyclopropylmethyl group and a carbamate group (-NH-CO-NH-) which is linked to a chiral center (a carbon with a methyl group and a hydrogen atom) which is part of a five-membered ring containing a nitrogen atom.		A
204	 Chemical structure of compound 204: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group (-CH₂-SO₂-C(CH₃)₃) and a carbamate group (-NH-CO-NH-). The carbamate is linked to a chiral center (a carbon with a methyl group and a hydrogen atom) which is part of a five-membered ring containing a nitrogen atom. This five-membered ring is further substituted with a cyclopropylmethyl group and a carbamate group (-NH-CO-NH-) which is linked to a chiral center (a carbon with a methyl group and a hydrogen atom) which is part of a five-membered ring containing a nitrogen atom. This five-membered ring is further substituted with a cyclopropylmethyl group and a carbamate group (-NH-CO-NH-) which is linked to a chiral center (a carbon with a methyl group and a hydrogen atom) which is part of a five-membered ring containing a nitrogen atom.		A

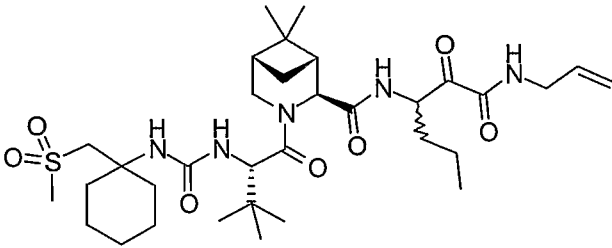
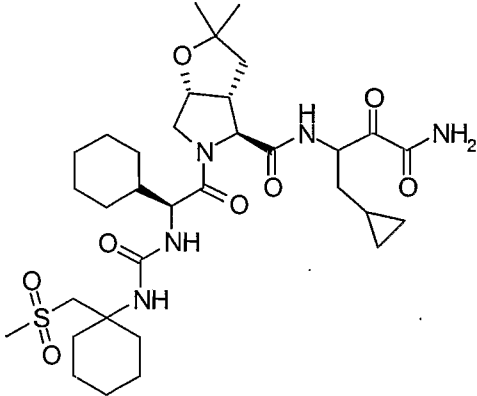
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
205			A
206		FABMS; MH ⁺ , 676.7.	A

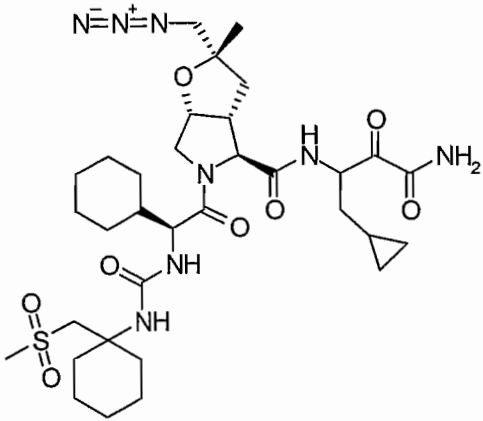
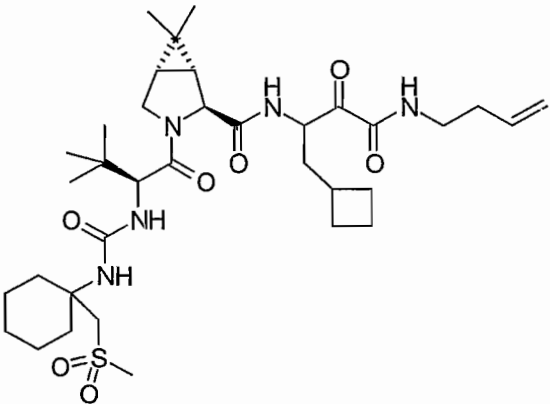
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
207	 Chemical structure of compound 207: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopropyl group at the 2-position (dashed bond), a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is linked to a side chain containing a cyclopropyl group and a primary amide group (NH₂). The carbonyl at the 4-position is linked to a side chain containing a cyclopropyl group and a primary amide group (NH₂). The pyrrolidine ring is also substituted with a cyclopropyl group at the 1-position (dashed bond). The side chain at the 3-position is linked to a cyclopropyl group and a primary amide group (NH₂). The side chain at the 4-position is linked to a cyclopropyl group and a primary amide group (NH₂).		A
208	 Chemical structure of compound 208: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopropyl group at the 2-position (dashed bond), a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is linked to a side chain containing a cyclopropyl group and a primary amide group (NH₂). The carbonyl at the 4-position is linked to a side chain containing a cyclopropyl group and a primary amide group (NH₂). The pyrrolidine ring is also substituted with a cyclopropyl group at the 1-position (dashed bond). The side chain at the 3-position is linked to a cyclopropyl group and a primary amide group (NH₂). The side chain at the 4-position is linked to a cyclopropyl group and a primary amide group (NH₂).		A

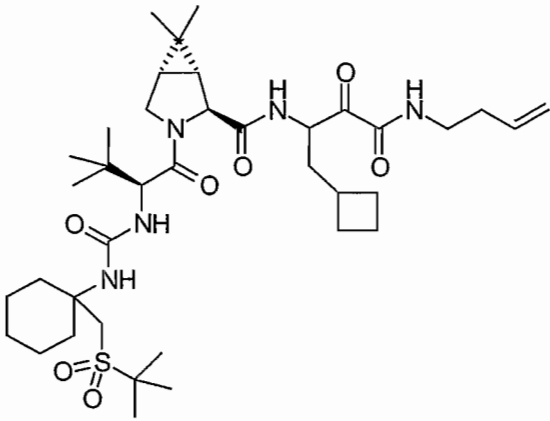
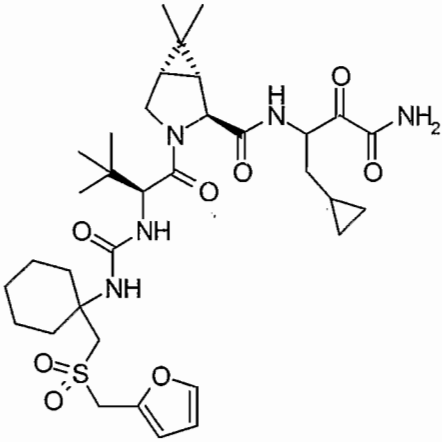
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
209	 Chemical structure of compound 209: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂NH-) and an amide group (-NH-C(=O)-). This amide is linked to a side chain containing a pyrrolidine ring substituted with a tert-butyl group and a methyl group. The side chain also includes a propargyl group (CH₂CH₂C≡CH) and a terminal alkyne group (CH₂C≡CH).	FABMS; MH ⁺ , 688.3.	A
210	 Chemical structure of compound 210: Similar to compound 209, but the terminal alkyne group is replaced by a terminal alkene group (CH₂CH=CH₂).	FABMS; MH ⁺ , 704.4.	A

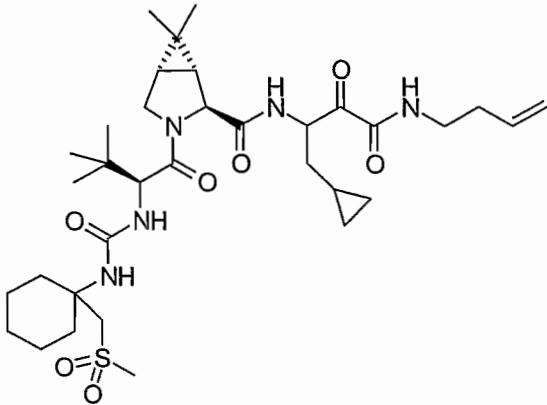
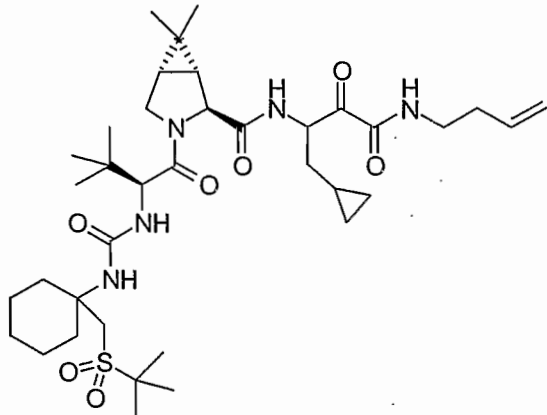
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i * range
213			A
214			A

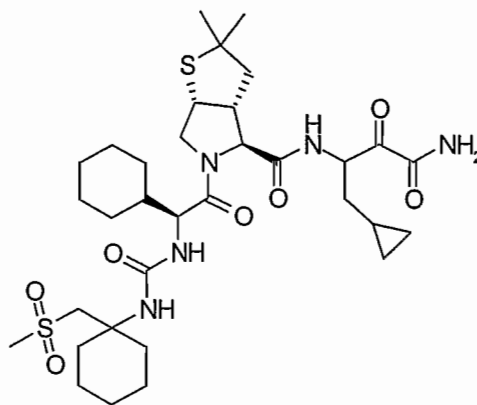
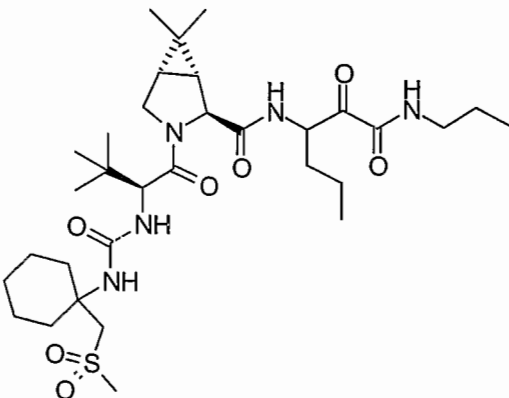
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
215	 Chemical structure of compound 215: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂NH-) and an amide group (-NH-C(=O)-). This amide is linked to a side chain containing a pyrrolidine ring, a carbonyl group, and a cyclobutane ring. The side chain also includes an amide group (-NH-C(=O)-) and a terminal vinyl group (-CH=CH₂).	FABMS; MH ⁺ , 678.6.	A
216	 Chemical structure of compound 216: Similar to compound 215, but the sulfonamide group on the cyclohexane ring is substituted with a tert-butyl group (C(CH₃)₃).	FABMS; MH ⁺ , 720.6.	A

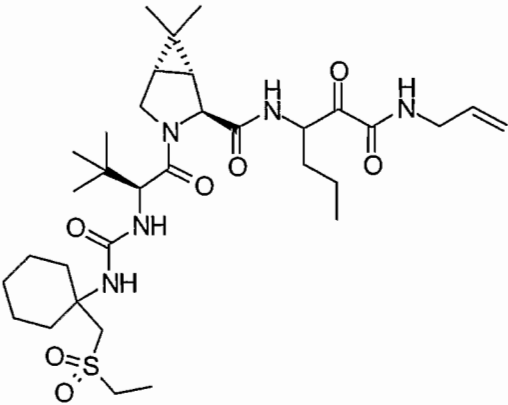
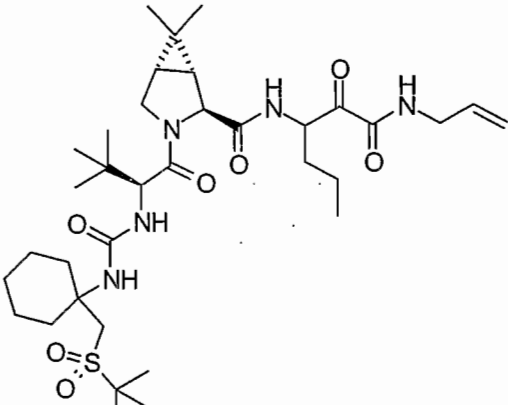
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
217	 Chemical structure of compound 217: A complex molecule featuring a cyclohexane ring substituted with a methylsulfonyl group and a carbamate. This carbamate is linked to a bicyclic amide system, which is further connected to a chain containing a ketone, an amide, and a terminal allyl group.		A
218	 Chemical structure of compound 218: A complex molecule featuring a cyclohexane ring substituted with a methylsulfonyl group and a carbamate. This carbamate is linked to a bicyclic amide system, which is further connected to a chain containing a ketone, an amide, and a terminal amide group.		A

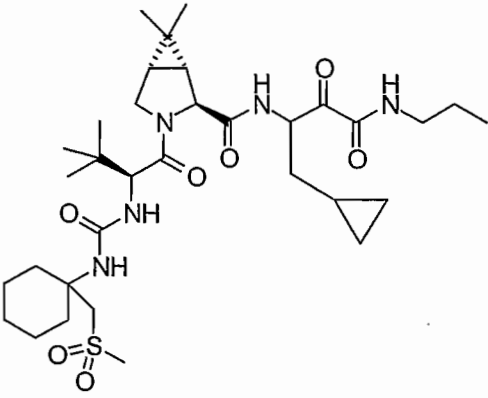
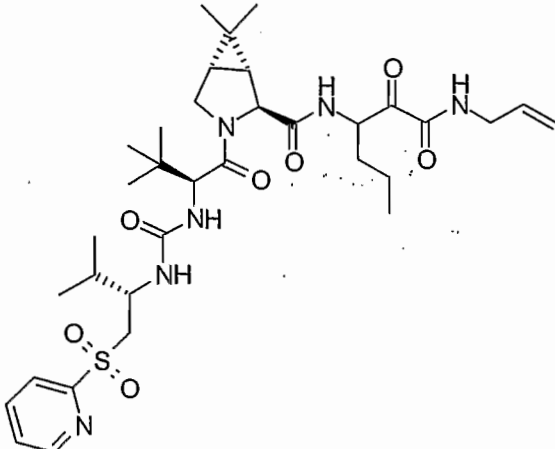
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
219	 Chemical structure of compound 219: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine is substituted with a 1,1,1-trifluoroethyl group (N=N⁺=N⁻), a cyclohexyl group, and a carbonyl group. The carbonyl is linked to a chain containing a cyclopropyl group, an amide group, and a carboxamide group.		A
220	 Chemical structure of compound 220: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine is substituted with a 1,1,1-trimethyl-2-propenyl group, a cyclohexyl group, and a carbonyl group. The carbonyl is linked to a chain containing a cyclobutyl group, an amide group, and a carboxamide group.	FABMS; MH ⁺ , 692.5.	A

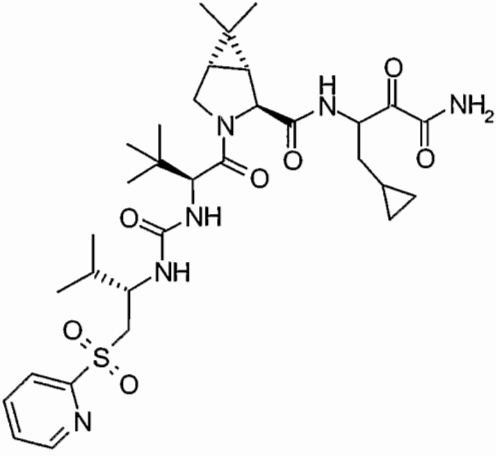
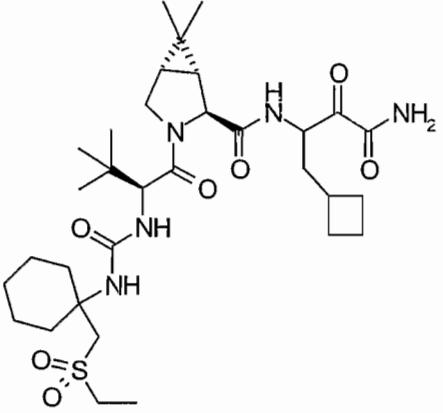
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
221	 Chemical structure of compound 221: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH₂NH-C(=O)-NH-), a tert-butyl group, and a side chain containing a pyrrolidine ring, a carbonyl group, and a vinyl group.	FABMS; MH ⁺ , 734.5.	A
222	 Chemical structure of compound 222: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH₂NH-C(=O)-NH-), a tert-butyl group, and a side chain containing a pyrrolidine ring, a carbonyl group, and an amide group.		A

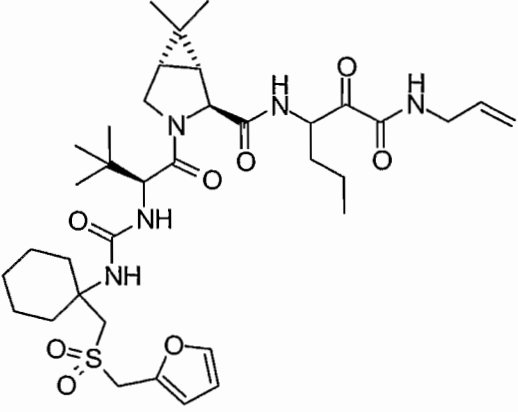
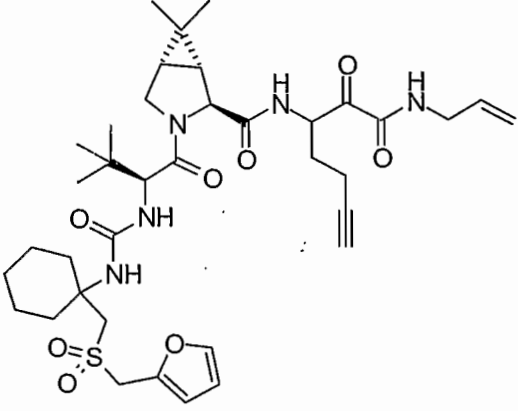
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
223		FABMS; MH ⁺ , 678.4.	A
224		FABMS; MH ⁺ , 720.8.	A

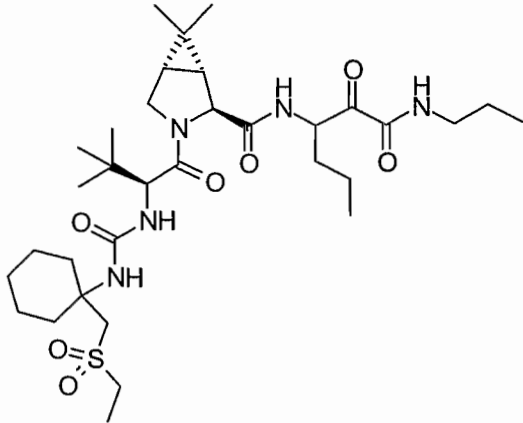
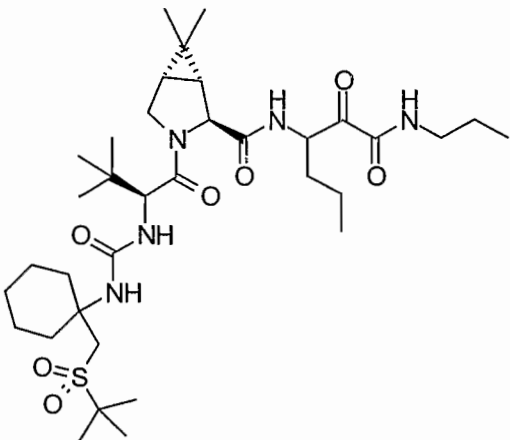
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
225	 Chemical structure of compound 225: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a cyclohexylmethyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a cyclopropylmethyl group, which is further substituted with a primary amide group (-NH₂). The pyrrolidine ring is also linked via an amide bond to a cyclohexylmethyl group, which is further substituted with a primary amide group (-NH₂).		B
226	 Chemical structure of compound 226: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a cyclohexylmethyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a propylmethyl group, which is further substituted with a primary amide group (-NH₂). The pyrrolidine ring is also linked via an amide bond to a cyclohexylmethyl group, which is further substituted with a primary amide group (-NH₂).	LCMS; MH ⁺ , 654.1.	A

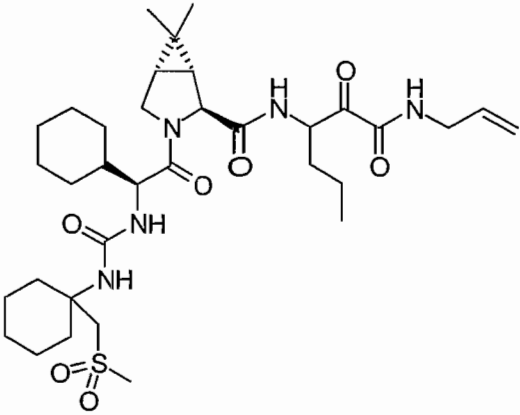
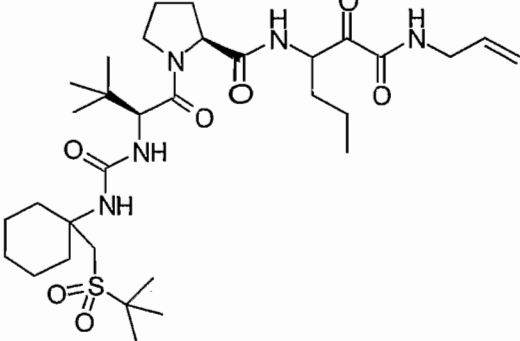
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
227	 Chemical structure of compound 227: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂Et) and an amide group (NH-C(=O)-CH(CH₃)-). This amide is linked to a pyrrolidine ring, which is further substituted with a methyl group and a side chain containing a ketone and an amide group (NH-C(=O)-CH(CH₃)-CH₂-CH₂-C(=O)-NH-CH₂-CH=CH₂).		A
228	 Chemical structure of compound 228: Similar to compound 227, but the sulfonamide group is substituted with a tert-butyl group (SO₂tBu) instead of an ethyl group.		A

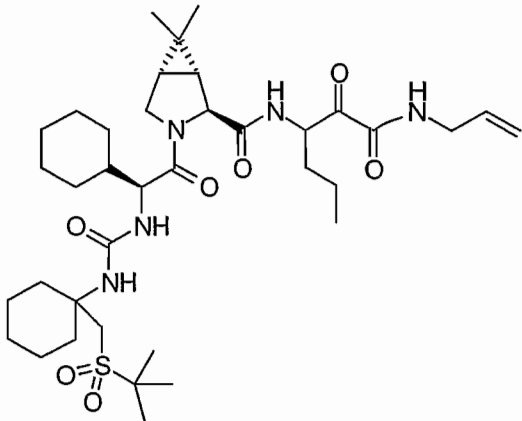
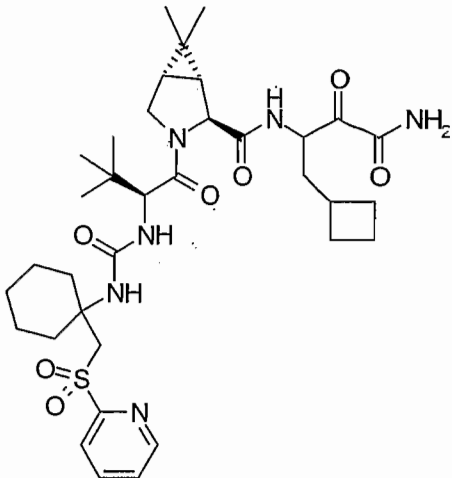
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
229	 Chemical structure of compound 229: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a side chain containing a cyclopropylmethyl group and a propylamide group. The carbonyl at the 4-position is part of an amide linkage to a side chain containing a cyclohexylmethyl group and a sulfonamide group.	FABMS; MH ⁺ , 666.5.	A
230	 Chemical structure of compound 230: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is part of an amide linkage to a side chain containing a propyl group and an allyl group. The carbonyl at the 4-position is part of an amide linkage to a side chain containing a pyridine ring and a sulfonamide group.		C

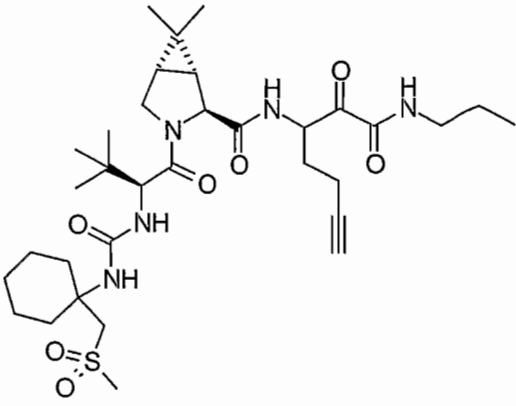
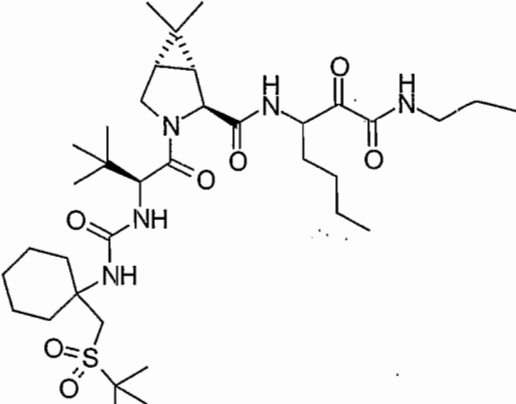
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i * range
231			A
232			A

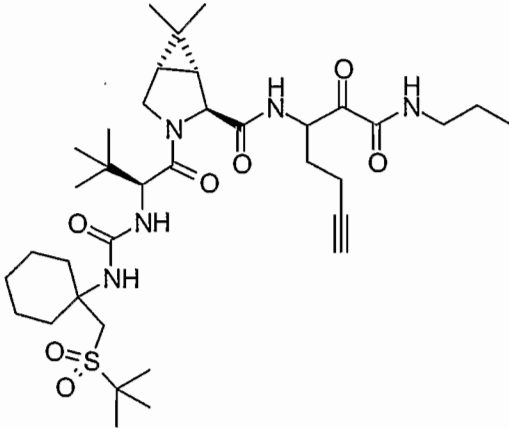
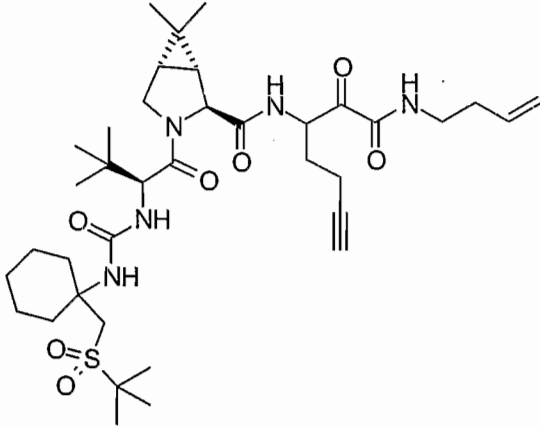
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K ⁱ * range
236	 Chemical structure of compound 236: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂ attached to a furan ring) and a carbamate group (NH-C(=O)-CH(CH₃)-). This carbamate is linked to a pyrrolidine ring, which is further substituted with a tert-butyl group and a side chain containing a ketone and an amide group ending in a vinyl group (CH=CH₂).		A
237	 Chemical structure of compound 237: Similar to compound 236, but the side chain of the pyrrolidine ring contains an alkyne group (C≡C) instead of a ketone and an amide group.		A

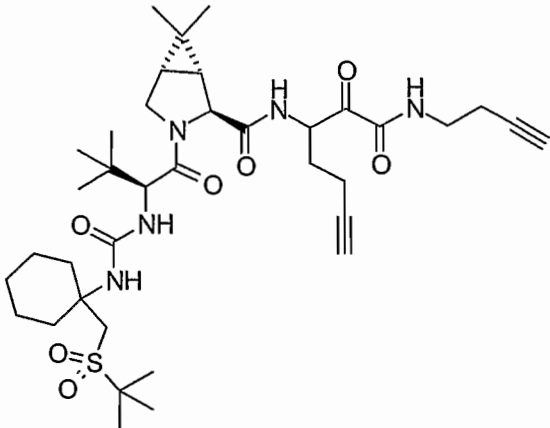
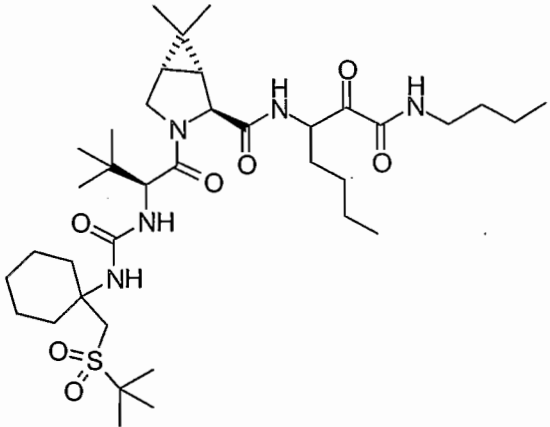
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
238			A
239			A

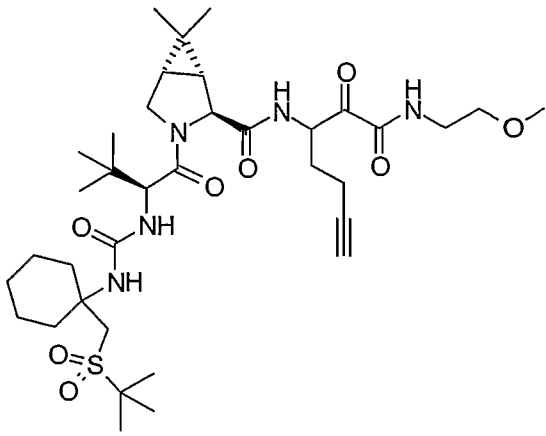
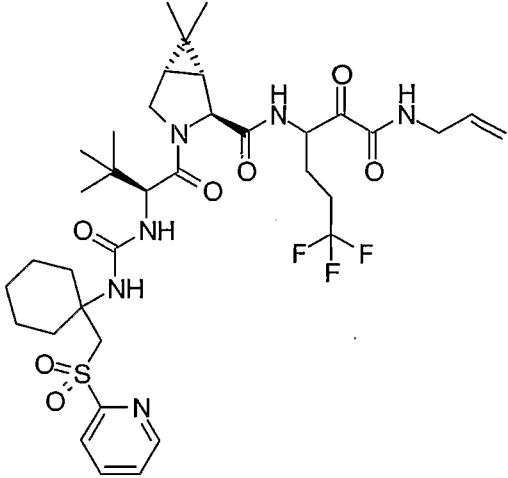
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
242	 Chemical structure of compound 242: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH₂NH-) and an amide group (-NHCO-). The amide is linked to a pyrrolidine ring, which is further substituted with a methyl group and a side chain containing a ketone and an amide group ending in a vinyl group (CH=CH₂).		A
243	 Chemical structure of compound 243: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH₂NH-) and an amide group (-NHCO-). The amide is linked to a pyrrolidine ring, which is further substituted with a methyl group and a side chain containing a ketone and an amide group ending in a vinyl group (CH=CH₂).		C

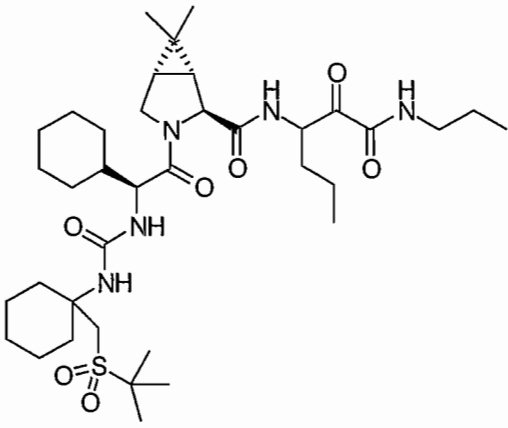
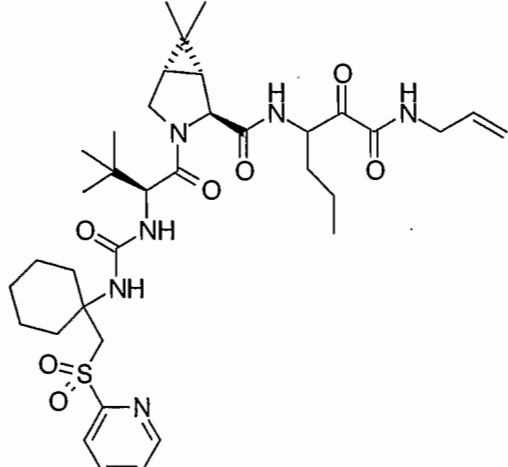
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
244	 Chemical structure of compound 244: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclohexyl group, a carbonyl group, and a terminal vinyl group. There is also a sulfonamide group attached to the side chain.		A
245	 Chemical structure of compound 245: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclohexyl group, a carbonyl group, and a terminal amide group. There is also a sulfonamide group attached to the side chain.		A

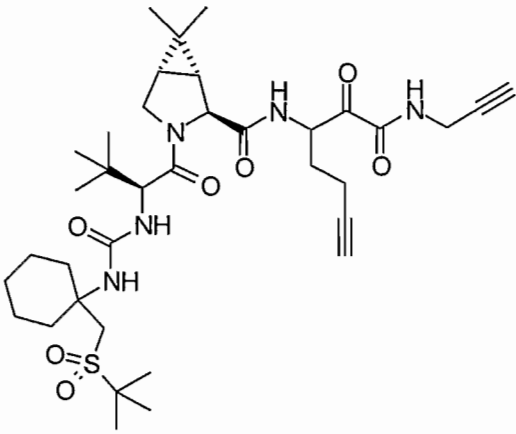
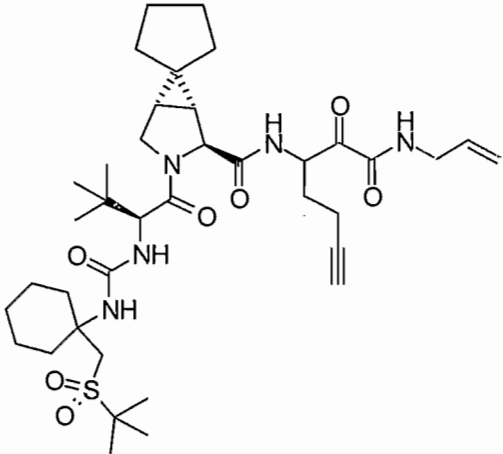
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
246		FABMS; MH ⁺ , 664.2.	A
247		FABMS; MH ⁺ , 710.3.	A

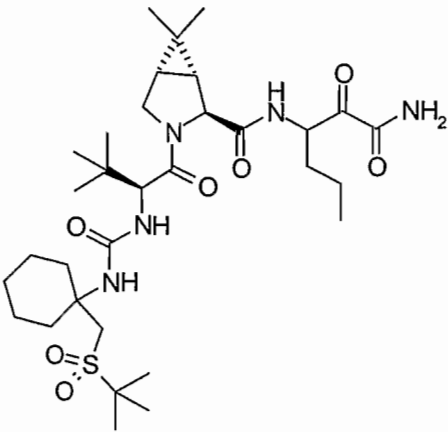
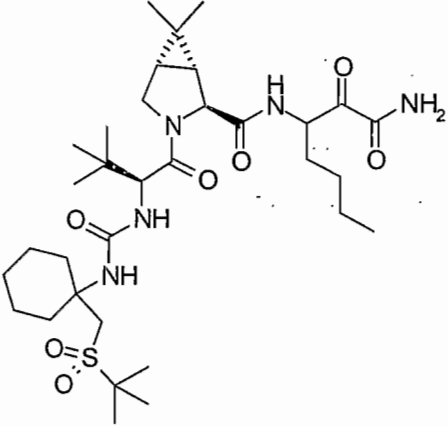
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
248	 Chemical structure of compound 248: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group and a side chain containing a pyrrolidine ring, a carbonyl group, and a propargyl group. The side chain also includes a propanamide moiety.	FABMS; MH ⁺ , 706.5.	A
249	 Chemical structure of compound 249: Similar to compound 248, but the terminal group of the side chain is a propenamide moiety instead of a propanamide moiety.	FABMS; MH ⁺ , 718.2.	A

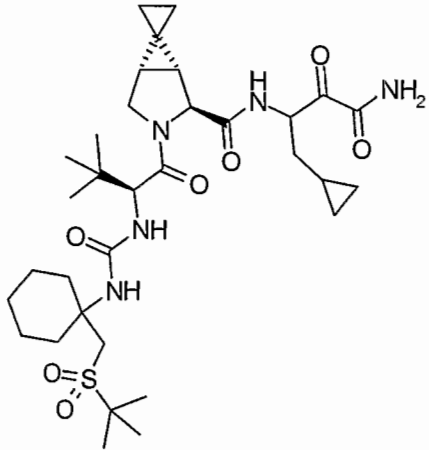
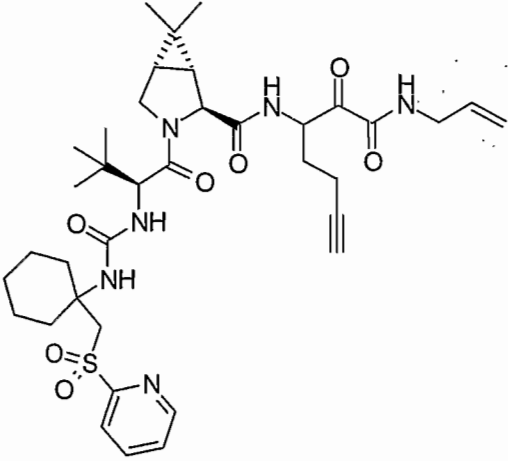
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
250	 Chemical structure of compound 250: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a side chain containing a carbamate and a propargyl group. This is linked via an amide bond to another side chain containing a carbamate and a propargyl group. A third side chain, containing a carbamate and a cyclohexyl group, is also attached to the central pyrrolidine ring. The molecule is further substituted with a tert-butyl sulfonamide group.		A
251	 Chemical structure of compound 251: Similar to compound 250, but the propargyl group is replaced by a propyl group.	FABMS; MH ⁺ , 724.5.	A

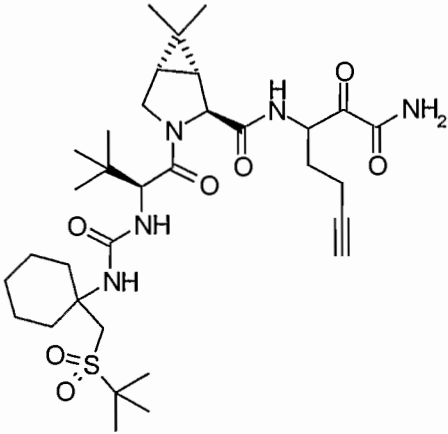
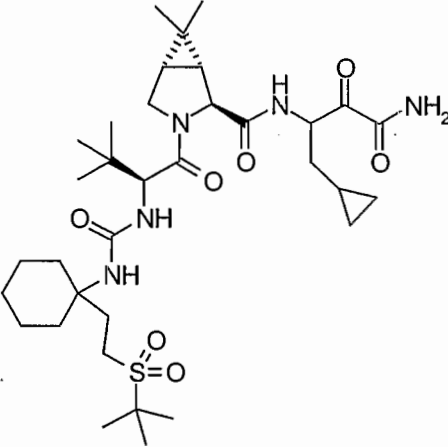
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
254	 Chemical structure of compound 254: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂NH-) and a carbamate group (-NHCOO-). The carbamate is linked to a chain containing a pyrrolidine ring, a carbonyl group, and a terminal methoxy group (-OCH₃). The chain also includes a propargyl group (-C≡CH).	FABMS; MH ⁺ , 722.1.	A
255	 Chemical structure of compound 255: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂NH-) and a carbamate group (-NHCOO-). The carbamate is linked to a chain containing a pyrrolidine ring, a carbonyl group, and a terminal vinyl group (-CH=CH₂). The chain also includes a trifluoromethyl group (-CF₃).		A

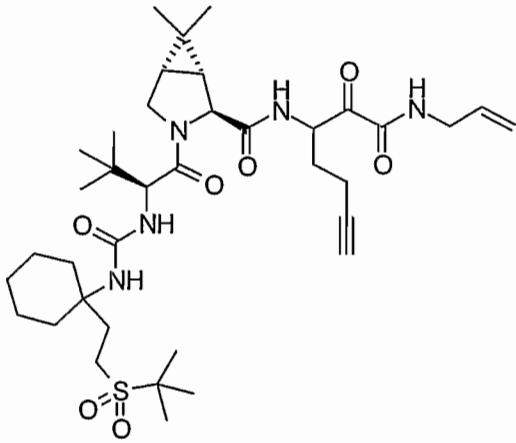
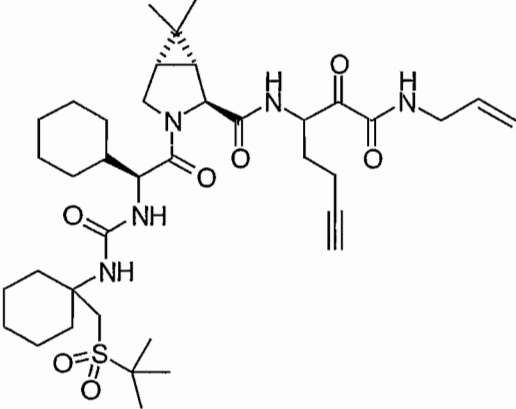
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
256	 Chemical structure of compound 256: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a cyclohexylmethyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a propanamide group (CH₂CH₂CONHCH₂CH₂CH₃) and a cyclohexylmethyl group attached to the amide nitrogen. The cyclohexylmethyl group is further substituted with a tert-butylsulfonyl group (SO₂C(CH₃)₃).		A
257	 Chemical structure of compound 257: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a cyclohexylmethyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a propanamide group (CH₂CH₂CONHCH₂CH₂CH=CH₂) and a cyclohexylmethyl group attached to the amide nitrogen. The cyclohexylmethyl group is further substituted with a pyridine-2-sulfonyl group (SO₂C₅H₄N).		A

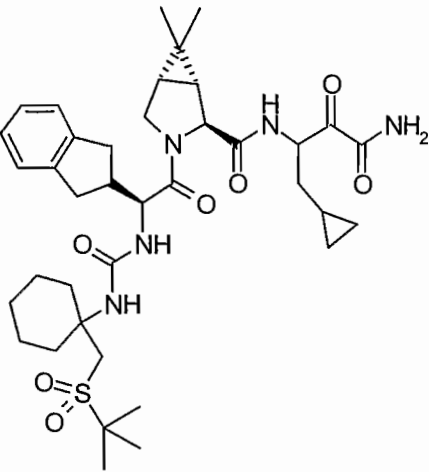
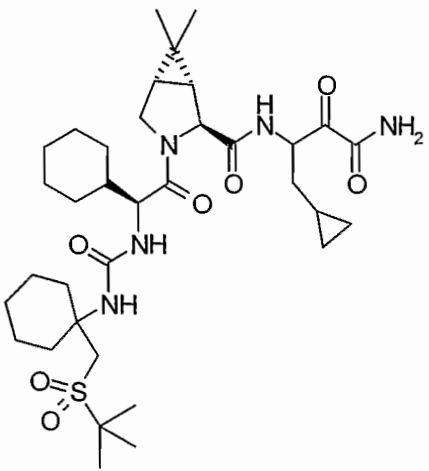
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
258	 Chemical structure of compound 258: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (dashed bond), a carbonyl group (solid bond), and a side chain containing a ketone and an alkyne. The side chain is further substituted with a carbonyl group and an alkyne. The pyrrolidine ring is also substituted with a carbonyl group and a side chain containing a ketone and an alkyne. The side chain is further substituted with a carbonyl group and an alkyne. The pyrrolidine ring is also substituted with a carbonyl group and a side chain containing a ketone and an alkyne. The side chain is further substituted with a carbonyl group and an alkyne.	FABMS; MH ⁺ , 702.3.	A
259	 Chemical structure of compound 259: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopentyl group (dashed bond), a carbonyl group (solid bond), and a side chain containing a ketone and an alkyne. The side chain is further substituted with a carbonyl group and an alkyne. The pyrrolidine ring is also substituted with a carbonyl group and a side chain containing a ketone and an alkyne. The side chain is further substituted with a carbonyl group and an alkyne. The pyrrolidine ring is also substituted with a carbonyl group and a side chain containing a ketone and an alkyne. The side chain is further substituted with a carbonyl group and an alkyne.	FABMS; MH ⁺ , 730.5.	A

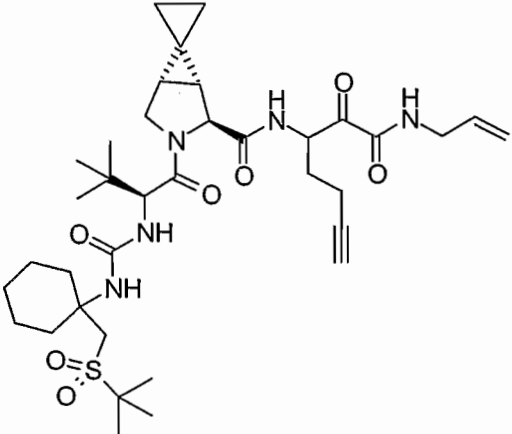
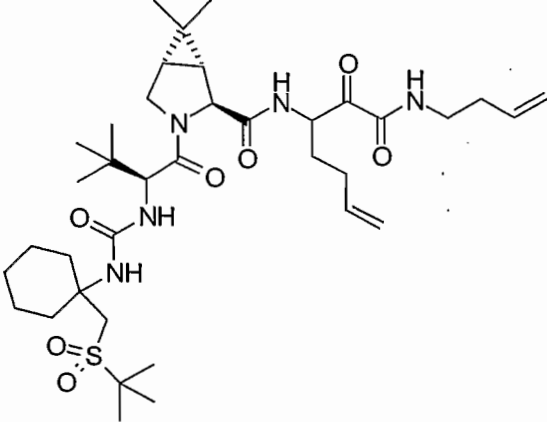
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
262	 The chemical structure of compound 262 is a complex molecule. It features a central pyrrolidine ring. Attached to the pyrrolidine ring is a side chain containing a carbonyl group, an amide group, and a carboxamide group. Another side chain on the pyrrolidine ring is a cyclohexyl group. A third side chain is a tert-butyl sulfonamide group. The structure is drawn with stereochemistry indicated by wedges and dashes.		A
263	 The chemical structure of compound 263 is identical to the structure of compound 262. It features a central pyrrolidine ring with a side chain containing a carbonyl group, an amide group, and a carboxamide group, a cyclohexyl group, and a tert-butyl sulfonamide group. The structure is drawn with stereochemistry indicated by wedges and dashes.		A

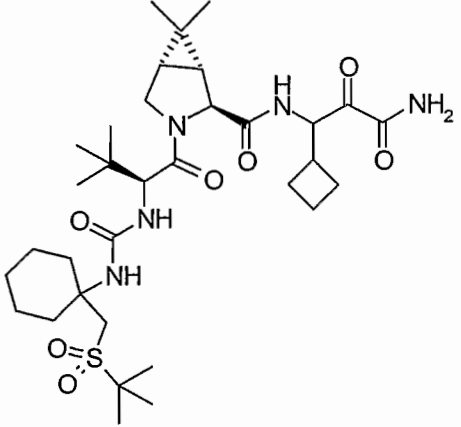
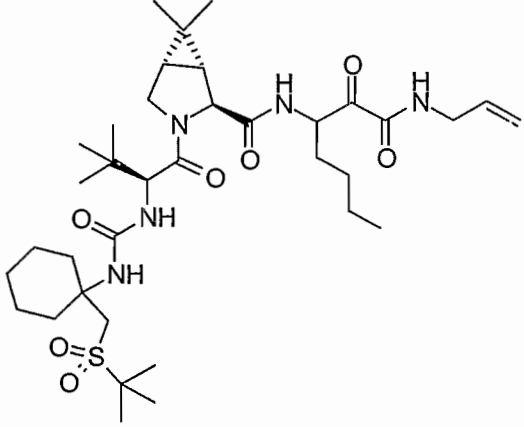
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
264	 Chemical structure of compound 264: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂NR₂) and an amide group (NH-CO-). The amide group is linked to a pyrrolidine ring, which is further substituted with a cyclopropyl group and an amide group (NH-CO-). The amide group is linked to a cyclopropyl group, which is further substituted with an amide group (NH-CO-). The amide group is linked to a cyclopropyl group, which is further substituted with an amide group (NH-CO-).	FABMS; MH ⁺ , 664.4.	A
265	 Chemical structure of compound 265: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂NR₂) and an amide group (NH-CO-). The amide group is linked to a pyrrolidine ring, which is further substituted with a cyclopropyl group and an amide group (NH-CO-). The amide group is linked to a cyclopropyl group, which is further substituted with an amide group (NH-CO-). The amide group is linked to a cyclopropyl group, which is further substituted with an amide group (NH-CO-).		A

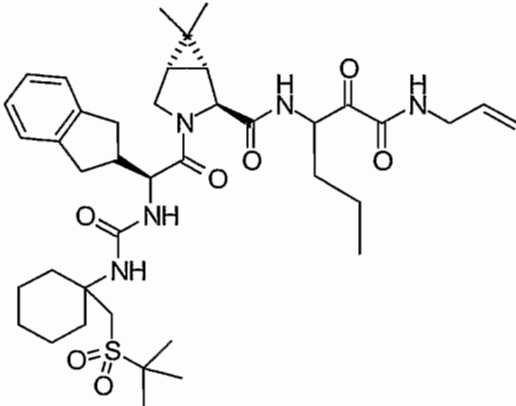
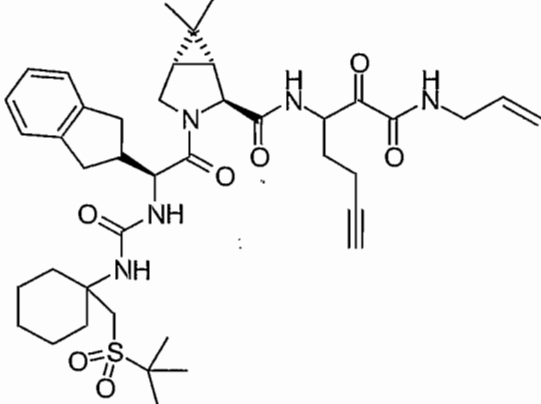
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
266	 Chemical structure of compound 266: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge), a methyl group (dash), and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain containing a cyclopropylmethyl group and a primary amide. Another amide linkage connects the pyrrolidine ring to a side chain containing a cyclohexylmethyl group and a sulfonamide group (SO₂CH₃).	FABMS; MH ⁺ , 664.2.	A
267	 Chemical structure of compound 267: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge), a methyl group (dash), and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain containing a cyclopropylmethyl group and a primary amide. Another amide linkage connects the pyrrolidine ring to a side chain containing a cyclohexylmethyl group and a sulfonamide group (SO₂CH₃).		B

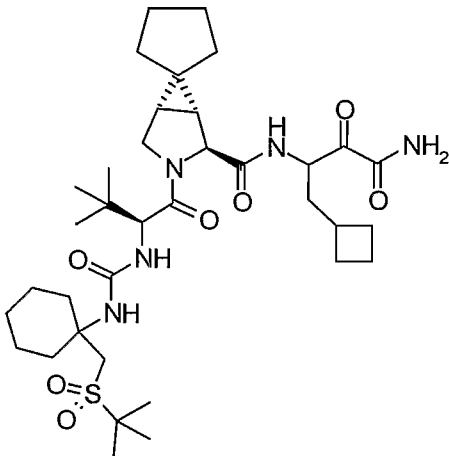
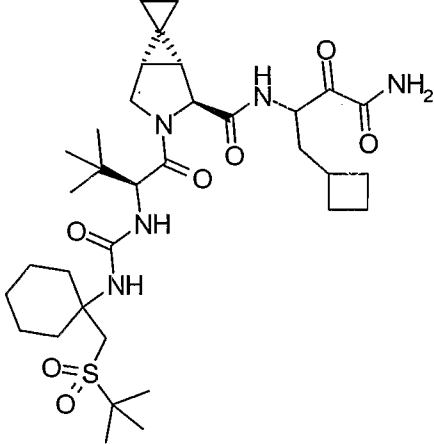
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
268	 Chemical structure of compound 268: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position (dashed bond), a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is linked to a chain containing a terminal vinyl group. The carbonyl at the 4-position is linked to a chain containing a terminal alkyne group. A cyclohexyl group is attached to the nitrogen of the pyrrolidine ring via a carbonyl group. A tert-butyl sulfonamide group is attached to the cyclohexyl ring via a carbonyl group.		B
269	 Chemical structure of compound 269: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position (dashed bond), a carbonyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl at the 3-position is linked to a chain containing a terminal vinyl group. The carbonyl at the 4-position is linked to a chain containing a terminal alkyne group. A cyclohexyl group is attached to the nitrogen of the pyrrolidine ring via a carbonyl group. A tert-butyl sulfonamide group is attached to the cyclohexyl ring via a carbonyl group.		A

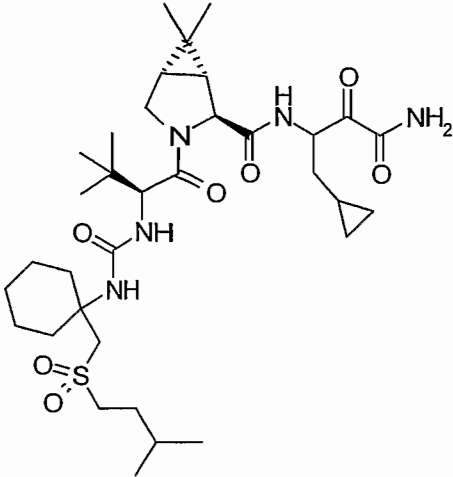
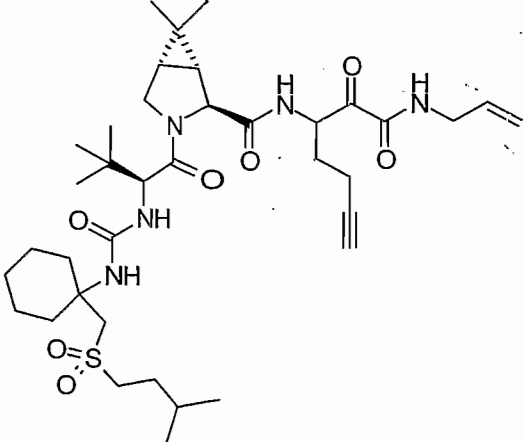
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
270	 Chemical structure of compound 270: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-sulfonyl group at the 2-position, a 1-aminocyclopropyl group at the 3-position, and a 1-aminocyclohexyl group at the 4-position. The pyrrolidine ring is also substituted with a 1-aminocyclopropyl group at the 3-position and a 1-aminocyclohexyl group at the 4-position. The pyrrolidine ring is also substituted with a 1-aminocyclopropyl group at the 3-position and a 1-aminocyclohexyl group at the 4-position.		A
271	 Chemical structure of compound 271: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-sulfonyl group at the 2-position, a 1-aminocyclopropyl group at the 3-position, and a 1-aminocyclohexyl group at the 4-position. The pyrrolidine ring is also substituted with a 1-aminocyclopropyl group at the 3-position and a 1-aminocyclohexyl group at the 4-position. The pyrrolidine ring is also substituted with a 1-aminocyclopropyl group at the 3-position and a 1-aminocyclohexyl group at the 4-position.		A

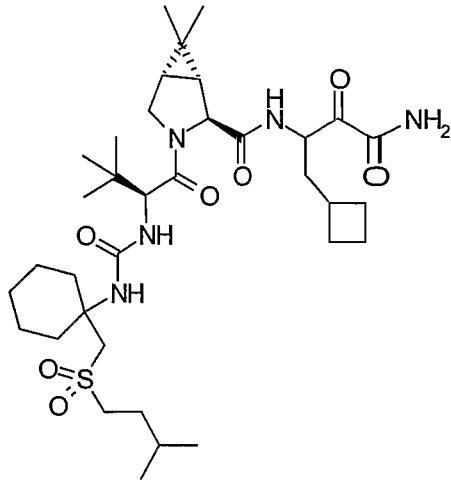
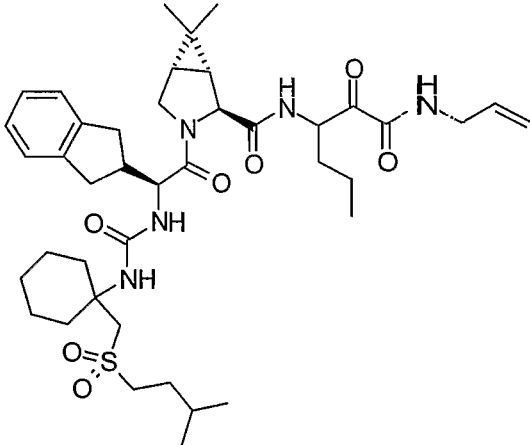
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i [*] range
272	 Chemical structure of compound 272: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group (-SO₂NH-t-Bu) and a side chain containing a cyclopropane ring, a pyrrolidine ring, and a dipeptide-like structure with a terminal vinyl group and an internal alkyne.	FABMS; MH ⁺ , 702.3.	A
273	 Chemical structure of compound 273: Similar to compound 272, but with a different side chain configuration, specifically a terminal vinyl group and an internal alkene instead of an alkyne.	FABMS; MH ⁺ , 720.5.	A

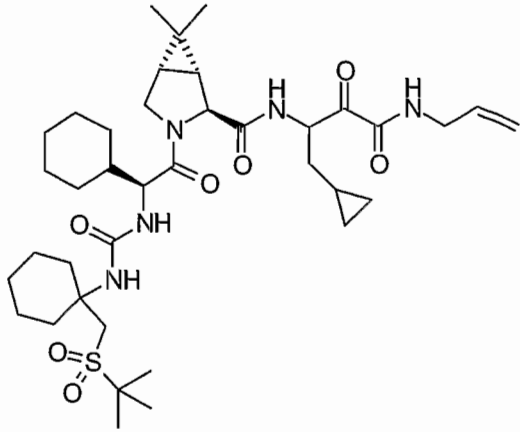
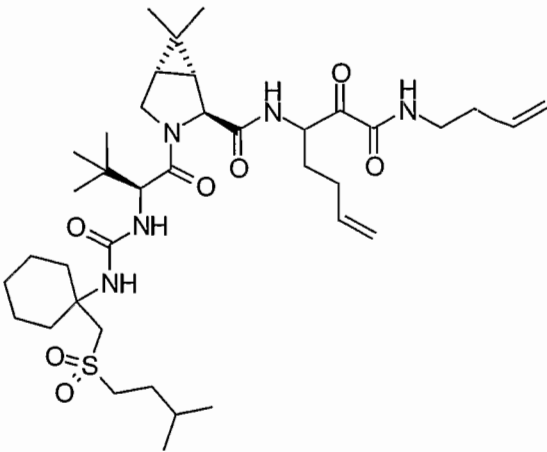
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
274	 Chemical structure of compound 274: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂NH-) and a carbamate group (-NHCOO-). The carbamate is linked to a pyrrolidine ring, which is further substituted with a tert-butyl group and a side chain containing a cyclobutyl ring and a primary amide group (-CONH₂).		A
275	 Chemical structure of compound 275: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂NH-) and a carbamate group (-NHCOO-). The carbamate is linked to a pyrrolidine ring, which is further substituted with a tert-butyl group and a side chain containing a propyl group and a secondary amide group (-NHCH₂CH=CH₂).		A

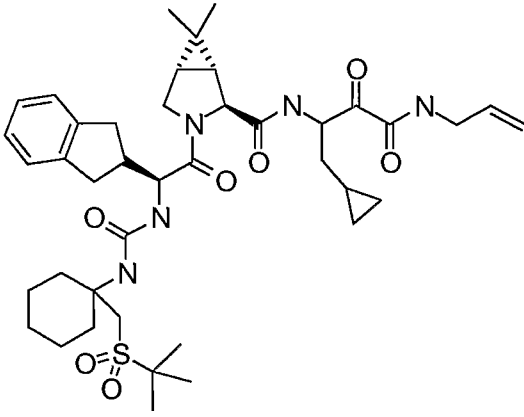
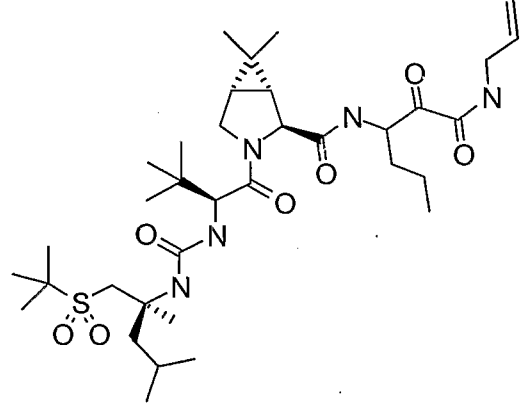
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
276	 Chemical structure of compound 276: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 1,2,3,4-tetrahydronaphthalen-1-yl group at the 2-position, a tert-butylsulfonyl group at the 3-position, and a 2-allyl-3-oxobutyl group at the 4-position. The 2-allyl-3-oxobutyl group is further substituted with a 2-allyl-3-oxobutyl group at the 2-position.		A
277	 Chemical structure of compound 277: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 1,2,3,4-tetrahydronaphthalen-1-yl group at the 2-position, a tert-butylsulfonyl group at the 3-position, and a 2-allyl-3-oxobutyl group at the 4-position. The 2-allyl-3-oxobutyl group is further substituted with a 2-allyl-3-oxobutyl group at the 2-position.	FABMS; MH ⁺ , 764.8.	A

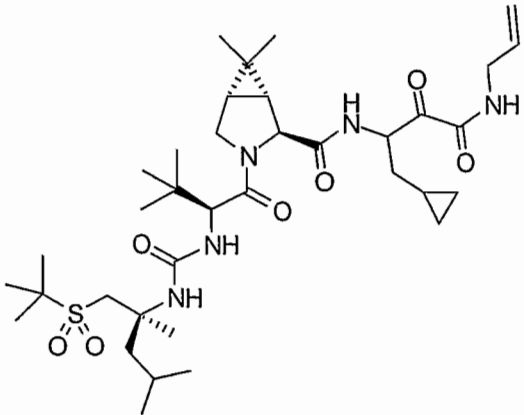
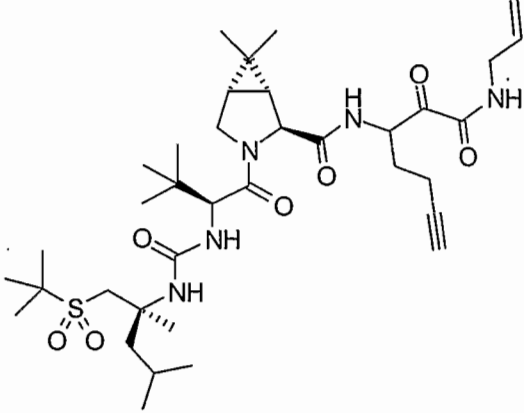
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
278		LCMS; MH ⁺ , 706.2.	A
279		FABMS; MH ⁺ , 678.2.	A

Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
280	 Chemical structure of compound 280: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a cyclopropylmethyl group, a carbonyl group, and a primary amide group (NH₂). The pyrrolidine ring is also substituted with a tert-butyl group at the 4-position. The side chain is further substituted with a cyclopropylmethyl group and a carbonyl group. The side chain is further substituted with a cyclopropylmethyl group and a carbonyl group. The side chain is further substituted with a cyclopropylmethyl group and a carbonyl group.		A
281	 Chemical structure of compound 281: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain includes a propargyl group (alkyne), a carbonyl group, and a primary amide group (NH₂). The pyrrolidine ring is also substituted with a tert-butyl group at the 4-position. The side chain is further substituted with a propargyl group and a carbonyl group. The side chain is further substituted with a propargyl group and a carbonyl group. The side chain is further substituted with a propargyl group and a carbonyl group.		A

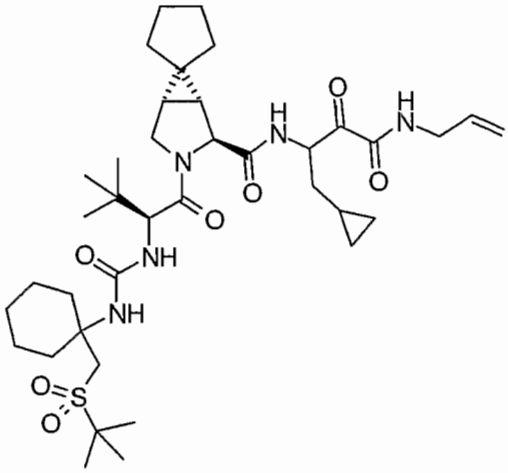
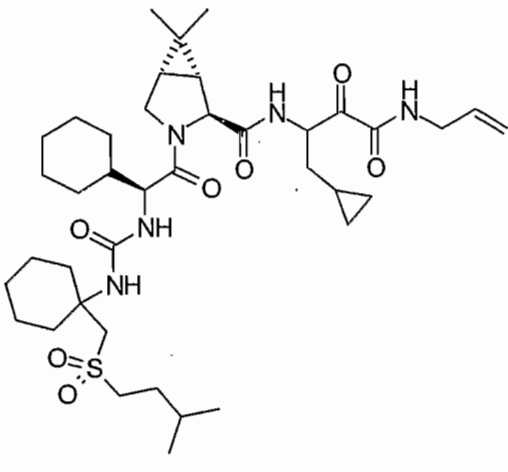
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
282	 Chemical structure of compound 282: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a carbonyl group (double bond), and an amide group (NH). The amide group is connected to a chain containing a cyclobutane ring, a carbonyl group, and an amide group (NH₂). The pyrrolidine ring is also connected to a chain containing a carbonyl group, an amide group (NH), and a cyclohexane ring. The cyclohexane ring is substituted with a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃).		A
283	 Chemical structure of compound 283: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a carbonyl group (double bond), and an amide group (NH). The amide group is connected to a chain containing a carbonyl group, an amide group (NH), and a cyclohexane ring. The cyclohexane ring is substituted with a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃). The pyrrolidine ring is also connected to a chain containing a carbonyl group, an amide group (NH), and a cyclohexane ring. The cyclohexane ring is substituted with a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃).		A

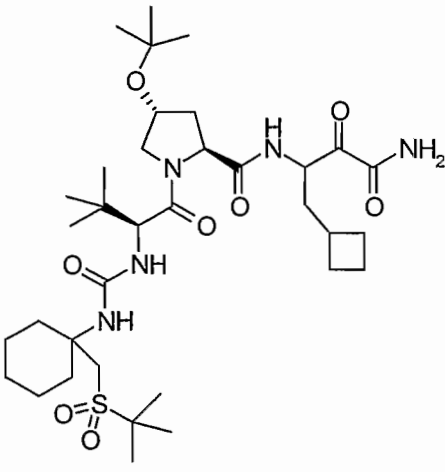
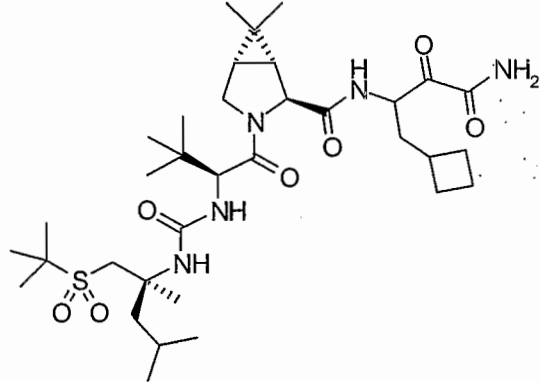
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
284	 Chemical structure of compound 284: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a cyclohexylmethyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a cyclopropylmethyl group, a carbonyl group, and an amide linkage to a 3-allylpropyl group. Additionally, the pyrrolidine ring is linked via a carbonyl group to a cyclohexylmethyl group, which is further linked via an amide to a cyclohexylmethyl group. The cyclohexylmethyl group is also linked via a carbonyl group to a tert-butyl group.		A
285	 Chemical structure of compound 285: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a cyclohexylmethyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a 3-allylpropyl group, a carbonyl group, and an amide linkage to a cyclohexylmethyl group. Additionally, the pyrrolidine ring is linked via a carbonyl group to a cyclohexylmethyl group, which is further linked via an amide to a cyclohexylmethyl group. The cyclohexylmethyl group is also linked via a carbonyl group to a tert-butyl group.		A

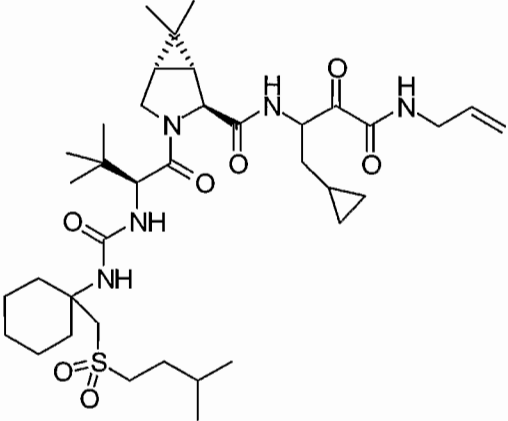
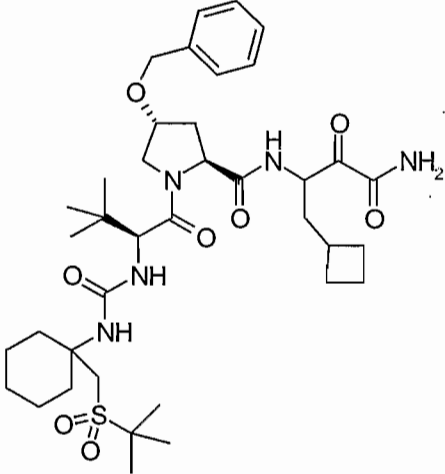
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
286	 Chemical structure of compound 286: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-allyl-3-oxopropyl group, and a 2-((2-allyl-3-oxopropyl)amino)-1-phenylpropan-1-yl group. The pyrrolidine ring is also substituted with a 2-((2-allyl-3-oxopropyl)amino)-1-phenylpropan-1-yl group. The molecule is further substituted with a 2-((2-allyl-3-oxopropyl)amino)-1-phenylpropan-1-yl group.	LCMS; MH ⁺ , 766.2.	A
287	 Chemical structure of compound 287: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-allyl-3-oxopropyl group, and a 2-((2-allyl-3-oxopropyl)amino)-1-phenylpropan-1-yl group. The pyrrolidine ring is also substituted with a 2-((2-allyl-3-oxopropyl)amino)-1-phenylpropan-1-yl group. The molecule is further substituted with a 2-((2-allyl-3-oxopropyl)amino)-1-phenylpropan-1-yl group.		C

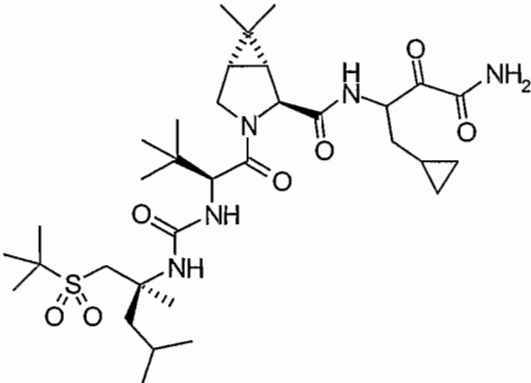
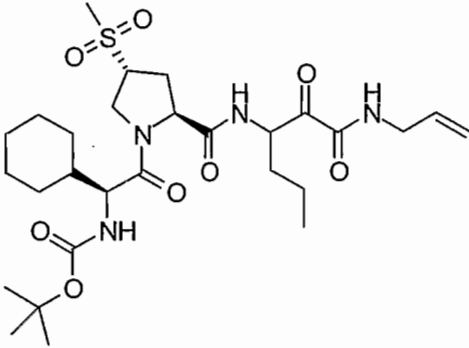
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
288	 Chemical structure of compound 288: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a (1S,2S)-2-((tert-butylsulfonyl)amino)-3-methylbutanamide group at the 3-position, and a (1S,2S)-2-((tert-butylsulfonyl)amino)-3-methylbutanamide group at the 4-position. The pyrrolidine ring is also linked via an amide bond to a cyclopropane ring, which is further substituted with a (1S,2S)-2-((tert-butylsulfonyl)amino)-3-methylbutanamide group.		C
289	 Chemical structure of compound 289: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a (1S,2S)-2-((tert-butylsulfonyl)amino)-3-methylbutanamide group at the 3-position, and a (1S,2S)-2-((tert-butylsulfonyl)amino)-3-methylbutanamide group at the 4-position. The pyrrolidine ring is also linked via an amide bond to a cyclopropane ring, which is further substituted with a (1S,2S)-2-((tert-butylsulfonyl)amino)-3-methylbutanamide group.		B

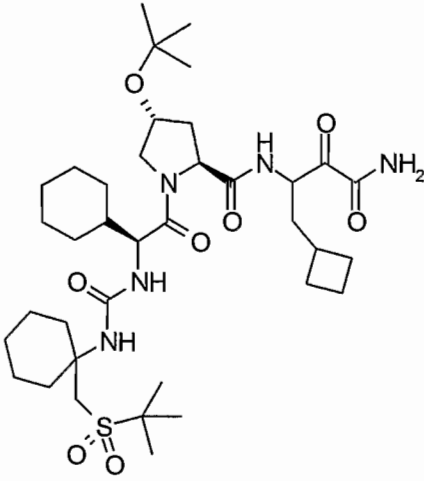
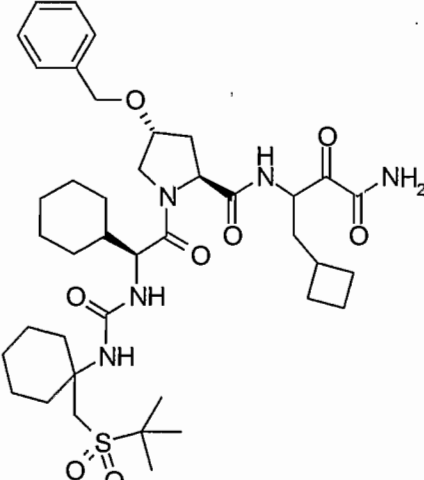
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
290			A
291			A

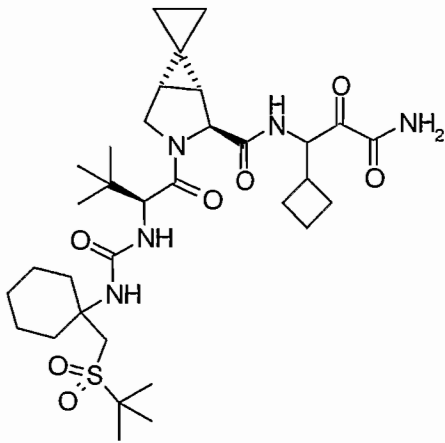
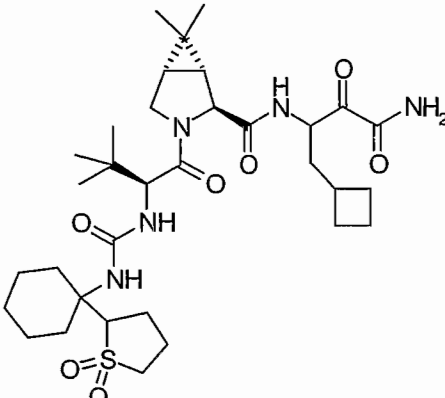
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
292	 Chemical structure of compound 292: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopentyl group (wedge bond), a tert-butyl group (dash bond), and a carbonyl group. The carbonyl group is part of an amide linkage to a cyclopropylmethyl group. The cyclopropylmethyl group is further substituted with a carbonyl group and an amide linkage to a vinyl group. The pyrrolidine ring is also substituted with a carbonyl group and an amide linkage to a cyclohexylmethyl group. The cyclohexylmethyl group is further substituted with a carbonyl group and an amide linkage to a tert-butyl group.		A
293	 Chemical structure of compound 293: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopentyl group (wedge bond), a tert-butyl group (dash bond), and a carbonyl group. The carbonyl group is part of an amide linkage to a cyclopropylmethyl group. The cyclopropylmethyl group is further substituted with a carbonyl group and an amide linkage to a vinyl group. The pyrrolidine ring is also substituted with a carbonyl group and an amide linkage to a cyclohexylmethyl group. The cyclohexylmethyl group is further substituted with a carbonyl group and an amide linkage to a tert-butyl group.		A

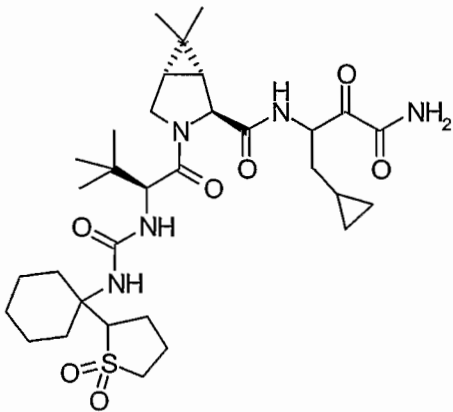
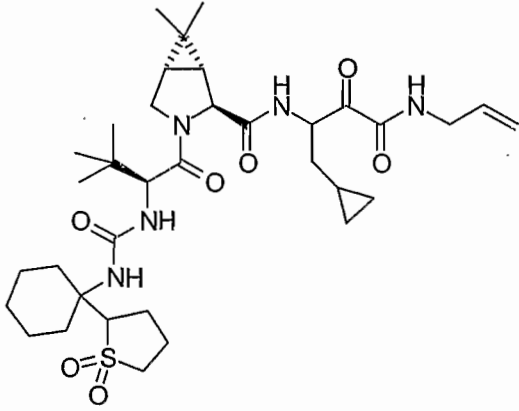
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
296	 Chemical structure of compound 296: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group and a side chain containing a pyrrolidine ring, a carbamate, and a cyclobutyl group.	LCMS; MH ⁺ , 712.3.	A
297	 Chemical structure of compound 297: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group and a side chain containing a pyrrolidine ring, a carbamate, and a cyclobutyl group.		A

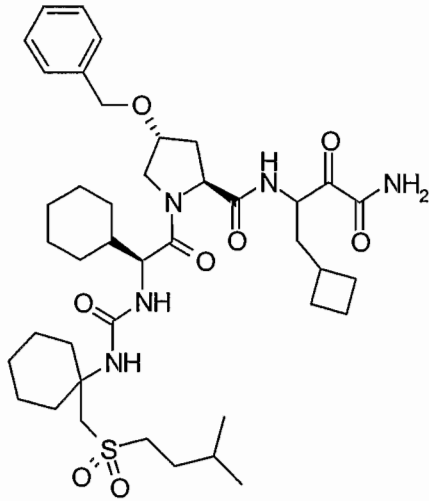
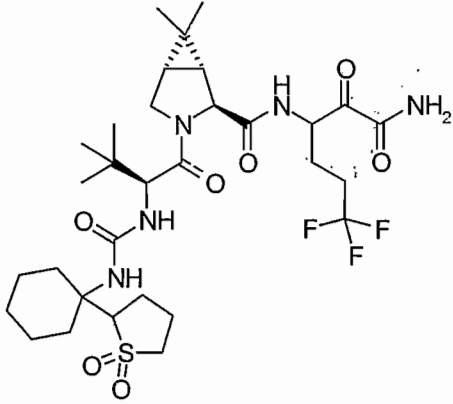
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
298			A
299		LCMS; MH ⁺ , 746.2.	A

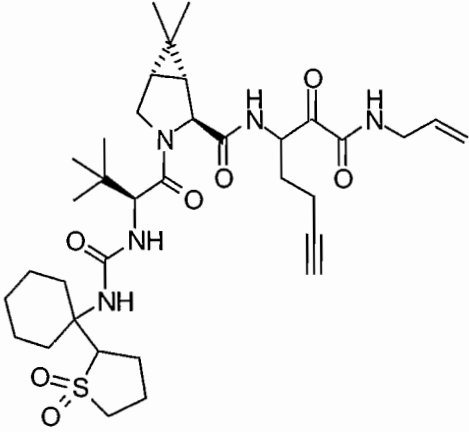
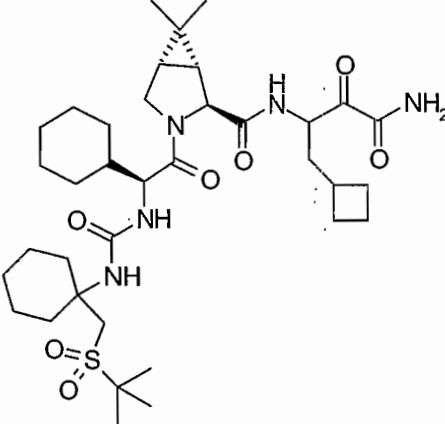
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i * range
300	 Chemical structure of compound 300: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a methyl group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a cyclopropylmethyl group, which is further substituted with an amide group and a primary amine (NH₂). The pyrrolidine ring is also linked via an amide to a side chain containing a sulfonamide group (SO₂NH₂) and a tert-butyl group.		B
301	 Chemical structure of compound 301: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group at the 2-position, a carbonyl group at the 3-position, and a sulfonamide group (SO₂NH₂) at the 4-position. The carbonyl group is part of an amide linkage to a side chain containing a cyclohexylmethyl group, which is further substituted with an amide group and a primary amine (NH₂). The pyrrolidine ring is also linked via an amide to a side chain containing a tert-butyl group and a carbonyl group.		A

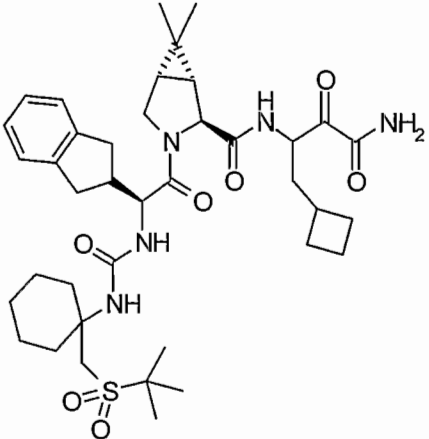
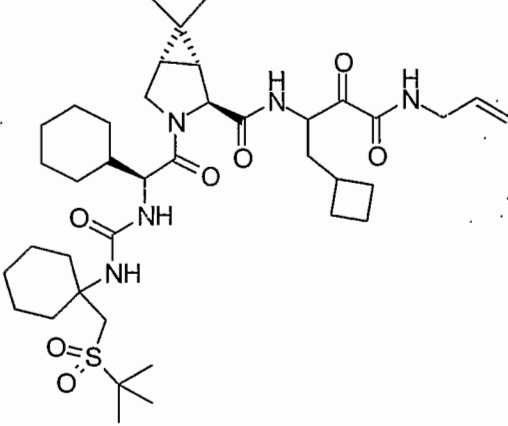
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
302	 Chemical structure of compound 302: A complex molecule featuring a central amide linkage. The left side includes a cyclohexyl ring attached to a chiral center, which is further linked to a sulfonamide group (SO₂CH₃) and a cyclohexyl ring. The right side includes a cyclohexyl ring attached to a chiral center, which is further linked to a sulfonamide group (SO₂CH₃) and a cyclohexyl ring. The central amide linkage connects a cyclohexyl ring to a cyclohexyl ring.		A
303	 Chemical structure of compound 303: A complex molecule featuring a central amide linkage. The left side includes a cyclohexyl ring attached to a chiral center, which is further linked to a sulfonamide group (SO₂CH₃) and a cyclohexyl ring. The right side includes a cyclohexyl ring attached to a chiral center, which is further linked to a sulfonamide group (SO₂CH₃) and a cyclohexyl ring. The central amide linkage connects a cyclohexyl ring to a cyclohexyl ring.		B

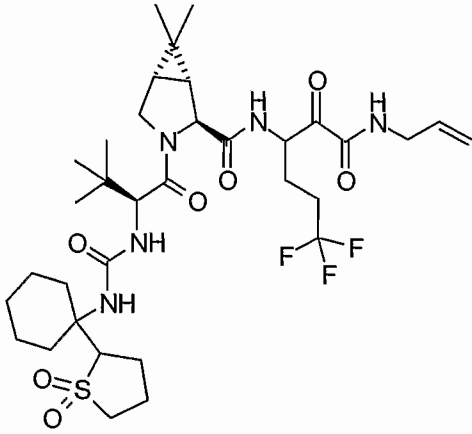
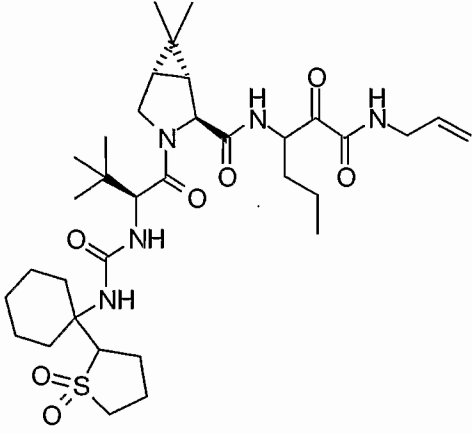
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
304	 Chemical structure of compound 304: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopropyl group at the 2-position (dashed bond), a tert-butyl group at the 3-position (wedged bond), and an amide group at the 4-position. The amide group is connected to a chain containing a cyclobutyl group and a primary amide group. The pyrrolidine ring is also connected to a chain containing a cyclohexyl group and a sulfonamide group.	LCMS; MH ⁺ , 664.1.	C
305	 Chemical structure of compound 305: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopropyl group at the 2-position (dashed bond), a tert-butyl group at the 3-position (wedged bond), and an amide group at the 4-position. The amide group is connected to a chain containing a cyclobutyl group and a primary amide group. The pyrrolidine ring is also connected to a chain containing a cyclohexyl group and a sulfonamide group.		B

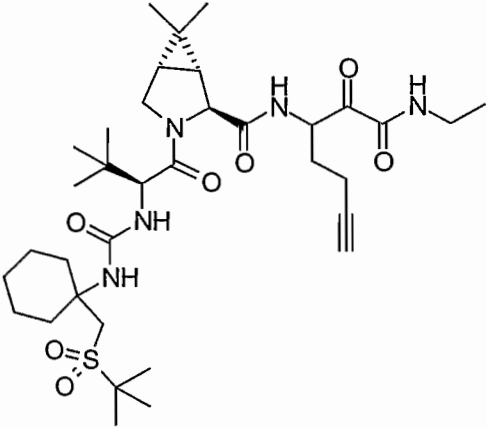
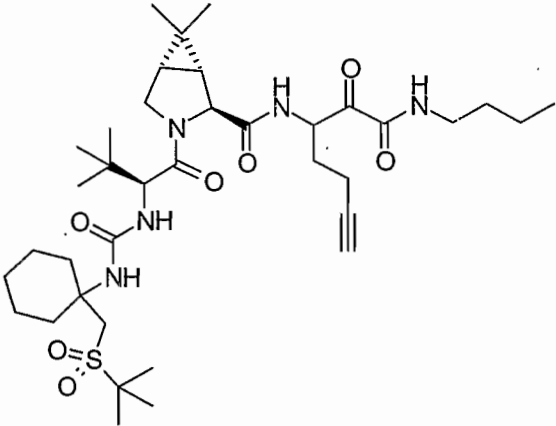
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
306	 Chemical structure of compound 306: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂). The pyrrolidine ring is also linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂). The pyrrolidine ring is further linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂). The pyrrolidine ring is also linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂).		A
307	 Chemical structure of compound 307: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂). The pyrrolidine ring is also linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂). The pyrrolidine ring is further linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂). The pyrrolidine ring is also linked to a chain containing a cyclopropylmethyl group and a primary amide group (NH₂).		A

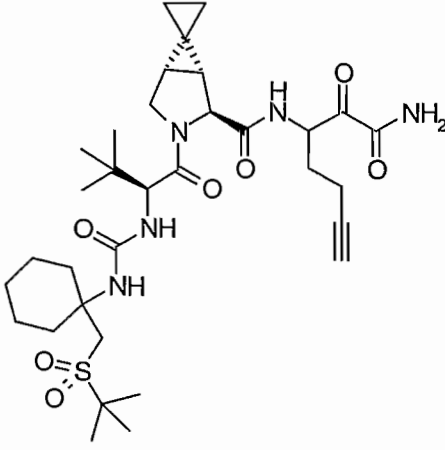
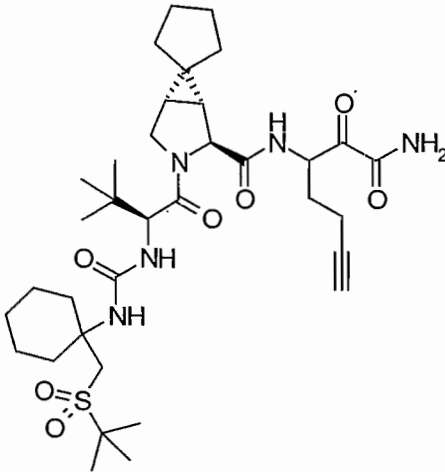
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
310	 Chemical structure of compound 310: A complex molecule featuring a central amide linkage. The left side includes a cyclohexyl ring attached to a carbonyl group, which is further linked to a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃). The right side includes a cyclohexyl ring attached to a carbonyl group, which is further linked to a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃). The central amide linkage connects a cyclohexyl ring to a carbonyl group, which is further linked to a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃).		A
311	 Chemical structure of compound 311: A complex molecule featuring a central amide linkage. The left side includes a cyclohexyl ring attached to a carbonyl group, which is further linked to a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃). The right side includes a cyclohexyl ring attached to a carbonyl group, which is further linked to a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃). The central amide linkage connects a cyclohexyl ring to a carbonyl group, which is further linked to a sulfonamide group (SO₂CH₂CH₂CH₂CH₂CH₃).		A

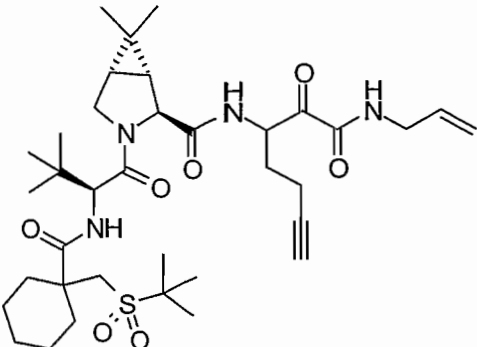
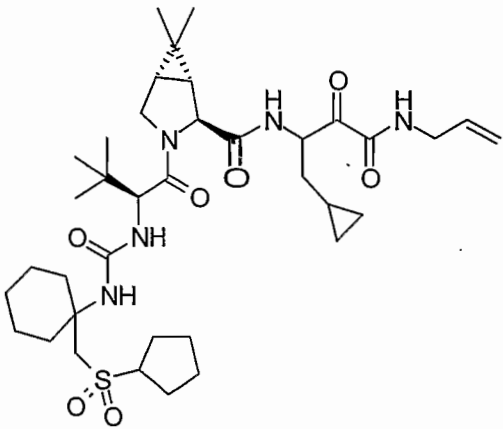
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
312	 Chemical structure of compound 312: A complex molecule featuring a central amide linkage. The left side includes a cyclohexane ring substituted with a sulfonamide group (SO₂NH-) and a carbonyl group. The right side includes a pyrrolidine ring substituted with a carbonyl group and a propargyl group (CH₂CH₂C≡CH). The central amide linkage connects the two main fragments.		A
313	 Chemical structure of compound 313: A complex molecule featuring a central amide linkage. The left side includes a cyclohexane ring substituted with a sulfonamide group (SO₂NH-) and a carbonyl group. The right side includes a pyrrolidine ring substituted with a carbonyl group and a cyclobutyl group. The central amide linkage connects the two main fragments.		A

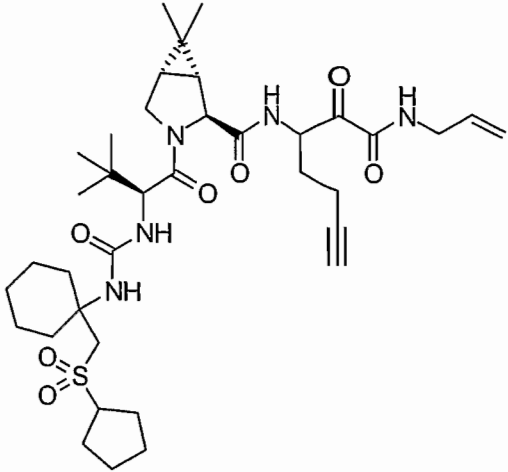
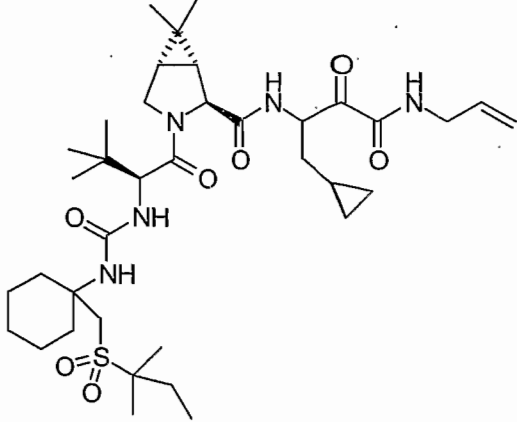
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
314	 Chemical structure of compound 314: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 2-position, a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 3-position, and a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 4-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 5-position. The molecule includes a cyclohexyl group, a cyclobutyl group, and a sulfonamide group.		A
315	 Chemical structure of compound 315: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 2-position, a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 3-position, and a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 4-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1,3-dioxane-5-carboxamide group at the 5-position. The molecule includes a cyclohexyl group, a cyclobutyl group, and a sulfonamide group.		A

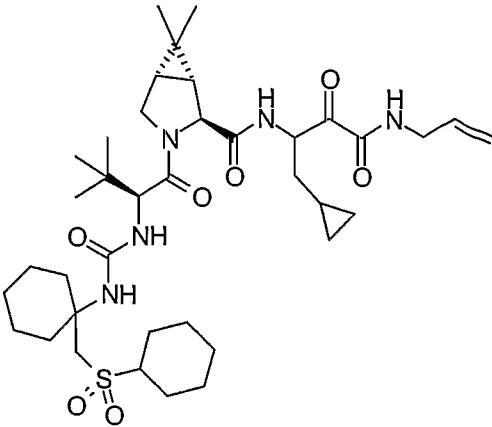
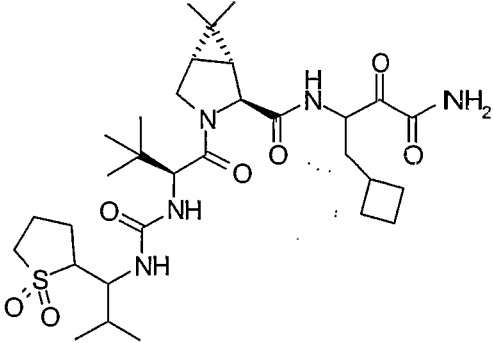
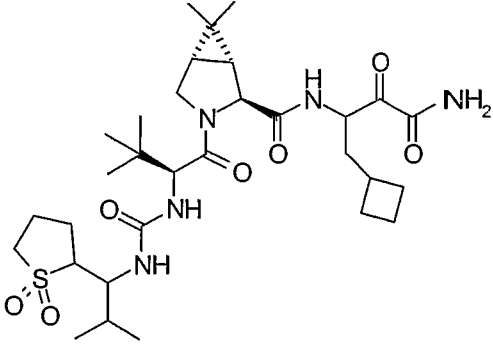
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
316	 Chemical structure of compound 316: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group, a dimethylamino group, and a carbonyl group. This carbonyl is part of an amide linkage to a side chain containing a trifluoromethyl group and a terminal vinyl group. Another amide linkage connects the pyrrolidine to a cyclohexane ring, which is further substituted with a sulfonamide group.		A
317	 Chemical structure of compound 317: Similar to compound 316, but the side chain contains an ethyl group instead of a trifluoromethyl group.		A

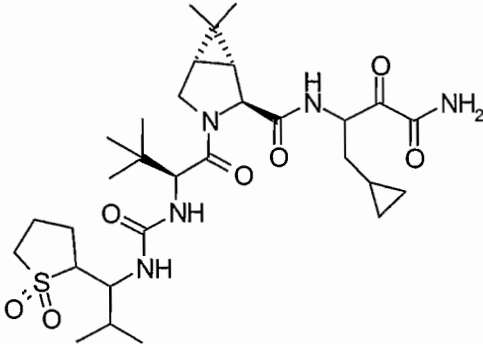
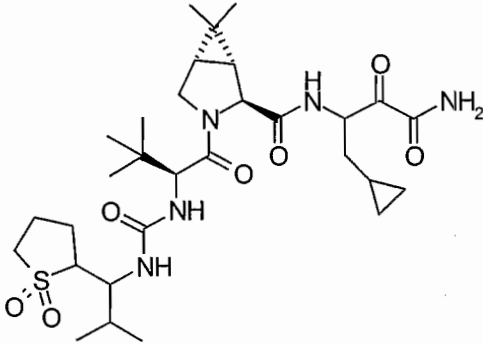
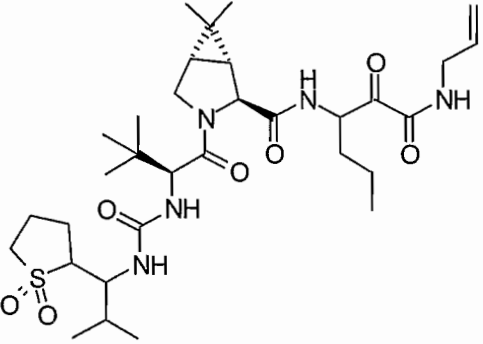
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K ⁱ * range
320	 Chemical structure of compound 320: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group and a side chain containing a pyrrolidine ring, a carbonyl group, and a terminal ethyl amide group. The side chain also includes a propargyl group (alkyne).	692.3LC MS; MH ⁺ , 692.2.	A
321	 Chemical structure of compound 321: A complex molecule featuring a cyclohexane ring substituted with a tert-butyl sulfonamide group and a side chain containing a pyrrolidine ring, a carbonyl group, and a terminal butyl amide group. The side chain also includes a propargyl group (alkyne).	LCMS; MH ⁺ , 720.2.	B

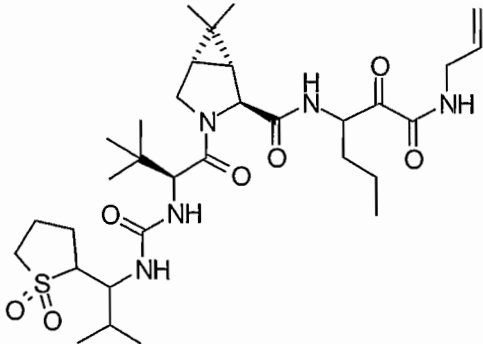
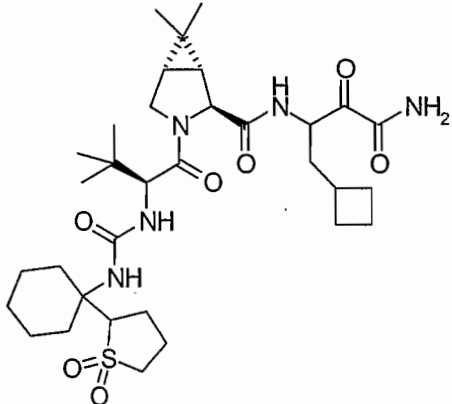
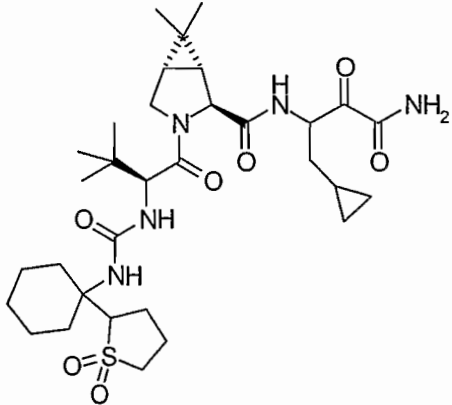
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
322	 Chemical structure of compound 322: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopropyl group (dashed bond), a carbonyl group (solid bond), and a side chain containing a carbonyl group, an amide group, and a terminal amide group. The side chain also includes a propargyl group (triple bond). The amide group is connected to a cyclohexyl ring, which is further substituted with a sulfonamide group (SO₂ group) and a tert-butyl group.		B
323	 Chemical structure of compound 323: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclopentyl group (dashed bond), a carbonyl group (solid bond), and a side chain containing a carbonyl group, an amide group, and a terminal amide group. The side chain also includes a propargyl group (triple bond). The amide group is connected to a cyclohexyl ring, which is further substituted with a sulfonamide group (SO₂ group) and a tert-butyl group.		A

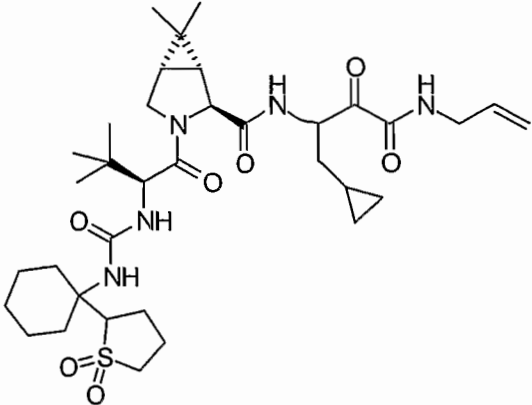
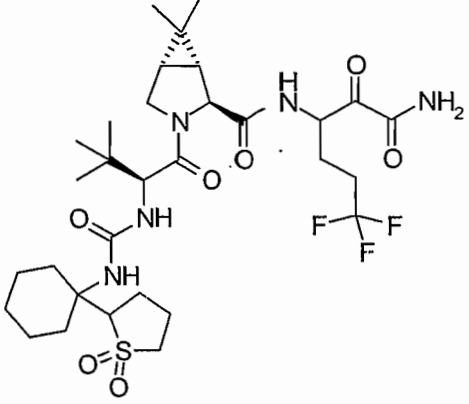
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
324			A
325			A

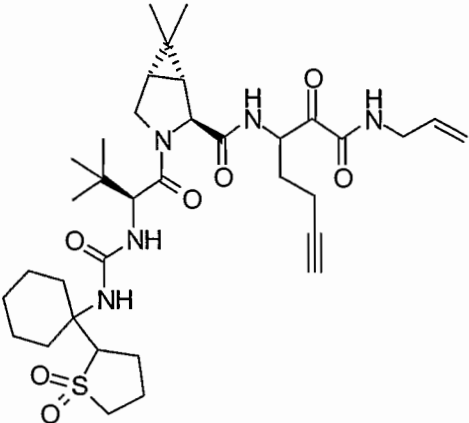
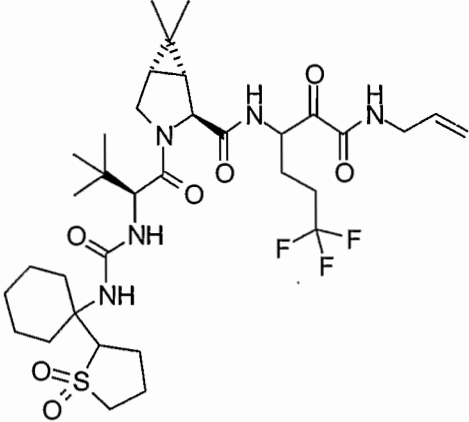
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K _i ⁺ range
326	 Chemical structure of compound 326: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a carbonyl group (double bond to oxygen), and an amide group (NH-C=O). The amide group is further substituted with a cyclohexyl ring (wedge bond) and a sulfonamide group (SO₂-NH₂). The sulfonamide group is further substituted with a cyclopentyl ring (wedge bond). The carbonyl group is further substituted with a propyl chain (wedge bond) and a terminal vinyl group (CH=CH₂).		A
327	 Chemical structure of compound 327: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (wedge bond), a carbonyl group (double bond to oxygen), and an amide group (NH-C=O). The amide group is further substituted with a cyclohexyl ring (wedge bond) and a sulfonamide group (SO₂-NH₂). The sulfonamide group is further substituted with a cyclopentyl ring (wedge bond). The carbonyl group is further substituted with a propyl chain (wedge bond) and a terminal vinyl group (CH=CH₂).	LCMS; MH ⁺ , 720.2.	C

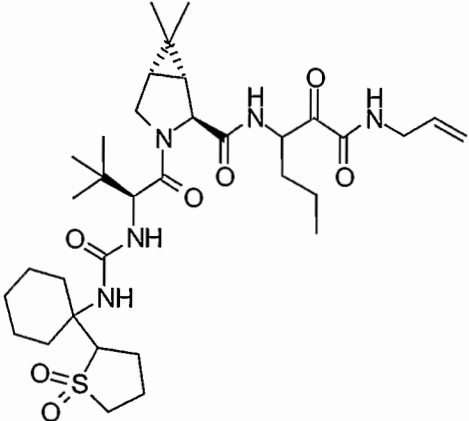
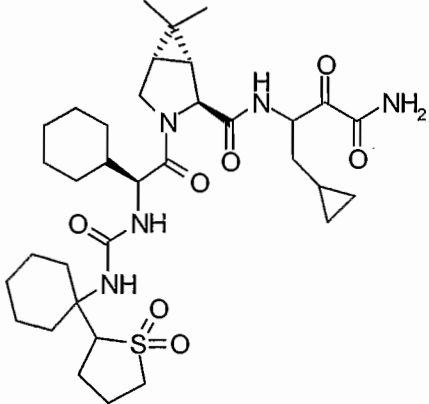
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328			NA
329			A
330			C

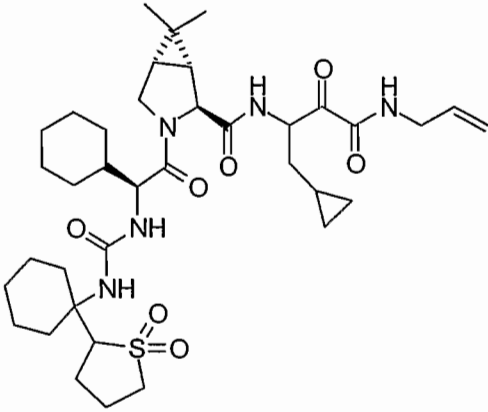
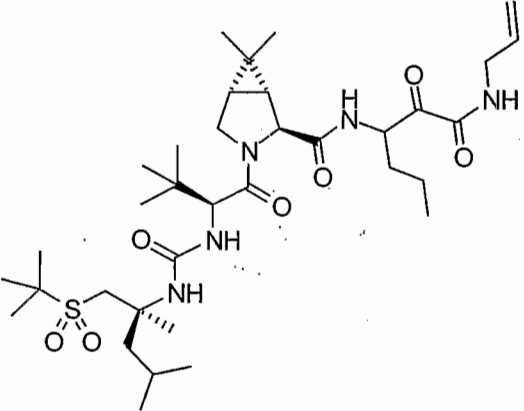
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
331			A
332			C
333			C

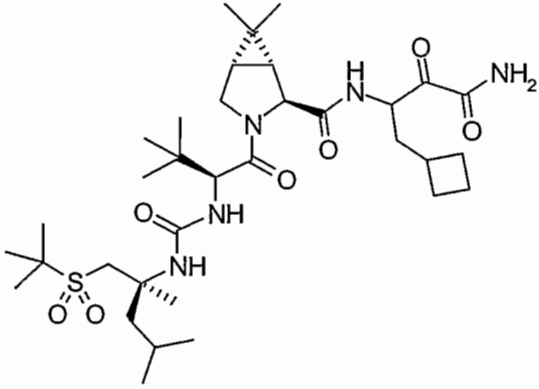
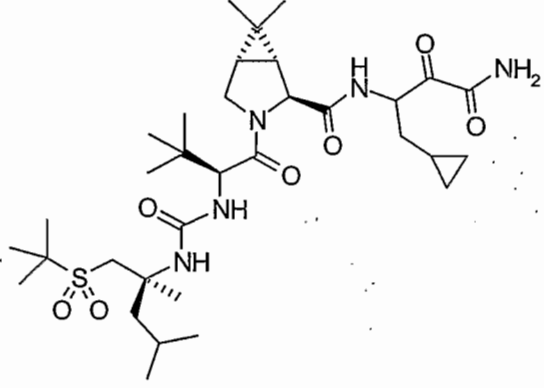
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
334	 Chemical structure of compound 334: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a methyl group. It is linked via amide bonds to a side chain containing a cyclopentyl sulfonamide group, a secondary amide, and a terminal allyl amide group.		A
335	 Chemical structure of compound 335: Similar to 334, but the side chain is modified to include a cyclobutyl ring and a terminal primary amide group (NH₂).		A
336	 Chemical structure of compound 336: Similar to 335, but the side chain is modified to include a cyclopropyl ring and a terminal primary amide group (NH₂).		A

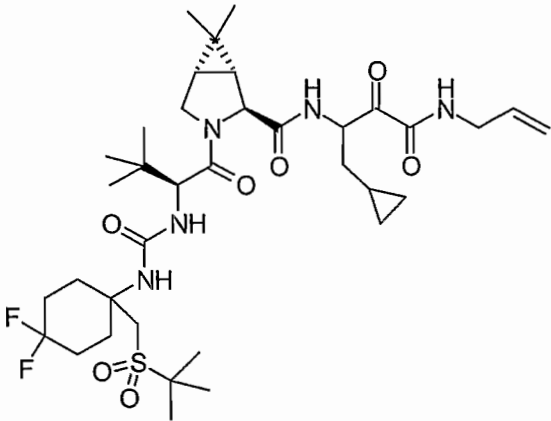
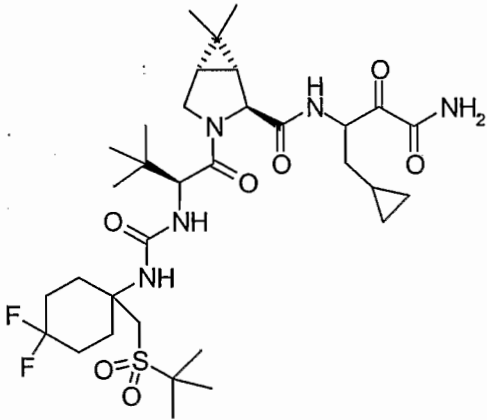
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
337	 Chemical structure of compound 337: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a methyl group. It is linked via amide bonds to a cyclopropylmethyl group and a 2-allylamino-3-oxopropyl group. Additionally, it contains a sulfonamide moiety consisting of a cyclohexyl ring fused to a cyclopentyl ring, which is substituted with a sulfonamide group.		A
338	 Chemical structure of compound 338: Similar to compound 337, it features the same central pyrrolidine and sulfonamide moieties. However, the amide linkage to the right is different, connecting to a 2-amino-3-oxopropyl group substituted with a trifluoromethyl group.		A

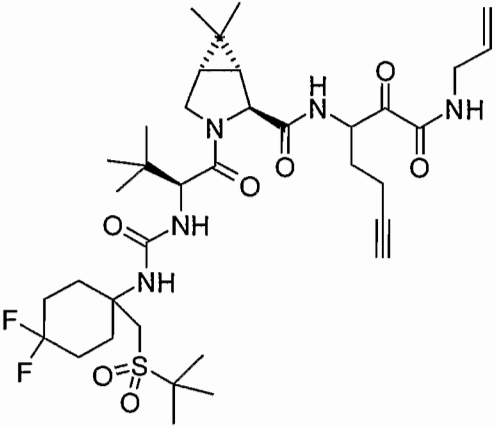
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
339	 Chemical structure of compound 339: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-5-yl group, a 2-allyl-4-oxo-1,2,3,4-tetrahydropyridine-5-yl group, and a 2-((cyclohexylideneamino)sulfonyl)ethyl group. The pyrrolidine ring also has a 2,2-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-5-yl group attached to its nitrogen atom.		A
340	 Chemical structure of compound 340: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-5-yl group, a 2-allyl-4-oxo-1,2,3,4-tetrahydropyridine-5-yl group, and a 2-((cyclohexylideneamino)sulfonyl)ethyl group. The pyrrolidine ring also has a 2,2-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-5-yl group attached to its nitrogen atom. The side chain is identical to compound 339, but the terminal group is a trifluoromethyl group (CF₃) instead of an ethynyl group.		A

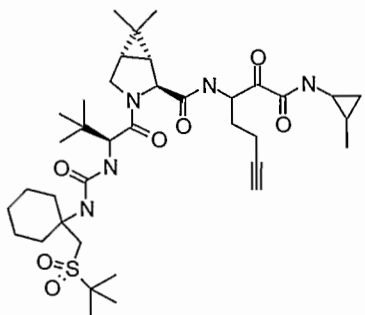
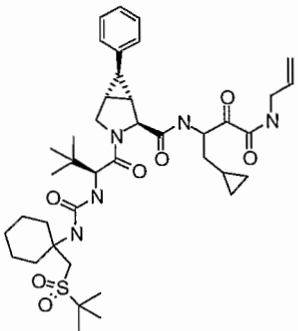
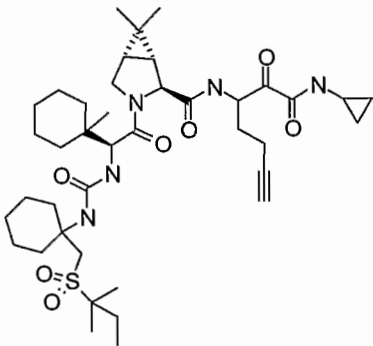
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
341	 Chemical structure of compound 341: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a dimethylamino group. This pyrrolidine is linked via an amide bond to a side chain containing a propyl group and a terminal allyl amide. Another amide branch connects the central pyrrolidine to a spirocyclic system consisting of a cyclohexane ring fused to a cyclopentane ring, which is further substituted with a sulfonamide group.		A
342	 Chemical structure of compound 342: Similar to compound 341, it features a central pyrrolidine ring with a tert-butyl group and a dimethylamino group. The amide linkage to the side chain is present, but the terminal group is a primary amide (NH₂) instead of an allyl amide. The spirocyclic sulfonamide system remains unchanged.		A

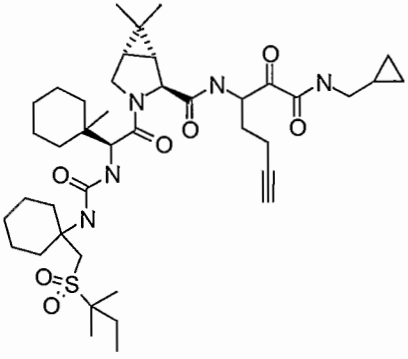
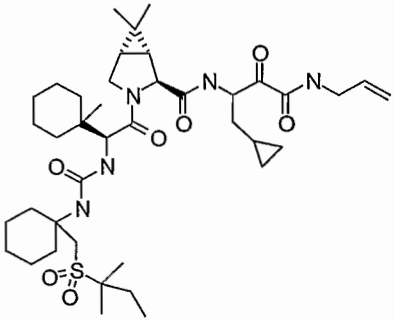
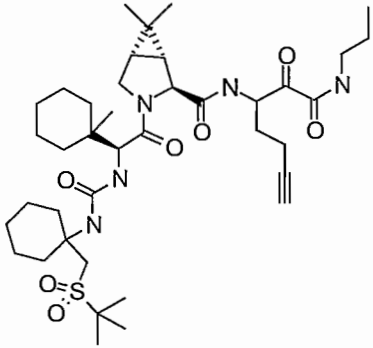
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
343	 Chemical structure of compound 343: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group, a methyl group, and a carbonyl group. The carbonyl group is part of an amide linkage to a cyclopropyl group. The cyclopropyl group is further substituted with a carbonyl group, which is part of another amide linkage to a vinyl group. The pyrrolidine ring is also substituted with a carbonyl group, which is part of an amide linkage to a cyclohexyl group. The cyclohexyl group is further substituted with a carbonyl group, which is part of another amide linkage to a vinyl group.		A
344	 Chemical structure of compound 344: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group, a carbonyl group, and a carbonyl group. The carbonyl group is part of an amide linkage to a cyclopropyl group. The cyclopropyl group is further substituted with a carbonyl group, which is part of another amide linkage to a vinyl group. The pyrrolidine ring is also substituted with a carbonyl group, which is part of an amide linkage to a cyclohexyl group. The cyclohexyl group is further substituted with a carbonyl group, which is part of another amide linkage to a vinyl group.		C

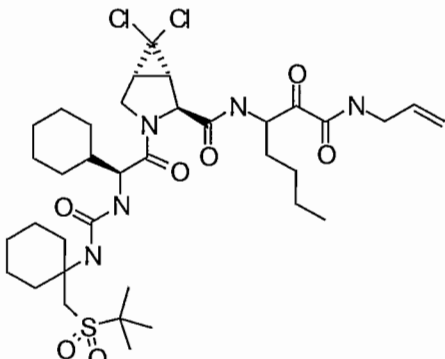
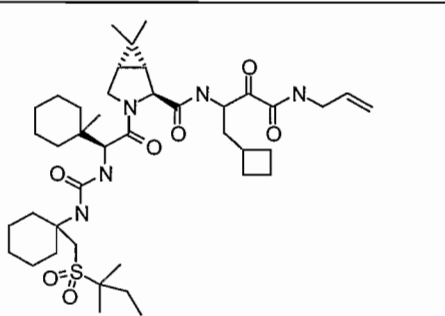
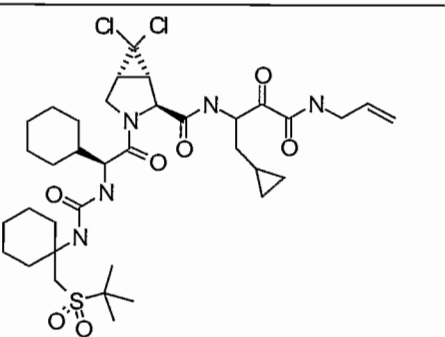
Prep. Ex.	COMPOUND	Select Mass Spectral Data	K ⁱ * range
347	 Chemical structure of compound 347: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a methyl group. The pyrrolidine ring is linked via an amide bond to a cyclobutane ring, which is further substituted with an amide group and a primary amine group. The molecule also contains a sulfonamide group and a chiral center.		B
348	 Chemical structure of compound 348: A complex molecule featuring a central pyrrolidine ring substituted with a tert-butyl group and a methyl group. The pyrrolidine ring is linked via an amide bond to a cyclopropane ring, which is further substituted with an amide group and a primary amine group. The molecule also contains a sulfonamide group and a chiral center.		B

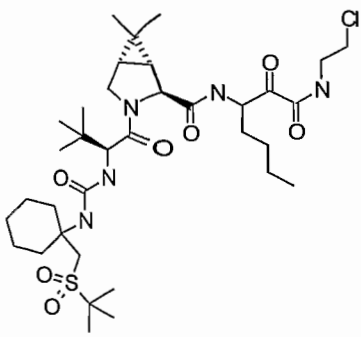
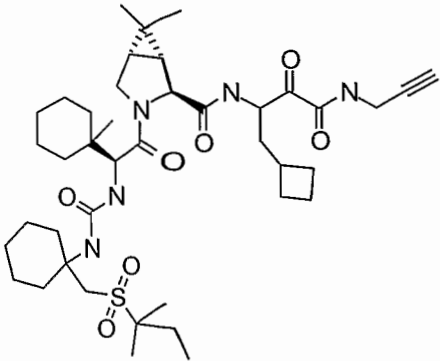
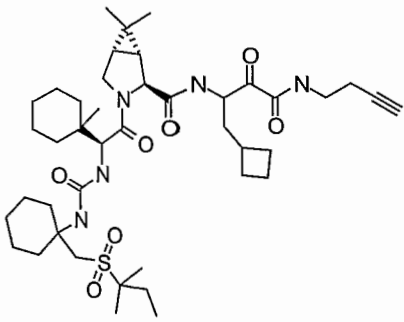
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
349	 Chemical structure of compound 349: A complex molecule featuring a 4,4-difluorocyclohexyl group connected via a methylene bridge to a sulfonamide group (SO₂NH-). This sulfonamide is linked to a chiral center (a carbon atom bonded to a methyl group, a hydrogen atom, and a carbonyl group). The carbonyl group is part of a five-membered ring containing a nitrogen atom, which is also substituted with a methyl group. This five-membered ring is connected via an amide bond to a cyclopropylmethyl group, which is further substituted with a carbonyl group and an amide group (NH-CH₂-CH=CH₂).		A
350	 Chemical structure of compound 350: A complex molecule featuring a 4,4-difluorocyclohexyl group connected via a methylene bridge to a sulfonamide group (SO₂NH-). This sulfonamide is linked to a chiral center (a carbon atom bonded to a methyl group, a hydrogen atom, and a carbonyl group). The carbonyl group is part of a five-membered ring containing a nitrogen atom, which is also substituted with a methyl group. This five-membered ring is connected via an amide bond to a cyclopropylmethyl group, which is further substituted with a carbonyl group and an amide group (NH-C(=O)-NH₂).		A

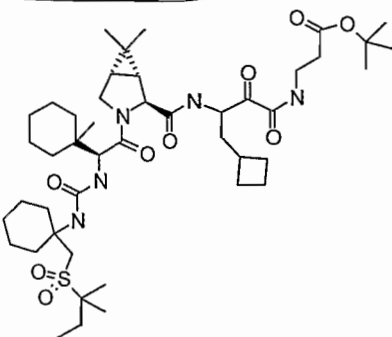
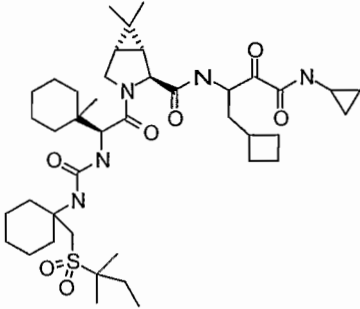
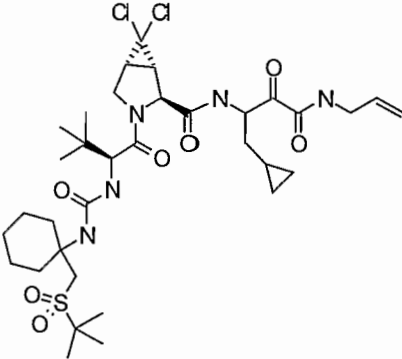
Prep. Ex.	COMPOUND	Select Mass Spectral Data	Ki* range
351	 The chemical structure of compound 351 is a complex molecule featuring a central pyrrolidine ring. This ring is substituted with a tert-butyl group at the 2-position, a (2-((tert-butylsulfonyl)amino)-2-fluorocyclohexyl)amino group at the 3-position, and a (2-((2-((2-allylamino)-2-oxoethyl)amino)-3-butynyl)-2-oxoethyl)amino group at the 4-position. The pyrrolidine ring also has a methyl group at the 5-position.		A

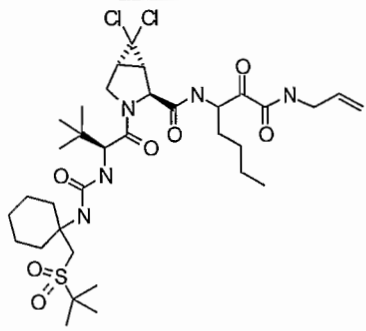
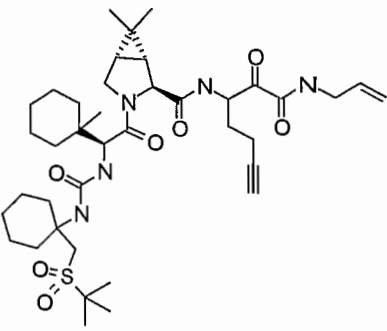
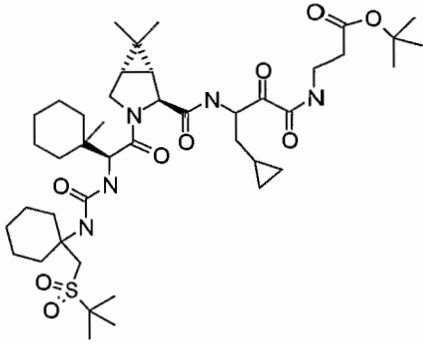
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	C	754.0095
	7	758.0414

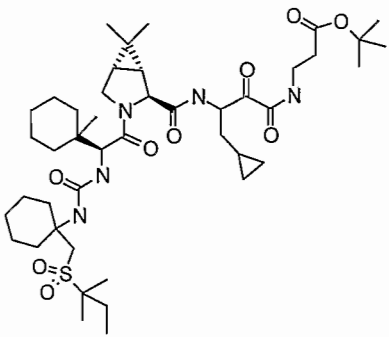
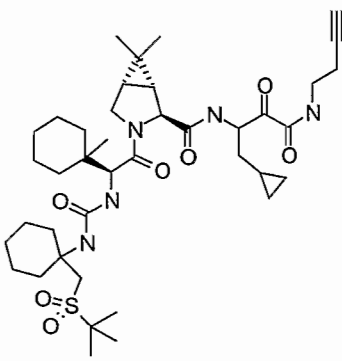
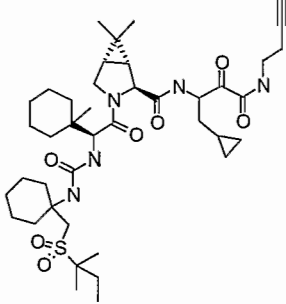
	10	772.0685
	14	760.0574
	4	746.0303

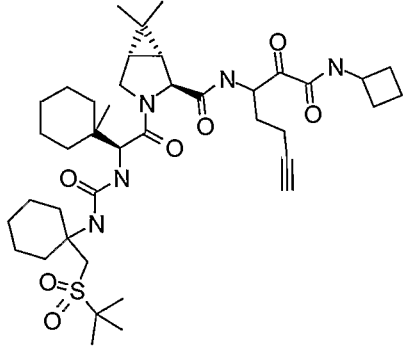
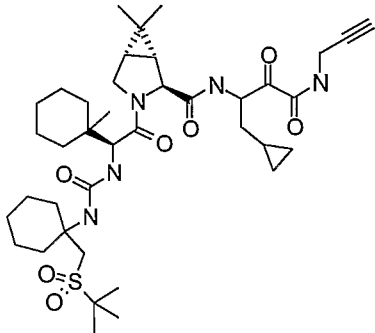
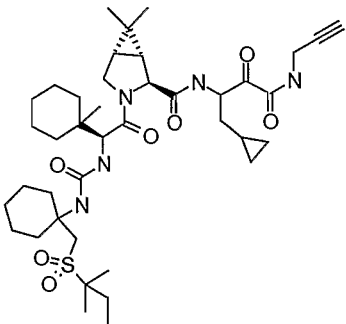
	5	774.855
	37	774.0844
	18	772.8391

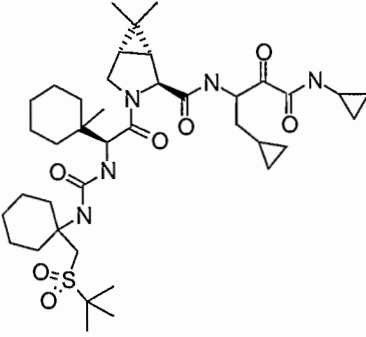
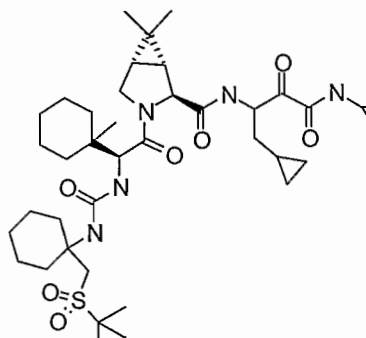
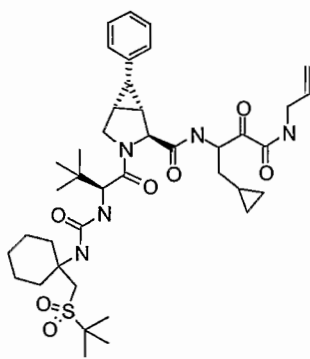
	27	730.4148
	34	772.0685
	48	786.0956

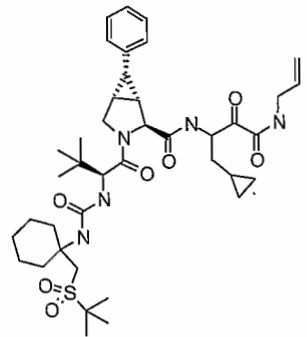
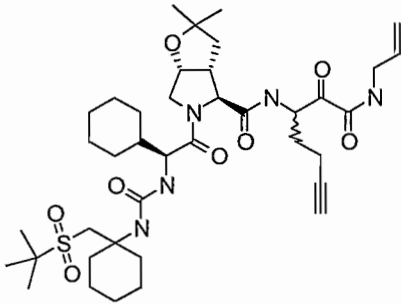
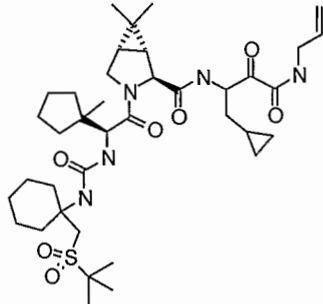
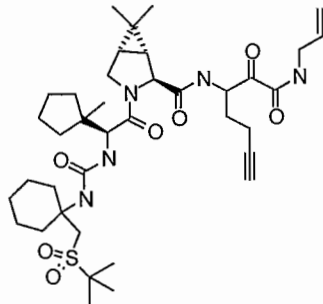
	52	862.1916
	54	774.0844
	9	746.8008

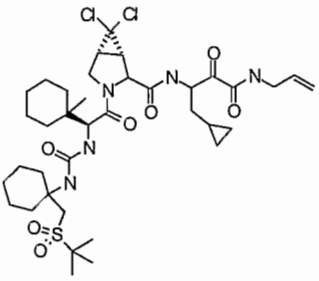
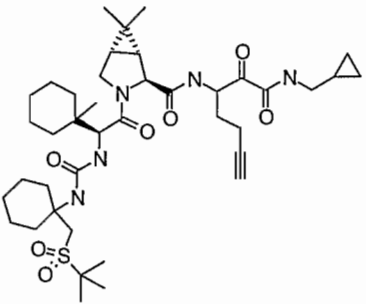
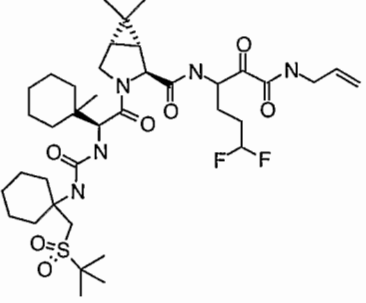
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	5	744.0143
	17	834.1374

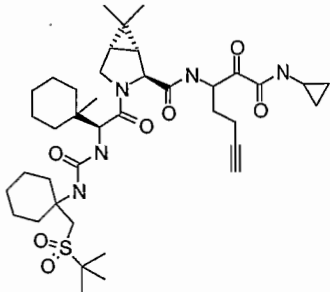
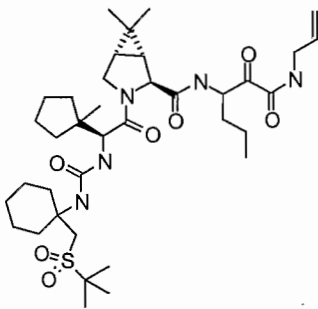
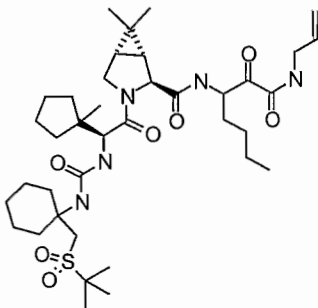
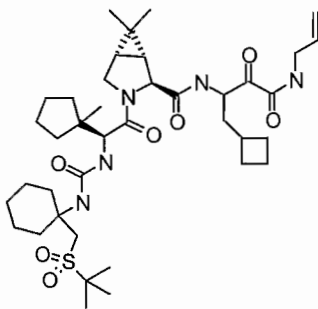
	19	848.1645
	17	758.0414
	20	772.0685

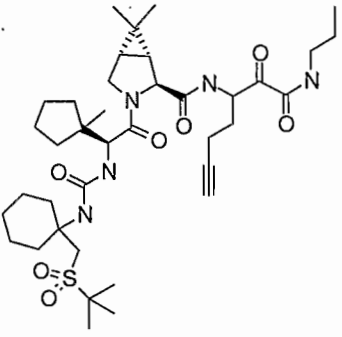
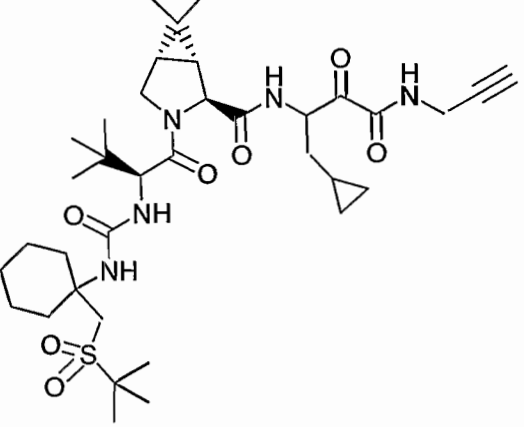
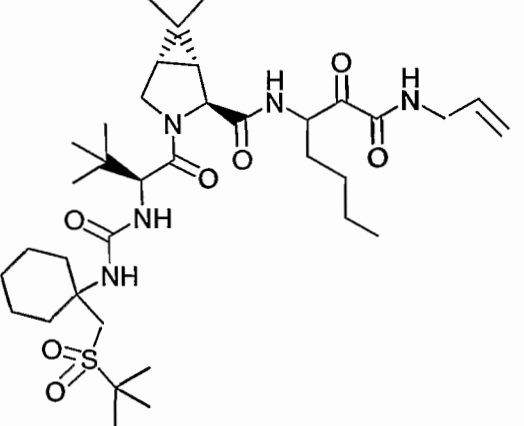
	10	758.0414
	8	744.0143
	17	758.0414

	12	746.0303
	13	760.0574
	C	754.0095

	C	754.0095
	23	760.0137
	12	732.0032
	2.4	729.9872

	B	786.8661
	4	758.0414
	6	770

	6	744.0143
	22	719.992
	22	734.0191
	34	746.0303

	13	732.0032
		
		

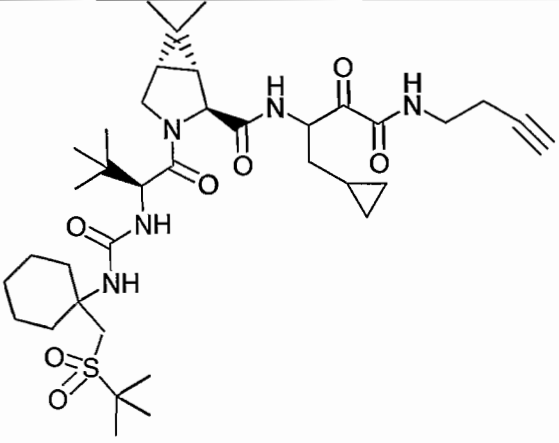
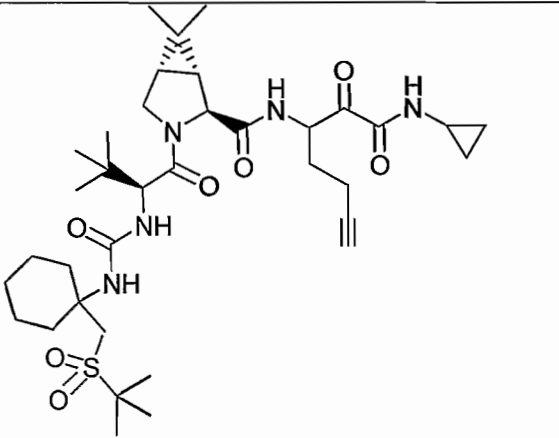
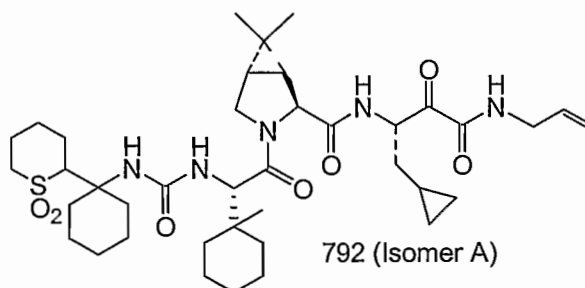
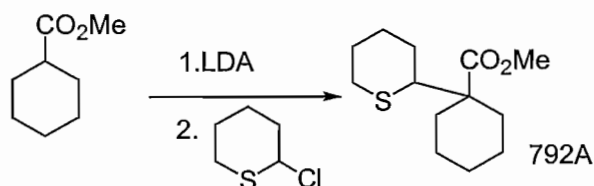
		
		

Table 3A lists additional compounds made in accordance with this invention. The following experimental procedures describe the preparation of the compounds shown in **Table 3A** which follows the experimentals.

5 Example 792



Step1

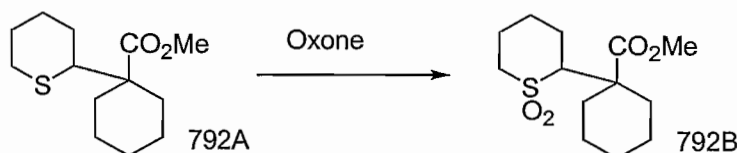


To a solution of pentamethylene sulfide (10.09g) in dry benzene (120ml) was added, portionwise (over a period of 40 min.), N-chlorosuccinimide (13.02g) while maintaining the internal temperature below 9°C. The resulting reaction mixture was stirred below 15°C for 45 min. The precipitate was filtered and the supernatant was concentrated under reduced pressure. The residue was diluted with cold hexane, filtered and the supernatant concentrated under reduced pressure to provide the chloride as a yellow oil (11.88g).

To diisopropylamine (12.5ml) in anhydrous THF (15ml) was added n-BuLi (53ml of a 1.6M solution in hexanes) at -78°C, under an atmosphere of nitrogen, and the resulting mixture was maintained at this temperature for a period of 15 min., before the addition of methyl cyclohexanecarboxylic acid (12.47ml) and the reaction was maintained at -78°C for a further 40 min. The chloride in anhydrous THF (50ml) was added to the reaction mixture and the flask was removed from the cooling bath and allowed to warm slowly to room temperature. The reaction was quenched with 5% aq. KH₂PO₄ (100ml) containing conc. aq. HCl (2.7ml). The organics were extracted into

Et₂O/EtOAc, dried (MgSO₄) and concentrated under reduced pressure to yield a residue which was purified by silica gel column chromatography using 0-2% EtOAc in hexanes as eluent. Gave the bicycle (792A; 8.12g) as a yellow oil.

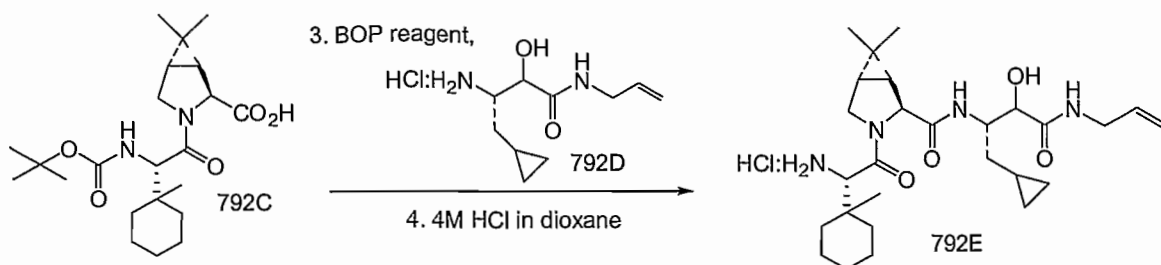
5 Step 2



A solution of the sulfide (792A; 0.780g) in 50% aq. MeOH (8ml) was cooled to 0°C and added to a cooled (0°C) suspension of oxone (5.97g) in 50% aq. MeOH (8ml) and the reaction was allowed to warm to room

10 temperature overnight before partitioning between methylene chloride and water. The aqueous layer was further extracted with methylene chloride and the combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using (25-35%) EtOAc in hexanes to give the sulfone (792B; 0.1598g). The reaction was repeated using the sulfide (792A; 8.12g), oxone (62.06g), methanol (30ml), water (30ml) to give the sulfone (792B; 4.73g).

The racemic mixture (792B; 0.4925g) was further purified by chiral HPLC using a preparatory Chiralpak AS column using 40% i-PrOH in hexanes (45ml/min; monitored at 218nm. Gave (792B-enantiomer A; 0.247g; retention time 37 min.) followed by (792B-enantiomer B; 0.249g; retention time 63min). Steps 3 and 4:



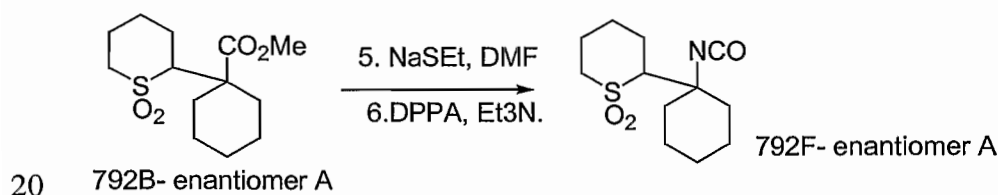
Step 3

- 5 To a solution of the carboxylic acid (792C; 0.172g) and the hydrochloride salt (792D) in dichloromethane (5ml) was added BOP reagent (0.246g) followed by triethylamine (0.232ml) and the resulting reaction mixture was stirred overnight at room temperature. The reaction mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. NaHCO₃, water, dried (MgSO₄) and the volatiles were removed under reduced pressure to yield a residue which was used in step 4 without purification.

Step 4

- 15 To the residue from step 3 was added 4M HCl in dioxane (10ml) and the solution was allowed to stand at room temperature for a period of 2h. The volatiles were removed under reduced pressure to yield the hydrochloride salt (792E), used without purification.

Steps 5 and 6



Step 5

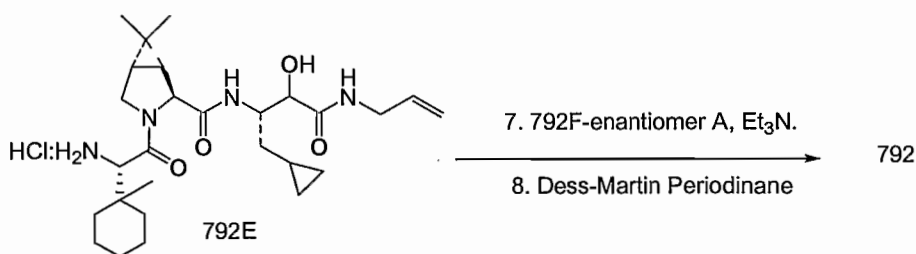
To a solution of the methyl ester (792B-enantiomer A; 0.100g) was dissolved in anhydrous DMF (1ml) and sodium ethanethiolate (0.122g) was added and the reaction mixture was allowed to stir at room temperature for approx 72h. The reaction was partitioned between EtOAc and 10% aq. HCl.

- 5 The organic phase was separated, washed with water (X4), dried (MgSO_4) and the volatiles were removed under reduced pressure.

Step 6

- 10 To the residue from step 5 was dissolved in anhydrous toluene (2ml) and DPPA (0.083ml) and Et_3N (0.054ml) were added and the reaction was heated to 120°C , under an atmosphere of nitrogen for 1h. After cooling, the reaction was partitioned between EtOAc and sat. aq. NaHCO_3 . The organic phase was separated, dried (MgSO_4) and the volatiles were removed under reduced pressure to provide the isocyanate (792F-enantiomer A), used without purification.

- 15 Steps 7 and 8



Step 7

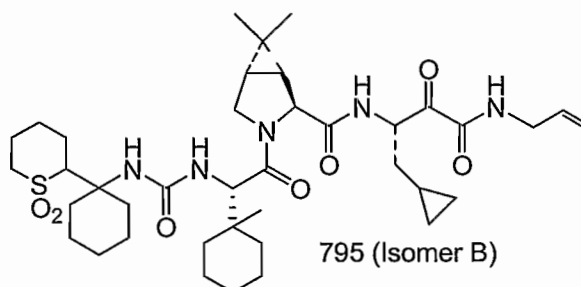
- 20 To the hydrochloride salt (792E; 0.050g) in dichloromethane (3ml) was added triethylamine (0.100ml) followed by the isocyanate (792F; approx. 0.040g) in toluene (1ml) and the reaction mixture was stirred at room temperature overnight. The reaction mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (MgSO_4). The volatiles were removed under

reduced pressure to yield a residue which was used without purification in step 8.

Step 8

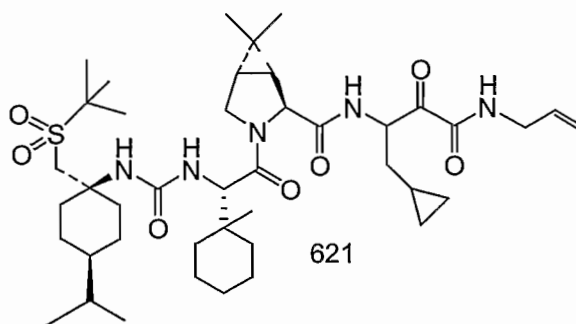
The residue from step 7 was dissolved in dichloromethane (3ml) and Dess-Martin peridinanone (0.100g) was added and the reaction was stirred at room temperature for 1h. The reaction was partitioned between EtOAc and 10% aq. sodium thiosulfate. The organic phase was separated, washed with sat. aq. sodium bicarbonate, dried (MgSO₄) and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc-hexanes (1:1) as eluent to give the keto-amide (792; 0.0436g) as a white solid.

Example 795

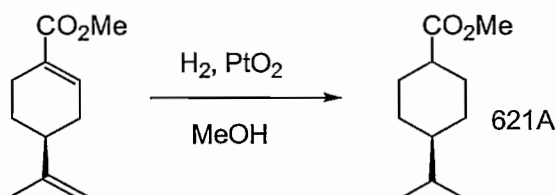


Using the procedures described for the preparation of 792, 792B-
15 enantiomer B was transformed into the corresponding isocyanate as
described in steps 5 and 6. Further by utilizing 792E and steps 7 and 8 and
the isocyanate derived from 792B-enantiomer B, 795 was produced.

Example 621:

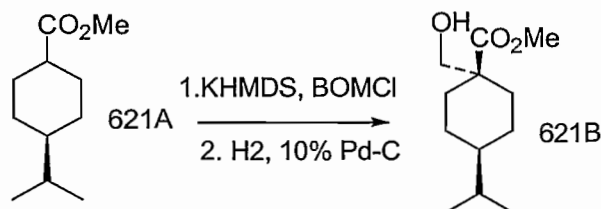


Steps 1



To Methyl Perillate (3g) in methanol (20ml) was added PtO₂ (0.3g) and the resulting suspension was placed under an atmosphere of hydrogen (balloon) overnight. The suspension was filtered through a pad of celite and the solid was washed thoroughly with methanol. The filtrate was concentrated under reduced pressure to yield the cyclohexane (621A; 2.93g), a mixture of diastereomers, as a colorless oil.

Steps 2 and 3



Step 2

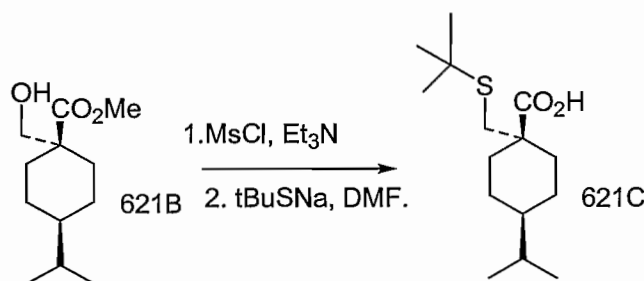
The carboxylic esters (621A; 3.75g) were dissolved in anhydrous diethyl ether (50ml) and cooled to -78°C, under an atmosphere of nitrogen. KHMDS (69ml of a 0.5M solution in toluene) was added dropwise and the resulting mixture was stirred for a further 15 min., before the addition of BOMCl (1.7eq.) and the reaction flask was removed from the cooling vessel and allowed to

warm slowly to room temperature. Water (approx. 10ml) was added and the mixture was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (MgSO_4), and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc:Hexanes (1:20) as eluent, providing the intermediate benzyl ether (3.01g), a colorless oil.

Step 3

To the benzyl ether from step 2 (2g) was added methanol (10ml) followed by 10% Pd-C (1g) and the black suspension was placed under an atmosphere of hydrogen (balloon) overnight. The reaction was filtered through a pad of celite and the solid was washed thoroughly with methanol. The filtrate was concentrated to provide the desired alcohol (621B; 1.362g) as a colorless oil.

Steps 4 and 5



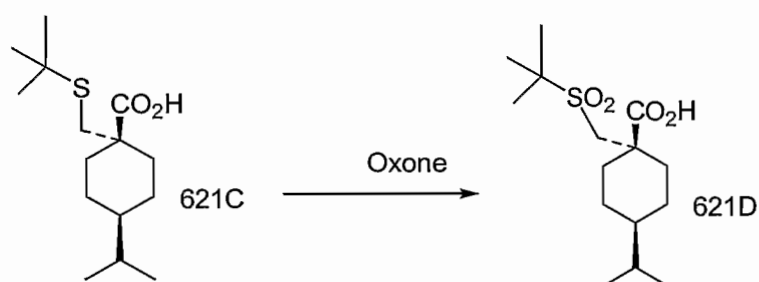
Step 4

The alcohol (621B; 0.32g) was dissolved in dichloromethane (5ml) and methane sulfonyl chloride (0.166ml) followed by triethylamine (0.37ml) were added and the resulting reaction was stirred for 0.5h before partitioning between EtOAc and 10% aq. HCl. The organic phase was separated washed with sat. aq. sodium bicarbonate, water, dried (MgSO_4) and the volatiles removed under reduced pressure to yield a residue which was used in step 5 without purification.

Step 5

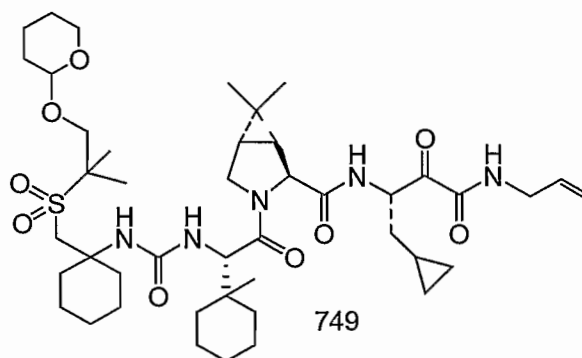
The residue from step 4 was dissolved in DMF (10ml) and sodium tert-butyl thiolate was added and the resulting reaction mixture was stirred at room temperature under an atmosphere of nitrogen overnight. The reaction mixture was partitioned between EtOAc and aq. 10% HCl. The organic phase was separated, washed with water (X4), dried (MgSO₄) and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc-Hexanes (3:7) as eluent to give the carboxylic acid (621C; 0.214g).

10 Step 6

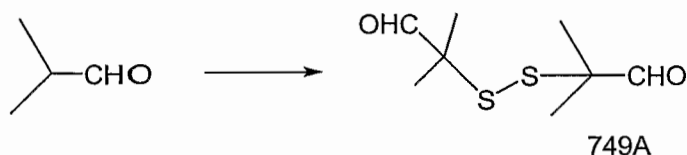


Using the sulfide (621C; 0.090g), oxone (0.61g), methanol (2ml), water (2ml) and the procedure set forth in example 792 (Step 2), the sulfone (621D; 0.091g) was obtained as a white solid.

15 As described above (Example 792; Steps 6 through 8), the sulfone-carboxylic acid was converted to compound 621.

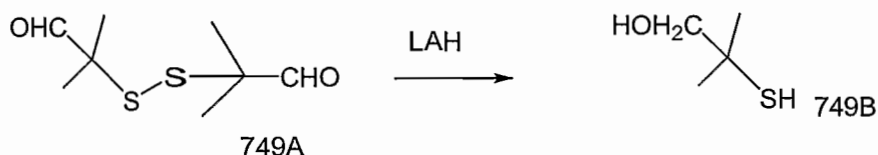
Example 749:

Step 1



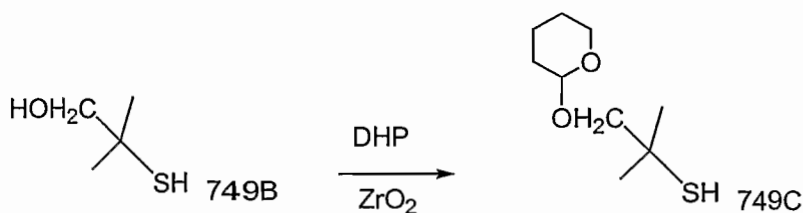
Procedure: To Isobutyraldehyde (59g, 0.69mol) in CCl₄ was added sulfur monochloride (27.6mL, 0.345mol, 0.5eq.) dropwise at 50°C. After a short lag (10min), evolution of HCl gas began. After HCl evolution ceased, the mixture was stirred at 55°C for 2.5hrs, which TLC indicated the reaction almost completed. Then cooled to room temperature. Crude was concentrated it to dryness. The oily residue, the disulfide (749A), was used without purification.

10 Step 2



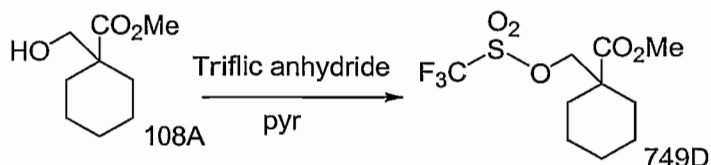
To the disulfide (749A; 7.5g, 36mmol) in THF was added LiAlH₄ (2.76g, 72.7mmol, 2eq.) at 0°C very slowly. The mixture was stirred at RT for 3hrs then Sat. Na₂SO₄ was added dropwise until white grey solid appeared. Stirred at RT for 10min. Diltued it with CH₂Cl₂. Dried over MgSO₄. Filtered and concentrated to dryness. Purified it by HPFC with 2~20% EtOAc in hexane to give the alcohol (749B; 6.81g). Yield 89%.

20 Step 3



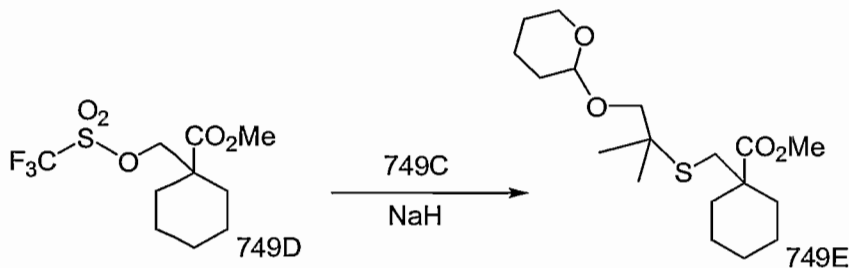
To the alcohol (749B; 10g, 94.2mmol) was added 3,4-dihydro-2H-pyran (8.8mL, 94.2mmol, 1equiv) and ZrO_2 . (2.0g, 20% w/w). The mixture was stirred at 80°C for 2hrs. reaction was diluted it with CH_2Cl_2 and filtered. The filtrate was concentrated to dryness and purified by HPFC with 2~10% EtOAc in hexane to give 14.3g of product (749C). Yield 80%.

Step 4



To the alcohol (108A; 3.0g, 17.4mmol, 1equiv) in CH_2Cl_2 was added pyridine (2.4mL, 29.6mmol, 1.7equiv) and triflic anhydride (3.8mL, 22.6mmol, 1.3equiv) at -20°C. The reaction was stirred at -20~10°C for 2hr which MS and TLC indicated the reaction completed. Diluted it with EtOAc, Washed with sat. NH_4Cl and brine. Dried over MgSO_4 . Concentrated it to dryness to give the sulfonate (749D; 5.21g). Yield 98%.

Step 5

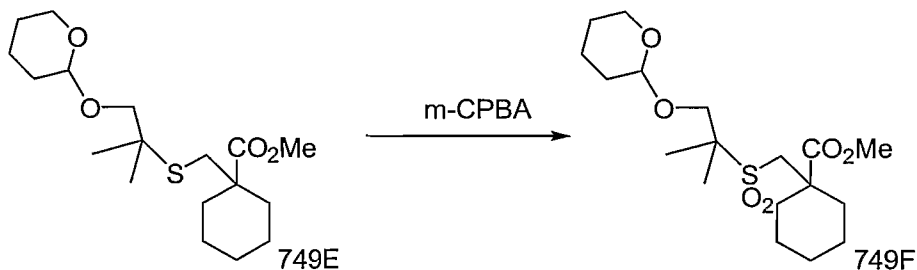


To THF at 0°C was added NaH(1.02g, 25.6mmol, 1.5eq.), then (749C; 4.88g, 25.6mmol, 1.5eq.) . The mixture was stirred at 0°C for 10min, then (749D; 5.21g, 17.1mmol) was added at 0°C. The reaction was stirred at RT for 1hr, which TLC indicated no starting materials. Diluted it with EtOAc and water. Extracted aqueous layer with EtOAc. Combined organic layer was

washed with H₂O and brine. Organic layer was dried over MgSO₄.

Concentrated it to dryness. Purified it by HPFC with 2~8% EtOAc in hexane to give (749E;5.89g) of product. Yield 100%.

Step 6



5

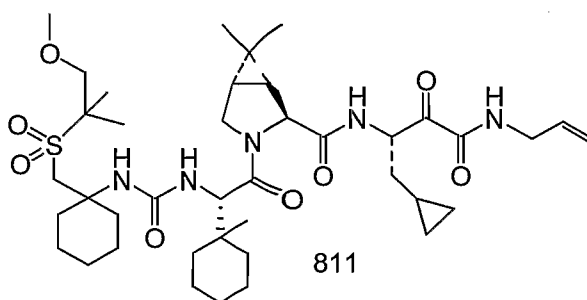
To the sulfide (749E; 0.17g, 0.49mmol) in CH₂Cl₂ was added NaHCO₃ (0.205g, 2.45mmol, 5equiv) , mCPBA(0.304g, 1.23mmol, 2.5eq.) at 0°C . The reaction was stirred at RT for 2hrs, which TLC and MS showed the reaction completed. Diluted with CH₂Cl₂. Washed with sat. NaHCO₃ and brine. Dried over MgSO₄. Purified it by HPFC with 5~20% EtOAc in hexane to give 0.14g of the sulfone (749F). Yield 76%.

10

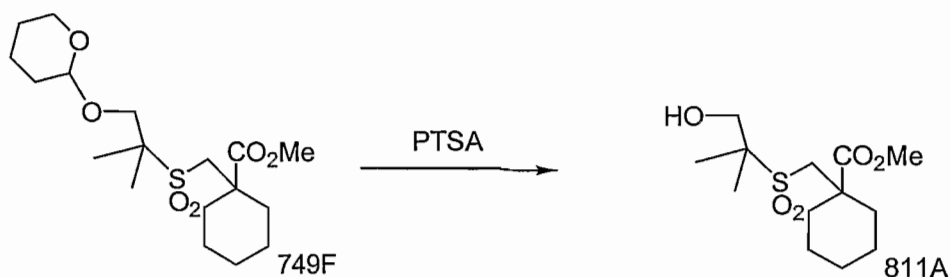
The methyl ester (749F) can be converted to the corresponding carboxylic acid and subsequently the isocyanate (Example 108; Steps 5 and 6) and converted to 749 (Example 792; Steps 7 and 8).

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Example 811:

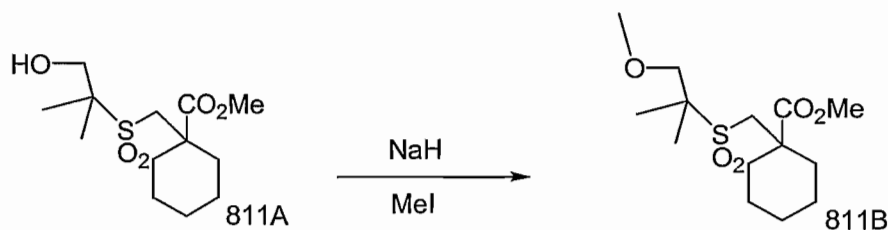


Step 1



To 749F (70mg, 0.18mmol) in MeOH was added pTsOH. The reaction was stirred at RT for overnight. MS showed the reaction almost completed.

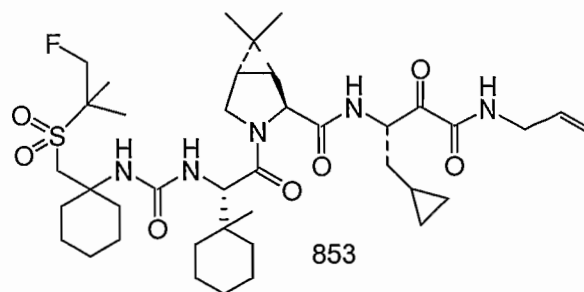
- 5 Concentrated it to dryness. Diluted with EtOAc. Washed with sat NaHCO₃, brine. Purified by HPFC with 10 ~40% EtOAc in hexane to give 52mg of the alcohol (811A) Yield 99%.



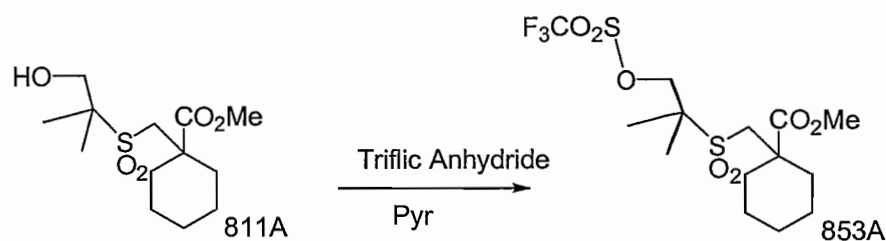
- 10 To NaH (88mg, 2.21mmol, 1.3equiv) in DMF at 0°C was added the alcohol (811A; 0.5g, 1.7mmol) and MeI (0.16mL, 2.56mmol, 1.5equiv). The reaction was stirred at RT for 2hrs which TLC indicated the reaction didn't completed. 1 equiv MeI was added again. The reaction was stirred at RT for overnight. Diluted it with EtOAc. Washed with water, brine. Dried over
- 15 MgSO₄. Purified it by HPFC with 2~10~40% EtOAc in hexane to give the ether (811B; 0.283g) Yield 54%.

The methyl ester (811B) can be converted to the corresponding carboxylic acid and subsequently the isocyanate (Example 108; Steps 5 and 6) and converted to 749 (Example 792; Steps 7 and 8).

- 20 Example 853:



Step 1



To the alcohol (811A; 56mg, 0.19mmol, 1equiv) in CH_2Cl_2 was added pyridine (0.026mL, 0.32mmol, 1.7equiv) and triflic anhydride (0.042mL, 0.25mmol, 1.3equiv) at -20°C . The reaction was stirred at $-20\sim 10^\circ\text{C}$ for 2hr which MS and TLC indicated the reaction completed. Diluted it with EtOAc, Washed with sat. NH_4Cl and brine. Dried over MgSO_4 . Concentrated it to dryness to give 75.9 mg of crude product (853A)

10

Step2

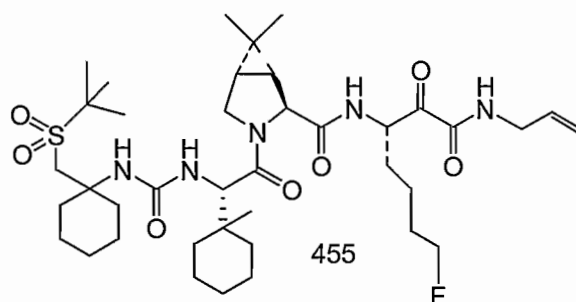


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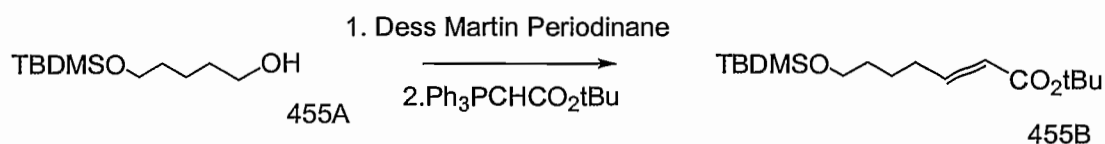
To 853A (75.9mg, 0.18mmol, 1equiv) in ether was added tetra-n-butyl ammonium fluoride (0.23mL, 0.23mmol, 1.3equiv) dropwise at -15°C. The reaction was stirred at RT for over night. Diluted it with ether, washed with sat. NH₄Cl and brine. Dried over MgSO₄. Purified it with 2~10% EtOAc in hexane to give 32mg of the fluoride (853B). Yield 60%.

The methyl ester (853B) can be converted to the corresponding carboxylic acid and subsequently the isocyanate (Example 108; Steps 5 and 6) and converted to 749 (Example 792; Steps 7 and 8).

Example 455:



Steps 1 and 2

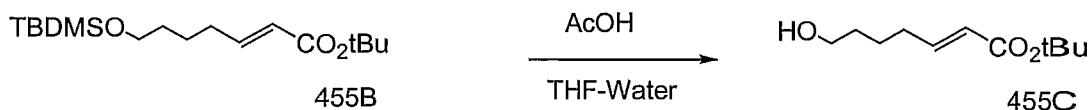


Steps 1 and 2 ('one-pot')

Dess-Martin Periodinane (21.35g) was added to a solution of the alcohol (455A; 10.00g) in dichloromethane (100ml) and stirred for 45 min., before the addition of the phosphorane (17.42g) and stirred overnight. The reaction mixture was partitioned between 5% aq. sodium thiosulfate and EtOAc and the organic phase was separated, washed with sat. aq. sodium bicarbonate,

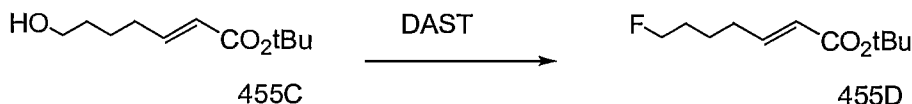
water, dried (MgSO_4) and concentrated under reduced pressure. Hexanes was added to the residue and the resulting suspension was stirred vigorously for 2h and filtered. The filtrate was concentrated under reduced pressure and purified by silica gel column chromatography using EtOAc-hexanes (1:99) as eluent to give the desired alkene (455B; 7.33g) as a yellow oil.

Step 3



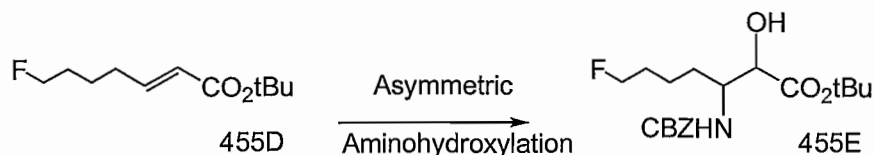
Acetic acid (26ml) was added to a solution of the silyl ether in THF (6ml) and water (14ml) and the resulting mixture was stirred at room temperature overnight. The reaction was partitioned between EtOAc and sat. aq. sodium bicarbonate. The organic phase was separated, washed with water, dried (MgSO_4) and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc-hexanes (1:5) as eluent to give the alcohol (455C; 4.46g) as a colorless oil.

Step 4



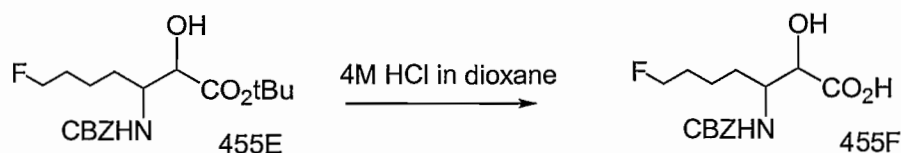
DAST (1.32ml) was added to a stirred solution of the alcohol (455C; 2.00g) in dichloromethane (50ml) at -78°C , under an atmosphere of nitrogen. When the addition was complete the cooling bath was removed and the reaction allowed to stir at room temperature for 2h., before partitioning between EtOAc and water. The organic phase was separated, dried (MgSO_4) and the volatiles removed under reduced pressure before purification by column chromatography. Gave the fluoride (455D; 0.758g).

Step 5



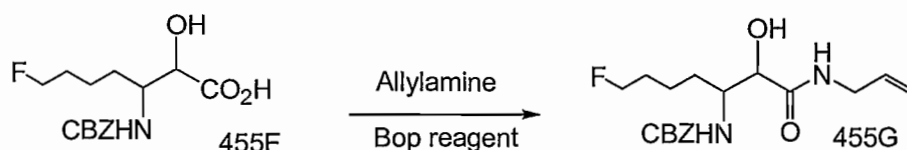
Using benzylcarbamate (2.06g) in n-PrOH (18ml), the alkene (455D; 0.881g), NaOH (0.537g), freshly prepared tBuOCl (1.54ml), (DHQ)₂PHAL (0.176g) in nPrOH (16ml), potassium osmate (0.065g) and the procedure set for in Angewandte Int. Ed. (Engl), 1996, 35, 2813 a crude product was formed which was purified by silica gel column chromatography using EtOAc-Hexanes (1:5) as eluent to give the desired hydroxyamide (455E; 0.892g).

10 Step 6



4M HCl in dioxane (25ml) (ex. Aldrich) was added to the t-Bu ester (455E; 0.69g) and the resulting solution was allowed to stand at room temperature for 2h. The volatiles were removed under reduced pressure to yield the carboxylic acid (455F; 0.613g), used in subsequent reactions without purification.

Step 7

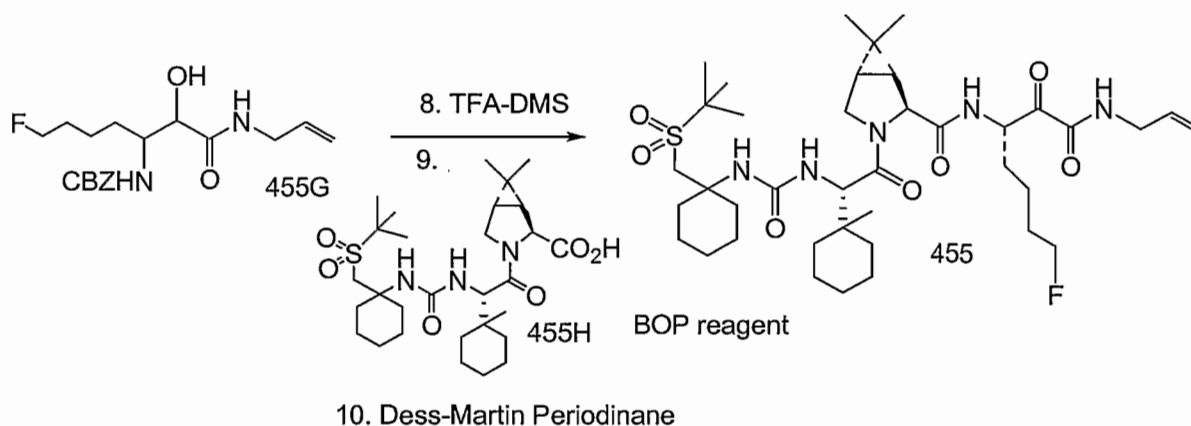


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Bop reagent (0.254g) followed by triethylamine (0.240ml) were added to a mixture of the carboxylic acid (455F; 0.15g) and allylamine (0.043ml) in

dichloromethane (5ml) and the resulting reaction mixture was stirred at room temperature overnight. The reaction was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (MgSO_4) and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography on silica gel using EtOAc:Hexanes (7:3) as eluent to give the amide (455G; 0.151g) as a white solid.

Steps 8, 9 and 10



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Step 8

To the benzylcarbamate (455G; 0.037g) was added TFA (2ml) followed by methylsulfide (0.5ml) and the resulting solution was allowed to stand at room temperature for 3h., before removal of the volatiles. The crude reaction product was used in step 9, below, without purification.

15

Step 9

To the residue from step 8 was added dichloromethane (3ml), the carboxylic acid (455H; 0.050g), Bop reagent (0.047g) and finally triethylamine (0.044ml) and the resulting mixture was stirred at room temperature overnight. The reaction was partitioned between EtOAc and 10% aq. HCl. The organic phase was separated, washed with sat. aq. sodium bicarbonate, dried

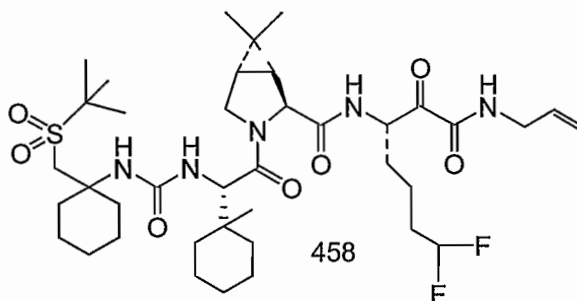
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(MgSO₄) and the volatiles removed under reduced pressure to yield a residue which was used, in step 10, below, without purification.

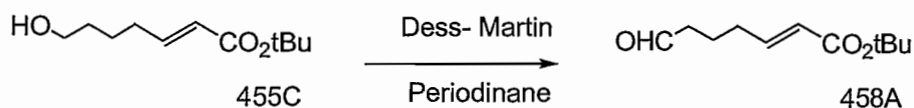
Step 10

To the residue from step 9, was added dichloromethane (3ml) followed by
5 Dess-Martin periodinane (0.075g) and the suspension was stirred at room
temperature for 2h., before partitioning between EtOAc and 5% aq. sodium
thiosulfate. The organic phase was separated, washed with sat. aq. sodium
bicarbonate, water, dried (MgSO_4) and the volatiles removed under reduced
pressure. The crude reaction product was purified by silica gel column
10 chromatography to give the desired keto-amide (455; 0.0467g) as a white
solid.

Example 458:



Step 1



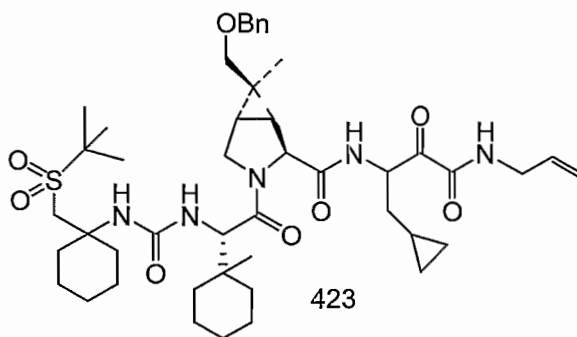
To a solution of the alcohol (455C; 1.66g) in dichloromethane (20ml) was added Dess-Martin periodinane (4.22g) and the resulting mixture stirred at room temperature for a period of 1h., before partitioning between EtOAc and 5% aq. sodium thiosulfate. The organic phase was separated, washed with sat. aq. sodium bicarbonate, water, dried (MgSO_4) and the volatiles removed under reduced to yield the aldehyde (458A; 0.775g) used with purification.

Step 2

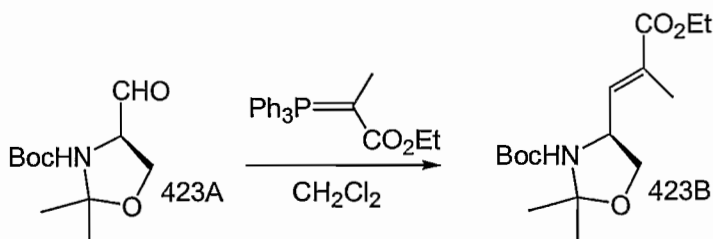


DAST (1.11ml) was added dropwise to a stirred solution of the aldehyde (458A; 0.755g) in dichloromethane (50 ml) while cooled in an ice bath, under an atmosphere of nitrogen. After completion of the addition the resulting mixture was stirred at room temperature for a period of 2h., before partitioning between EtOAc and water. The organic phase was separated, dried (MgSO_4) and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography to give the desired difluoride (458B; 0.758g).

Using 458B and the procedures outlined in example 455 (Steps 5 through 10) target 458 was produced.

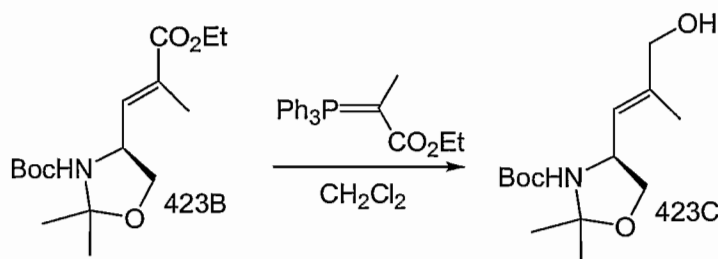
Example 423:

Step 1



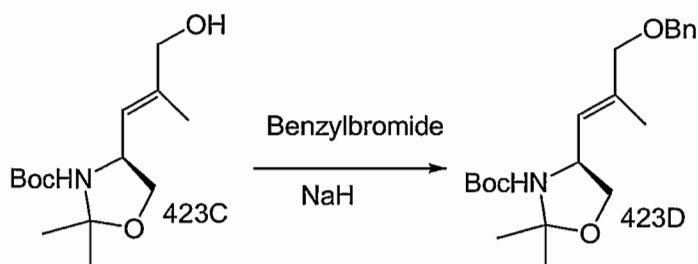
To a solution of Garner aldehyde (423A; 10.7g) in dichloromethane (110ml) was added (carbethoxyethylidene)triphenylphosphorane (28.75g) the resulting solution was stirred at room temperature overnight. The volatiles were removed under reduced pressure and the residue purified by silica gel column chromatography using 4-10% EtOAc in hexanes to give the desired alkene (423B; 12.7g), as a colorless oil.

Step 2



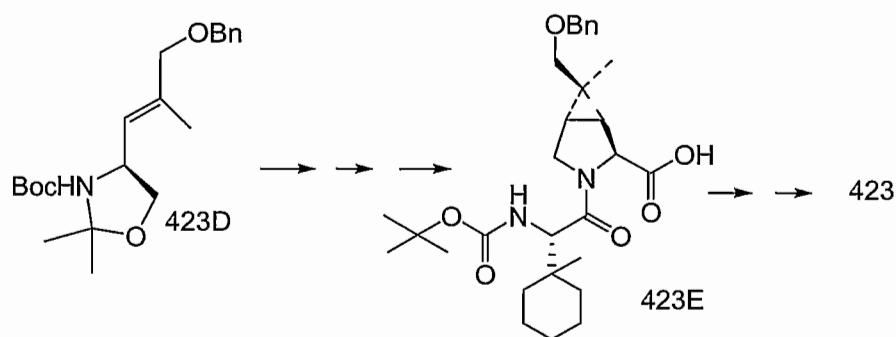
To a solution of the ethyl ester (423B; 12.72g) in dichloromethane (20ml) was added DIBAL-H (90ml of a 1M solution in dichloromethane) at -78°C , under an atmosphere of nitrogen. When the addition was complete the reaction was maintained at this temperature for a further 30 min then at room temperature for 1h., before the addition of MeOH (3ml) and sat aq. potassium sodium tartrate (3ml) and EtOAc. The organic phase was separated, washed with 1M aq HCl, brine, dried (MgSO_4). The volatiles were removed under reduced pressure and the residue purified by silica gel column chromatography using 6-35% EtOAc in hexanes to give the alcohol (9.06g), as a colorless oil.

Step 3

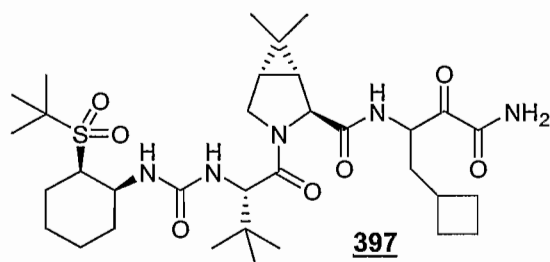


To a solution of the alcohol (423C; 8.66g) in anhydrous DMF (30ml), while cooled in an ice bath, was added NaH (1.38g) and the resulting mixture was maintained at that temperature for 45 min., before the addition of benzyl bromide (5ml). The reaction was allowed to warm to room temperature overnight before the addition of ether followed by 10% aq. HCl. The organic phase was separated, washed with sat aq. sodium bicarbonate, brine, dried (Na_2SO_4). The volatiles were removed under reduced pressure to yield a residue which was purified by silica gel column chromatography using 8% EtOAc in hexanes to yield the benzyl ether (8.10g) as a yellow oil.

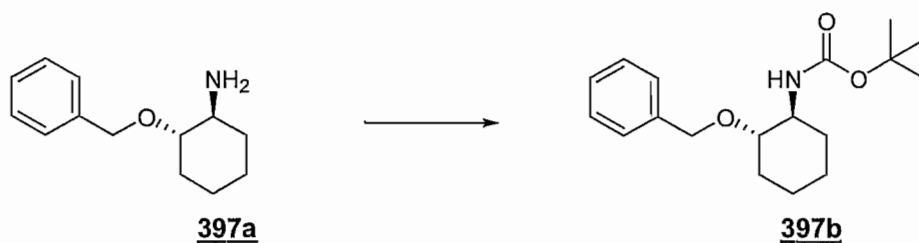
Using analogous procedures described above for the conversion of 22.03 to 22.01, 423D was transformed into 423E



15 Example 397:

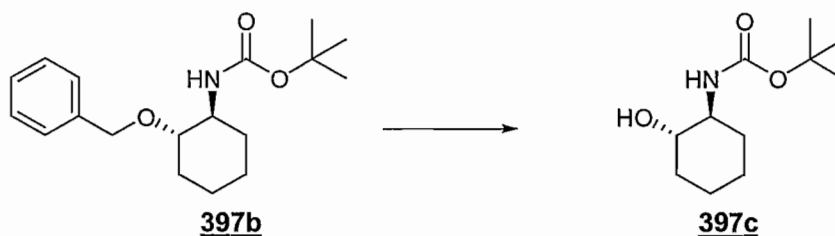


Step A



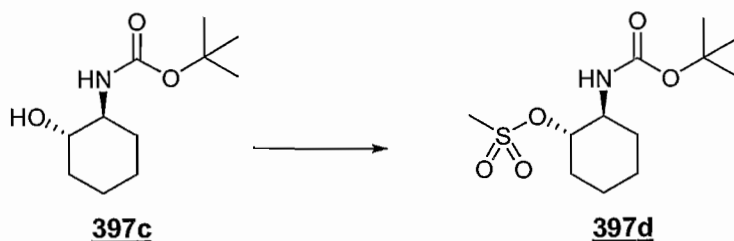
A solution of benzyloxycyclohexyl amine **397a** (10.6 g, Lancaster) and N-methylmorpholine (8.5 mL, d 0.920) in 200 mL of dry dichloromethane was cooled to -78 °C. Boc-anhydride in 100 mL of dry dichloromethane was added over 15 min using an addition funnel. After addition was completed, the cooling bath was removed and the mixture was stirred of further 30 min. The reaction mixture was partitioned between 300 mL of ether and 100 mL of aqueous 1N HCl. The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford the product **397b** (15.7 g; 99 %) as a white solid which was used without further purification.

Step B



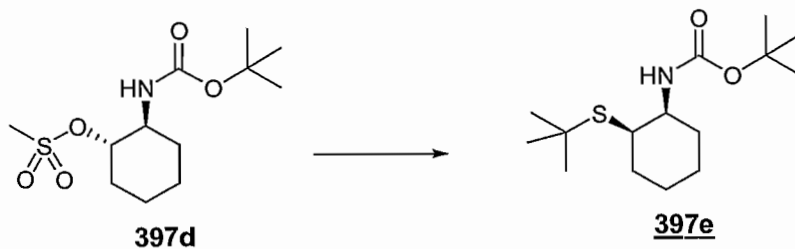
20% palladium dihydroxide on carbon (30 mol%; 10.8 g) was added to a solution of benzyl ether **397b** (15.7 g) in 300 mL of methanol. The heterogeneous mixture was subjected to hydrogenation at 40 psi until no more starting material was detected by TLC (ethyl acetate/hexanes; 2:8). The mixture was filtered thru celite and the filtrate was concentrated under reduced pressure. No further purification was carried out for the product **397c** (11.1 g; 99%).

Step C



Pyridine (25.0 mL) was added to a solution of cyclohexanol **397c** in 300 mL of dry dichloromethane at 0 °C. Methanesulfonyl chloride (8.0 mL) in 100 mL of dry dichloromethane was added over 15 min. The reaction mixture turned to a homogeneous yellow solution. The reaction mixture was stirred at 0 °C for 15 min and then the cooling bath was removed. Reaction was stirred at room temp for about 3 h. The mixture was partitioned between ether (500 mL) and aqueous 1N HCl (100 mL). The organic layer was washed with aqueous saturated sodium bicarbonate (100 mL), brine (100 mL), dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: ethyl acetate/(hexanes-dichloromethane, 1:1); 0:10 to 2:8) to afford the product **397d** (9.7 g; 64 %) as a white solid.

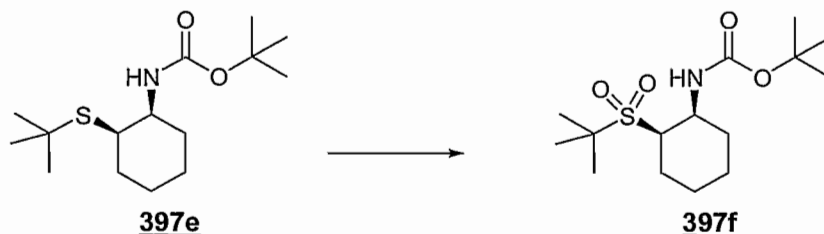
Step D



A 250 mL-flask was charged with mesylate **397d** (3.0 g) and t-butylthiol sodium salt (3.44 g). The flask was flushed with nitrogen and 100 mL of dry DMF were added. The resulting solution was degassed (vacuum/nitrogen-flush) and heated to 70 °C. The flow of the reaction was monitored by TLC (ethyl acetate/hexanes; 2:8). All the starting material was consumed in about

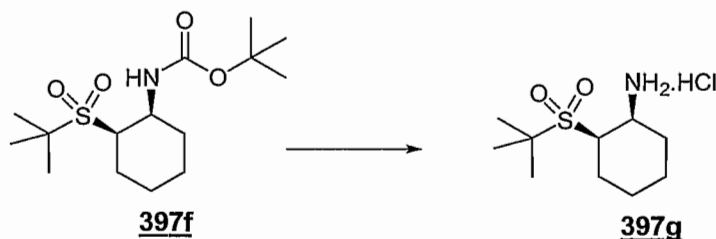
3 h. The reaction mixture was dissolved in 300 mL of ethyl acetate and washed with water (3 x 50 mL) and brine (1 x 50 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated. No further purification was done for the product **397e** (2.78 g; 95 %).

5 Step E



A solution of sulfide **397e** (10.22 mmol) in dry dichloromethane (60 mL) was treated with m-CPBA (5.28 g; 60%). The homogeneous mixture was heated at 45 °C for about 3 h. TLC analysis (ethyl acetate/hexanes; 1:9) showed that all the starting material had been consumed. The mixture was concentrated under reduced pressure and the residue was dissolved in 20 mL of ether and treated with aqueous sodium thiosulfate solution at 0 °C. The mixture was diluted with ether (350 mL) and washed with aqueous saturated sodium bicarbonate (5 x 30 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexane; 3:97 to 2:8) to afford the product **397f** (2.45 g; 75 %) as a white solid.

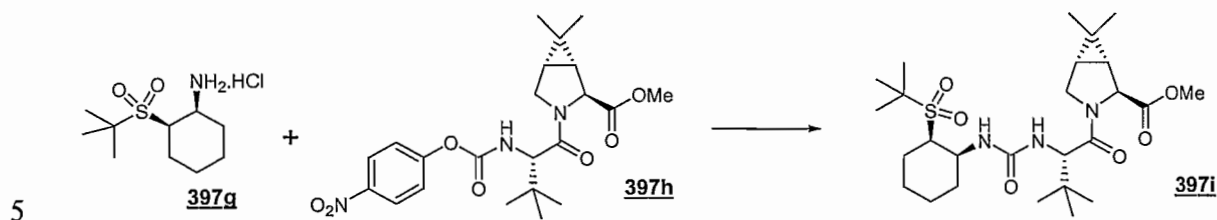
Step F



20 The N-Boc protected amine **397f** (2.43 g) was dissolved in 20 mL of 4M HCl in dioxanes. The mixture was stirred at room temperature until all the starting

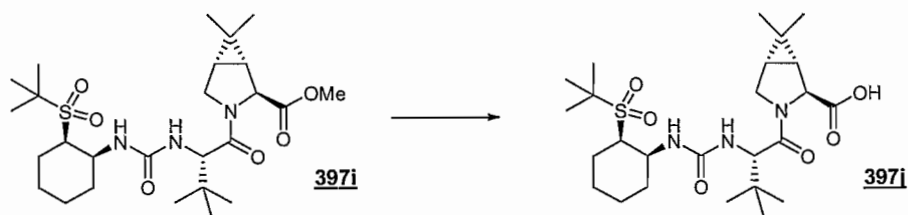
material had been consumed as determined by TLC analysis (ethyl acetate/hexanes; 2:8). After 3 h, all the volatiles were removed under reduced pressure to afford the product **397g** (1.90 g; 98 %) as a white solid.

Step G



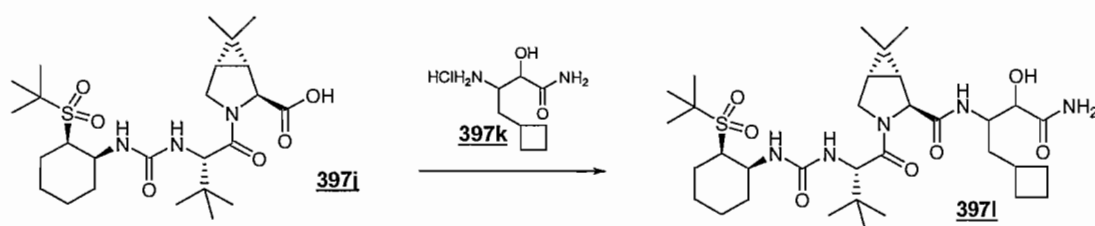
A solution of the p-nitrophenylcarbamate **397h** (640 mg) in 10 mL of acetonitrile was treated with amine hydrochloride **397g** (350 mg). N-methylmorpholine (0.37 mL, d 0.920) was added to the heterogeneous mixture and the reaction mixture was stirred at room temperature. The reaction was completed after 7 h as determined by TLC analysis (acetone/hexanes; 2:8). The reaction mixture was concentrated under reduced pressure. The residue was dissolved in 150 mL of dichloromethane and washed with aqueous 1N HCl (1 x 30 mL), and aqueous saturated sodium bicarbonate (2 x 30 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The product was purified on silica gel (gradient: acetone/hexanes; 1:9 to 4:6) to afford the product **397i** (625 mg; 87 %) as a white solid.

Step H



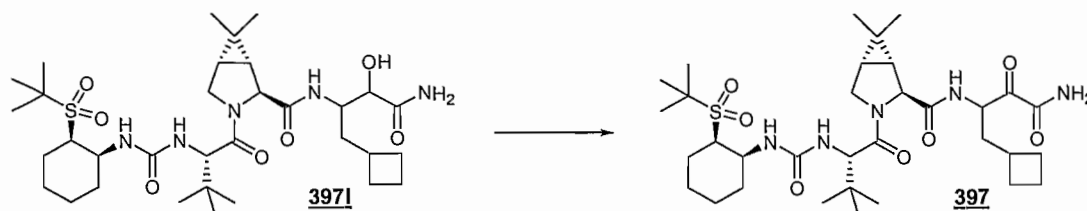
A solution of methyl ester **397i** (610 mg) in 15 mL of a mixture of THF/MeOH/water (1:1:1) was treated with lithium hydroxide monohydrate (121 mg). Reaction was stirred at room temperature and monitored by TLC (acetone/hexanes; 3:7). After 3 h, all the volatiles were removed under reduced pressure. The residue was partitioned between 30 mL of aqueous 1N HCl and 100 mL of dichloromethane. The aqueous layer was back extracted with dichloromethane (2 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford the product **397j** (570 mg; 96 %) as a white solid.

Step I



A solution of acid **397j** (120 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (124 mg). The amine hydrochloride **397k** (63 mg) was added followed by addition of N-methylmorpholine (0.10 mL, d 0.920). The reaction mixture was gradually warmed to room temperature and stirred overnight. All the volatiles were removed under vacuum and the residue was taken into 100 mL of ethyl acetate. The organic layer was washed with aqueous 1N HCl (15 mL), aqueous saturated sodium bicarbonate (15 mL), and brine (15 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford the desired product **397l** (150 mg; 96 %) which was used without further purification.

Step J

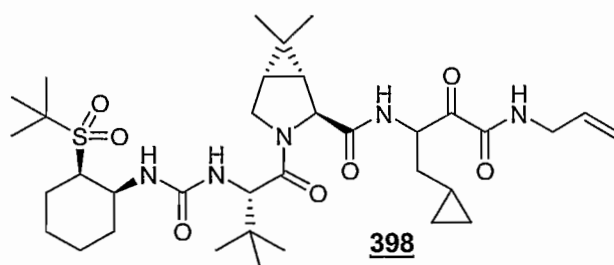


A solution of **397I** (150 mg) in 6 mL of a 1:1 mixture of toluene/DMSO was treated with EDCI (430 mg) and dichloroacetic acid (0.09 mL, d 1.563).

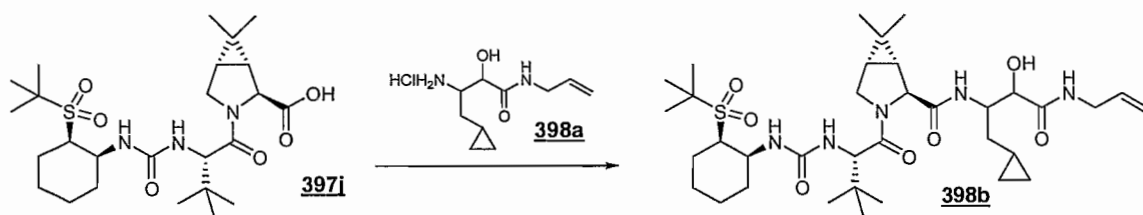
Reaction mixture was stirred at room temperature for about 2 h. The reaction

- 5 mixture was diluted with dichloromethane (100 mL) and washed with aqueous saturated sodium bicarbonate (15 mL), aqueous 1N HCl (15 mL), and brine (15 mL). The organic layer was dried over magnesium sulfate, filtrated, and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 2:8 to 5:5) to afford the product **397** (94
- 10 mg; 64 %) as a white solid. HRMS calcd for $C_{33}H_{56}N_5O_7S$ $[M+H]^+$: 666.3900, found 666.3883.

Example 398:

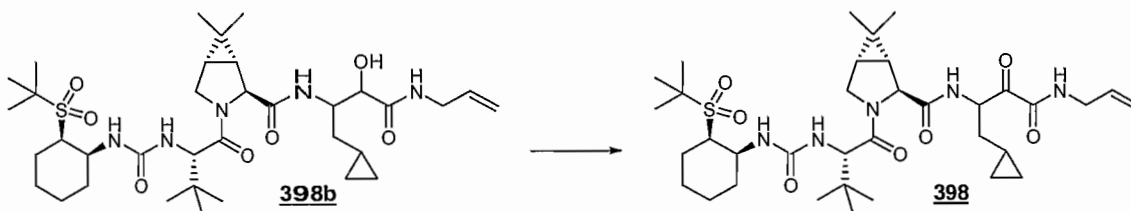


15 **Step A**



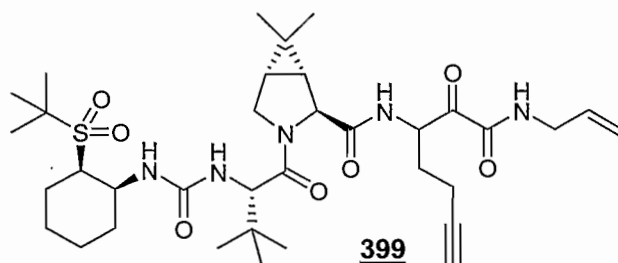
A solution of acid **397j** (100 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (103 mg). The amine hydrochloride **398a** (60 mg) was added followed by addition of N-methylmorpholine (0.09 mL, d 0.920). The reaction mixture was gradually warmed to room temperature and stirred overnight. All the volatiles were removed under vacuum and the residue was taken into 100 mL of ethyl acetate. The organic layer was washed with aqueous 1N HCl (15 mL), aqueous saturated sodium bicarbonate (15 mL), and brine (15 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford the desired product **398b** (115 mg; 86 %).

Step B

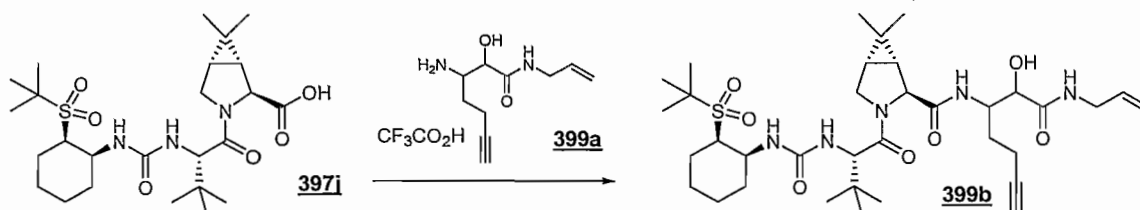


A solution of hydroxyamide **398b** (115 mg) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (210 mg). Reaction mixture was stirred at room temperature for 1 h. The mixture was treated with aqueous 1M sodium sulfite solution (10 mL) and aqueous saturated sodium bicarbonate (10 mL) and stirred for 15 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 2:8 to 5:5) to afford the product **398** (60 mg; 53 %) as a white solid. HRMS calcd for $C_{35}H_{58}N_5O_7S$ $[M+H]^+$: 692.4057, found 692.4081.

Example 399:

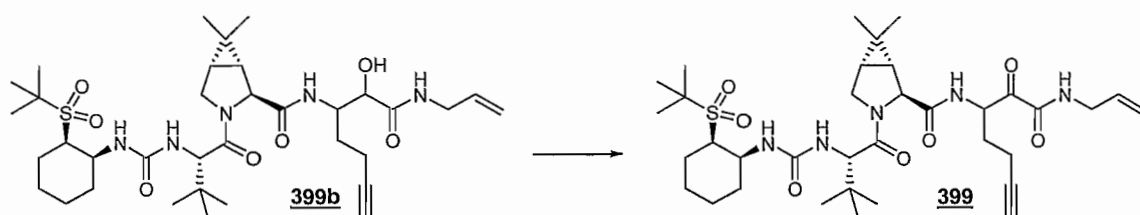


Step A



- 5 A solution of acid **397j** (100 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (106 mg). A solution of the amine salt **399a** (0.252 mmol) and N-methyl morpholine (0.09 mL, d 0.920) in 1 mL of dichloromethane was added dropwise. The reaction mixture was gradually warmed to room temperature and stirred overnight. All the
- 10 volatiles were removed under vacuum and the residue was taken into 100 mL of ethyl acetate. The organic layer was washed with aqueous 1N HCl (15 mL), aqueous saturated sodium bicarbonate (15 mL), and brine (15 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford the desired product **399b** (85 mg; 63 %).

15 Step B



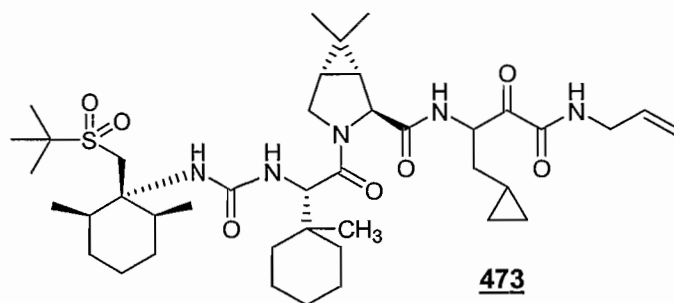
A solution of hydroxyamide **399b** (85 mg) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (157 mg). Reaction mixture was stirred at room temperature for 1 h. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and aqueous saturated sodium

bicarbonate (10 mL) and stirred for 15 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was

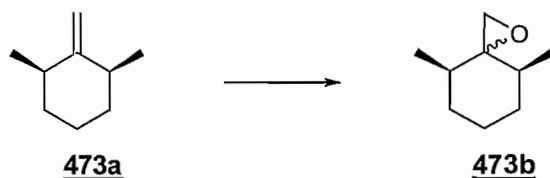
chromatographed on silica gel (gradient: acetone/hexanes; 2:8 to 4:6) to afford the product **399** (50 mg; 60 %) as a white solid. HRMS calcd for

$C_{33}H_{55}N_6O_7S$ $[M+H]^+$: 679.3853, found 679.3834.

Example 473:



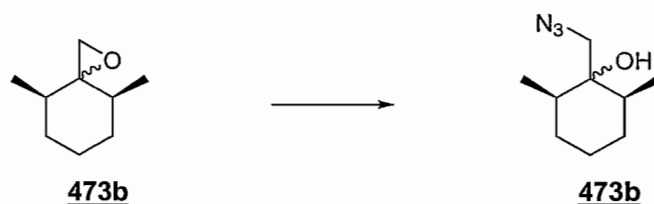
Step A



Cis-2,6-dimethyl-1-methylene cyclohexane (3.0 g, ChemSamp Co.) was added to a stirred suspension of solid sodium bicarbonate (6 eq, 12.19 g) in 150 mL of dichloromethane. The mixture was cooled to 0 °C and a slurry of 70% m-CPBA (3 eq, 17.4 g) in 150 mL of dichloromethane was added in small portions. After addition was completed, the cooling bath was removed and the mixture was stirred for about 2h. The excess m-CPBA was quenched at 0 °C by careful addition of aqueous saturated sodium thiosulfate solution.

The mixture was washed with aqueous saturated sodium bicarbonate solution (100 mL). The organic layer was concentrated in the rotavap (ice-water bath was used). The residue was dissolved in ether (80 mL) and hexanes (120 mL) and washed several times with aqueous saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure (ice-water bath). The residue was chromatographed on silica gel (gradient: ether/hexanes; 0:10 to 8:92) to afford the product **473b** (3.0 g; 90 %) as a colorless oil.

Step B



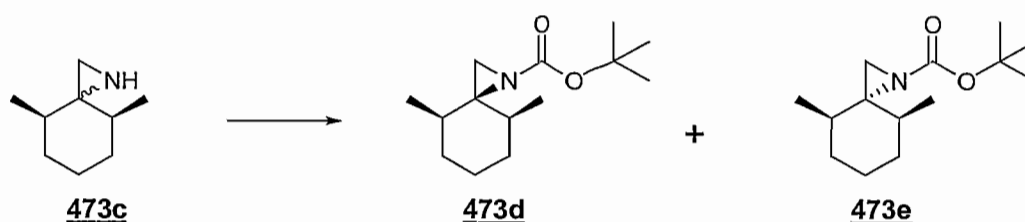
A heterogeneous mixture of epoxide **473b** (3 g) and ammonium chloride (5 eq, 5.72 g) in 80 mL of methanol was treated with sodium azide (5 eq, 7.17 g) and heated at 65 °C for 3 h. TLC analysis showed some starting material left and more ammonium chloride (1.5 eq, 1.71 g) and sodium azide (1.5 eq, 2.15 g) were added. The mixture was heated (65 °C) overnight. The reaction mixture was diluted with 30 mL of water and extracted with ether (3 x 100 mL). The combined organic extracts were dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: ether/hexanes; 0:10 to 2:8) to afford the corresponding diastereomeric product **473b** (2.73 g; 71 %) as a colorless oil.

Step C



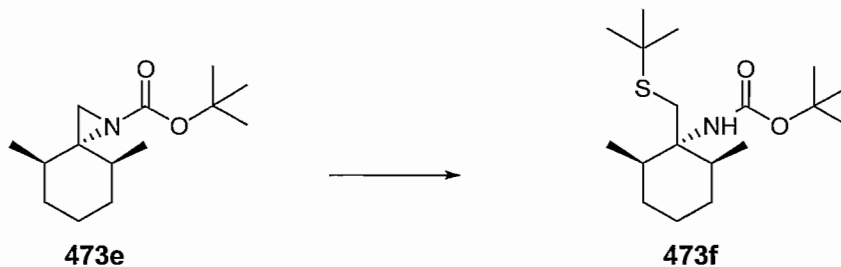
A solution of azidoalcohol **473b** (1.73 g) in 50 mL of acetonitrile was treated with triphenylphosphine (1.1 eq, 2.69 g) and refluxed for 1 h. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel (gradient: ether/hexanes; 5:5 to 9:1) to afford the desired aziridine product **473c** (2.0 g; 98 %).

Step D



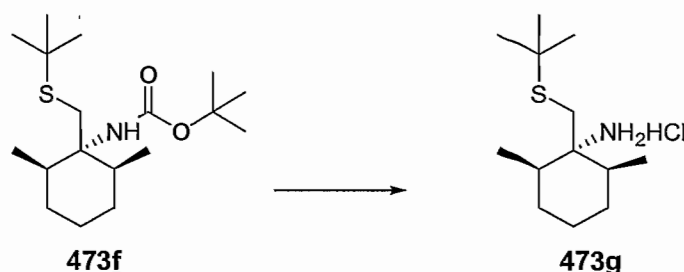
A solution of aziridine **473c** (aprox 1.5 g) in dry dichloromethane (50 mL) was cooled to 0 °C and treated with di-tert-butylidene carbonate (1.3 eq, 3.0 g) in 50 mL of dry dichloromethane. N-methylmorpholine (2.5 eq, 2.9 mL, d 0.920) was added dropwise and the mixture was stirred overnight (temp: 0 to 25 °C). The mixture was diluted with ether (300 mL) and washed with aqueous 1M HCl (100 mL), aqueous saturated sodium bicarbonate (80 mL) and brine (80 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: ether/hexanes; 0:10 to 1:9) to afford the products **473d** and **473e** as clear oils (970 mg).

Step E



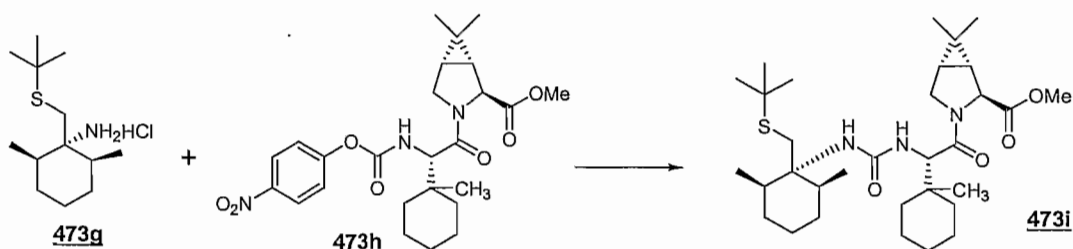
A 20 mL vial was charged with a solution of N-Boc-aziridine **473e** (469 mg) in 20 mL of dry DMF and sodium tert-butylthiolate (2 eq, 438 mg). The reaction was carried out in a microwave oven at 130 °C for 30 min. The reaction mixture was diluted with 100 mL of ether and washed with water (3 x 30 mL) and brine (20 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: hexanes to ether/hexanes, 4:96) to afford the product **473e** (140 mg) as a white solid and unreacted starting material (120 mg).

Step F



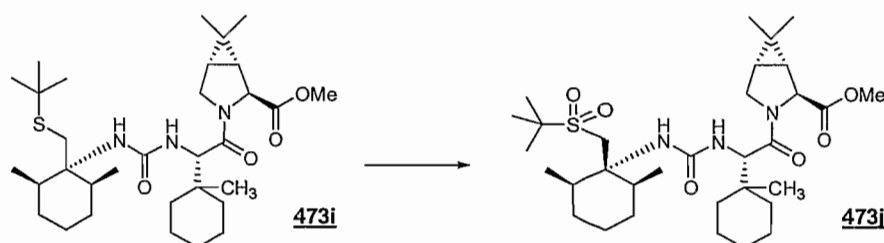
The N-Boc protected amine **473f** (140 mg) was dissolved in 10 mL of 4M HCl solution in dioxanes. The resulting solution was stirred at room temperature for 30 min until all the starting material had been consumed as determined by TLC analysis (ether/hexanes; 5:95). All the volatiles were removed under reduced pressure and the residue was placed under high vacuum for 3 h to afford the product **473g** (112 mg; 98 %) as a white solid.

Step G



A solution of the p-nitrophenylcarbamate **473h** (1.05 eq, 212 mg) in 3 mL of acetonitrile was treated with amine hydrochloride **473g** (110 mg) in 2 mL of acetonitrile. N-methylmorpholine (2.5 eq, 0.11 mL, d 0.920) was added and the resulting yellow solution was stirred at room temperature for 8 h. The reaction mixture was concentrated under reduced pressure and the residue was dissolved in 100 mL of dichloromethane and washed with aqueous 1N HCl (1 x 20 mL), and aqueous saturated sodium bicarbonate solution (2 x 20 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The product was purified on silica gel (gradient: hexanes to acetone/hexanes, 2:8) to afford the product **473i** (150 mg; 63 %).

Step H

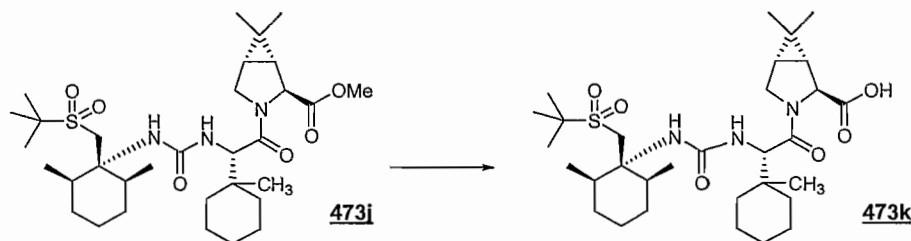


A solution of sulfide **473i** (150 mg) in dry dichloromethane (15 mL) was treated with 60% m-CPBA (3 eq, 134 mg). The homogeneous mixture was heated at 45 °C for about 1.5 h. Excess m-CPBA was quenched by addition of aqueous sodium thiosulfate solution (20 mL) and stirring was continued for 10 min. Aqueous saturated sodium bicarbonate solution (20 mL) was added and the product was taken into ethyl acetate (100 mL). The organic layer was

concentrated and the residue was dissolved in ethyl acetate (80 mL). The organic layer was washed with aqueous saturated sodium bicarbonate solution (3 x 10 mL) and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated. The residue was

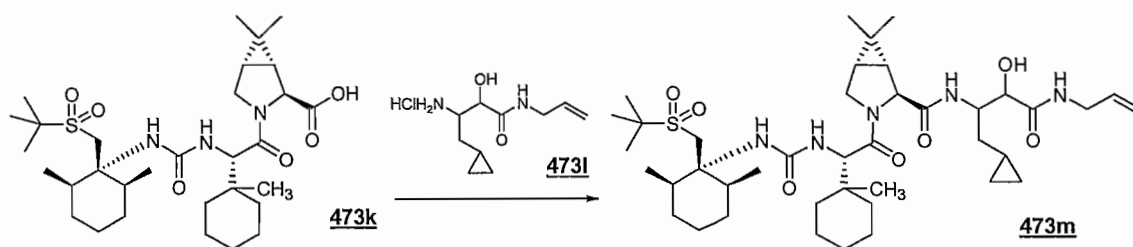
- 5 chromatographed on silica gel (gradient: ethyl acetate/hexanes; 1:3 to 5:5) to afford the product **473j** (120 mg; 76%) as a colorless oil.

Step I



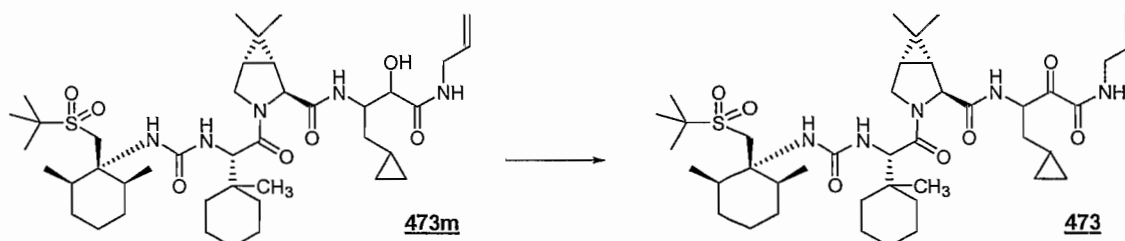
- A solution of methyl ester **473j** (110 mg) in 10 mL of a 1:1:1 mixture of THF/water/MeOH was cooled to 0 °C and treated with lithium hydroxide monohydrate (2.5 eq, 19 mg). The cooling bath was removed after 30 min and the mixture was stirred at room temp for further 2 h until all the starting material had been consumed as determined by TLC analysis (ethyl acetate/hexanes; 3:7). The reaction mixture was treated with 20 mL of aqueous 1M HCl (pH of mixture = 1) and the organic solvents were removed under reduced pressure. The aqueous residue was extracted with dichloromethane (3 x 50 mL). The combined organic extracts were dried over magnesium sulfate, filtered and concentrated under reduced pressure to afford the product **473k** (105 mg; 98 %) as a clear oil.

- 20 Step J



A solution of acid **473k** (50 mg) in 2 mL of dry dichloromethane and 1 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 44 mg). The amine salt (1.3 eq, 25 mg) was added followed by N-methylmorpholine (4 eq, 0.036 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (20 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **473m** (64 mg) was used without further purification.

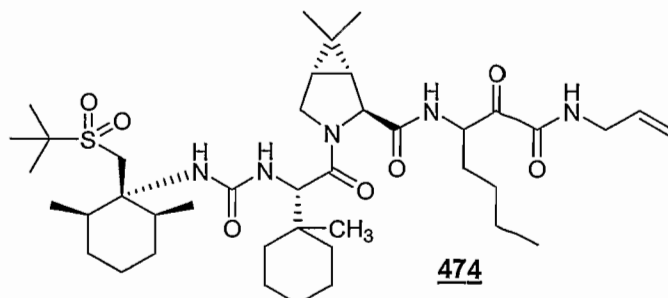
Step K



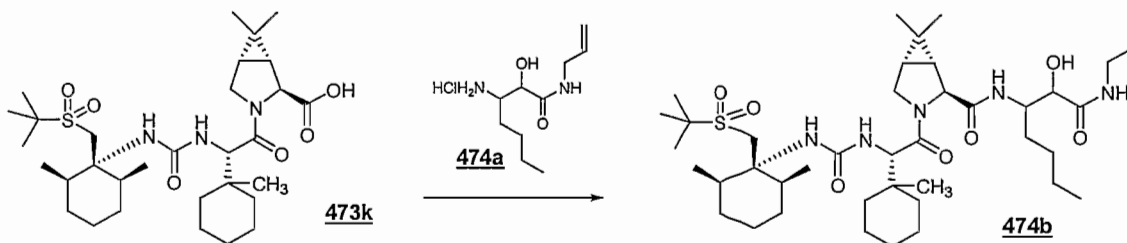
A solution of hydroxyamide **473m** (0.083 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 70 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (20 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers

were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 1:9 to 4:6) to afford the product **473** (40 mg; 62% for two steps) as white solid. HRMS calcd for $C_{41}H_{68}N_5O_7S$ $[M+H]^+$: 774.4839, found 774.4834.

5 Example 474:

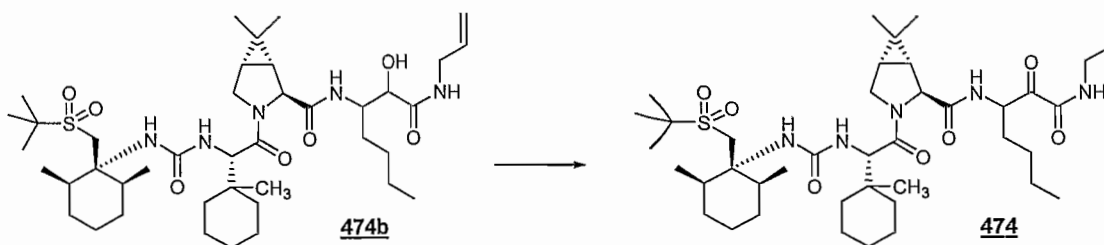


Step A



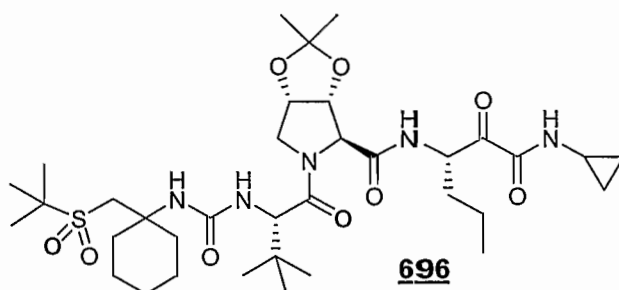
- 10 A solution of acid **473k** (50 mg) in 2 mL of dry dichloromethane and 1 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 44 mg). The amine salt **474a** (1.3 eq, 25 mg) was added followed by N-methylmorpholine (4 eq, 0.036 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was
- 15 dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (20 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **474b** (65 mg) was used without further purification.

20 Step B

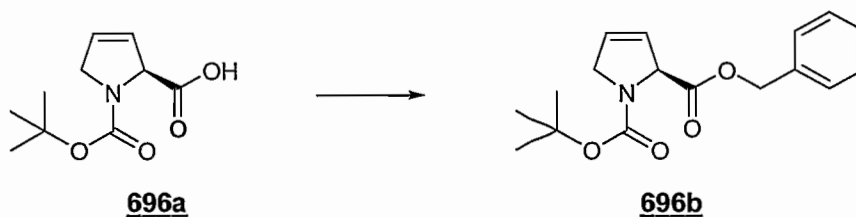


A solution of hydroxyamide **474b** (0.083 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 70 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (20 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 1:9 to 4:6) to afford the product **474** (40 mg; 62% for two steps) as white solid. HRMS calcd for $C_{41}H_{70}N_5O_7S$ $[M+H]^+$: 776.4995, found 776.5005.

Example 696:

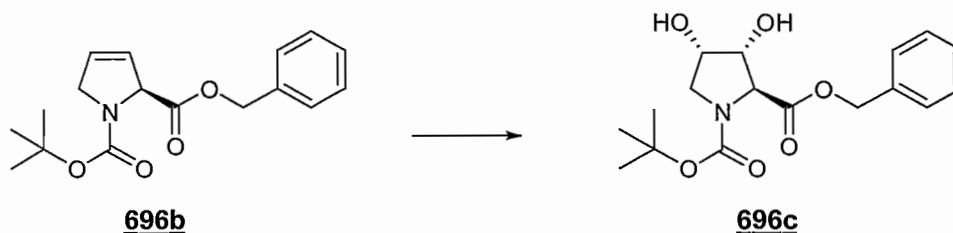


15 **Step A**



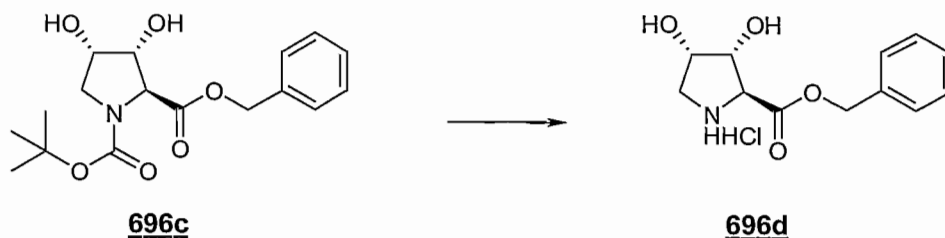
A solution of acid **696a** (3.0 g) in 140 mL of dry DMF was cooled to 0 °C and treated with cesium carbonate (1.1 eq, 5.04 g) followed by addition of benzyl bromide (1.2 eq, 2.00 mL, d 1.438). The reaction mixture was stirred for 24 h (temp: 0 to 25 °C). The mixture was diluted with ethyl acetate (350 mL) and washed with water (3 x 50 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: hexanes to ethyl acetate/hexanes 25:75) to afford the product **696b** (3.82 g; 90 %) as a clear oil.

Step B



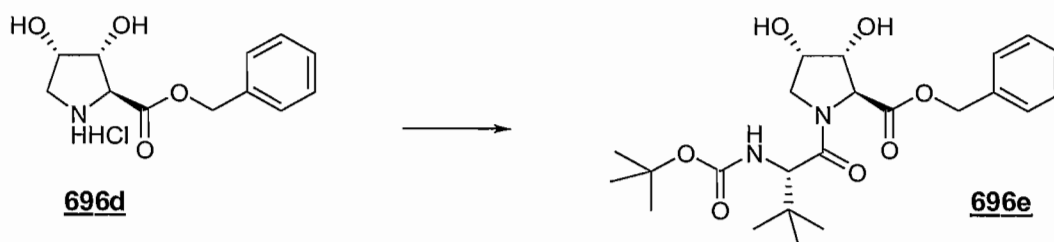
A solution of N-methylmorpholine-N-oxide (1.3 eq, 1.9 g) in tert-butanol (20 mL), THF (7 mL) and water (3.5 mL) under argon atmosphere was treated with osmium tetroxide (0.1 eq, 318 mg). The resulting pale yellow solution was stirred for 5 min followed by dropwise addition of benzylester **696b** (3.8 g) in 30 mL of THF. The reaction mixture was stirred at room temperature for 20 h. The mixture was filtered thru a short path of silica gel and the solids were washed with ethyl acetate (500 mL). The organic layer was washed with brine (80 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 2:8 to 55:45) to afford the product **696c** (3.5 g; 83 %) as a paste.

Step C



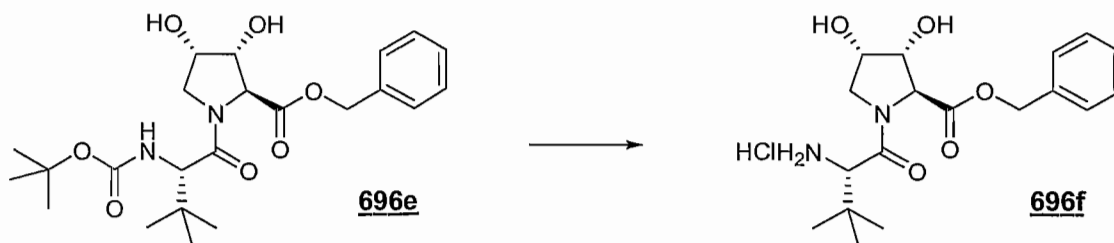
The N-Boc amine **696c** (3.5 g) was dissolved in 60 mL of 4M HCl in dioxane. The resulting solution was stirred at room temperature for about 2 h. All the volatiles were removed under reduced pressure to afford the product **696d** (2.8 g; 98 %) which was used without further purification.

Step D



A solution of N-Boc-tert-butyl glycine (2.15 g) in 100 mL of dry dichloromethane and 20 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 4.96 g). The amine salt **696d** (1.1 eq, 2.8 g) was added in 30 mL of DMF followed by addition of N-methylmorpholine (4 eq, 4.08 mL, d 0.920). The reaction mixture was stirred at 0 °C overnight. All the volatiles were removed under vacuum and the residue was dissolved in 300 mL of ethyl acetate. The organic layer was washed with water (1 x 100 mL), aqueous 1M HCl (100 mL), aqueous saturated sodium bicarbonate solution (100 mL), and brine (100 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (ethyl acetate/hexanes; 6:4) to afford the product **696e** (3.29 g; 79 %) as a colorless oil.

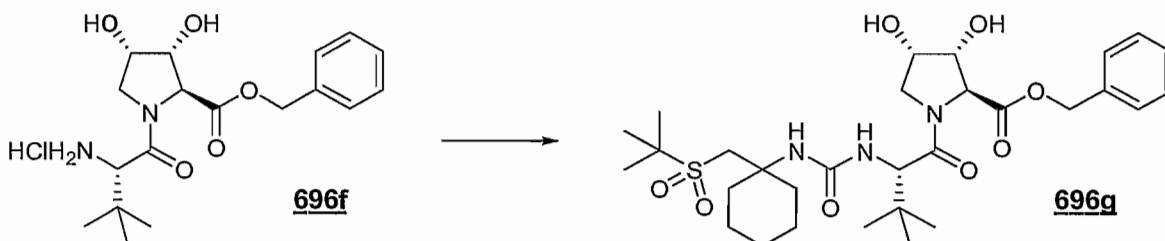
Step E



The N-Boc amine **696e** (1.24 g) was dissolved in 30 mL of 4M HCl in dioxane. The resulting solution was stirred at room temperature for about 2h. All the volatiles were removed under reduced pressure to afford the product **696f**

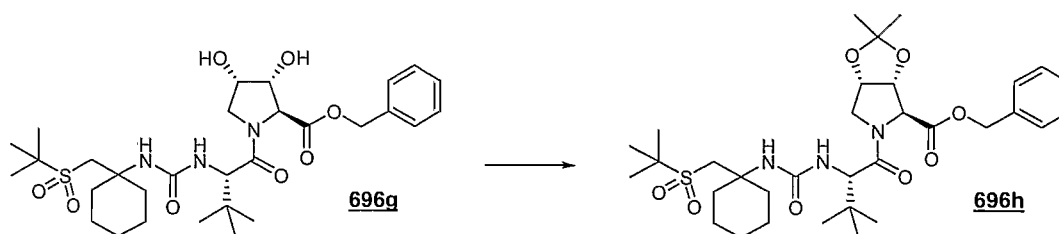
5 (1.06 g; 98 %) as a white solid.

Step F



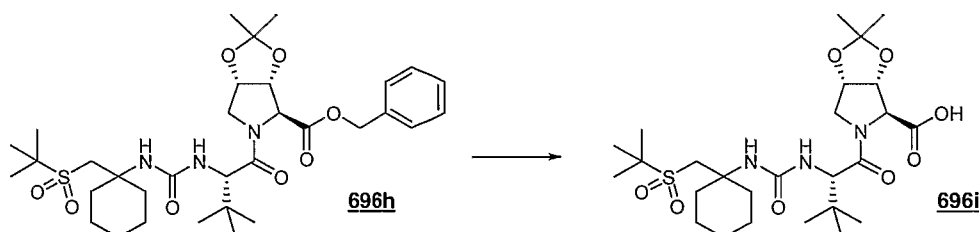
N-methyl morpholine (1.3 eq, 0.39 mL, d 0.920) was added to a heterogeneous mixture of amine-diol **696f** (1.06 g) in 50 mL of dichloromethane. After 5 min, a solution of isocyanate (1.05 eq, 9.63 mL of a 0.3M soln in toluene) was added. DMF (5 mL) was also added and the slurry was stirred at room temperature. The mixture gradually converted (over 4 h) to a clear homogeneous solution. The mixture was diluted with ethyl acetate (300 mL) and washed with aqueous 1M HCl. The aqueous layer was back extracted with 100 mL of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 3:7 to 6:4) to give the product **696g** (1.6 g; 98 %) as a colorless oil.

Step G



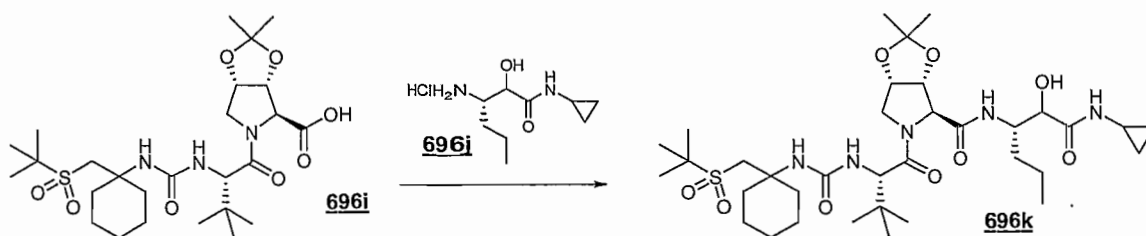
A solution of diol **696g** (1.5 g) was treated with 2,2-dimethoxypropane (2 eq, 0.6 mL, d 0.847) and a catalytic amount of pyridinium p-toluenesulfonic acid (0.1 eq, 62 mg). The mixture was stirred overnight at 50 °C. The mixture was diluted with 200 mL of ethyl acetate and washed with 50 mL of aqueous saturated sodium bicarbonate soln. The aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were dried over magnesium sulfate, filtered and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 5:95 to 35:65) to afford the product **696h** (1.33 g; 83 %) as a white solid.

Step H



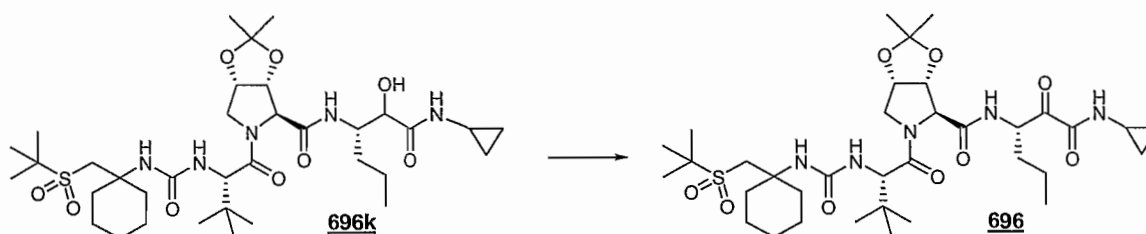
The benzyl ester **696h** (1.33 g) was dissolved in 70 mL of ethyl acetate and treated with 20% palladium dihydroxide on carbon (0.1 mol%; 144 mg). The heterogeneous mixture was hydrogenated at 50 psi for 3 h. The mixture was diluted with 200 mL of dichloromethane and filtered thru a short path of celite. The filtrate was concentrated under reduced pressure to afford the product **696i** (1.14 g; 98 %) as a white solid.

Step I



A solution of acid **696i** (100 mg) in 3 mL of dry dichloromethane and 3 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 93 mg). The amine salt **696j** (1.2 eq, 47 mg) was added followed by N-methylmorpholine (4 eq, 0.08 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (10 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **696k** was used without further purification.

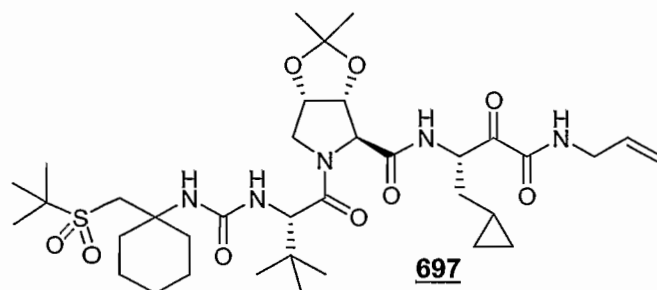
Step J



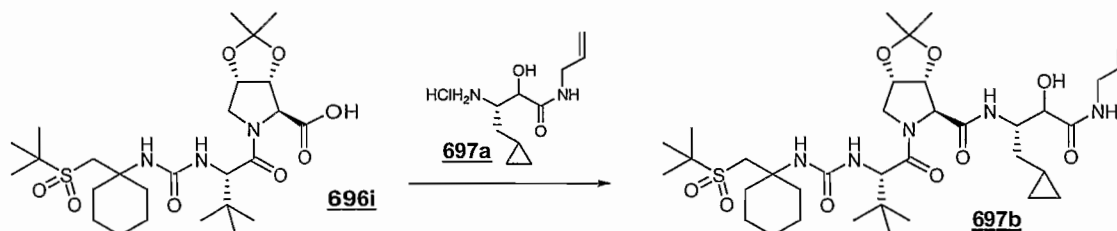
A solution of hydroxyamide **696k** (0.178 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 150 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (10 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers

were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 15:85 to 1:1) to afford the product **696** (120 mg; 93 %) as white solid. HRMS calcd for $C_{35}H_{60}N_5O_9S$ $[M+H]^+$: 726.4112, found 726.4128.

5 Example 697:

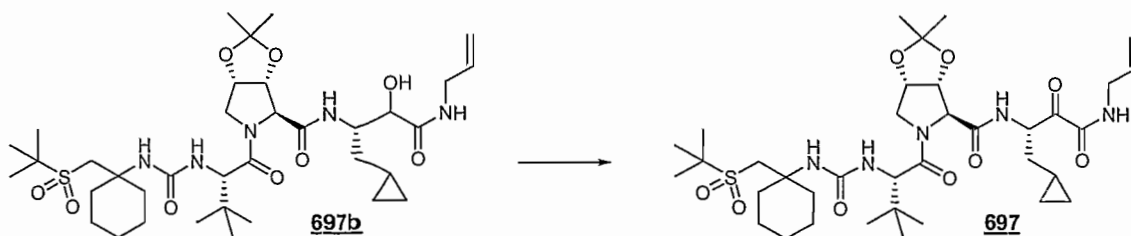


Step A



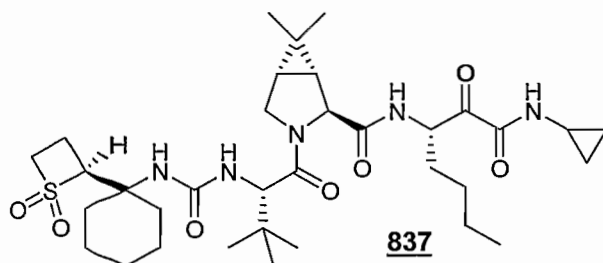
- 10 A solution of acid **696i** (100 mg) in 3 mL of dry dichloromethane and 3 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 93 mg). The amine salt **697a** (1.2 eq, 50 mg) was added followed by N-methylmorpholine (4 eq, 0.08 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was
- 15 dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (10 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **697b** was used without further purification.

20 Step B

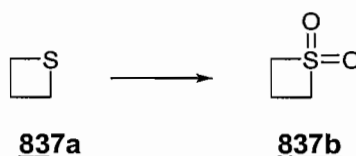


A solution of hydroxyamide **697b** (0.178 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 150 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (10 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 15:85 to 1:1) to afford the product **697** (120 mg; 91 %) as white solid. HRMS calcd for $C_{36}H_{60}N_5O_9S$ $[M+H]^+$: 738.4112, found 738.4092.

Example 837:



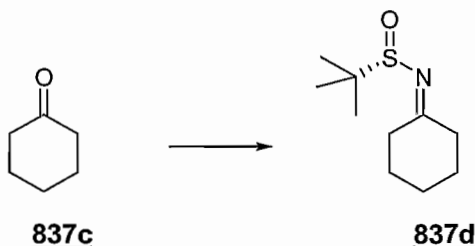
15 Step A



A solution of thietane (10 g, 9.727 mL, d 1.028, Aldrich) in 200 mL of dichloromethane was treated with a slurry of m-chloroperoxybenzoic acid (2.3

eq, 76 g of 70% m-CPBA) in dichloromethane (400 mL) at 0 °C. The cooling bath was removed and the mixture was stirred for 3 h. The solids were removed by filtration and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (400 mL) and the solution was extensively washed with aqueous saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography to afford the product **837b** as a white solid.

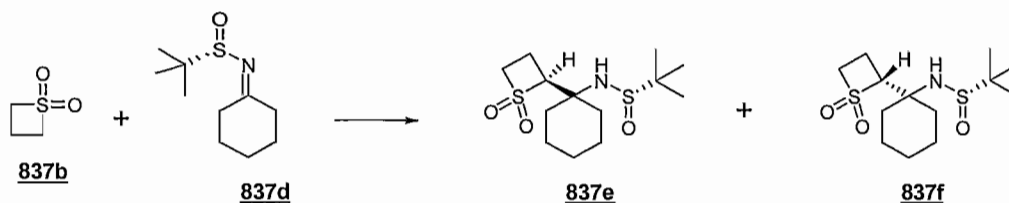
Step B



Titanium tetraethoxide (2 eq, 24.2 mL, d 1.088) was added to a solution of cyclohexanone (1.2 eq, 7.18 mL, d 0.947) in 150 mL of dry THF under nitrogen atmosphere. After 5 min, t-butanedisulfonamide (7.0 g, Aldrich) in 50 mL of THF was added dropwise. The mixture was heated to 60 °C overnight.

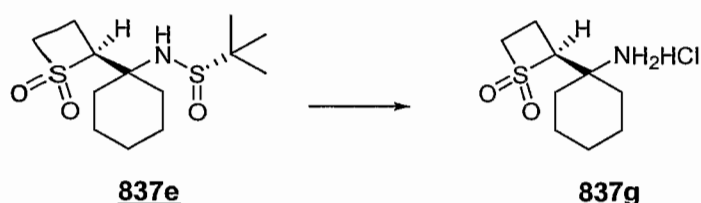
The reaction mixture was poured into an equal volume of aqueous saturated sodium bicarbonate solution with rapid stirring and immediately filtered through filter paper whatman #1. The filter cake was washed with ethyl acetate (100 mL). The layers in the filtrate were separated and the aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were washed with aqueous saturated sodium bicarbonate solution (100 mL), dried over magnesium sulfate, filtered and concentrated. The residue was chromatographed on silica gel (ethyl acetate/hexanes; 3:7) to afford the product **837d** (7.5 g; 55 %) as a colorless oil. The product is kept under inert atmosphere at -20 °C.

Step C



n-Butyl lithium (1.1 eq, 7.6 mL of a 1.6M soln in cyclohexane) was added dropwise to a cooled (-78 °C) solution of sulfone **837b** (1.15 eq, 1.35 g) in 100 mL of dry THF under anhydrous atmosphere. The mixture was stirred for 1 h at that temperature and then transferred via cannula to a pre-cooled (-78 °C) solution of sulfinylimine **837d** (2.23 g) in 100 mL of dry THF. The resulting mixture was stirred at -78 °C and monitored by TLC (acetone/hexanes; 3:7). All the sulfinylimine **837d** starting material was consumed in 2 h. The reaction was quenched by addition of aqueous saturated ammonium chloride solution (5 mL). The mixture was allowed to reach room temperature and partitioned between ethyl acetate (200 mL) and aqueous saturated sodium bicarbonate (80 mL). The aqueous layer was back extracted with ethyl acetate (2 x 60 mL). The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: dichloromethane to acetone/dichloromethane; 3:7) to afford the corresponding diastereomeric products **837e** and **837f** as a 1.4:1 mixture (1.64 g; 50 % comb.yield).

Step D



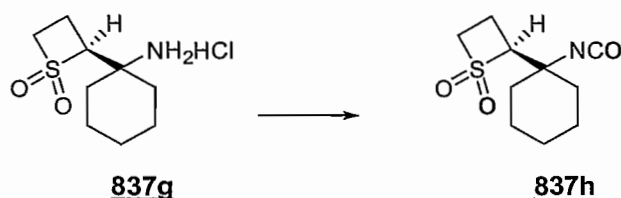
The sulfonamide **837e** (910 mg) was dissolved in 50 mL of methanol and treated with 20 mL of 4M HCl solution in dioxane. The mixture was stirred for

about 1 h until all the starting material had been consumed as determined by TLC (acetone/hexanes; 1:9). The mixture was concentrated to dryness.

Dichloromethane (10 mL) was added to make a homogeneous solution then ether was added (80 mL) and a white precipitate was formed. The amine

5 hydrochloride product **837g** (700 mg; 98 %) was recovered by filtration as a white solid.

Step E



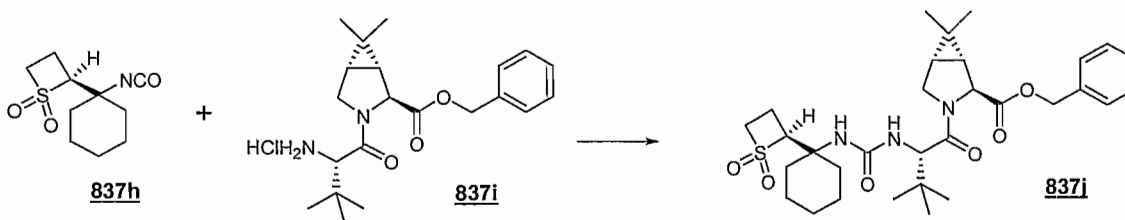
A solution of amine hydrochloride **837g** (2.960 mmol) in 40 mL of

10 dichloromethane was treated with 20 mL of aqueous saturated sodium bicarbonate solution and stirred vigorously for 10 min at 0 °C. Stirring was stopped and layers were allowed to separate. Phosgene (10 mL of 20% soln in toluene) was added through a needle to the organic layer (lower layer) in one portion. The mixture was vigorously stirred immediately after addition for

15 10 min at 0 °C and further stirred at room temp for 3 h. The mixture was diluted with 100 mL of dichloromethane and layers were separated. The organic layer was washed with 50 mL of cold aqueous saturated sodium bicarbonate solution and dried over magnesium sulfate. The organic layer was filtered and diluted with 50 mL of toluene. The resulting solution was

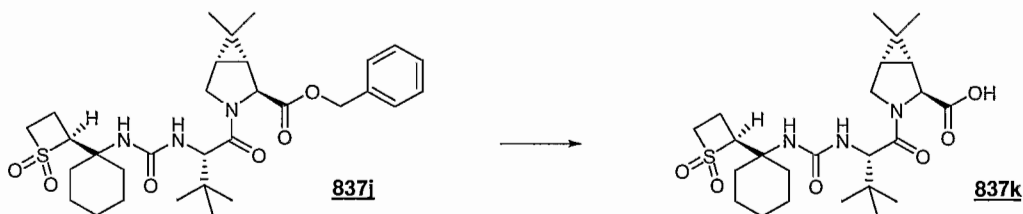
20 concentrated and kept as a 0.118M solution in toluene.

Step F



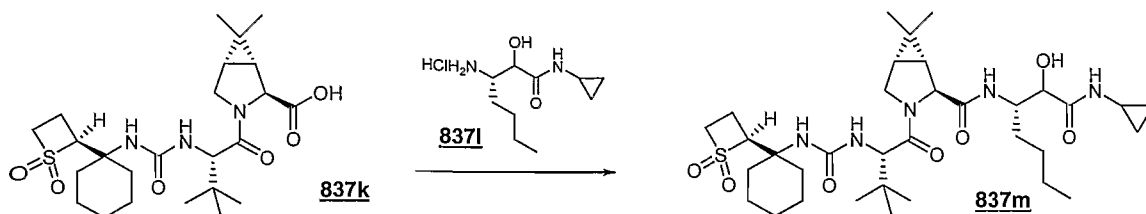
A solution of amine hydrochloride **837i** (1.5 mmol) in 30 mL of dichloromethane was treated with 5 mL of aqueous saturated sodium bicarbonate. The mixture was stirred for 10 min followed by addition of the isocyanate **837h** (1.03 eq, 13.1 mL of a 0.118M solution in toluene. The reaction mixture was stirred overnight. The reaction mixture was diluted with dichloromethane (200 mL) and washed with aqueous saturated sodium bicarbonate solution (40 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 1:9 to 1:1) to afford the product **837j** (740 mg; 84 %) as a white solid.

Step G



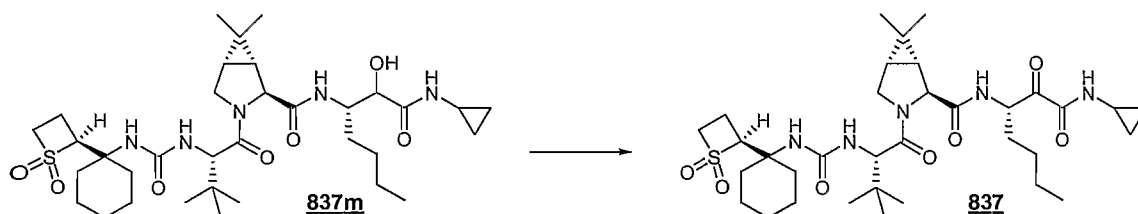
The benzyl ester **837j** (740 mg) was dissolved in 20 mL of methanol and treated with 20% palladium dihydroxide on carbon (0.1 mol%; 90 mg). The heterogeneous mixture was hydrogenated at 50 psi for 2 h. TLC (acetone/hexanes; 35:65) showed that all the starting material had been consumed. The mixture was diluted with 100 mL of dichloromethane and filtered thru a short path of celite. The filtrate was concentrated under reduced pressure to afford the product **837k** (620 mg; 98 %) as a white solid.

Step H



A solution of acid **837k** (69 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 74 mg). The amine salt **837l** (1.2 eq, 39 mg) was added followed by N-methylmorpholine (4 eq, 0.06 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (10 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **837m** was used without further purification.

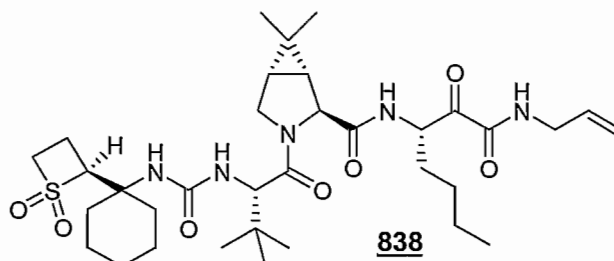
Step I



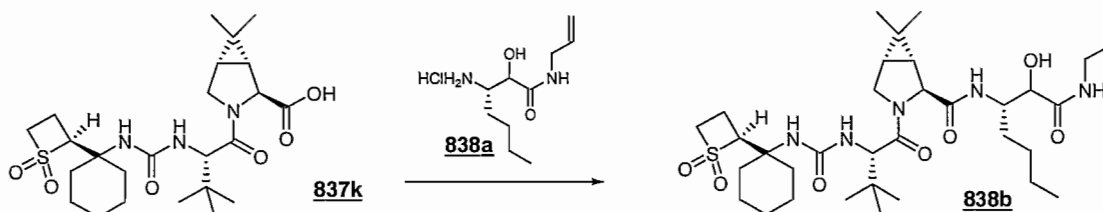
A solution of hydroxyamide **837m** (0.138 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 117 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (10 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers

were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 2:8 to 1:1) to afford the product **837** (66 mg; 70 %) as white solid. HRMS calcd for $C_{34}H_{56}N_5O_7S$ $[M+H]^+$: 678.3900, found 678.3883.

5 Example 838:

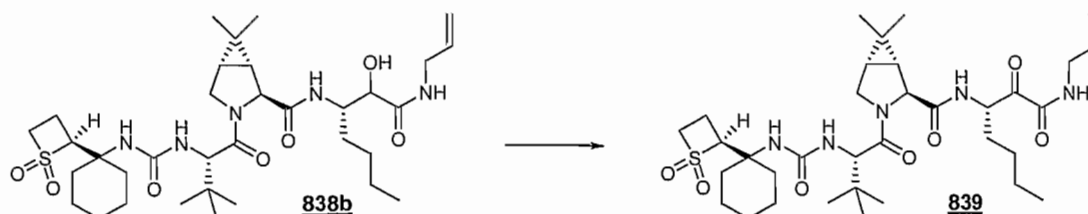


Step A



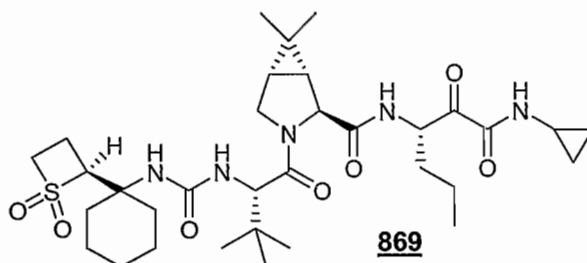
A solution of acid **837k** (69 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 74 mg). The amine salt **838a** (1.2 eq, 39 mg) was added followed by N-methylmorpholine (4 eq, 0.06 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (10 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **838b** was used without further purification.

Step B

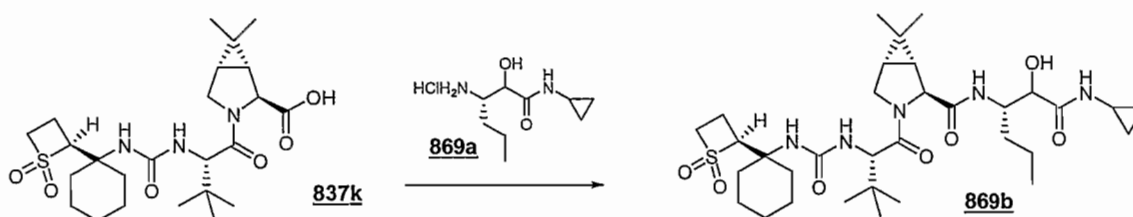


A solution of hydroxyamide **838b** (0.138 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 117 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (10 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 1:9 to 4:6) to afford the product **838** (71 mg; 76 %) as white solid. HRMS calcd for $C_{34}H_{56}N_5O_7S$ $[M+H]^+$: 678.3900, found 678.3883.

Example 869:

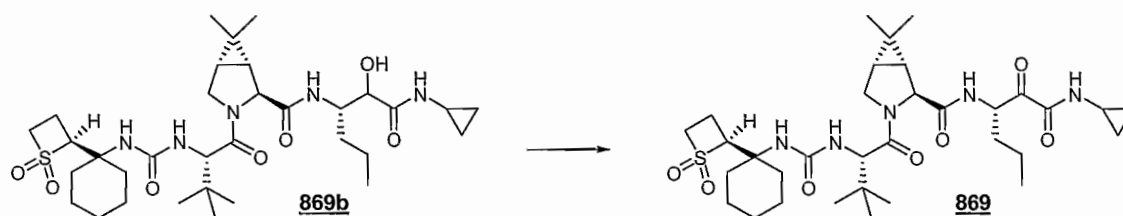


15 Step A



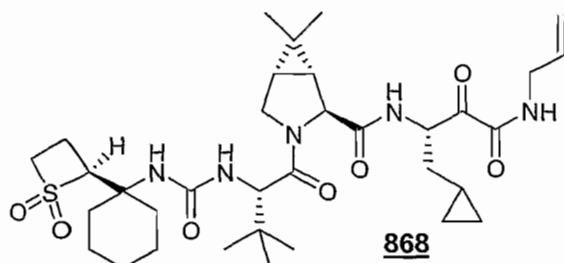
WO 2005/087731

A solution of acid **837k** (69 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 74 mg). The amine salt **869a** (1.2 eq, 37 mg) was added followed by N-methylmorpholine (4 eq, 0.06 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (10 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **869b** was used without further purification.

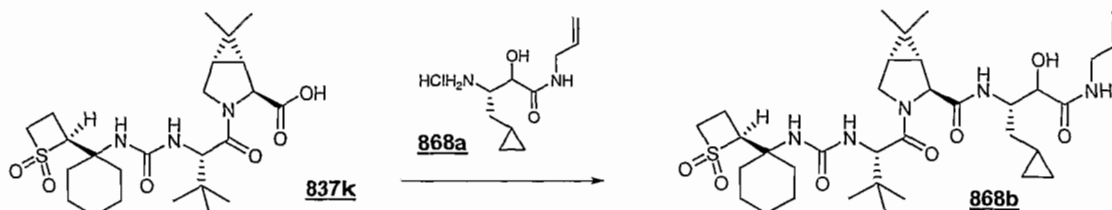
Step B

A solution of hydroxyamide **869b** (0.138 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 117 mg). The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (10 mL) was also added and stirring was continued for further 10 min. The mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 18:85 to 45:55) to afford the product **869** (69 mg; 75 %) as white solid.

Preparative Example 868:

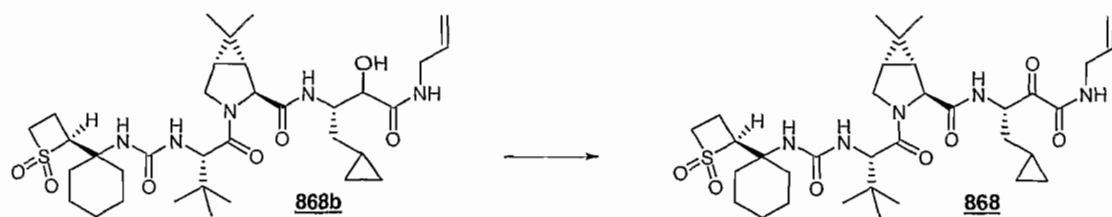


Step A



A solution of acid **837k** (69 mg) in 2 mL of dry dichloromethane and 2 mL of dry DMF was stirred at 0 °C and treated with HATU (1.4 eq, 74 mg). The amine salt **868a** (1.2 eq, 39 mg) was added followed by N-methylmorpholine (4 eq, 0.06 mL, d 0.920). The reaction mixture was stirred overnight (temp 0 to 25 °C). All the volatiles were removed under vacuum and the residue was dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (10 mL), aqueous 1M HCl (10 mL), aqueous saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product **868b** was used without further purification.

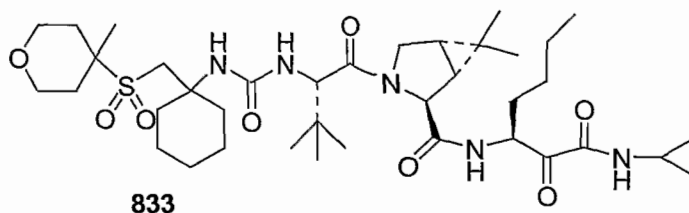
Step B



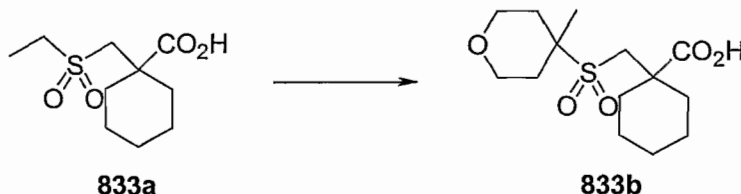
A solution of hydroxamide **868b** (0.138 mmol) in 10 mL of dry dichloromethane was treated with Dess-Martin periodinane (2.0 eq, 117 mg).

The reaction mixture was stirred at room temperature for 30 min. The mixture was treated with aqueous 1M sodium thiosulfate solution (10 mL) and stirred for 5 min. Aqueous saturated sodium bicarbonate solution (10 mL) was also added and stirring was continued for further 10 min. The mixture was
5 extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel (gradient: acetone/hexanes; 1:9 to 4:6) to afford the product **868** (73 mg; 78 %) as white solid.

Example **833**:



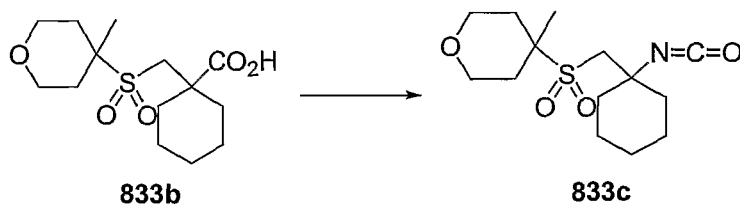
Step 1



To a solution of ethylsulfone acid **833a** (2.06 g, 8.79 mmol) in anhydrous THF at -78°C under N₂ was added LiHMDS solution (19.3 mL, 1.0
15 Min THF). The mixture was stirred at -78°C for 30 min before it was allowed to warmed to 0°C along with a cold acetone bath. It was then re-cooled to -78°C and to it was added 2-bromoethyl ether (1.8 mL, 13.2 mmol). After stirred at -78°C for 30 min, the mixture was warmed to rt and stirred for 2 h. It was again re-cooled to -78°C and to it was added LiHMDS solution (10.6 mL, 10.6
20 mmol). After stirred at -78°C for 30 min, the mixture was warmed to rt and stirred for 3 h before it was quenched with 1 N aqueous HCl solution until the pH is about 1-2. The solution was extracted with CH₂Cl₂ (2x450 mL).

Combined organic solution was dried (MgSO_4), filtered and concentrated. The crude product was dissolved in 1 N NaOH solution (300 mL) and extracted with EtOAc (100 mL). After layers were separated, the organic solution was washed with 1 N NaOH (2x150 mL). The combined aqueous solution was acidified to pH~1 using 6 N HCl solution. It was extracted with EtOAc (3 x 300 mL). The organic solutions were combined, dried (MgSO_4), filtered and concentrated to give 2.3 g product (**833b**; 7.56 mmol, 89%).

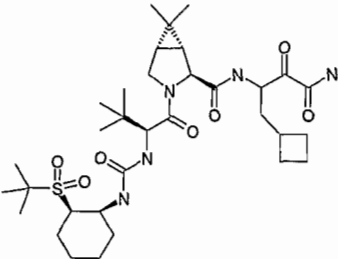
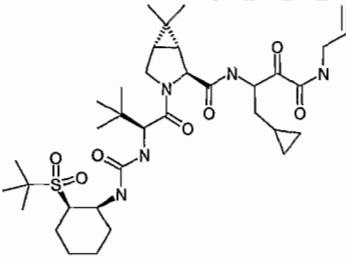
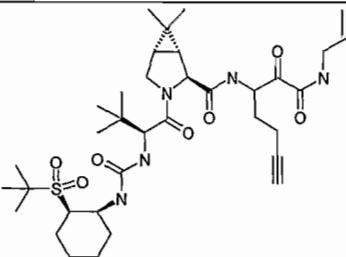
Step 2

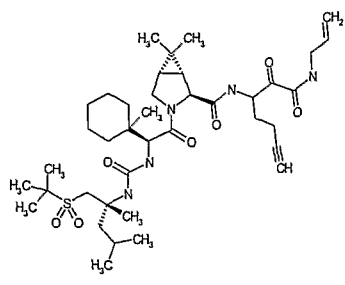
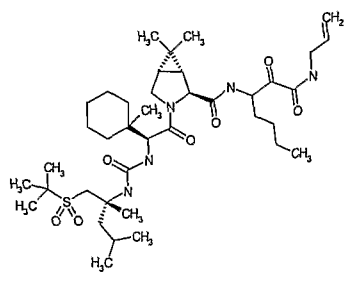


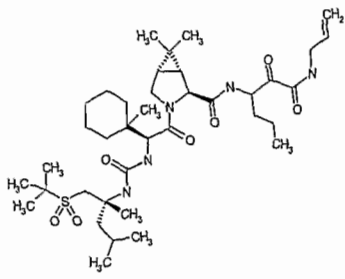
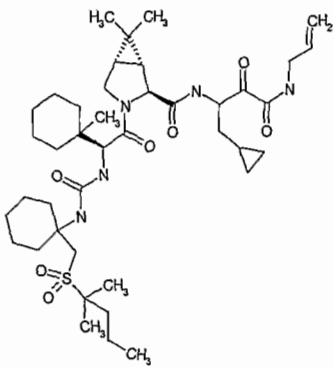
To the acid **833b** (2.30 g, 7.56 mmol) in toluene at rt under N_2 was added triethylamine (1.15 mL, 8.32 mmol) and diphenylphosphoryl azide (1.79 mL, 8.32 mmol). The resulting mixture was stirred at rt for 30 min and heated to reflux for 5.5 h. After it was cooled to rt, more toluene was added to make up a 0.19 M solution of the isocyanate **833c**, which was used without further purification.

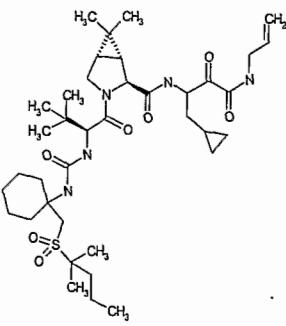
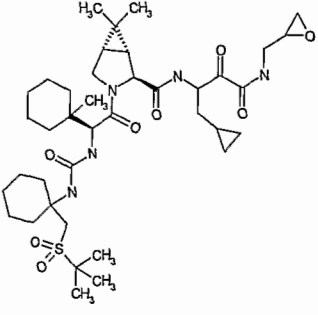
Using the aforementioned procedures **833c** was transformed into **833**.

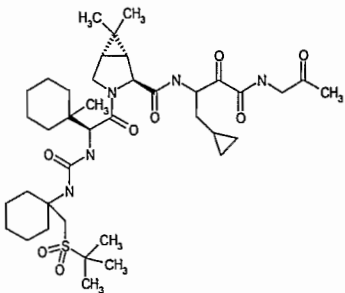
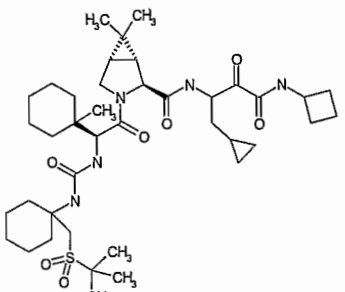
Table 3A

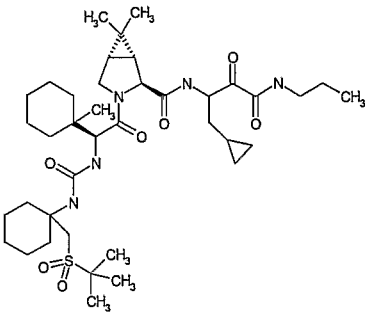
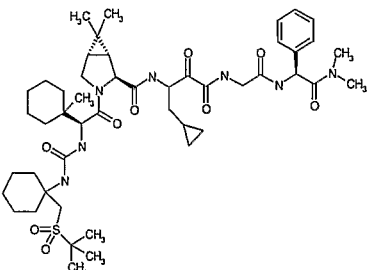
Compo-und #	structure	mol weight structure	Select LC-MS Data (M+H)	Ki* Range
397		665.887	666.3	B
398		691.925	692.4	C
399		689.909	690.3	B

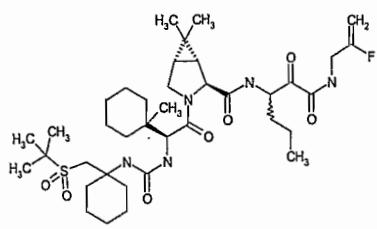
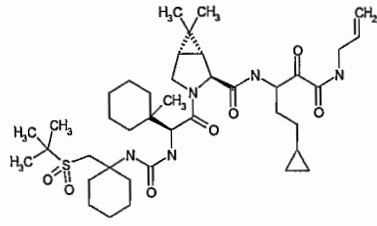
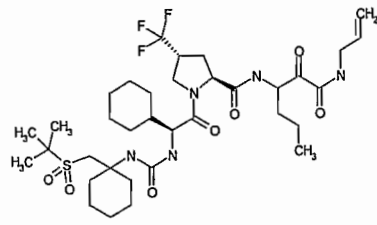
402	 Chemical structure of compound 402: A complex molecule featuring a cyclohexane ring substituted with a tert-butylsulfonyl group, a 2-methyl-2-propionyl-1-oxazolidinone ring, and a 2-allyl-3-oxobutyl group. Stereochemistry is indicated with wedges and dashes.	746.0303	746.2	A
403	 Chemical structure of compound 403: A complex molecule featuring a cyclohexane ring substituted with a tert-butylsulfonyl group, a 2-methyl-2-propionyl-1-oxazolidinone ring, and a 2-propyl-3-oxobutyl group. Stereochemistry is indicated with wedges and dashes.	750.0621	750.4	A

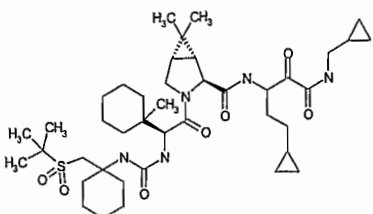
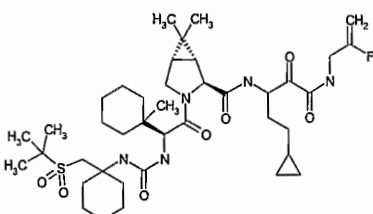
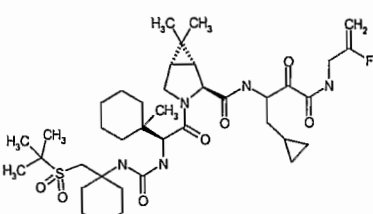
404		736.0351	736.4	A
405		774.0844		A

406		734.0191		A
407		762.0297		A

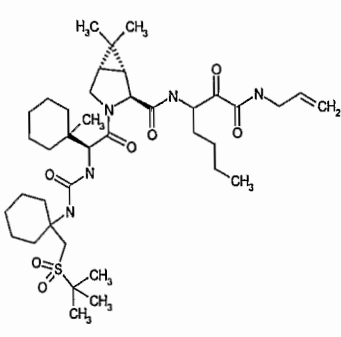
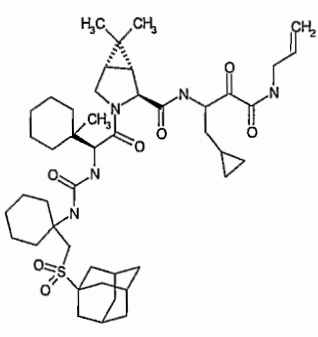
412	 Chemical structure of compound 412: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The nitrogen atom is part of a larger structure that includes a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The nitrogen atom is also part of a side chain that includes a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The structure is highly symmetrical and complex, with multiple rings and functional groups.	762.0297		A
413	 Chemical structure of compound 413: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The nitrogen atom is part of a larger structure that includes a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The nitrogen atom is also part of a side chain that includes a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The structure is highly symmetrical and complex, with multiple rings and functional groups.	760.0574		A

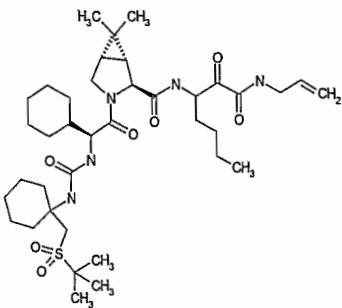
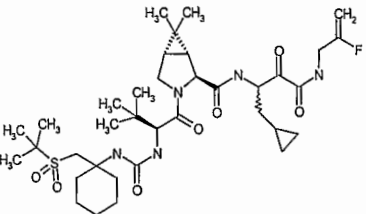
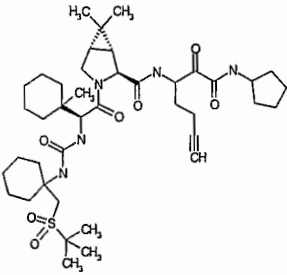
414	 Chemical structure of compound 414: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A cyclopropyl group is attached to the amide nitrogen. Another amide group is attached to the cyclopropyl group, which is further substituted with a propyl group. A sulfonamide group is also present, attached to the cyclohexane ring via a methylene group. The sulfonamide group is a dimethylsulfonamide.	748.0462		A
415	 Chemical structure of compound 415: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A cyclopropyl group is attached to the amide nitrogen. Another amide group is attached to the cyclopropyl group, which is further substituted with a propyl group. A sulfonamide group is also present, attached to the cyclohexane ring via a methylene group. The sulfonamide group is a dimethylsulfonamide.	924.2225		B

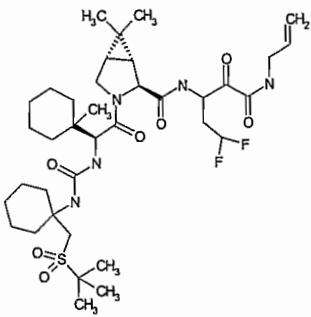
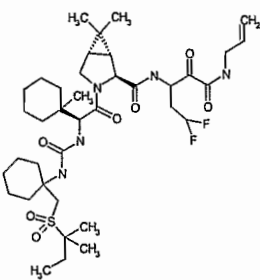
416		752.0095		A
417		760.0574		A
418		747.9251		A

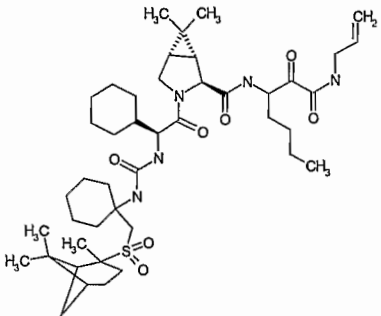
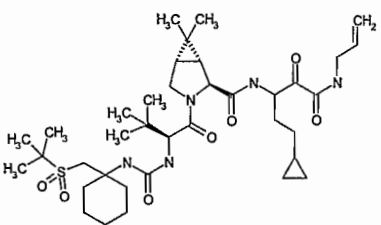
419		774.0844		A
420		778.0478		A
421		764.0207		A

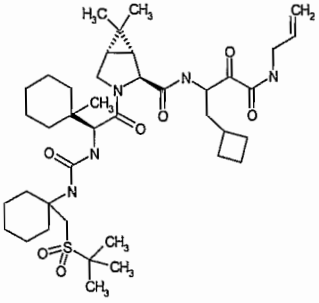
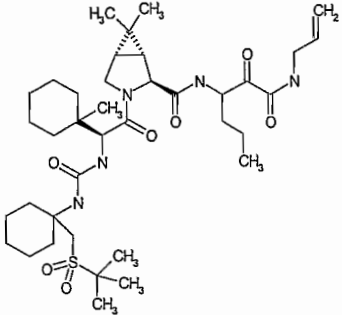
422	 <chem>CC1(C)C(=O)N(C1C2CCCCC2)C(=O)N(C3CCCCC3)C(=O)N(C4CCCC4)C#C</chem>	772.0685		A
423	 <chem>CC1(C)C(=O)N(C1C2CCCCC2)C(=O)N(C3CCCCC3)C(=O)N(C4CCCCC4)C=C</chem>	852.1555	852.5	A

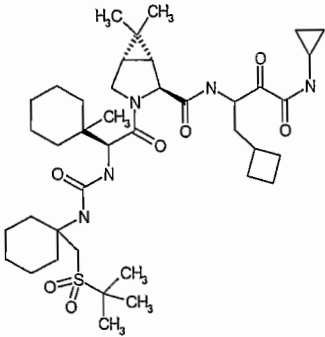
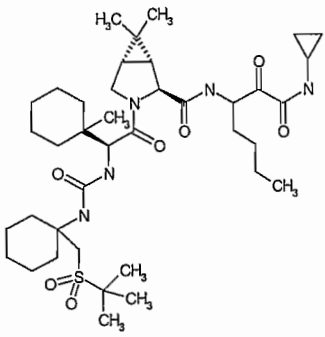
424		748.0462		A
425		824.145		A

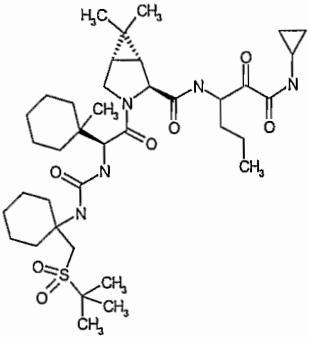
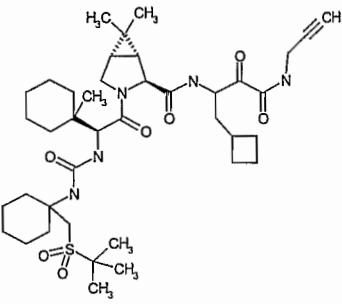
426		734.0191		A
427		723.9554		A
428		772.0685		A

429		755.9729		A
430		770		A

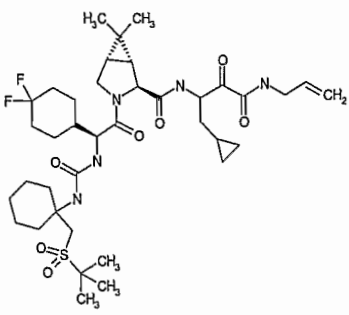
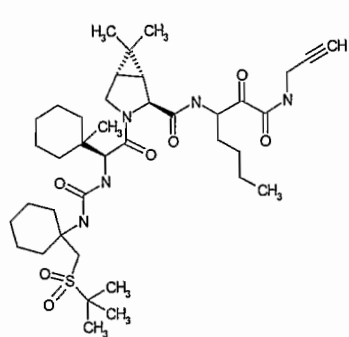
431		814.1498		A
432		719.992		A

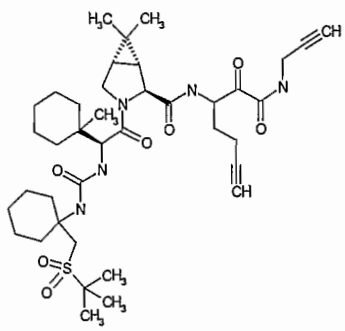
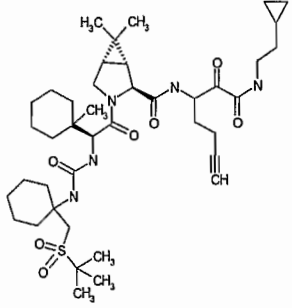
433		760.0574		A
434		734.0191		A

435	 Chemical structure of compound 435: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a cyclopropylmethyl group. Another side chain on the cyclohexane ring includes a carbonyl group, a nitrogen atom, and a tert-butyl group. A third side chain on the cyclohexane ring consists of a carbonyl group, a nitrogen atom, and a cyclopropylmethyl group. The molecule also includes a cyclobutylmethyl group and a cyclopropylmethyl group.	760.0574		A
436	 Chemical structure of compound 436: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a propyl group. Another side chain on the cyclohexane ring includes a carbonyl group, a nitrogen atom, and a tert-butyl group. A third side chain on the cyclohexane ring consists of a carbonyl group, a nitrogen atom, and a propyl group. The molecule also includes a cyclobutylmethyl group and a cyclopropylmethyl group.	748.0462		A

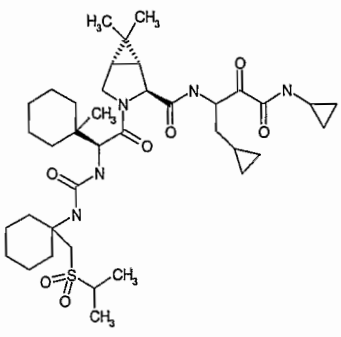
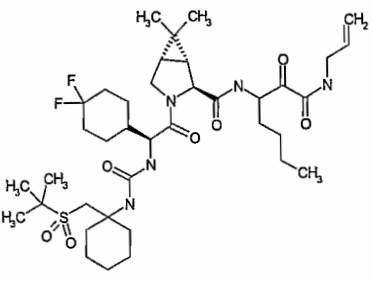
437	 Chemical structure of compound 437: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a cyclopropylmethyl group and a methyl group. Another side chain features a sulfonamide group (SO₂NH-) attached to a cyclohexane ring, which is further substituted with a methyl group and a carbonyl group. The molecule also contains a cyclohexane ring with a methyl group and a carbonyl group, and a side chain with a methyl group and a carbonyl group.	734.0191		A
438	 Chemical structure of compound 438: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a cyclopropylmethyl group and a methyl group. Another side chain features a sulfonamide group (SO₂NH-) attached to a cyclohexane ring, which is further substituted with a methyl group and a carbonyl group. The molecule also contains a cyclohexane ring with a methyl group and a carbonyl group, and a side chain with a methyl group and a carbonyl group.	758.0414		A

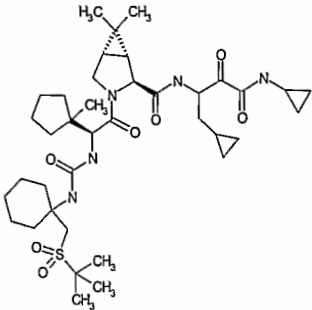
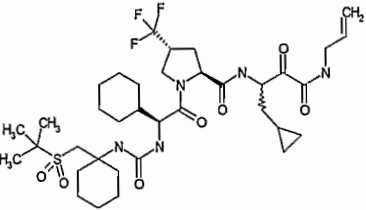
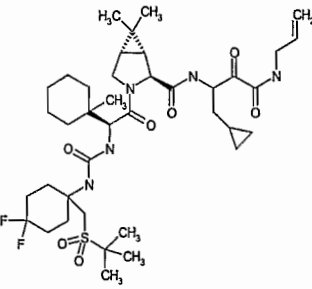
441		784.0271	784.2	A
442		755.9729	756.2	A

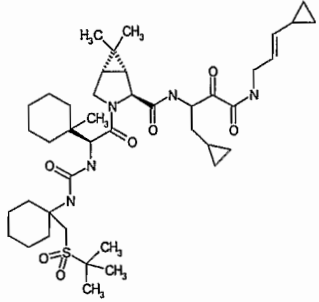
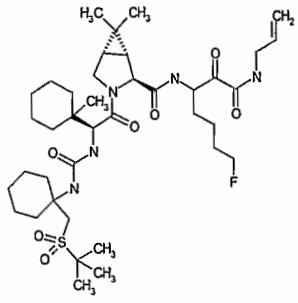
443		767.984	768.4	A
444		746.0303		A

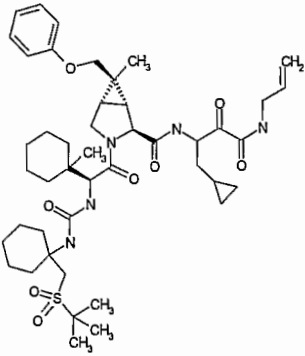
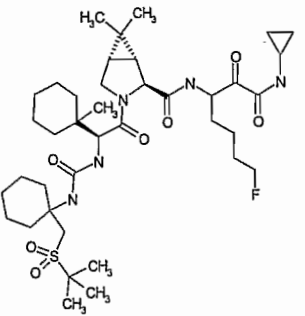
445	 Chemical structure of compound 445: A complex molecule featuring a central bicyclic system (a cyclohexane ring fused to a five-membered ring containing a nitrogen atom). The nitrogen atom is part of a carbamate group. The five-membered ring is substituted with a methyl group and a carbonyl group. The carbonyl group is part of a carbamate chain that includes a terminal alkyne group (CH≡CH). The cyclohexane ring is also substituted with a carbonyl group, which is part of a carbamate chain that includes a terminal alkyne group (CH≡CH). The cyclohexane ring is further substituted with a sulfonamide group (SO₂CH₃).	741.9984		A
446	 Chemical structure of compound 446: A complex molecule featuring a central bicyclic system (a cyclohexane ring fused to a five-membered ring containing a nitrogen atom). The nitrogen atom is part of a carbamate group. The five-membered ring is substituted with a methyl group and a carbonyl group. The carbonyl group is part of a carbamate chain that includes a terminal alkyne group (CH≡CH). The cyclohexane ring is also substituted with a carbonyl group, which is part of a carbamate chain that includes a terminal alkyne group (CH≡CH). The cyclohexane ring is further substituted with a sulfonamide group (SO₂CH₃).	772.0685		A

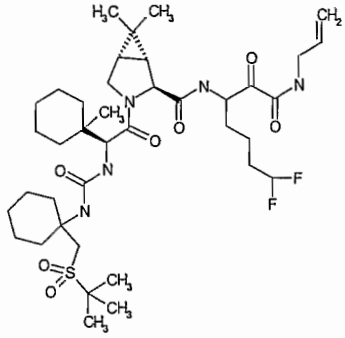
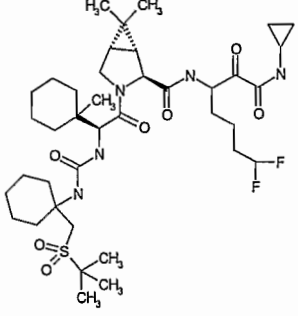
447	The structure shows a bicyclic sulfonamide core. A cyclopropane ring is attached to the sulfonamide nitrogen. The sulfonamide group is a methanesulfonyl derivative. A cyclopropane ring is also attached to the sulfonamide sulfur. The sulfonamide nitrogen is part of a larger bicyclic system. A vinyl group is attached to the sulfonamide nitrogen.	703.949	704.4	A
448	The structure shows a bicyclic sulfonamide core. A cyclopropane ring is attached to the sulfonamide nitrogen. The sulfonamide group is a methanesulfonyl derivative. A cyclopropane ring is also attached to the sulfonamide sulfur. The sulfonamide nitrogen is part of a larger bicyclic system. A vinyl group is attached to the sulfonamide nitrogen.	774.0844		A

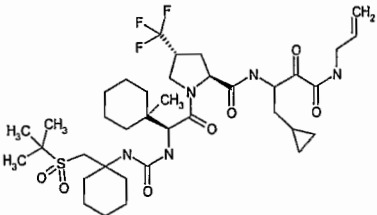
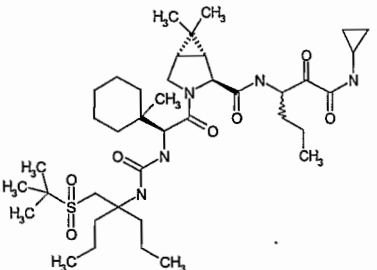
449	 Chemical structure of compound 449: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (H₃C) and a methyl group (CH₃) at the 2-position. It is also substituted with a cyclohexyl group at the 3-position. The pyrrolidine ring is connected via amide bonds to a cyclohexyl group and a cyclopropyl group. The cyclohexyl group is further substituted with a sulfonamide group (SO₂CH₃).	732.0032		A
450	 Chemical structure of compound 450: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (H₃C) and a methyl group (CH₃) at the 2-position. It is also substituted with a cyclohexyl group at the 3-position. The pyrrolidine ring is connected via amide bonds to a cyclohexyl group and a cyclopropyl group. The cyclohexyl group is further substituted with a sulfonamide group (SO₂CH₃).	770	770.2	A

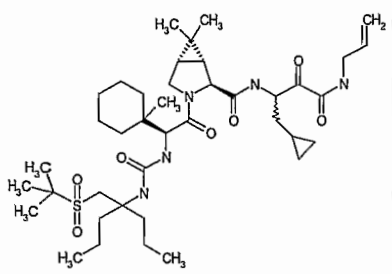
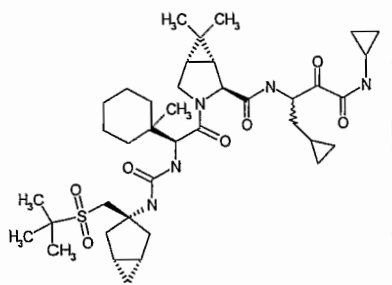
451		732.0032	732.2	A
452		759.9362		A
453		782.0111		A

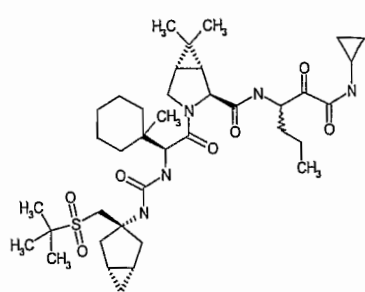
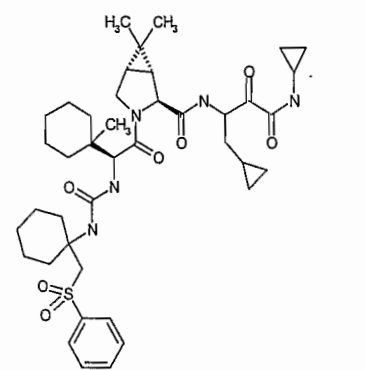
454	 Chemical structure of compound 454: A complex molecule featuring a central amide linkage. The left side consists of a cyclohexane ring substituted with a tert-butyl sulfonamide group and a 2-methyl-2-propionyl-1-azetidinyl group. The right side consists of a cyclopropane ring substituted with a 2-((cyclopropylmethylidene)amino)acetyl group. Stereochemistry is indicated with wedges and dashes.	786.0956		A
455	 Chemical structure of compound 455: A complex molecule featuring a central amide linkage. The left side consists of a cyclohexane ring substituted with a tert-butyl sulfonamide group and a 2-methyl-2-propionyl-1-azetidinyl group. The right side consists of a cyclopropane ring substituted with a 2-((cyclopropylmethylidene)amino)acetyl group. Stereochemistry is indicated with wedges and dashes.	766.0366		A

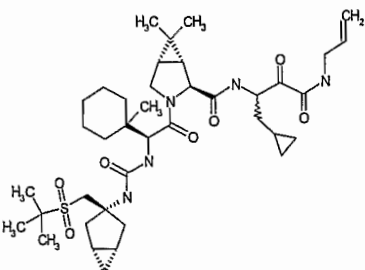
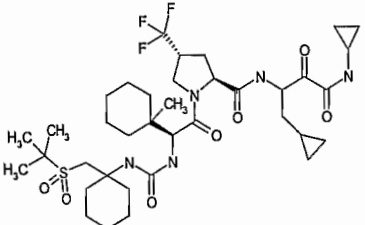
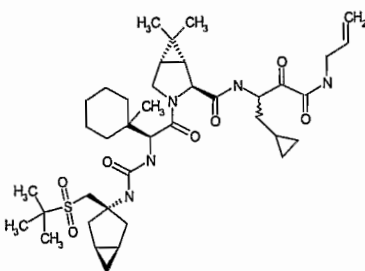
456	 Chemical structure of compound 456: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a benzyl group (CH₂Ph) and a methyl group (CH₃). It is also connected to a cyclohexane ring via a carbonyl group (C=O). The cyclohexane ring is further substituted with a methyl group (CH₃) and a sulfonamide group (SO₂CH₃). The pyrrolidine ring is also connected to a cyclopropane ring via a carbonyl group (C=O). The cyclopropane ring is substituted with a methyl group (CH₃) and a vinyl group (CH=CH₂).	838.1284		B
457	 Chemical structure of compound 457: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a methyl group (CH₃). It is also connected to a cyclohexane ring via a carbonyl group (C=O). The cyclohexane ring is further substituted with a methyl group (CH₃) and a sulfonamide group (SO₂CH₃). The pyrrolidine ring is also connected to a cyclopropane ring via a carbonyl group (C=O). The cyclopropane ring is substituted with a methyl group (CH₃) and a fluorine atom (F).	766.0366	766.4	A

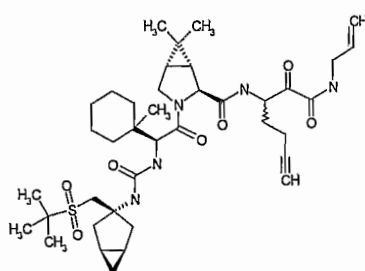
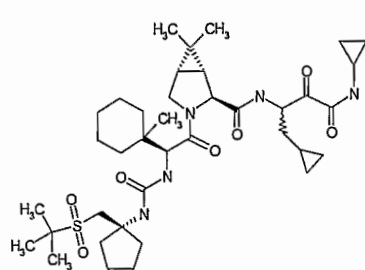
458	 Chemical structure of compound 458: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a sulfonamide group. The sulfonamide group is further substituted with a cyclohexylmethyl group and a dimethylsulfonyl group. The side chain also includes a fluorinated alkyl group and a vinyl group.	784.0271	784.4	A
459	 Chemical structure of compound 459: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a sulfonamide group. The sulfonamide group is further substituted with a cyclohexylmethyl group and a dimethylsulfonyl group. The side chain also includes a fluorinated alkyl group and a cyclopropyl group.	784.0271	784.2	A

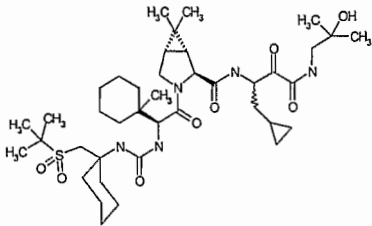
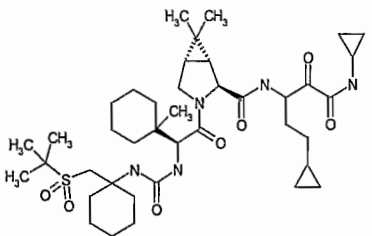
460		773.9633		A
461		750.0621	750.9	B

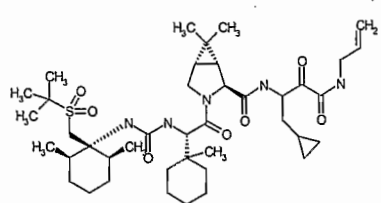
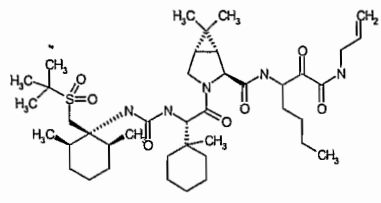
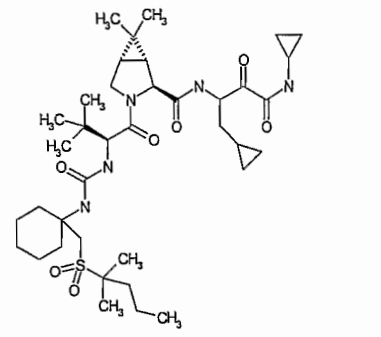
462		762.0733	762.41	C
463		744.0143	744.2	B

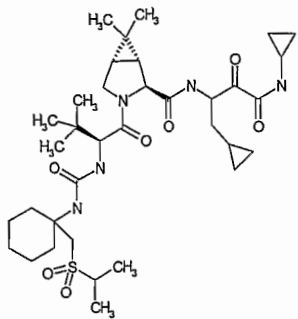
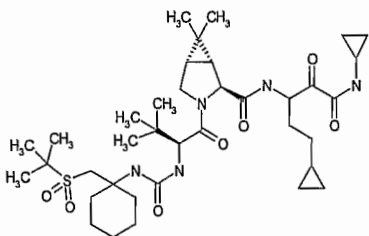
464		732.0032	732.4	A
465		766.0207		B

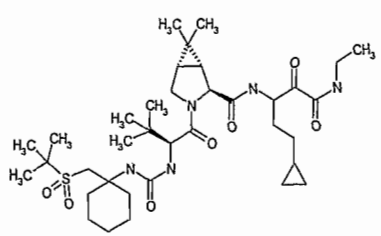
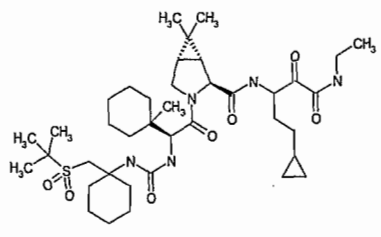
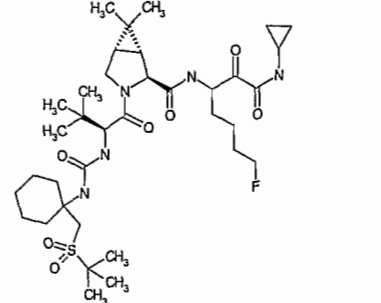
466		744.0143	744.4	A
467		773.9633		B
468		744.0143	744.70	B

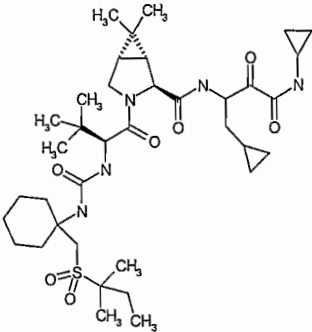
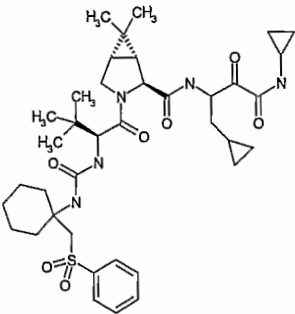
469	 Chemical structure of compound 469: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. This is linked via an amide bond to a five-membered ring containing a methyl group and a carbonyl group. This five-membered ring is further linked via an amide bond to a chain containing a carbonyl group, a propargyl group (CH₂CH₂C≡CH), and a terminal vinyl group (CH=CH₂). Another branch from the five-membered ring leads to a carbonyl group, which is linked via an amide bond to a cyclopropylmethyl group. A tert-butylsulfonyl group (SO₂CH₂C(CH₃)₃) is attached to the cyclopropylmethyl group.	741.9984	742.40	A
470	 Chemical structure of compound 470: Similar to compound 469, it features a cyclohexane ring substituted with a methyl group and a carbonyl group. This is linked via an amide bond to a five-membered ring containing a methyl group and a carbonyl group. This five-membered ring is further linked via an amide bond to a chain containing a carbonyl group and a cyclopropyl group. Another branch from the five-membered ring leads to a carbonyl group, which is linked via an amide bond to a cyclopropylmethyl group. A tert-butylsulfonyl group (SO₂CH₂C(CH₃)₃) is attached to the cyclopropylmethyl group.	744.0143	744.38	B

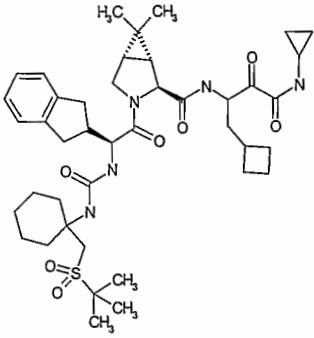
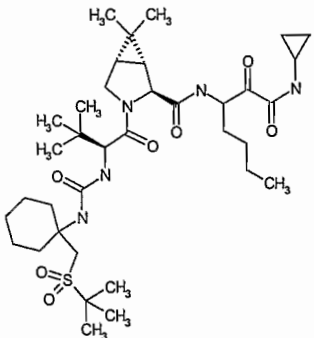
471	 Chemical structure of compound 471: A complex molecule featuring a central cyclohexane ring. Attached to the ring is a side chain containing a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The nitrogen is part of a larger structure that includes a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The molecule also contains a sulfonamide group (SO₂CH₃) and a hydroxyl group (OH).	778.0727	778.7	B
472	 Chemical structure of compound 472: A complex molecule featuring a central cyclohexane ring. Attached to the ring is a side chain containing a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The nitrogen is part of a larger structure that includes a cyclopropylmethyl group, a carbonyl group, and a nitrogen atom. The molecule also contains a sulfonamide group (SO₂CH₃) and a hydroxyl group (OH).	760.0574		A

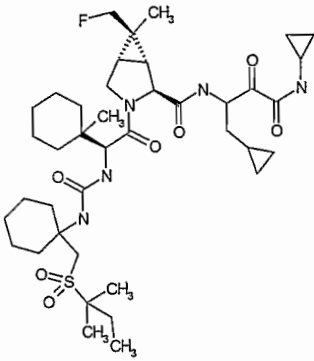
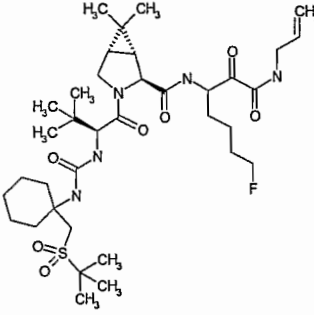
473		774.0844	774.4	A
474		776.1004	776.5	A
475		734.0191		A

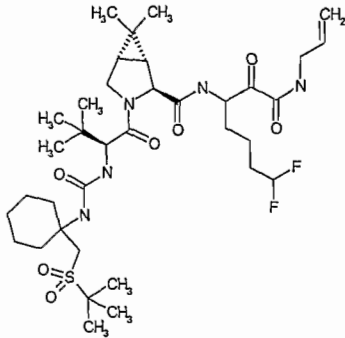
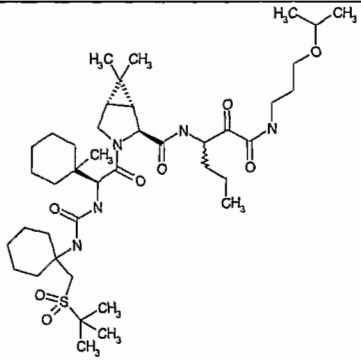
476		691.9378		B
477		719.992		A

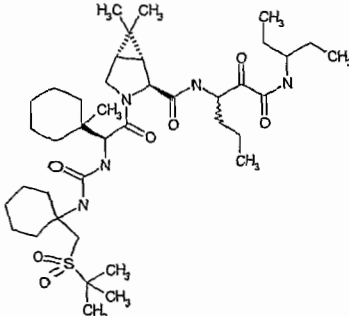
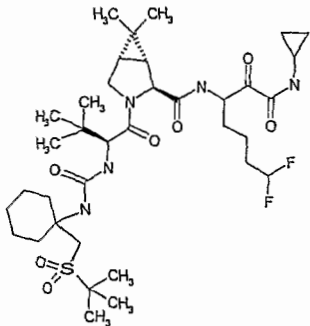
478		707.9809		A
479		748.0462		A
480		725.9713	726.4	A

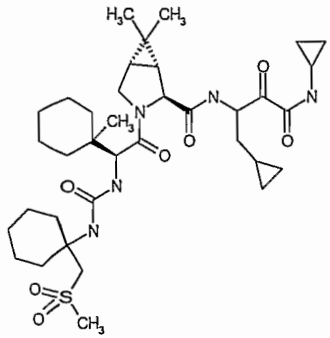
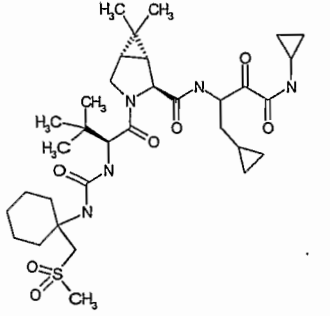
481		719.992		A
482		725.9554		B

483	 Chemical structure of compound 483: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2-phenyl-1H-inden-3-yl group, a 2-methyl-2-butyl group, and a 2-cyclobutyl-1H-imidazole-4-carboxamide group. The pyrrolidine ring is also substituted with a 2-methyl-2-butyl group and a 2-cyclobutyl-1H-imidazole-4-carboxamide group. The pyrrolidine ring is also substituted with a 2-methyl-2-butyl group and a 2-cyclobutyl-1H-imidazole-4-carboxamide group.	780.0478		B
484	 Chemical structure of compound 484: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2-phenyl-1H-inden-3-yl group, a 2-methyl-2-butyl group, and a 2-cyclobutyl-1H-imidazole-4-carboxamide group. The pyrrolidine ring is also substituted with a 2-methyl-2-butyl group and a 2-cyclobutyl-1H-imidazole-4-carboxamide group. The pyrrolidine ring is also substituted with a 2-methyl-2-butyl group and a 2-cyclobutyl-1H-imidazole-4-carboxamide group.	707.9809		A

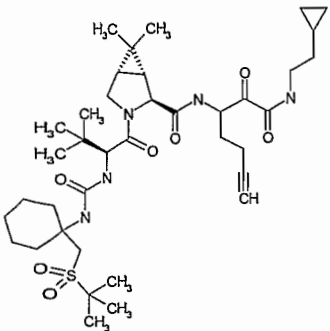
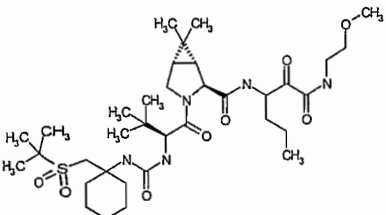
485	 Chemical structure of compound 485: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group, a methyl group, and a fluoromethyl group. It is also linked via amide bonds to a cyclopropyl group and a cyclohexyl group. A sulfonamide group is attached to the cyclohexyl group.	778.0478		B
486	 Chemical structure of compound 486: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group, a methyl group, and a fluoromethyl group. It is also linked via amide bonds to a cyclopropyl group and a cyclohexyl group. A sulfonamide group is attached to the cyclohexyl group.	725.9713		A

487	 Chemical structure of compound 487: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a carbamate group. The carbamate is linked to a pyrazole ring, which is further substituted with a methyl group and a side chain containing a ketone, a fluorine atom, and a terminal vinyl group.	743.9617		A
488	 Chemical structure of compound 488: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a carbamate group. The carbamate is linked to a pyrazole ring, which is further substituted with a methyl group and a side chain containing a ketone, a methyl group, and a terminal isopropoxy group.	794.1157	794.2	B

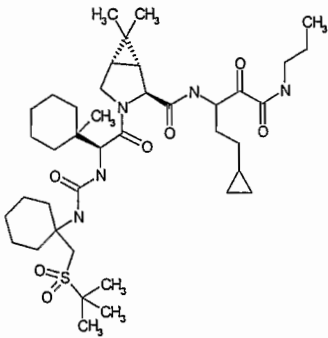
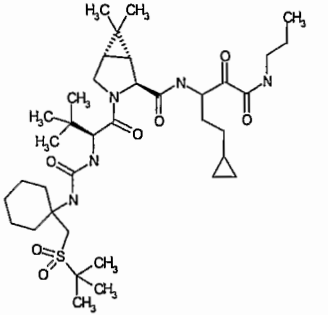
489	 Chemical structure of compound 489: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group, a dimethylamino group, and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain containing a cyclohexyl group, a sulfonamide group, and a dimethylamino group. The side chain also includes a cyclohexyl group and a dimethylamino group.	764.0892	764.1	B
490	 Chemical structure of compound 490: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group, a dimethylamino group, and a carbonyl group. The carbonyl group is part of an amide linkage to a side chain containing a cyclohexyl group, a sulfonamide group, and a dimethylamino group. The side chain also includes a cyclohexyl group and a dimethylamino group.	743.9617	744.4	A

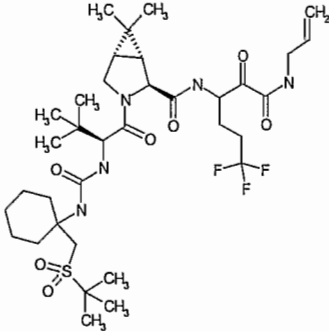
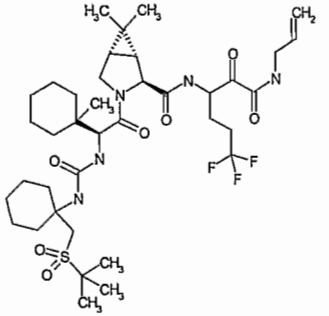
491	 Chemical structure of compound 491: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a cyclohexyl group. It is also linked via amide bonds to a cyclopropylmethyl group and a cyclohexylmethyl group. The cyclohexylmethyl group is further substituted with a sulfonamide group (SO₂CH₃).	703.949		A
492	 Chemical structure of compound 492: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a cyclohexyl group. It is also linked via amide bonds to a cyclopropylmethyl group and a cyclohexylmethyl group. The cyclohexylmethyl group is further substituted with a sulfonamide group (SO₂CH₃).	663.8837		A

[illegible]

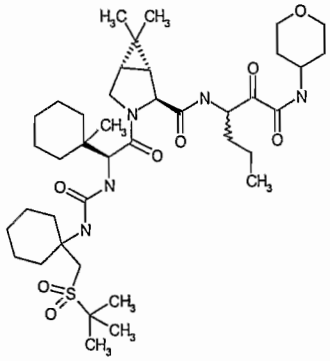
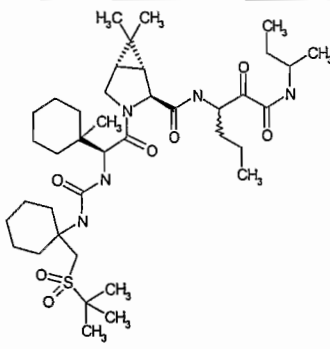
495	 Chemical structure of compound 495: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom connected to a side chain. The side chain includes a carbonyl group, a nitrogen atom, and a terminal group consisting of a cyclopropylmethyl group and a propargyl group (CH₂C≡CH).	732.0032		A
496	 Chemical structure of compound 496: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom connected to a side chain. The side chain includes a carbonyl group, a nitrogen atom, and a terminal group consisting of a methoxymethyl group (CH₂OCH₃) and a methyl group (CH₃).	712		A

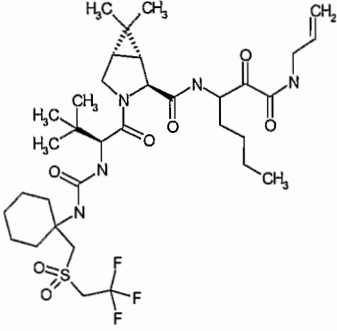
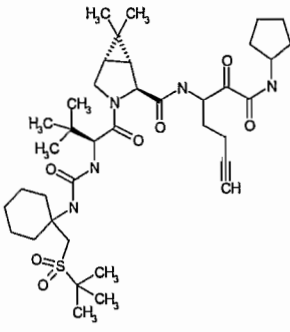
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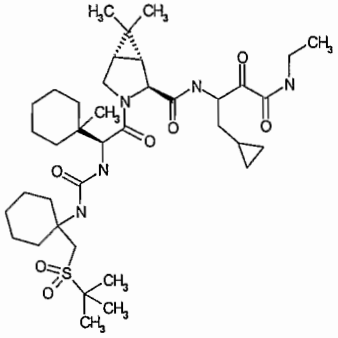
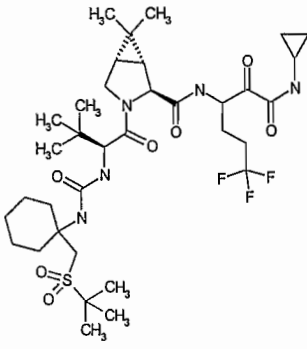
501		762	A	
502		722	A	

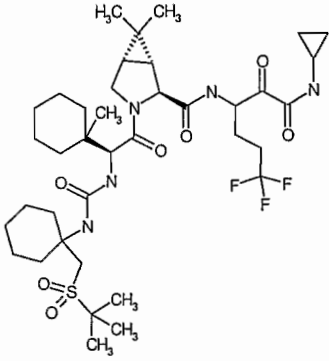
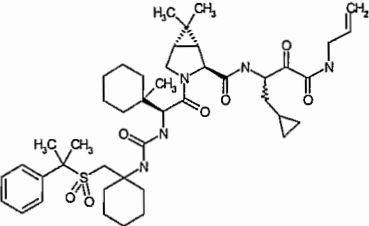
503		748		A
504		788		A

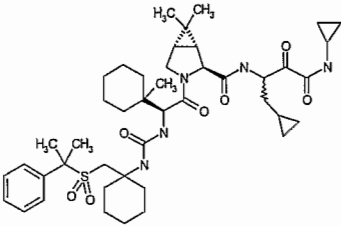
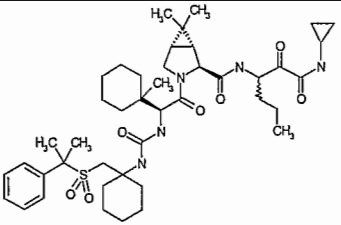
505		774		A
506		734		A

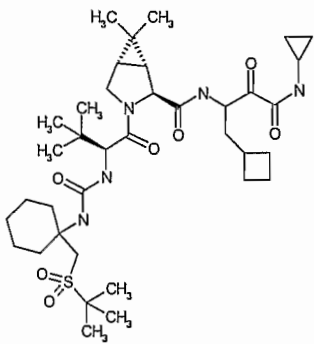
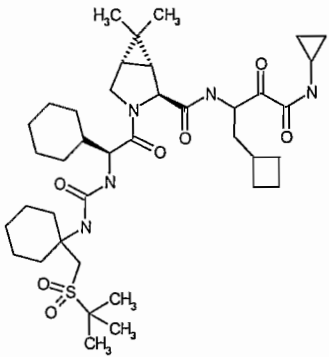
507	 Chemical structure of compound 507: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a sulfonamide group (SO₂NH-) attached to a cyclohexane ring, which is further substituted with a methyl group and a carbonyl group. The molecule also contains a morpholine ring and a methyl group.	778	778.2	C
508	 Chemical structure of compound 508: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a sulfonamide group (SO₂NH-) attached to a cyclohexane ring, which is further substituted with a methyl group and a carbonyl group. The molecule also contains a morpholine ring and a methyl group.	750	750.5	B

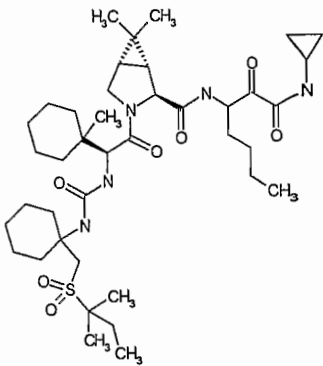
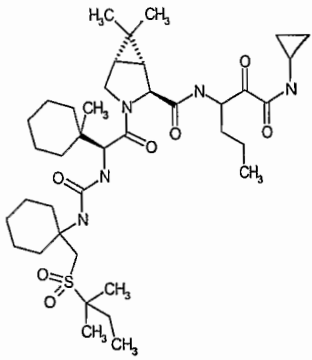
511	 Chemical structure of compound 511: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CF₃) and a nitrogen atom. This nitrogen is part of a larger system including a pyrrolidine ring, a carbonyl group, and a side chain with a terminal vinyl group (CH=CH₂). The side chain also includes a carbonyl group and a methyl group.	734		A
512	 Chemical structure of compound 512: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom. This nitrogen is part of a larger system including a pyrrolidine ring, a carbonyl group, and a side chain with a terminal alkyne group (C≡CH). The side chain also includes a carbonyl group and a methyl group.	732	733.4	A

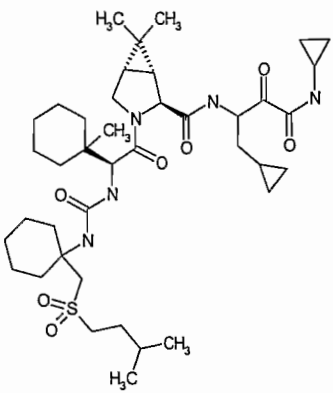
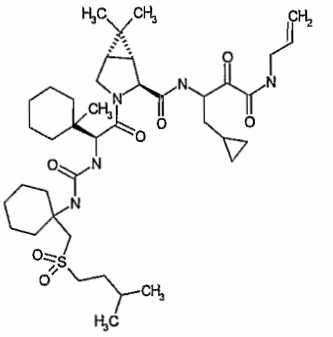
513	 Chemical structure of compound 513: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group at the 2-position, a dimethylamino group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is linked to a side chain containing a cyclopropyl group, a carbonyl group, and a dimethylamino group. The side chain also includes a sulfonamide group (SO₂CH₃) and a dimethylamino group.	734	734.4	A
514	 Chemical structure of compound 514: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group at the 2-position, a dimethylamino group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is linked to a side chain containing a cyclopropyl group, a carbonyl group, and a dimethylamino group. The side chain also includes a sulfonamide group (SO₂CH₃) and a dimethylamino group.	748		A

515	 <chem>CC1(C)C(C2CCCCC2C1C(=O)N(C)C(=O)N(C)C(F)(F)F)C(=O)N(C)C(=O)N3CCCCC3C(S(=O)(=O)C(C)(C)C)C4CCCCC4</chem>	788		A
516	 <chem>CC1(C)C(C2CCCCC2C1C(=O)N(C)C(=O)N(C)C=C)C(=O)N(C)C(=O)N3CCCCC3C(S(=O)(=O)C4=CC=CC=C4)C5CCCCC5</chem>	808.102	809.1	A

517		808.102	809.1	B
518		796.0908	797.1	A

519		719.992		A
520		746.0303		B

521	 Chemical structure of compound 521: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a cyclopropyl group. Another side chain on the cyclohexane ring includes a carbonyl group, a nitrogen atom, and a cyclohexyl group. A third side chain on the cyclohexane ring consists of a carbonyl group, a nitrogen atom, and a cyclohexyl group. The molecule also contains a sulfonamide group (SO₂CH₃) and a cyclopropyl group.	762.0733		A
522	 Chemical structure of compound 522: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a cyclopropyl group. Another side chain on the cyclohexane ring includes a carbonyl group, a nitrogen atom, and a cyclohexyl group. A third side chain on the cyclohexane ring consists of a carbonyl group, a nitrogen atom, and a cyclohexyl group. The molecule also contains a sulfonamide group (SO₂CH₃) and a cyclopropyl group.	748.0462		A

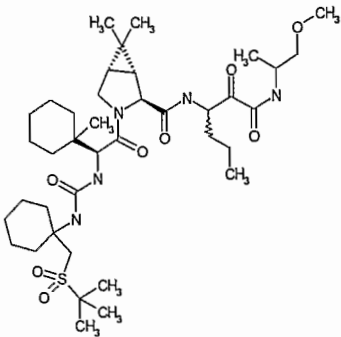
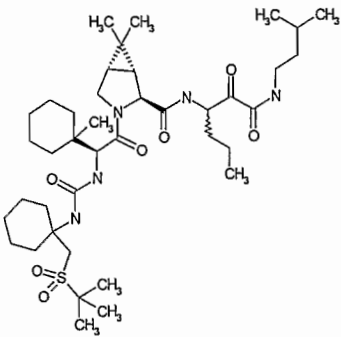
523		760.0574		A
524		760.0574		A

525		771.9474	A
526		693.9538	A

CN(C)C(=O)N(CCC1CCCC1)C(=O)N[C@@H]2C[C@H](C)[C@H](C)[C@H]2C(=O)N(C)C(=O)N(CCCC3CCCC3)C(=O)N=C/C=C\

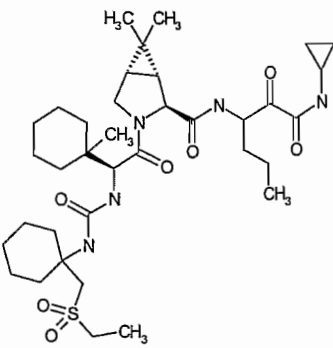
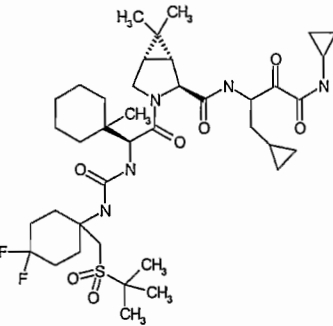
529		717.9761		A
530		717.9761		A

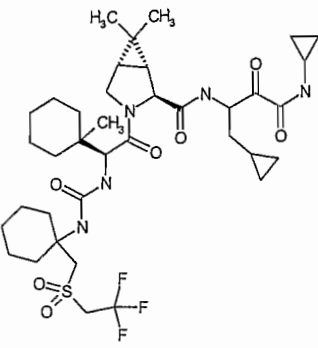
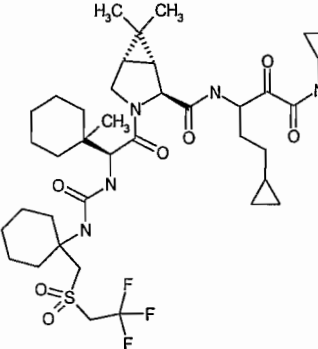
The chemical structure is a complex molecule featuring a central cyclohexane ring. Attached to this ring is a carbamate group (N-C(=O)-O-CH₂-C₆H₅) and a sulfonamide group (N-C(=O)-SO₂-C(CH₃)₃). The sulfonamide group is further substituted with a cyclopropylmethyl group. The carbamate group is also substituted with a cyclopropylmethyl group. The molecule is highly branched and contains multiple functional groups, including amide, carbamate, sulfonamide, and ether linkages.

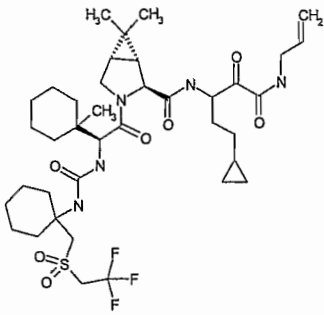
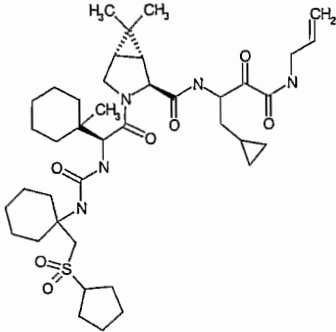
533	 Chemical structure of compound 533: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopropane ring with a methyl group and a methyl ester group. The cyclohexane ring is also substituted with a sulfonamide group (SO₂CH₃) and a carbamate group (NHCOCH₃). The carbamate group is further substituted with a methyl group and a methyl ester group.	766.0615	766.4	B
534	 Chemical structure of compound 534: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopropane ring with a methyl group and a methyl ester group. The cyclohexane ring is also substituted with a sulfonamide group (SO₂CH₃) and a carbamate group (NHCOCH₃). The carbamate group is further substituted with a methyl group and a methyl ester group.	764.0892	764.4	C

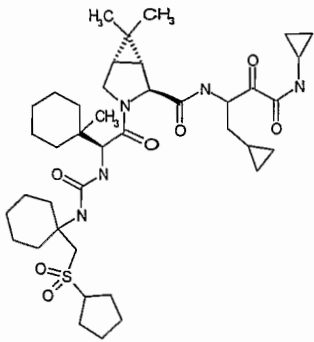
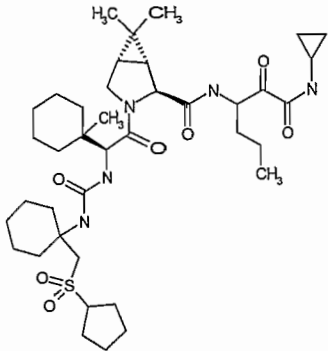
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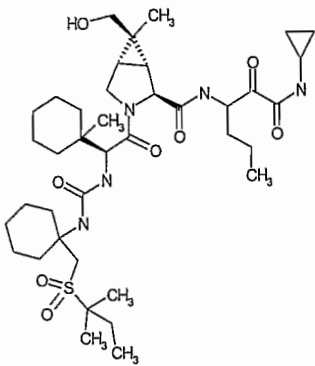
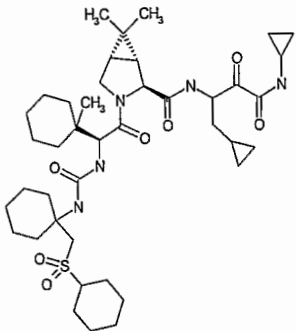
CN(C)C(=O)N(CC1CC1)C(=O)N[C@@H](C)[C@H](C)C(=O)N2C[C@H](OC3(C)C)C[C@H]2C(=O)NC(=O)N(CCCC4CCCCC4)S(=O)(=O)C(C)(C)C

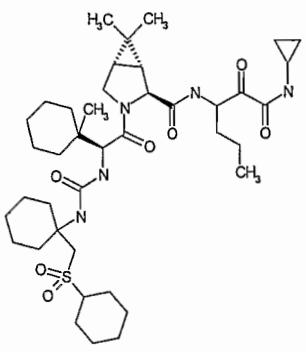
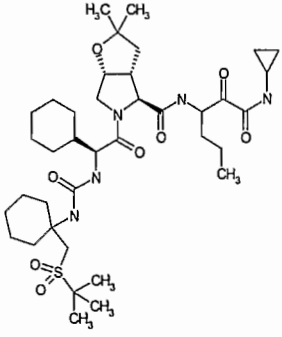
539	 Chemical structure of compound 539: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopropane ring with two methyl groups (H₃C, CH₃) and a carbonyl group. The cyclohexane ring also has a methyl group (CH₃) and a carbonyl group. A sulfonamide group (SO₂CH₂CH₃) is attached to the cyclohexane ring. The molecule also includes a cyclopropylmethyl group and a carbonyl group.	705.9649		A
540	 Chemical structure of compound 540: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopropane ring with two methyl groups (H₃C, CH₃) and a carbonyl group. The cyclohexane ring also has a methyl group (CH₃) and a carbonyl group. A sulfonamide group (SO₂CH₂CH₃) is attached to the cyclohexane ring. The molecule also includes a cyclopropylmethyl group and a carbonyl group.	782.0111		A

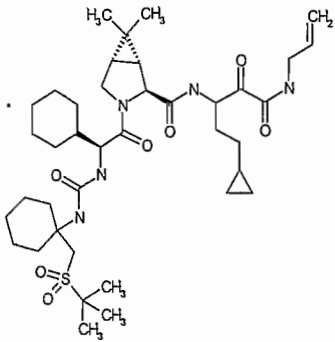
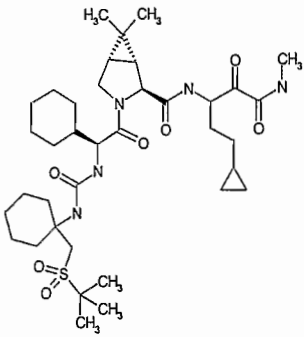
541		771.9474		A
542		785.9745		A

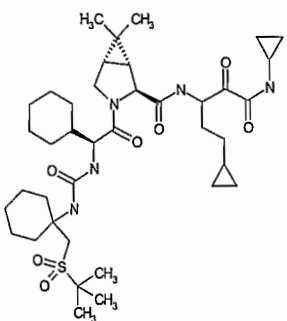
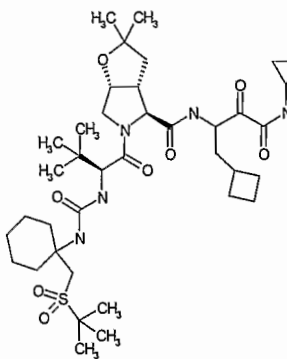
543		785.9745		A
544		758.0414		A

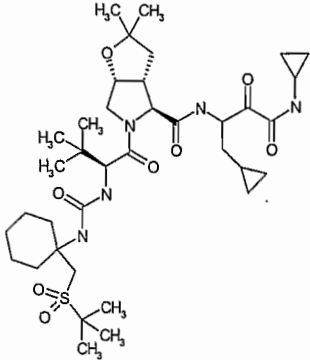
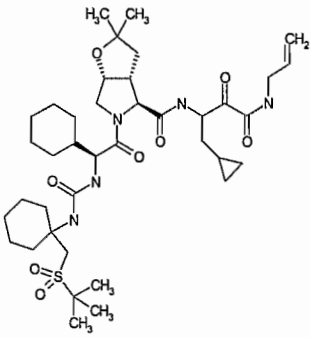
545		758.0414		A
546		746.0303		A

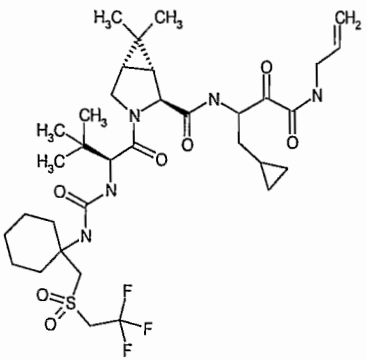
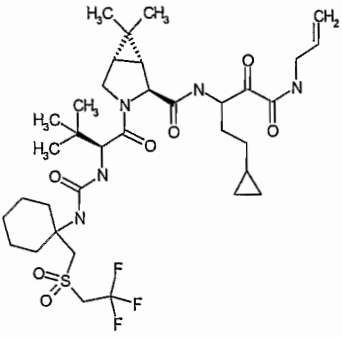
549		764.0456		A
550		772.0685		A

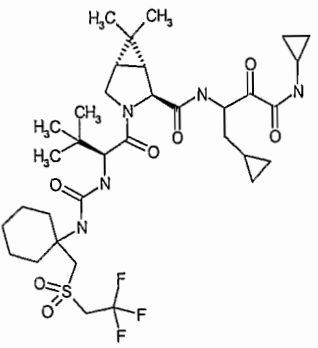
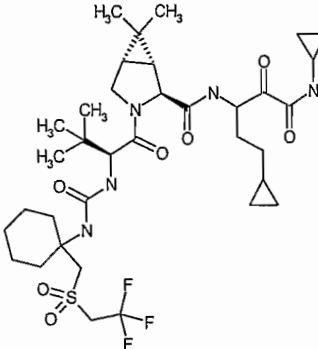
551	 Chemical structure of compound 551: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a cyclohexyl group. It is also linked via amide bonds to a side chain containing a methyl group (CH₃) and a cyclopropyl group. Additionally, the pyrrolidine ring is connected to a sulfonamide group, which is further substituted with a cyclohexyl group.	760.0574		A
552	 Chemical structure of compound 552: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a cyclohexyl group. It is also linked via amide bonds to a side chain containing a methyl group (CH₃) and a cyclopropyl group. Additionally, the pyrrolidine ring is connected to a sulfonamide group, which is further substituted with a cyclohexyl group.	750.0185	750.1	B

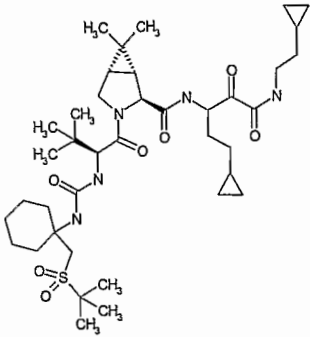
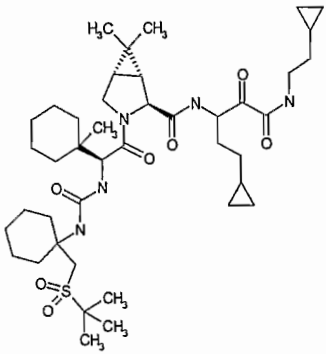
553		746.0303		A
554		719.992		A

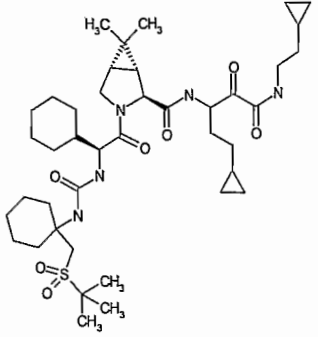
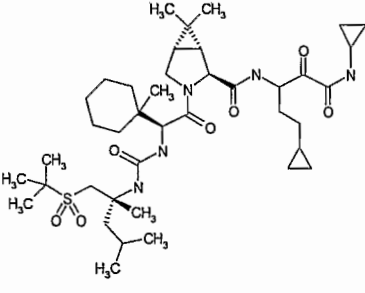
555		746.0303		A
556		750.0185	750.1	B

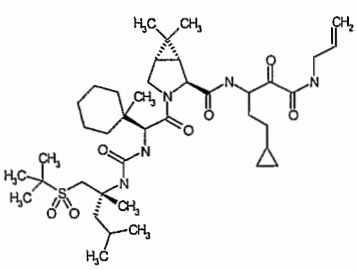
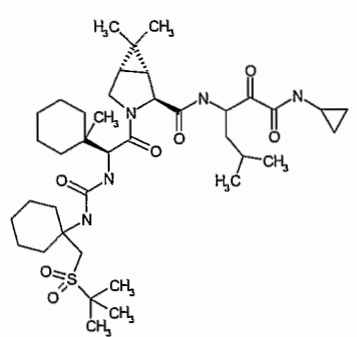
559	 Chemical structure of compound 559: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1,3-dioxolane group at the 2-position, a 2,2,3-trimethylbutyramide group at the 3-position, and a 2,2,3-trimethylbutyramide group at the 4-position. The 2,2,3-trimethylbutyramide group at the 3-position is further substituted with a 2,2,3-trimethylbutyramide group at the 2-position. The 2,2,3-trimethylbutyramide group at the 4-position is further substituted with a 2,2,3-trimethylbutyramide group at the 2-position. The 2,2,3-trimethylbutyramide group at the 2-position is further substituted with a 2,2,3-trimethylbutyramide group at the 2-position.	735.9914		B
560	 Chemical structure of compound 560: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1,3-dioxolane group at the 2-position, a 2,2,3-trimethylbutyramide group at the 3-position, and a 2,2,3-trimethylbutyramide group at the 4-position. The 2,2,3-trimethylbutyramide group at the 3-position is further substituted with a 2,2,3-trimethylbutyramide group at the 2-position. The 2,2,3-trimethylbutyramide group at the 4-position is further substituted with a 2,2,3-trimethylbutyramide group at the 2-position. The 2,2,3-trimethylbutyramide group at the 2-position is further substituted with a 2,2,3-trimethylbutyramide group at the 2-position.	762.0297		A

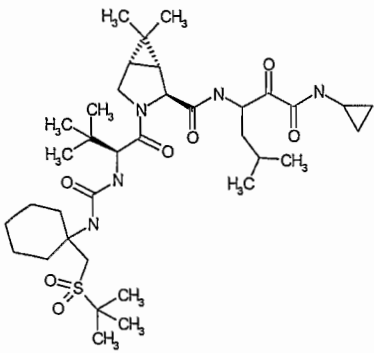
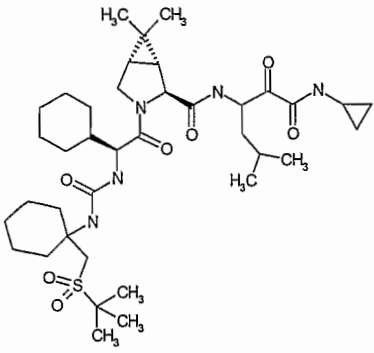
563	 Chemical structure of compound 563: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CF₃) and a carbamate group. The carbamate is linked to a pyrrolidine ring, which is further substituted with a methyl group and a vinyl group. The pyrrolidine ring is also linked to a carbonyl group, which is part of a larger amide structure.	731.882		A
564	 Chemical structure of compound 564: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CF₃) and a carbamate group. The carbamate is linked to a pyrrolidine ring, which is further substituted with a methyl group and a vinyl group. The pyrrolidine ring is also linked to a carbonyl group, which is part of a larger amide structure.	745.9091		A

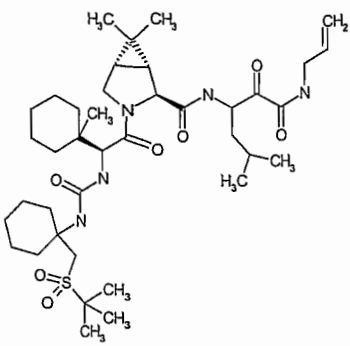
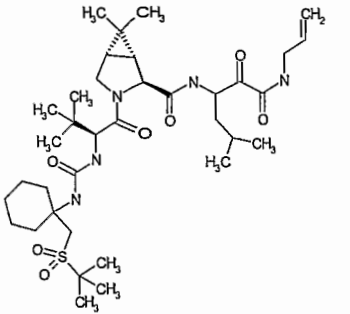
565		731.882		A
566		745.9091		1A

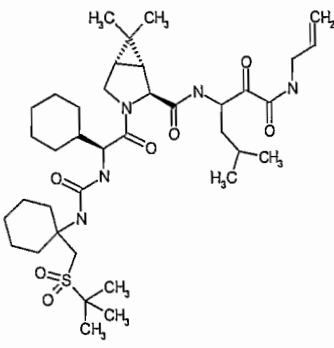
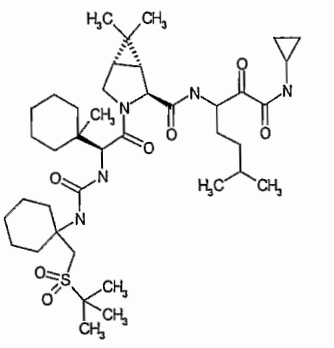
567		748.0462		A
568		788.1115		A

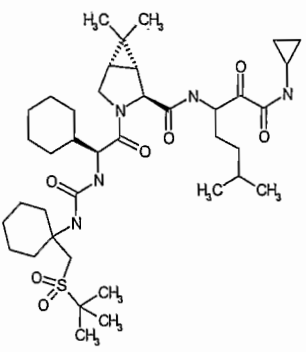
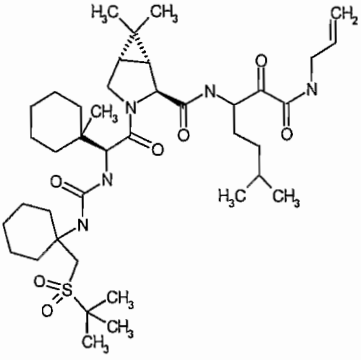
569	 Chemical structure of compound 569: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group at the 2-position, a dimethylamino group at the 3-position, and a side chain at the 4-position. The side chain consists of a carbonyl group linked to a methylene group, which is further linked to a carbonyl group, and finally to a cyclopropylmethyl group. The cyclohexyl group is also substituted with a dimethylsulfonylmethyl group at the 1-position.	774.0844		A
570	 Chemical structure of compound 570: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group at the 2-position, a dimethylamino group at the 3-position, and a side chain at the 4-position. The side chain consists of a carbonyl group linked to a methylene group, which is further linked to a carbonyl group, and finally to a cyclopropylmethyl group. The cyclohexyl group is also substituted with a dimethylsulfonylmethyl group at the 1-position.	762.0733	763.1	A

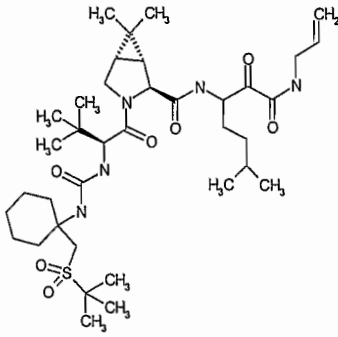
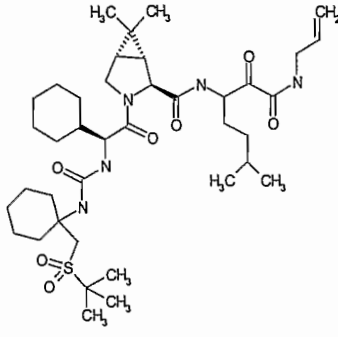
571	 Chemical structure of compound 571: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a cyclopropyl group, a carbonyl group, and a terminal vinyl group. Another side chain includes a sulfonamide group and a methyl group.	762.0733	763.1	A
572	 Chemical structure of compound 572: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a cyclopropyl group, a carbonyl group, and a methyl group. Another side chain includes a sulfonamide group and a methyl group.	748.0462		B

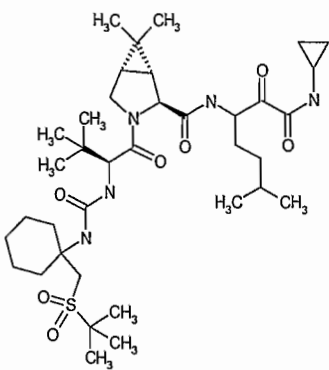
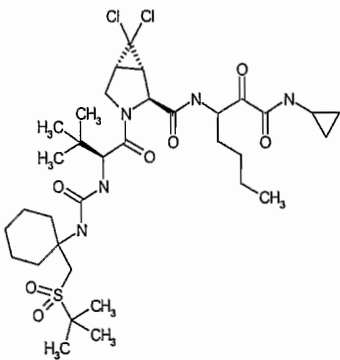
573		707.9809		B
574		734.0191		B

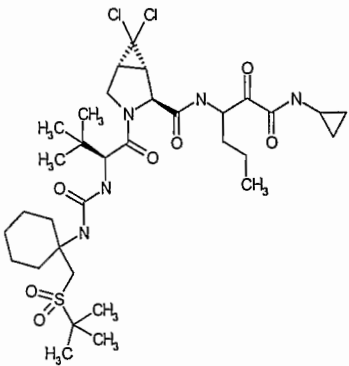
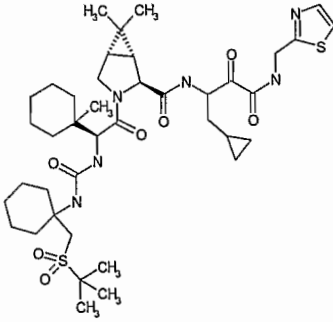
575		748.0462		B
576		707.9809		B

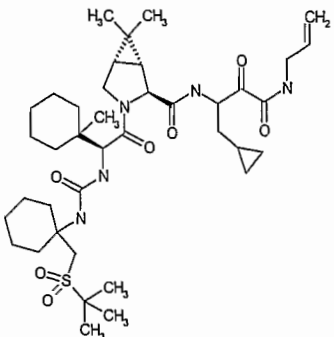
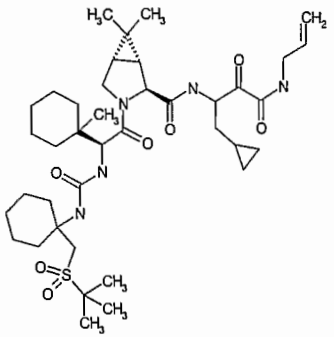
577	 Chemical structure of compound 577: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a sulfonamide group. The sulfonamide group is further substituted with a cyclohexylmethyl group and a dimethylsulfonyl group. The nitrogen atom is also part of a larger ring system that includes a carbonyl group and a dimethylsulfonyl group. The molecule is highly branched and contains multiple functional groups.	734.0191		C
578	 Chemical structure of compound 578: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a sulfonamide group. The sulfonamide group is further substituted with a cyclohexylmethyl group and a dimethylsulfonyl group. The nitrogen atom is also part of a larger ring system that includes a carbonyl group and a dimethylsulfonyl group. The molecule is highly branched and contains multiple functional groups.	762.0733	762.4	B

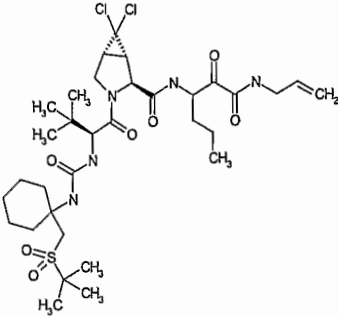
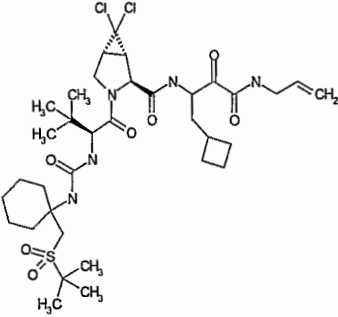
579	 Chemical structure of compound 579: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group at the 2-position, a dimethylamino group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a methylene group, a carbonyl group, and a nitrogen atom. The nitrogen atom is substituted with a cyclopropyl group and a dimethylamino group. The side chain also includes a dimethylamino group and a carbonyl group. The molecule is further substituted with a dimethylamino group and a carbonyl group.	748.0462	748.4	A
580	 Chemical structure of compound 580: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a cyclohexyl group at the 2-position, a dimethylamino group at the 3-position, and a carbonyl group at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a methylene group, a carbonyl group, and a nitrogen atom. The nitrogen atom is substituted with a cyclopropyl group and a dimethylamino group. The side chain also includes a dimethylamino group and a carbonyl group. The molecule is further substituted with a dimethylamino group and a carbonyl group.	762.0733		A

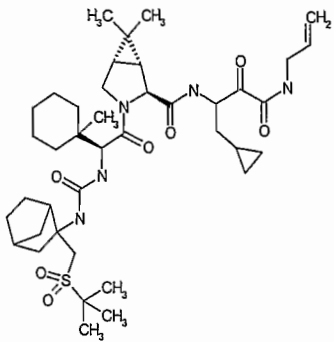
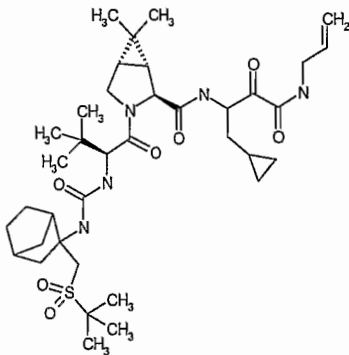
581		722.008		A
582		748.0462		A

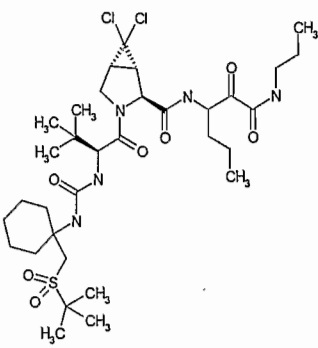
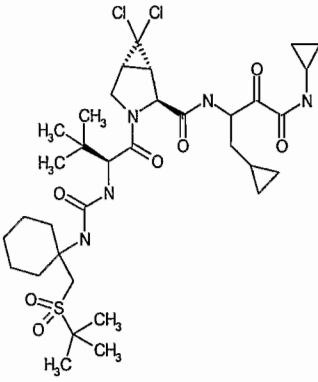
583	 Chemical structure of compound 583: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom. This nitrogen is part of a chain containing a carbonyl group, a tertiary amine, and a cyclopropylmethyl group. The chain also includes a carbonyl group and a cyclopropylmethyl group. The molecule is further substituted with a dimethylamino group and a carbonyl group.	722.008	722.4	A
584	 Chemical structure of compound 584: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom. This nitrogen is part of a chain containing a carbonyl group, a tertiary amine, and a cyclopropylmethyl group. The chain also includes a carbonyl group and a cyclopropylmethyl group. The molecule is further substituted with a dimethylamino group and a carbonyl group.	748.8168	748.4	A

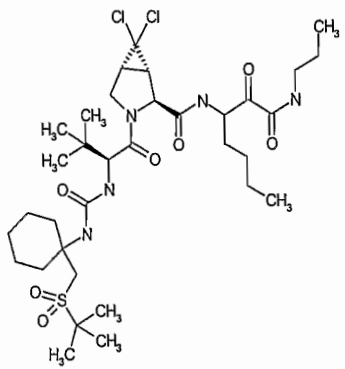
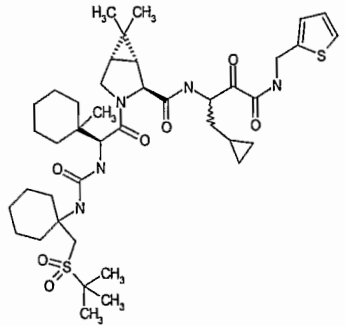
585		734.7897	734.4	A
586		803.1041	803.4	A

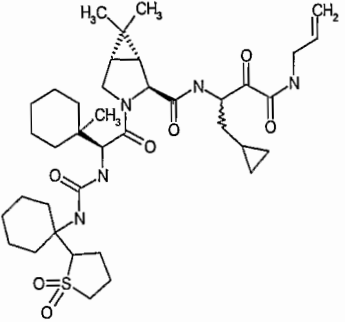
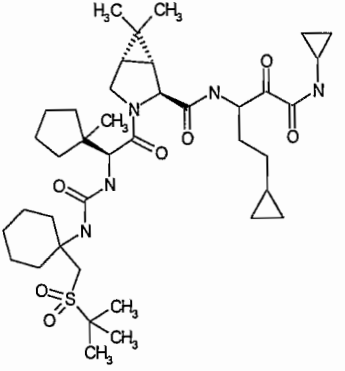
587	 The chemical structure shows a cyclohexane ring substituted with a sulfonamide group (-SO₂CH₂-) and a pyrrolidine ring. The pyrrolidine ring is further substituted with a cyclopropyl group and a vinyl group (-CH=CH₂). The sulfonamide group is attached to a cyclohexane ring via a methylene bridge.	746.0303		C
588	 The chemical structure is identical to the one in row 587, showing a cyclohexane ring substituted with a sulfonamide group (-SO₂CH₂-) and a pyrrolidine ring. The pyrrolidine ring is further substituted with a cyclopropyl group and a vinyl group (-CH=CH₂). The sulfonamide group is attached to a cyclohexane ring via a methylene bridge.	746.0303		6

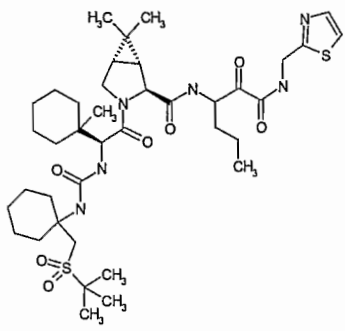
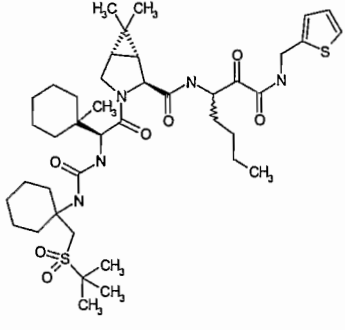
589	 Chemical structure of compound 589: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom connected to a carbonyl group. This carbonyl is part of a larger amide system, which includes a cyclopropane ring substituted with two chlorine atoms (Cl₂). The molecule also contains a vinyl group (CH=CH₂) and a methyl group (CH₃).	734.7897	734.1	A
590	 Chemical structure of compound 590: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₃) and a nitrogen atom connected to a carbonyl group. This carbonyl is part of a larger amide system, which includes a cyclopropane ring substituted with two chlorine atoms (Cl₂). The molecule also contains a vinyl group (CH=CH₂) and a methyl group (CH₃).	760.8279	760.1	A

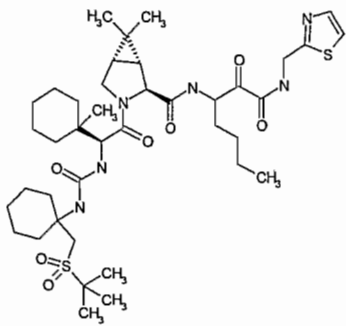
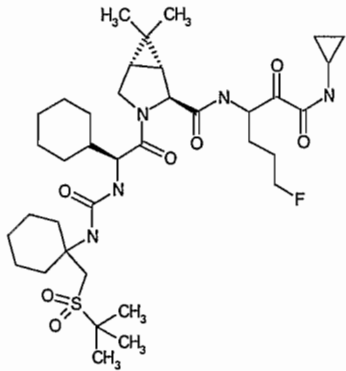
591		758.0414		A
592		717.9761		A

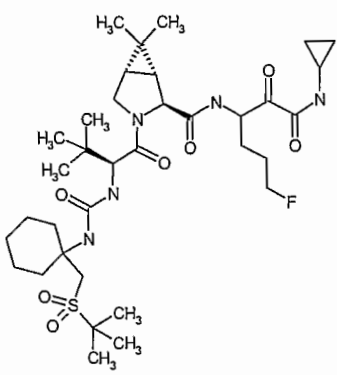
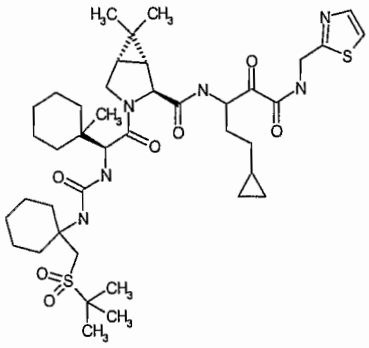
593	 Chemical structure of compound 593: A complex molecule featuring a central pyrrolidine ring substituted with two chlorine atoms. This ring is connected via amide bonds to a cyclohexylidene-protected amine and a side chain containing a ketone and a terminal ethyl group. A tert-butyl sulfonamide group is also attached to the cyclohexylidene moiety.	736.8056	736.1	A
594	 Chemical structure of compound 594: Similar to compound 593, but the side chain contains a ketone and a terminal cyclopropyl group instead of an ethyl group.	746.8008	746.1	A

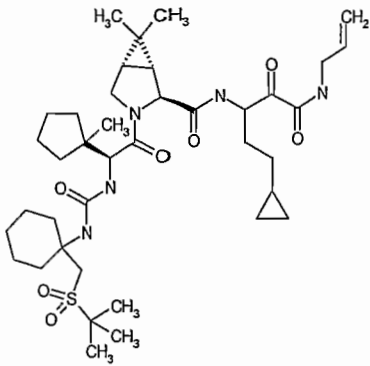
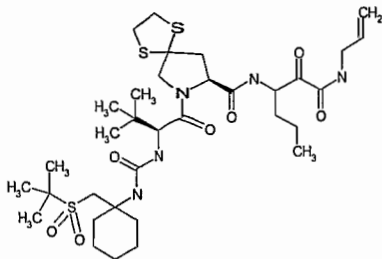
595	 Chemical structure of compound 595: A complex molecule featuring a cyclohexane ring substituted with a tert-butylsulfonyl group and a carbamate group. The carbamate is linked to a cyclopropane ring, which is further substituted with a dichloromethyl group and a carbonyl group. This carbonyl is part of a larger amide structure that includes a propyl chain and a terminal carbamate group.	750.8327	750.4	A
596	 Chemical structure of compound 596: A complex molecule featuring a cyclohexane ring substituted with a tert-butylsulfonyl group and a carbamate group. The carbamate is linked to a cyclopropane ring, which is further substituted with a methyl group and a carbonyl group. This carbonyl is part of a larger amide structure that includes a thienylmethyl group and a carbonyl group.	802.1166	802.5	A

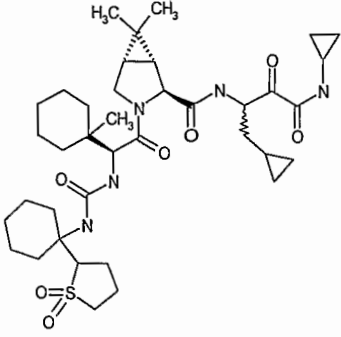
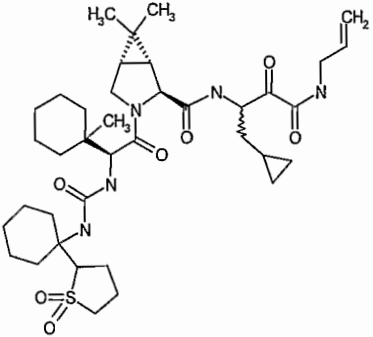
597	 Chemical structure of compound 597: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge and dash), a 2-methyl-2-(cyclohexyl) group, and a 2-((2-methyl-2-(cyclohexyl)ethyl)thio)ethyl group. The pyrrolidine ring is also substituted with a 2-((2-methyl-2-(cyclohexyl)ethyl)thio)ethyl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a vinyl group.	729.9872	731.4	A
598	 Chemical structure of compound 598: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge and dash), a 2-methyl-2-(cyclohexyl) group, and a 2-((2-methyl-2-(cyclohexyl)ethyl)thio)ethyl group. The pyrrolidine ring is also substituted with a 2-((2-methyl-2-(cyclohexyl)ethyl)thio)ethyl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a vinyl group.	746.0303	746.4	A

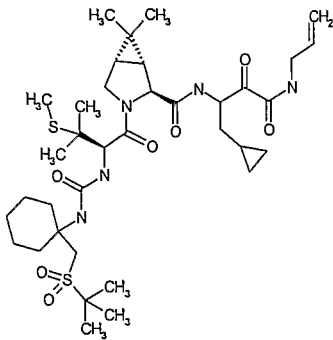
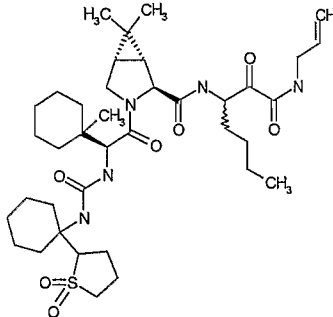
599		791.093	791.4	A
600		804.1325	804.5	A

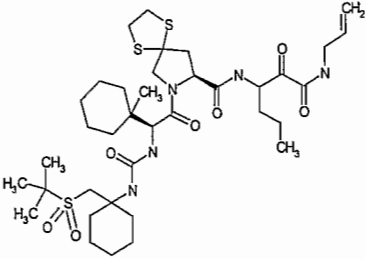
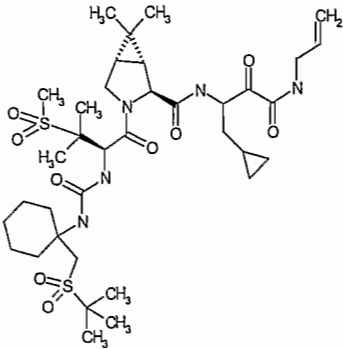
601	 Chemical structure of compound 601: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a thiazole ring, a carbonyl group, and a propyl group. Another side chain features a sulfonamide group and a cyclohexyl ring.	805.1201	805.4	A
602	 Chemical structure of compound 602: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl group is part of a larger amide structure. A side chain includes a carbonyl group, a propyl group, and a fluorine atom. Another side chain features a sulfonamide group and a cyclohexyl ring.	737.9825		A

603	 Chemical structure of compound 603: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a methyl group (CH₃) at the 2-position, and a methyl group (CH₃) at the 3-position. The pyrrolidine ring is also substituted with a methyl group (CH₃) at the 4-position. The pyrrolidine ring is connected via a carbonyl group (C=O) to a nitrogen atom (N), which is further connected to a carbonyl group (C=O) and a fluorine atom (F). The pyrrolidine ring is also connected via a carbonyl group (C=O) to a nitrogen atom (N), which is further connected to a carbonyl group (C=O) and a fluorine atom (F). The pyrrolidine ring is also connected via a carbonyl group (C=O) to a nitrogen atom (N), which is further connected to a carbonyl group (C=O) and a fluorine atom (F).	711.9442		A
604	 Chemical structure of compound 604: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a methyl group (CH₃) at the 2-position, and a methyl group (CH₃) at the 3-position. The pyrrolidine ring is also substituted with a methyl group (CH₃) at the 4-position. The pyrrolidine ring is connected via a carbonyl group (C=O) to a nitrogen atom (N), which is further connected to a carbonyl group (C=O) and a fluorine atom (F). The pyrrolidine ring is also connected via a carbonyl group (C=O) to a nitrogen atom (N), which is further connected to a carbonyl group (C=O) and a fluorine atom (F). The pyrrolidine ring is also connected via a carbonyl group (C=O) to a nitrogen atom (N), which is further connected to a carbonyl group (C=O) and a fluorine atom (F).	817.1312	817.4	A

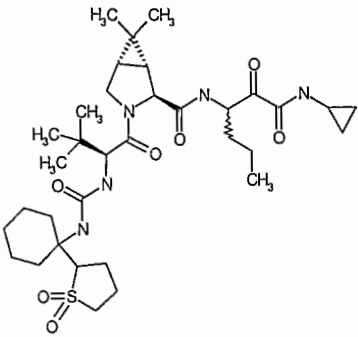
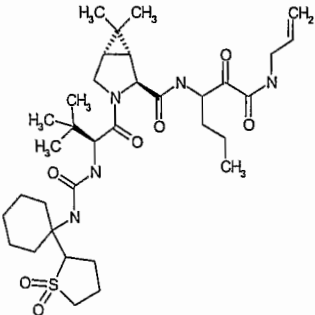
605	 Chemical structure of compound 605: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N). The nitrogen atom is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N). The nitrogen atom is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N). The nitrogen atom is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N).	746.0303	746.4	A
606	 Chemical structure of compound 606: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N). The nitrogen atom is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N). The nitrogen atom is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N). The nitrogen atom is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group (C=O) and a nitrogen atom (N).	744.0547	745.1	A

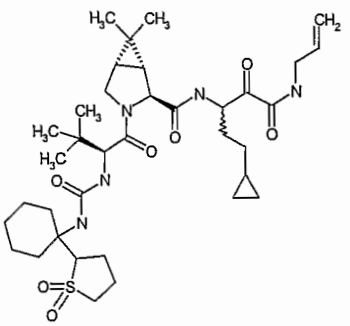
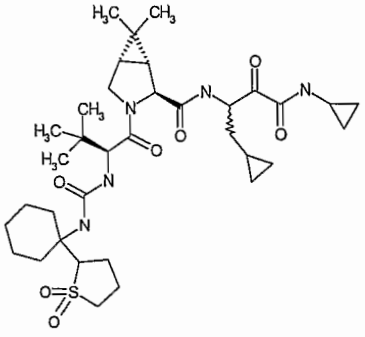
607	 Chemical structure of compound 607: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge bond to methyl, dash bond to propyl), a methyl group, and a carbonyl group. This pyrrolidine is linked via an amide bond to a cyclopropane ring, which is further substituted with a carbonyl group and a 1-cyclopropyl-2-oxoethyl group. Another amide branch from the central pyrrolidine leads to a cyclohexane ring, which is substituted with a carbonyl group and a 1-cyclohexyl-2-sulfonyl-1-cyclopentyl group.	729.9872		A
608	 Chemical structure of compound 608: Similar to compound 607, but the 1-cyclopropyl-2-oxoethyl group is replaced by a 1-cyclopropyl-2-oxo-3-vinylethyl group, where the vinyl group is represented as -CH=CH₂.	729.9872	730.4	A

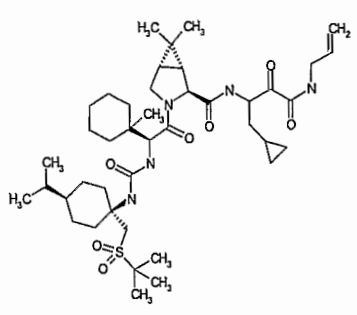
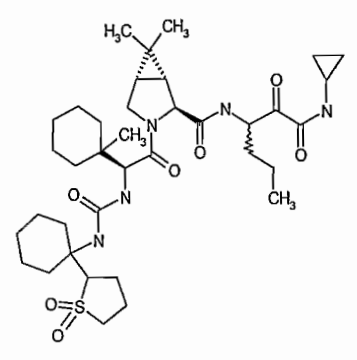
609		738.0289	738.1	A
610		732.0032	732.1	A

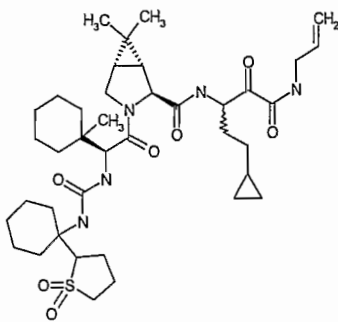
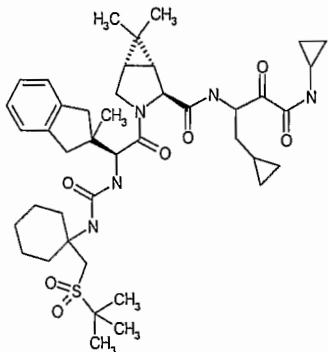
613		784.12	784.2	A
614		770.0277	770.2	B

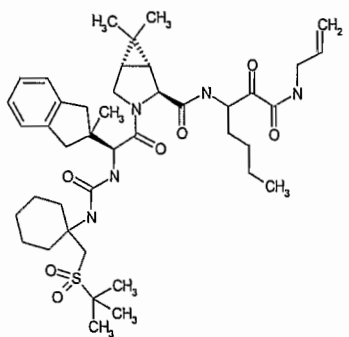
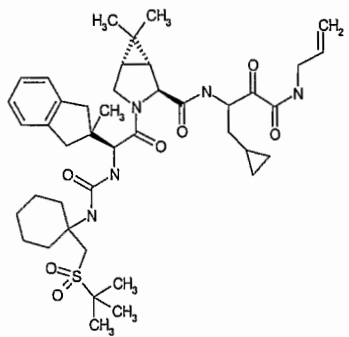
615		717.9761		A
616		689.9219		A

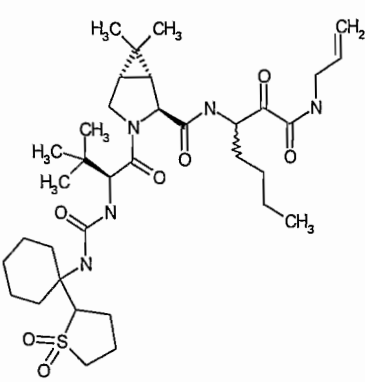
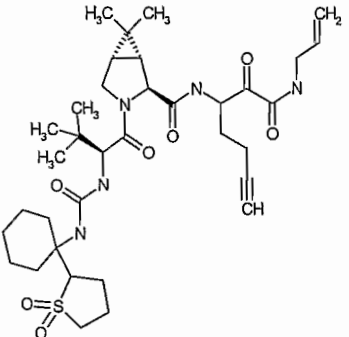
617	 Chemical structure of compound 617: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyl group, a 2,2,3-trimethylbutyl group, and a 2,2,3-trimethylbutyl group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutyl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a cyclopentyl group.	677.9108	678.4	A
618	 Chemical structure of compound 618: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyl group, a 2,2,3-trimethylbutyl group, and a 2,2,3-trimethylbutyl group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutyl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a cyclopentyl group.	677.9108	678.4	A

619	 Chemical structure of compound 619: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,3-trimethylbutan-3-yl group, a 2,2,3-trimethylbutan-3-yl group, and a 2,2,3-trimethylbutan-3-yl group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutan-3-yl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a vinyl group.	703.949	704.4	A
620	 Chemical structure of compound 620: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,3-trimethylbutan-3-yl group, a 2,2,3-trimethylbutan-3-yl group, and a 2,2,3-trimethylbutan-3-yl group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutan-3-yl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a vinyl group.	689.9219	690.4	A

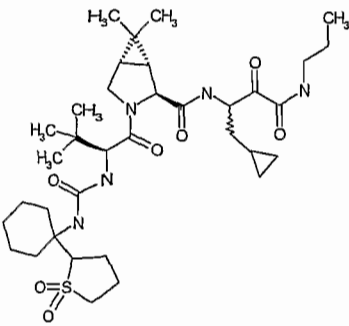
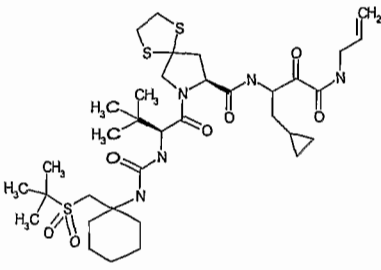
621	 Chemical structure of compound 621: A complex molecule featuring a central cyclohexane ring. One carbon of the cyclohexane is part of a bicyclic system with a cyclopropane ring fused to it. Another carbon of the cyclohexane is attached to a nitrogen atom, which is part of a five-membered ring containing a carbonyl group. This five-membered ring is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group and a terminal vinyl group. A third carbon of the cyclohexane is attached to a nitrogen atom, which is part of a five-membered ring containing a carbonyl group. This five-membered ring is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group and a terminal vinyl group. A fourth carbon of the cyclohexane is attached to a nitrogen atom, which is part of a five-membered ring containing a carbonyl group. This five-membered ring is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group and a terminal vinyl group.	788.1115	789.4	C
622	 Chemical structure of compound 622: A complex molecule featuring a central cyclohexane ring. One carbon of the cyclohexane is part of a bicyclic system with a cyclopropane ring fused to it. Another carbon of the cyclohexane is attached to a nitrogen atom, which is part of a five-membered ring containing a carbonyl group. This five-membered ring is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group and a terminal vinyl group. A third carbon of the cyclohexane is attached to a nitrogen atom, which is part of a five-membered ring containing a carbonyl group. This five-membered ring is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group and a terminal vinyl group. A fourth carbon of the cyclohexane is attached to a nitrogen atom, which is part of a five-membered ring containing a carbonyl group. This five-membered ring is further substituted with a cyclopropylmethyl group and a side chain containing a carbonyl group and a terminal vinyl group.	717.9761	718.1	A

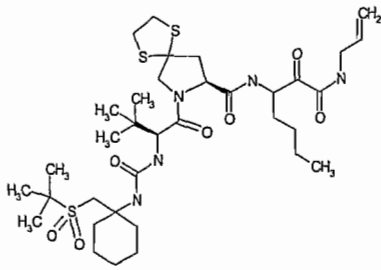
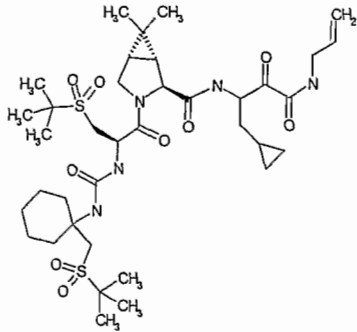
623		744.0143	744.1	A
624		780.0478	780.5	B

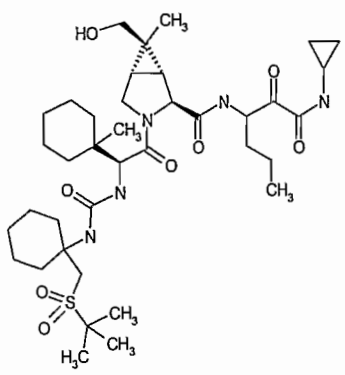
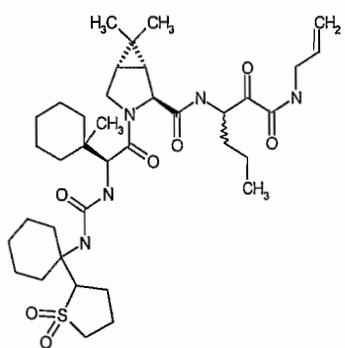
625	 Chemical structure of compound 625: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2-methyl-2-phenyl-1,3-dioxane-5-carbonyl group, a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group, and a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group.	782.0637	782.5	A
626	 Chemical structure of compound 626: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2-methyl-2-phenyl-1,3-dioxane-5-carbonyl group, a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group, and a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-(propylsulfonyl)-1,3-dioxane-5-carbonyl group.	780.0478	780.5	A

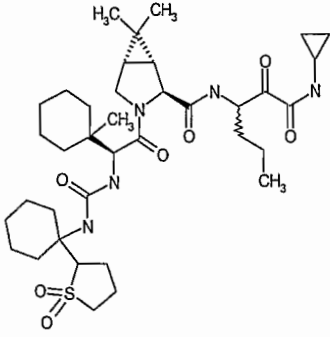
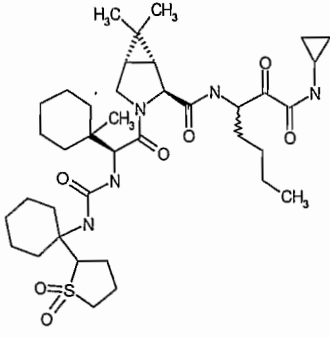
629	 Chemical structure of compound 629: A complex molecule featuring a cyclohexane ring fused to a cyclopentane ring, which is substituted with a sulfone group (SO₂). This is connected via a nitrogen atom to a carbonyl group, which is further linked to a chain containing a cyclopropane ring substituted with two methyl groups (H₃C, CH₃). The chain continues with a carbonyl group, a methylene group, and another carbonyl group, ending in a vinyl group (CH=CH₂).	691.9378	692.4	A
630	 Chemical structure of compound 630: Similar to compound 629, but the terminal vinyl group (CH=CH₂) is replaced by a terminal alkyne group (C≡CH).	687.906	688.4	A

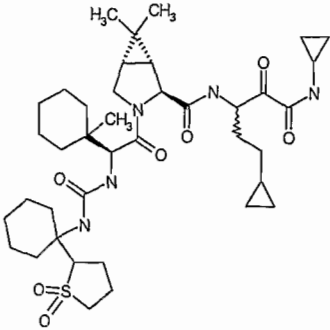
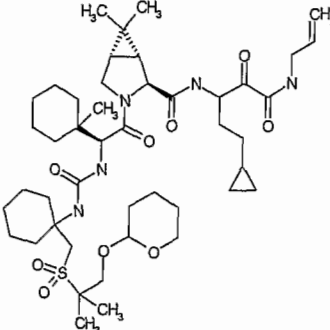
631		732.0032	732.4	A
632		679.9267	680.4	A

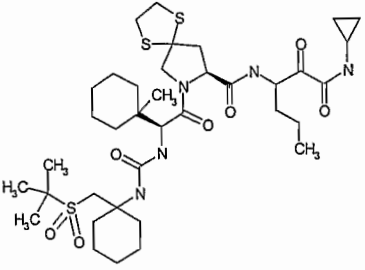
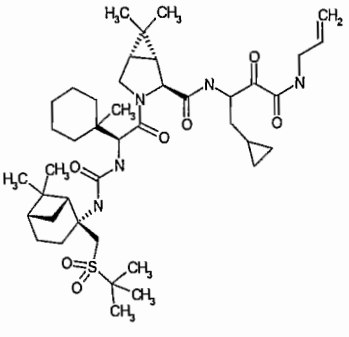
633		691.9378	692.4	A
634		756.0658	756.1	A

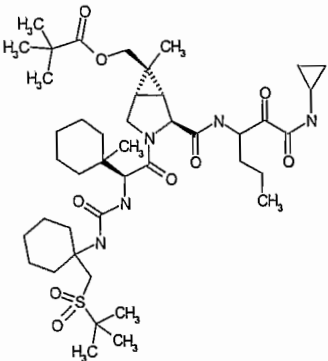
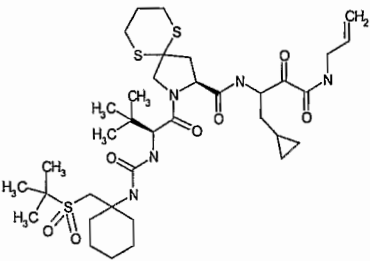
635		758.0818	758.1	A
636		784.0548	784.2	C

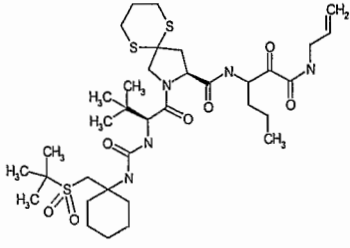
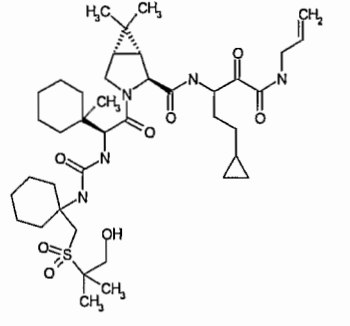
637	 Chemical structure of compound 637: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl is part of a larger amide system. A side chain includes a hydroxyl group, a methyl group, and a carbonyl group. Another side chain features a sulfonamide group (SO₂NH₂) and a methyl group.	750.0185		B
638	 Chemical structure of compound 638: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl is part of a larger amide system. A side chain includes a methyl group and a carbonyl group. Another side chain features a sulfonamide group (SO₂NH₂) and a methyl group.	717.9761	718.4	A

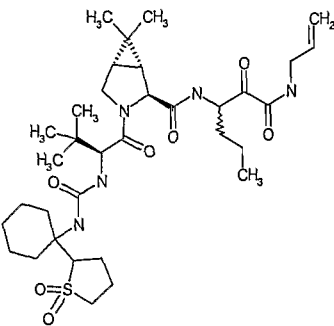
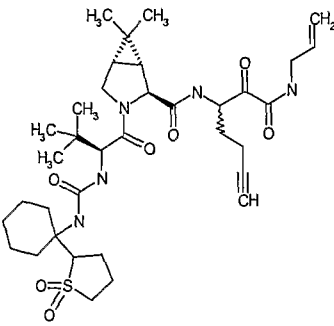
639	 Chemical structure of compound 639: A complex molecule featuring a central cyclopentane ring substituted with a methyl group and a dimethylamino group. This ring is connected via an amide bond to a side chain containing a cyclopropylmethyl ketone and a morpholine ring. Another amide branch connects the central ring to a cyclohexylmethyl ketone, which is further linked to a morpholine ring. A sulfonamide group is also present, attached to a cyclohexylmethyl ketone.	717.9761	718.4	A
640	 Chemical structure of compound 640: Similar to compound 639, but with a different side chain. The side chain contains a propylmethyl ketone instead of a cyclopropylmethyl ketone. The rest of the molecule, including the central cyclopentane ring, the dimethylamino group, and the sulfonamide branch, is identical to compound 639.	732.0032	732.4	A

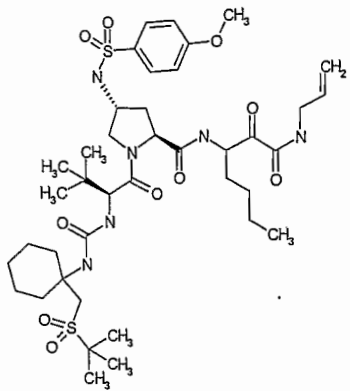
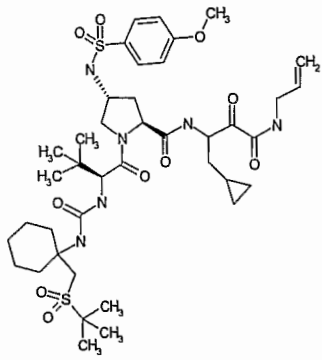
641		744.0143	744.4	A
642		860.1757		A

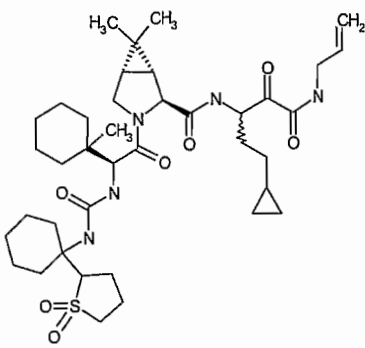
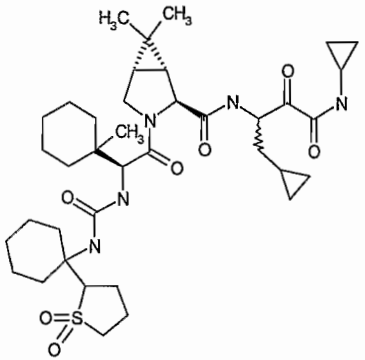
643	 Chemical structure of compound 643: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a sulfonamide group (SO₂CH₃). This cyclohexane is linked via an amide bond to a five-membered ring containing a sulfur atom and a methyl group. This five-membered ring is further linked via an amide bond to a side chain containing a methyl group, a carbonyl group, and a cyclopropyl group.	784.12		B
644	 Chemical structure of compound 644: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a sulfonamide group (SO₂CH₃). This cyclohexane is linked via an amide bond to a five-membered ring containing a sulfur atom and a methyl group. This five-membered ring is further linked via an amide bond to a side chain containing a methyl group, a carbonyl group, and a cyclopropyl group.	786.0956		B

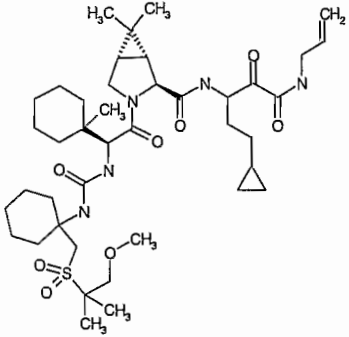
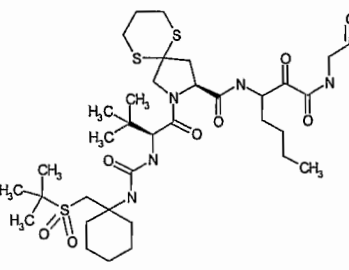
645		834.1374		B
646		770.0929	770.2	A

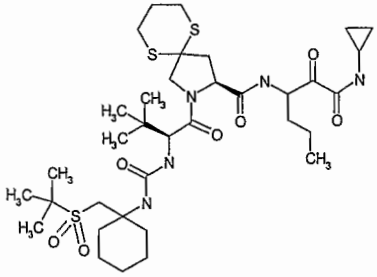
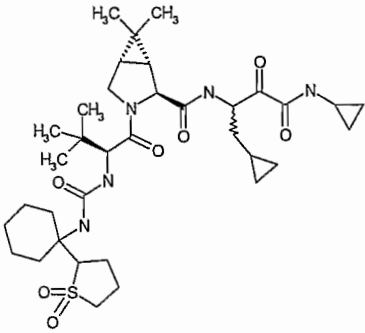
647	 Chemical structure of compound 647: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group. The 1,3-dithiane is also substituted with a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group. The 1,3-dithiane is also substituted with a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group.	758.0818	758.2	A
648	 Chemical structure of compound 648: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group. The 1,3-dithiane is also substituted with a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group. The 1,3-dithiane is also substituted with a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-sulfonyl group.	776.0568		A

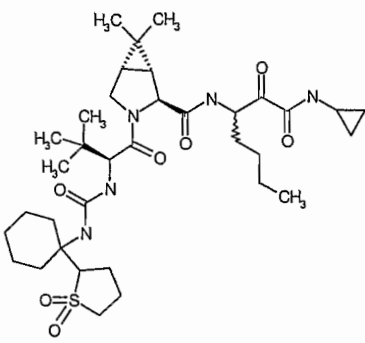
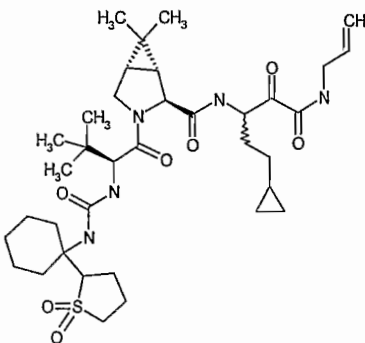
649	 Chemical structure of compound 649: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group, a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group, and a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group. The molecule includes a sulfonamide group, a cyclohexyl group, and a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group.	677.9108	678.2	A
650	 Chemical structure of compound 650: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group, a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group, and a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group. The molecule includes a sulfonamide group, a cyclohexyl group, and a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group.	687.906	688.2	A

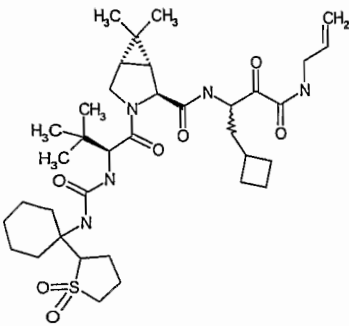
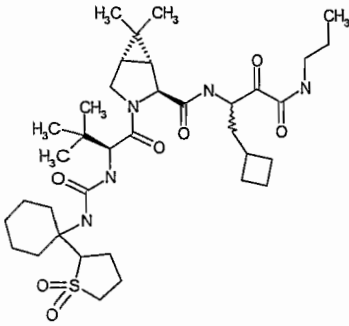
653	 Chemical structure of compound 653: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a (4-methoxyphenyl)sulfonyl group at the 2-position, a (1-oxo-2-methylpropyl) group at the 3-position, and a (1-oxo-2-methylpropyl) group at the 4-position. The pyrrolidine ring is also linked to a (1-oxo-2-methylpropyl) group at the 1-position. The (1-oxo-2-methylpropyl) group at the 3-position is further substituted with a (1-oxo-2-methylpropyl) group. The (1-oxo-2-methylpropyl) group at the 4-position is further substituted with a (1-oxo-2-methylpropyl) group. The (1-oxo-2-methylpropyl) group at the 1-position is further substituted with a (1-oxo-2-methylpropyl) group.	853.1183	853.4	C
654	 Chemical structure of compound 654: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a (4-methoxyphenyl)sulfonyl group at the 2-position, a (1-oxo-2-methylpropyl) group at the 3-position, and a (1-oxo-2-methylpropyl) group at the 4-position. The pyrrolidine ring is also linked to a (1-oxo-2-methylpropyl) group at the 1-position. The (1-oxo-2-methylpropyl) group at the 3-position is further substituted with a (1-oxo-2-methylpropyl) group. The (1-oxo-2-methylpropyl) group at the 4-position is further substituted with a (1-oxo-2-methylpropyl) group. The (1-oxo-2-methylpropyl) group at the 1-position is further substituted with a (1-oxo-2-methylpropyl) group.	851.1023	851.4	C

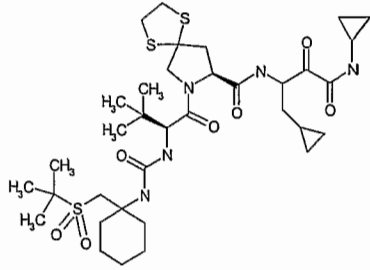
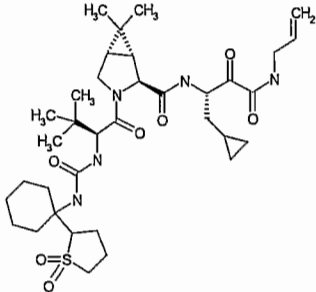
655	 Chemical structure of compound 655: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge and dash), a methyl group, and a carbonyl group. This pyrrolidine is linked via an amide bond to a side chain containing a cyclopropylmethyl group, a carbonyl group, and a terminal vinyl group (CH=CH₂). Another amide branch from the pyrrolidine connects to a sulfonamide group, which is further linked to a cyclohexyl ring and a sulfonamide group attached to a cyclopentyl ring.	744.0143	744.1	A
656	 Chemical structure of compound 656: Similar to compound 655, but the side chain is modified. It features a cyclopropylmethyl group, a carbonyl group, and a terminal cyclopropyl group instead of a vinyl group. The rest of the molecule, including the central pyrrolidine and the sulfonamide-linked rings, remains identical to compound 655.	729.9872	730.1	A

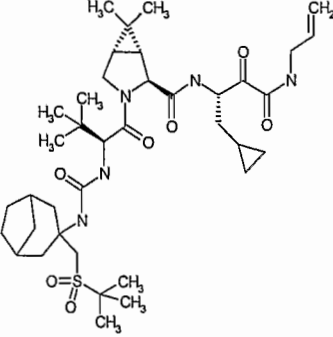
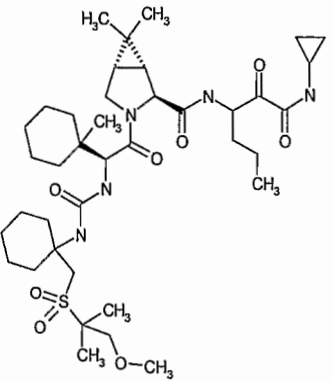
657		790.0838		A
658		772.1089	772.2	A

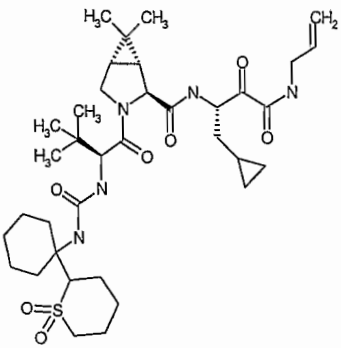
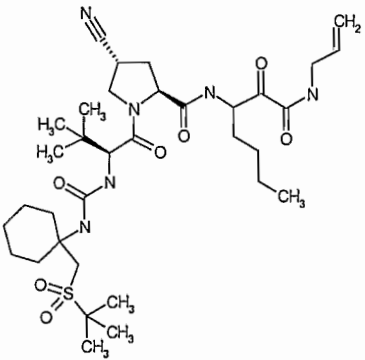
659	 Chemical structure of compound 659: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group. The 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group. The 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group.	758.0818	758.2	A
660	 Chemical structure of compound 660: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group and a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group. The 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group. The 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group.	689.9219	690.1	A

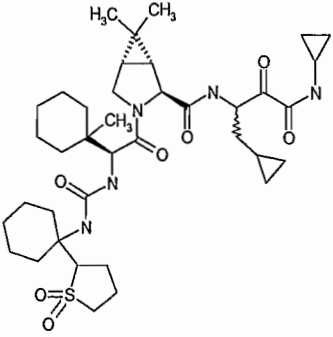
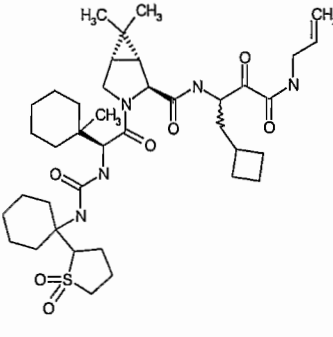
661	 Chemical structure of compound 661: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 2-position and a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 4-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 3-position. The pyrrolidine ring is further substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 5-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 6-position.	691.9378	692.1	A
662	 Chemical structure of compound 662: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 2-position and a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 4-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 3-position. The pyrrolidine ring is further substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 5-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 6-position.	703.949	704.1	A

663	 Chemical structure of compound 663: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group, a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group, and a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group. The molecule includes a sulfonamide group, a cyclobutyl group, and a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group.	703.949	704.1	A
664	 Chemical structure of compound 664: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-1,3-dioxolane-5-carbonyl group, a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group, and a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group. The molecule includes a sulfonamide group, a cyclobutyl group, and a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group.	705.9649	706.2	A

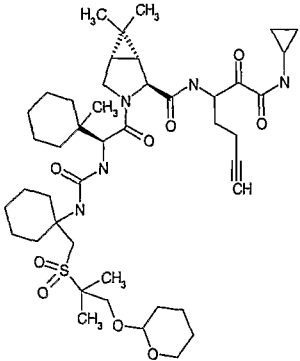
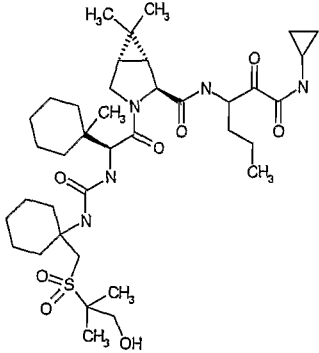
665		756.0658		B
666		689.9219		A

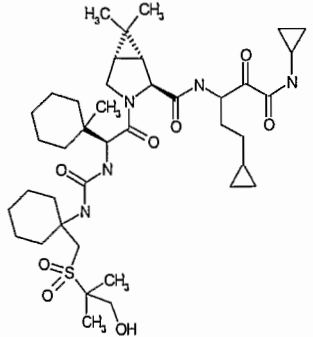
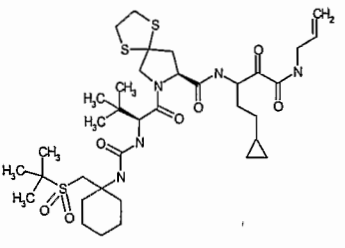
667		732.0032		A
668		764.0456		A

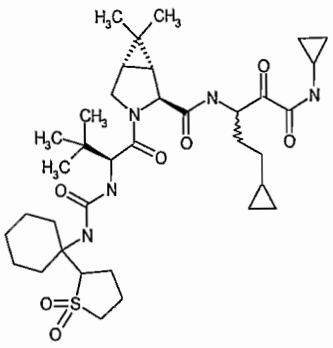
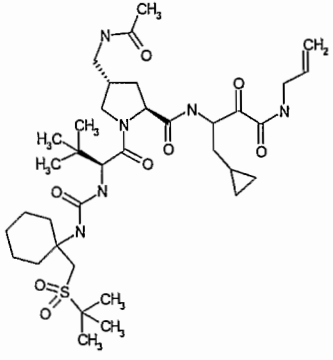
669	 Chemical structure of compound 669: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a cyclopropylmethyl group, and a side chain containing a carbonyl group and a terminal vinyl group. The pyrrolidine ring is also connected to a cyclohexane ring via a carbonyl group. The cyclohexane ring is further substituted with a sulfonamide group and a cyclopropylmethyl group.	703.949		A
670	 Chemical structure of compound 670: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group, a nitrile group, and a side chain containing a carbonyl group and a terminal vinyl group. The pyrrolidine ring is also connected to a cyclohexane ring via a carbonyl group. The cyclohexane ring is further substituted with a sulfonamide group and a cyclopropylmethyl group.	692.9254	693.3	C

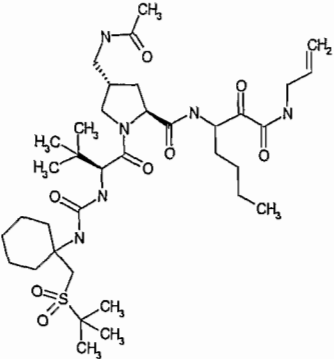
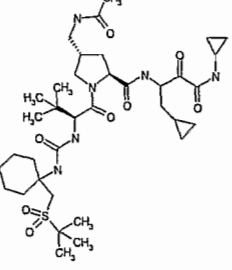
671	 Chemical structure of compound 671: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopentylidene sulfone group (a five-membered ring with a sulfur atom double-bonded to two oxygen atoms). Another attachment is a carbonyl group linked to a nitrogen atom, which is further connected to a cyclohexylidene group. A third attachment is a carbonyl group linked to a nitrogen atom, which is connected to a cyclohexylidene group. A fourth attachment is a carbonyl group linked to a nitrogen atom, which is connected to a cyclohexylidene group. The molecule also includes a cyclopropylidene group and a cyclohexylidene group.	729.9872	730.1	A
672	 Chemical structure of compound 672: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopentylidene sulfone group (a five-membered ring with a sulfur atom double-bonded to two oxygen atoms). Another attachment is a carbonyl group linked to a nitrogen atom, which is further connected to a cyclohexylidene group. A third attachment is a carbonyl group linked to a nitrogen atom, which is connected to a cyclohexylidene group. A fourth attachment is a carbonyl group linked to a nitrogen atom, which is connected to a cyclohexylidene group. The molecule also includes a cyclopropylidene group and a cyclohexylidene group.	744.0143	744.1	A

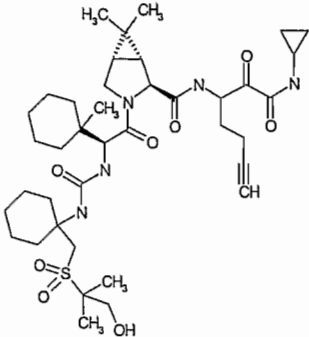
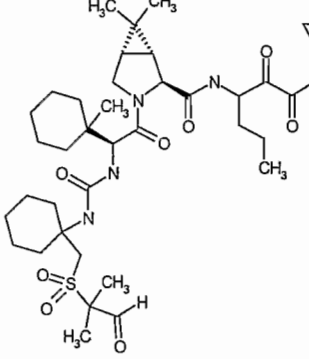
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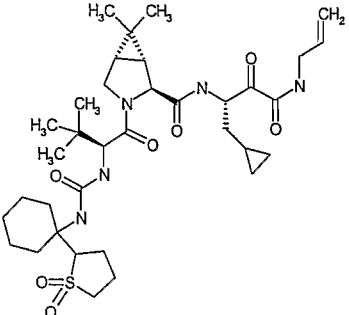
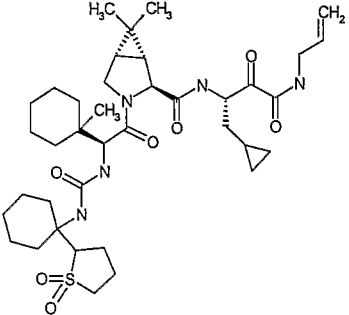
677		844.1326		A
678		750.0185		A

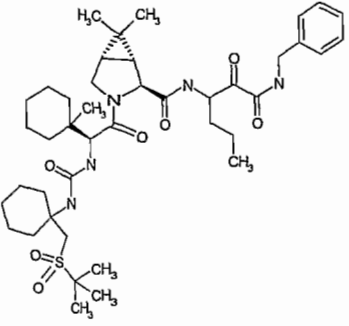
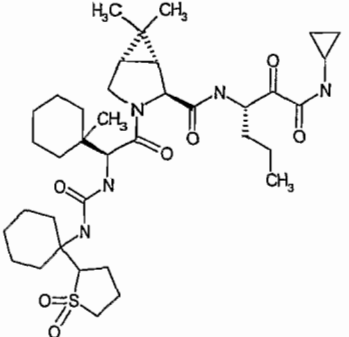
679		776.0568		A
680		770.0929	770.4	A

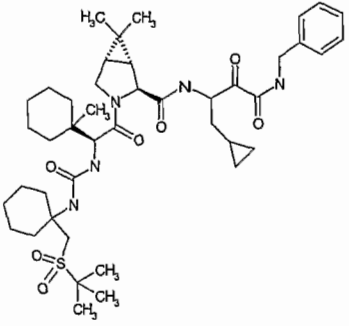
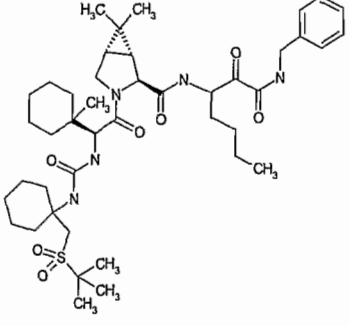
681	 Chemical structure of compound 681: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (C(CH₃)₃) at the 2-position, a carbonyl group (C=O) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl at the 3-position is linked to a nitrogen atom, which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O). The carbonyl at the 4-position is linked to a nitrogen atom, which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O). The nitrogen at the 1-position of the pyrrolidine ring is linked to a carbonyl group (C=O), which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O). The nitrogen at the 1-position of the pyrrolidine ring is also linked to a carbonyl group (C=O), which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O).	703.949	704.2	A
682	 Chemical structure of compound 682: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (C(CH₃)₃) at the 2-position, a carbonyl group (C=O) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl at the 3-position is linked to a nitrogen atom, which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O). The carbonyl at the 4-position is linked to a nitrogen atom, which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O). The nitrogen at the 1-position of the pyrrolidine ring is linked to a carbonyl group (C=O), which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O). The nitrogen at the 1-position of the pyrrolidine ring is also linked to a carbonyl group (C=O), which is further substituted with a cyclopropylmethyl group and a carbonyl group (C=O).	736.979	737.5	C

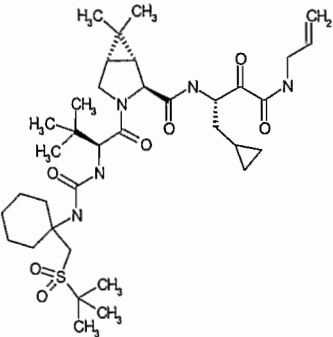
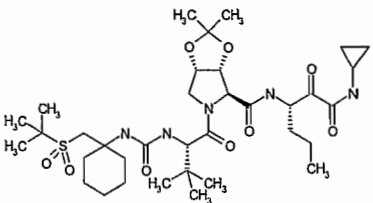
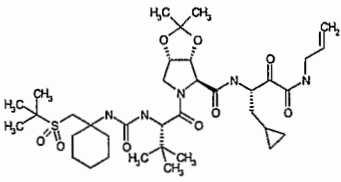
683	 Chemical structure of compound 683: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂) and a carbamate group (N-C(=O)-O-). The carbamate is linked to a pyrazole ring, which is further substituted with a methyl group and a side chain containing a ketone and an amide group. The amide is linked to a side chain with a ketone and a terminal vinyl group (CH=CH₂).	738.9949	739.4	C
684	 Chemical structure of compound 684: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂) and a carbamate group (N-C(=O)-O-). The carbamate is linked to a pyrazole ring, which is further substituted with a methyl group and a side chain containing a ketone and an amide group. The amide is linked to a side chain with a ketone and a terminal cyclopropyl group.	736.979	737.4	C

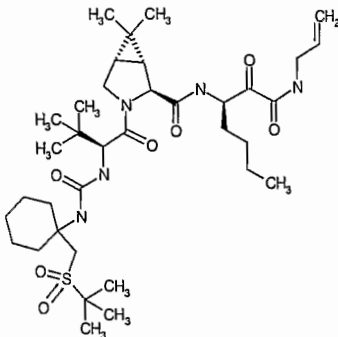
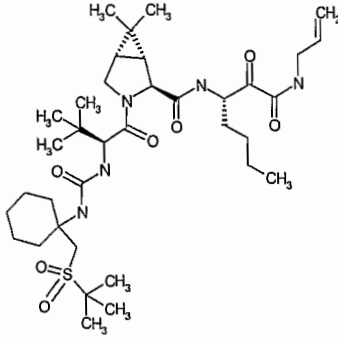
685	 <chem>CC(C)(O)S(=O)(=O)C1(CCCCC1)N(C(=O)N2C(CCCC2C(C)C)C(=O)N(C(=O)N(C)CC#CC(=O)N3C4CCCC4C3)C5=CC=CC=C5)C6=CC=CC=C6</chem>	760.0137		A
686	 <chem>CC(C)C(=O)S(=O)(=O)C1(CCCCC1)N(C(=O)N2C(CCCC2C(C)C)C(=O)N(C(=O)N(C)CC(C)C(=O)N3C4CCCC4C3)C5=CC=CC=C5)C6=CC=CC=C6</chem>	748.0026		A

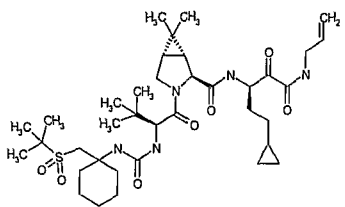
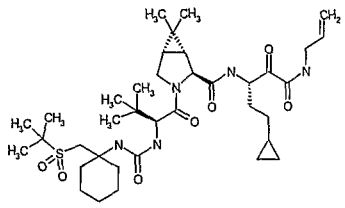
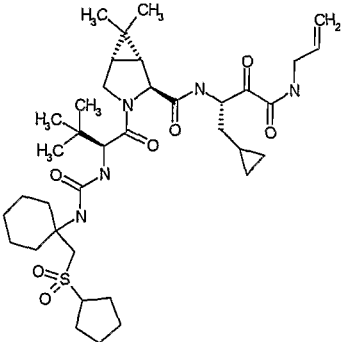
689	 Chemical structure of compound 689: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group, a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group, and a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group. The molecule includes a cyclopropylmethyl group and a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group.	689.9219	690.2	A
690	 Chemical structure of compound 690: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group, a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group, and a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group. The molecule includes a cyclopropylmethyl group and a 2-methyl-2-propyl-1,3-dioxolane-5-sulfonyl group.	729.9872	730.2	A

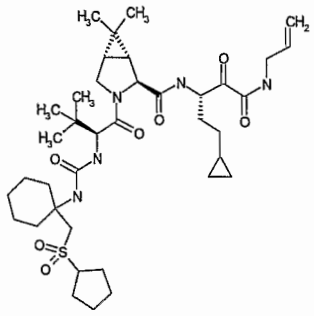
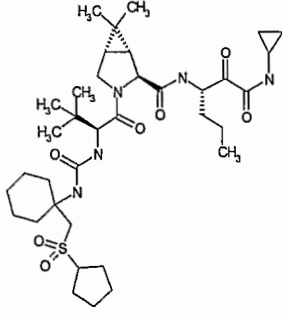
691	 Chemical structure of compound 691: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl-1,3-dioxane-5-carboxamide group, a 2-methyl-2-propyl-1,3-dioxane-5-carboxamide group, and a 2-methyl-2-propyl-1,3-dioxane-5-carboxamide group. The structure includes a cyclohexyl ring, a sulfonamide group, and a benzyl group.	784.0797	784.2	A
692	 Chemical structure of compound 692: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl-1,3-dioxane-5-carboxamide group, a 2-methyl-2-propyl-1,3-dioxane-5-carboxamide group, and a 2-methyl-2-propyl-1,3-dioxane-5-carboxamide group. The structure includes a cyclohexyl ring, a sulfonamide group, and a cyclopropyl group.	717.9761		A

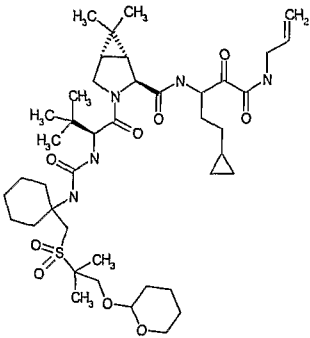
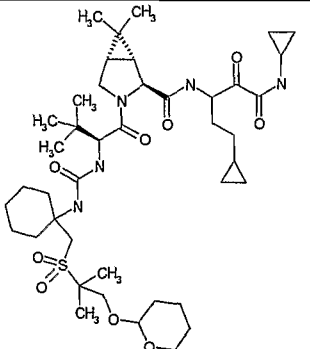
693	 Chemical structure of compound 693: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopropylmethyl group (with two methyl groups on the cyclopropyl ring), a carbonyl group, and a nitrogen atom. The nitrogen atom is part of a side chain that includes a carbonyl group, a benzyl group, and a cyclopropylmethyl group. Another nitrogen atom is attached to the cyclohexane ring, which is part of a side chain containing a carbonyl group and a cyclopropylmethyl group. A sulfonamide group is also present, consisting of a sulfonyl group attached to a cyclohexylmethyl group.	796.0908	796.2	A
694	 Chemical structure of compound 694: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a cyclopropylmethyl group (with two methyl groups on the cyclopropyl ring), a carbonyl group, and a nitrogen atom. The nitrogen atom is part of a side chain that includes a carbonyl group, a benzyl group, and a propyl group. Another nitrogen atom is attached to the cyclohexane ring, which is part of a side chain containing a carbonyl group and a cyclopropylmethyl group. A sulfonamide group is also present, consisting of a sulfonyl group attached to a cyclohexylmethyl group.	798.1067	798.2	A

695		705.9649		5
696		725.9526	726.4	A
697		737.9637	738.4	A

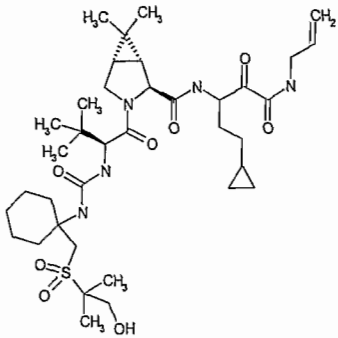
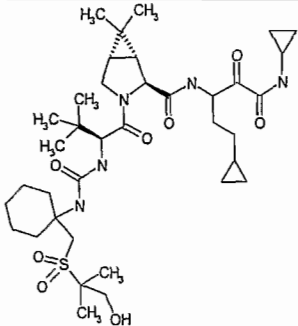
698		707.9809	708.4	B
699		707.9809	708.4	A

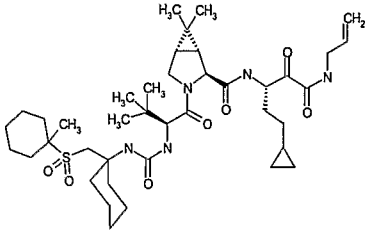
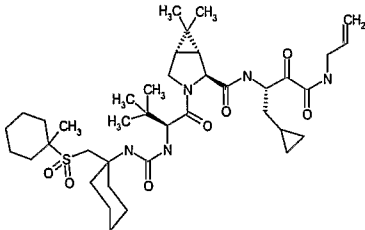
700		719.992		A
701		719.992		6
702		717.9761	718.60	A

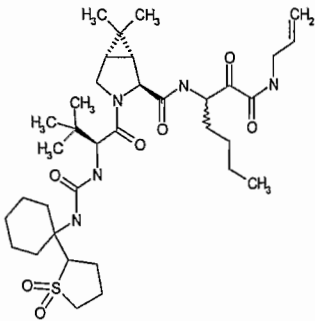
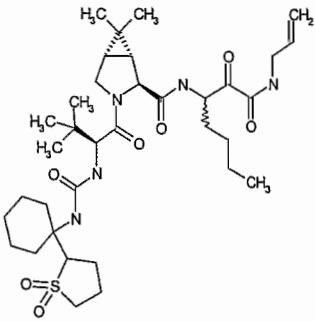
703	 Chemical structure of compound 703: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group, a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group, and a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a vinyl group.	732.0032	732.6	A
704	 Chemical structure of compound 704: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group, a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group, and a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclopropylmethyl)pyrrolidin-1-yl group. The molecule includes a sulfonamide group, a cyclopropyl group, and a methyl group.	705.9649	706.6	A

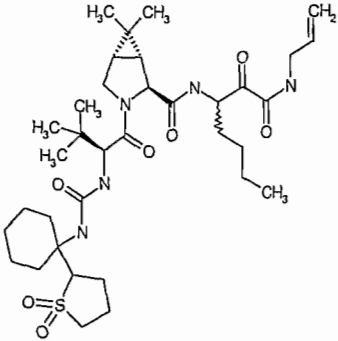
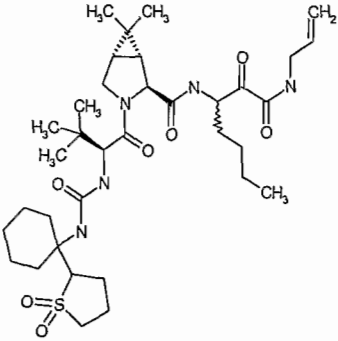
705		820.1103	A	
706		820.1103	A	

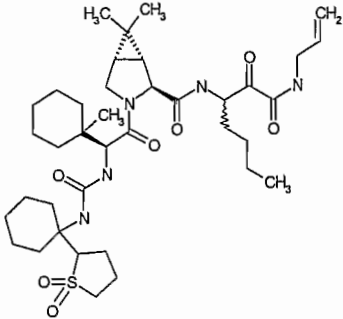
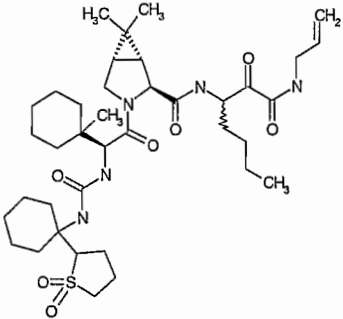
707		794.0721	A
708		794.0721	A

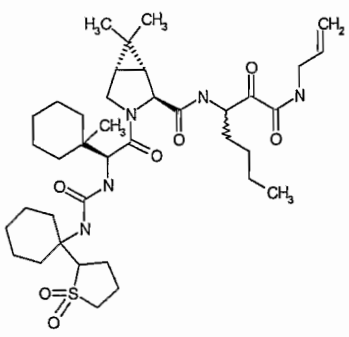
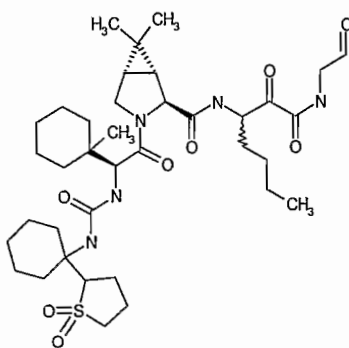
709	 Chemical structure of compound 709: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH₂OH) and a nitrogen atom connected to a pyrazole ring. The pyrazole ring is substituted with a methyl group and a carbonyl group. The carbonyl group is connected to a nitrogen atom, which is further connected to a cyclopropylmethyl group. The cyclopropylmethyl group is substituted with a vinyl group (CH=CH₂).	735.9914		A
710	 Chemical structure of compound 710: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH₂OH) and a nitrogen atom connected to a pyrazole ring. The pyrazole ring is substituted with a methyl group and a carbonyl group. The carbonyl group is connected to a nitrogen atom, which is further connected to a cyclopropylmethyl group. The cyclopropylmethyl group is substituted with a vinyl group (CH=CH₂).	735.9914		A

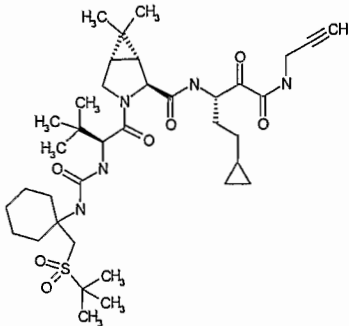
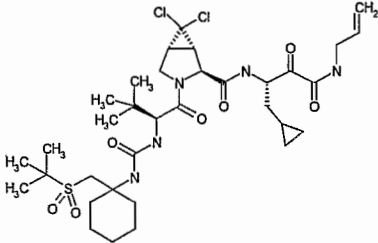
711	 Chemical structure of compound 711: A complex molecule featuring a cyclohexylmethyl sulfonamide group, a cyclopropylmethyl carbamate group, and a central amide linkage. The structure includes a cyclohexane ring with a methyl group and a sulfonamide group, connected to a cyclopropane ring via a carbamate linkage. The cyclopropane ring is further substituted with a methyl group and a carbamate group. The central amide linkage connects the cyclopropane ring to a cyclohexane ring via a carbamate linkage.	760.0574		A
712	 Chemical structure of compound 712: A complex molecule featuring a cyclohexylmethyl sulfonamide group, a cyclopropylmethyl carbamate group, and a central amide linkage. The structure includes a cyclohexane ring with a methyl group and a sulfonamide group, connected to a cyclopropane ring via a carbamate linkage. The cyclopropane ring is further substituted with a methyl group and a carbamate group. The central amide linkage connects the cyclopropane ring to a cyclohexane ring via a carbamate linkage.	746.0303		A

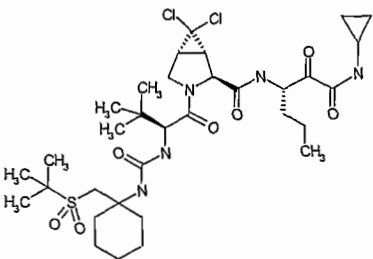
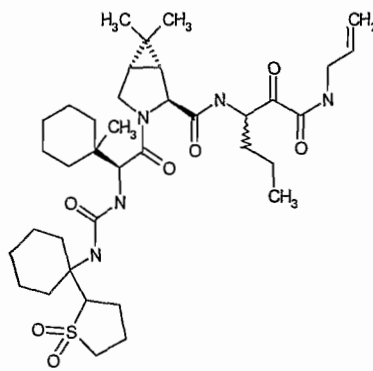
713	 The chemical structure shows a cyclohexane ring substituted with a sulfonamide group (-SO₂-NH-) and a side chain. The side chain includes a carbonyl group, a nitrogen atom, and a vinyl group (-CH=CH₂). There are also methyl groups and a propyl chain attached to the structure.	691.9378	692.2	B
714	 The chemical structure is identical to the one in row 713, showing a cyclohexane ring with a sulfonamide group and a side chain containing a carbonyl, nitrogen, and vinyl group, along with methyl and propyl substituents.	691.9378	692.2	A

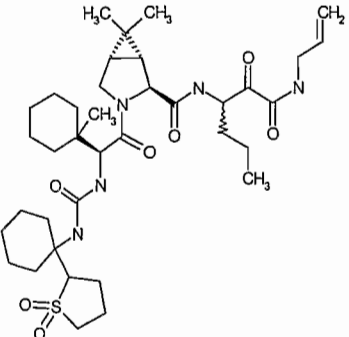
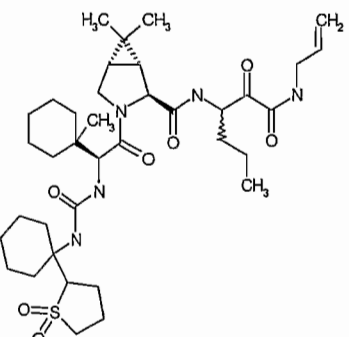
715	 The chemical structure shows a cyclohexane ring substituted with a sulfone group (-SO₂-) and a nitrogen atom. This nitrogen is part of a pyrrolidine ring system. The pyrrolidine ring is further substituted with a side chain that includes a carbonyl group, a methylene group, and a terminal vinyl group (-CH=CH₂). The side chain also features a methyl group and a propyl group.	691.9378	692.2	A
716	 The chemical structure is identical to the one in row 715, showing a cyclohexane ring substituted with a sulfone group (-SO₂-) and a nitrogen atom. This nitrogen is part of a pyrrolidine ring system. The pyrrolidine ring is further substituted with a side chain that includes a carbonyl group, a methylene group, and a terminal vinyl group (-CH=CH₂). The side chain also features a methyl group and a propyl group.	691.9378	692.2	A

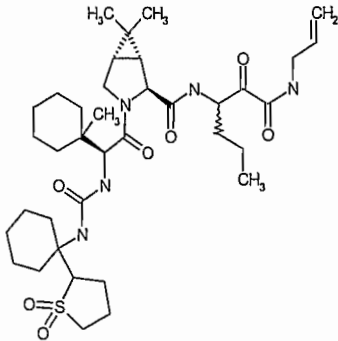
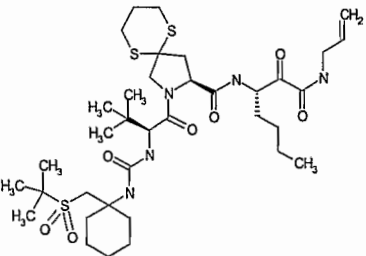
717	 The chemical structure shows a cyclohexane ring substituted with a carbamate group (-NH-C(=O)-O-CH2-CH=CH2) and a sulfonamide group (-SO2NH2). The carbamate group is further substituted with a vinyl group (-CH=CH2). The sulfonamide group is attached to a cyclohexane ring via a sulfonamide linkage (-SO2NH-). The structure is a complex derivative of a cyclohexane ring.	732.0032	732.2	B
718	 The chemical structure is identical to the one in row 717, showing a cyclohexane ring substituted with a carbamate group (-NH-C(=O)-O-CH2-CH=CH2) and a sulfonamide group (-SO2NH2). The carbamate group is further substituted with a vinyl group (-CH=CH2). The sulfonamide group is attached to a cyclohexane ring via a sulfonamide linkage (-SO2NH-). The structure is a complex derivative of a cyclohexane ring.	732.0032	732.2	B

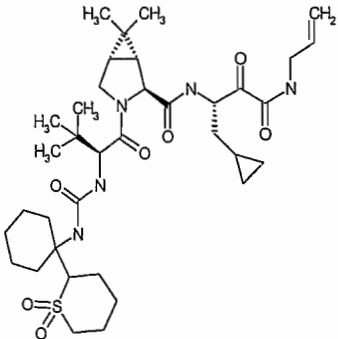
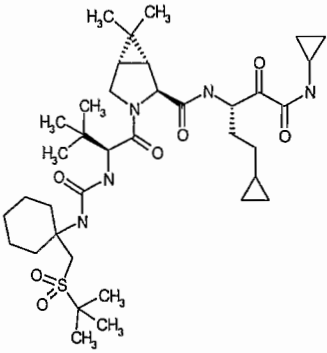
719	 The chemical structure shows a cyclohexane ring substituted with a methyl group and a side chain. The side chain includes a sulfonamide group (SO₂NH-) and a complex amide linkage. A vinyl group (CH=CH₂) is attached to the side chain. Stereochemistry is indicated with wedges and dashes.	732.0032	732.2	A
720	 This chemical structure is identical to the one in row 719, showing a cyclohexane ring, a sulfonamide group, and a side chain with a vinyl group, with the same stereochemistry.	732.0032	732.2	A

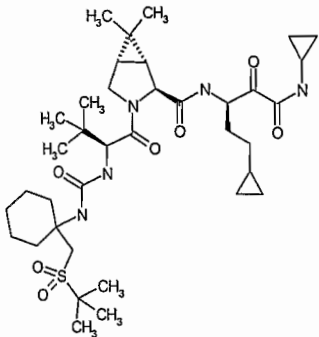
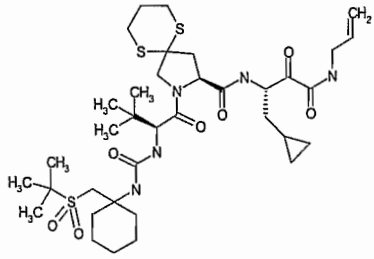
721		717.9761	718.1	A
722		746.8008		A

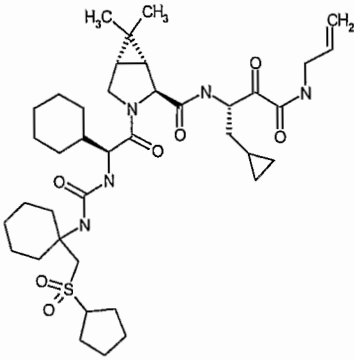
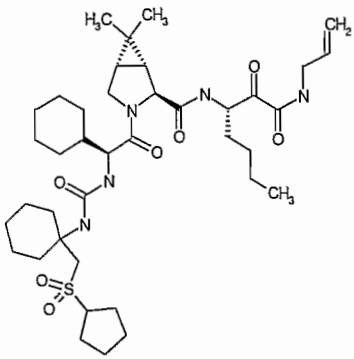
723		734.7897		A
724		717.9761	718.2	B

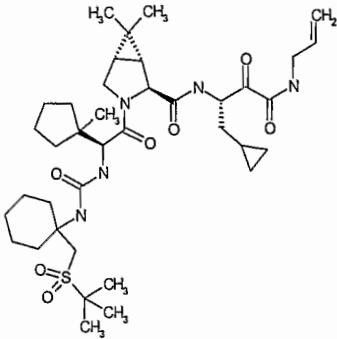
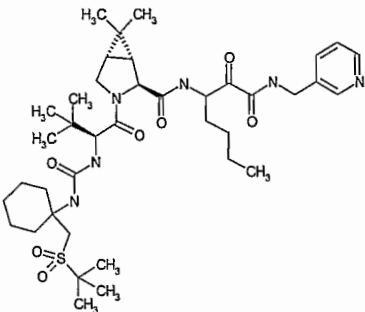
725	 The chemical structure is a complex molecule. It features a central cyclohexane ring. Attached to one carbon of the cyclohexane is a pyrrolidine ring. The pyrrolidine ring has a methyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a methylene group, a chiral center (indicated by a wavy bond), a carbonyl group, and a terminal vinyl group. Another substituent on the cyclohexane ring is a sulfonamide group, which is a cyclopentyl ring with a sulfonamide group attached to one of its carbons.	717.9761	718.2	A
726	 The chemical structure is identical to the one in row 725. It features a central cyclohexane ring. Attached to one carbon of the cyclohexane is a pyrrolidine ring. The pyrrolidine ring has a methyl group at the 2-position and a carbonyl group at the 3-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a methylene group, a chiral center (indicated by a wavy bond), a carbonyl group, and a terminal vinyl group. Another substituent on the cyclohexane ring is a sulfonamide group, which is a cyclopentyl ring with a sulfonamide group attached to one of its carbons.	717.9761	718.2	A

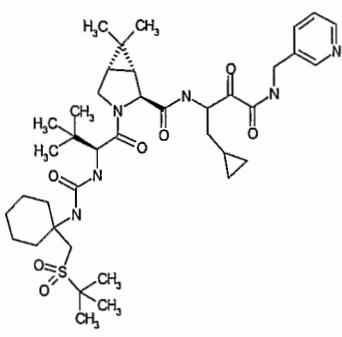
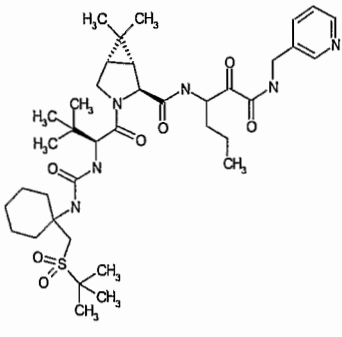
727		717.9761	718.2	A
728		772.1089		A

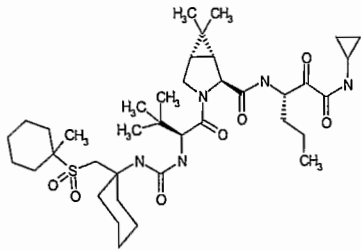
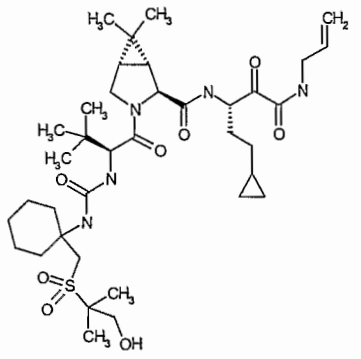
729	 Chemical structure of compound 729: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2,3-trimethylbutan-3-yl group (indicated with stereochemistry), a 2-oxo-2-(cyclopropylmethyl)ethyl group, and a 2-oxo-2-(cyclopropylmethyl)ethyl group. The pyrrolidine ring is also connected to a 2-oxo-2-(cyclopropylmethyl)ethyl group. The molecule includes a sulfonamide group (SO₂), a cyclohexyl group, and a vinyl group (CH=CH₂).	703.949	704.2	A
730	 Chemical structure of compound 730: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2,3-trimethylbutan-3-yl group (indicated with stereochemistry), a 2-oxo-2-(cyclopropylmethyl)ethyl group, and a 2-oxo-2-(cyclopropylmethyl)ethyl group. The pyrrolidine ring is also connected to a 2-oxo-2-(cyclopropylmethyl)ethyl group. The molecule includes a sulfonamide group (SO₂), a cyclohexyl group, and a vinyl group (CH=CH₂).	719.992		5.6

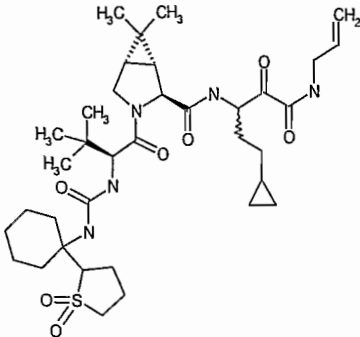
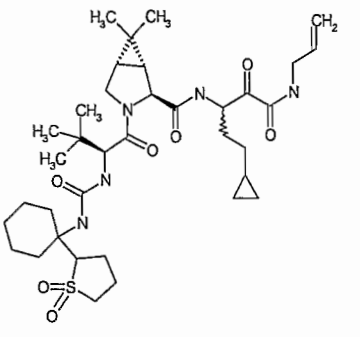
731	 Chemical structure of compound 731: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group, a dimethylamino group, and a side chain containing a carbonyl group and a cyclopropylmethyl group. The side chain also includes a sulfonamide group and a dimethylsulfonyl group.	719.992		64
732	 Chemical structure of compound 732: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group, a dimethylamino group, and a side chain containing a carbonyl group and a cyclopropylmethyl group. The side chain also includes a sulfonamide group and a dimethylsulfonyl group.	770.0929	770.2	A

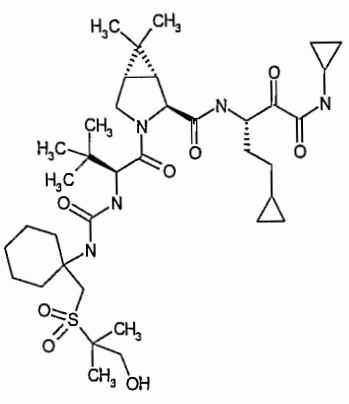
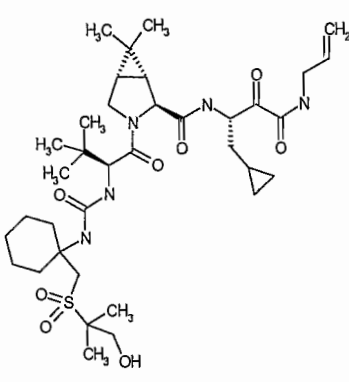
733	 Chemical structure of compound 733: A complex molecule featuring a central pyrrolidine ring substituted with a cyclohexyl group, a dimethylallyl group, and a side chain containing a carbamate and a cyclopropylmethyl ketone. It is also linked via a carbamate to a spirocyclic system consisting of a cyclohexane ring and a cyclopentane ring with a sulfonamide group.	744.0143	744.3	A
734	 Chemical structure of compound 734: Similar to compound 733, but the side chain of the pyrrolidine ring is a propyl group instead of a cyclopropylmethyl ketone. The rest of the molecule, including the spirocyclic sulfonamide system, remains the same.	746.0303	746.2	A

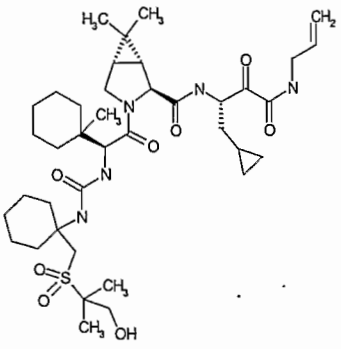
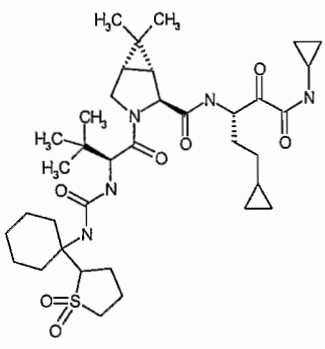
735		732.0032	732.4	A
736		759.029	759.4	A

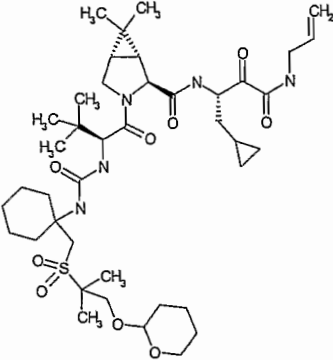
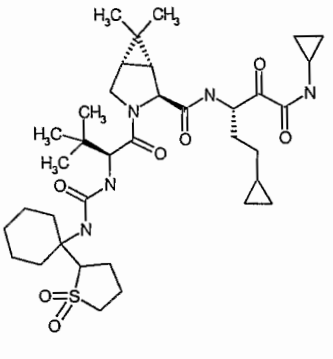
737	 Chemical structure of compound 737: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a (4-pyridylmethyl)carbamoyl group at the 3-position, and a (cyclopropylmethyl)carbamoyl group at the 4-position. The nitrogen of the pyrrolidine ring is part of a carbamate linkage to a cyclohexylmethyl group, which is further substituted with a tert-butylsulfonyl group.	757.0131	757.4	A
738	 Chemical structure of compound 738: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group at the 2-position, a (4-pyridylmethyl)carbamoyl group at the 3-position, and a (propylmethyl)carbamoyl group at the 4-position. The nitrogen of the pyrrolidine ring is part of a carbamate linkage to a cyclohexylmethyl group, which is further substituted with a tert-butylsulfonyl group.	745.0019	745.4	A

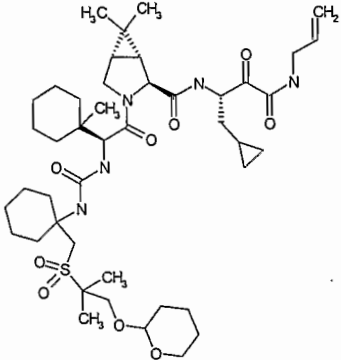
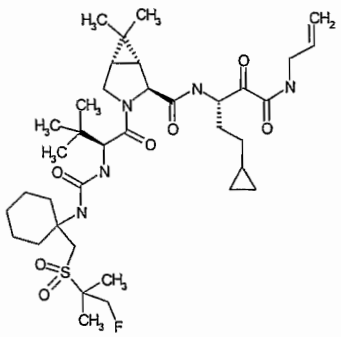
739	 Chemical structure of compound 739: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (-SO₂-NH-). This sulfonamide is linked to a bicyclic system (bicyclo[2.2.1]heptane) which is further substituted with a methyl group and a carbamate group (-NH-CO-O-). The carbamate is connected to a cyclopropane ring, which is also substituted with a methyl group and a carbamate group (-NH-CO-O-). The final carbamate group is linked to a cyclopropane ring, which is substituted with a methyl group and a carbamate group (-NH-CO-O-).	734.0191	734.3	18
740	 Chemical structure of compound 740: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (-SO₂-NH-). This sulfonamide is linked to a bicyclic system (bicyclo[2.2.1]heptane) which is further substituted with a methyl group and a carbamate group (-NH-CO-O-). The carbamate is connected to a cyclopropane ring, which is also substituted with a methyl group and a carbamate group (-NH-CO-O-). The final carbamate group is linked to a cyclopropane ring, which is substituted with a methyl group and a carbamate group (-NH-CO-O-).	735.9914		A

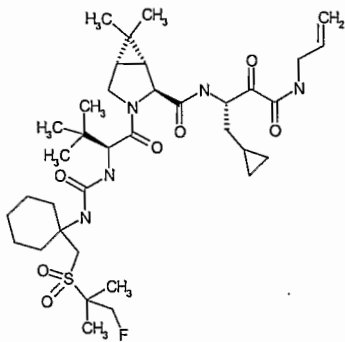
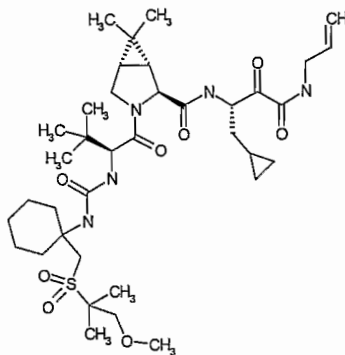
741		703.949	704.2	A
742		703.949	704.2	A

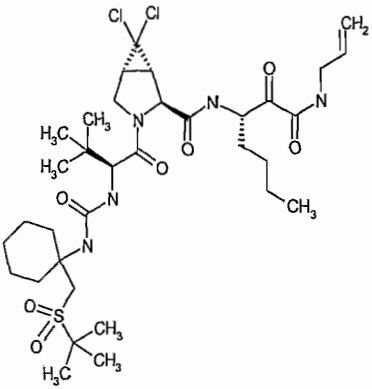
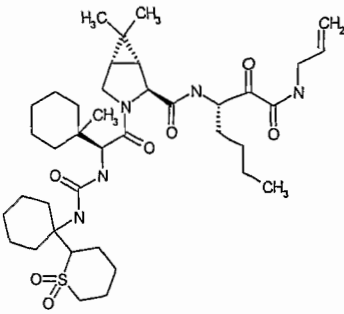
743	 Chemical structure of compound 743: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂OH) and a carbamate group (N-C(=O)-O-C(=O)-N). The carbamate group is further substituted with a cyclopropylmethyl group and a side chain containing a ketone and a cyclopropylmethyl group. The molecule also includes a quaternary carbon atom bonded to two methyl groups and a cyclopropylmethyl group.	735.9914		A
744	 Chemical structure of compound 744: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂OH) and a carbamate group (N-C(=O)-O-C(=O)-N). The carbamate group is further substituted with a cyclopropylmethyl group and a side chain containing a ketone and a vinyl group (CH=CH₂). The molecule also includes a quaternary carbon atom bonded to two methyl groups and a cyclopropylmethyl group.	721.9643		A

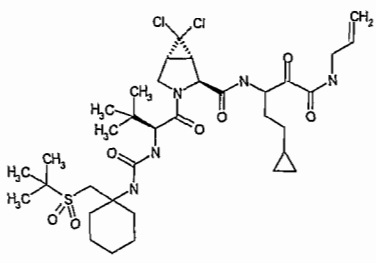
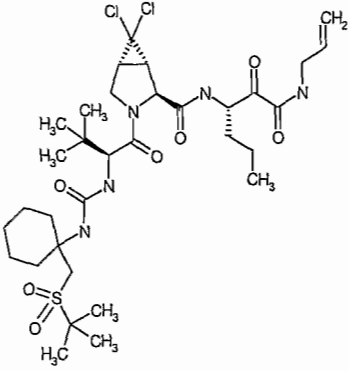
745	 Chemical structure of compound 745: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2-methyl-2-(prop-1-en-1-yl)acetyl group at the 2-position, a 1-(cyclohexyl)pyrrolidin-2-yl group at the 3-position, and a 1-(cyclohexyl)pyrrolidin-2-yl group at the 4-position. The pyrrolidine ring is also substituted with a 1-(cyclohexyl)pyrrolidin-2-yl group at the 5-position. The molecule contains multiple amide and ester functional groups.	762.0297		A
746	 Chemical structure of compound 746: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2-methyl-2-(prop-1-en-1-yl)acetyl group at the 2-position, a 1-(cyclohexyl)pyrrolidin-2-yl group at the 3-position, and a 1-(cyclohexyl)pyrrolidin-2-yl group at the 4-position. The pyrrolidine ring is also substituted with a 1-(cyclohexyl)pyrrolidin-2-yl group at the 5-position. The molecule contains multiple amide and ester functional groups.	703.949	704.2	A

747		806.0832		A
748		703.949	704.2	A

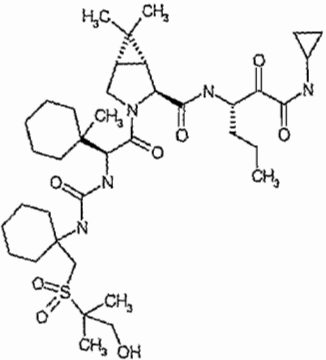
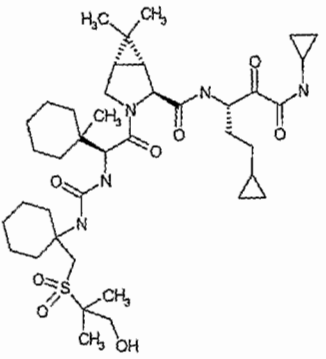
749		846.1486		A
750		737.9825		A

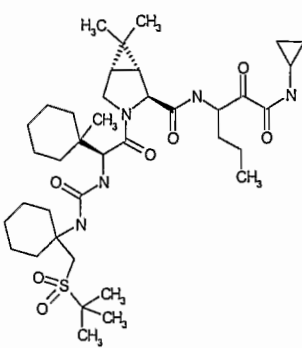
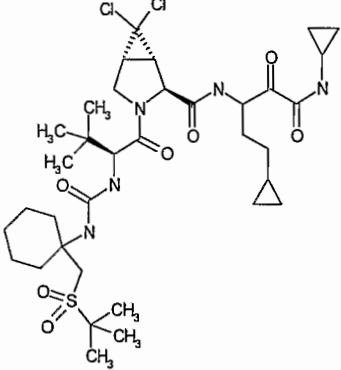
751	 Chemical structure of compound 751: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂CH₂CH₃), a carbamate group (NHCOCH₂CH₂CH₃), and a cyclopropylmethyl group. The cyclohexane ring is also substituted with a carbamate group (NHCOCH₂CH₂CH₃) and a cyclopropylmethyl group. The molecule contains multiple chiral centers and functional groups including amides, carbamates, and sulfonamides.	723.9554		A
752	 Chemical structure of compound 752: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂CH₂CH₃), a carbamate group (NHCOCH₂CH₂CH₃), and a cyclopropylmethyl group. The cyclohexane ring is also substituted with a carbamate group (NHCOCH₂CH₂CH₃) and a cyclopropylmethyl group. The molecule contains multiple chiral centers and functional groups including amides, carbamates, and sulfonamides.	735.9914		A

755	 Chemical structure of compound 755: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a dichloromethyl group (CHCl₂) at the 2-position, a tert-butyl group (C(CH₃)₃) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a propyl group (CH₂CH₂CH₃) attached to a carbonyl group (C=O), which is further attached to a nitrogen atom (N) that is part of another amide linkage to a vinyl group (CH=CH₂). Additionally, the pyrrolidine ring is substituted with a cyclohexyl group (C₆H₁₁) at the 1-position and a sulfonamide group (SO₂CH₂C(CH₃)₃) at the 5-position.	748.8168	748.1	A
756	 Chemical structure of compound 756: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) at the 2-position, a methyl group (CH₃) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl group is part of an amide linkage to a side chain. The side chain consists of a propyl group (CH₂CH₂CH₃) attached to a carbonyl group (C=O), which is further attached to a nitrogen atom (N) that is part of another amide linkage to a vinyl group (CH=CH₂). Additionally, the pyrrolidine ring is substituted with a cyclohexyl group (C₆H₁₁) at the 1-position and a sulfonamide group (SO₂CH₂C(CH₃)₃) at the 5-position.	746.0303	746.1	A

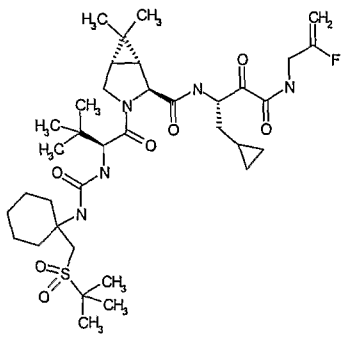
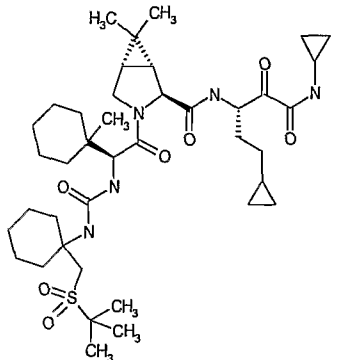
757		760.8279	760.1	A
758		734.7897	734.1	A

759		748.8168	748.1	A
760		746.0303		A

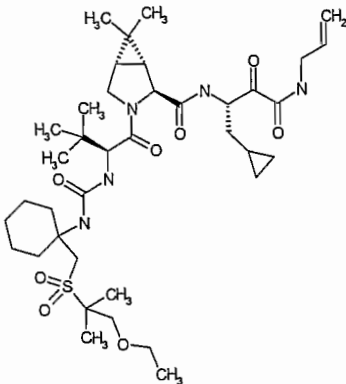
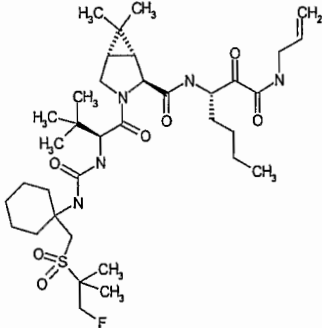
761	 Chemical structure of compound 761: A complex molecule featuring a central bicyclic system (a cyclohexane ring fused to a cyclopentane ring). The cyclohexane ring is substituted with a cyclopropylmethyl group and a sulfonamide group (SO₂CH₂CH₂CH₂OH). The cyclopentane ring is substituted with a methyl group and a carbonyl group (C=O). The carbonyl group is part of a larger amide structure, which includes a cyclopropylmethyl group and a sulfonamide group (SO₂CH₂CH₂CH₂OH).	750.0185		A
762	 Chemical structure of compound 762: A complex molecule featuring a central bicyclic system (a cyclohexane ring fused to a cyclopentane ring). The cyclohexane ring is substituted with a cyclopropylmethyl group and a sulfonamide group (SO₂CH₂CH₂CH₂OH). The cyclopentane ring is substituted with a methyl group and a carbonyl group (C=O). The carbonyl group is part of a larger amide structure, which includes a cyclopropylmethyl group and a sulfonamide group (SO₂CH₂CH₂CH₂OH).	776.0568		A

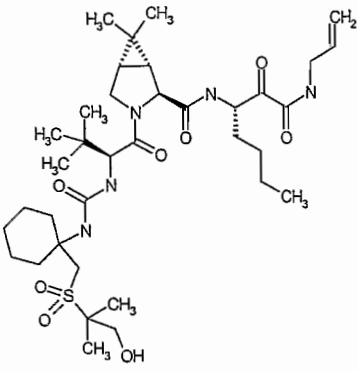
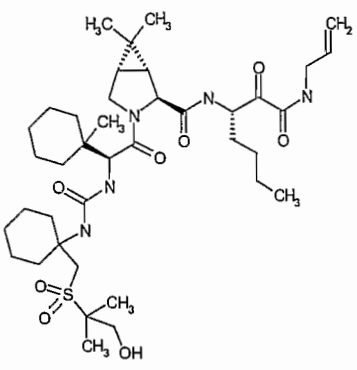
763		734.0191		B
764		760.8279	760.1	A

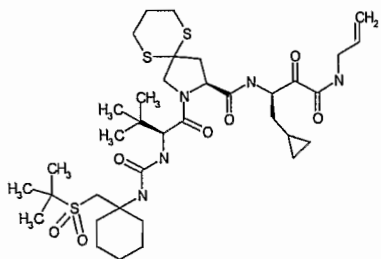
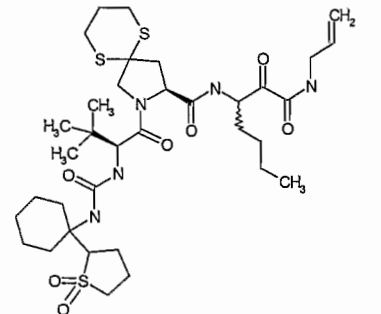
767		738.0074		A
768		709.9532		A

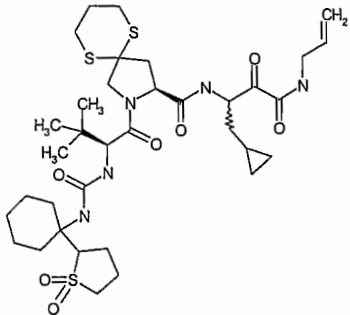
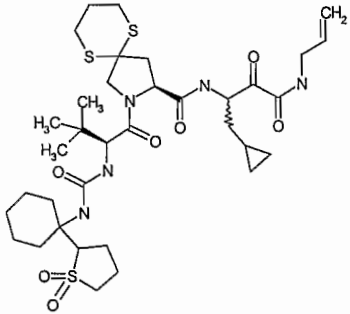
769	 Chemical structure of compound 769: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a carbonyl group (C=O). The carbonyl group is part of an amide linkage to a cyclopropylmethyl group. The pyrrolidine ring is also linked to a cyclohexylmethyl group via a carbonyl group. The cyclohexylmethyl group is further substituted with a sulfonamide group (SO₂CH₃) and a methyl group (CH₃). The cyclopropylmethyl group is linked to a carbonyl group, which is part of an amide linkage to a cyclopropylmethyl group. The cyclopropylmethyl group is further substituted with a methyl group (CH₃) and a carbonyl group (C=O).	723.9554		A
770	 Chemical structure of compound 770: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a carbonyl group (C=O). The carbonyl group is part of an amide linkage to a cyclopropylmethyl group. The pyrrolidine ring is also linked to a cyclohexylmethyl group via a carbonyl group. The cyclohexylmethyl group is further substituted with a sulfonamide group (SO₂CH₃) and a methyl group (CH₃). The cyclopropylmethyl group is linked to a carbonyl group, which is part of an amide linkage to a cyclopropylmethyl group. The cyclopropylmethyl group is further substituted with a methyl group (CH₃) and a carbonyl group (C=O).	760.0574		A

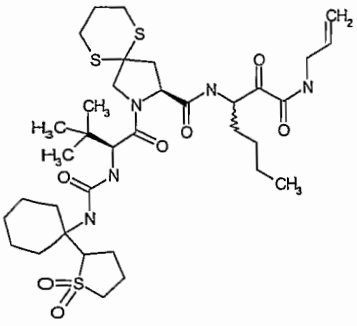
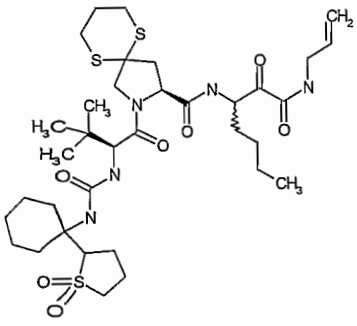
771		764.0456	A
772		746.0303	A

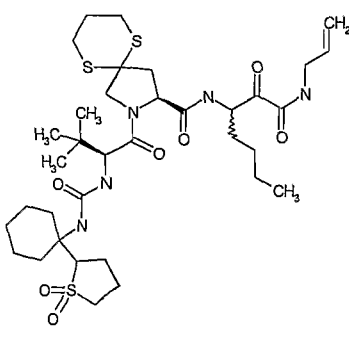
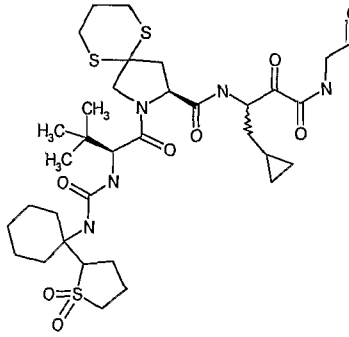
773		750.0185	A
774		725.9713	A

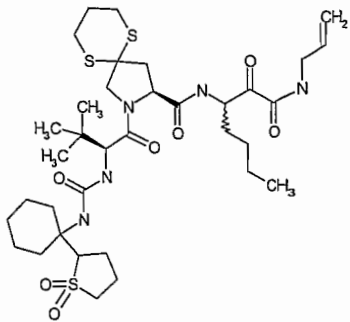
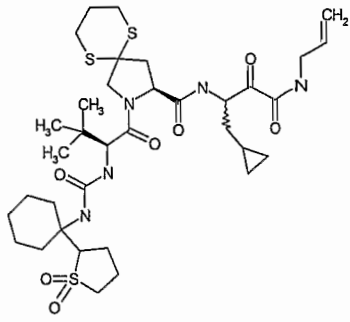
775	 Chemical structure of compound 775: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂OH) and a carbamate group (NHC(=O)CH(CH₃)₂). The carbamate is linked to a pyrazole ring, which is further substituted with a methyl group and a side chain containing a ketone and an allyl group.	723.9803		A
776	 Chemical structure of compound 776: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂CH₂CH(CH₃)₂OH) and a carbamate group (NHC(=O)CH(CH₃)₂). The carbamate is linked to a pyrazole ring, which is further substituted with a methyl group and a side chain containing a ketone and an allyl group.	764.0456		A

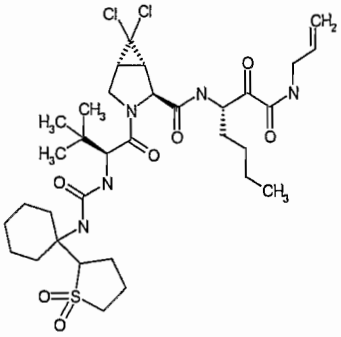
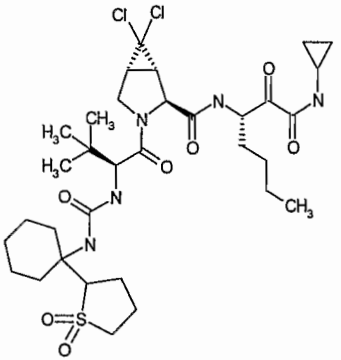
777		770.0929	770.2	B
778		756.0658	756.1	A

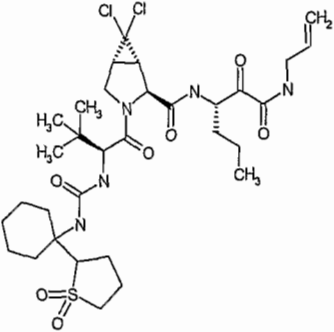
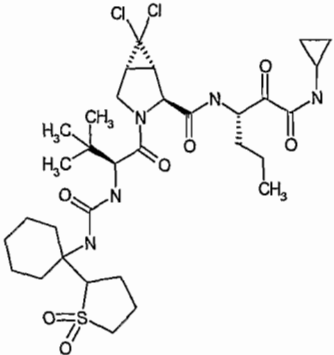
779	 Chemical structure of compound 779: A complex molecule featuring a central pyrazole ring substituted with a cyclohexylmethyl group, a dimethylamino group, and a side chain containing a thietane ring, a carbonyl group, and a vinyl group.	754.0499	754.1	A
780	 Chemical structure of compound 780: A complex molecule featuring a central pyrazole ring substituted with a cyclohexylmethyl group, a dimethylamino group, and a side chain containing a thietane ring, a carbonyl group, and a vinyl group.	754.0499	754.1	A

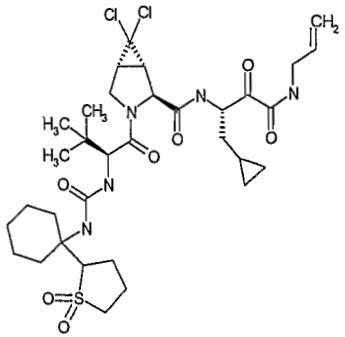
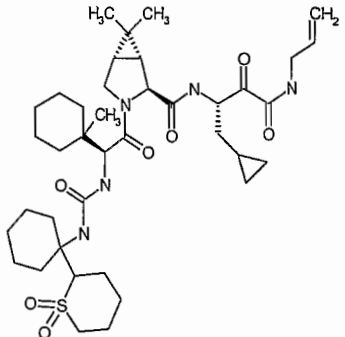
781	 Chemical structure of compound 781: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group. The amide nitrogen is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group. The amide nitrogen is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group. The amide nitrogen is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group.	756.0658	756.1	A
782	 Chemical structure of compound 782: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group. The amide nitrogen is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group. The amide nitrogen is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group. The amide nitrogen is further substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group.	756.0658	756.1	A

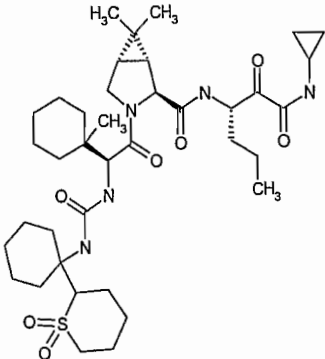
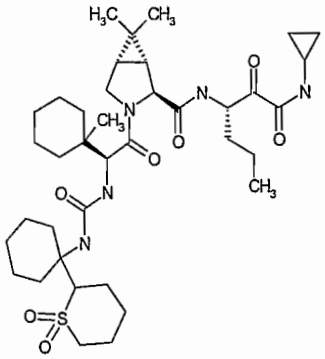
783	 Chemical structure of compound 783: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group and a 2-((cyclohexylmethyl)amino)-2-sulfonyl-1,3-dioxane-5-carboxamide group. The 2,2,4-trimethyl-1,3-dioxane-5-carboxamide is further substituted with a 2-((cyclohexylmethyl)amino)-2-sulfonyl-1,3-dioxane-5-carboxamide group. The 2,2,4-trimethyl-1,3-dioxane-5-carboxamide is further substituted with a 2-((cyclohexylmethyl)amino)-2-sulfonyl-1,3-dioxane-5-carboxamide group.	756.0658	756.1	A
784	 Chemical structure of compound 784: A complex molecule featuring a 1,3-dithiane ring system. The 1,3-dithiane is substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carboxamide group and a 2-((cyclohexylmethyl)amino)-2-sulfonyl-1,3-dioxane-5-carboxamide group. The 2,2,4-trimethyl-1,3-dioxane-5-carboxamide is further substituted with a 2-((cyclohexylmethyl)amino)-2-sulfonyl-1,3-dioxane-5-carboxamide group. The 2,2,4-trimethyl-1,3-dioxane-5-carboxamide is further substituted with a 2-((cyclohexylmethyl)amino)-2-sulfonyl-1,3-dioxane-5-carboxamide group.	754.0499	754.1	A

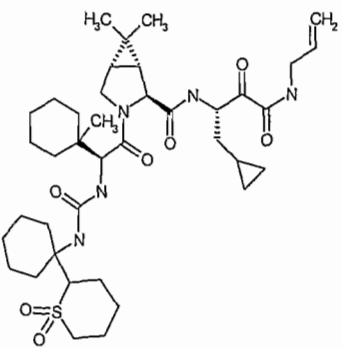
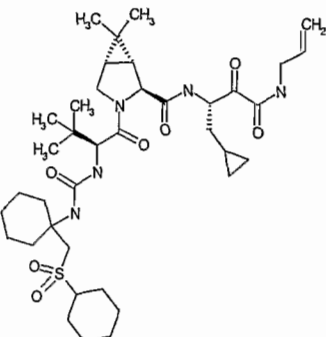
785		756.0658	756.1	A
786		754.0499	754.1	A

787	 Chemical structure of compound 787: A complex molecule featuring a central pyrrolidine ring substituted with two chlorine atoms. This ring is connected via an amide bond to a side chain containing a ketone, a secondary amine, and a terminal vinyl group. Another amide branch from the central ring connects to a quaternary carbon atom bonded to two methyl groups and a nitrogen atom. This nitrogen is part of a sulfonamide group, which is further linked to a cyclohexane ring and a sulfonamide group.	732.7737	732.1	A
788	 Chemical structure of compound 788: Similar to compound 787, but the side chain is modified. The terminal vinyl group is replaced by a cyclopropyl group, and the amide linkage is altered to a different configuration.	732.7737	732.1	A

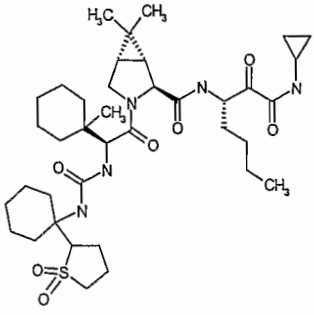
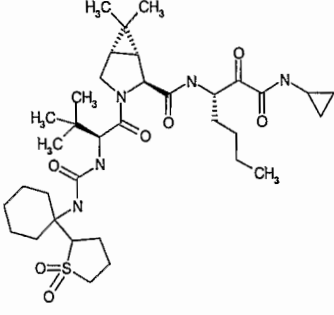
789	 Chemical structure of compound 789: A complex molecule featuring a central pyrrolidine ring substituted with a dichloromethyl group, a dimethylamino group, and a carbonyl group. This pyrrolidine is linked via an amide bond to a side chain containing a methyl group, a carbonyl group, and a terminal vinyl group. Another amide branch connects the pyrrolidine to a cyclohexane ring, which is further substituted with a sulfonamide group and a cyclopentyl ring.	718.7466	718.2	A
790	 Chemical structure of compound 790: Similar to compound 789, but the side chain is modified. The terminal vinyl group is replaced by a cyclopropyl group, and the methyl group in the side chain is explicitly labeled as CH₃.	718.7466	718.2	A

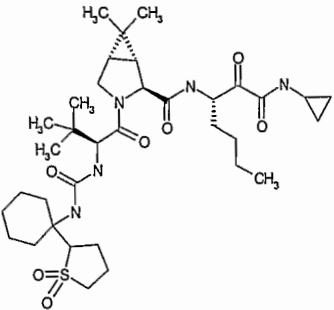
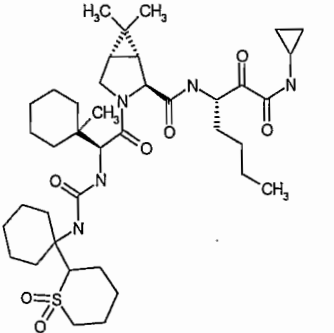
791	 Chemical structure of compound 791: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 1,1-dichloroethyl group, a 2-methyl-2-propionyl-1-methylpyrrolidine-3-carboxamide group, and a 2-methyl-2-propionyl-1-methylpyrrolidine-3-carboxamide group. The pyrrolidine ring is also substituted with a 2-methyl-2-propionyl-1-methylpyrrolidine-3-carboxamide group. The molecule includes a sulfonamide group and a cyclopropylmethyl group.	730.7578	730.2	A
792	 Chemical structure of compound 792: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 1,1-dichloroethyl group, a 2-methyl-2-propionyl-1-methylpyrrolidine-3-carboxamide group, and a 2-methyl-2-propionyl-1-methylpyrrolidine-3-carboxamide group. The pyrrolidine ring is also substituted with a 2-methyl-2-propionyl-1-methylpyrrolidine-3-carboxamide group. The molecule includes a sulfonamide group and a cyclopropylmethyl group.	744.0143		A

793	 The chemical structure shows a cyclohexane ring substituted with a sulfone group (-SO₂-) and a cyclopropyl group. The cyclohexane ring is also substituted with a carbonyl group (-C(=O)-) and a nitrogen atom. The nitrogen atom is part of a larger structure that includes a cyclopropyl group and a carbonyl group. The structure is highly complex and contains multiple functional groups.	732.0032	732.1	A
794	 The chemical structure is identical to the one in row 793, showing a cyclohexane ring substituted with a sulfone group (-SO₂-) and a cyclopropyl group. The cyclohexane ring is also substituted with a carbonyl group (-C(=O)-) and a nitrogen atom. The nitrogen atom is part of a larger structure that includes a cyclopropyl group and a carbonyl group. The structure is highly complex and contains multiple functional groups.	732.0032		A

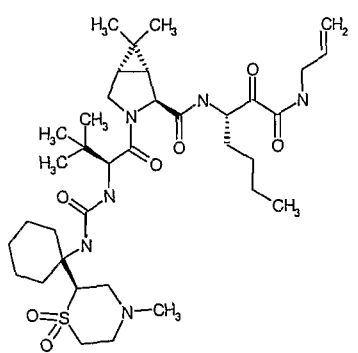
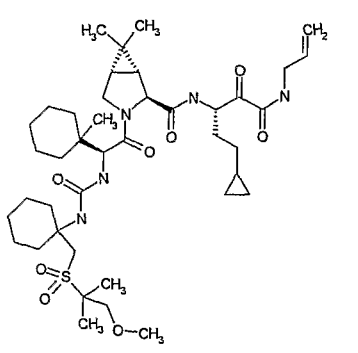
795	 Chemical structure of compound 795: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge bond to methyl, dash bond to propyl), a 2-((cyclohexylmethyl)amino)-2-oxoethyl group, and a 2-((cyclopropylmethyl)amino)-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-((cyclohexylmethyl)amino)-2-oxoethyl group. The molecule includes a sulfonamide group (cyclohexylmethyl sulfonamide) and a cyclopropylmethyl group.	744.0143		A
796	 Chemical structure of compound 796: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge bond to methyl, dash bond to propyl), a 2-((cyclohexylmethyl)amino)-2-oxoethyl group, and a 2-((cyclopropylmethyl)amino)-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-((cyclohexylmethyl)amino)-2-oxoethyl group. The molecule includes a sulfonamide group (cyclohexylmethyl sulfonamide) and a cyclopropylmethyl group.	732.0032	732.1	A

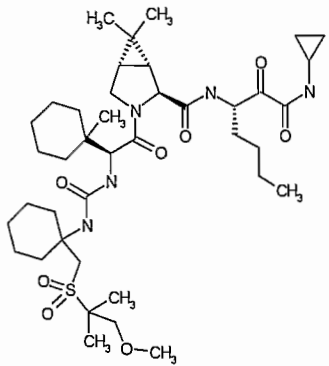
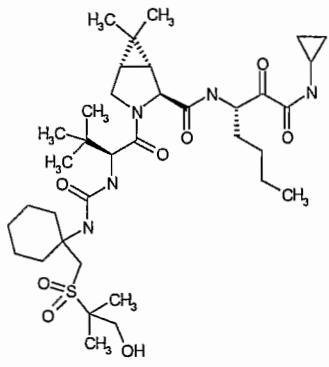
797	 <chem>CC(C)(C)C(=O)N1C(=O)C(C2CCCCC2)C(=O)N1C(=O)N(C)C(=O)N(C)C(=O)N3CCCC3S(=O)(=O)C4CCCCC4</chem>	746.0303		A
798	 <chem>CC(C)(C)C(=O)N1C(=O)C(C2CCCCC2)C(=O)N1C(=O)N(C)C(=O)N(C)C(=O)N3CCCC3S(=O)(=O)C4CCCCC4</chem>	677.9108	678.1	A

799	 Chemical structure of compound 799: A complex molecule featuring a central pyrrolidine ring substituted with a cyclohexyl group, a dimethyl-substituted cyclopropyl group, and a side chain containing a carbamate and a cyclopropyl group. It is also linked to a sulfonamide moiety via a carbonyl group.	732.0032	732.2	A
800	 Chemical structure of compound 800: Similar to compound 799, but with an additional methyl group on the side chain, resulting in a different stereochemistry and molecular weight.	691.9378	692.2	A

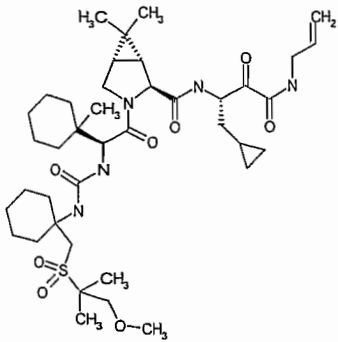
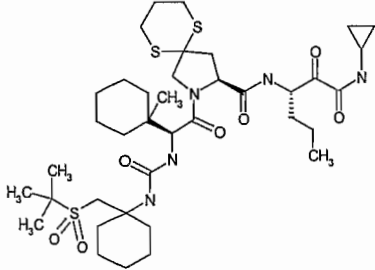
801		692	692.2	A
802		746.0303		A

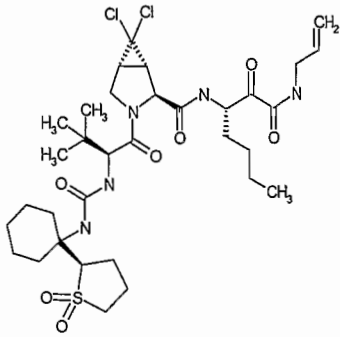
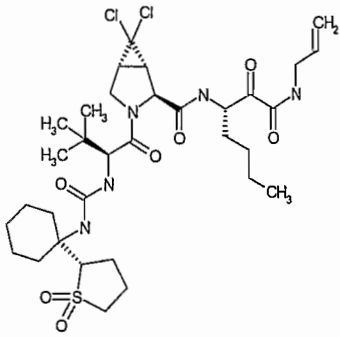
A

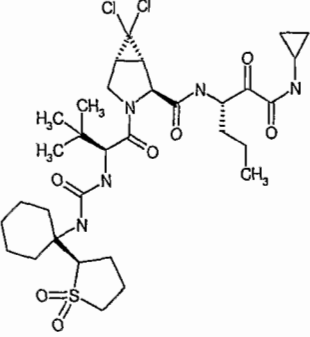
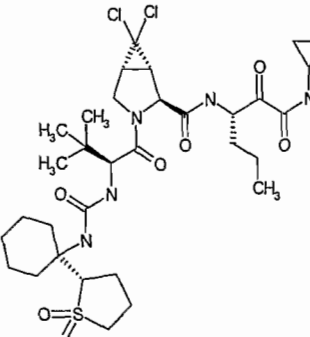
805		720.9796	A
806		790.0838	A

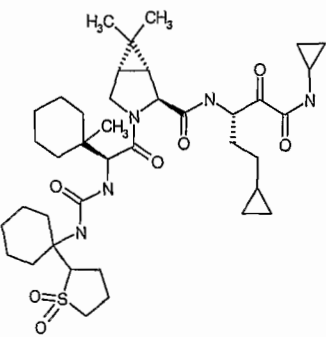
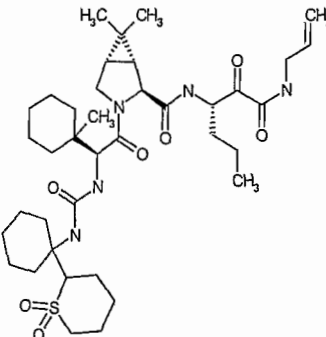
807		778.0727		A
808		723.9803		A

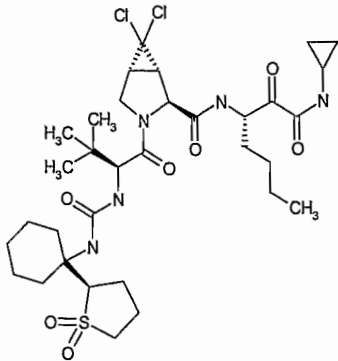
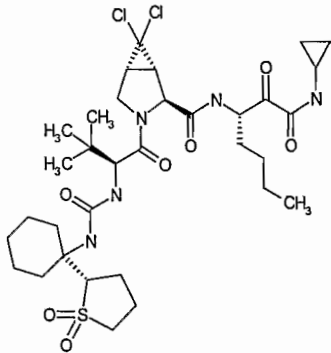
809		764.0456		A
810		705.9649	706.4	A

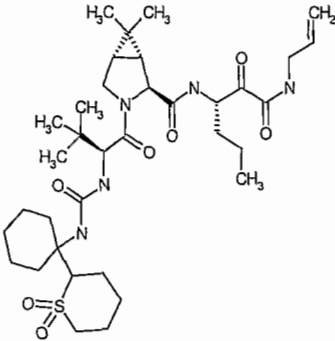
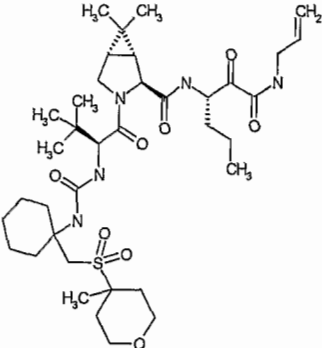
811	 Chemical structure of compound 811: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl is part of a larger system including a nitrogen atom bonded to a cyclopropylmethyl group and a sulfonamide group. The sulfonamide group is further substituted with a methoxy group and a methyl group. The molecule also contains a cyclopropylmethyl group and a vinyl group.	776.0568		A
812	 Chemical structure of compound 812: A complex molecule featuring a cyclohexane ring substituted with a methyl group and a carbonyl group. The carbonyl is part of a larger system including a nitrogen atom bonded to a cyclopropylmethyl group and a sulfonamide group. The sulfonamide group is further substituted with a methoxy group and a methyl group. The molecule also contains a cyclopropylmethyl group and a vinyl group.	798.1471	798.4	A

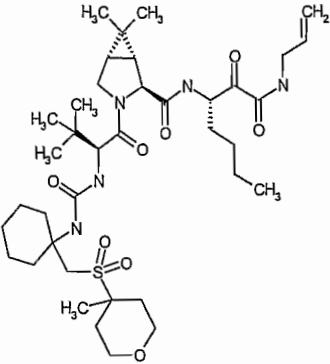
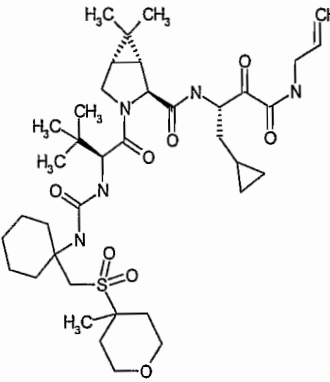
813		732.7737	732.1	A
814		732.7737	732.1	A

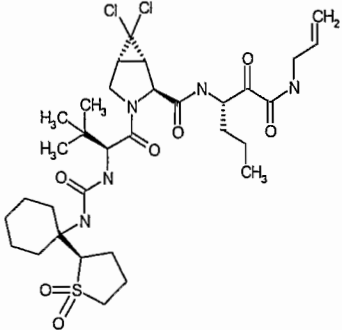
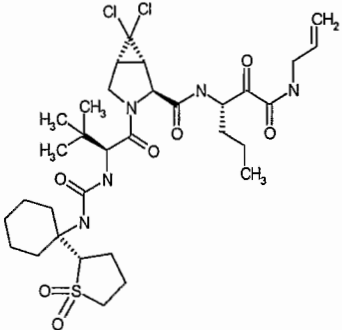
815		718.7466	718.1	A
816		718.7466	718.1	A

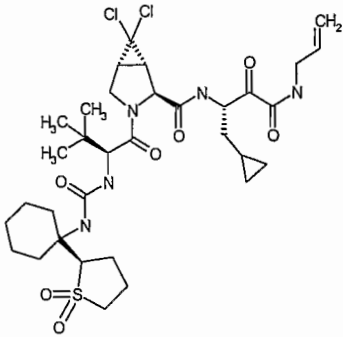
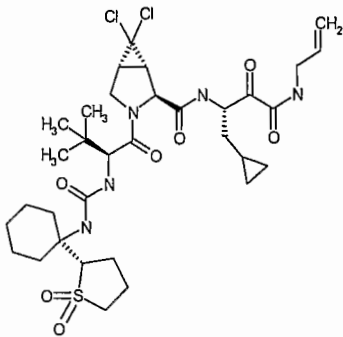
817		744.0143	744.1	A
818		732.0032	732.1	A

819		732.7737	732.1	A
820		732.7737	732.1	A

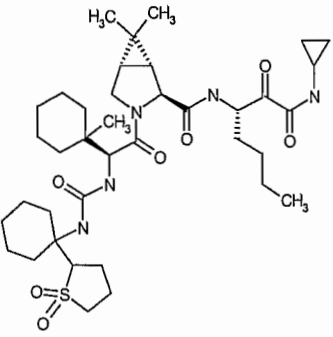
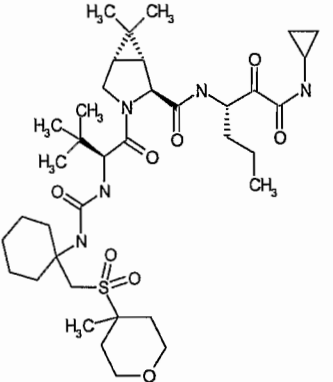
821		691.9378	692.1	A
822		735.9914	736.1	A

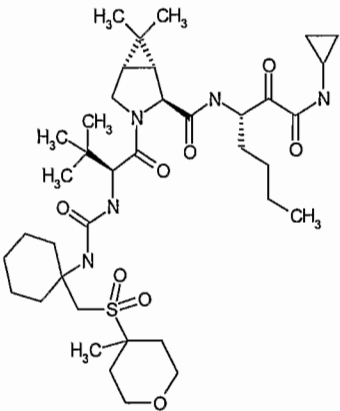
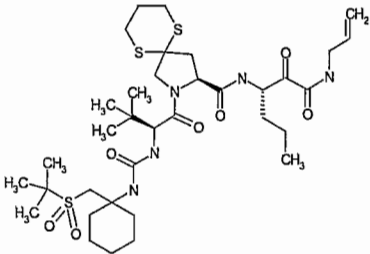
823	 Chemical structure of compound 823: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a carbonyl group (C=O). The carbonyl group is part of a larger amide structure. The pyrrolidine ring is also connected to a sulfonamide group (SO₂NH-) which is linked to a cyclohexyl ring. The cyclohexyl ring is further substituted with a methyl group (CH₃) and a tetrahydropyran ring. The tetrahydropyran ring is also substituted with a methyl group (CH₃). The molecule contains several other functional groups, including a vinyl group (CH=CH₂) and a carbonyl group (C=O).	750.0185	750.1	A
824	 Chemical structure of compound 824: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a methyl group (CH₃) and a carbonyl group (C=O). The carbonyl group is part of a larger amide structure. The pyrrolidine ring is also connected to a sulfonamide group (SO₂NH-) which is linked to a cyclohexyl ring. The cyclohexyl ring is further substituted with a methyl group (CH₃) and a tetrahydropyran ring. The tetrahydropyran ring is also substituted with a methyl group (CH₃). The molecule contains several other functional groups, including a vinyl group (CH=CH₂) and a carbonyl group (C=O).	748.0026	748.1	A

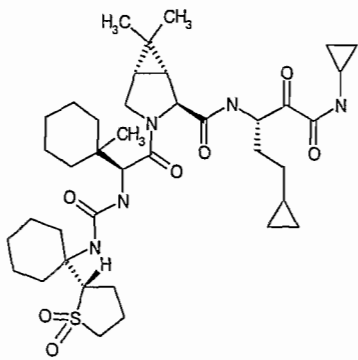
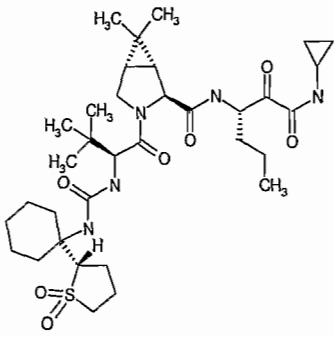
825	 The chemical structure shows a cyclohexane ring substituted with a sulfonamide group (-SO₂NH-) and a pyrrolidine ring. The pyrrolidine ring is further substituted with a side chain containing a vinyl group (-CH=CH₂) and a methyl group (-CH₃). The structure also includes a carbonyl group and a chlorine atom.	718.7466	718.2	A
826	 The chemical structure is identical to the one in row 825, showing a cyclohexane ring substituted with a sulfonamide group (-SO₂NH-) and a pyrrolidine ring. The pyrrolidine ring is further substituted with a side chain containing a vinyl group (-CH=CH₂) and a methyl group (-CH₃). The structure also includes a carbonyl group and a chlorine atom.	718.7466	718.2	A

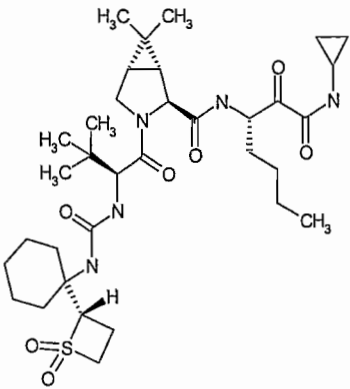
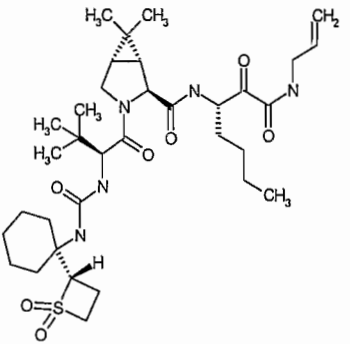
827	 Chemical structure of compound 827: A complex molecule featuring a central pyrrolidine ring substituted with a dichloromethyl group (CHCl₂), a tert-butyl group, and a carbonyl group. This pyrrolidine is linked via an amide bond to a cyclopropylmethyl group, which is further connected to a carbonyl group. Another amide branch from the central pyrrolidine leads to a cyclohexyl ring, which is substituted with a sulfonamide group (SO₂NH₂).	730.7578	730.2	A
828	 Chemical structure of compound 828: A complex molecule featuring a central pyrrolidine ring substituted with a dichloromethyl group (CHCl₂), a tert-butyl group, and a carbonyl group. This pyrrolidine is linked via an amide bond to a cyclopropylmethyl group, which is further connected to a carbonyl group. Another amide branch from the central pyrrolidine leads to a cyclohexyl ring, which is substituted with a sulfonamide group (SO₂NH₂).	730.7578	730.2	A

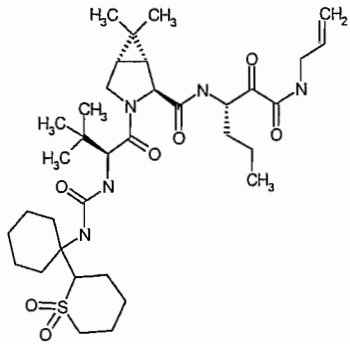
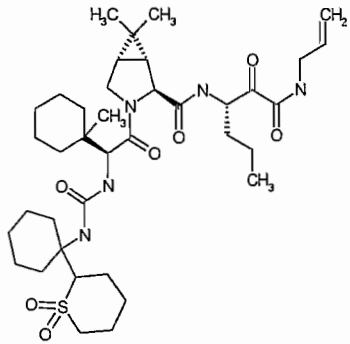
CC(C)[C@H]1CC[C@@H](C(=O)N(CCC(=O)N2CC2)C(=O)N3C(=O)C(C)C3)[C@@H](C)C1C(=O)N(C(=O)N4C(=O)C5CCCCC4S(=O)(=O)C5)CCC(C)C1CCC(CC1)S(=O)(=O)C2(C)C(C)C(=O)N2C(=O)N3C(C)C(C)C3C(=O)N[C@@H](CCCC)C(=O)N[C@H](C=C)C=CC=C

831		732.0032	732.2	A
832		735.9914	736.1	A

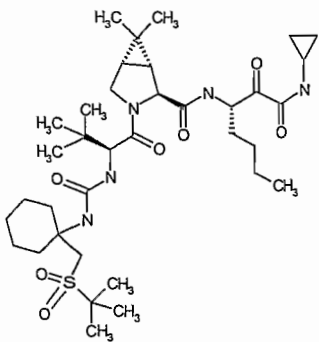
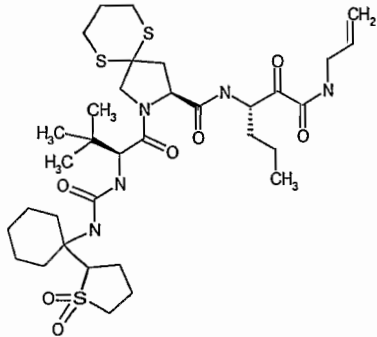
833	 Chemical structure of compound 833: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (H₃C, CH₃, H₃C) at the 2-position, a carbonyl group (C=O) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl group at the 3-position is linked to a side chain containing a cyclopropyl group (triangle) and a propyl group (CH₂, CH₂, CH₃). The carbonyl group at the 4-position is linked to a side chain containing a cyclopropyl group (triangle) and a propyl group (CH₂, CH₂, CH₃). The pyrrolidine ring is also linked to a side chain containing a cyclopropyl group (triangle) and a propyl group (CH₂, CH₂, CH₃). The side chain is linked to a sulfonamide group (SO₂) which is further linked to a cyclohexyl group (hexagon) and a morpholine ring (six-membered ring with one oxygen atom).	750.0185	750.1	A
834	 Chemical structure of compound 834: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (H₃C, CH₃, H₃C) at the 2-position, a carbonyl group (C=O) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl group at the 3-position is linked to a side chain containing a cyclopropyl group (triangle) and a propyl group (CH₂, CH₂, CH₃). The carbonyl group at the 4-position is linked to a side chain containing a cyclopropyl group (triangle) and a propyl group (CH₂, CH₂, CH₃). The pyrrolidine ring is also linked to a side chain containing a cyclopropyl group (triangle) and a propyl group (CH₂, CH₂, CH₃). The side chain is linked to a sulfonamide group (SO₂) which is further linked to a cyclohexyl group (hexagon) and a morpholine ring (six-membered ring with one oxygen atom).	758.0818	758.2	A

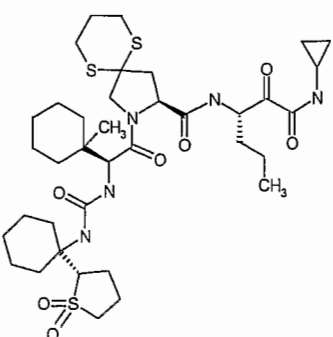
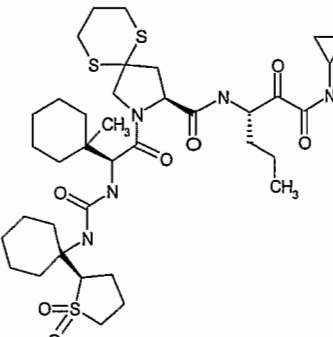
835		744.0143	744.1	A
836		677.9108		A

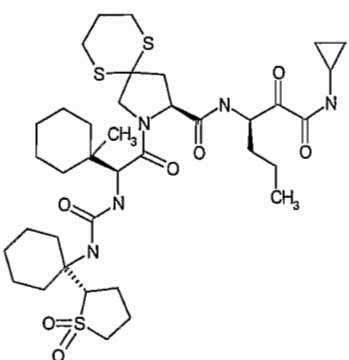
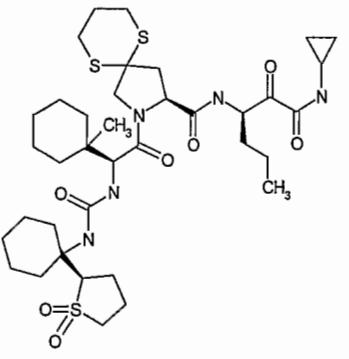
837	 Chemical structure of compound 837: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂ group) and a carbamate group. The carbamate group is linked to a chiral center (marked with a wedge bond) which is part of a larger amide structure. This amide structure includes a pyrrolidine ring substituted with a methyl group and a carbamate group. The carbamate group is further substituted with a propyl chain and a cyclopropyl group.	677.9108	678.3	A
838	 Chemical structure of compound 838: A complex molecule featuring a cyclohexane ring substituted with a sulfonamide group (SO₂ group) and a carbamate group. The carbamate group is linked to a chiral center (marked with a wedge bond) which is part of a larger amide structure. This amide structure includes a pyrrolidine ring substituted with a methyl group and a carbamate group. The carbamate group is further substituted with a propyl chain and a vinyl group (CH=CH₂).	677.9108	678.3	A

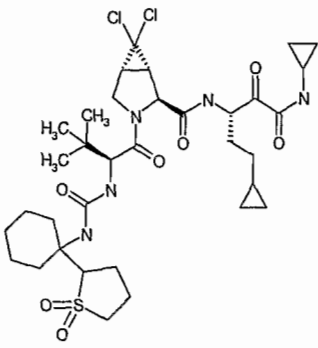
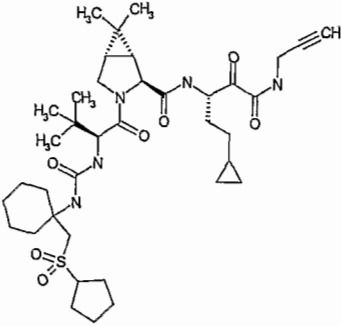
839	 Chemical structure of compound 839: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 2-position, a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 3-position, and a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 4-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 5-position. The molecule contains multiple amide and sulfonamide groups, and a cyclohexylmethyl group.	691.9378		A
840	 Chemical structure of compound 840: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 2-position, a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 3-position, and a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 4-position. The pyrrolidine ring is also substituted with a 2,2-dimethyl-1-(cyclohexylmethyl)pyrrolidine-1-carboxamide group at the 5-position. The molecule contains multiple amide and sulfonamide groups, and a cyclohexylmethyl group.	732.0032		A

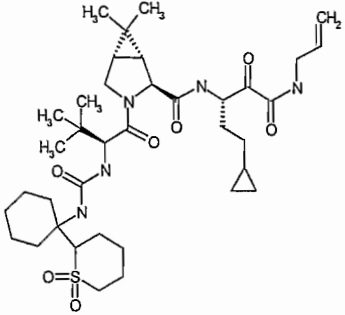
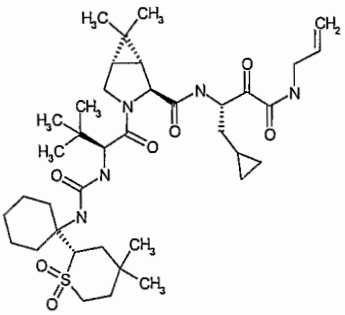
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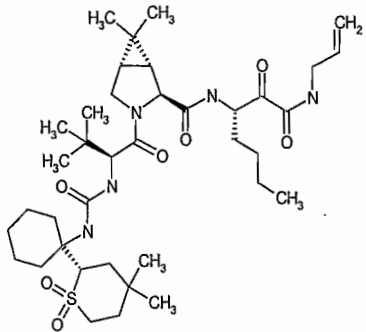
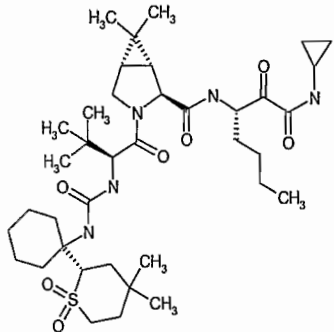
843		707.9809	708.4	11
845		742.0388	742.4	A

846		782.1041	782.4	A
847		782.1041	782.4	A

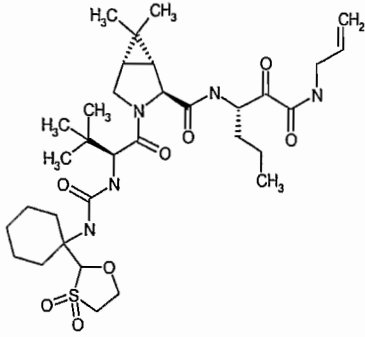
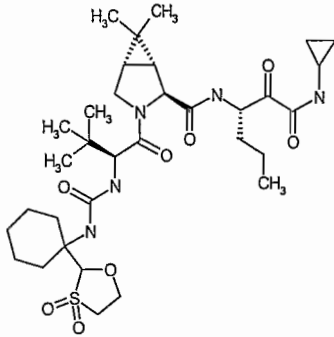
848	 The chemical structure shows a thietane ring (four-membered ring with one sulfur atom) connected to a cyclohexane ring. The cyclohexane ring is substituted with a methyl group and a sulfonamide group. The sulfonamide group is further substituted with a cyclopropyl group. The structure is a complex molecule with multiple rings and functional groups.	782.1041	782.4	B
849	 The chemical structure is identical to the one in row 848. It features a thietane ring connected to a cyclohexane ring, which is substituted with a methyl group and a sulfonamide group. The sulfonamide group is further substituted with a cyclopropyl group.	782.1041	782.4	B

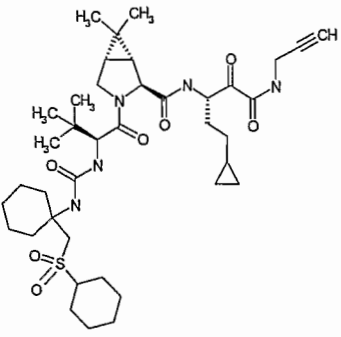
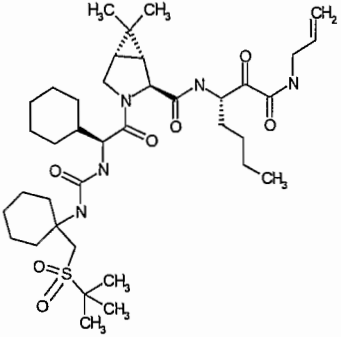
854	 Chemical structure of compound 854: A complex molecule featuring a central pyrrolidine ring substituted with a dichloromethyl group, a tert-butyl group, and a carbonyl group. This pyrrolidine is linked via an amide bond to a side chain containing a cyclopropylmethyl group and a carbonyl group. The side chain is further connected to a nitrogen atom that is part of a larger system including a cyclohexyl ring and a sulfonamide group.	744.7849	744.4	A
855	 Chemical structure of compound 855: Similar to compound 854, but the side chain is modified to include a terminal alkyne group (CH₂C≡CH) instead of a cyclopropylmethyl group. The rest of the molecule, including the central pyrrolidine and the sulfonamide-containing side chain, remains the same.	729.9872	730.2	A

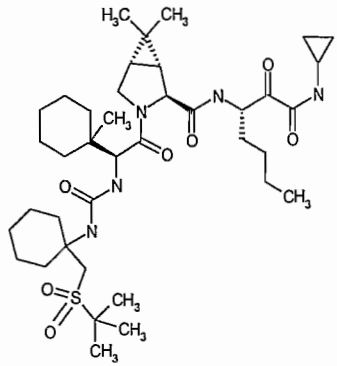
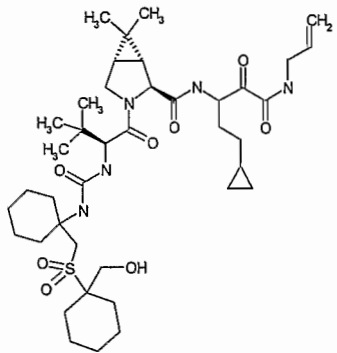
856		717.9761		5
857		732.0032	732.4	A

858	 Chemical structure of compound 858: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyl group, a 2,2,3-trimethylbutyl group, and a 2,2,3-trimethylbutyl group. The pyrrolidine ring is connected via a carbonyl group to a side chain containing a 2,2,3-trimethylbutyl group, a 2,2,3-trimethylbutyl group, and a 2,2,3-trimethylbutyl group. The side chain also includes a 2,2,3-trimethylbutyl group and a 2,2,3-trimethylbutyl group. The molecule is further substituted with a 2,2,3-trimethylbutyl group and a 2,2,3-trimethylbutyl group.	734.0191	734.4	A
859	 Chemical structure of compound 859: A complex molecule featuring a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyl group, a 2,2,3-trimethylbutyl group, and a 2,2,3-trimethylbutyl group. The pyrrolidine ring is connected via a carbonyl group to a side chain containing a 2,2,3-trimethylbutyl group, a 2,2,3-trimethylbutyl group, and a 2,2,3-trimethylbutyl group. The side chain also includes a 2,2,3-trimethylbutyl group and a 2,2,3-trimethylbutyl group. The molecule is further substituted with a 2,2,3-trimethylbutyl group and a 2,2,3-trimethylbutyl group.	734.0191	734.41	A

860		746.0303	746.5	A
861		691.8942	692.4	A

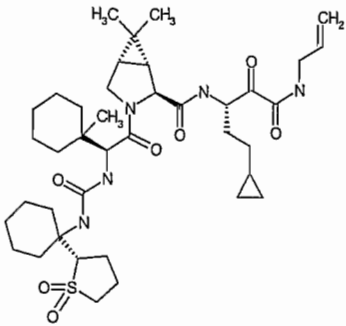
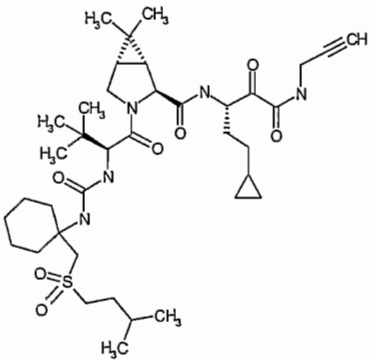
862	 Chemical structure of compound 862: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (C(CH₃)₃) at the 2-position, a carbonyl group (C=O) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl group at the 3-position is linked to a side chain: -CH(CH₃)-CH₂-C(=O)-N-CH=CH₂. The carbonyl group at the 4-position is linked to a side chain: -CH(CH₃)-CH₂-C(=O)-N-CH=CH₂. The pyrrolidine ring is also linked to a cyclohexane ring via a carbonyl group (C=O) at the 1-position. The cyclohexane ring is further substituted with a sulfonamide group (-SO₂-NH-) and a methoxy group (-OCH₃).	679.8831	680.38	A
863	 Chemical structure of compound 863: A complex molecule featuring a central pyrrolidine ring. The pyrrolidine ring is substituted with a tert-butyl group (C(CH₃)₃) at the 2-position, a carbonyl group (C=O) at the 3-position, and a carbonyl group (C=O) at the 4-position. The carbonyl group at the 3-position is linked to a side chain: -CH(CH₃)-CH₂-C(=O)-N-CH₂-CH₂-C(=O)-N-cyclopropyl. The carbonyl group at the 4-position is linked to a side chain: -CH(CH₃)-CH₂-C(=O)-N-cyclopropyl. The pyrrolidine ring is also linked to a cyclohexane ring via a carbonyl group (C=O) at the 1-position. The cyclohexane ring is further substituted with a sulfonamide group (-SO₂-NH-) and a methoxy group (-OCH₃).	679.8831	680.4	A

864		744.0143	744.1	A
865		734.0191	734.4	A

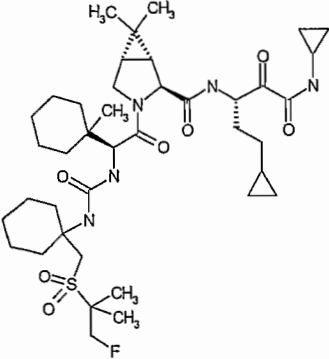
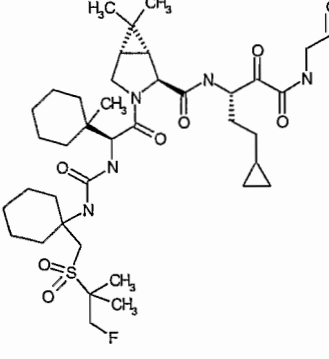
866		748.0462	748.4	A
867		776.0568		A

868		675.8948		A
869		663.8837		A

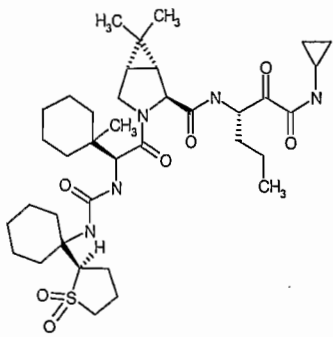
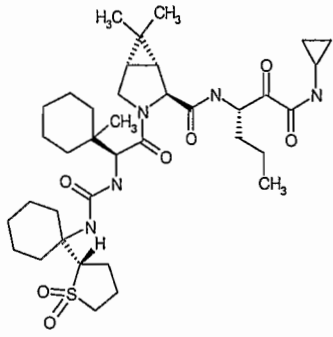
870		717.9761		A
871		744.0143		A

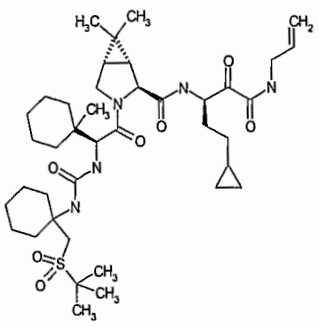
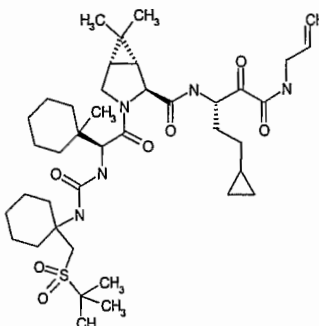
872	 Chemical structure of compound 872: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge bond to methyl, dash bond to isopropyl), a 2-((2-cyclohexyl-2-((2-cyclohexyl-1-methyl-1-sulfonyl-1,2,3,4-tetrahydropyridin-1-yl)amino)ethyl)amino)acetyl group, and a 2-((2-cyclopropyl-2-oxoethyl)amino)acetyl group. The side chain includes a vinyl group (-CH=CH₂).	744.0143		A
873	 Chemical structure of compound 873: A complex molecule featuring a central pyrrolidine ring substituted with a 2-methyl-2-propyl group (wedge bond to methyl, dash bond to isopropyl), a 2-((2-cyclohexyl-2-((2-cyclohexyl-1-methyl-1-sulfonyl-1,2,3,4-tetrahydropyridin-1-yl)amino)ethyl)amino)acetyl group, and a 2-((2-cyclopropyl-2-oxoethyl)amino)acetyl group. The side chain includes a cyano group (-C≡CH).	732.0032	732.1	A

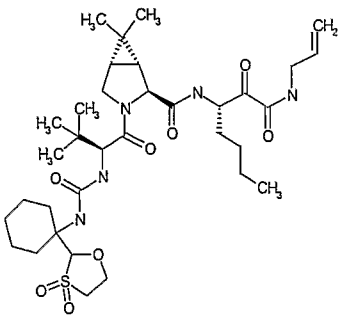
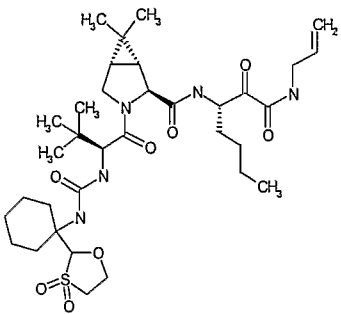
874		734.0191	734.1	A
875		719.9484		A

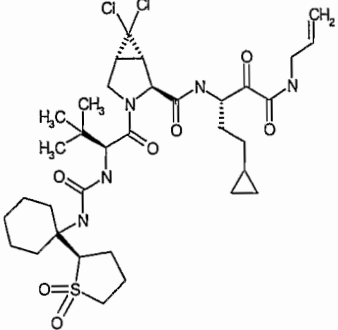
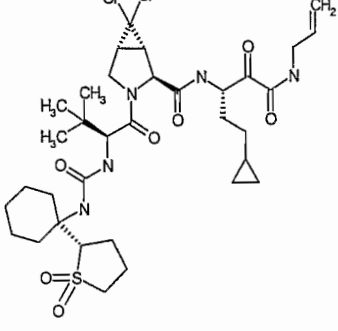
876		778.0478		A
877		778.0478		A

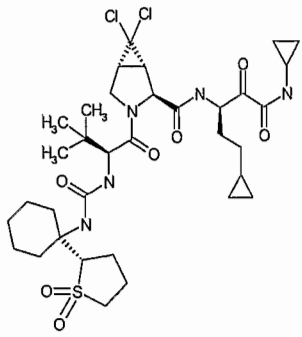
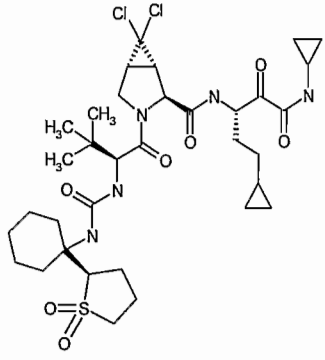
878		766.0366		A
879		766.0366		A

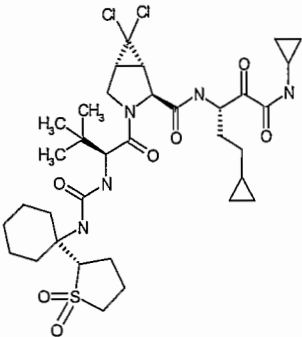
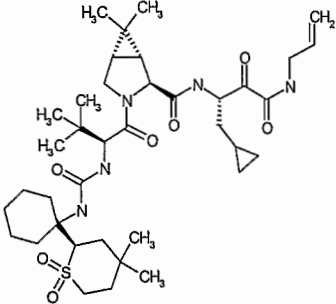
880	 The chemical structure shows a cyclohexane ring substituted with a methyl group and a pyrrolidine ring. The pyrrolidine ring is further substituted with a methyl group and a sulfonamide group. The sulfonamide group is connected to a cyclopropylmethyl group. The structure is drawn with stereochemistry indicated by wedges and dashes.	717.9761	718.1	A
881	 The chemical structure is identical to the one in row 880, showing a cyclohexane ring substituted with a methyl group and a pyrrolidine ring. The pyrrolidine ring is further substituted with a methyl group and a sulfonamide group. The sulfonamide group is connected to a cyclopropylmethyl group. The structure is drawn with stereochemistry indicated by wedges and dashes.	717.9761	718.1	A

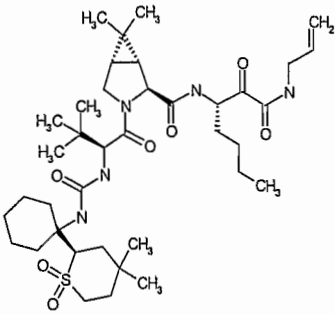
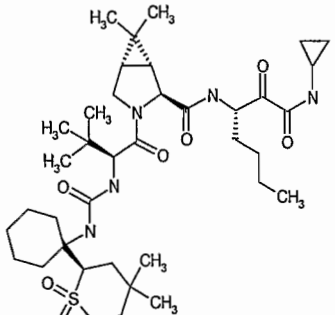
883-a	 Chemical structure of compound 883-a. It features a central bicyclic system (a cyclohexane ring fused to a five-membered ring containing a nitrogen atom). This system is substituted with a tert-butyl sulfonamide group, a cyclopropylmethyl group, and a side chain containing a carbamate and an allyl group. Stereochemistry is indicated with wedges and dashes.	760.0574		B
883-b	 Chemical structure of compound 883-b. It is similar to 883-a but with different stereochemistry at the chiral centers, as indicated by the different wedge/dash configurations.	760.0574		A

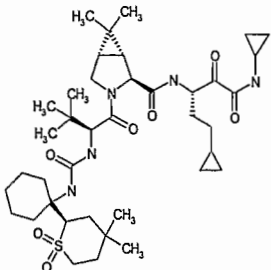
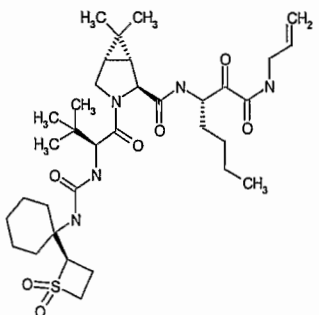
883-c	 The chemical structure of compound 883-c is a complex molecule. It features a central pyrrolidine ring. Attached to the pyrrolidine ring is a side chain containing a carbonyl group, a methylene group, and a terminal vinyl group. Another side chain on the pyrrolidine ring includes a carbonyl group, a methylene group, and a terminal vinyl group. A third side chain on the pyrrolidine ring is a cyclohexyl group. A fourth side chain on the pyrrolidine ring is a sulfonamide group, which is further substituted with a cyclohexyl group and a sulfonamide group.	693.9102		3
883-d	 The chemical structure of compound 883-d is identical to the structure of compound 883-c, as shown above.	693.9102		A

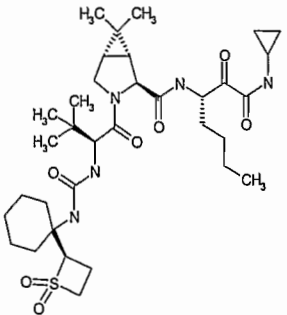
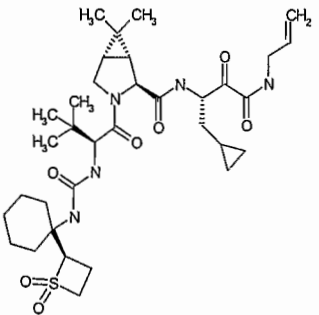
883-e	 The chemical structure of compound 883-e is a complex molecule. It features a central pyrrolidine ring substituted with a 1,1-dichloroethyl group (wedge bond), a 2-((cyclopropylmethyl)amino)-2-oxoethyl group (dash bond), and a 2-((cyclohexylamino)carbonyl)-2-methylpropanoyl group (wedge bond). The cyclohexylamino group is further substituted with a 2-oxo-2-sulfolanylmethyl group (wedge bond).	744.7849		A
883-f	 The chemical structure of compound 883-f is identical to that of compound 883-e. It features a central pyrrolidine ring substituted with a 1,1-dichloroethyl group (wedge bond), a 2-((cyclopropylmethyl)amino)-2-oxoethyl group (dash bond), and a 2-((cyclohexylamino)carbonyl)-2-methylpropanoyl group (wedge bond). The cyclohexylamino group is further substituted with a 2-oxo-2-sulfolanylmethyl group (wedge bond).	744.7849		A

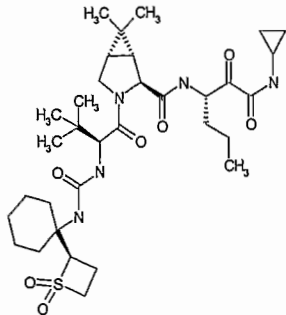
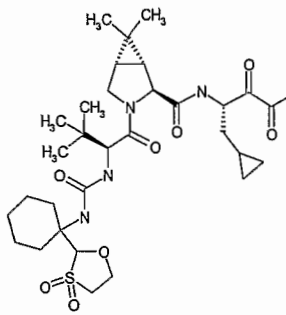
	 Chemical structure of compound 883-fa: A complex molecule featuring a central pyrrolidine ring substituted with a dichloromethyl group, a tert-butyl group, and a carbonyl group. This carbonyl is linked via an amide bond to a side chain containing a cyclopropylmethyl group and a carbonyl group. Another amide branch from the side chain leads to a cyclopropylmethyl group. The pyrrolidine nitrogen is also part of a larger system including a cyclohexyl ring and a sulfonamide group.	744.7849		A
883-fa				
	 Chemical structure of compound 883-g: Similar to 883-fa, but with a different stereochemistry at the chiral center of the side chain, indicated by a dashed bond to the cyclopropylmethyl group.	744.7849		A
883-g				

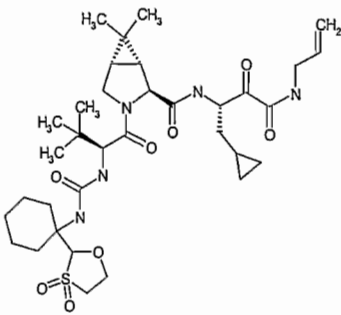
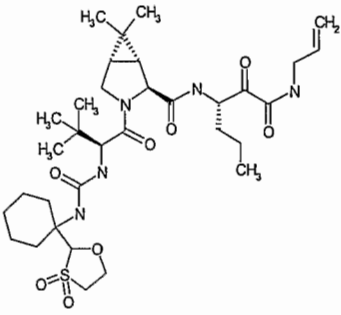
883-h	 Chemical structure of compound 883-h. It features a central pyrrolidine ring substituted with a 1,1-dichloroethyl group, a 2,2,3-trimethylbutyramide group, and a 2-((cyclohexylamino)sulfonyl)cyclopentyl group. The pyrrolidine ring is also linked via an amide bond to a side chain containing a cyclopropylmethyl group and a 2-(cyclopropylamino)acrylamide group.	744.7849		A
883-i	 Chemical structure of compound 883-i. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyramide group and a 2-((cyclohexylamino)sulfonyl)-2-methylcyclopentyl group. The pyrrolidine ring is also linked via an amide bond to a side chain containing a cyclopropylmethyl group and a 2-(cyclopropylamino)acrylamide group.	732.0032		A

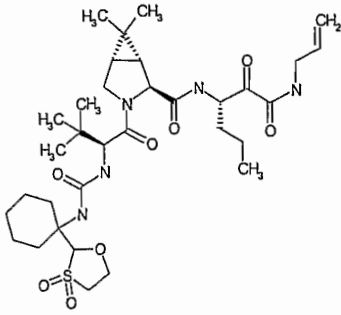
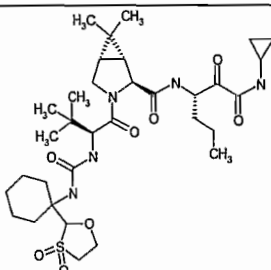
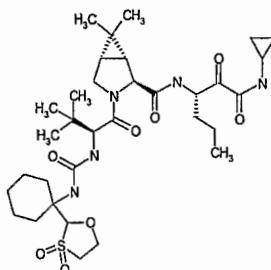
883-j	 Chemical structure of compound 883-j. It features a central bicyclic sulfonamide core. The core consists of a cyclohexane ring fused to a five-membered ring containing a sulfonamide group (SO₂NH-). The nitrogen of the sulfonamide is substituted with a cyclohexyl group. The five-membered ring also has a carbonyl group (C=O) and a nitrogen atom. This nitrogen is part of a five-membered ring that also contains a carbonyl group and a methyl group. The nitrogen of this ring is substituted with a propyl group. The carbonyl carbon of this ring is substituted with a methyl group and a vinyl group (CH=CH₂).	734.0191		A
883-k	 Chemical structure of compound 883-k. It features a central bicyclic sulfonamide core, similar to 883-j. The core consists of a cyclohexane ring fused to a five-membered ring containing a sulfonamide group (SO₂NH-). The nitrogen of the sulfonamide is substituted with a cyclohexyl group. The five-membered ring also has a carbonyl group (C=O) and a nitrogen atom. This nitrogen is part of a five-membered ring that also contains a carbonyl group and a methyl group. The nitrogen of this ring is substituted with a propyl group. The carbonyl carbon of this ring is substituted with a methyl group and a cyclopropyl group.	734.0191		A

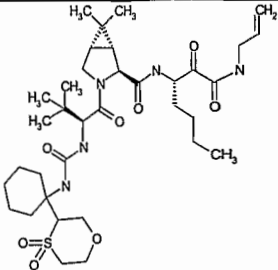
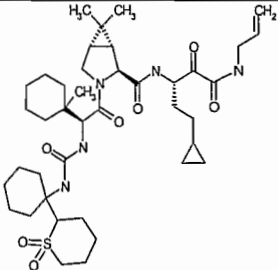
883-l	 Chemical structure of compound 883-l. It features a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-cyclopropyl-2-oxoethyl group, and a 2-cyclopropyl-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-cyclopropyl-2-oxoethyl group. The structure is complex, with multiple chiral centers and functional groups.	746.0303		A
883-m	 Chemical structure of compound 883-m. It features a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-cyclopropyl-2-oxoethyl group, and a 2-cyclopropyl-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-cyclopropyl-2-oxoethyl group. The structure is complex, with multiple chiral centers and functional groups.	677.9108		A

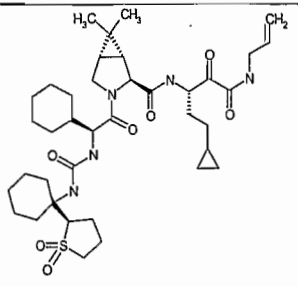
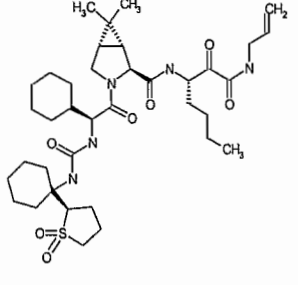
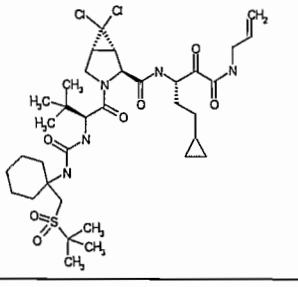
883-n	 Chemical structure of compound 883-n. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutanamide group, a 2,2,3-trimethylbutanamide group, and a 2,2,3-trimethylbutanamide group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutanamide group. The structure includes a cyclohexyl group, a sulfonamide group, and a 2,2,3-trimethylbutanamide group.	677.9108		A
883-o	 Chemical structure of compound 883-o. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutanamide group, a 2,2,3-trimethylbutanamide group, and a 2,2,3-trimethylbutanamide group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutanamide group. The structure includes a cyclohexyl group, a sulfonamide group, and a 2,2,3-trimethylbutanamide group.	675.8948		A

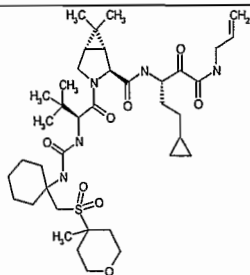
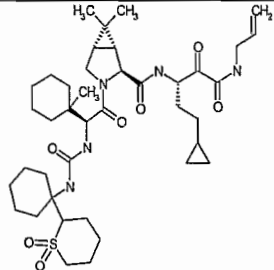
883-p	 Chemical structure of compound 883-p. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutanamide group, a 2,2,3-trimethylbutanamide group, and a 2,2,3-trimethylbutanamide group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutanamide group. The structure includes a sulfonamide group, a cyclopropyl group, and a 2,2,3-trimethylbutanamide group.	663.8837		A
883-q	 Chemical structure of compound 883-q. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutanamide group, a 2,2,3-trimethylbutanamide group, and a 2,2,3-trimethylbutanamide group. The pyrrolidine ring is also substituted with a 2,2,3-trimethylbutanamide group. The structure includes a sulfonamide group, a cyclopropyl group, and a 2,2,3-trimethylbutanamide group.	691.8942		A

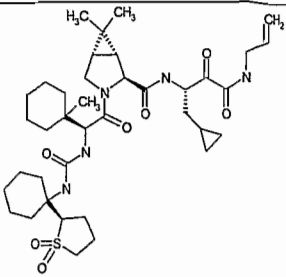
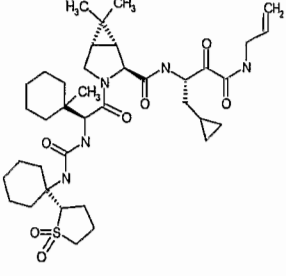
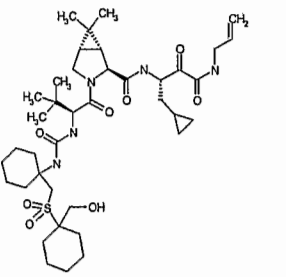
883-r	 The chemical structure of compound 883-r is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutanamide group (top), a 2,2,3-trimethylbutanamide group (left), and a 2-((cyclohexylmethyl)amino)-2-oxo-1,3-dioxolane-5-sulfonyl group (bottom). The 2,2,3-trimethylbutanamide group on the left is further substituted with a 2-((cyclohexylmethyl)amino)-2-oxo-1,3-dioxolane-5-sulfonyl group. The 2,2,3-trimethylbutanamide group on the top is further substituted with a 2-((cyclohexylmethyl)amino)-2-oxo-1,3-dioxolane-5-sulfonyl group.	691.8942		A
883-s	 The chemical structure of compound 883-s is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutanamide group (top), a 2,2,3-trimethylbutanamide group (left), and a 2-((cyclohexylmethyl)amino)-2-oxo-1,3-dioxolane-5-sulfonyl group (bottom). The 2,2,3-trimethylbutanamide group on the left is further substituted with a 2-((cyclohexylmethyl)amino)-2-oxo-1,3-dioxolane-5-sulfonyl group. The 2,2,3-trimethylbutanamide group on the top is further substituted with a 2-((cyclohexylmethyl)amino)-2-oxo-1,3-dioxolane-5-sulfonyl group.	679.8831		A

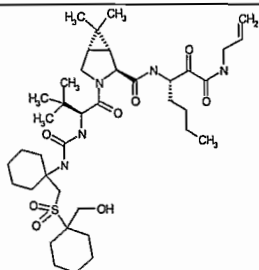
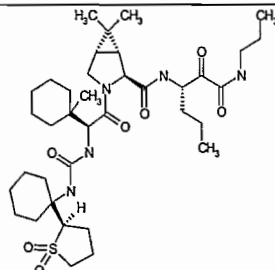
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883-u		679.8831		A
883-v		679.8831		A

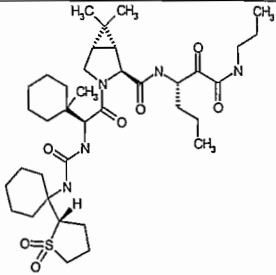
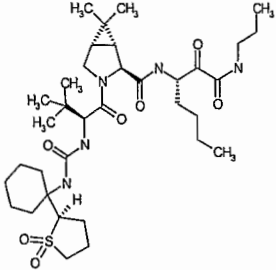
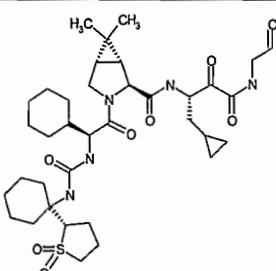
883-w	 The chemical structure of compound 883-w is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group, a 2-(cyclohexylmethyl)carbamoyl group, and a 2-(2-ethyl-3-oxo-1-(2-allylaminoethyl)-1-oxoethyl)carbamoyl group. The pyrrolidine ring is also substituted with a 2-(2-allylaminoethyl)-3-oxo-1-oxoethyl group.	707.9372		3
883-x	 The chemical structure of compound 883-x is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethyl-1,3-dioxolane-5-carbonyl group, a 2-(cyclohexylmethyl)carbamoyl group, and a 2-(2-cyclopropyl-3-oxo-1-(2-allylaminoethyl)-1-oxoethyl)carbamoyl group. The pyrrolidine ring is also substituted with a 2-(2-allylaminoethyl)-3-oxo-1-oxoethyl group.	758.0414		A

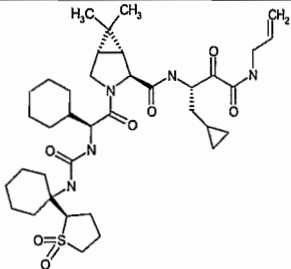
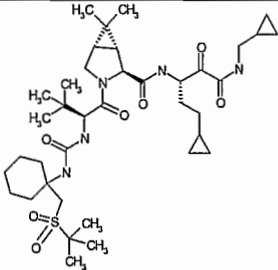
883-y	 Chemical structure of compound 883-y. It features a central pyrrolidine ring substituted with a cyclohexyl group, a dimethyl-substituted cyclopropyl group, and a side chain containing a carbamate and a vinyl group. This pyrrolidine is linked via an amide bond to a second pyrrolidine, which is further substituted with a cyclohexyl group and a sulfonamide group.	729.9872		A
883-z	 Chemical structure of compound 883-z. It is similar to 883-y but the side chain of the first pyrrolidine is a propyl group instead of a vinyl group.	717.9761		A
883-aa	 Chemical structure of compound 883-aa. It features a central pyrrolidine ring substituted with a dimethyl-substituted cyclopropyl group, a dichloromethyl-substituted cyclopropyl group, and a side chain containing a carbamate and a vinyl group. This pyrrolidine is linked via an amide bond to a second pyrrolidine, which is further substituted with a cyclohexyl group and a sulfonamide group.	760.8279		A

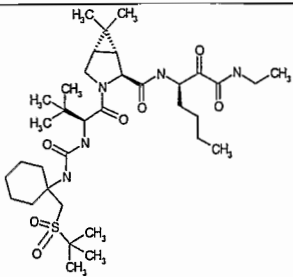
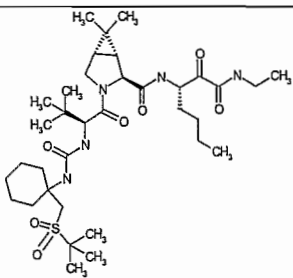
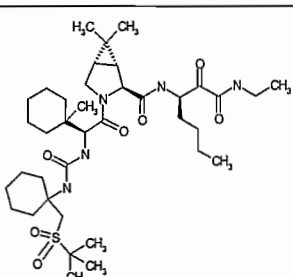
883-ab	 Chemical structure of compound 883-ab. It features a central cyclopropane ring substituted with a methyl group and a 2-methyl-2-butenoate group. This cyclopropane is linked via an amide bond to a 2-methyl-2-butenoate group, which is further linked via an amide bond to a 2-methyl-2-butenoate group. The structure also includes a cyclohexyl ring, a sulfonamide group, and a morpholine ring.	762.0297		A
883-ac	 Chemical structure of compound 883-ac. It features a central cyclopropane ring substituted with a methyl group and a 2-methyl-2-butenoate group. This cyclopropane is linked via an amide bond to a 2-methyl-2-butenoate group, which is further linked via an amide bond to a 2-methyl-2-butenoate group. The structure also includes a cyclohexyl ring, a sulfonamide group, and a morpholine ring.	758.0414		A

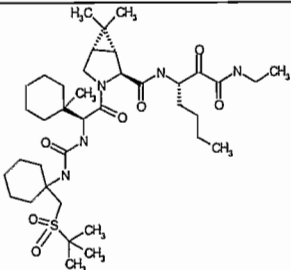
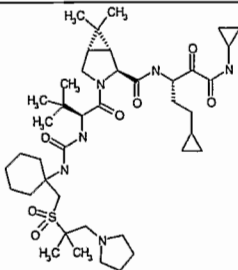
883-ad	 Chemical structure of compound 883-ad. It features a central pyrrolidine ring substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group, a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group, and a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group. The structure is complex, involving multiple rings and functional groups.	729.9872		A
883-ae	 Chemical structure of compound 883-ae. It is similar to 883-ad, but the central pyrrolidine ring is substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group, a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group, and a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group. The structure is complex, involving multiple rings and functional groups.	729.9872		A
883-af	 Chemical structure of compound 883-af. It is similar to 883-ad, but the central pyrrolidine ring is substituted with a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group, a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group, and a 2-methyl-2-propyl-1,3-dioxolane-5-carbonyl group. The structure is complex, involving multiple rings and functional groups.	762.0297		A

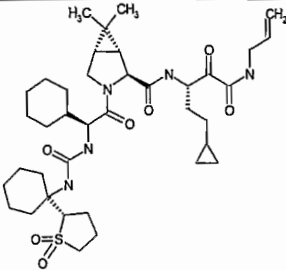
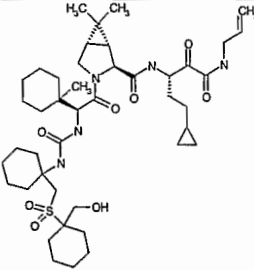
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883-ah		719.992	A	

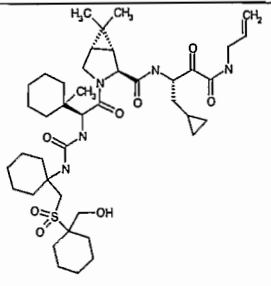
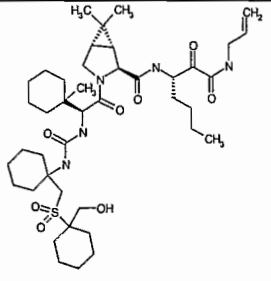
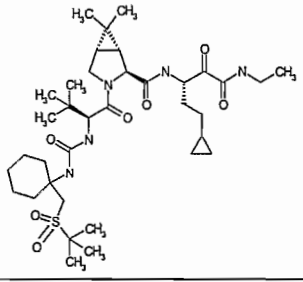
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883-aj		693.9538		A
883-ak		715.9601		A

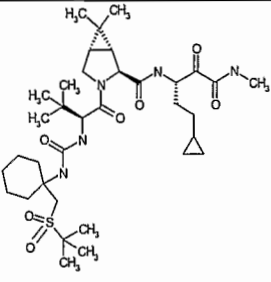
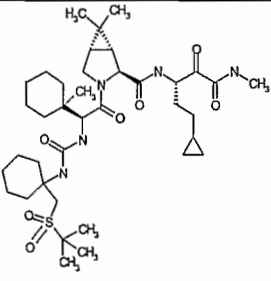
883-al	 Chemical structure of compound 883-al. It features a central pyrrolidine ring substituted with a 2-methylprop-1-en-1-yl group, a 2-oxo-2-(cyclohexylmethyl)ethyl group, and a 2-oxo-2-(cyclohexylmethyl)ethyl group. The pyrrolidine ring is also substituted with a 2-oxo-2-(cyclohexylmethyl)ethyl group. The structure includes a sulfonamide group and a cyclopropylmethyl group.	715.9601		A
883-am	 Chemical structure of compound 883-am. It features a central pyrrolidine ring substituted with a 2-methylprop-1-en-1-yl group, a 2-oxo-2-(cyclohexylmethyl)ethyl group, and a 2-oxo-2-(cyclohexylmethyl)ethyl group. The pyrrolidine ring is also substituted with a 2-oxo-2-(cyclohexylmethyl)ethyl group. The structure includes a sulfonamide group and a cyclopropylmethyl group.	734.0191		A

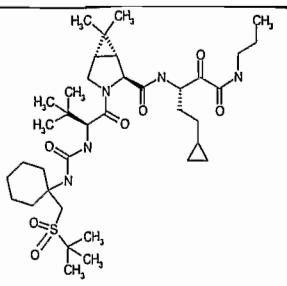
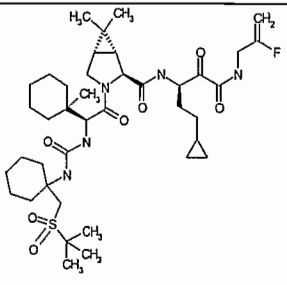
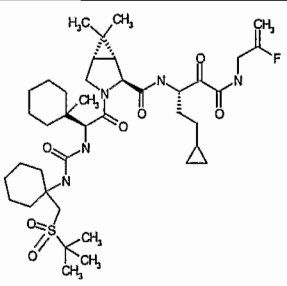
883-an		695.9697		C
883-ao		695.9697		A
883-ap		736.0351		B

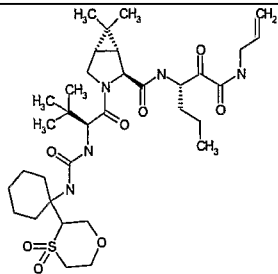
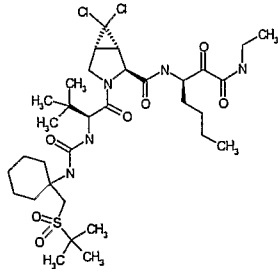
883-aq	 Chemical structure of compound 883-aq: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a sulfonamide group. The sulfonamide group is further substituted with a cyclopropylmethyl group and a dimethylamino group. The side chain also includes a carbonyl group and a nitrogen atom, which is part of a larger amide structure. The molecule is highly branched and contains multiple functional groups.	736.0351		A
883-ar	 Chemical structure of compound 883-ar: A complex molecule featuring a central cyclohexane ring. Attached to this ring is a side chain containing a carbonyl group, a nitrogen atom, and a sulfonamide group. The sulfonamide group is further substituted with a cyclopropylmethyl group and a dimethylamino group. The side chain also includes a carbonyl group and a nitrogen atom, which is part of a larger amide structure. The molecule is highly branched and contains multiple functional groups.	789.0991		A

883-av		729.9872		A
883-aw		816.1221		A

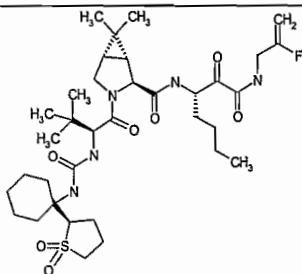
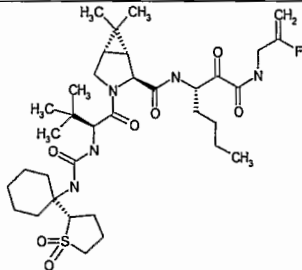
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883-ay		804.1109		A
883-az		707.9809		A

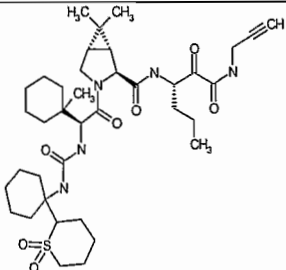
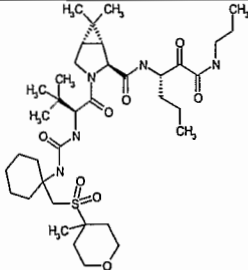
883-ba	 The chemical structure of 883-ba is a complex molecule. It features a central pyrrolidine ring. Attached to the pyrrolidine ring is a cyclopropylmethyl group. Another attachment point on the pyrrolidine ring is a carbonyl group, which is part of a larger amide structure. This amide structure includes a cyclohexyl ring and a sulfonamide group (SO₂CH₃). The molecule also contains a cyclopropylmethyl group and a carbonyl group. Stereochemistry is indicated with wedges and dashes.	693.9538		A
883-bb	 The chemical structure of 883-bb is similar to 883-ba. It features a central pyrrolidine ring. Attached to the pyrrolidine ring is a cyclopropylmethyl group. Another attachment point on the pyrrolidine ring is a carbonyl group, which is part of a larger amide structure. This amide structure includes a cyclohexyl ring and a sulfonamide group (SO₂CH₃). The molecule also contains a cyclopropylmethyl group and a carbonyl group. Stereochemistry is indicated with wedges and dashes.	734.0191		A

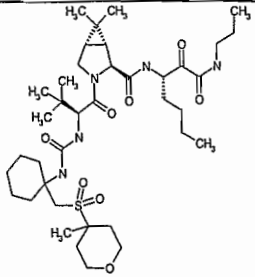
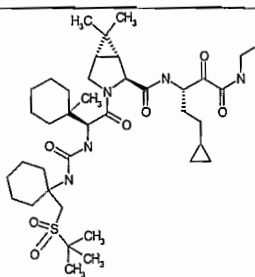
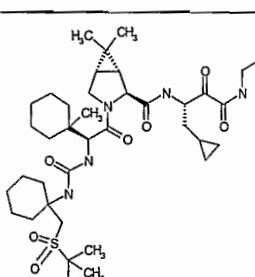
883-bc	 Chemical structure of compound 883-bc. It features a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-cyclopropyl-2-oxoethyl group, and a 2-((2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl)amino)ethyl group. The pyrrolidine ring is also substituted with a 2-cyclopropyl-2-oxoethyl group and a 2-((2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl)amino)ethyl group.	722.008		A
883-bd	 Chemical structure of compound 883-bd. It features a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-cyclopropyl-2-oxoethyl group, and a 2-((2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl)amino)ethyl group. The pyrrolidine ring is also substituted with a 2-cyclopropyl-2-oxoethyl group and a 2-((2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl)amino)ethyl group.	778.0478		b
883-be	 Chemical structure of compound 883-be. It features a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-cyclopropyl-2-oxoethyl group, and a 2-((2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl)amino)ethyl group. The pyrrolidine ring is also substituted with a 2-cyclopropyl-2-oxoethyl group and a 2-((2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl)amino)ethyl group.	778.0478		A

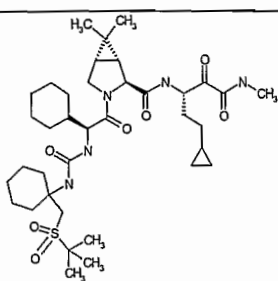
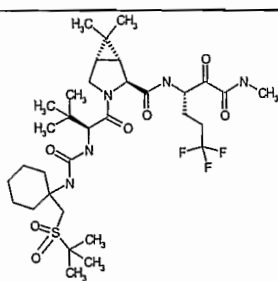
883-bf	 Chemical structure of compound 883-bf: A complex molecule featuring a cyclohexane ring fused to a sulfonamide group (SO₂), which is connected via a nitrogen atom to a carbonyl group. This carbonyl is part of a larger amide system, including a pyrrolidine ring substituted with two methyl groups and a side chain containing a ketone and an imine group.	693.9102		A
883-bg	 Chemical structure of compound 883-bg: A complex molecule featuring a cyclohexane ring fused to a sulfonamide group (SO₂), which is connected via a nitrogen atom to a carbonyl group. This carbonyl is part of a larger amide system, including a pyrrolidine ring substituted with two methyl groups and a side chain containing a ketone and an imine group.	736.8056		B

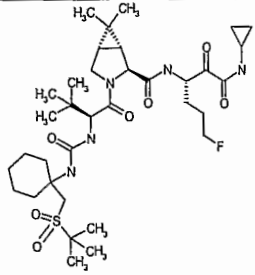
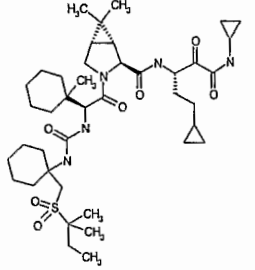
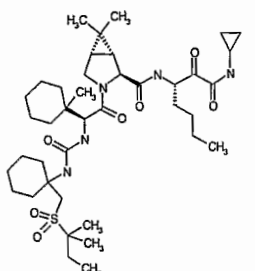
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883-bi		709.9283		B
883-bj		709.9283		B

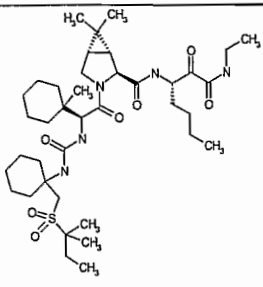
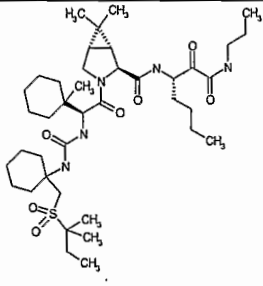
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883-bk				
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883-bl				

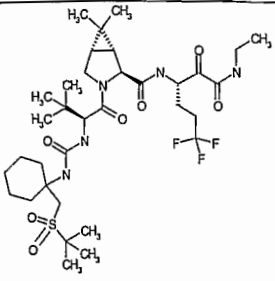
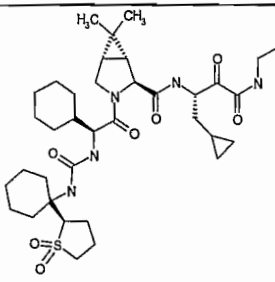
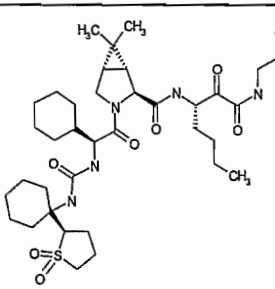
883-bp		729.9872		A
883-bq		738.0074		A

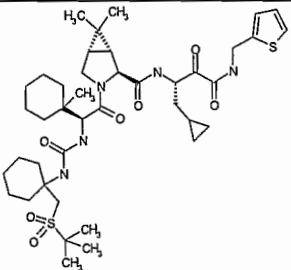
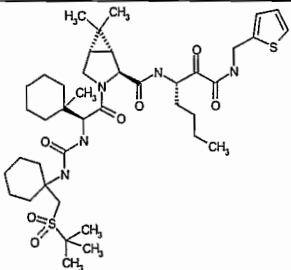
883-br	 Chemical structure of compound 883-br. It features a central pyrrolidine ring substituted with a 2-ethyl-2-oxoethyl group, a 2-ethyl-2-oxoethyl group, and a 2-ethyl-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-ethyl-2-oxoethyl group. The structure includes a cyclohexyl group, a sulfonamide group, and a 2-ethyl-2-oxoethyl group.	752.0345		A
883-bs	 Chemical structure of compound 883-bs. It features a central pyrrolidine ring substituted with a 2-ethyl-2-oxoethyl group, a 2-ethyl-2-oxoethyl group, and a 2-ethyl-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-ethyl-2-oxoethyl group. The structure includes a cyclohexyl group, a sulfonamide group, and a 2-ethyl-2-oxoethyl group.	748.0462		A
883-bt	 Chemical structure of compound 883-bt. It features a central pyrrolidine ring substituted with a 2-ethyl-2-oxoethyl group, a 2-ethyl-2-oxoethyl group, and a 2-ethyl-2-oxoethyl group. The pyrrolidine ring is also substituted with a 2-ethyl-2-oxoethyl group. The structure includes a cyclohexyl group, a sulfonamide group, and a 2-ethyl-2-oxoethyl group.	764.0207		A

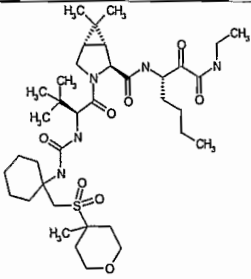
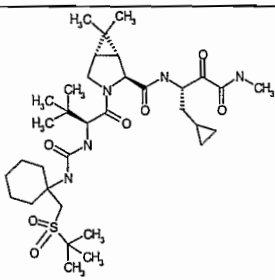
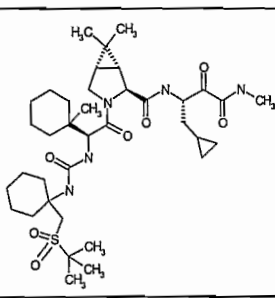
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883-bu				
		721.8868	A	
883-bv				

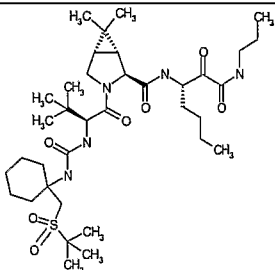
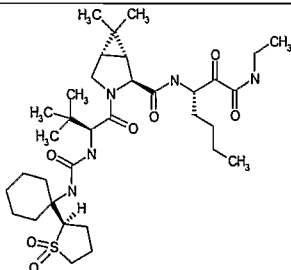
	 Chemical structure of compound 883-bw. It features a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group, and a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group. The side chain includes a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group and a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group.	711.9442		A
883-bw				
	 Chemical structure of compound 883-bx. It features a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group, and a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group. The side chain includes a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group and a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group.	774.0844		A
883-bx				
	 Chemical structure of compound 883-by. It features a central pyrrolidine ring substituted with a 2,2,4,4-tetramethyl-1,3-dioxane-5-carbonyl group, a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group, and a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group. The side chain includes a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group and a 2-(2,2,4,4-tetramethyl-1,3-dioxan-5-yl)propanoate group.	762.0733		A
883-by				

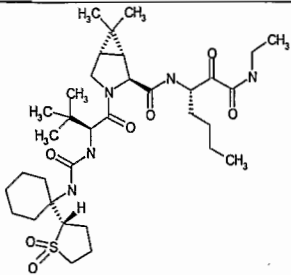
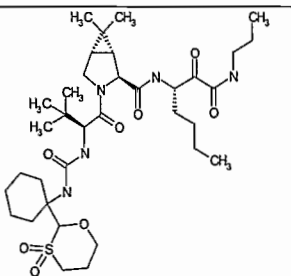
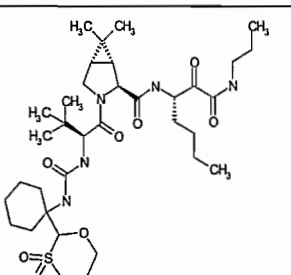
883-bz	 The chemical structure of 883-bz is a complex molecule. It features a central cyclohexane ring substituted with a methyl group and a 1-methyl-2-oxo-2-(propylamino)ethyl group. This cyclohexane ring is further substituted with a 1-methyl-2-oxo-2-(propylamino)ethyl group and a 1-methyl-2-oxo-2-(propylamino)ethyl group. The molecule also contains a sulfonamide group and a 1-methyl-2-oxo-2-(propylamino)ethyl group.	750.0621		A
883-ca	 The chemical structure of 883-ca is a complex molecule. It features a central cyclohexane ring substituted with a methyl group and a 1-methyl-2-oxo-2-(propylamino)ethyl group. This cyclohexane ring is further substituted with a 1-methyl-2-oxo-2-(propylamino)ethyl group and a 1-methyl-2-oxo-2-(propylamino)ethyl group. The molecule also contains a sulfonamide group and a 1-methyl-2-oxo-2-(propylamino)ethyl group.	764.0892		A

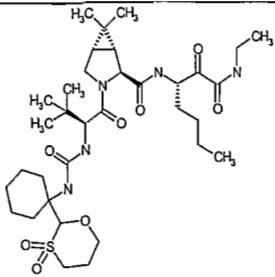
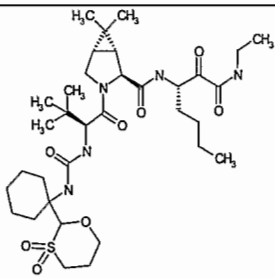
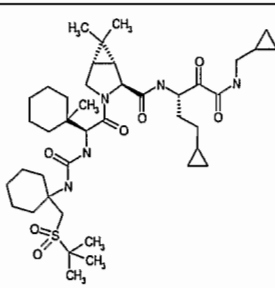
883-cb	 Chemical structure of compound 883-cb. It features a central amide linkage connecting a substituted pyrrolidine ring (with a methyl group and a cyclohexylmethyl group) to a chain containing a trifluoromethyl group and a dimethylsulfonyl group.	735.9139		A
883-cc	 Chemical structure of compound 883-cc. It features a central amide linkage connecting a substituted pyrrolidine ring (with a methyl group and a cyclohexylmethyl group) to a chain containing a cyclopropyl group and a dimethylsulfonyl group.	717.9761		A
883-cd	 Chemical structure of compound 883-cd. It features a central amide linkage connecting a substituted pyrrolidine ring (with a methyl group and a cyclohexylmethyl group) to a chain containing a propyl group and a dimethylsulfonyl group.	719.992		A

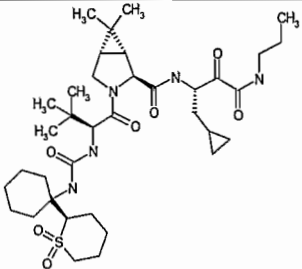
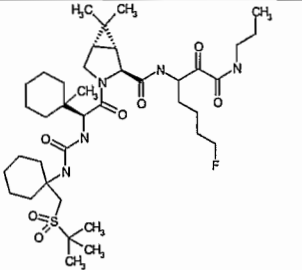
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883-cf		804.1325		A

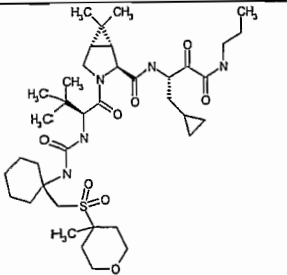
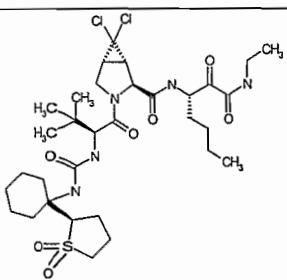
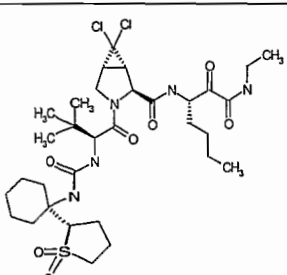
883-cg	 Chemical structure of compound 883-cg. It features a central pyrrolidine ring substituted with a 1-methyl-2-(propylamino)propanoyl group, a 1-methyl-2-(cyclopropylamino)propanoyl group, and a 1-methyl-2-(cyclohexylamino)propanoyl group. The pyrrolidine ring is also substituted with a 1-methyl-2-(cyclohexylamino)propanoyl group.	738.0074		A
883-ch	 Chemical structure of compound 883-ch. It features a central pyrrolidine ring substituted with a 1-methyl-2-(propylamino)propanoyl group, a 1-methyl-2-(cyclopropylamino)propanoyl group, and a 1-methyl-2-(cyclohexylamino)propanoyl group. The pyrrolidine ring is also substituted with a 1-methyl-2-(cyclohexylamino)propanoyl group.	679.9267		A
883-ci	 Chemical structure of compound 883-ci. It features a central pyrrolidine ring substituted with a 1-methyl-2-(propylamino)propanoyl group, a 1-methyl-2-(cyclopropylamino)propanoyl group, and a 1-methyl-2-(cyclohexylamino)propanoyl group. The pyrrolidine ring is also substituted with a 1-methyl-2-(cyclohexylamino)propanoyl group.	719.992		A

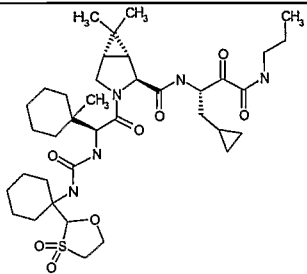
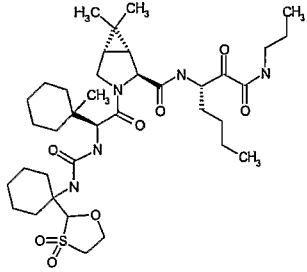
883-cj	 Chemical structure of compound 883-cj. It features a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-ethyl-3-methylbutanamide group, and a 2-ethyl-3-methylbutanamide group. The pyrrolidine ring is also substituted with a 2-ethyl-3-methylbutanamide group. The structure is complex, showing multiple amide and ester linkages.	709.9968		A
883-ck	 Chemical structure of compound 883-ck. It features a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-ethyl-3-methylbutanamide group, and a 2-ethyl-3-methylbutanamide group. The pyrrolidine ring is also substituted with a 2-ethyl-3-methylbutanamide group. The structure is complex, showing multiple amide and ester linkages.	679.9267		A

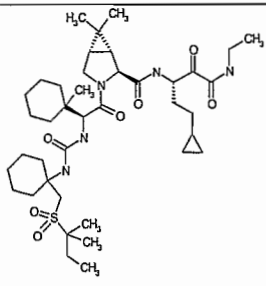
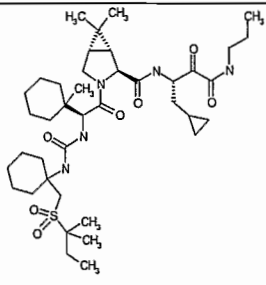
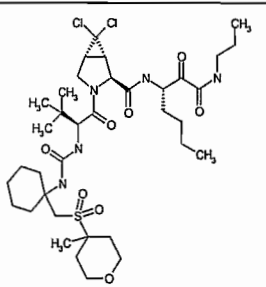
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883-cn		709.9532		A

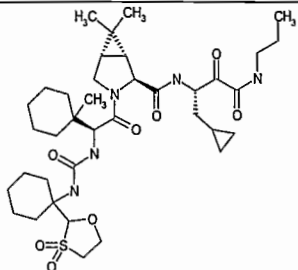
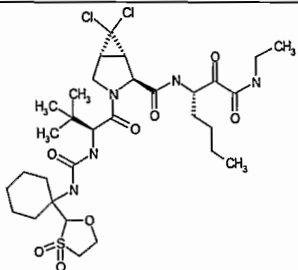
883-cq	 Chemical structure of compound 883-cq. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-(2-oxo-2-(propylthio)ethyl) group, and a 1-(2-oxo-2-(propylthio)ethyl) group. The pyrrolidine ring is also substituted with a 1-(2-oxo-2-(propylthio)ethyl) group. The structure includes a sulfonamide group and a cyclohexyl ring.	695.9261		A
883-cr	 Chemical structure of compound 883-cr. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-(2-oxo-2-(propylthio)ethyl) group, and a 1-(2-oxo-2-(propylthio)ethyl) group. The pyrrolidine ring is also substituted with a 1-(2-oxo-2-(propylthio)ethyl) group. The structure includes a sulfonamide group and a cyclohexyl ring.	695.9261		B
883-cs	 Chemical structure of compound 883-cs. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-(2-oxo-2-(propylthio)ethyl) group, and a 1-(2-oxo-2-(propylthio)ethyl) group. The pyrrolidine ring is also substituted with a 1-(2-oxo-2-(propylthio)ethyl) group. The structure includes a sulfonamide group and a cyclohexyl ring.	774.0844		A

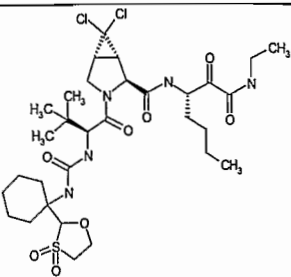
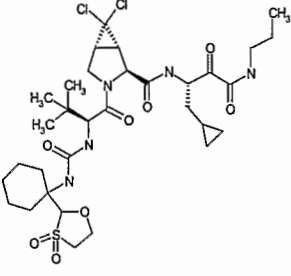
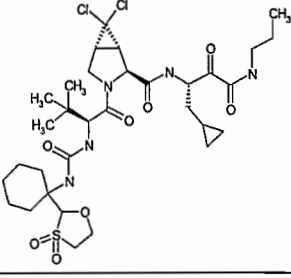
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883-cu		768.0526		A

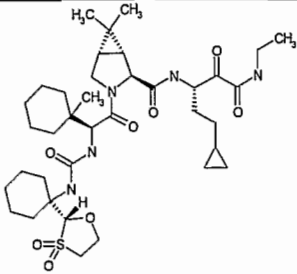
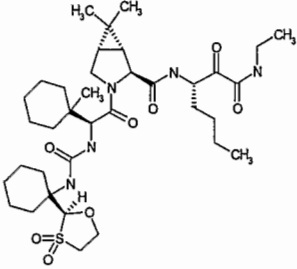
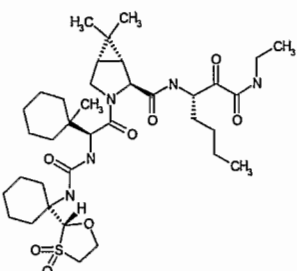
883-cv	 Chemical structure of compound 883-cv. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1,1-dimethyl-2-oxoethyl group, and a 1-cyclohexyl-2-sulfonyl group. The sulfonyl group is further substituted with a 1-methyl-2-oxoethyl group.	750.0185		A
883-cw	 Chemical structure of compound 883-cw. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1,1-dimethyl-2-oxoethyl group, and a 1-cyclohexyl-2-sulfonyl group. The sulfonyl group is further substituted with a 1-methyl-2-oxoethyl group.	720.7626		A
883-cx	 Chemical structure of compound 883-cx. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1,1-dimethyl-2-oxoethyl group, and a 1-cyclohexyl-2-sulfonyl group. The sulfonyl group is further substituted with a 1-methyl-2-oxoethyl group.	720.7626		A

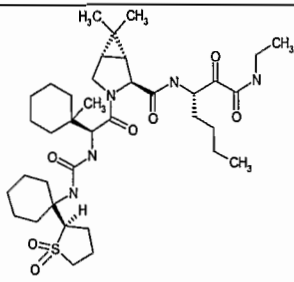
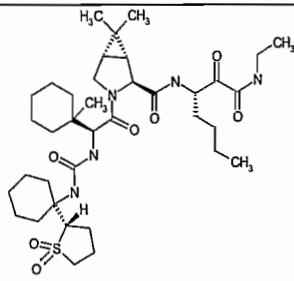
883-cy		733.9755		A
883-cz		735.9914		A

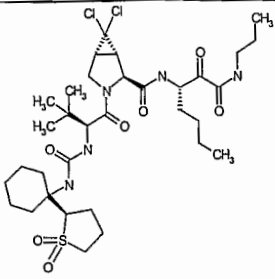
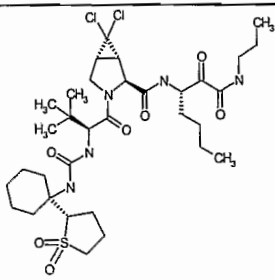
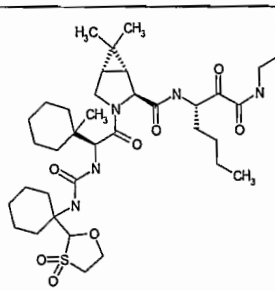
883-da	 Chemical structure of compound 883-da: A complex molecule featuring a central pyrrolidine ring substituted with a cyclohexyl group, a dimethylamino group, and a side chain containing a carbamate and a cyclopropyl group. It is also linked to a sulfonamide moiety via a carbonyl group.	762.0733		A
883-db	 Chemical structure of compound 883-db: A complex molecule featuring a central pyrrolidine ring substituted with a cyclohexyl group, a dimethylamino group, and a side chain containing a carbamate and a cyclopropyl group. It is also linked to a sulfonamide moiety via a carbonyl group.	762.0733		A
883-dc	 Chemical structure of compound 883-dc: A complex molecule featuring a central pyrrolidine ring substituted with a cyclohexyl group, a dimethylamino group, and a side chain containing a carbamate and a cyclopropyl group. It is also linked to a sulfonamide moiety via a carbonyl group.	792.8703		A

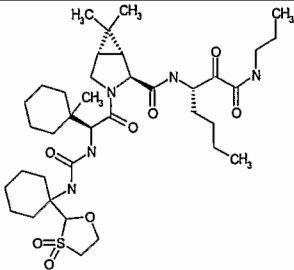
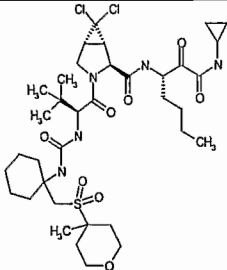
883-dd	 Chemical structure of compound 883-dd. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-methyl-2-oxo-2-(cyclopropylmethyl)ethyl group, and a 1-methyl-2-oxo-2-(cyclohexylmethyl)ethyl group. The pyrrolidine ring is also substituted with a 1-methyl-2-oxo-2-(cyclohexylmethyl)ethyl group. The structure includes a sulfonamide group and a cyclopropylmethyl group.	733.9755		A
883-de	 Chemical structure of compound 883-de. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-methyl-2-oxo-2-(cyclopropylmethyl)ethyl group, and a 1-methyl-2-oxo-2-(cyclohexylmethyl)ethyl group. The pyrrolidine ring is also substituted with a 1-methyl-2-oxo-2-(cyclohexylmethyl)ethyl group. The structure includes a sulfonamide group and a cyclopropylmethyl group.	722.7349		A

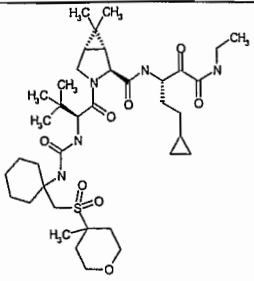
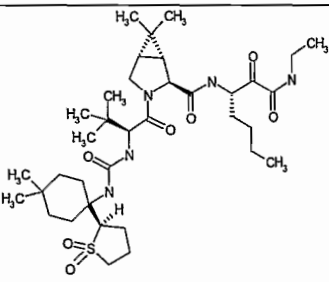
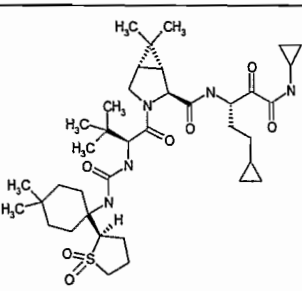
883-df	 The chemical structure of compound 883-df features a central pyrrolidine ring substituted with a dichloromethyl group (CHCl₂) and a carbonyl group. This carbonyl is part of an amide linkage to a side chain containing a propyl group and a terminal ethylcarbamate group. Another carbonyl group on the pyrrolidine ring is linked to a quaternary carbon atom bonded to two methyl groups and a 1-(cyclohexylmethyl)pyrrolidine-2-sulfonamide moiety.	722.7349		A
883-dg	 The chemical structure of compound 883-dg is similar to 883-df, but the side chain amide is linked to a cyclopropylmethyl group instead of a propyl group.	734.746		A
883-dh	 The chemical structure of compound 883-dh is identical to compound 883-dg, featuring a cyclopropylmethyl side chain.	734.746		A

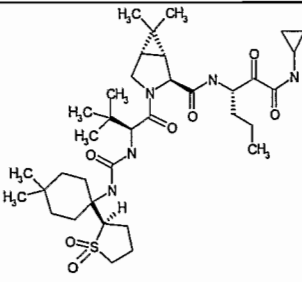
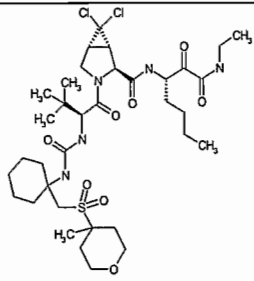
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883-dm		721.9643		A

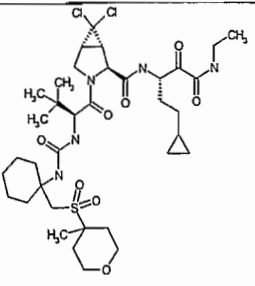
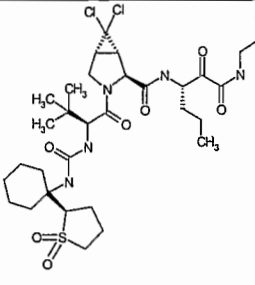
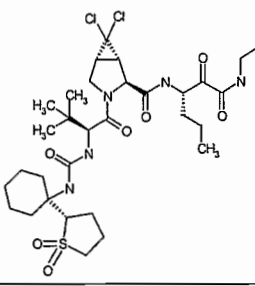
		719.992	A	
883-dn		719.992	A	
883-do				

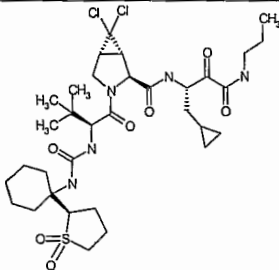
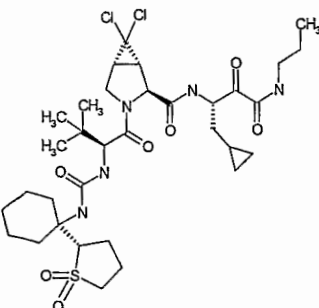
883-dp	 The chemical structure of 883-dp features a central pyrrolidine ring substituted with a 1,1-dichloroethyl group, a 2-ethyl-2-oxoethyl group, and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group. This pyrrolidine is further substituted with a 2-((2-ethyl-2-oxoethyl)amino)acetyl group and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group. The structure also includes a 2-ethyl-2-oxoethyl group and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group.	734.7897		A
883-dq	 The chemical structure of 883-dq is identical to 883-dp, featuring a central pyrrolidine ring substituted with a 1,1-dichloroethyl group, a 2-ethyl-2-oxoethyl group, and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group. This pyrrolidine is further substituted with a 2-((2-ethyl-2-oxoethyl)amino)acetyl group and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group. The structure also includes a 2-ethyl-2-oxoethyl group and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group.	734.7897		A
883-dr	 The chemical structure of 883-dr features a central pyrrolidine ring substituted with a 1,1-dimethyl-2-ethyl-2-oxoethyl group, a 2-ethyl-2-oxoethyl group, and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group. This pyrrolidine is further substituted with a 2-((2-ethyl-2-oxoethyl)amino)acetyl group and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group. The structure also includes a 2-ethyl-2-oxoethyl group and a 2-((2-ethyl-2-oxoethyl)amino)acetyl group.	735.9914		A

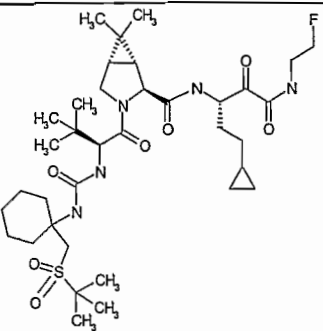
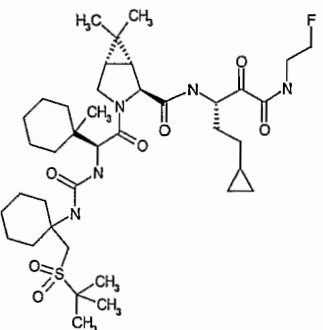
883-ds		735.9914		A
883-dt		790.8544		A

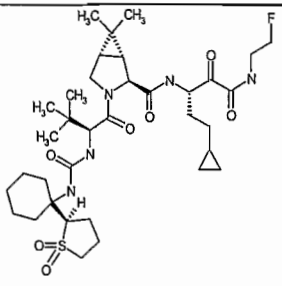
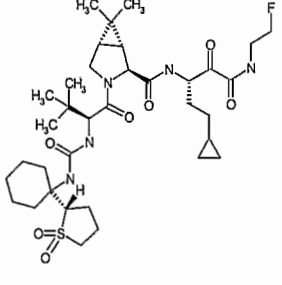
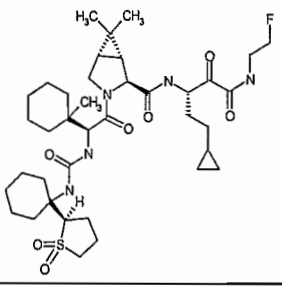
883-du	 Chemical structure of compound 883-du. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-cyclopropyl-3-oxopropyl group, and a 1-(4-methyl-1,3-dioxol-2-yl)sulfonyl group. The pyrrolidine ring is also substituted with a 1-(4-methyl-1,3-dioxol-2-yl)sulfonyl group.	750.0185		A
883-dv	 Chemical structure of compound 883-dv. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-cyclopropyl-3-oxopropyl group, and a 1-(4-methyl-1,3-dioxol-2-yl)sulfonyl group. The pyrrolidine ring is also substituted with a 1-(4-methyl-1,3-dioxol-2-yl)sulfonyl group.	707.9809		A
883-dw	 Chemical structure of compound 883-dw. It features a central pyrrolidine ring substituted with a 1-ethyl-3-oxopropyl group, a 1-cyclopropyl-3-oxopropyl group, and a 1-(4-methyl-1,3-dioxol-2-yl)sulfonyl group. The pyrrolidine ring is also substituted with a 1-(4-methyl-1,3-dioxol-2-yl)sulfonyl group.	732.0032		A

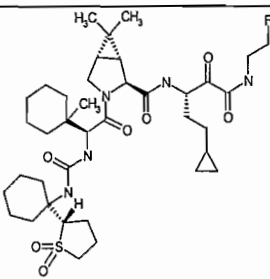
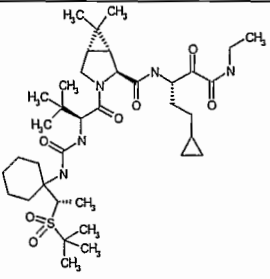
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883-dx				
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883-dy				

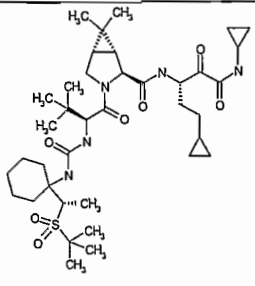
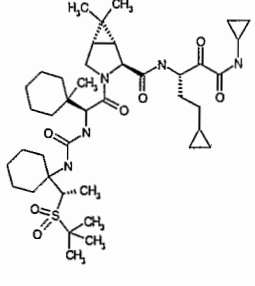
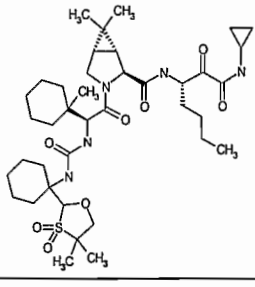
883-dz		790.8544		A
883-ea		720.7626		A
883-eb		720.7626		A

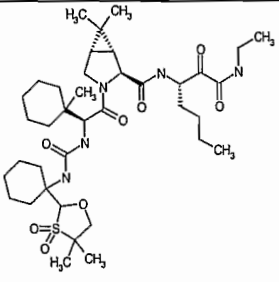
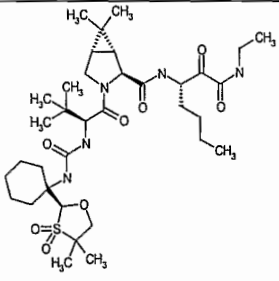
883-ec	 The chemical structure of compound 883-ec is a complex molecule. It features a central pyrrolidine ring substituted with a dichloromethyl group (CHCl₂) and a carbonyl group. This carbonyl is part of an amide linkage to a cyclopropylmethyl group. Another carbonyl group is attached to the pyrrolidine ring, which is further substituted with a tert-butyl group and a cyclohexylmethyl group. The cyclohexylmethyl group is connected to a cyclopentylmethyl group, which is in turn connected to a sulfonamide group (SO₂NH-).	732.7737	A	
883-ed	 The chemical structure of compound 883-ed is identical to that of compound 883-ec. It features a central pyrrolidine ring substituted with a dichloromethyl group (CHCl₂) and a carbonyl group. This carbonyl is part of an amide linkage to a cyclopropylmethyl group. Another carbonyl group is attached to the pyrrolidine ring, which is further substituted with a tert-butyl group and a cyclohexylmethyl group. The cyclohexylmethyl group is connected to a cyclopentylmethyl group, which is in turn connected to a sulfonamide group (SO₂NH-).	732.7737	A	

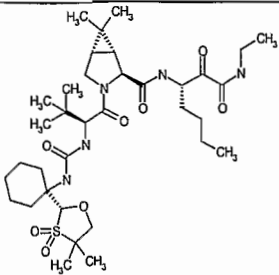
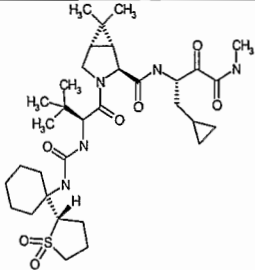
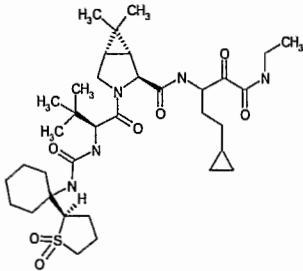
883-ee	 Chemical structure of compound 883-ee. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyl group, a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group, and a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group. The structure includes a cyclopropylmethyl group and a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group.	725.9713		A
883-ef	 Chemical structure of compound 883-ef. It features a central pyrrolidine ring substituted with a 2,2,3-trimethylbutyl group, a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group, and a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group. The pyrrolidine ring is also substituted with a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group. The structure includes a cyclopropylmethyl group and a 2-(2,2,3-trimethylbutyl)-2-oxo-1,3-dioxane-5-carbonyl group.	766.0366		A

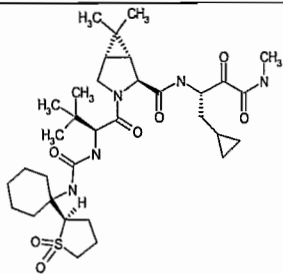
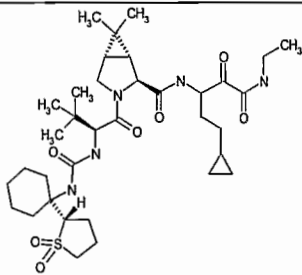
883-eg	 The chemical structure of 883-eg is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,4-trimethyl-1,3-dioxane-5-carbonyl group, a 2-(2,2,4-trimethyl-1,3-dioxan-5-yl)propanoate group, and a 2-(2,2,4-trimethyl-1,3-dioxan-5-yl)propanoate group. The pyrrolidine ring is also substituted with a 2-(2,2,4-trimethyl-1,3-dioxan-5-yl)propanoate group. The molecule contains multiple chiral centers and a sulfonamide group.	709.9283		A
883-eh	 The chemical structure of 883-eh is identical to the structure of 883-eg, showing a complex molecule with multiple chiral centers and a sulfonamide group.	709.9283		A
883-ei	 The chemical structure of 883-ei is identical to the structures of 883-eg and 883-eh, showing a complex molecule with multiple chiral centers and a sulfonamide group.	749.9936		A

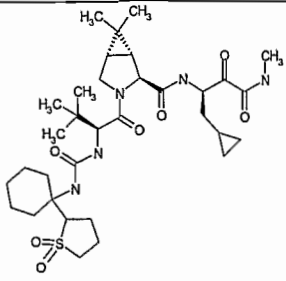
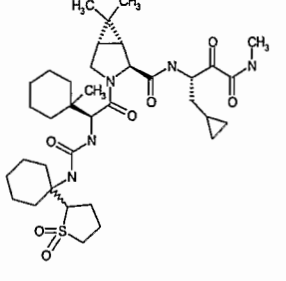
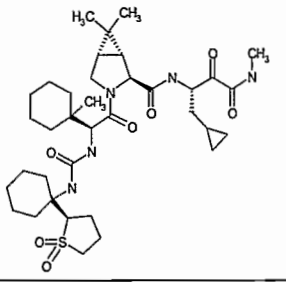
883-ej		749.9936	A	
883-ek		722.008	A	

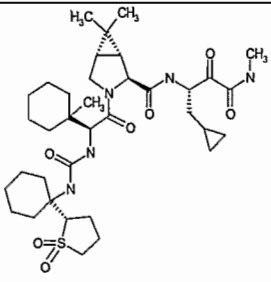
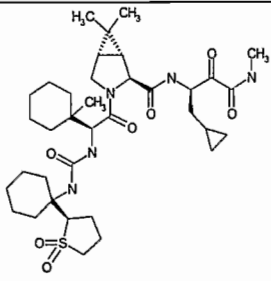
883-el		734.0191		A
883-em		774.0844		A
883-en		762.0297		A

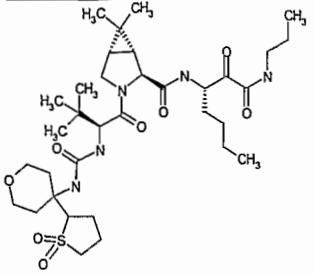
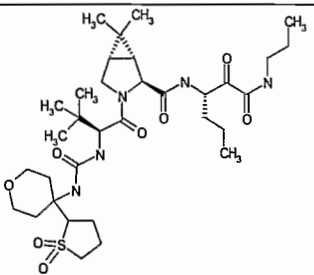
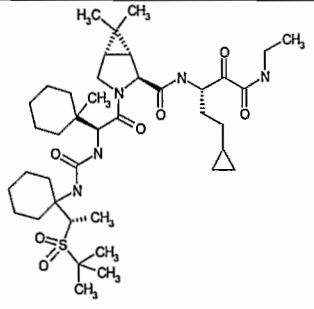
883-eo		750.0185		A
883-ep		709.9532		A

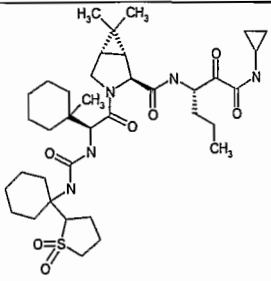
883-eq		709.9532		A
883-er		663.8837		A
883-es		691.9378		A

883-et		663.8837		A
883-eu		691.9378		A

883-ev	 The chemical structure of 883-ev is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethyl-1,3-dioxolane group, a 2-methyl-2-cyclohexyl group, and a 2-(2-methyl-2-cyclohexyl)ethyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-cyclohexyl group and a 2-(2-methyl-2-cyclohexyl)ethyl group. The molecule is further substituted with a 2-methyl-2-cyclohexyl group and a 2-(2-methyl-2-cyclohexyl)ethyl group.	663.8837		A
883-ew	 The chemical structure of 883-ew is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethyl-1,3-dioxolane group, a 2-methyl-2-cyclohexyl group, and a 2-(2-methyl-2-cyclohexyl)ethyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-cyclohexyl group and a 2-(2-methyl-2-cyclohexyl)ethyl group. The molecule is further substituted with a 2-methyl-2-cyclohexyl group and a 2-(2-methyl-2-cyclohexyl)ethyl group.	703.949		A
883-ex	 The chemical structure of 883-ex is a complex molecule. It features a central pyrrolidine ring substituted with a 2,2,3-trimethyl-1,3-dioxolane group, a 2-methyl-2-cyclohexyl group, and a 2-(2-methyl-2-cyclohexyl)ethyl group. The pyrrolidine ring is also substituted with a 2-methyl-2-cyclohexyl group and a 2-(2-methyl-2-cyclohexyl)ethyl group. The molecule is further substituted with a 2-methyl-2-cyclohexyl group and a 2-(2-methyl-2-cyclohexyl)ethyl group.	703.949		A

883-ey	 The chemical structure is a complex molecule. It features a central cyclohexane ring. Attached to this ring is a sulfonamide group (a cyclopentyl ring with a sulfonyl group) and a cyclopropyl group. There are also several amide and ester linkages connecting different parts of the molecule, including a cyclopropyl group and a methyl group.	703.949		A
883-ez	 The chemical structure is identical to the one in the row above. It features a central cyclohexane ring with a sulfonamide group (a cyclopentyl ring with a sulfonyl group) and a cyclopropyl group. There are also several amide and ester linkages connecting different parts of the molecule, including a cyclopropyl group and a methyl group.	703.949		A

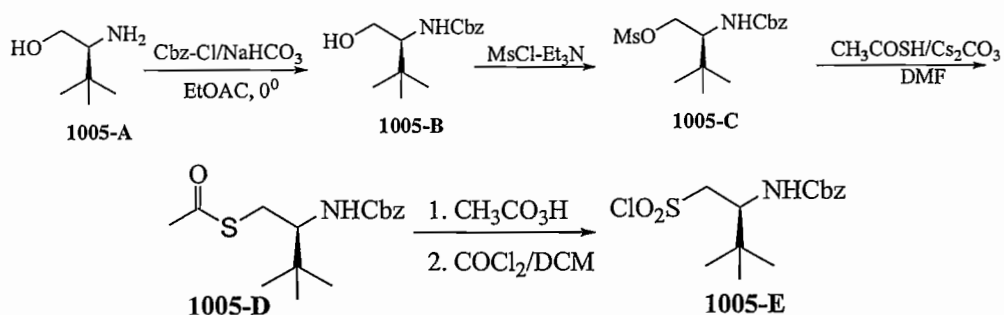
883-fa		695.9261		B
883-fb		681.899		A
883-fc		762.0733		A

883-fd		717.9761		A
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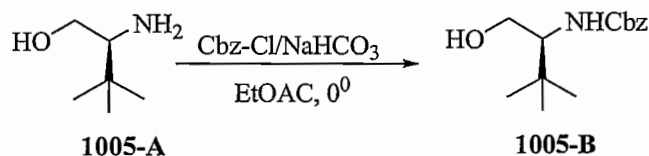
Also disclosed are the following compounds in **Table 4** and **Table 4A**.

- 5 The preparation of the compounds in **Table 4** and **Table 4A** is described below:

EXAMPLE 1005:



STEP 1



- 15 To a solution of 5g of **1005-A** (commercially available from Aldrich) in 100 ml of EtOAc at 0°C were added 40 ml of saturated NaHCO₃ solution followed by 6.5 ml of Cbz-Cl in one portion. The resulting mixture was stirred for 2h and layers were separated. The aqueous layer was back extracted with

50 ml of EtOAc. The combined organic layer was washed once with brine, dried over MgSO_4 and concentrated to a colorless liquid which solidified on standing. 10.7g of **1005-B** as white solids were obtained.

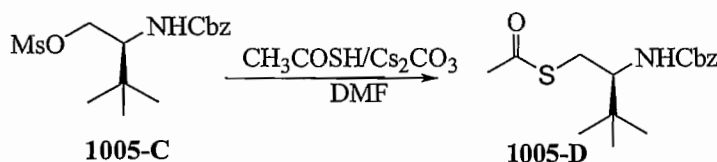
MS: 274 $[\text{M}+\text{Na}]^+$.

5 STEP 2



To a solution of 10.7g of **1005-B** in 120 ml of DCM at 0°C were added 7.04 ml of triethylamine and 4.05 ml of methanesulfonyl chloride. The mixture was stirred at 0°C for 10 minutes and 1.5h at room temperature. The mixture was washed with 1M KHSO_4 solution, water, brine and dried over MgSO_4 . Concentration of solvent gave the crude product which was purified on silica gel column eluted with DCM. 13g of **1005-C** were obtained as colorless thick oil. MS: 352 $[\text{M}+\text{Na}]^+$.

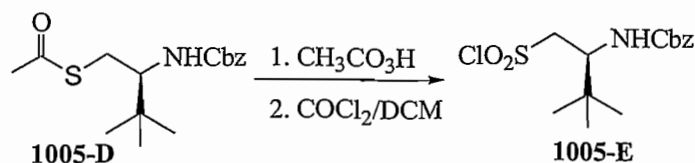
STEP 3



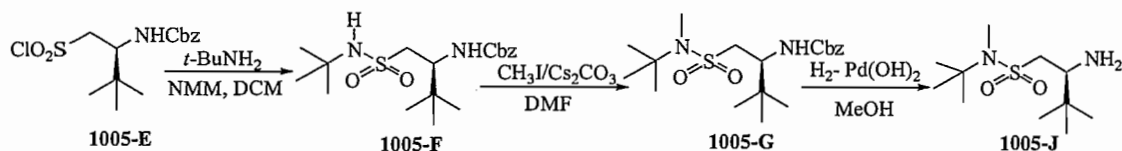
To a suspension of 8.3g of Cs_2CO_3 in 100 ml of anhydrous DMF were added 3.3 ml of thioacetic acid. To the dark brown slurry was added a solution of 12.97g of **1005-C** in 30 ml of anhydrous DMF. The resulting mixture was stirred overnight at room temperature, diluted with 300 ml of ice-water and extracted with 2x250 ml of EtOAc. The combined organic layer was washed with water, brine and dried over MgSO_4 . Evaporation of solvent gave ~10g of the crude product which was purified over silica gel column with 10% EtOAc in hexane. 4.8g of **1005-D** as white solids were obtained. MS: 310 $[\text{M}+\text{H}]^+$,

332 $[M+Na]^+$.

STEP 4



To a solution of 4.4g of **1005-D** in 15 ml of AcOH was added a solution of 15 ml of 30% H_2O_2 and 30 ml of AcOH. The resulting solution was stirred at room temperature for 20 h. 75 mg of 10% Pd/C were added and the mixture was stirred for 1h, filtered through a celite pad and rinsed with MeOH. The combined filtrate was concentrated and co-evaporated with 3x100 ml of toluene to give solids. 90 ml of anhydrous DCM were added to dissolve solids and to the solution was added 15 ml of 20% phosgene in toluene (Fluka) followed by 1.8 ml of anhydrous DMF. Gas evolved and the mixture was stirred at room temperature for 2 h and concentrated to yield solid residue. Purification on silica gel eluted with DCM gave 3.94 g of **1005-E** as solids. MS: 356, 358 $[M+Na]^+$.



STEP 5

A mixture of 900 mg of **1005-E**, 1.0 ml of t-Butylamine and 0.4 ml of NMM in 40 ml of DCM was stirred at room temperature for 0.5 h, washed with 1M $KHSO_4$ solution, brine and dried over $MgSO_4$. Evaporation of solvent gave 445 mg of the crude product which was purified on silica gel with DCM and 5% EtOAc in DCM. 617 mg of **1005-F** were obtained. MS: 379 $[M+Na]^+$.

STEP 6

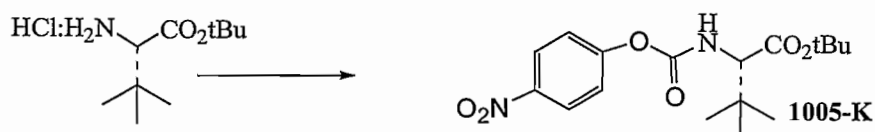
A mixture of 600 mg of **1005-F**, 2.64 g of cesium carbonate and 0.5 ml methyl iodide in 10 ml of anhydrous DMF was stirred at room temperature

overnight, diluted with 50 ml of ice-cold water and extracted with 2x50 ml EtOAc. The combined organic solution was washed twice with water, once with brine, dried over MgSO₄. Removal of solvent under vacuum gave 620 mg of **1005-G** as white solids. MS: 385 [M+H]⁺.

5 **STEP 7**

A solution of **1005-G** (600 mg) and Pd(OH)₂ (70mg) in MeOH was placed under an atmosphere of hydrogen overnight. The solids were filtered and washed thoroughly with MeOH. The volatiles were removed under reduced pressure to give the amine (**1005-J**; 380mg). MS: 251 [M+H]⁺.

10



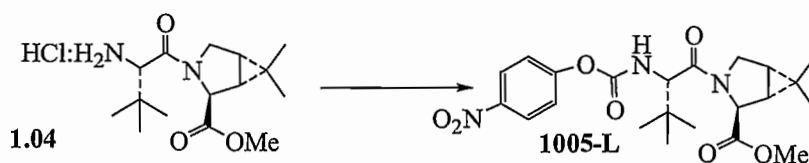
STEP 8

15

To a solution of the of the hydrochloride salt (Bachem; 2.24g) in dichloromethane (50ml) was added NMM (2.6ml) followed by the p-nitrophenyl chloroformate (2.42g) and the resulting mixture was stirred at room temperature overnight. The reaction mixture was washed with cold aq. 1N HCl, sat aq. sodium bicarbonate, dried and the volatiles were removed under reduced pressure. The crude reaction product by silica gel chromatography using EtOAc:hexanes (1:10) as eluent to give the carbamate (**1005-K**; 2.97g).

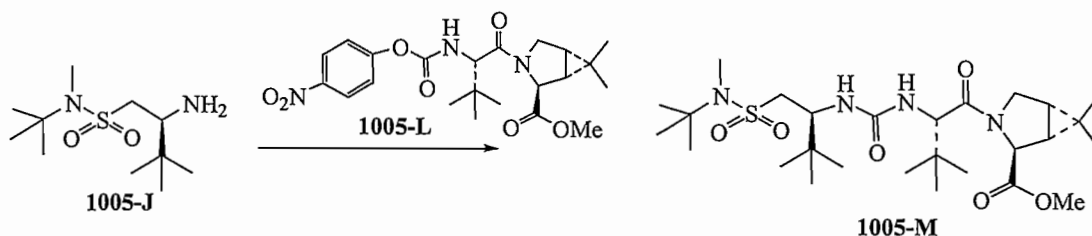
20

STEP 9



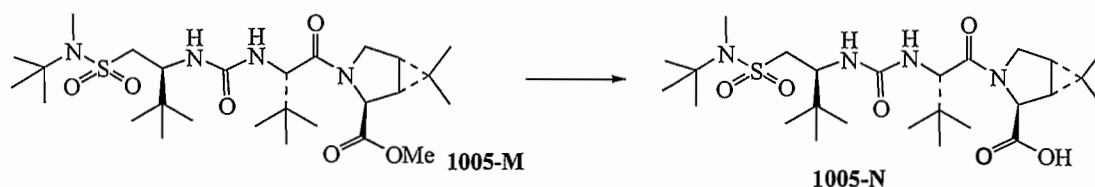
Using the procedure set forth in **STEP 8** the carbamate **1005-L** was prepared from the amine-hydrochloride salt **1.04**.

STEP 10



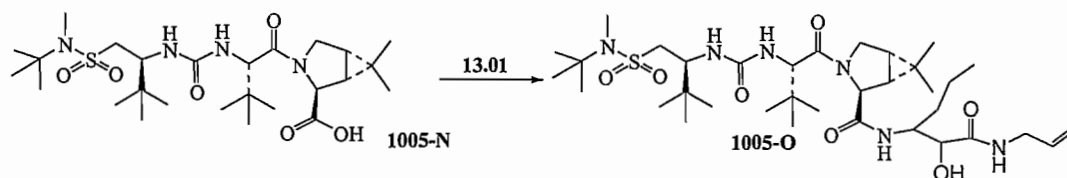
NMM (0.12ml) was added to a mixture of the amine (**1005-J**; 0.20g) and the carbamate (**1005-L**; 0.375g) in acetonitrile (15ml) and the resulting mixture was stirred at room temperature, under an atmosphere of nitrogen, overnight. The volatiles were removed under reduced pressure and the residue was partitioned between EtOAc and water. The organic phase was separated, dried and concentrated. The crude reaction product was purified by silica gel column chromatography using EtOAc: Hexanes (2:3) as eluent, providing the desired urea (**1005-M**; 0.43g). MS: 559.28 $[M+H]^+$.

STEP 11

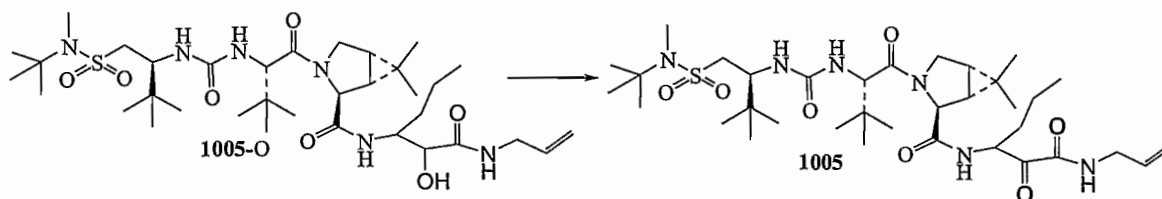


Lithium hydroxide (0.020g) in water (2ml) was added to a solution of the methyl ester (**1005-M**; 0.41g) in dioxane (15ml) and the resulting mixture was stirred at room temperature overnight. Aqueous HCl (0.01N) was added and the organics were extracted into EtOAc. The organic phase was separated, dried and concentrated to yield the carboxylic acid (**1005-N**; 0.395g). MS: 545.32 $[M+H]^+$.

STEP 12



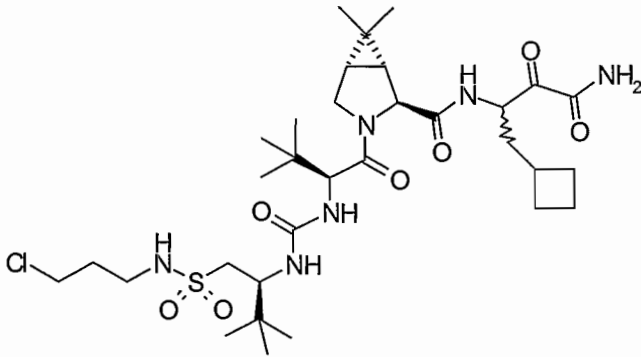
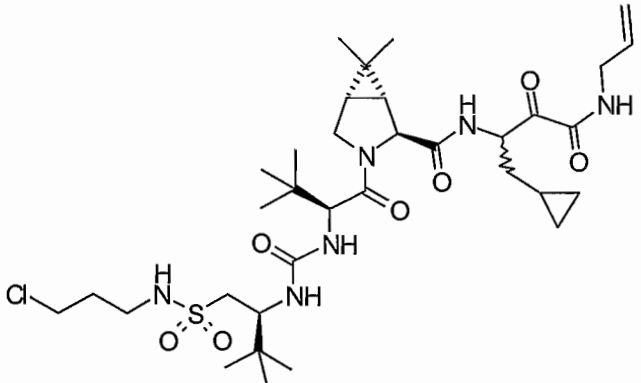
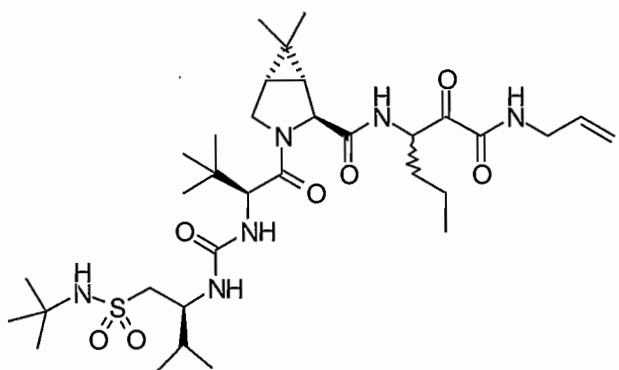
Hunigs base (0.050ml) was added to a mixture of the carboxylic acid (**1005-N**; 0.030g) and the hydrochloride salt (**13.01**; 0.015g) in dichloromethane (5ml) at -20C, under an atmosphere of nitrogen. The reaction was maintained at this temperature for a period of 20h. Aqueous work-up gave a crude reaction product (**1005-O**) which was used in **STEP 12**, below.

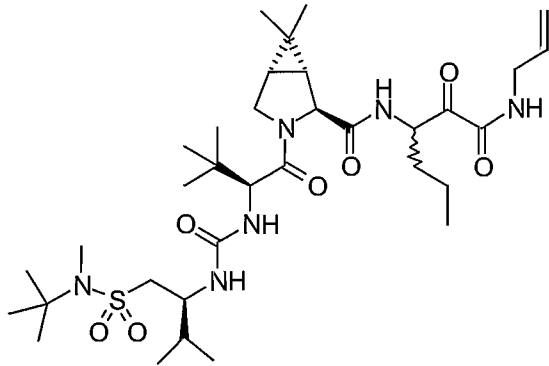
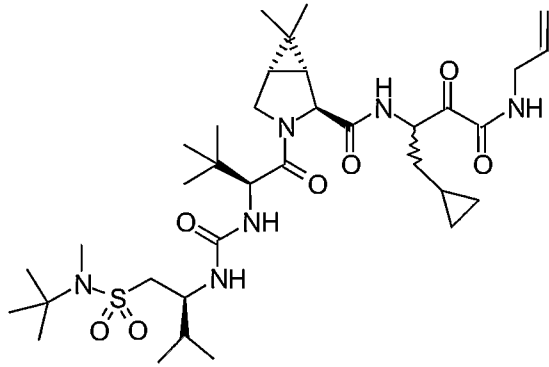
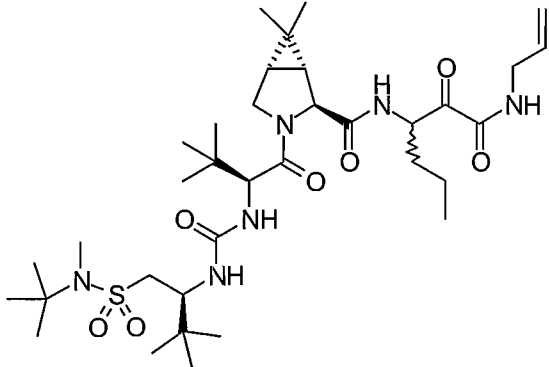
STEP 13

To crude (**1005-O**; above in **STEP 11**) in dichloromethane (3ml) was added Dess-Martin periodinane (0.050g) and the resulting mixture was stirred at room temperature for a period of 24h. Aqueous work-up and silica gel plate chromatography using dichloromethane:methanol (20:1) as eluent gave the desired α -keto-amide (0.0282g), as a white solid. K_i^* ranges are: A = <75 nM; B = 75 - 250 nM; C = >250 nM.

Table 4

Prep. Ex.	COMPOUND	FABMS: MH+	K_i^* range
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1000		703.7	A
1001		729.7	B
1002		683.3	C

1003		697.3	A
1004		709.3	A
1005		711.3	B

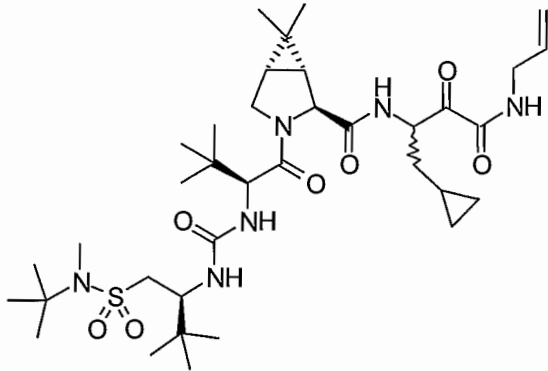
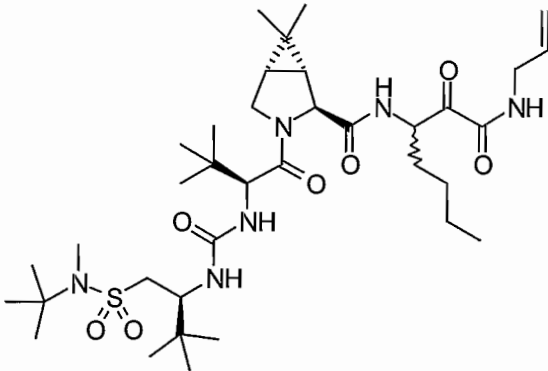
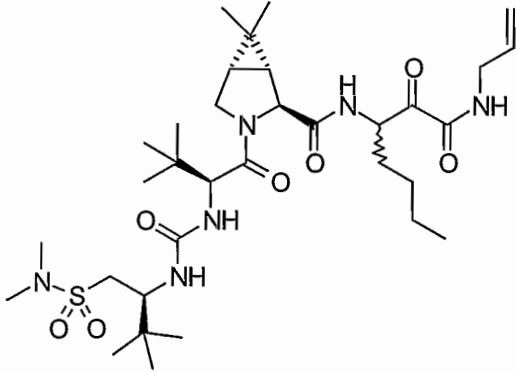
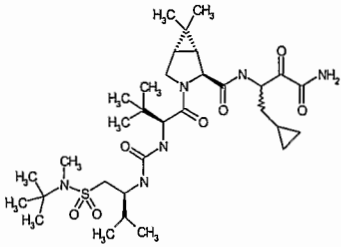
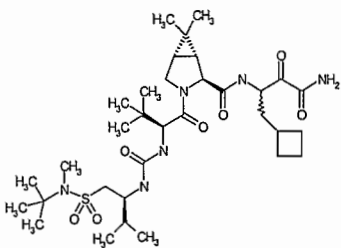
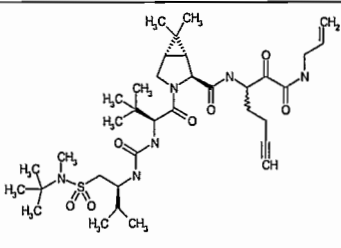
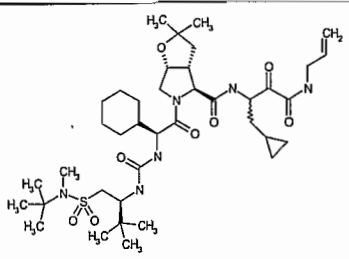
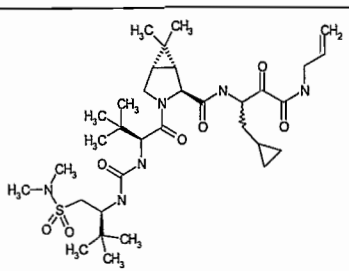
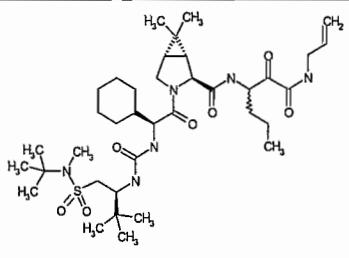
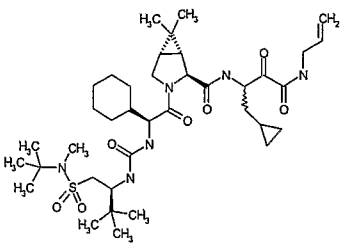
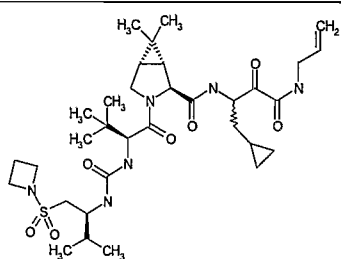
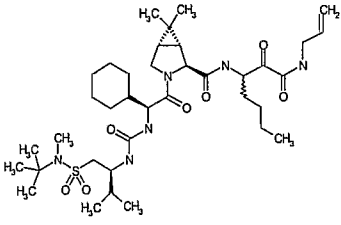
1006		723.3	B
1007		725.3	B
1008		683.3	B

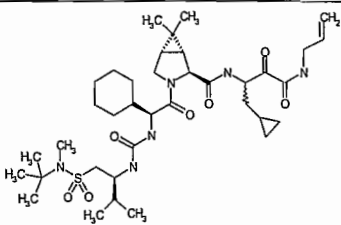
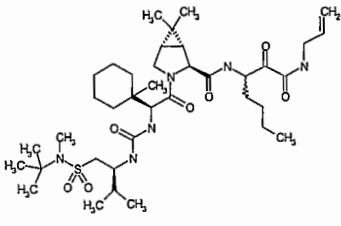
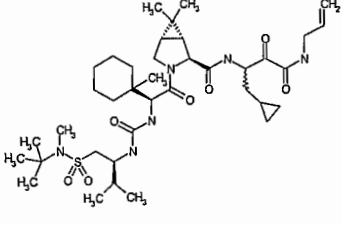
Table 4A lists still additional compounds representing the present invention:

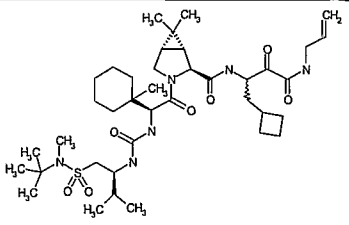
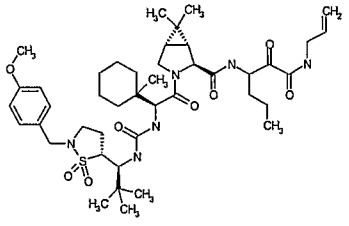
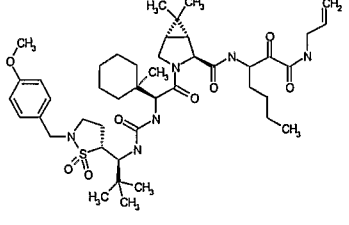
Table 4A

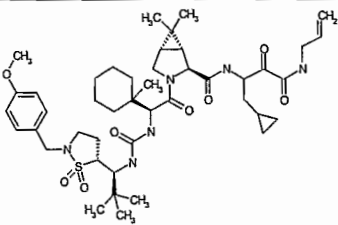
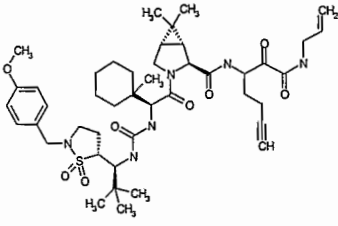
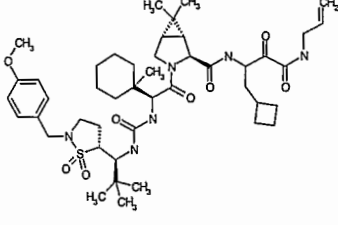
Prep. Ex.	Compound	Select Mass Spectra Data	Ki* Range
1100			A
1101			A
1102			A

1103			B
1104			B
1105			B

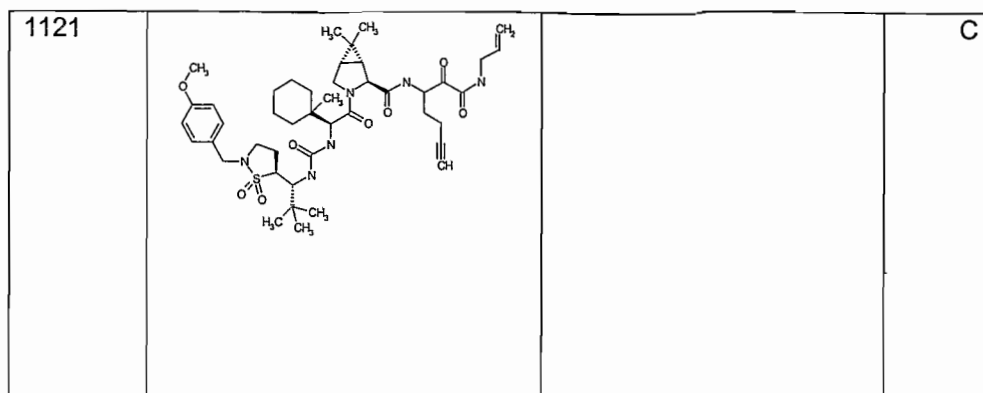
1106			B
1107			A
1108			A

1109			B
1110			A
1111			C

1112			A
1113			C
1114			C

1115			C
1116			C
1117			C

1118	 <chem>COc1ccc(cc1)CN2C(=O)N(C2)S(=O)(=O)C3(C)CC(C3)C(=O)N4C(=O)C(C4)C(=O)N5C(=O)CC(C5)C=CC</chem>		C
1119	 <chem>COc1ccc(cc1)CN2C(=O)N(C2)S(=O)(=O)C3(C)CC(C3)C(=O)N4C(=O)C(C4)C(=O)N5C(=O)CC(C5)C=CC</chem>		C
1120	 <chem>COc1ccc(cc1)CN2C(=O)N(C2)S(=O)(=O)C3(C)CC(C3)C(=O)N4C(=O)C(C4)C(=O)N5C(=O)CC(C5)C=CC</chem>		



The present invention relates to novel HCV protease inhibitors. This utility can be manifested in their ability to inhibit the HCV NS2/NS4a serine protease. A general procedure for such demonstration is illustrated by the following *in vitro* assay.

Assay for HCV Protease Inhibitory Activity:

Spectrophotometric Assay: Spectrophotometric assay for the HCV serine protease can be performed on the inventive compounds by following the procedure described by R. Zhang *et al*, *Analytical Biochemistry*, 270 (1999) 268-275, the disclosure of which is incorporated herein by reference. The assay based on the proteolysis of chromogenic ester substrates is suitable for the continuous monitoring of HCV NS3 protease activity. The substrates are derived from the P side of the NS5A-NS5B junction sequence (Ac-DTEDVVX(Nva), where X = A or P) whose C-terminal carboxyl groups are esterified with one of four different chromophoric alcohols (3- or 4-nitrophenol, 7-hydroxy-4-methyl-coumarin, or 4-phenylazophenol). Illustrated below are the synthesis, characterization and application of these novel spectrophotometric ester substrates to high throughput screening and detailed kinetic evaluation of HCV NS3 protease inhibitors.

Materials and Methods:

Materials: Chemical reagents for assay related buffers are obtained from Sigma Chemical Company (St. Louis, Missouri). Reagents for peptide synthesis were from Aldrich Chemicals, Novabiochem (San Diego, California), Applied Biosystems (Foster City, California) and Perseptive Biosystems (Framingham, Massachusetts). Peptides are synthesized manually or on an automated ABI model 431A synthesizer (from Applied Biosystems). UV/VIS Spectrometer model LAMBDA 12 was from Perkin Elmer (Norwalk, Connecticut) and 96-well UV plates were obtained from Corning (Corning, New York). The prewarming block can be from USA Scientific (Ocala, Florida) and the 96-well plate vortexer is from Labline Instruments (Melrose Park, Illinois). A Spectramax Plus microtiter plate reader with monochromator is obtained from Molecular Devices (Sunnyvale, California).

Enzyme Preparation: Recombinant heterodimeric HCV NS3/NS4A protease (strain 1a) is prepared by using the procedures published previously (D. L. Sali *et al*, *Biochemistry*, 37 (1998) 3392-3401). Protein concentrations are determined by the Biorad dye method using recombinant HCV protease standards previously quantified by amino acid analysis. Prior to assay initiation, the enzyme storage buffer (50 mM sodium phosphate pH 8.0, 300 mM NaCl, 10% glycerol, 0.05% lauryl maltoside and 10 mM DTT) is exchanged for the assay buffer (25 mM MOPS pH 6.5, 300 mM NaCl, 10% glycerol, 0.05% lauryl maltoside, 5 μ M EDTA and 5 μ M DTT) utilizing a Biorad Bio-Spin P-6 prepacked column.

Substrate Synthesis and Purification: The synthesis of the substrates is done as reported by R. Zhang *et al*, (*ibid.*) and is initiated by anchoring Fmoc-Nva-OH to 2-chlorotrityl chloride resin using a standard protocol (K. Barlos *et al*, *Int. J. Pept. Protein Res.*, 37 (1991), 513-520). The peptides are subsequently assembled, using Fmoc chemistry, either manually or on an automatic ABI model 431 peptide synthesizer. The N-acetylated and fully protected peptide

fragments are cleaved from the resin either by 10% acetic acid (HOAc) and 10% trifluoroethanol (TFE) in dichloromethane (DCM) for 30 min, or by 2% trifluoroacetic acid (TFA) in DCM for 10 min. The combined filtrate and DCM wash is evaporated azeotropically (or repeatedly extracted by aqueous
5 Na_2CO_3 solution) to remove the acid used in cleavage. The DCM phase is dried over Na_2SO_4 and evaporated.

The ester substrates are assembled using standard acid-alcohol coupling procedures (K. Holmber *et al*, *Acta Chem. Scand.*, B33 (1979) 410-412). Peptide fragments are dissolved in anhydrous pyridine (30-60 mg/ml) to
10 which 10 molar equivalents of chromophore and a catalytic amount (0.1 eq.) of para-toluenesulfonic acid (pTSA) were added. Dicyclohexylcarbodiimide (DCC, 3 eq.) is added to initiate the coupling reactions. Product formation is monitored by HPLC and can be found to be complete following 12-72 hour reaction at room temperature. Pyridine solvent is evaporated under vacuum
15 and further removed by azeotropic evaporation with toluene. The peptide ester is deprotected with 95% TFA in DCM for two hours and extracted three times with anhydrous ethyl ether to remove excess chromophore. The deprotected substrate is purified by reversed phase HPLC on a C3 or C8 column with a 30% to 60% acetonitrile gradient (using six column volumes).
20 The overall yield following HPLC purification can be approximately 20-30%. The molecular mass can be confirmed by electrospray ionization mass spectroscopy. The substrates are stored in dry powder form under desiccation.

Spectra of Substrates and Products: Spectra of substrates and the
25 corresponding chromophore products are obtained in the pH 6.5 assay buffer. Extinction coefficients are determined at the optimal off-peak wavelength in 1-cm cuvettes (340 nm for 3-Np and HMC, 370 nm for PAP and 400 nm for 4-Np) using multiple dilutions. The optimal off-peak wavelength is defined as

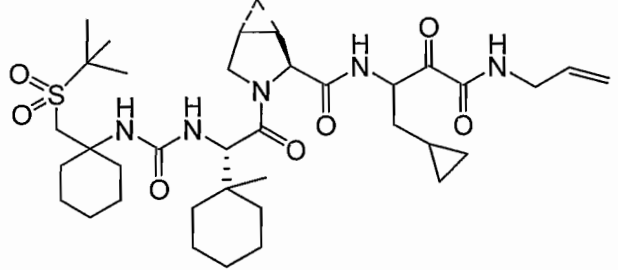
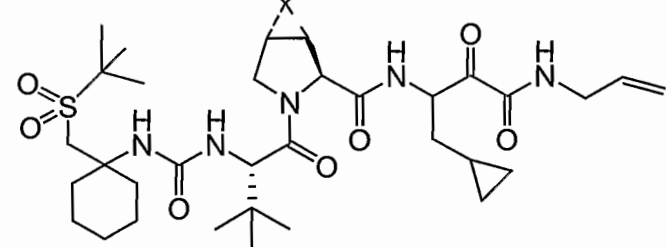
that wavelength yielding the maximum fractional difference in absorbance between substrate and product (product OD - substrate OD)/substrate OD).

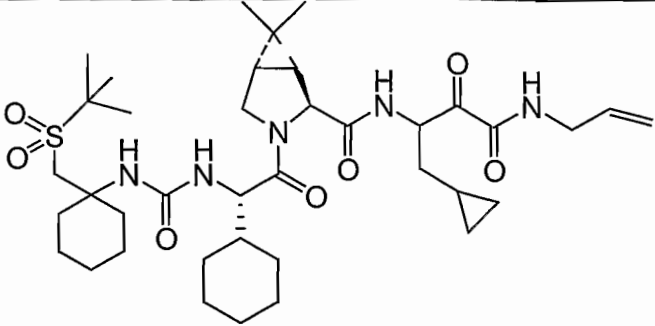
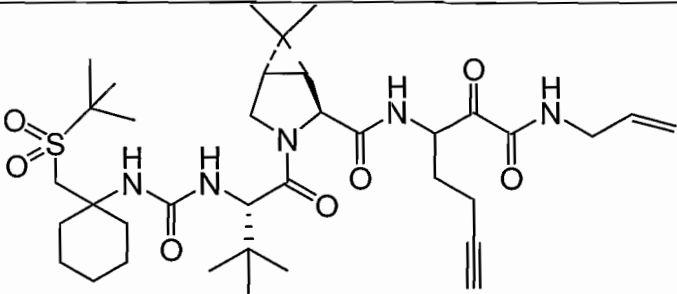
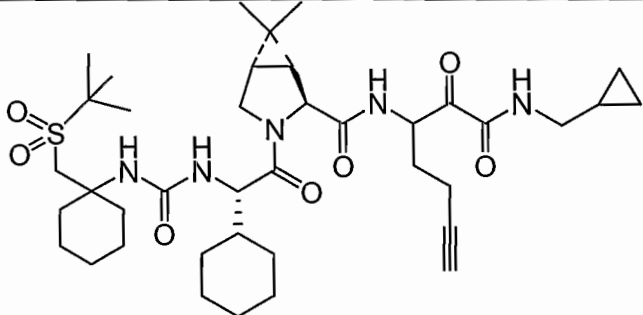
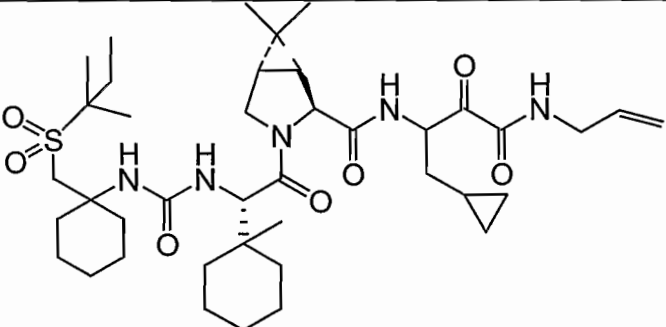
Protease Assay: HCV protease assays are performed at 30°C using a 200 µl reaction mix in a 96-well microtiter plate. Assay buffer conditions (25 mM

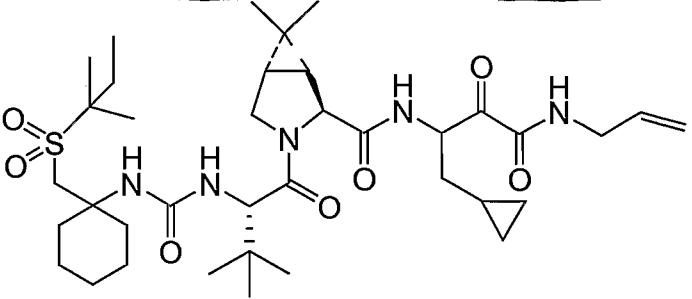
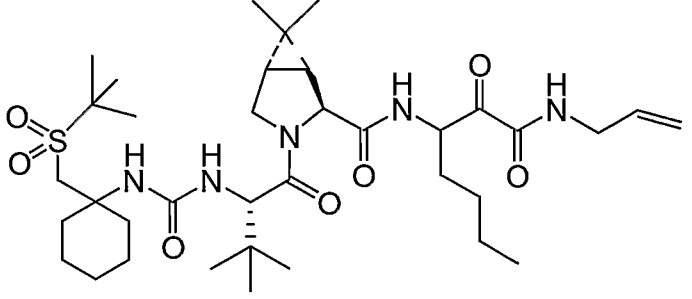
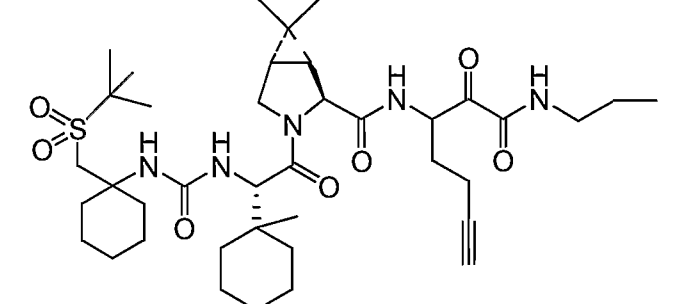
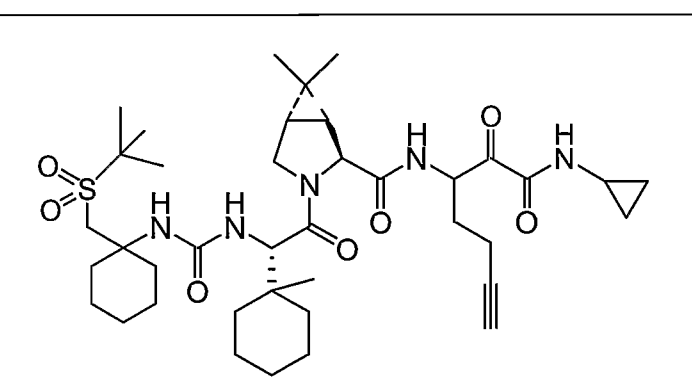
- 5 MOPS pH 6.5, 300 mM NaCl, 10% glycerol, 0.05% lauryl maltoside, 5 µM EDTA and 5 µM DTT) are optimized for the NS3/NS4A heterodimer (D. L. Sali *et al, ibid.*). Typically, 150 µl mixtures of buffer, substrate and inhibitor are placed in wells (final concentration of DMSO ≤ 4 % v/v) and allowed to preincubate at 30 °C for approximately 3 minutes. Fifty µls of prewarmed
- 10 protease (12 nM, 30°C) in assay buffer, is then used to initiate the reaction (final volume 200 µl). The plates are monitored over the length of the assay (60 minutes) for change in absorbance at the appropriate wavelength (340 nm for 3-Np and HMC, 370 nm for PAP, and 400 nm for 4-Np) using a Spectromax Plus microtiter plate reader equipped with a monochrometer
- 15 (acceptable results can be obtained with plate readers that utilize cutoff filters). Proteolytic cleavage of the ester linkage between the Nva and the chromophore is monitored at the appropriate wavelength against a no enzyme blank as a control for non-enzymatic hydrolysis. The evaluation of substrate kinetic parameters is performed over a 30-fold substrate concentration range
- 20 (~6-200 µM). Initial velocities are determined using linear regression and kinetic constants are obtained by fitting the data to the Michaelis-Menten equation using non-linear regression analysis (Mac Curve Fit 1.1, K. Raner). Turnover numbers (k_{cat}) are calculated assuming the enzyme is fully active.
- Evaluation of Inhibitors and Inactivators: The inhibition constants (K_i) for the
- 25 competitive inhibitors Ac-D-(D-Gla)-L-I-(Cha)-C-OH (27), Ac-DTEDVVA(Nva)-OH and Ac-DTEDVVP(Nva)-OH are determined experimentally at fixed concentrations of enzyme and substrate by plotting v_0/v_i vs. inhibitor

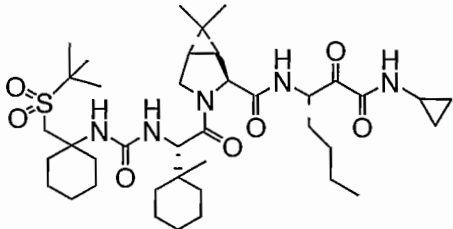
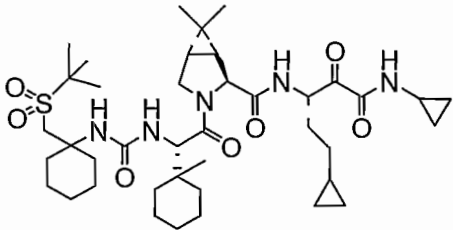
concentration ($[I]_0$) according to the rearranged Michaelis-Menten equation for competitive inhibition kinetics: $v_0/v_i = 1 + [I]_0 / (K_i (1 + [S]_0 / K_M))$, where v_0 is the uninhibited initial velocity, v_i is the initial velocity in the presence of inhibitor at any given inhibitor concentration ($[I]_0$) and $[S]_0$ is the substrate concentration used. The resulting data are fitted using linear regression and the resulting slope, $1/(K_i(1+[S]_0/K_M))$, is used to calculate the K_i value. The following **Table 5** lists the obtained K_i^* values (in nanoMolar) for some of the inventive compounds. Several others are noted in the **Tables** on earlier pages.

Table 5

Structure	K_i^* (nM)
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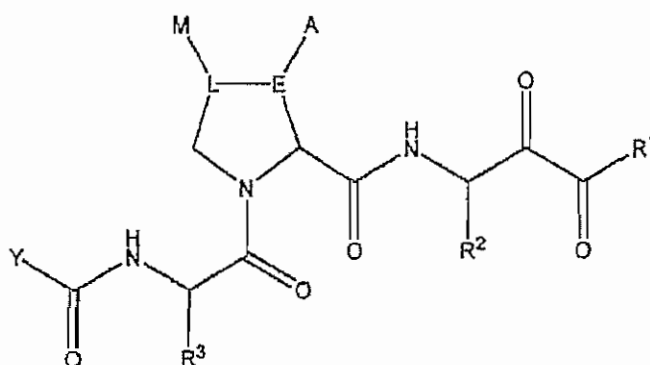
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While the present invention has been described with in conjunction with the specific embodiments set forth above, many alternatives, modifications and other variations thereof will be apparent to those of ordinary skill in the art. All such alternatives, modifications and variations are intended to fall within the spirit and scope of the present invention.

CLAIMS

1. A compound, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the general structure shown in Formula I:



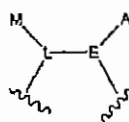
Formula I

wherein:

R¹ is H, OR⁸, NR⁹R¹⁰, or CHR⁹R¹⁰, wherein R⁸, R⁹ and R¹⁰ can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, heteroalkyl-, cycloalkyl-, heterocyclyl-, arylalkyl-, and heteroarylalkyl;

A and M can be the same or different, each being independently selected from R, OR, NHR, NRR', SR, SO₂R, and halo;

or A and M are connected to each other such that the moiety:



shown above in Formula I forms either a three, four, six, seven or eight-membered cycloalkyl, a four to eight-membered heterocyclyl, a six to ten-membered aryl, or a five to ten-membered heteroaryl;

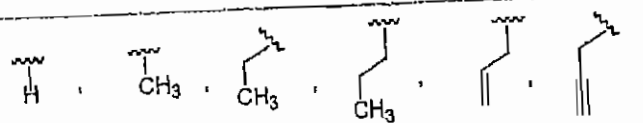
E is C(H) or C(R);

L is C(H), C(R), CH₂C(R), or C(R)CH₂;

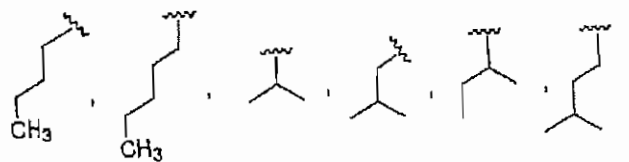
R, R', R², and R³ can be the same or different, each being independently selected from the group consisting of H, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or alternatively R and R' in NRR' are connected to each other such that NRR' forms a four to eight-membered heterocyclyl;

or R² is selected from the group consisting of the following moieties:

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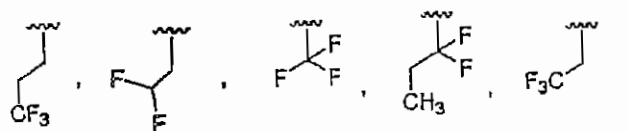


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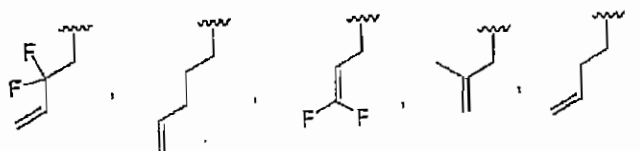


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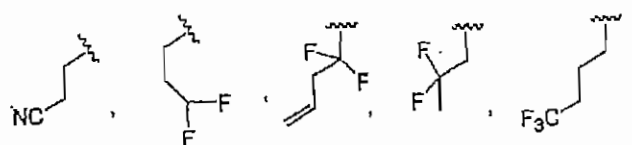


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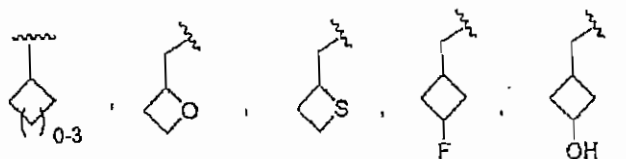
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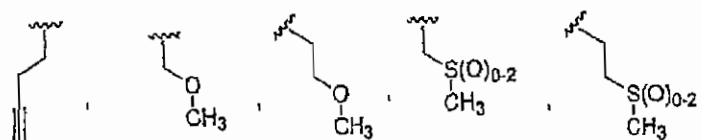
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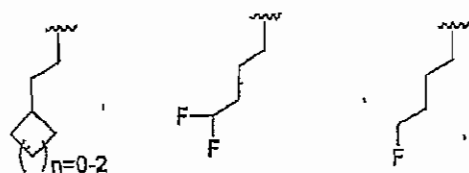
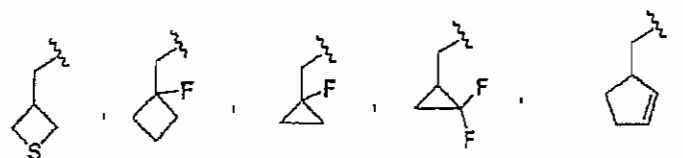
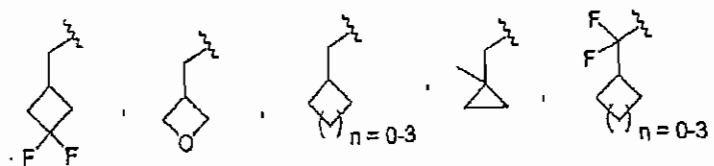
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and Y is selected from the following moieties:

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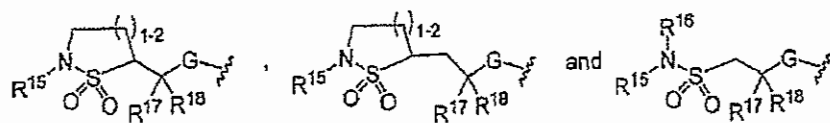
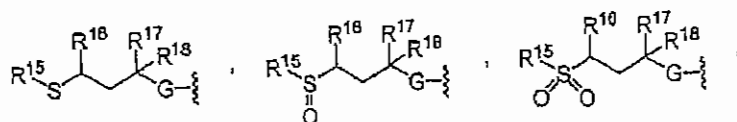
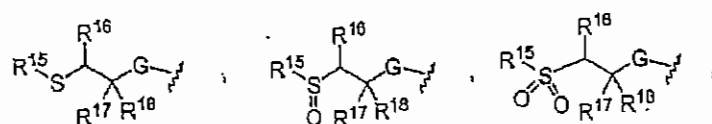
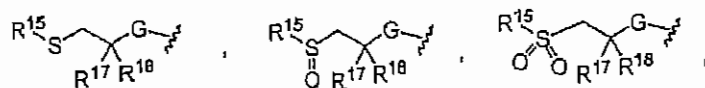
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wherein G is NH or O; and R¹⁵, R¹⁶, R¹⁷ and R¹⁸ can be the same or different, each being independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl, or alternately, (i) R¹⁵ and R¹⁶ are connected to each other to form a four to eight-membered cyclic structure, and (ii) likewise, independently R¹⁷ and R¹⁸ are connected to each other to form a three to eight-membered cycloalkyl or heterocyclyl; wherein each of said alkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl can be unsubstituted or optionally independently substituted with one or more moieties selected from the group consisting of: hydroxy, alkoxy, aryloxy, thio, alkylthio, arylthio, amino, amido, alkylamino, arylamino, alkylsulfonyl, arylsulfonyl, sulfonamido, alkylsulfonamido, arylsulfonamido, alkyl, aryl, heteroaryl, keto, carboxy, carbalkoxy, carboxamido, alkoxycarbonylamino, alkoxycarbonyloxy, alkylureido, arylureido, halo, cyano, and nitro,

wherein:

"alkyl" means an aliphatic hydrocarbon group which may be straight or branched and comprising 1 to 20 carbon atoms in the chain;

"alkenyl" means an aliphatic hydrocarbon group containing at least one carbon-carbon double bond and which may be straight or branched and comprising 2 to 15 carbon atoms in the chain;

"alkynyl" means an aliphatic hydrocarbon group containing at least one carbon-carbon triple bond and which may be straight or branched and comprising 2 to 15 carbon atoms in the chain;

"aryl" means an aromatic monocyclic or multicyclic ring system comprising 6 to 14 carbon atoms;

"heteroaryl" means an aromatic monocyclic or multicyclic ring system comprising 5 to 14 ring atoms, in which one or more of the ring atoms is an element other than carbon;

"aralkyl" or "arylkalkyl" means an aryl-alkyl- group in which the aryl and alkyl are as previously described wherein the bond to the parent moiety is through the alkyl;

"alkylaryl" means an alkyl-aryl- group in which the alkyl and aryl are as previously described wherein the bond to the parent moiety is through the aryl;

"cycloalkyl" means a non-aromatic mono- or multicyclic ring system comprising 3 to 10 carbon atoms;

"halogen" or "halo" means fluorine, chlorine, bromine, or iodine;

"heterocyclyl" means a non-aromatic saturated monocyclic or multicyclic ring system comprising 3 to 10 ring atoms in which one or more of the atoms in the ring system is an element other than carbon wherein there are no adjacent oxygen and/or sulfur atoms present in the ring system;

"alkynylalkyl" means an alkynyl-alkyl- group in which the alkynyl and alkyl are as previously described wherein the bond to the parent moiety is through the alkyl;

"heteroaralkyl" means a heteroaryl-alkyl- group in which the heteroaryl and alkyl are as previously described wherein the bond to the parent moiety is through the alkyl;

"alkoxy" means an alkyl-O- group in which the alkyl group is as previously described wherein the bond to the parent moiety is through the ether oxygen;

"aryloxy" means an aryl-O- group in which the aryl group is as previously described wherein the bond to the parent moiety is through the ether oxygen;

"alkylthio" means an alkyl-S- group in which the alkyl group is as previously described wherein the bond to the parent moiety is through the sulfur;

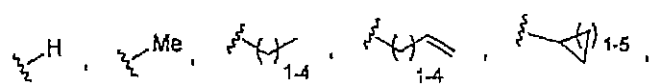
"arylthio" means an aryl-S- group in which the aryl group is as previously described wherein the bond to the parent moiety is through the sulfur;

"alkylsulfonyl" means an alkyl-S(O₂)- group wherein the bond to the parent moiety is through the sulfonyl; and

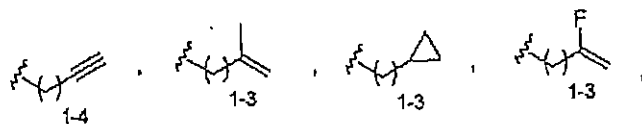
"arylsulfonyl" means an aryl-S(O₂)- group wherein the bond to the parent moiety is through the sulfonyl.

2. The compound of claim 1, wherein R¹ is NR⁹R¹⁰, and R⁹ is H, R¹⁰ is H, or R¹⁴ wherein R¹⁴ is H, alkyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, aryl-alkyl, alkenyl, alkynyl or heteroaryl-alkyl.

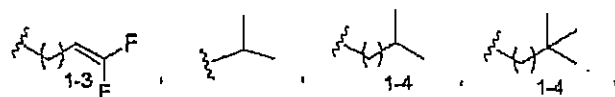
3. The compound of claim 2, wherein R¹⁴ is selected from the group consisting of:



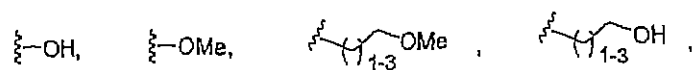
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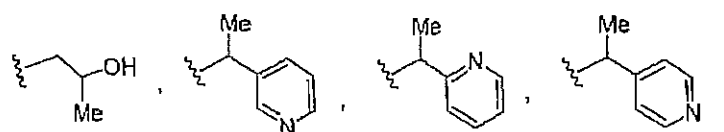
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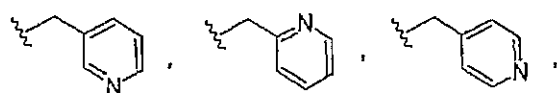
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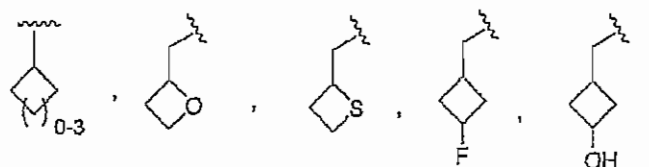
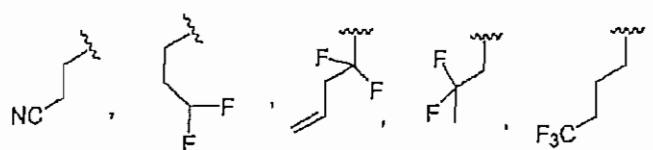
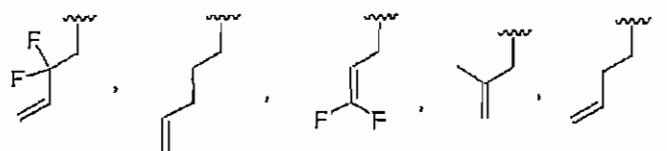
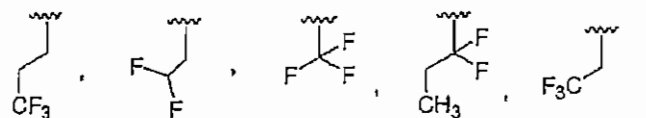
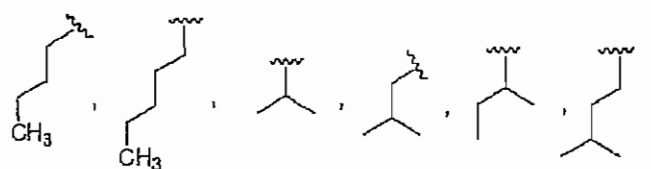
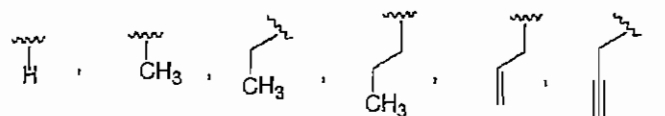


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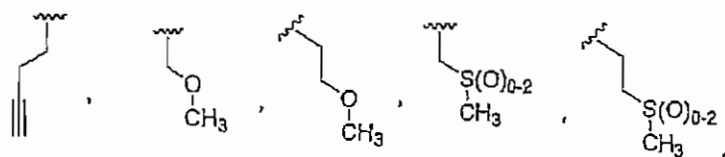
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4. The compound of claim 1, wherein R^2 is selected from the group consisting of the following moieties:



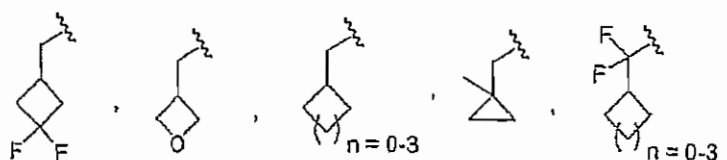
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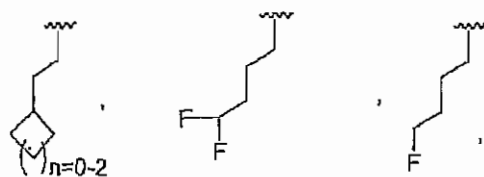


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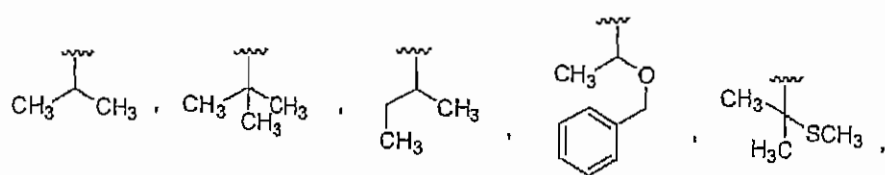
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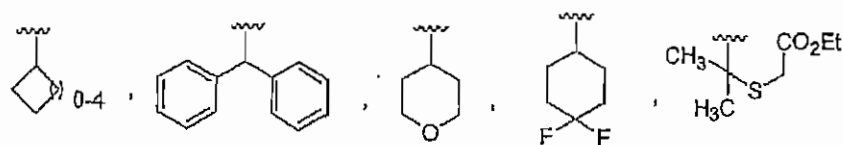
5. The compound of claim 1, wherein R^3 is selected from the group consisting of:

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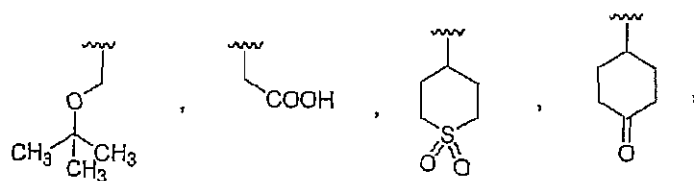
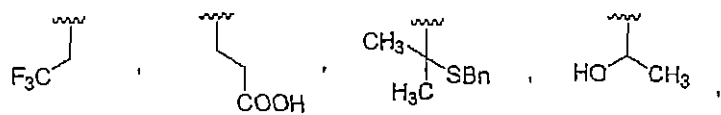
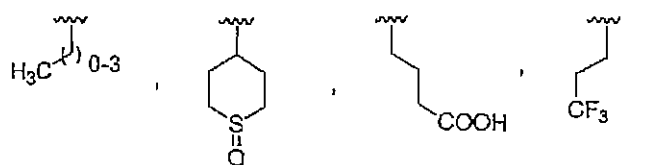
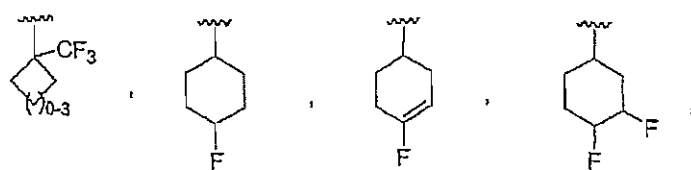
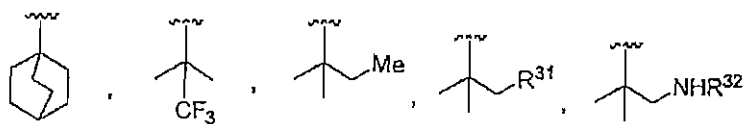
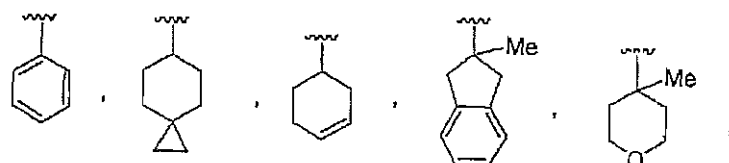
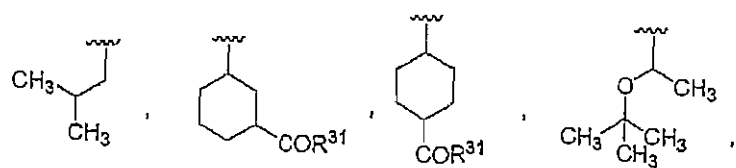
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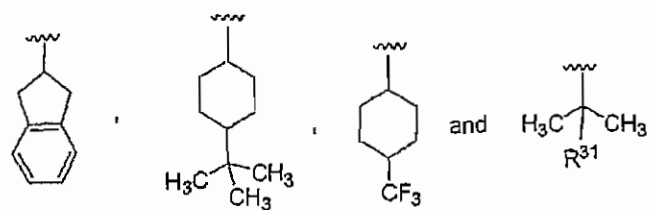
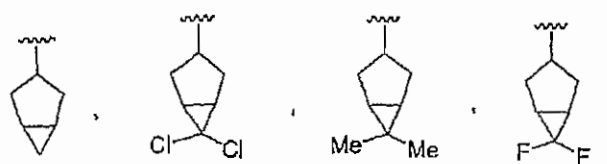
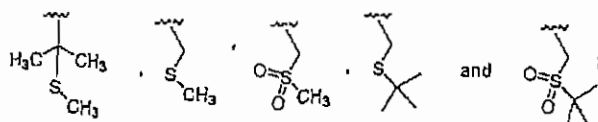
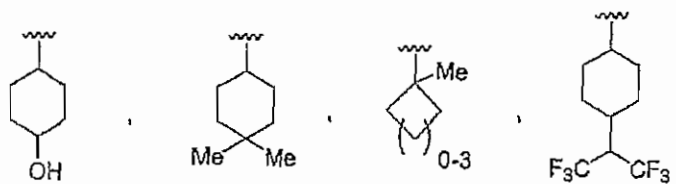
6. The compound of claim 5, wherein R^3 is selected from the group consisting of the following moieties:

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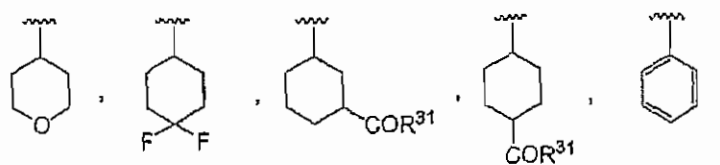
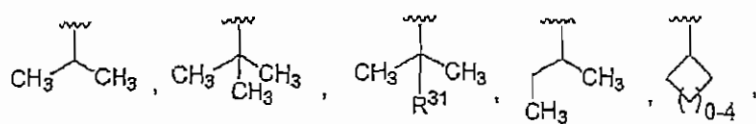
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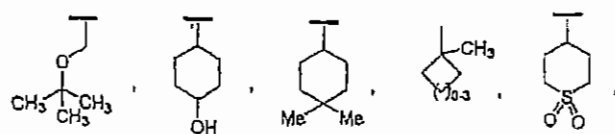
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wherein R^{31} is OH or O-alkyl; and
 R^{32} is H, $C(O)CH_3$, $C(O)OIBu$ or $C(O)N(H)IBu$.



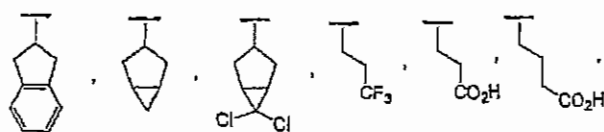
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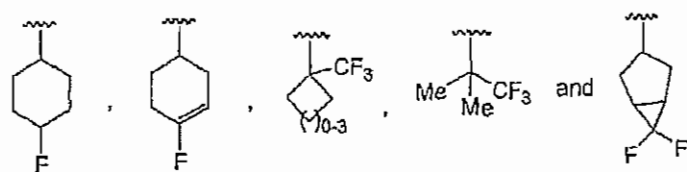
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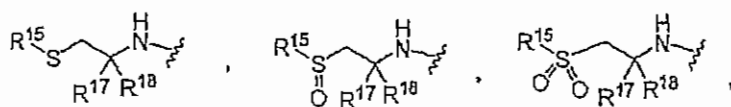
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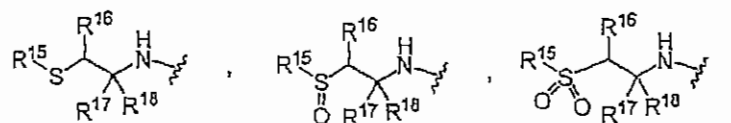
7. The compound of claim 1, wherein Y is selected from the following moieties:

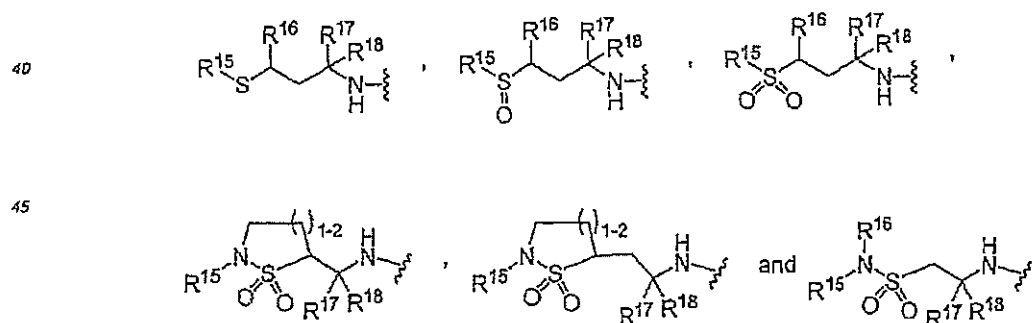
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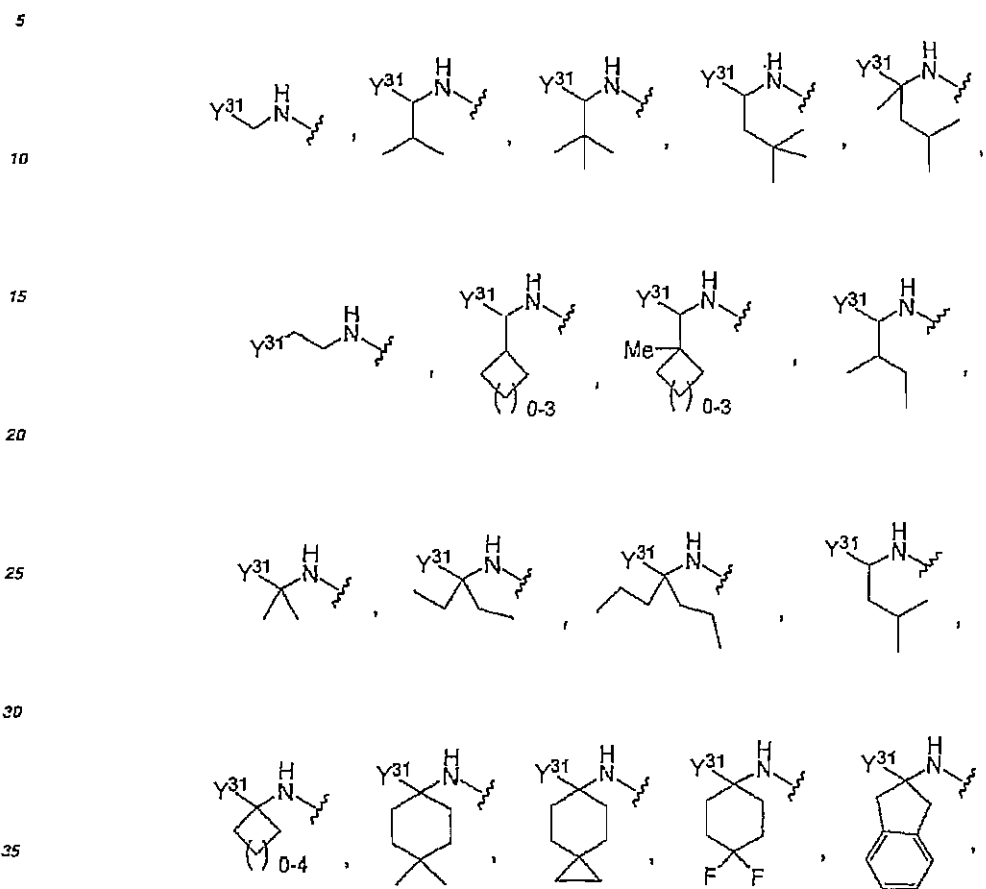


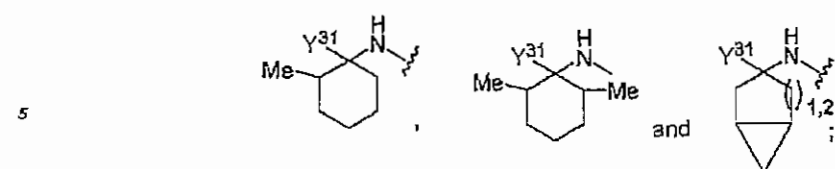
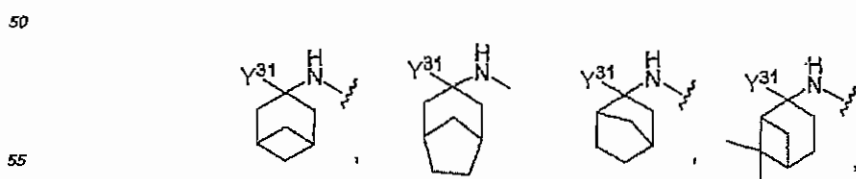
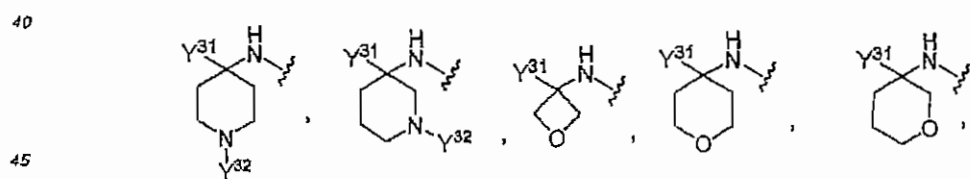


55 wherein R^{15} , R^{16} , R^{17} and R^{18} can be the same or different, each being independently selected from the group consisting of H, alkyl, heteroalkyl, alkenyl, heteroalkenyl, alkynyl, heteroalkynyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or alternately, R^{15} and R^{16} are connected to each other to form a four to eight-membered cycloalkyl or heterocyclic structure; R^{17} and R^{18} are connected to each other to form a three to eight-membered cycloalkyl or heterocyclyl, wherein each of said aryl, heteroaryl, cycloalkyl or heterocyclyl can be unsubstituted or optionally independently substituted with one or more moieties selected from the group consisting of: hydroxy, alkoxy, aryloxy, thio, alkylthio, arylthio, amino, amido, alkylamino, arylamino, alkylsulfonyl, arylsulfonyl, sulfonamido, alkylsulfonamido, arylsulfonamido, alkyl, aryl, heteroaryl, carboxy, carbalkoxy, carboxamido, alkoxy-

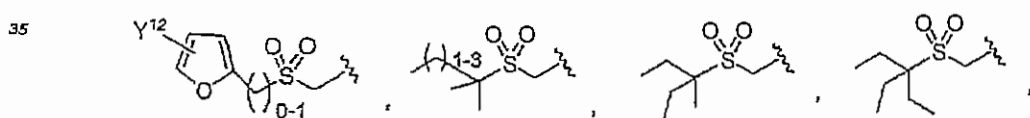
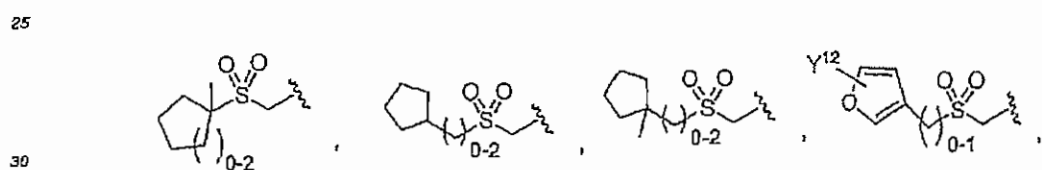
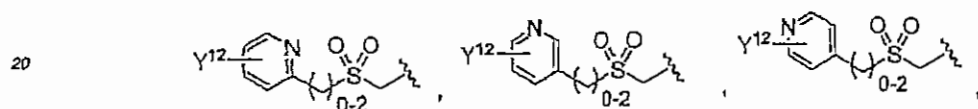
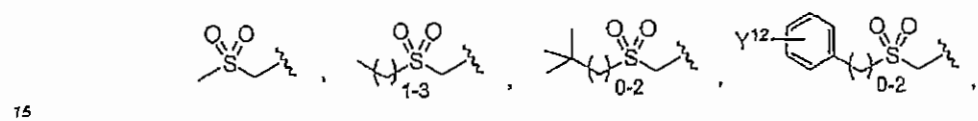
carbonylamino, alkoxy-carbonyloxy, alkylureido, arylureido, halo, cyano, and nitro.

B. The compound of claim 7, Y is selected from the group consisting of:

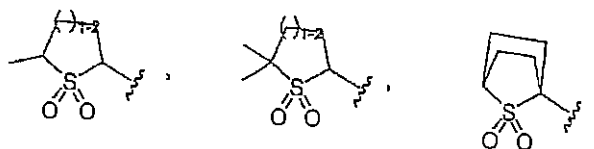




wherein Y³¹ is selected from the group consisting of:

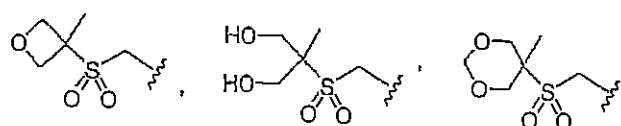


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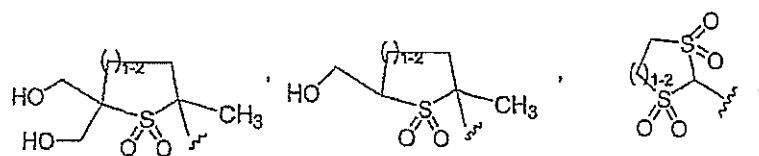


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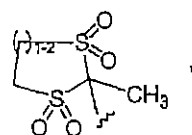
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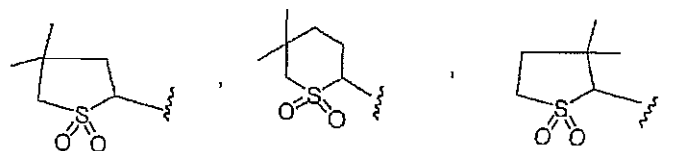


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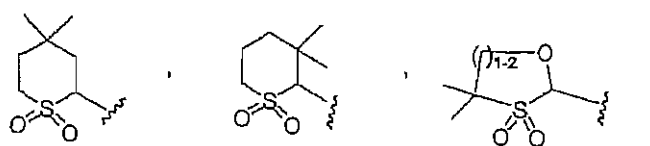
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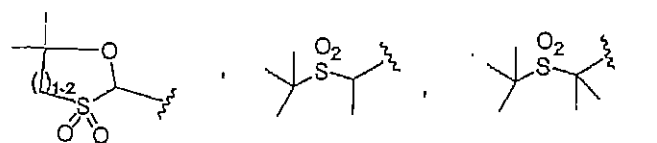


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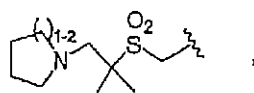


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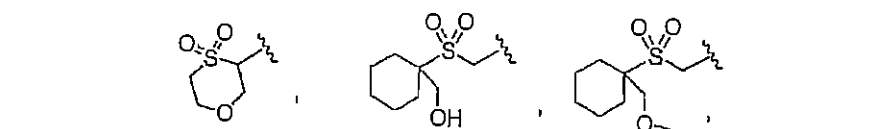
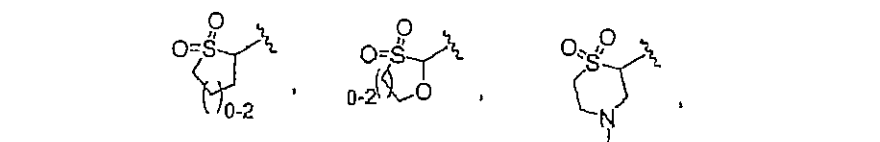
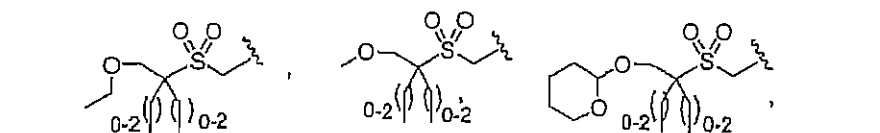
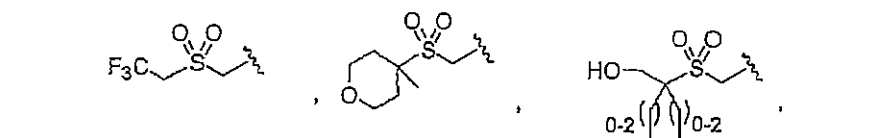
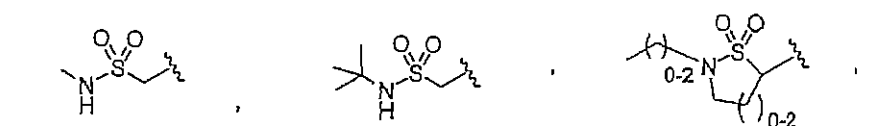
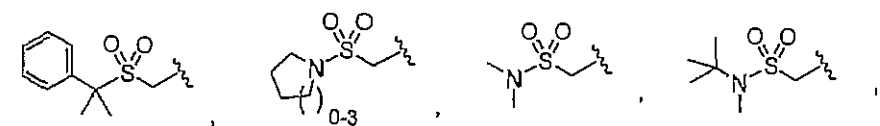
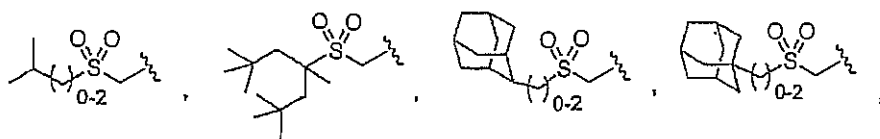
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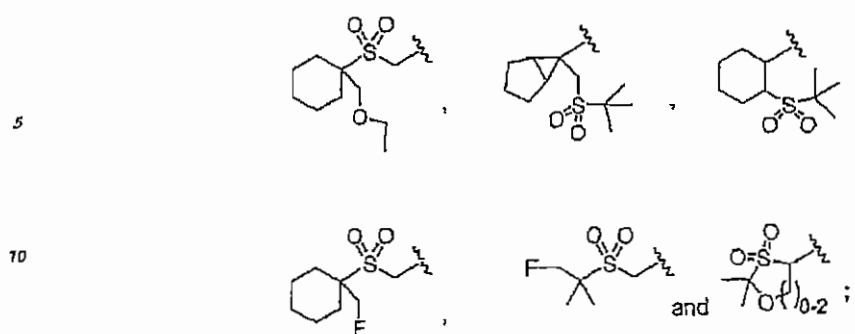
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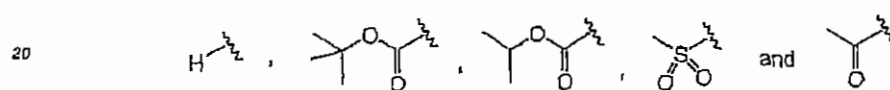
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Y^{32} is selected from the group consisting of:

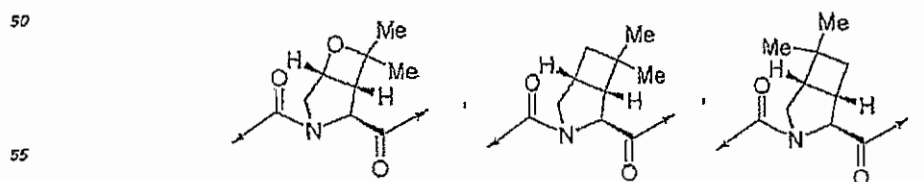
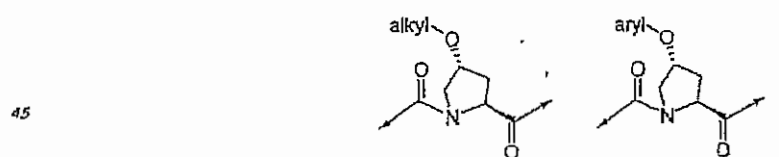


and Y^{12} is selected from the group consisting of H, CO_2H , CO_2Me , OMe, F, Cl, Br, NH_2 , $N(H)S(O_2)CH_3$, $N(H)C(O)CH_3$, NO_2 , $S(O_2)NH_2$, CF_3 , Me, OH, OCF_3 , and $C(O)NH_2$.

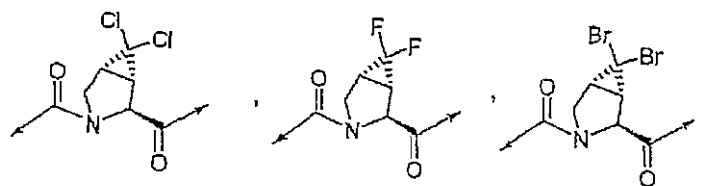
9. The compound of claim 1, wherein the moiety:



is selected from the following structures:

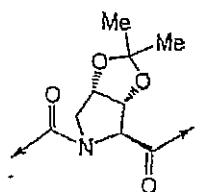


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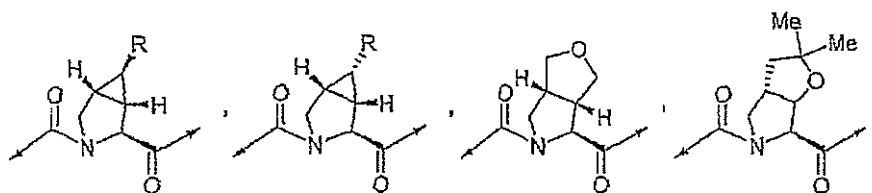
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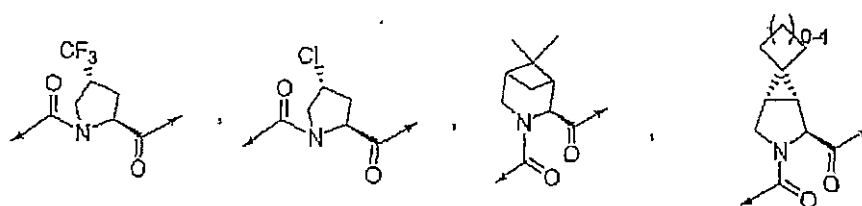
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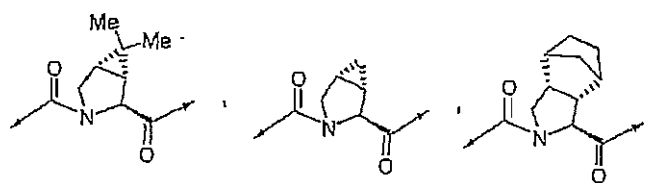
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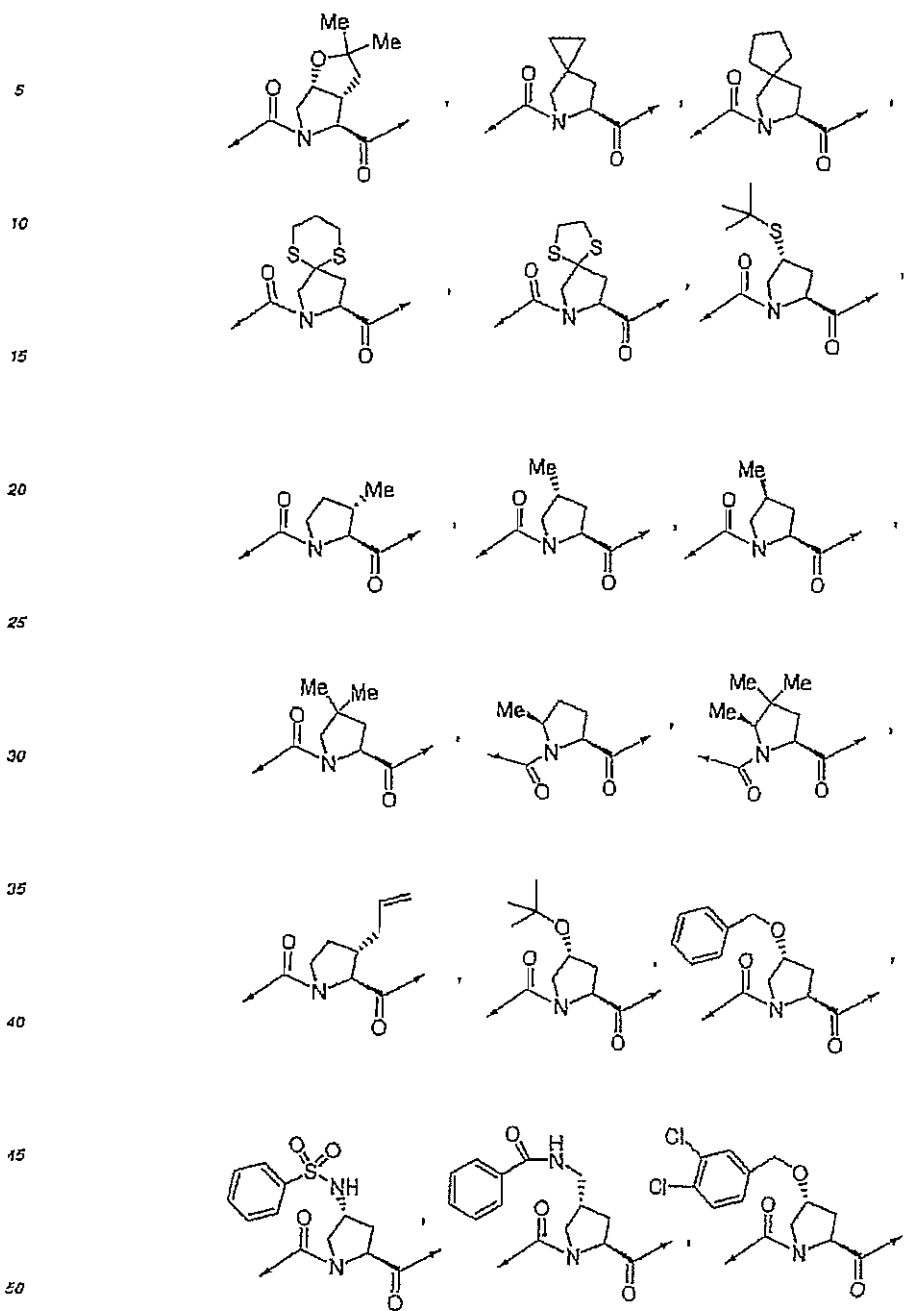
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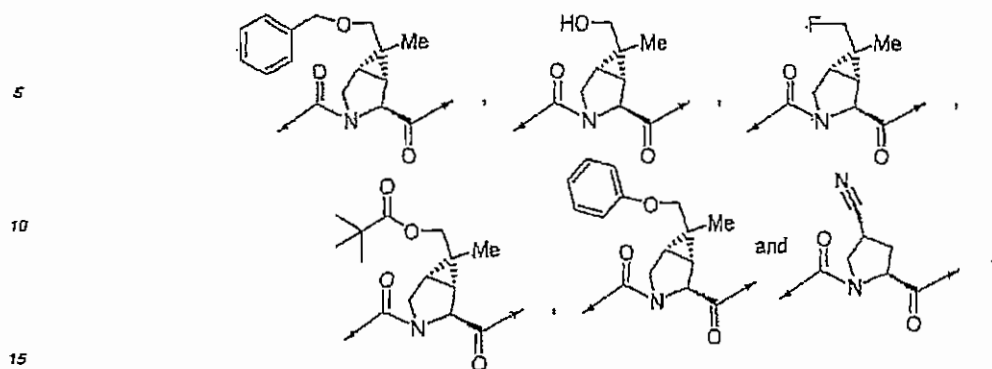
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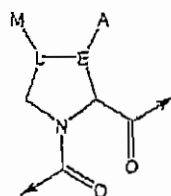




10. The compound of claim 9, wherein the moiety:

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is selected from the following structures:

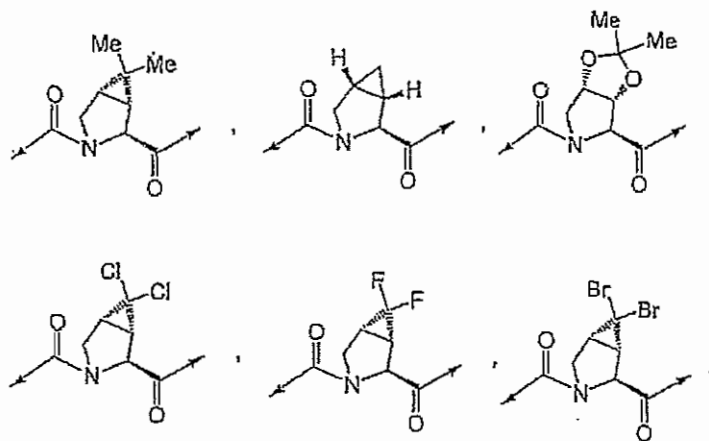
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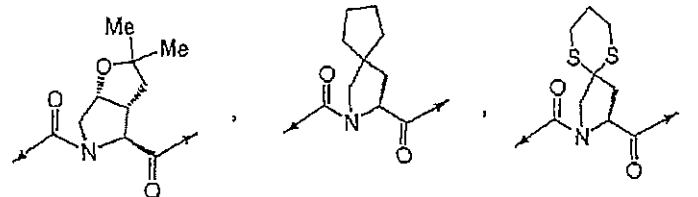
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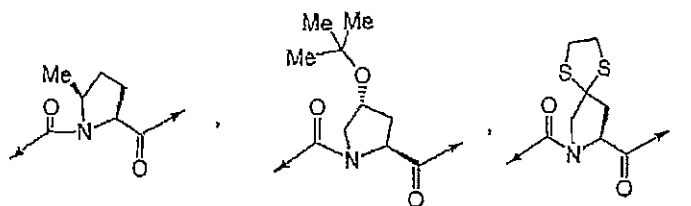


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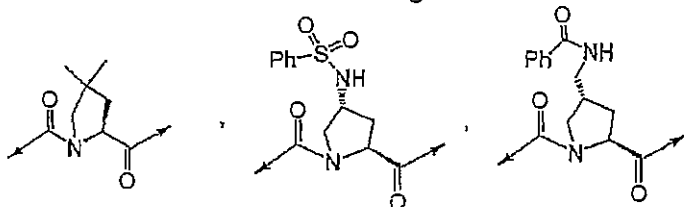
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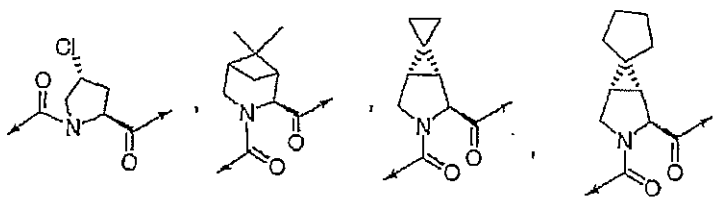
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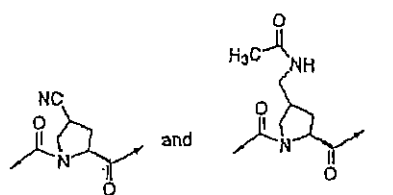
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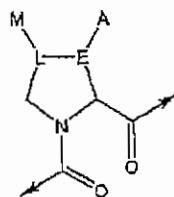
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11. The compound of claim 10, wherein the moiety:

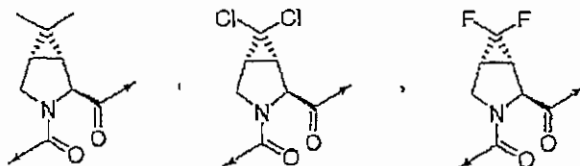
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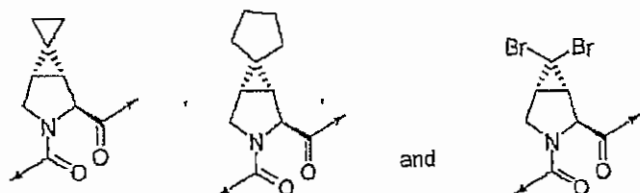
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is selected from the following structures:



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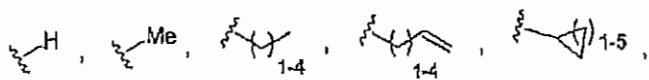
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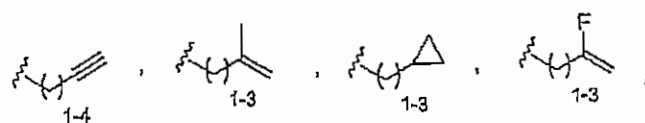
12. The compound of claim 1, wherein:

R^1 is NHR^{14} , where R^{14} is selected from the group consisting of:

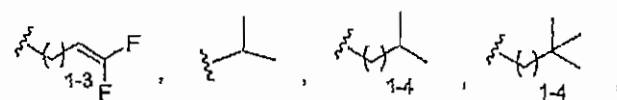
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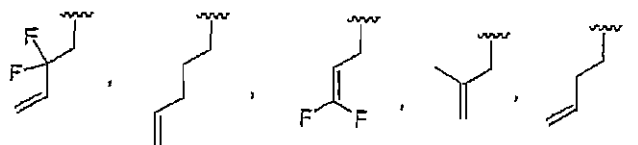
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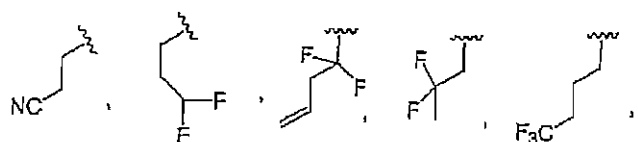


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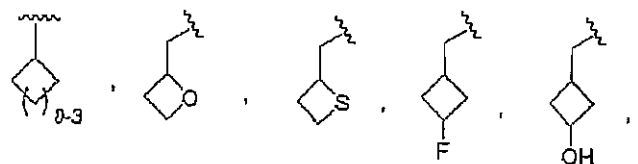
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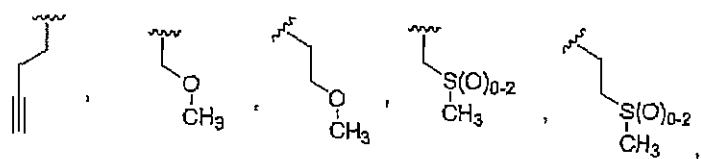
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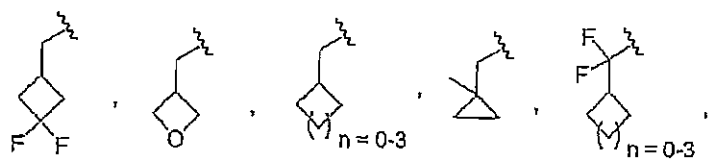
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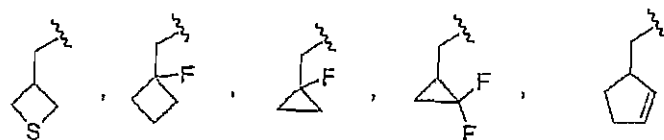
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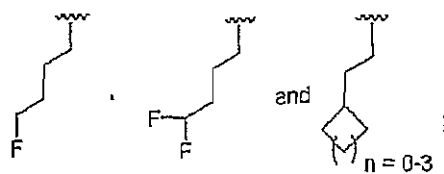


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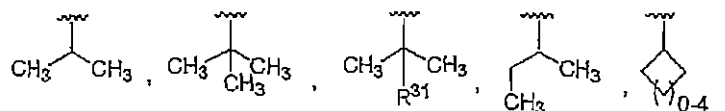
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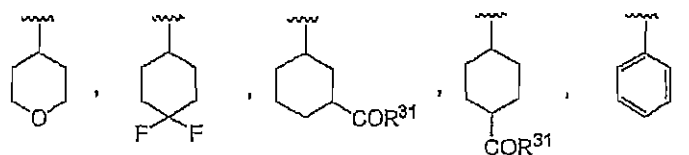
R^3 is selected from the group consisting of the following moieties:

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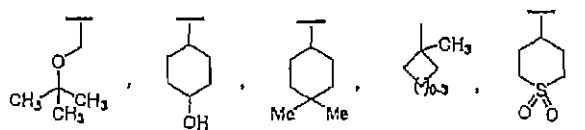
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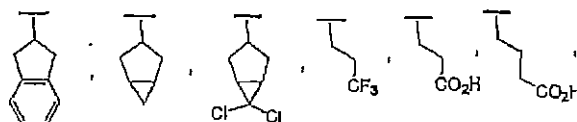


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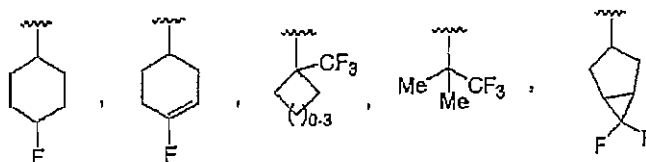


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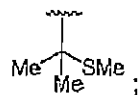


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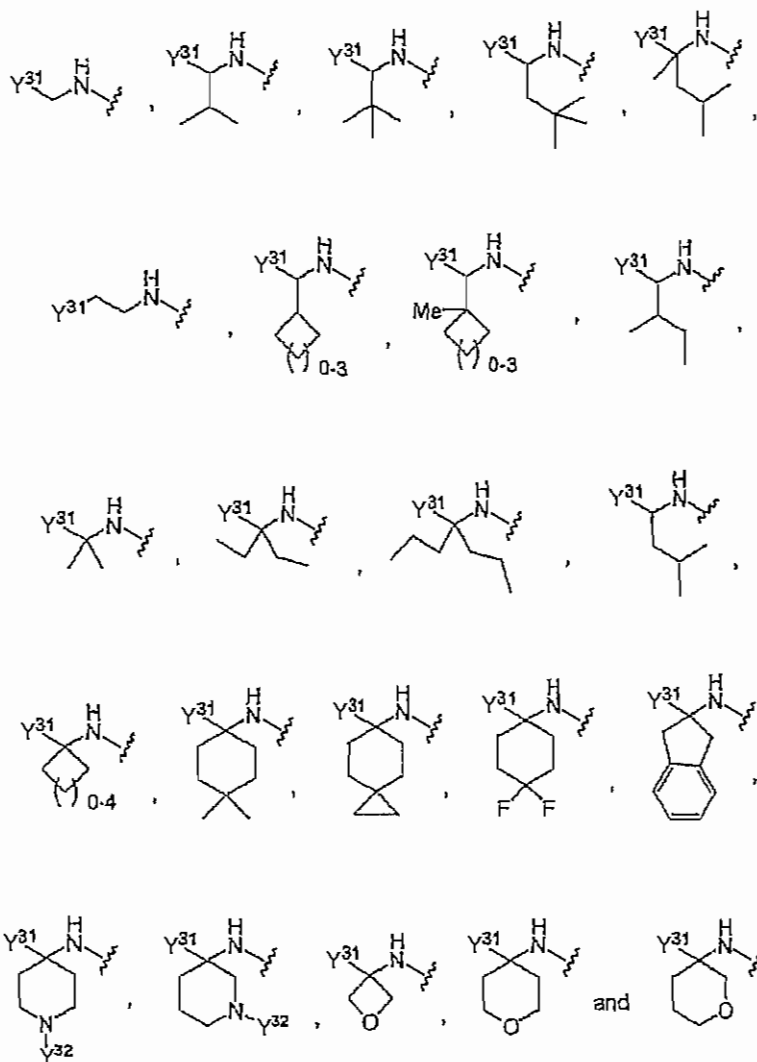
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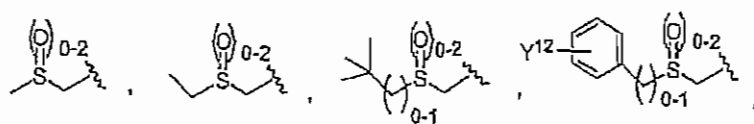
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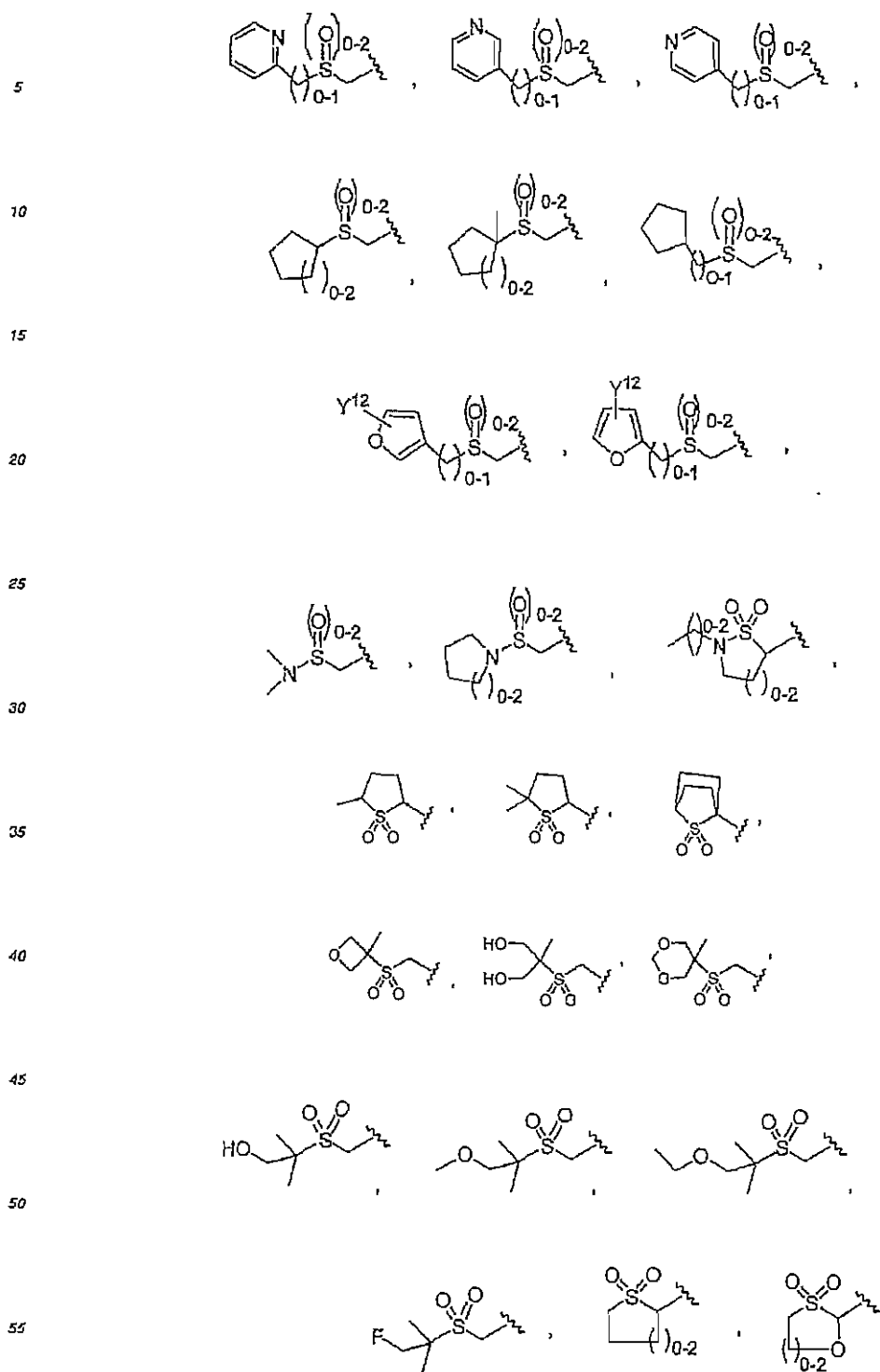


Y is selected from the group consisting of:

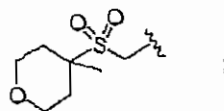


wherein Y³¹ is selected from the group consisting of:

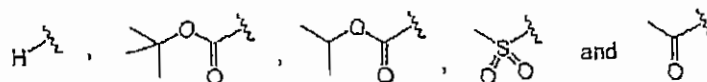




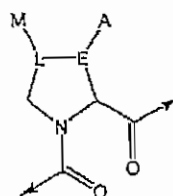
and



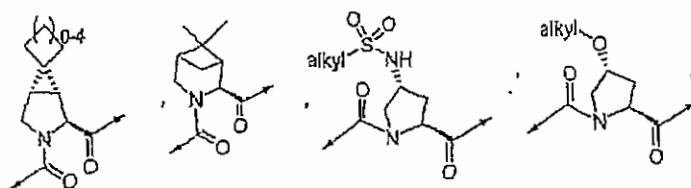
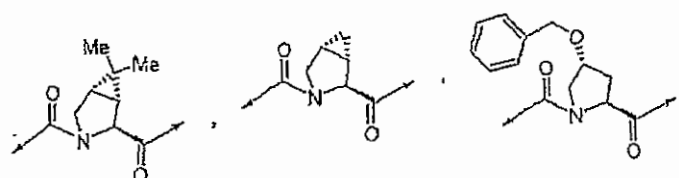
Y^{32} is selected from the group consisting of:

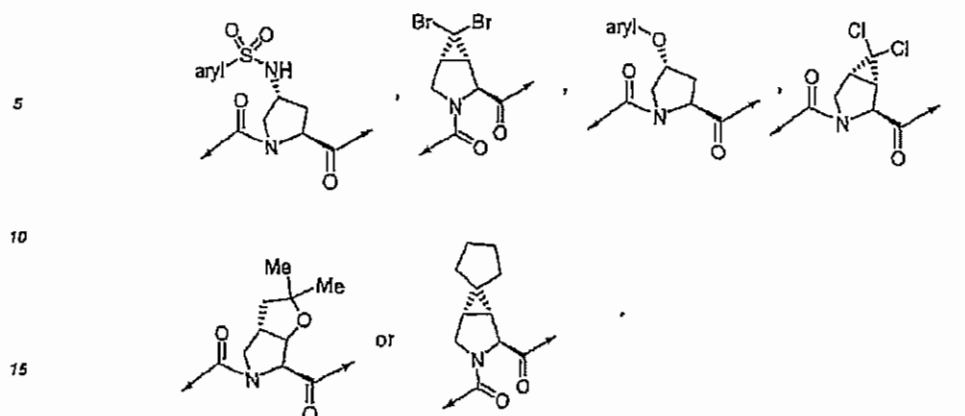


and Y^{12} is selected from the group consisting of H, CO_2H , CO_2Me , OMe, F, Cl, Br, NH_2 , $N(H)S(O_2)CH_3$, $N(H)C(O)CH_3$, NO_2 , $S(O_2)NH_2$, CF_3 , Me, OH, OCF_3 , and $C(O)NH_2$; and the moiety:



is:





13. A pharmaceutical composition comprising as an active ingredient at least one compound of claim 1.

14. The pharmaceutical composition of claim 13 for use in treating disorders associated with HCV.

15. The pharmaceutical composition of claim 13 additionally comprising at least one pharmaceutically acceptable carrier.

16. The pharmaceutical composition of claim 15, additionally containing at least one antiviral agent.

17. The pharmaceutical composition of claim 16, still additionally containing at least one interferon.

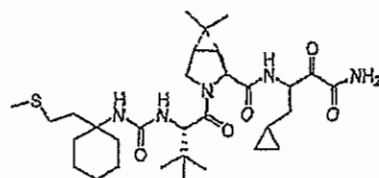
18. The pharmaceutical composition of claim 17, wherein said at least one antiviral agent is ribavirin and said at least one interferon is α -interferon or pegylated interferon.

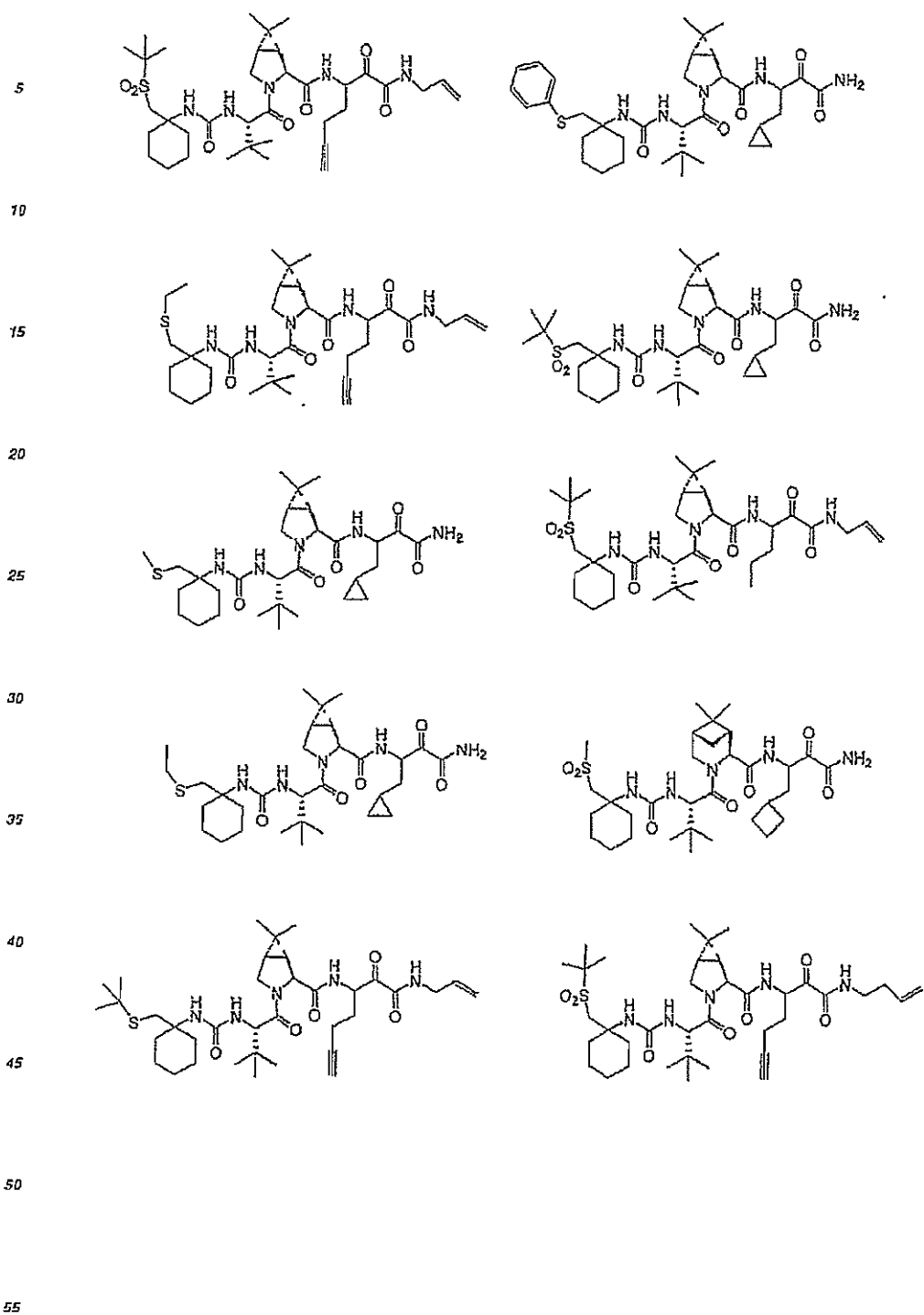
19. The use of at least one compound of claim 1 for the manufacture of a medicament for treating disorders associated with the HCV.

20. The use of claim 19, wherein said treatment comprises oral or subcutaneous administration of the medicament.

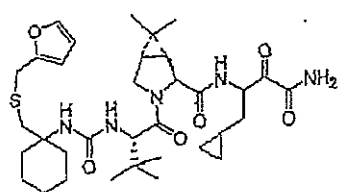
21. A method of preparing a pharmaceutical composition for treating the disorders associated with the HCV, said method comprising bringing into intimate contact at least one compound of claim 1 and at least one pharmaceutically acceptable carrier.

22. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate said compound, said compound being selected from the compounds of structures listed below:

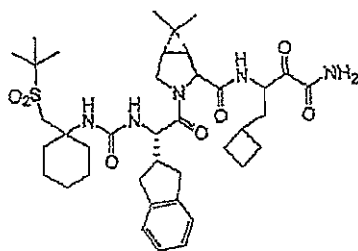




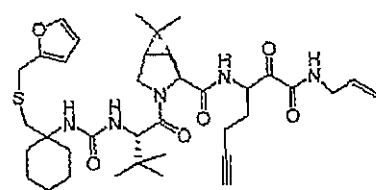
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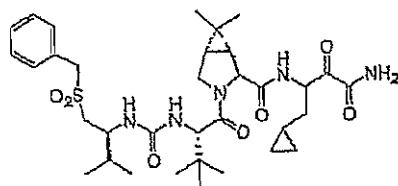
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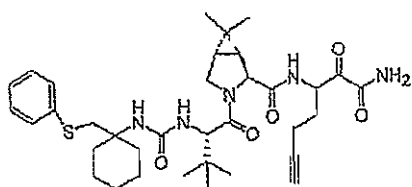


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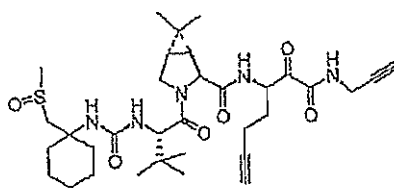


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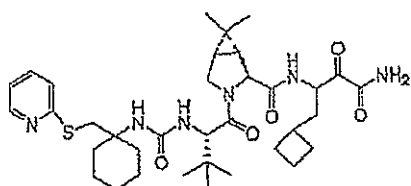
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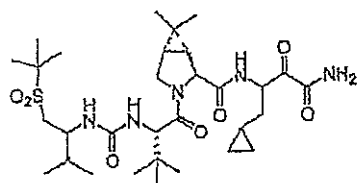
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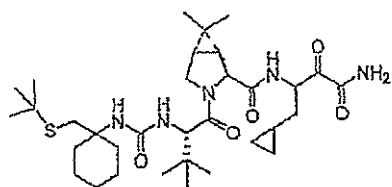
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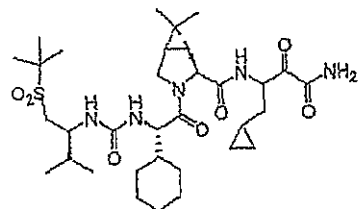
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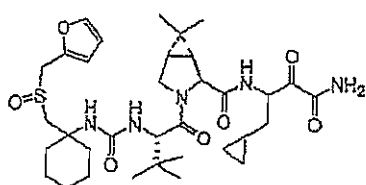
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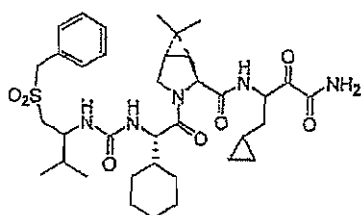
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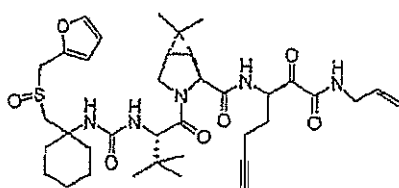
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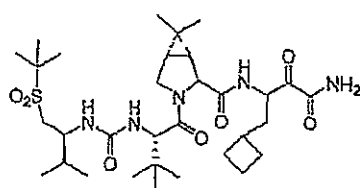
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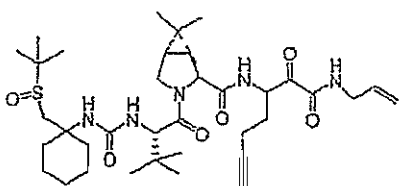
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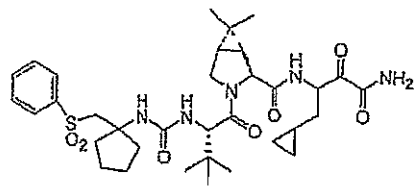
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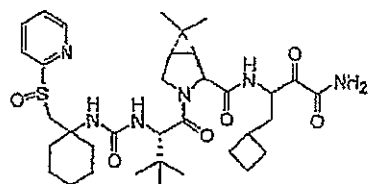
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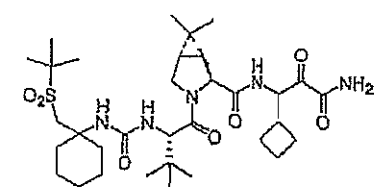
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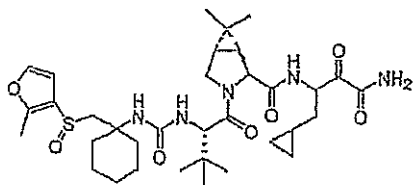


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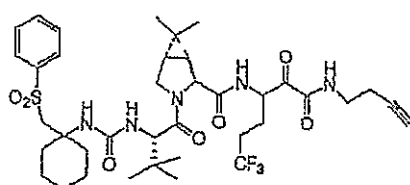


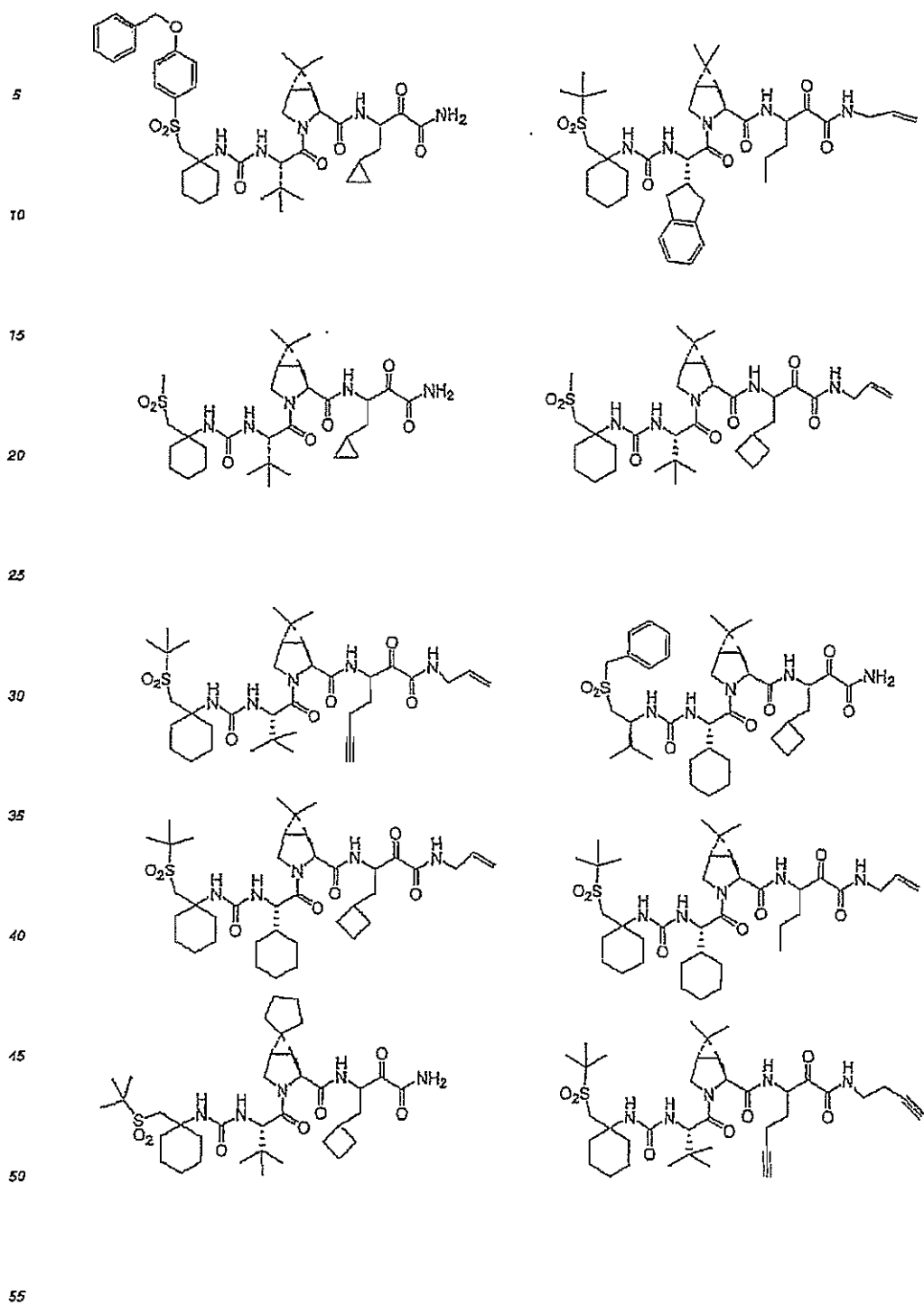
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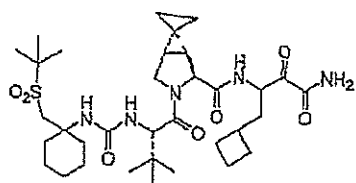


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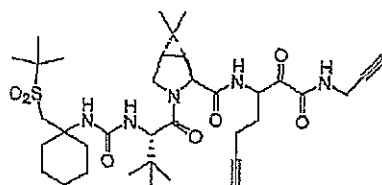




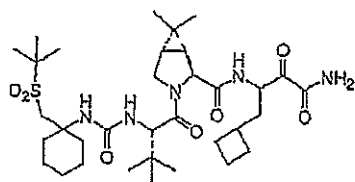
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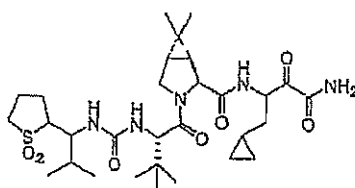
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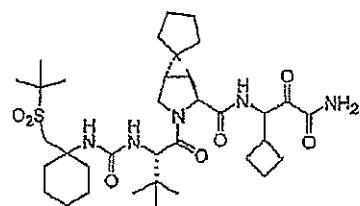
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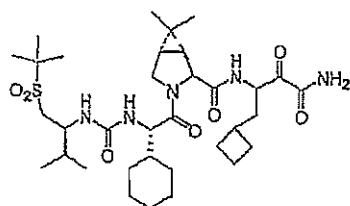
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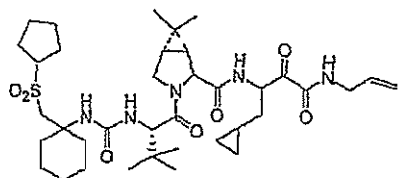
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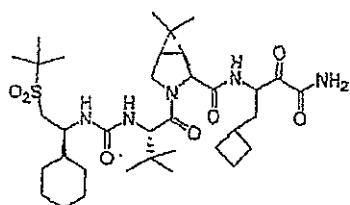
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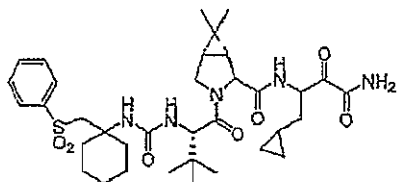
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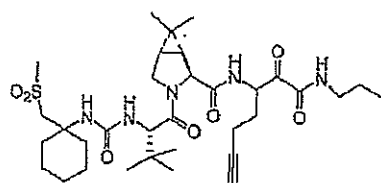
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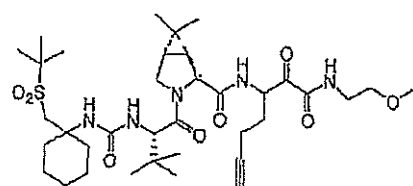
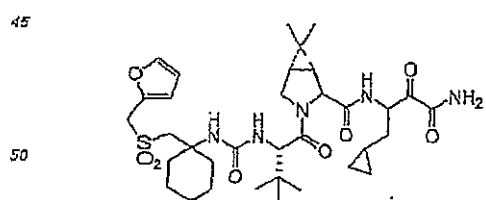
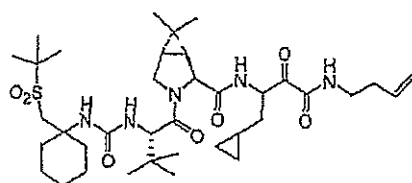
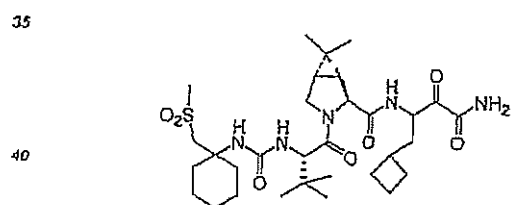
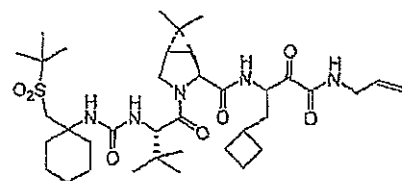
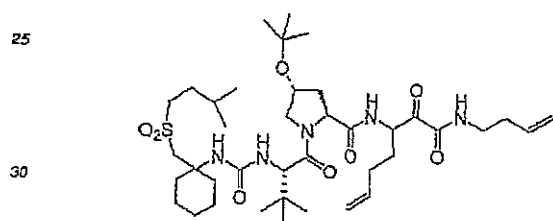
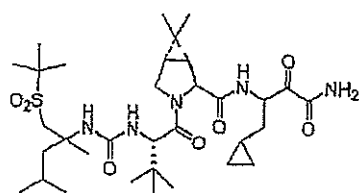
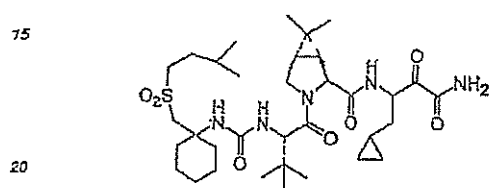
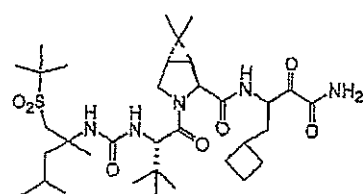
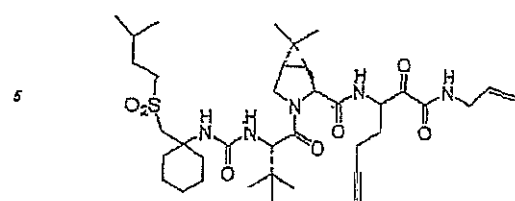
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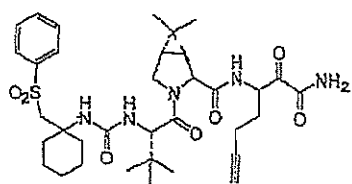
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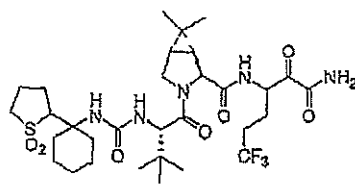
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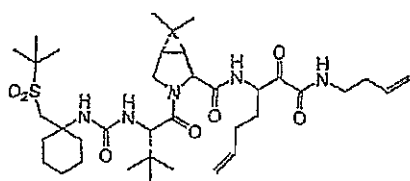
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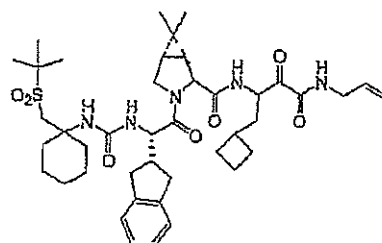
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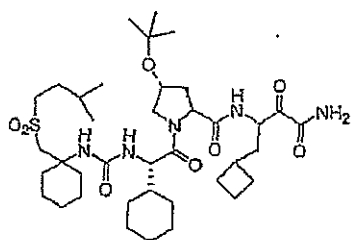
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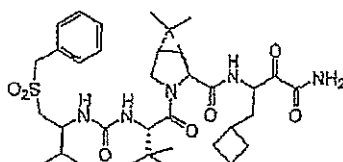
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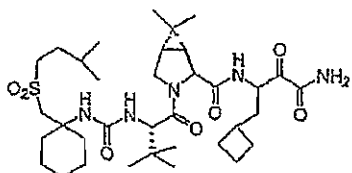
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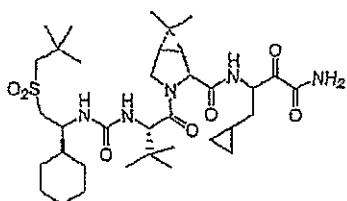
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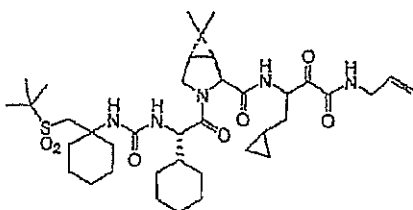
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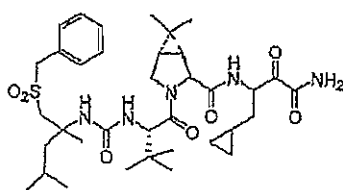
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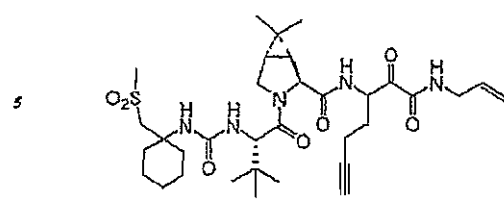
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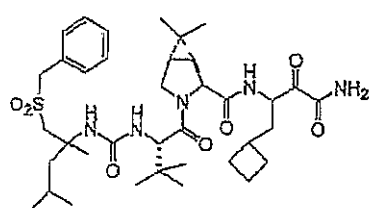
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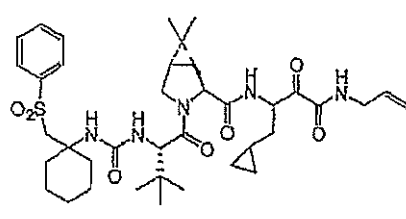
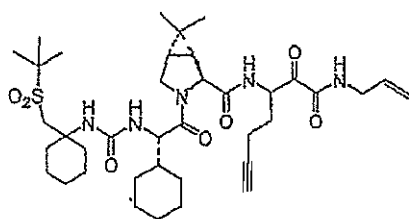
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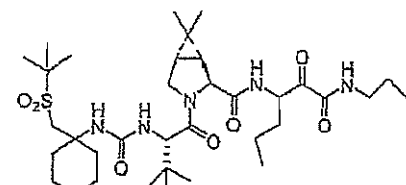
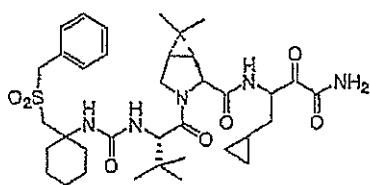
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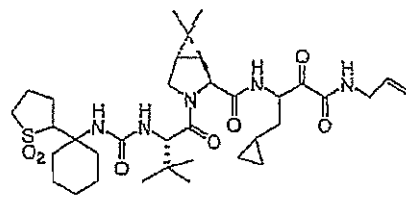
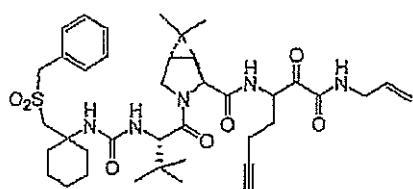
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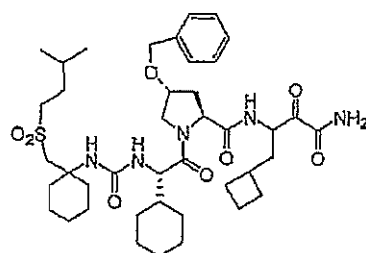
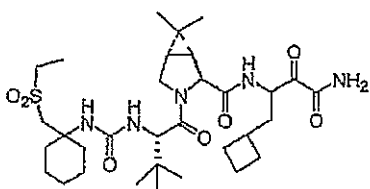
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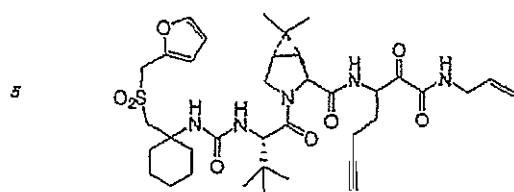
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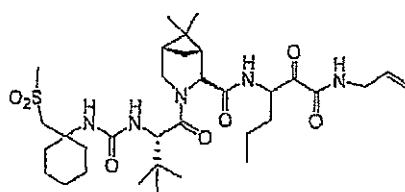
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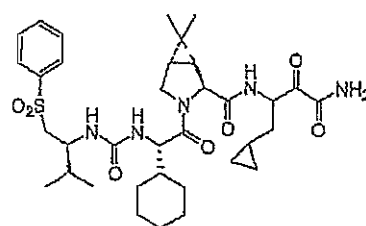
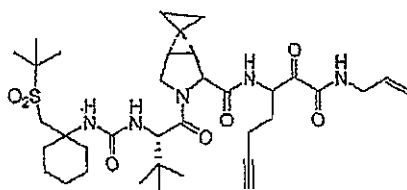


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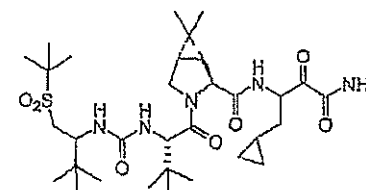
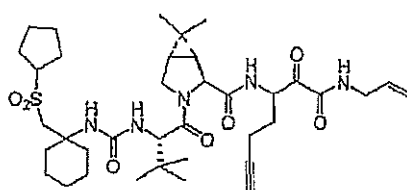
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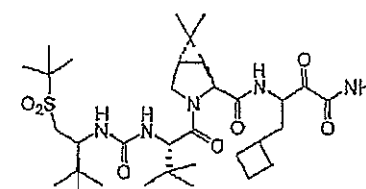
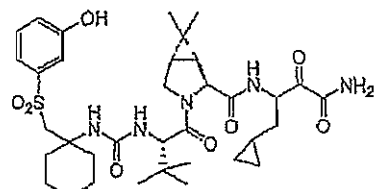
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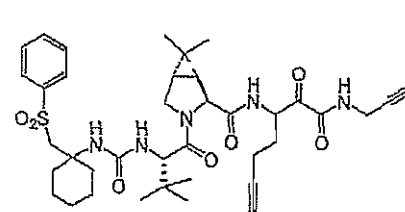
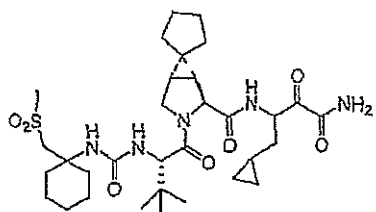
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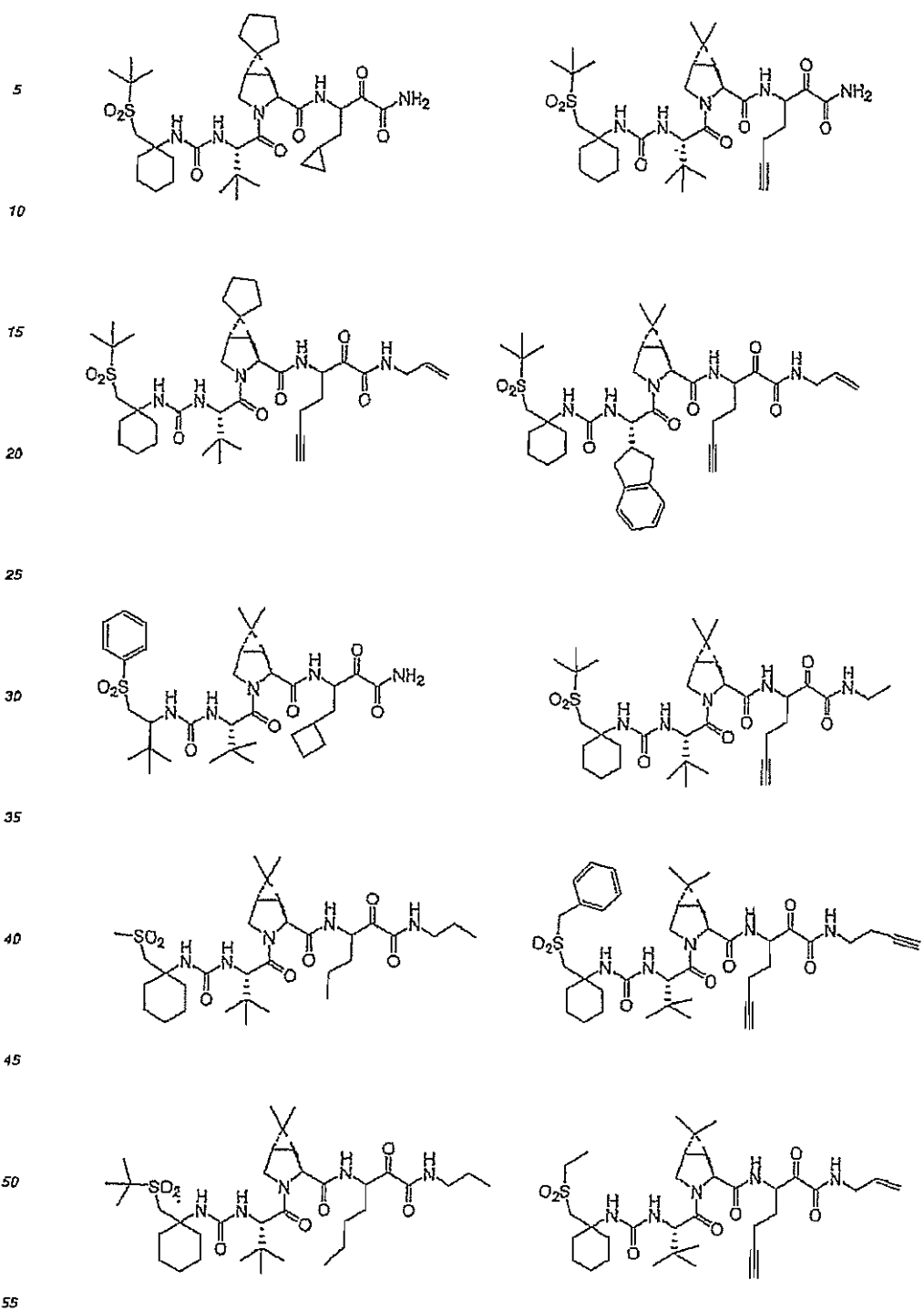


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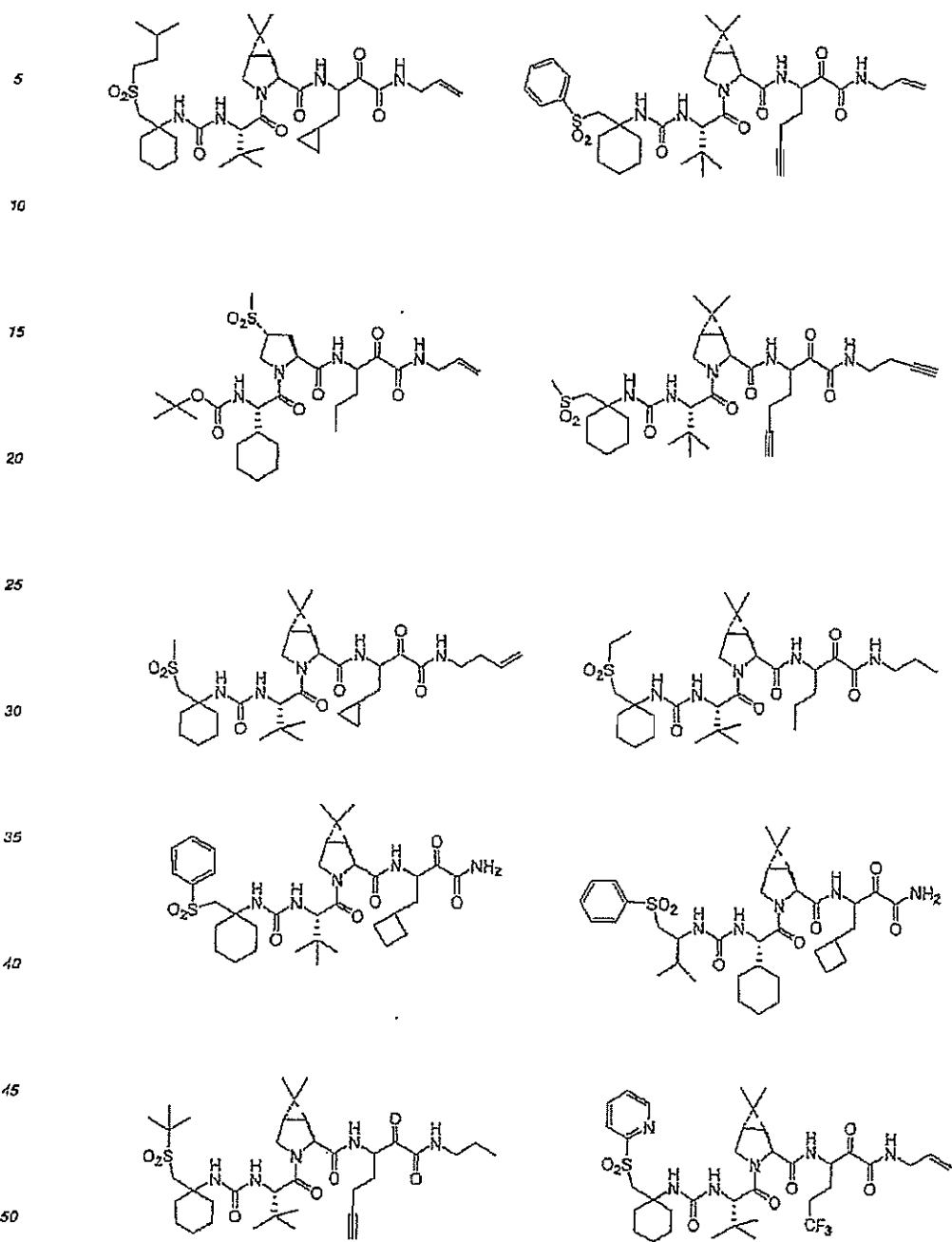
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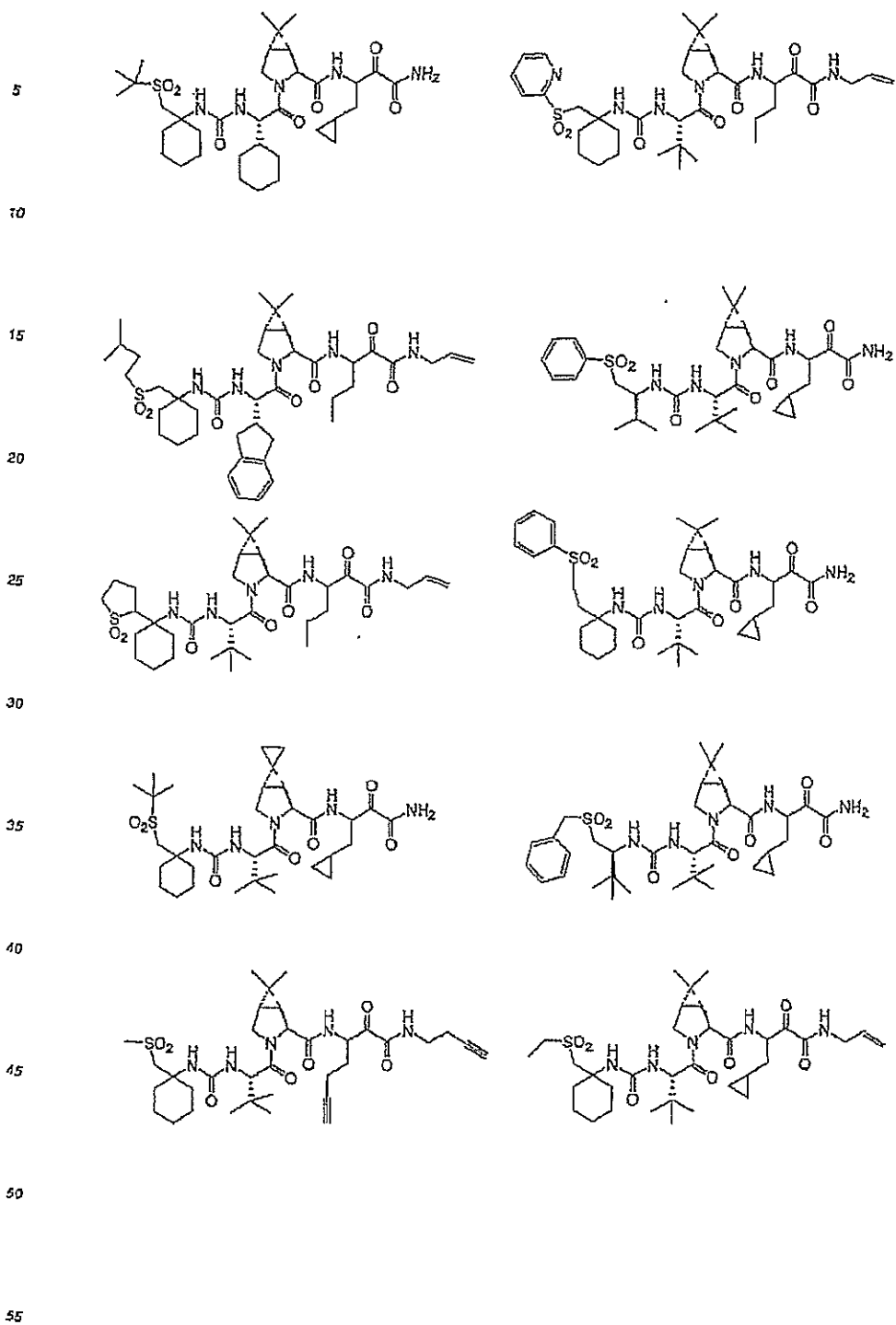


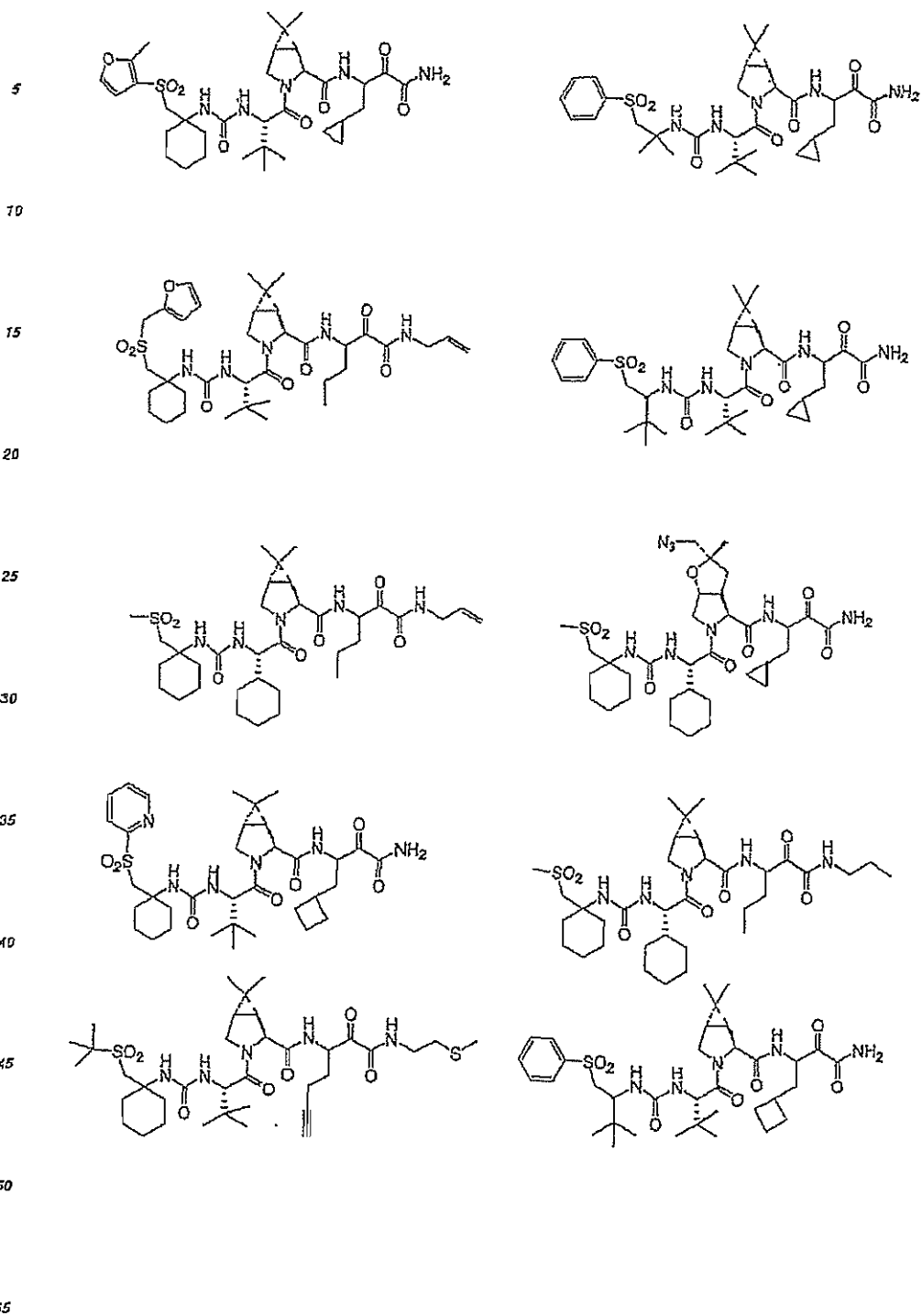
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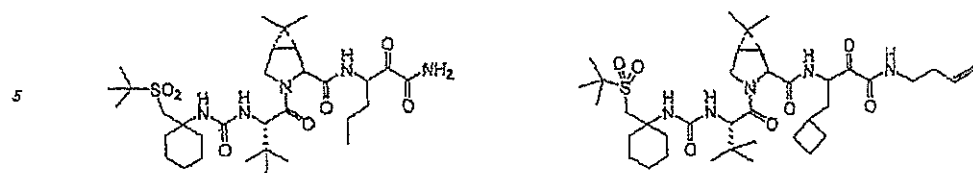




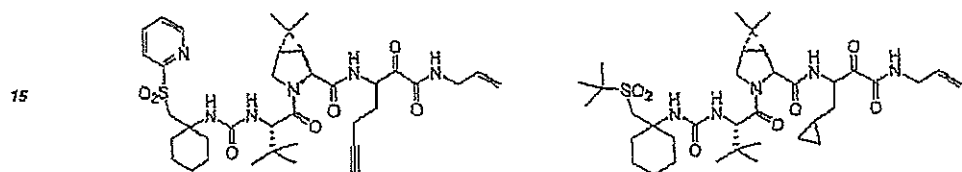




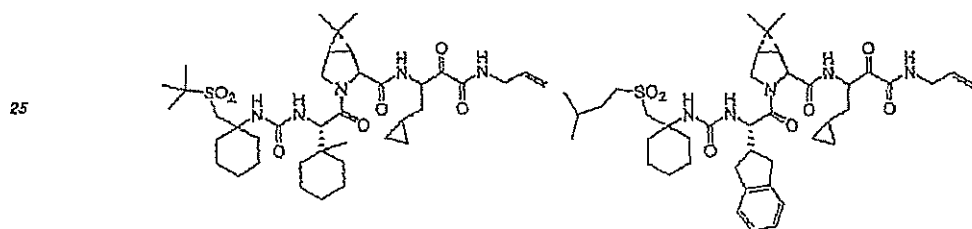




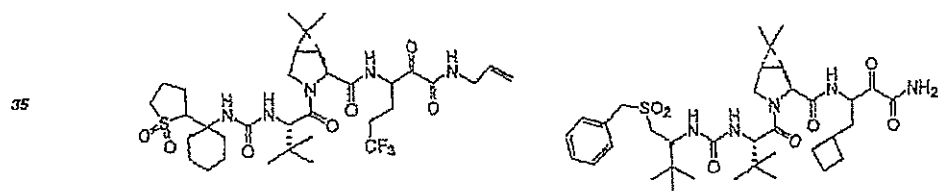
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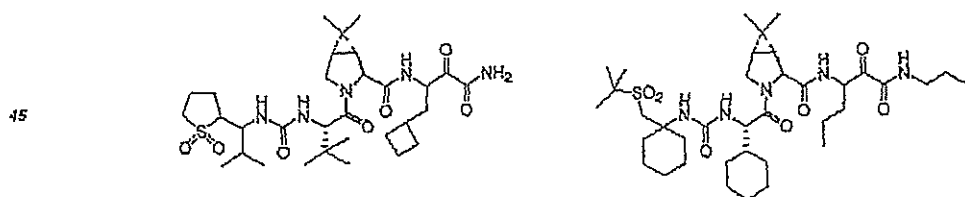
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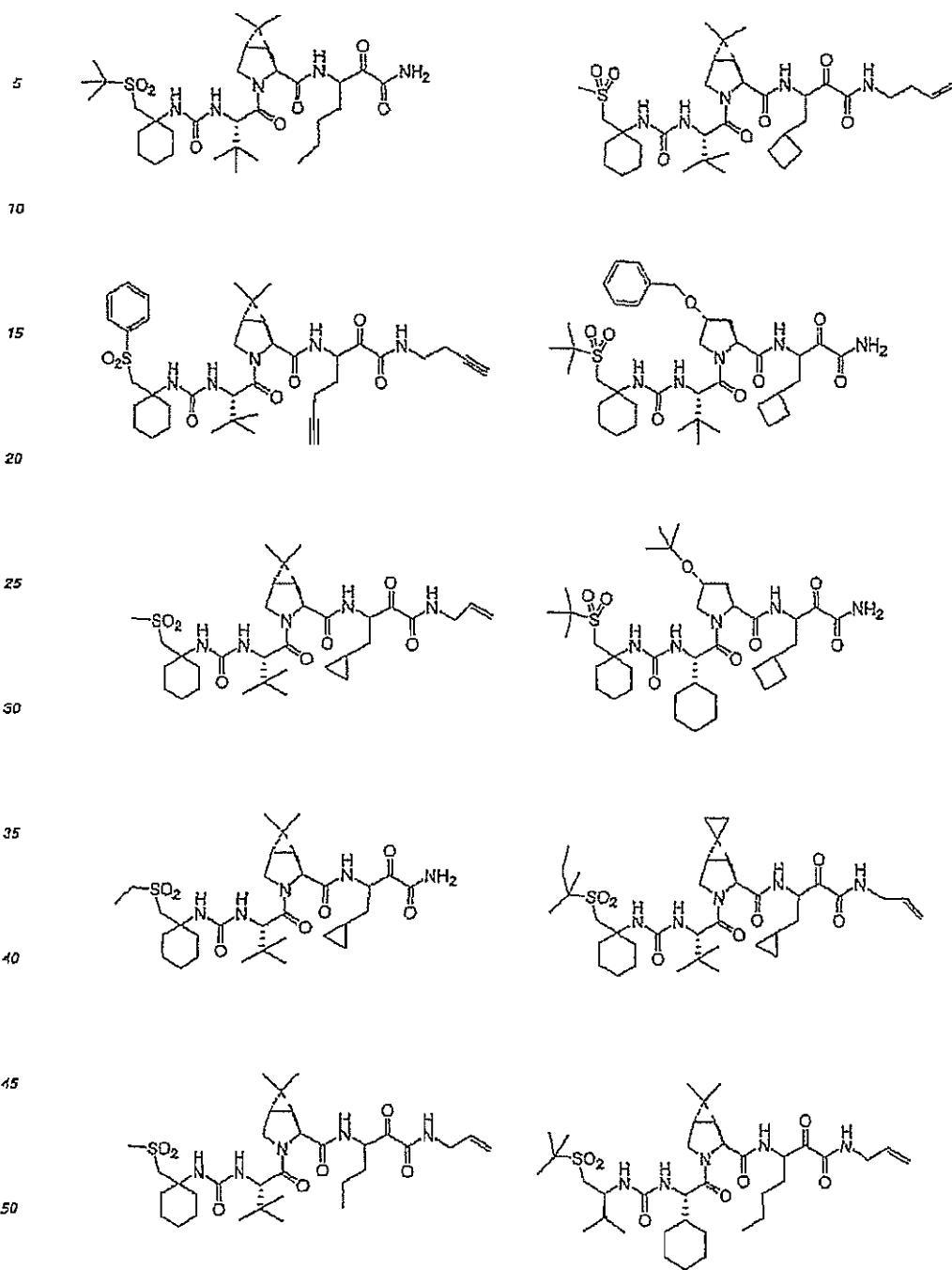


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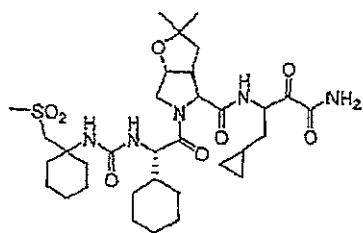


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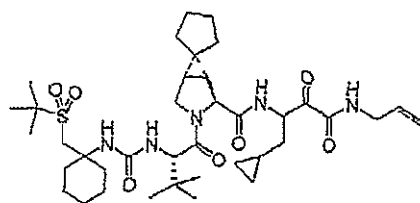
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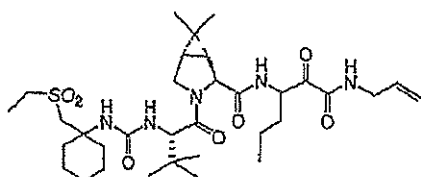
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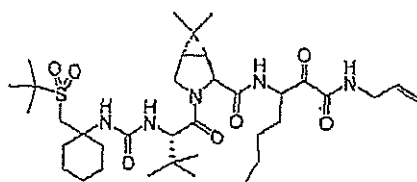
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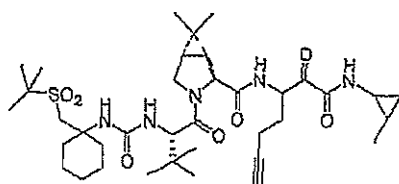
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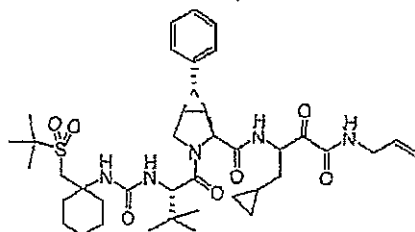
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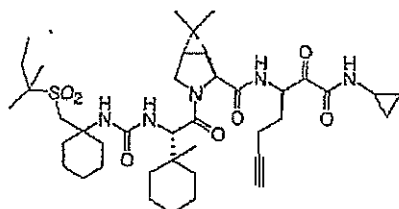
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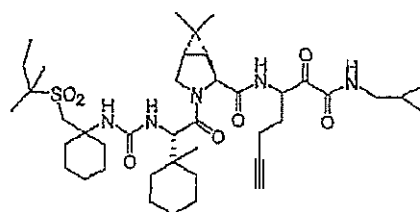
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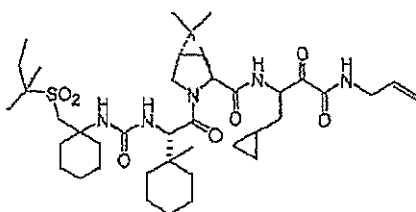
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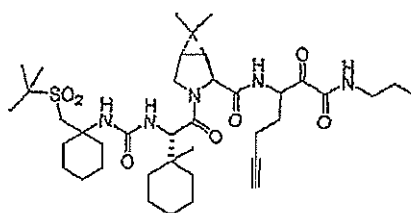
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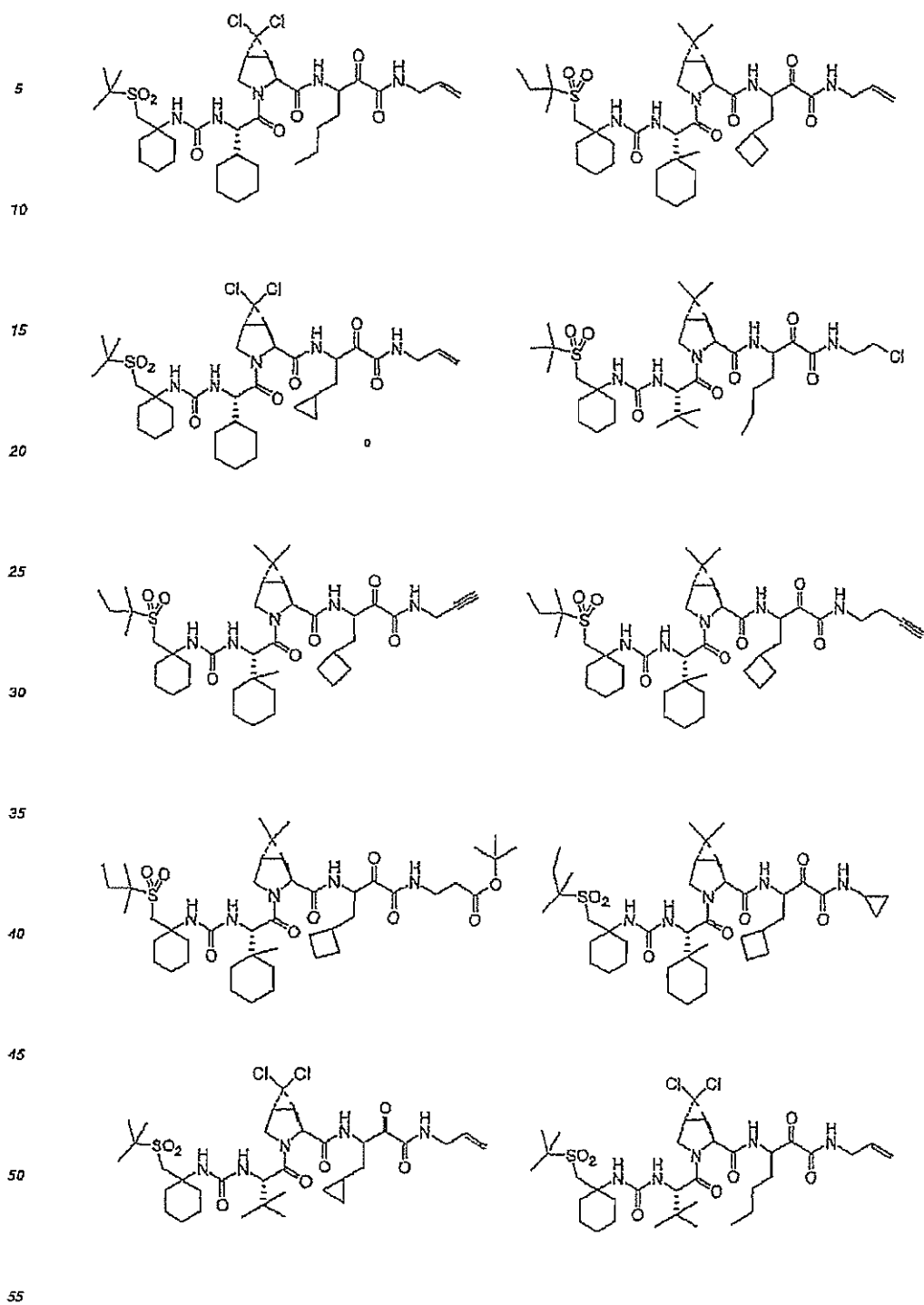
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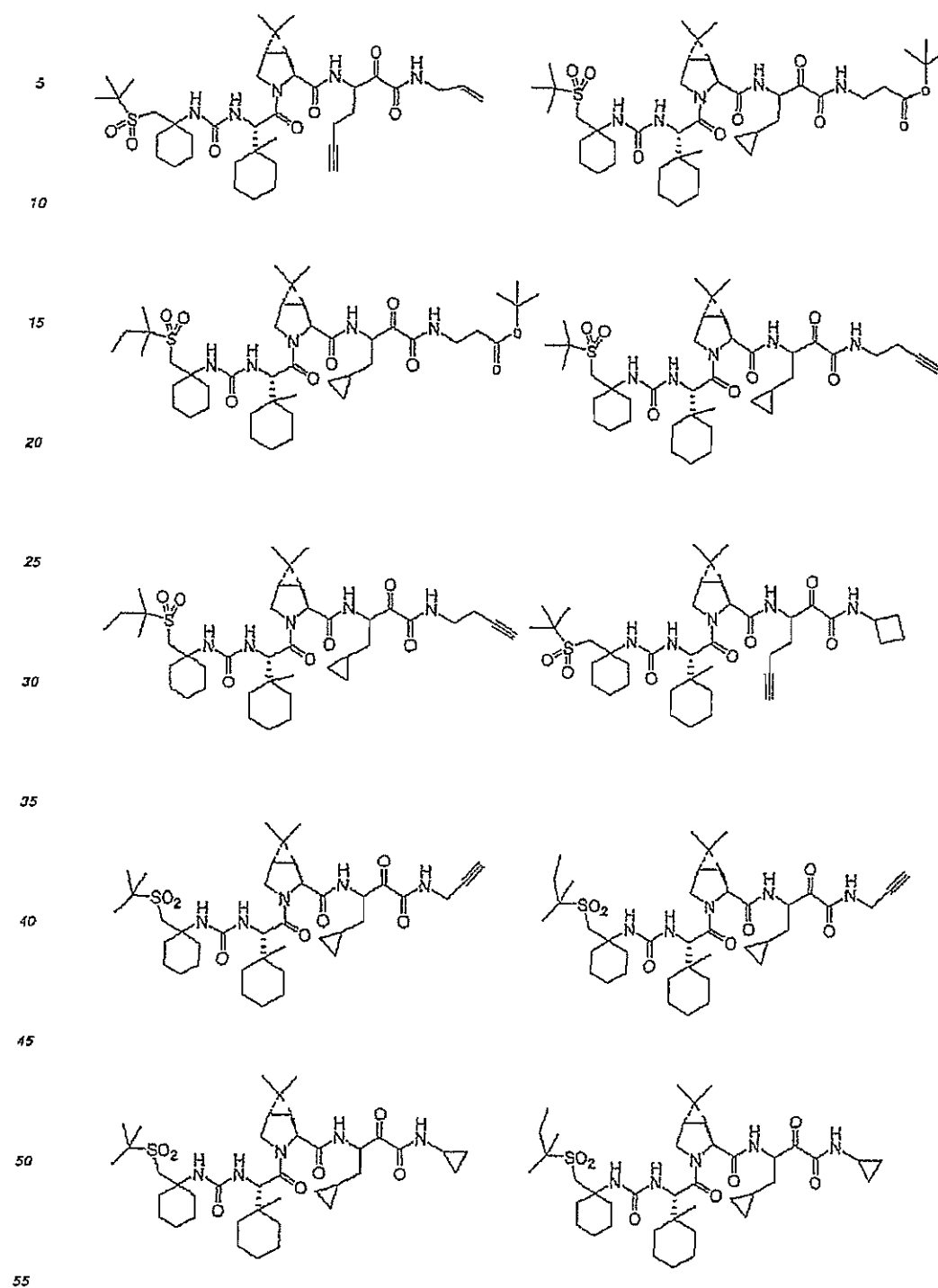


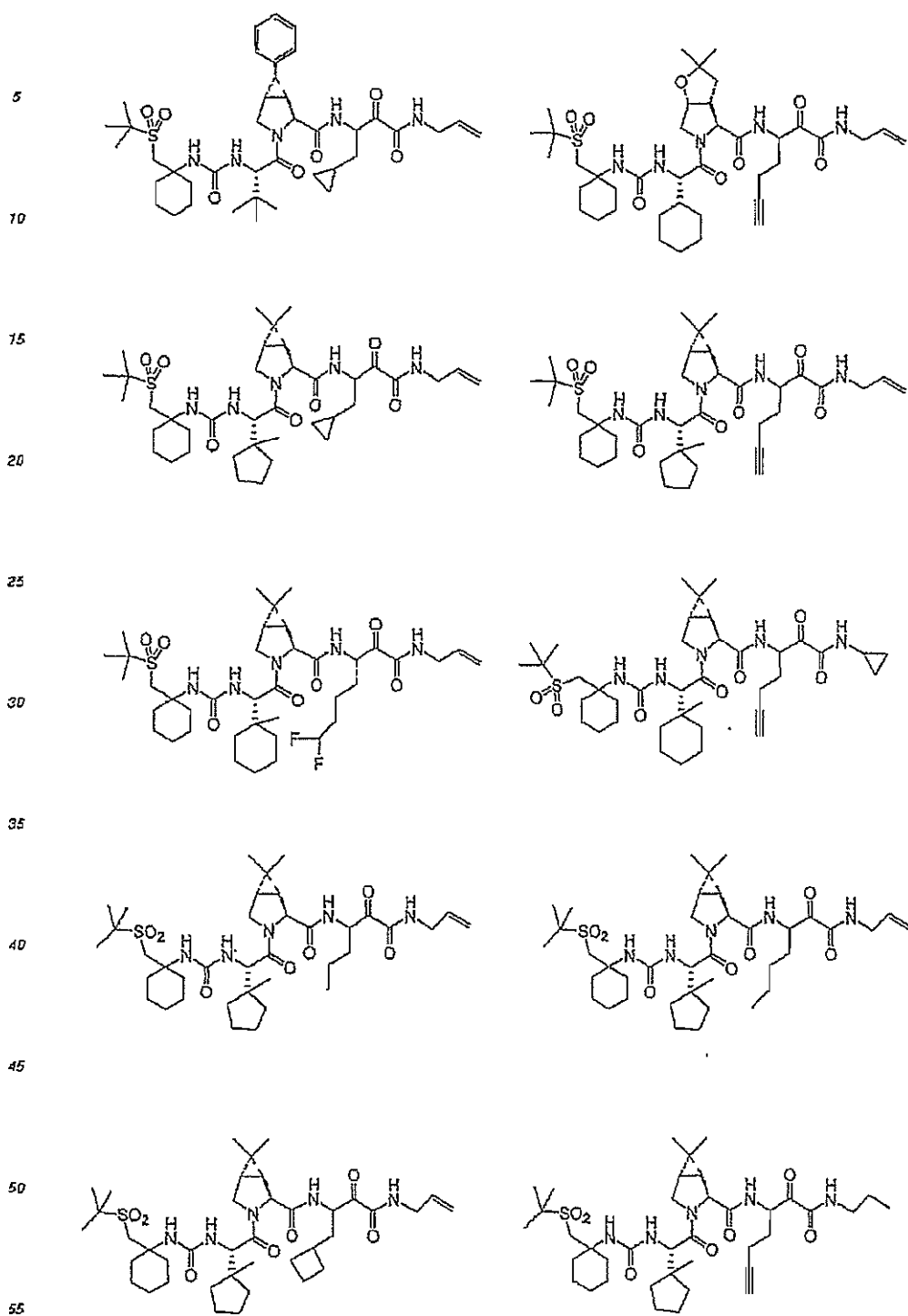
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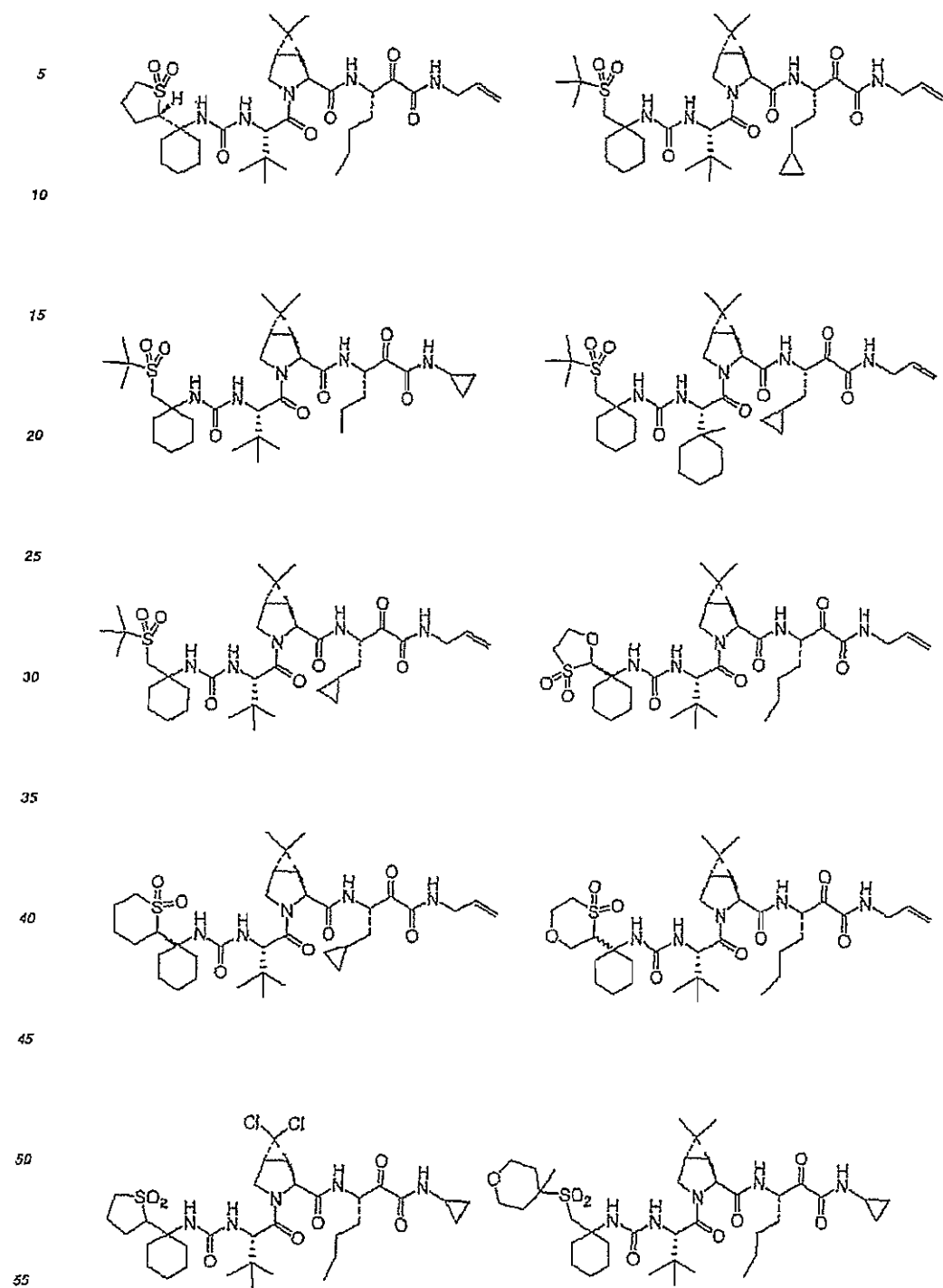


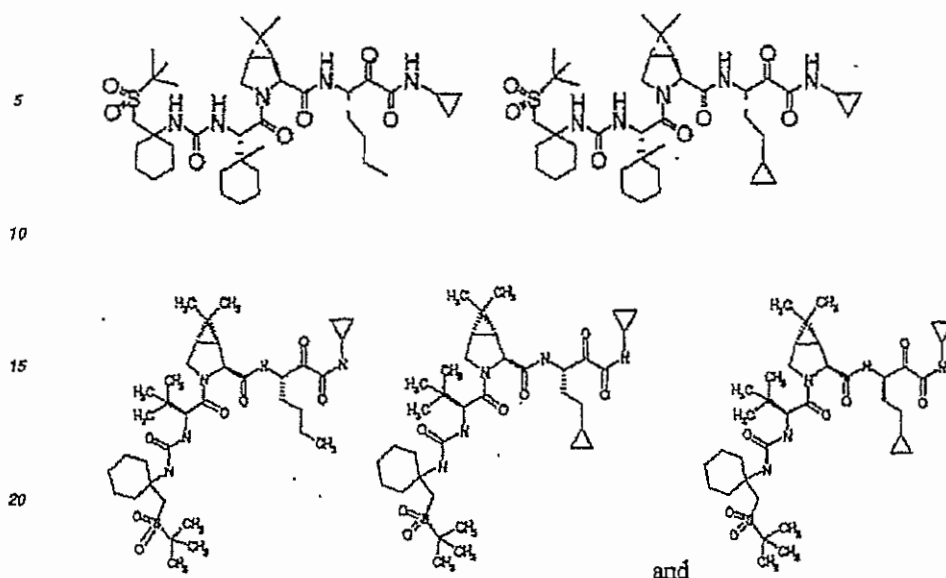
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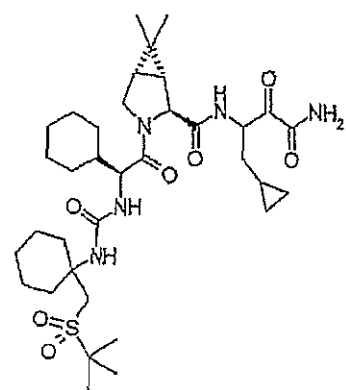
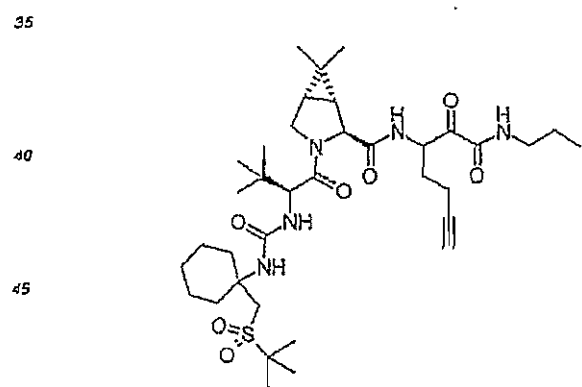
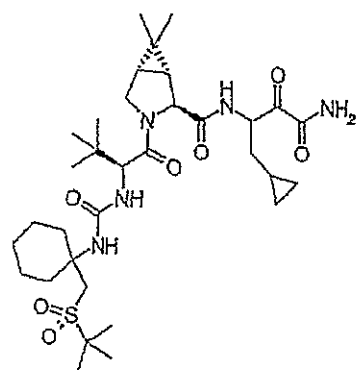
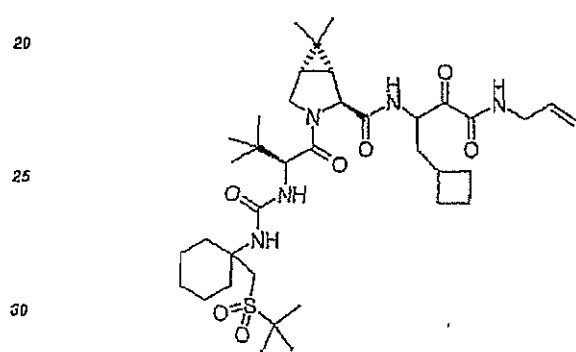
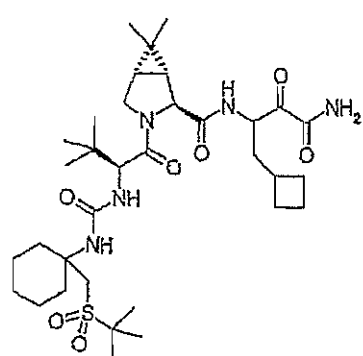
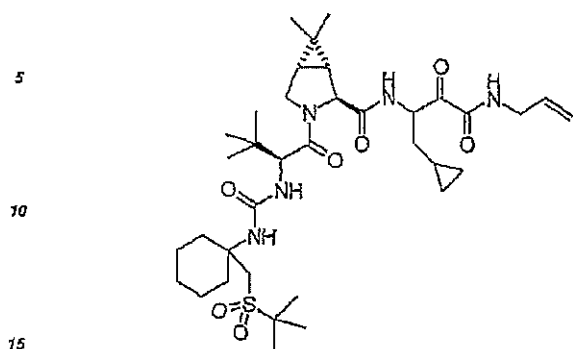


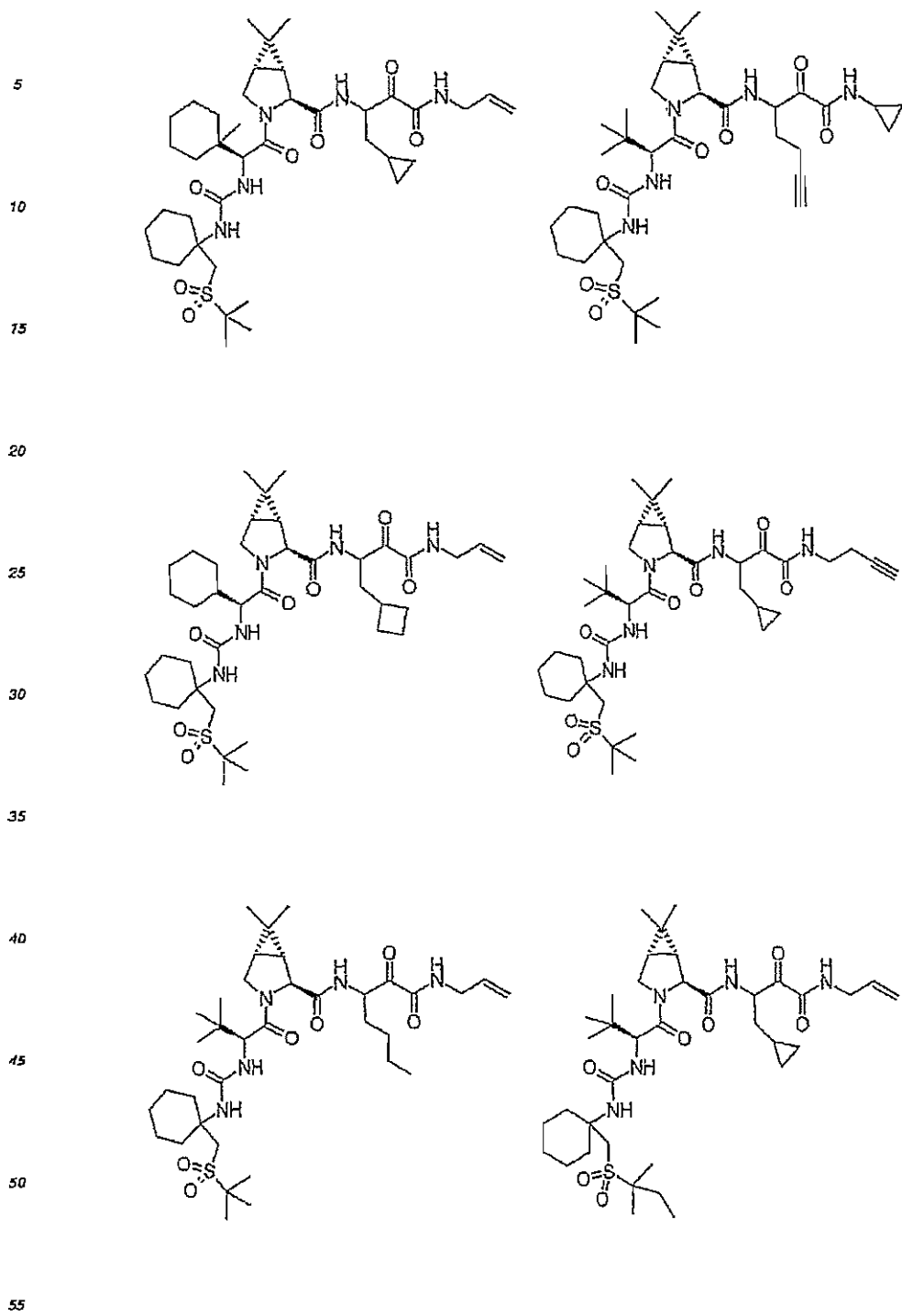


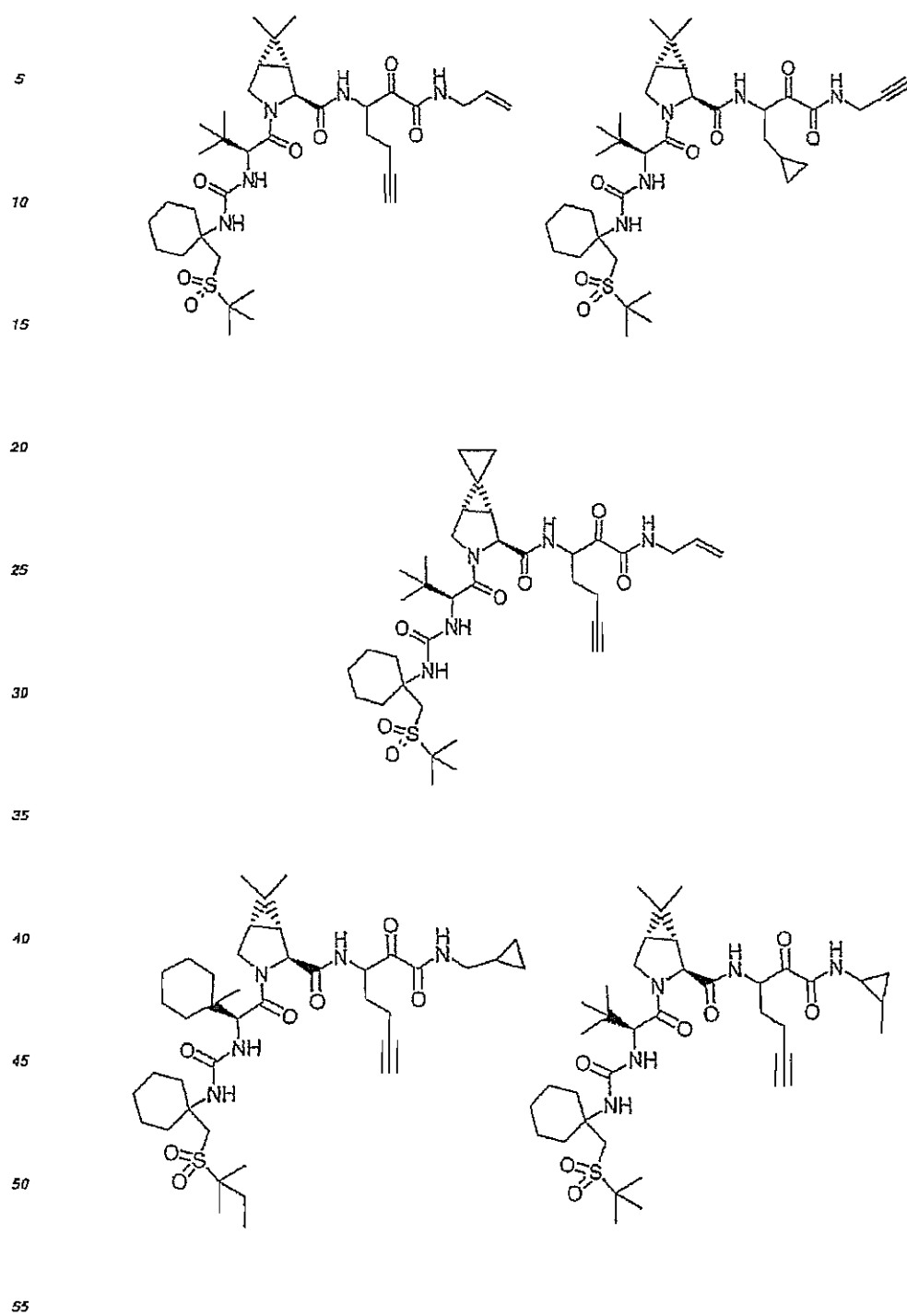


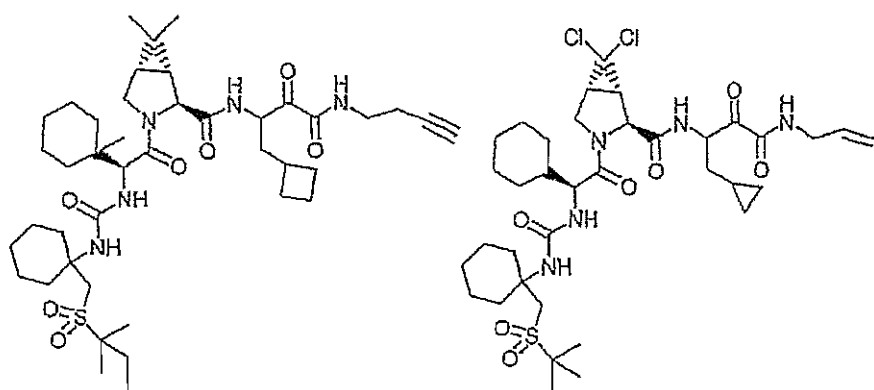
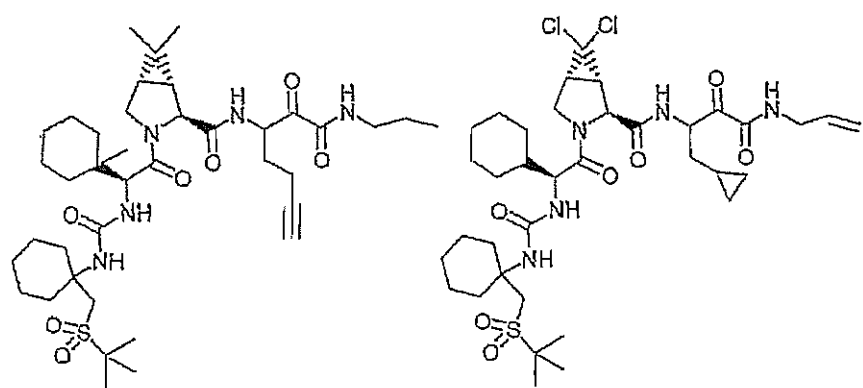
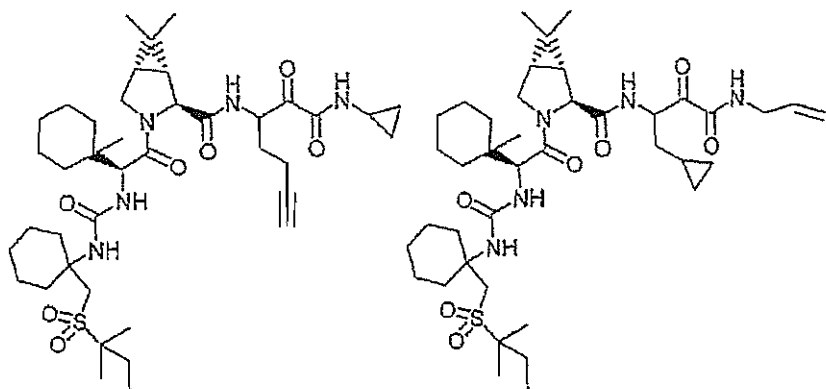


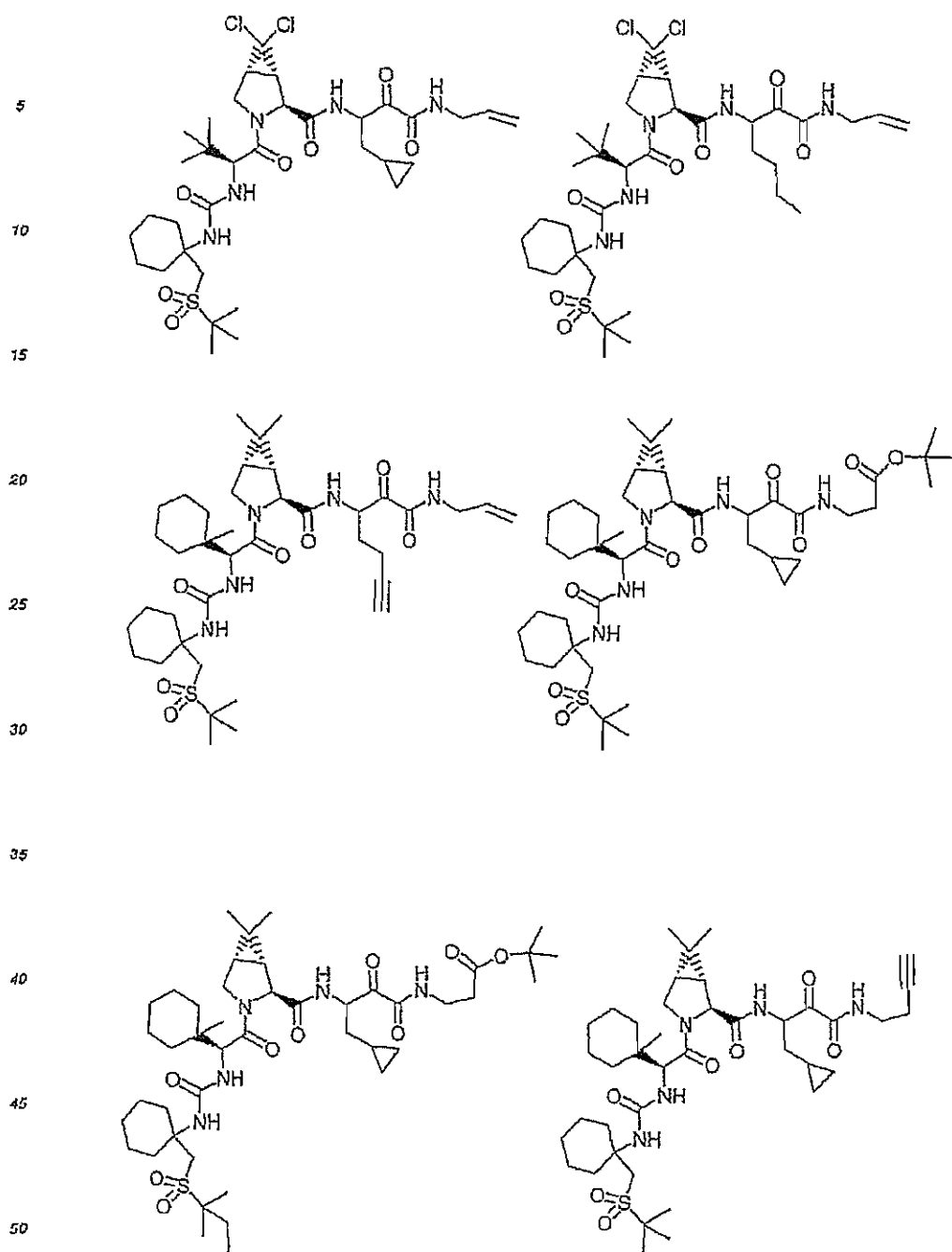
23. A pharmaceutical composition for treating disorders associated with the HCV, said composition comprising therapeutically effective amount of one or more compounds in claim 22 and a pharmaceutically acceptable carrier.
24. The pharmaceutical composition of claim 23, additionally containing at least one antiviral agent
25. The pharmaceutical composition of claim 24, still additionally containing at least one interferon or PEG-interferon alpha conjugate.
26. The pharmaceutical composition of claim 25, wherein said at least one antiviral agent is ribavirin and said at least one interferon is α -interferon or pegylated interferon.
27. The use of one or more compounds of claim 22 for the manufacture of a medicament for the treatment of a hepatitis C virus associated disorder.
28. The use of one or more compounds of claim 22 for the manufacture of a medicament for treating, preventing, or ameliorating one or more symptoms of hepatitis C.
29. The use of claim 28 wherein the one or more compounds modulate the activity of hepatitis C virus (HCV) protease.
30. The use of claim 29, wherein the HCV protease is the NS3/NS4a protease.
31. The use of claim 30, wherein the compound or compounds inhibit HCV NS3/NS4a protease.
32. The use at least one compound, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, for the manufacture of a medicament for treating disorders associated with the HCV, said compound being selected from the following:

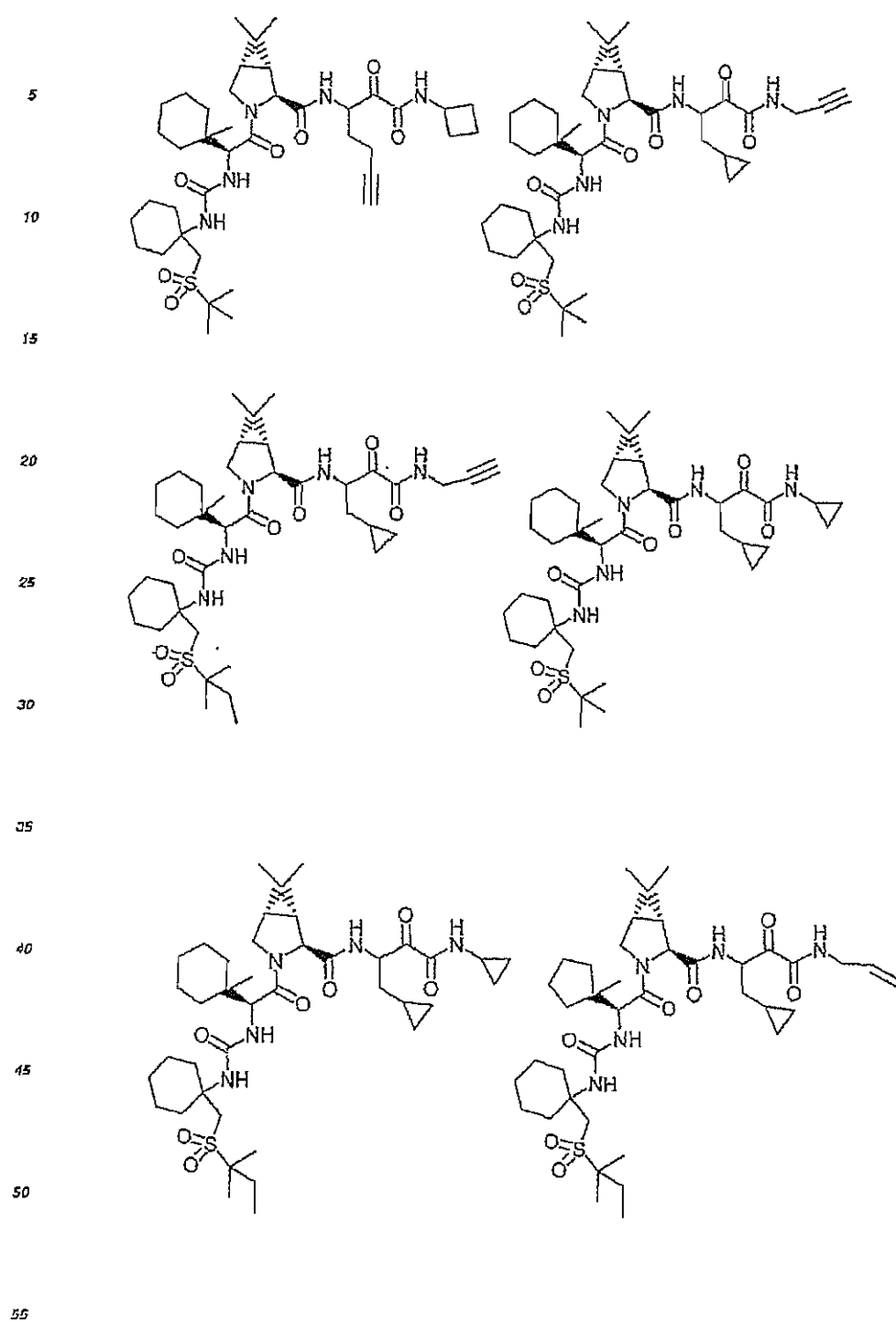


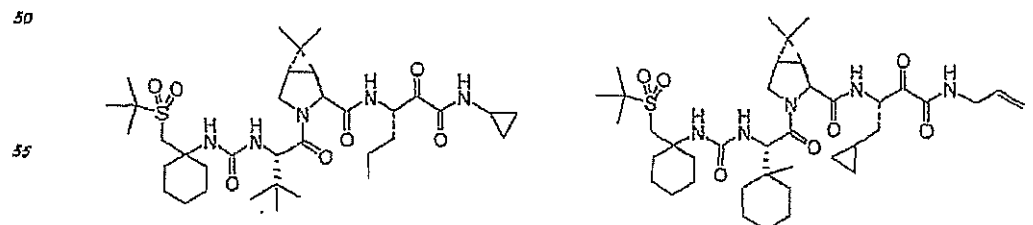
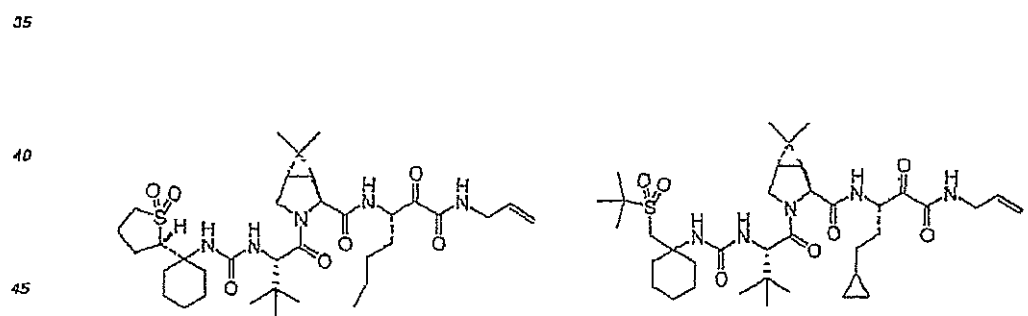
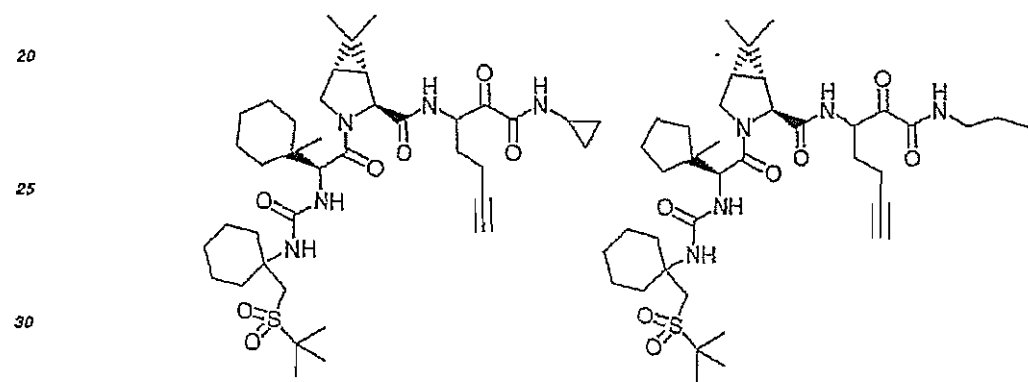
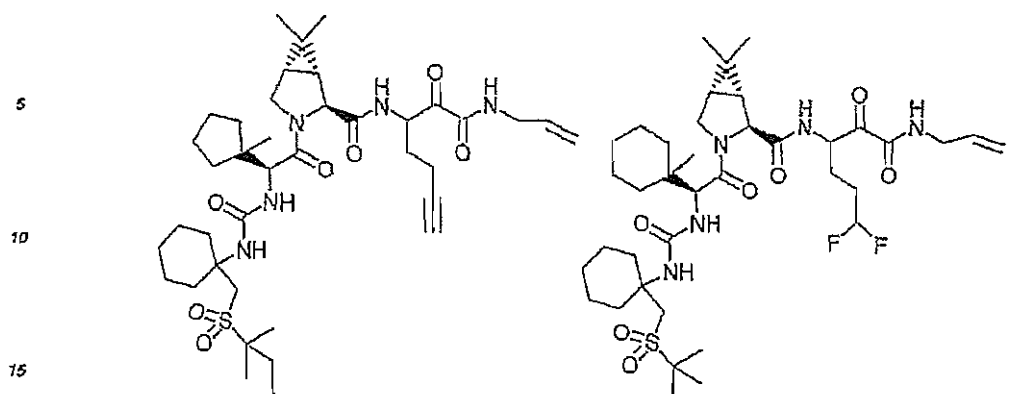


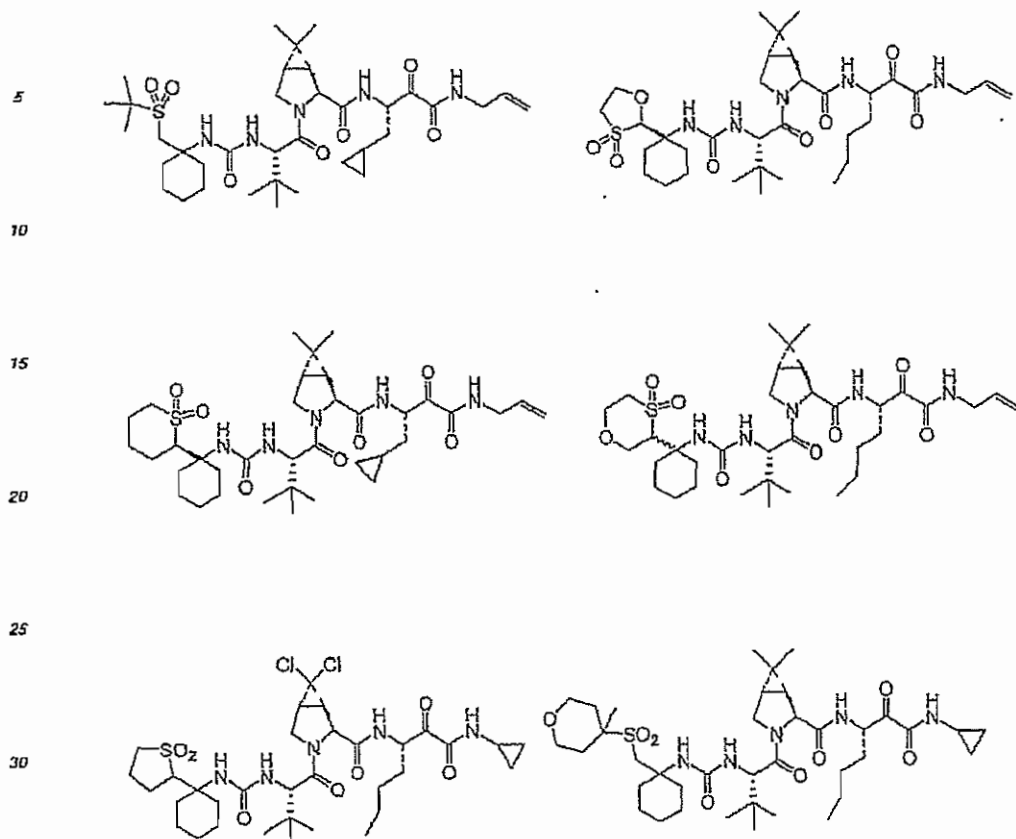




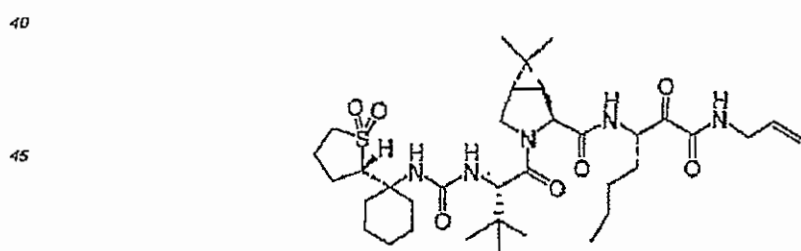








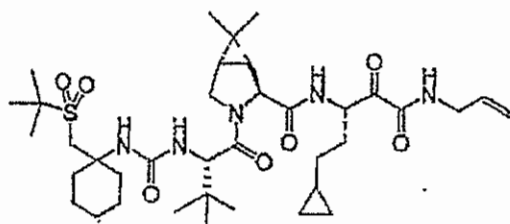
33. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:



34. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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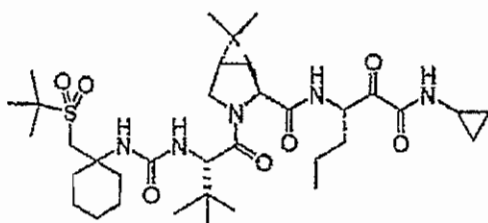


35. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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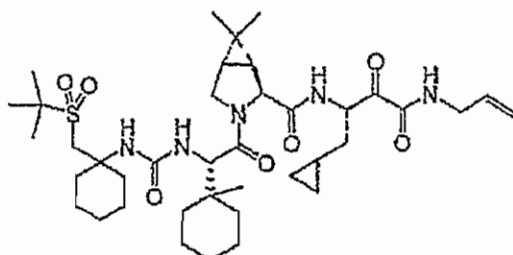


36. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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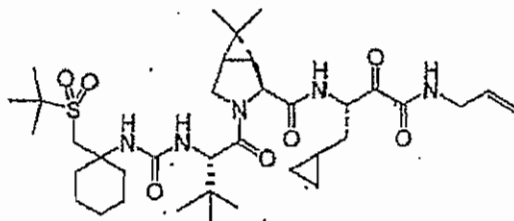


37. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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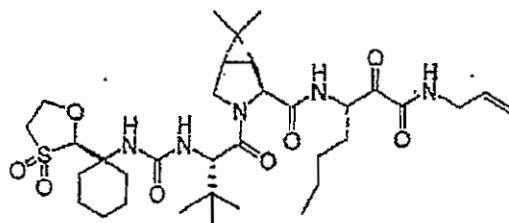


38. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tau-

tomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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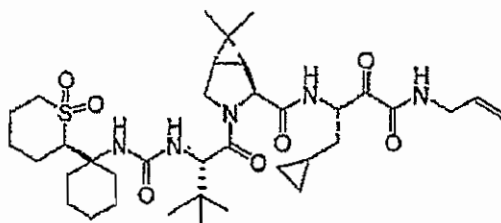


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39. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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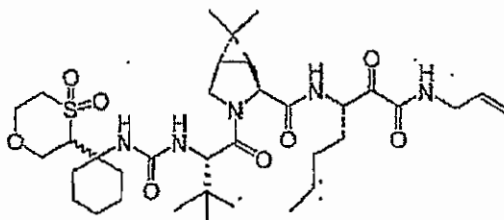


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40. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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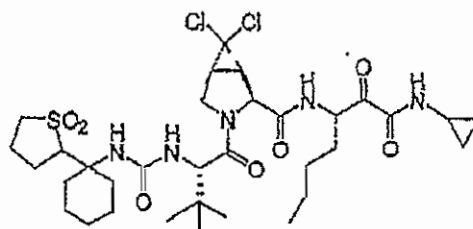


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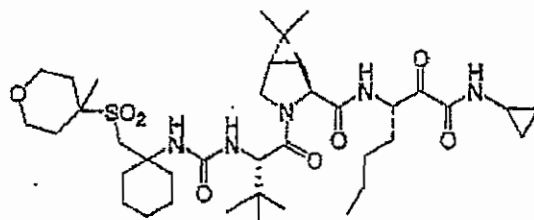
41. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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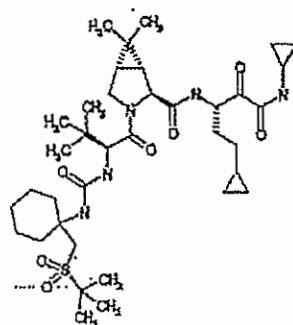
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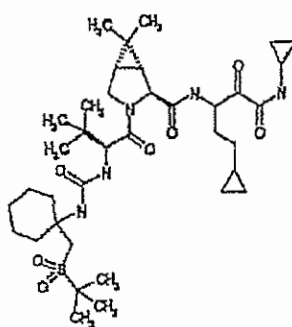
42. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:



43. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:



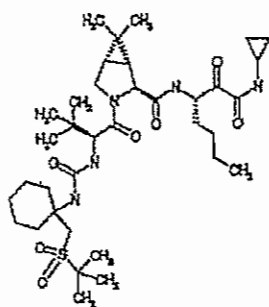
44. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:



45. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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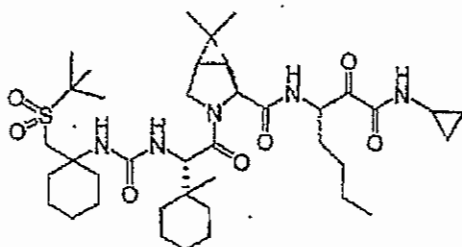
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- 15 46. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

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47. A compound of claim 1 exhibiting HCV protease inhibitory activity, or enantiomers, stereoisomers, rotamers, tautomers, and racemates of said compound, or a pharmaceutically acceptable salt or solvate of said compound, said compound having the structure:

