Office de la Propriété Intellectuelle du Canada
Un organisme d'Industrie Canada

Canadian Intellectual Property Office
An agency of Industry Canada

CA 2901471 A1 2014/10/02

(21) 2 901 471

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

(86) **Date de dépôt PCT/PCT Filing Date:** 2014/03/13
(87) **Date publication PCT/PCT Publication Date:** 2014/10/02
(85) **Entrée phase nationale/National Entry:** 2015/08/14
(86) **N° demande PCT/PCT Application No.:** US 2014/025674
(87) **N° publication PCT/PCT Publication No.:** 2014/160031
(30) **Priorité/Priority:** 2013/03/14 (US61/784,020)

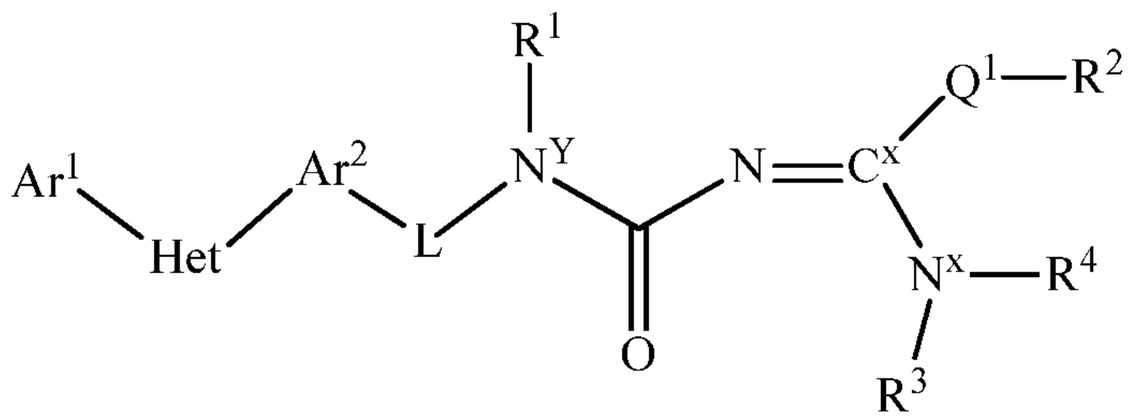
(51) **Cl.Int./Int.Cl.** ***C07D 401/00*** (2006.01),
A01N 43/647 (2006.01), ***A01P 19/00*** (2006.01),
A01P 7/00 (2006.01), ***A01P 9/00*** (2006.01),
A61K 31/4196 (2006.01)

(71) **Demandeur/Applicant:**
DOW AGROSCIENCES LCC, US

(72) **Inventeurs/Inventors:**
FISCHER, LINDSEY G., US;
BAUM, ERICH W., US;
CROUSE, GARY D., US;
DEAMICIS, CARL, US;
LORSBACH, BETH, US;
PETKUS, JEFF, US;

(54) **Titre : MOLECULES AYANT CERTAINES UTILITES PESTICIDES, ET DES INTERMEDIAIRES, DES COMPOSITIONS ET DES PROCEDES ASSOCIES A CELLES-CI**

(54) **Title: MOLECULES HAVING CERTAIN PESTICIDAL UTILITIES, AND INTERMEDIATES, COMPOSITIONS, AND PROCESSES RELATED THERETO**



(57) **Abrégé/Abstract:**
This disclosure relates to the field of molecules having pesticidal utility against pests in phyla Nematoda, Arthropoda, and/or Mollusca, processes to produce such molecules and intermediates used in such processes, compositions containing such molecules, and processes of using such molecules against such pests. These molecules may be used, for example, as nematicides, acaricides, insecticides, miticides, and/or molluscicides. This document discloses molecules having the following formula (Formula One).

CA 2901471 A1 2014/10/02

(21) **2 901 471**

(13) **A1**

(72) **Inventeurs(suite)/Inventors(continued):** SPARKS, THOMAS C., US; WHITEKER, GREGORY T., US; WARD, ANDREW L., US; ROSS, RONALD, US; HAO, YAN, US; GIAMPIETRO, NATALIE C., US

(74) **Agent:** SMART & BIGGAR

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 October 2014 (02.10.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/160031 A1

(51) **International Patent Classification**:
C07D 401/00 (2006.01) ***A01P 7/00*** (2006.01)
A61K 31/4196 (2006.01) ***A01P 9/00*** (2006.01)
A01N 43/647 (2006.01) ***A01P 19/00*** (2006.01)

(21) **International Application Number**:
PCT/US2014/025674

(22) **International Filing Date**:
13 March 2014 (13.03.2014)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
61/784,020 14 March 2013 (14.03.2013) US

(71) **Applicant**: **DOW AGROSCIENCES LLC** [US/US]; 9330 Zionsville Road, Indianapolis, IN 46268 (US).

(72) **Inventors**: **FISCHER, Lindsey G.**; 2239 Spur Point Dr, Apt H, Indianapolis, IN 46217 (US). **BAUM, Erich W.**; 772 Burr Oak Drive, Greenwood, IN 46143 (US). **CROUSE, Gary D.**; 5069 East 146th Street, Noblesville, IN 46062 (US). **DEAMICIS, Carl**; 11321 Echo Ridge Lane, Indianapolis, IN 46236 (US). **LORSBACH, Beth**; 6034 Haverford Avenue, Indianapolis, IN 46220 (US). **PETKUS, Jeff**; 12552 Geist Cove Dr., Indianapolis, IN 46236 (US). **SPARKS, Thomas C.**; 1322 Greenhills Road, Greenfield, IN 46140 (US). **WHITEKER, Gregory T.**; 337 Autumn Drive, Carmel, IN 46032 (US). **WARD, Andrew L.**; 460 Parkview Place #1, Carmel, IN 46032 (US). **ROSS, Ronald**; 445 West Hawthorne Street, Zionsville, IN 46077 (US). **HAO, Yan**; 3865 Castle Rock Drive, Zionsville, Indiana 46077 (US). **GIAMPIETRO, Natalie C.**; 3738 Dunellen Circle, Carmel, IN 46074 (US).

(74) **Agent**: **CORVIN, Carl**; Dow AgroSciences LLC, 9330 Zionsville Rd, Indianapolis, Indiana 46268 (US).

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

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

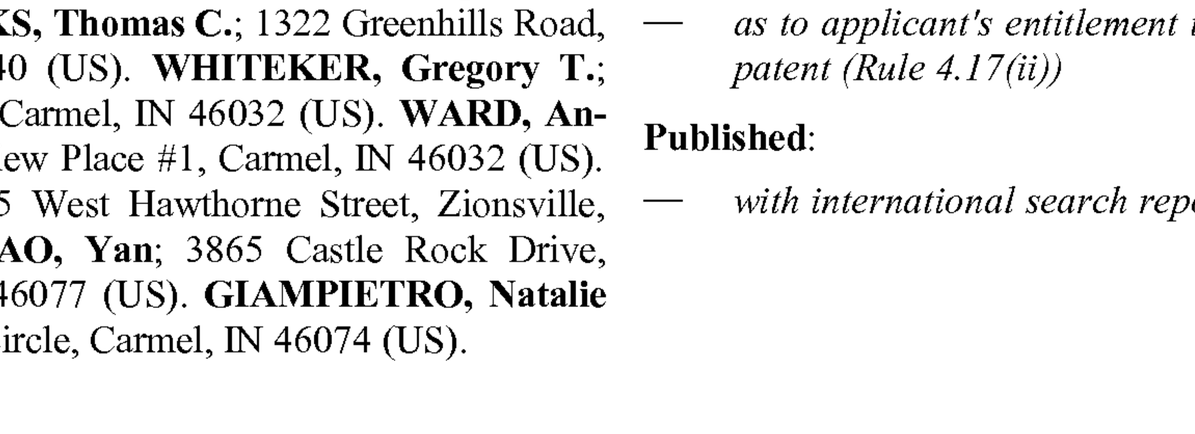
Declarations under Rule 4.17:

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

Published:

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

(54) **Title**: MOLECULES HAVING CERTAIN PESTICIDAL UTILITIES, AND INTERMEDIATES, COMPOSITIONS, AND PROCESSES RELATED THERETO



(57) **Abstract**: This disclosure relates to the field of molecules having pesticidal utility against pests in phyla Nematoda, Arthropoda, and/or Mollusca, processes to produce such molecules and intermediates used in such processes, compositions containing such molecules, and processes of using such molecules against such pests. These molecules may be used, for example, as nematicides, acaricides, insecticides, miticides, and/or molluscicides. This document discloses molecules having the following formula (Formula One).

WO 2014/160031 A1

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 503

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 503

NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

MOLECULES HAVING CERTAIN PESTICIDAL UTILITIES, AND INTERMEDIATES, COMPOSITIONS, AND PROCESSES RELATED THERETO

FIELD OF THE DISCLOSURE

This disclosure relates to the field of molecules having pesticidal utility against pests in Phyla Nematoda, Arthropoda, and Mollusca, processes to produce such molecules and intermediates used in such processes, compositions containing such molecules, and processes of using such molecules against such pests. These molecules may be used, for example, as nematicides, acaricides, insecticides, miticides, and molluscicides.

BACKGROUND OF THE DISCLOSURE

"Many of the most dangerous human diseases are transmitted by insect vectors" (Rivero, A. *et al.*, **Insect Control of Vector-Borne Diseases: When is Insect Resistance a Problem?** Public Library of Science Pathogens, 6(8) (2010)). Historically, vector-borne diseases, such as, malaria, dengue, yellow fever, plague, and louse-borne typhus, among others, were responsible for more human disease and death from the 1600's through the early 1900's than all other causes combined (Gubler D., **Resurgent Vector-Borne Diseases as a Global Health Problem**, Emerging Infectious Diseases, Vol.4, No. 3, July-September (1998)). Currently, vector-borne diseases are responsible for about 17% of the global parasitic and infectious diseases. It has been estimated that about 250 million people around the world have malaria and about 800,000 deaths occur each year - 85% of those deaths are children under the age of five. A further 250,000 to 500,000 cases of dengue hemorrhagic fever occur each year (Matthews, G., **Integrated Vector Management: controlling vectors of malaria and other insect vector borne diseases** (2011)). Vector control plays a critical role in the prevention and control of infectious diseases. However, insecticide resistance, including resistance to multiple insecticides, has arisen in all insect species that are major vectors of human diseases (Rivero, A. *et al.*).

Each year insects, plant pathogens, and weeds destroy more than 40% of all potential food production. This loss occurs despite the application of pesticides and

the use of a wide array of non-chemical controls, such as crop rotations and biological controls. If just some of this food could be saved, it could be used to feed the more than three billion people in the world who are malnourished (Pimental, D., **Pest Control in World Agriculture**, Agricultural Sciences - Vol. II (2009)).

Plant parasitic nematodes are among the most widespread pests, and are frequently one of the most insidious and costly. It has been estimated that losses attributable to nematodes are from about 9% in developed countries to about 15% in undeveloped countries. However, in the United States of America, a survey of 35 States on various crops indicated nematode-derived losses of up to 25% (Nicol, J. et al., **Current Nematode Threats to World Agriculture**, Genomic and Molecular Genetics of Plant –Nematode Interactions (Eds. Jones, J. et al.), Chapter 2, (2011)).

It is noted that gastropods (slugs and snails) are pests of less economic importance than insects or nematodes, but in certain areas, gastropods may reduce yields substantially, severely affecting the quality of harvested products, as well as transmitting human, animal, and plant diseases. While only a few dozen species of gastropods are serious regional pests, a handful of species are important pests on a world-wide scale. In particular, gastropods affect a wide variety of agricultural and horticultural crops, such as arable, pastoral, and fiber crops; vegetables; bush and tree fruits; herbs; and ornamentals (Speiser, B., **Molluscicides**, Encyclopedia of Pest Management (2002)).

Termites cause damage to all kinds of private and public structures, as well as to agricultural and forestry resources. In 2003, it was estimated that termites cause over US$20 billion in damage world-wide each year (Su, N.Y., **Overview of the global distribution and control of the Formosan subterranean termite**, *Sociobiology* 2003, 41, 177-192).

Therefore, for many reasons, including the above reasons, a need exists for new pesticides.

DEFINITIONS

The examples given in the definitions are generally non-exhaustive and must not be construed as limiting the molecules disclosed in this document. It is

understood that a substituent should comply with chemical bonding rules and steric compatibility constraints in relation to the particular molecule to which it is attached.

"**Alkenyl**" means an acyclic, unsaturated (at least one carbon-carbon double bond), branched or unbranched, substituent consisting of carbon and hydrogen, for example, vinyl, allyl, butenyl, pentenyl, and hexenyl.

"**Alkenyloxy**" means an alkenyl further consisting of a carbon-oxygen single bond, for example, allyloxy, butenyloxy, pentenyloxy, hexenyloxy.

"**Alkoxy**" means an alkyl further consisting of a carbon-oxygen single bond, for example, methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, and *tert*-butoxy.

"**Alkyl**" means an acyclic, saturated, branched or unbranched, substituent consisting of carbon and hydrogen, for example, methyl, ethyl, propyl, isopropyl, butyl, and *tert*-butyl.

"**Alkynyl**" means an acyclic, unsaturated (at least one carbon-carbon triple bond), branched or unbranched, substituent consisting of carbon and hydrogen, for example, ethynyl, propargyl, butynyl, and pentynyl.

"**Alkynyloxy**" means an alkynyl further consisting of a carbon-oxygen single bond, for example, pentynyloxy, hexynyloxy, heptynyloxy, and octynyloxy.

"**Aryl**" means a cyclic, aromatic substituent consisting of hydrogen and carbon, for example, phenyl, naphthyl, and biphenyl.

"**Cycloalkenyl**" means a monocyclic or polycyclic, unsaturated (at least one carbon-carbon double bond) substituent consisting of carbon and hydrogen, for example, cyclobutenyl, cyclopentenyl, cyclohexenyl, norbornenyl, bicyclo[2.2.2]octenyl, tetrahydronaphthyl, hexahydronaphthyl, and octahydronaphthyl.

"**Cycloalkenyloxy**" means a cycloalkenyl further consisting of a carbon-oxygen single bond, for example, cyclobutenyloxy, cyclopentenyloxy, norbornenyloxy, and bicyclo[2.2.2]octenyloxy.

"**Cycloalkyl**" means a monocyclic or polycyclic, saturated substituent consisting of carbon and hydrogen, for example, cyclopropyl, cyclobutyl, cyclopentyl, norbornyl, bicyclo[2.2.2]octyl, and decahydronaphthyl.

"**Cycloalkoxy**" means a cycloalkyl further consisting of a carbon-oxygen single bond, for example, cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, norbornyloxy, and bicyclo[2.2.2]octyloxy.

"**Halo**" means fluoro, chloro, bromo, and iodo.

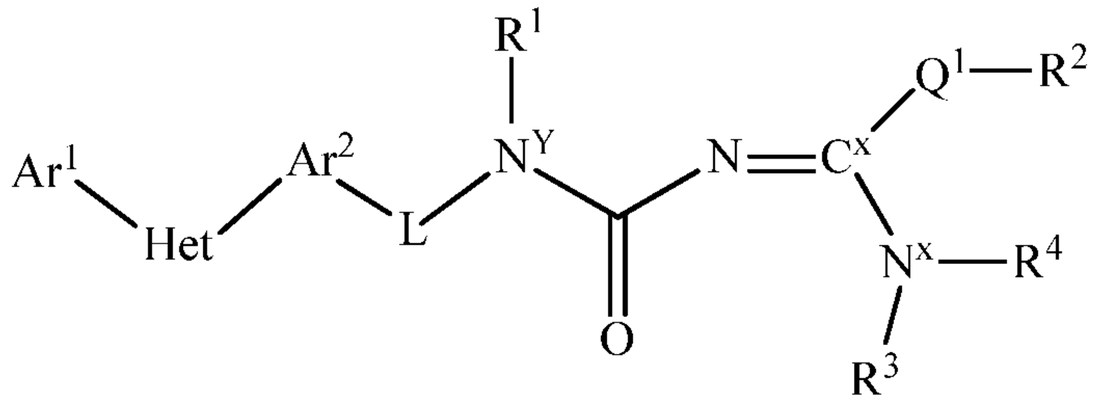
"**Haloalkoxy**" means an alkoxy further consisting of, from one to the maximum possible number of identical or different, halos, for example, fluoromethoxy, trifluoromethoxy, 2,2-difluoropropoxy, chloromethoxy, trichloromethoxy, 1,1,2,2-tetrafluoroethoxy, and pentafluoroethoxy.

"**Haloalkyl**" means an alkyl further consisting of, from one to the maximum possible number of, identical or different, halos, for example, fluoromethyl, trifluoromethyl, 2,2-difluoropropyl, chloromethyl, trichloromethyl, and 1,1,2,2-tetrafluoroethyl.

"**Heterocyclyl**" means a cyclic substituent that may be fully saturated, partially unsaturated, or fully unsaturated, where the cyclic structure contains at least one carbon and at least one heteroatom, where said heteroatom is nitrogen, sulfur, or oxygen. Examples of aromatic heterocyclyls include, but are not limited to, benzofuranyl, benzoisothiazolyl, benzoisoxazolyl, benzoxazolyl, benzothienyl, benzothiazolyl, cinnolinyl, furanyl, indazolyl, indolyl, imidazolyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, oxadiazolyl, oxazolinyl, oxazolyl, phthalazinyl, pyrazinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidinyl, pyrrolyl, quinazolinyl, quinolinyl, quinoxalinyl, tetrazolyl, thiazolinyl, thiazolyl, thienyl, triazinyl, and triazolyl. Examples of fully saturated heterocyclyls include, but are not limited to, piperazinyl, piperidinyl, morpholinyl, pyrrolidinyl, tetrahydrofuranyl, and tetrahydropyranyl. Examples of partially unsaturated heterocyclyls include, but are not limited to, 1,2,3,4-tetrahydro-quinolinyl, 4,5-dihydro-oxazolyl, 4,5-dihydro-1*H*-pyrazolyl, 4,5-dihydro-isoxazolyl, and 2,3-dihydro-[1,3,4]-oxadiazolyl.

DETAILED DESCRIPTION OF THE DISCLOSURE

This document discloses molecules having the following formula ("**Formula One**")



Formula One

wherein:

(A) Ar^1 is selected from

(1) phenyl, pyridazinyl, pyridyl, pyrimidinyl, or

(2) substituted phenyl, substituted pyridazinyl, substituted pyridyl, or substituted pyrimidinyl,

wherein said substituted phenyl, substituted pyridazinyl, substituted pyridyl, and substituted pyrimidinyl, have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6

alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, and phenoxy;

(B) Het is a 5- or 6-membered, saturated or unsaturated, heterocyclic ring, containing one or more heteroatoms independently selected from nitrogen, sulfur, or oxygen, and where Ar^1 and Ar^2 are not *ortho* to each other (but may be *meta* or *para*, such as, for a five-membered ring they are 1,3 and for a 6-membered ring they are either 1,3 or 1,4) and where said heterocyclic ring may also be substituted with one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n$(C_1-C_6 alkyl), $S(=O)_n$(C_1-C_6 haloalkyl), OSO_2(C_1-C_6 alkyl), OSO_2(C_1-C_6 haloalkyl), C(=O)NR^xR^y, (C_1-C_6 alkyl)NR^xR^y, C(=O)(C_1-C_6 alkyl), C(=O)O(C_1-C_6 alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n$(C_1-C_6 alkyl), $S(=O)_n$(C_1-C_6 haloalkyl), OSO_2(C_1-C_6 alkyl), OSO_2(C_1-C_6 haloalkyl), C(=O)H, C(=O)NR^xR^y, (C_1-C_6 alkyl)NR^xR^y, C(=O)(C_1-C_6 alkyl), C(=O)O(C_1-C_6 alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), phenyl, and phenoxy;

(C) Ar^2 is selected from

(1) phenyl, pyridazinyl, pyridyl, pyrimidinyl, or

(2) substituted phenyl, substituted pyridazinyl, substituted pyridyl, or substituted pyrimidinyl,

wherein said substituted phenyl, substituted pyridazinyl, substituted pyridyl, and substituted pyrimidinyl, have one or more substituents independently

selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, and phenoxy;

(D) R^1 is selected from H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$OC(=O)(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), and (C_1-C_6 alkyl)$OC(=O)O(C_1$-C_6 alkyl),

wherein each alkyl, cycloalkyl, cycloalkoxy, alkoxy, alkenyl, and alkynyl are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6

cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, and phenoxy;

(E) R^2 is selected from **(J)**, H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C(=O)(C_1-C_6 alkyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C_1-C_6 alkylphenyl, C_1-C_6 alkyl-O-phenyl, C(=O)(Het-1), (Het-1), (C_1-C_6 alkyl)-(Het-1), C_1-C_6 alkyl-O-C(=O)C_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)(C_1-C_6 alkyl), C_1-C_6 alkyl-O-C(=O)OC_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)NR^xR^y, C_1-C_6 alkyl C(=O)$N(R^x)C_1$-C_6 alkyl-(Het-1), C_1-C_6 alkylC(=O)(Het-1), C_1-C_6 alkylC(=O)$N(R^x)C_1$-C_6 alkyl($N(R^x)(R^y)$)(C(=O)OH), C_1-C_6 alkylC(=O)$N(R^x)C_1$-C_6 alkyl$N(R^x)(R^y)$, C_1-C_6 alkylC(=O)$N(R^x)C_1$-C_6 alkyl$N(R^x)$C(=O)-O-C_1-C_6 alkyl, C_1-C_6 alkylC(=O)$N(R^x)C_1$-C_6 alkyl($N(R^x)$C(=O)-O-C_1-C_6 alkyl)(C(=O)OH), C_1-C_6 alkylC(=O)(Het-1)C(=O)-O-C_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)-O-C_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)C_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)C_3-C_6 cycloalkyl, C_1-C_6 alkyl-O-C(=O)(Het-1), C_1-C_6 alkyl-O-C(=O)C_1-C_6 alkyl-$N(R^x)$C(=O)-O-C_1-C_6 alkyl, C_1-C_6 alkyl-NR^xR^y, (C_1-C_6 alkyl)S-(Het-1) or C_1-C_6 alkyl-O-(Het-1),

wherein each alkyl, cycloalkyl, alkenyl, alkynyl, phenyl, and (Het-1) are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, NR^xR^y, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n$(C_1-C_6 alkyl), $S(=O)_n$(C_1-C_6 haloalkyl), OSO_2(C_1-C_6 alkyl), OSO_2(C_1-C_6 haloalkyl), C(=O)H, C(=O)OH, C(=O)NR^xR^y, (C_1-C_6 alkyl)NR^xR^y, C(=O)(C_1-C_6 alkyl), C(=O)O(C_1-C_6 alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, phenoxy, $Si(C_1$-C_6 alkyl$)_3$, $S(=O)_nNR^xR^y$, or (Het-1);

(F) R^3 is selected from phenyl, C_1-C_6 alkylphenyl, C_1-C_6 alkyl-O-phenyl, C_2-C_6 alkenyl-O-phenyl, (Het-1), C_1-C_6 alkyl(Het-1), or C_1-C_6 alkyl-O-(Het-1),

wherein each alkyl, cycloalkyl, alkenyl, alkynyl, phenyl, and (Het-1) are optionally substituted with one or more substituents independently selected from F,

Cl, Br, I, CN, NO_2, NR^xR^y, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), $O(C_1$-C_6 alkyl), $S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, and (Het-1);

(G) R^4 is selected from **(J)**, H, or C_1-C_6 alkyl;

(H) Q^1 is selected from O or S,

(I) R^x and R^y are independently selected from H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), and phenyl,

wherein each alkyl, cycloalkyl, cycloalkoxy, alkoxy, alkenyl, alkynyl, phenyl, phenoxy, and (Het-1), are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, OH, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, C(=O)OH, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, halophenyl, phenoxy, and (Het-1),

or R^x and R^y together can optionally form a 5- to 7-membered saturated or unsaturated cyclic group which may contain one or more heteroatoms selected from nitrogen, sulfur, and oxygen, and where said cyclic group may be substituted with F,

Cl, Br, I, CN, oxo, thioxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), $(C_1$-C_6 alkyl)$O(C_1$-C_6 alkyl), $(C_1$-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, substituted phenyl, phenoxy, and (Het-1);

(J) R^2 and R^4 may be a 1- to 4-membered saturated or unsaturated, hydrocarbyl link, which may contain one or more heteroatoms selected from nitrogen, sulfur, and oxygen, and together with $C^x(Q^1)(N^x)$ forms a cyclic structure, wherein said hydrocarbyl link may optionally be substituted with one or more substituents independently selected from R^5, R^6, and R^7, wherein each R^5, R^6, and R^7 is selected from H, F, Cl, Br, I, CN, OH, C_1-C_6 alkyl, oxo, thioxo, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), $(C_1$-C_6 alkyl)$O(C_1$-C_6 alkyl), $(C_1$-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, substituted phenyl, phenoxy, or (Het-1);

(K) (Het-1) is a 5- or 6-membered, saturated or unsaturated, heterocyclic ring, containing one or more heteroatoms independently selected from nitrogen, sulfur or oxygen, wherein said heterocyclic ring may also be substituted with one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, $(C_1$-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6

alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy,

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n$(C_1-C_6 alkyl), $S(=O)_n$(C_1-C_6 haloalkyl), OSO_2(C_1-C_6 alkyl), OSO_2(C_1-C_6 haloalkyl), C(=O)H, C(=O)NR^xR^y, (C_1-C_6 alkyl)NR^xR^y, C(=O)(C_1-C_6 alkyl), C(=O)O(C_1-C_6 alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), phenyl, and phenoxy;

(L) L is linker selected from

(1) a saturated or unsaturated, substituted or unsubstituted, linear (C_1-C_4)hydrocarbyl linker, or

(2) a saturated or unsaturated, substituted or unsubstituted, cyclic (C_3-C_8)hydrocarbyl group linker,

wherein each of said linkers connects Ar^2 to N^Y and

wherein said substituted linear (C_1-C_4)hydrocarbyl linker and substituted cyclic (C_3-C_8)hydrocarbyl linker has one or more substituents independently selected from R^8, R^9, R^{10}, R^{11}, and R^{12}, wherein each R^8, R^9, R^{10}, R^{11}, and R^{12}, is selected from F, Cl, Br, I, CN, oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 haloalkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, C_3-C_6 halocycloalkyl, or phenyl; and

(M) n is each individually 0, 1, or 2.

In another embodiment Ar^1 is a substituted phenyl. This embodiment may be used in combination with the other embodiments of Het, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Ar^1 is a substituted phenyl that has one or more substituents selected from C_1-C_6 haloalkyl and C_1-C_6 haloalkoxy. This embodiment

may be used in combination with the other embodiments of Het, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Ar^1 is a substituted phenyl that has one or more substituents selected from CF_3, OCF_3, and OC_2F_5. This embodiment may be used in combination with the other embodiments of Het, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Het is selected from benzofuranyl, benzoisothiazolyl, benzoisoxazolyl, benzoxazolyl, benzothienyl, benzothiazolyl, cinnolinyl, furanyl, indazolyl, indolyl, imidazolyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, oxadiazolyl, oxazolinyl, oxazolyl, phthalazinyl, pyrazinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidinyl, pyrrolyl, quinazolinyl, quinolinyl, quinoxalinyl, tetrazolyl, thiazolinyl, thiazolyl, thienyl, triazinyl, triazolyl, piperazinyl, piperidinyl, morpholinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyranyl, 1,2,3,4-tetrahydro-quinolinyl, 4,5-dihydro-oxazolyl, 4,5-dihydro-1H-pyrazolyl, 4,5-dihydro-isoxazolyl, and 2,3-dihydro-[1,3,4]-oxadiazolyl.

In another embodiment Het is triazolyl. This embodiment may be used in combination with the other embodiments of Ar^1, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Het is 1,2,4 triazolyl. This embodiment may be used in combination with the other embodiments of Ar^1, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Het is oxadiazolyl. This embodiment may be used in combination with the other embodiments of Ar^1, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Het is 1,3,4 oxadiazolyl. This embodiment may be used in combination with the other embodiments of Ar^1, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Het is pyrazolyl. This embodiment may be used in combination with the other embodiments of Ar^1, Ar^2, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Ar^2 is phenyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Ar^2 is a substituted phenyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Ar^2 is a substituted phenyl that has one or more substituents selected from C_1-C_6 alkyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Ar^2 is a substituted phenyl that has one or more substituents wherein said substituent is CH_3. This embodiment may be used in combination with the other embodiments of Ar^1, Het, R^1, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^1 is H. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^2, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^2 is **(J)**, H, C_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)C_1-C_6 alkyl, C_1-C_6 alkyl-O-C(=O)N(R^xR^y), or (C_1-C_6 alkyl)S-(Het-1). This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^2 is **(J)**, H, CH_3, C_1-C_6 alkyl, $CH_2OC(=O)CH(CH_3)_2$, $CH_2OC(=O)N(H)(C(=O)OCH_2Ph)$, or CH_2S(3,4,5-trimethoxy-2-tetrahydropyran). This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^3, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^3 is substituted phenyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^3 is substituted phenyl wherein said substituted phenyl has one or more substituents selected from F, Cl, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and phenyl. This embodiment may be used in combination

with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^3 is substituted phenyl wherein said substituted phenyl has one or more substituents selected from F, CH_3, 2-$CH(CH_3)_2$, $CH(CH_3)(C_2H_5)$, OCH_3, and phenyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^3 is substituted phenyl wherein said substituted phenyl has more than one substituent and at least one pair of said substituents are not *ortho* to each other. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^3 is C_1-C_6 alkylphenyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^3 is (Het-1). This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^4, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^4 is H. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^3, Q^1, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment Q^1 is O. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^3, R^4, R^2 and R^4 hydrocarbyl links, and/or L.

In another embodiment R^2 and R^4 is a hydrocarbyl link wherein said hydrocarbyl link is substituted with oxo or C_1-C_6 alkyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^3, R^4, Q^1, and/or L.

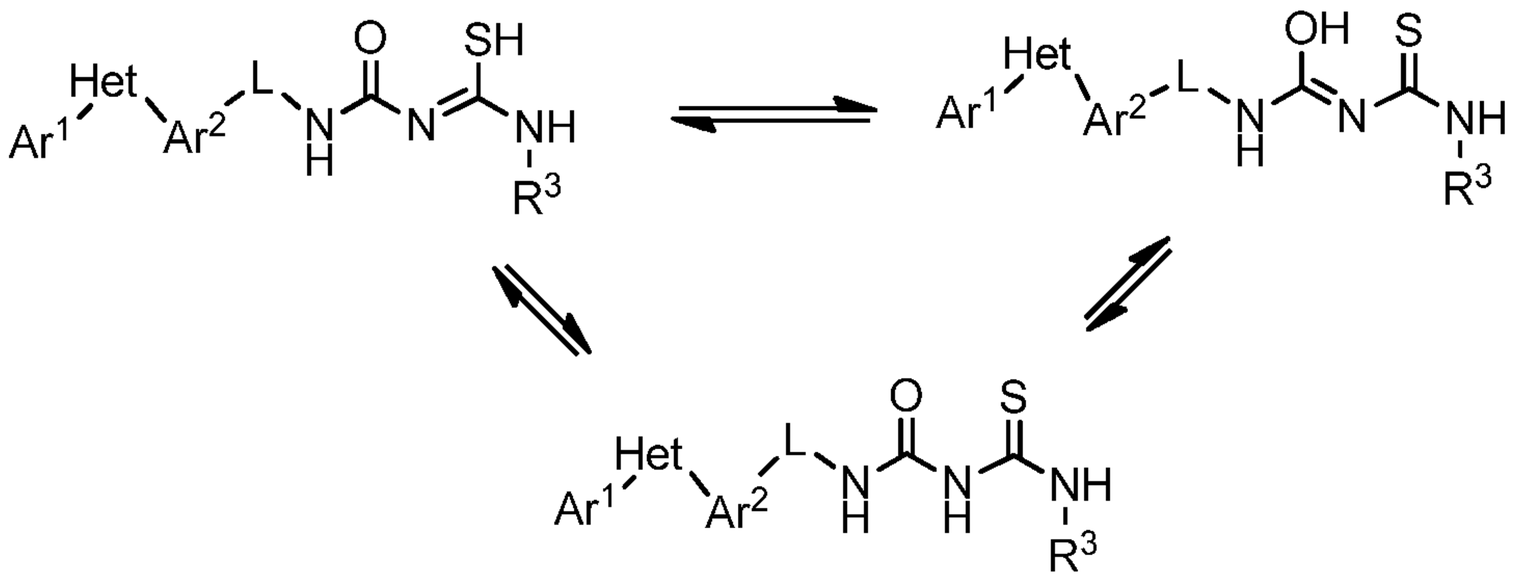
In another embodiment R^2 and R^4 is a hydrocarbyl link wherein said hydrocarbyl link is $CH_2C(=O)$, $C(C(OH)(CH_3)_2)C(=O)$, $C(cyclopropyl)C(=O)$, $C(CH_3)_2C(=O)$, $CFHC(=O)$, $CBrHC(=O)$, $CH(CH_3)C(=O)$, CH_2CH_2, $CH_2C(OH)(CH_3)$, $CH_2CH_2CH_2$, $CH_2CH_2C(=O)$, $CH_2CH(CH_3)CH_2$, $N(CH_3)C(=O)$, $N(CH_2CH_3)C(=O)$,

$CH=C(CH_3)$, or $CH_2CH(CH_3)$. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^3, R^4, Q^1, and/or L.

In another embodiment L is CH_2, CH_2CH_2, $CH_2CH(CH_3)$, $CH_2C(CH_3)_2$, $CH_2CH(CH_2CH_3)$, $CH=CH$, $CH(CH_3)CH_2$, $C(CH_3)_2CH_2$, $CHBrCH_2$, $CH_2C(cyclopropyl)$, $CH(CH_2CH_3)CH_2$, $C(CH_3)=CH$, $CH_2CH_2CH_2$, $CH(CH_3)CH(CH_3)$, $CH_2CH_2CH_2CH_2$, $C\equiv CCH_2CH_2$, cyclopropyl, or cyclohexyl. This embodiment may be used in combination with the other embodiments of Ar^1, Het, Ar^2, R^1, R^2, R^3, R^4, Q^1, and/or R^2 and R^4 hydrocarbyl links.

Many of the molecules of Formula One may be depicted in two or more tautomeric forms such as when R^1, R^2, or R^4, is H (see for example, “Scheme TAU” below). For the sake of simplifying the schemes, all molecules have been depicted as existing as a single tautomer. Any and all alternative tautomers are included within the scope of this Formula One, and no inference should be made as to whether the molecule exists as the tautomeric form in which it is drawn.

“Scheme TAU”



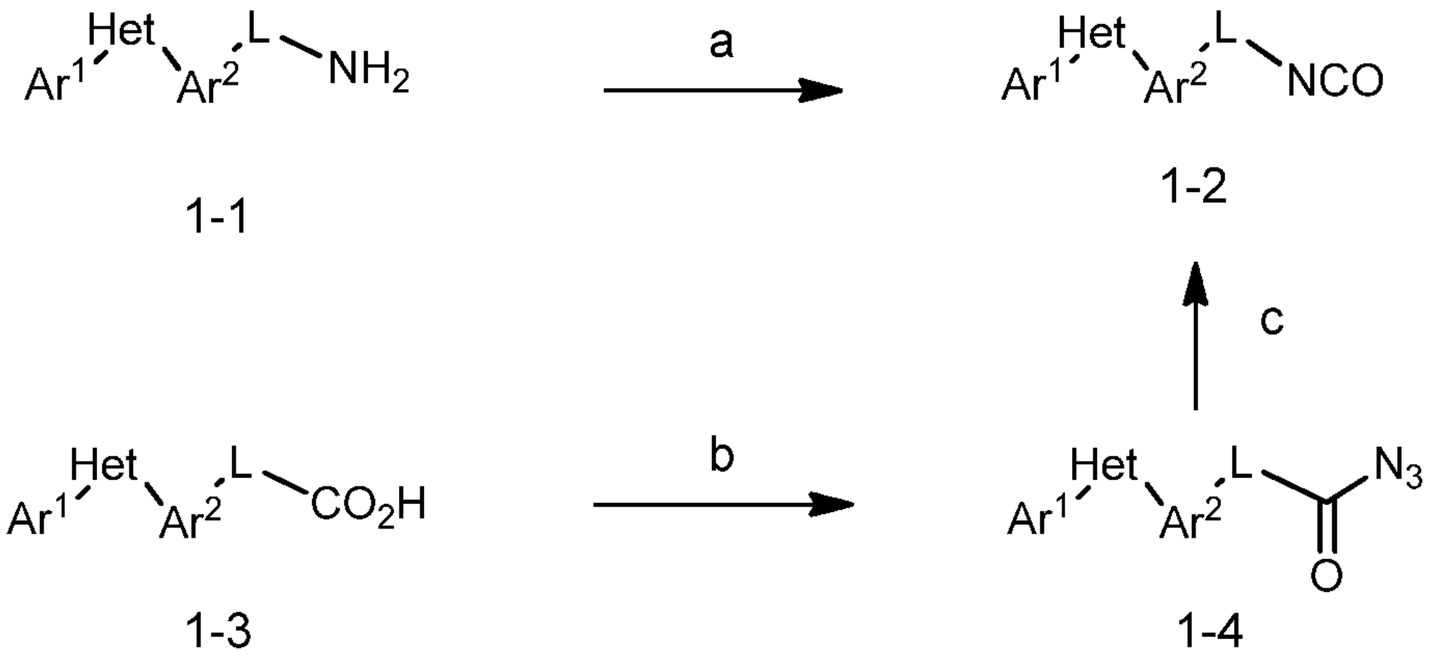
The molecules of Formula One will generally have a molecular mass of about 400 Daltons to about 1200 Daltons. However, it is generally preferred if the molecular mass is from about 300 Daltons to about 1000 Daltons, and it is even more generally preferred if the molecular mass is from about 400 Daltons to about 750 Daltons.

PREPARATION OF THIOBIURETS

Thiobiurets disclosed herein are prepared from the corresponding isocyanate, Ar^1-Het-Ar^2-L-NCO (1-2). Usually, these isocyanates are not isolated, but are instead generated *in situ* from a suitable precursor and used directly in the preparation of a

thiobiuret. One such suitable precursor is an amine (1-1) which can be converted into an isocyanate by using one of several common reagents such as phosgene, diphosgene, triphosgene, or carbonyldiimidazole (Scheme 1, step a), in a mixed solvent system such as dichloromethane and water or diethyl ether and water, in the presence of a base such as sodium bicarbonate or triethylamine, at temperatures from about -10 ºC to about 50 ºC.

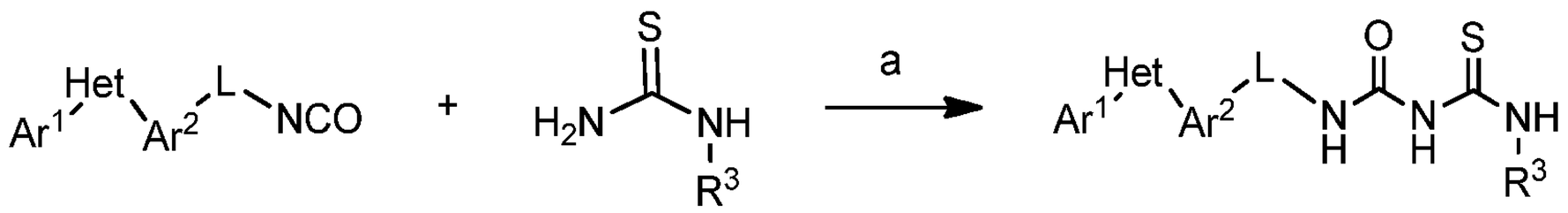
Scheme 1



Alternatively, the isocyanates may be generated *via* a Curtius rearrangement of an acyl azide, Ar^1-Het-Ar^2-L-C(O)N_3 (1-4), which is, in turn, prepared from the corresponding carboxylic acid precursor, Ar^1-Het-Ar^2-L-CO_2H (1-3). Formation of an acyl azide (Scheme 1, step b) occurs either by treatment of the acid with ethyl chloroformate and sodium azide in the presence of an amine base such as triethylamine, or with diphenylphosphoryl azide in the presence of an amine base such as triethylamine. The acyl azide is then made to undergo a Curtius rearrangement (which may need to be thermally induced), leading to the corresponding isocyanate (1-3). Depending on the nature of the particular acyl azide, this rearrangement may occur spontaneously at ambient temperature, or it may require heating from about 40 ºC to about 100 ºC in a suitable solvent, such as toluene, or acetonitrile, or an ethereal solvent such as dioxane or tetrahydrofuran. Azides of arylacetic acids are known, though frequently, due to their reactivity, they are not isolated as pure solids. Accordingly, the acyl azide intermediate is not always fully characterized, but may simply be heated directly without characterization, to generate the isocyanate.

An isocyanate, Ar^1-Het-Ar^2-L-NCO (1-2), can be treated directly with an *N*-aryl thiourea (2-1) in the presence of about 0.1 to about 2 equivalents of an inorganic base such as cesium carbonate or sodium hydride, resulting in the formation of a thiobiuret (2-2, Scheme 2). The reaction can be performed at temperatures from about 0 ºC to about 100 ºC, preferably from about 20 ºC to about 80 ºC, in an aprotic solvent or solvent mixture chosen from acetonitrile, acetone, toluene, tetrahydrofuran, 1,2-dichloroethane, dichloromethane, or mixtures thereof, but use of acetonitrile is preferred.

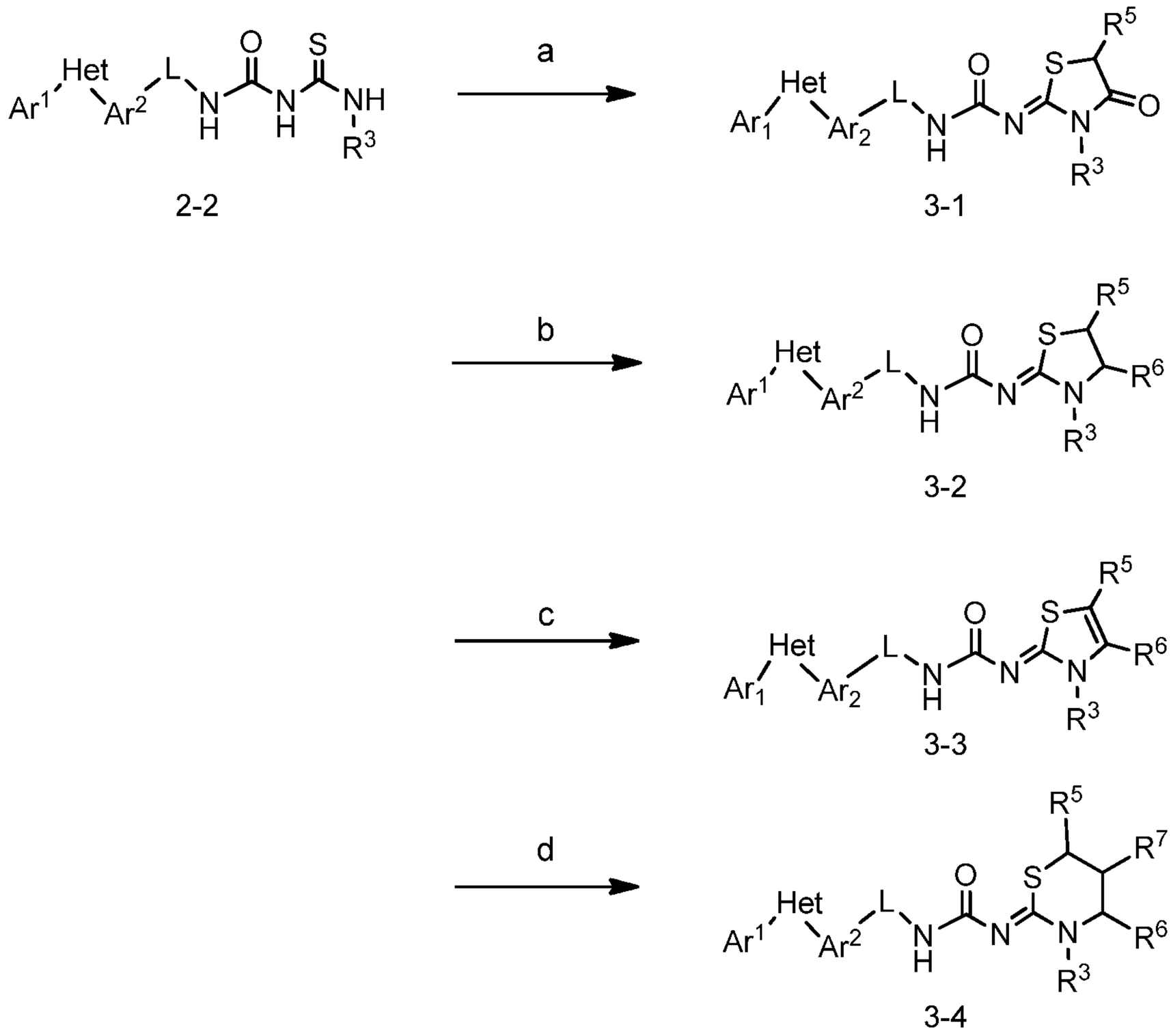
Scheme 2



1-2 2-1 2-2

Thiobiurets (2-2) generated *in situ* can be converted directly without purification into a variety of cyclized analogs (Scheme 3), or they can be isolated from the reaction medium prior to cyclization. Cyclization can be achieved by treatment with an α-halo ester such as methyl bromoacetate to form 2-imino 1,3-thiazolin-4-ones (3-1, step a) unsubstituted or mono- or di-substituted with R^5; vicinal dihalides such as 1-bromo-2-chloroethane or 1,2-dichloroethane, to form 2-imino-1,3-thiazolines (3-2, step b) unsubstituted or mono-substituted with R^5 or R^6; α-halo ketones such as chloroacetone to form 2-imino-1,3-thiazoles (3-3, step c) unsubstituted with R^5 or R^6; or 1,3-dihalopropanes such as 1-bromo-3-chloro-propane to form 2-imino-1,3-thiazinanes (3-4, step d) unsubstituted or mono-substituted with R^5 or R^6 or unsubstituted or mono- or di-substituted with R^7. With step a, use of sodium acetate in a protic solvent such as ethanol or methanol, at temperatures ranging from about 20 ºC to about 70 ºC is preferred. With step b, use of an inorganic base such as potassium carbonate in a solvent such as acetonitrile or (preferably) 2-butanone, at a temperature between about 0 ºC and about 80 ºC, is preferred.

Scheme 3

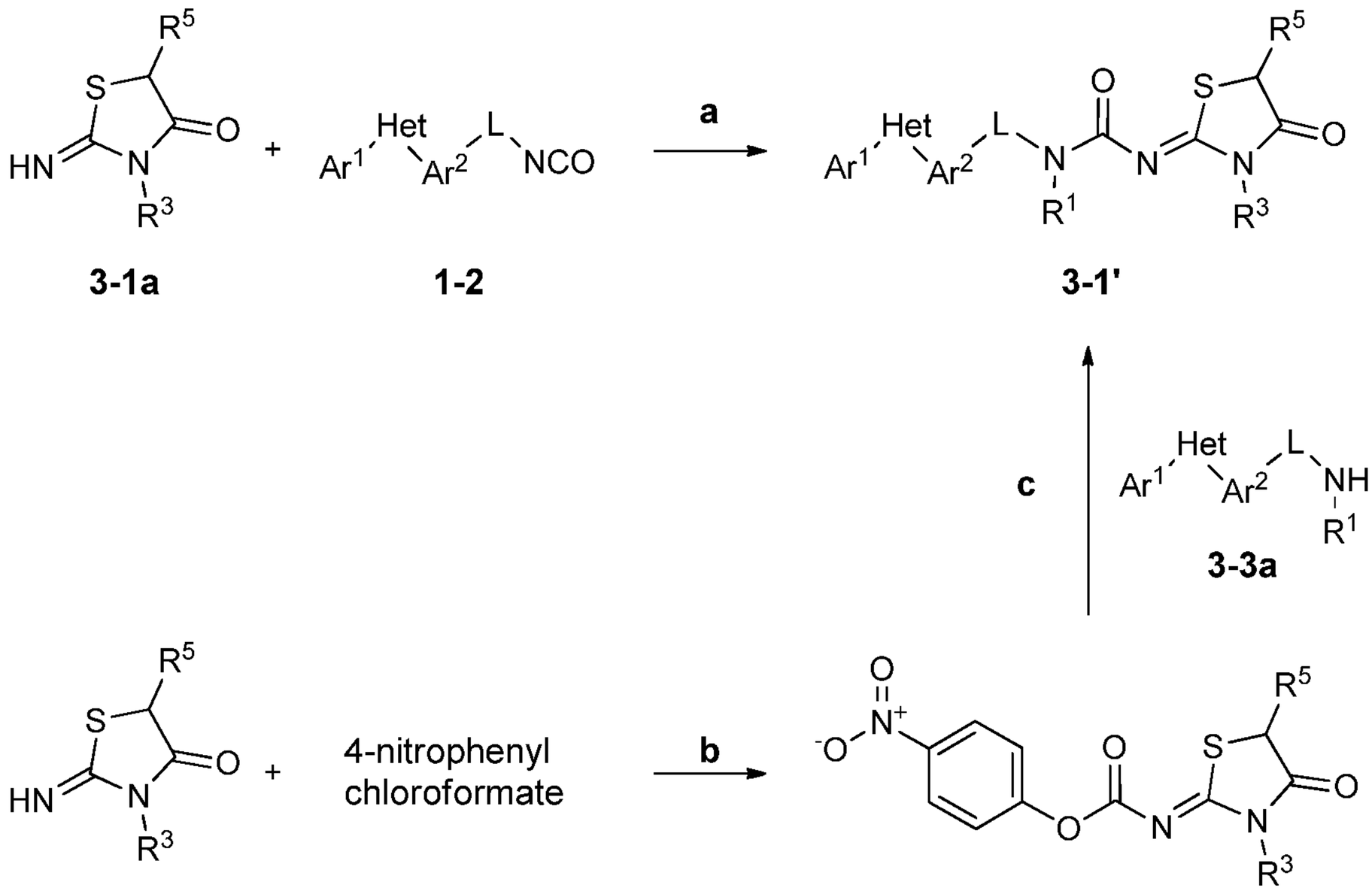


An alternative method for preparing analogs having the general structure 3-1' (Scheme 3) is described in Scheme 3a, Intermediate 2-iminolthiazolidin-4-one (3-1a, step a) is reacted directly with an isocyanate (1-2), in the presence of about 0.1 to about 2 equivalents of an inorganic base such as cesium carbonate or sodium hydride to form cyclized thiobiuret (3-1'). The reaction can be performed at temperatures from about 0 ºC to about 100 ºC, preferably from about 20 ºC to about 80 ºC, in an aprotic solvent or solvent mixture chosen from acetonitrile, acetone, toluene, tetrahydrofuran, 1,2-dichloroethane, dichloromethane, or mixtures thereof, but use of acetonitrile is preferred.

Alternatively, the 2-iminothiazolidin-2-one (3-1a) may be reacted with 4-nitrophenyl chloroformate (step b), forming a 4-nitrophenyl carbamate intermediate (3-2a). This reaction is conducted with equimolar quantities of the imine and the

chloroformate, in a polar aprotic solvent such as tetrahydrofuran or dioxane, and in the presence of from about 0.1 to about 2 equivalents of an inorganic base such as cesium carbonate or potassium carbonate, preferably at room temperature. The intermediate (3-2a) may be isolated by filtration from inorganic salts and evaporation of solvent, or it can be used directly in step c. In step c, treatment of 3-2a with a primary alkyl amine Ar_1-Het-Ar_2-L-NHR^1, wherein R^1 is H or alkyl, may generate cyclized thiobiuret (3-1'). Step c may also be conducted in the presence of an inorganic base such as cesium carbonate or potassium carbonate, from about 0.1 to about 2 equivalents, preferably about 1 to about 1.2 equivalents; it is also most conveniently run at room temperature, although it may be run at temperatures from about 0 ºC to about 100 ºC.

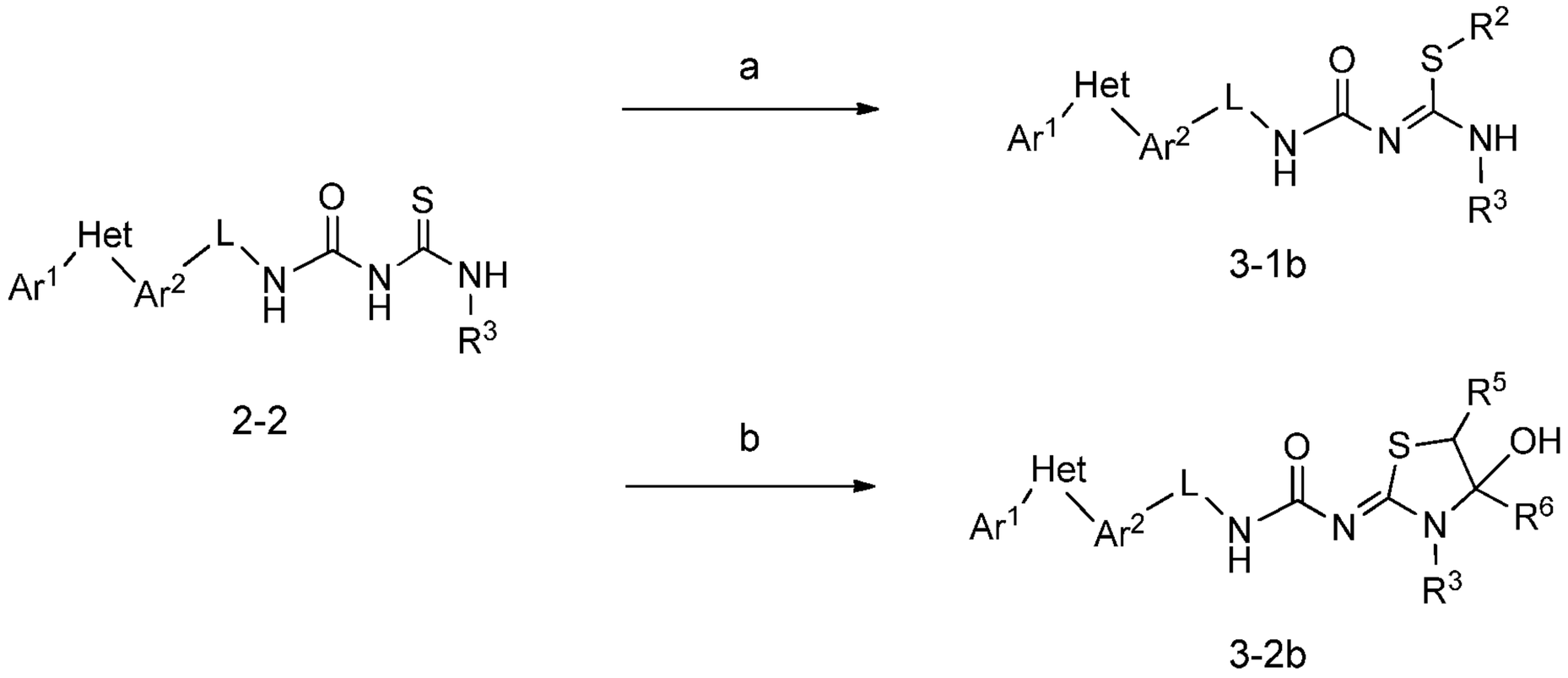
Scheme 3a



Thiobiurets (2-2) can also be converted into novel S-alkylated analogs as described in Scheme 3b. For example, reaction of a thiobiuret 2-2 with an alkyl iodide (step a), in a protic solvent such as ethanol, and in the presence of a base such as sodium acetate, at temperatures from about 0 ºC to about 60 ºC, results in

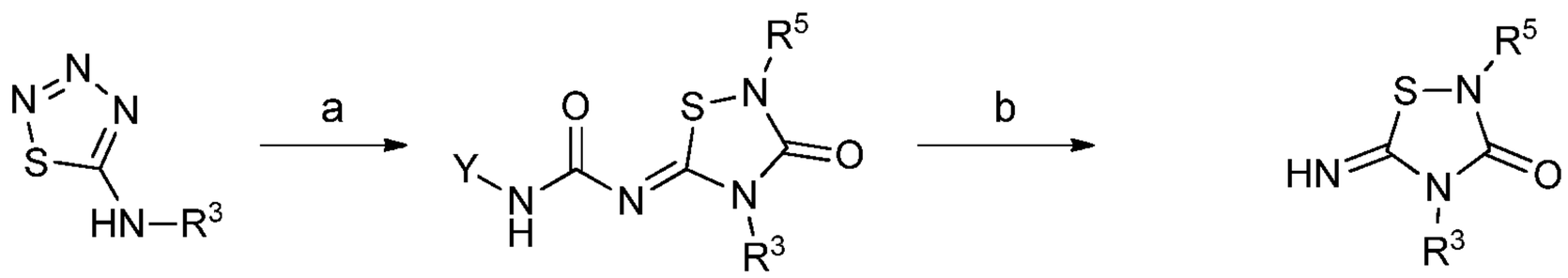
formation of an S-R^2 substituted product (3-1b). A variation of the reaction conditions described in Scheme 3, step c, employs careful control of reaction conditions to ensure that the temperature does not exceed 20 ºC. Under these conditions, 4-hydroxy-2-iminothiazolidines (3-2b, step b) may be isolated.

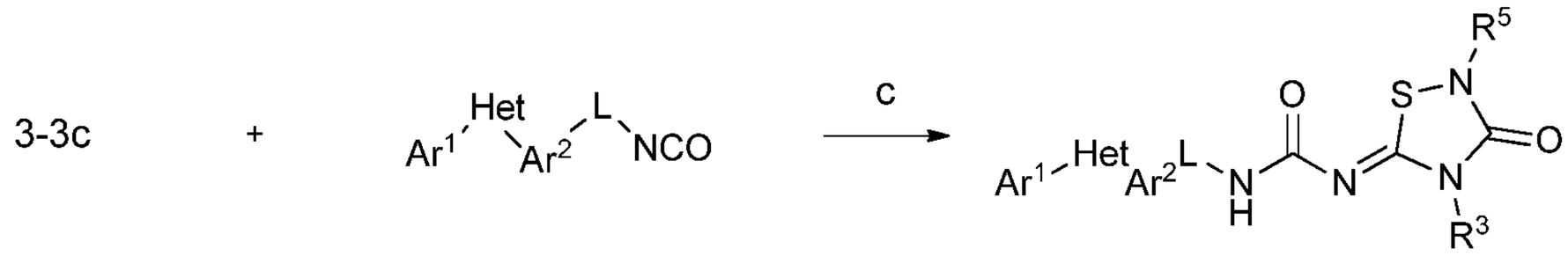
Scheme 3b



Analogs of Formula 1 wherein R^2 and R^4 are cyclized to form a 2-(R^5)-4-(R^3)-5-imino-1,2,4-thiadiazolidin-3-one (3-4c) may be constructed as described in Scheme 3c. Following the work described by Kaugers, *et al* (J. Org. Chem 1992, 57, 1671), an *N*-arylamino 1,2,3,4-thiatriazole (3-1c), prepared in one step from the corresponding N^3-aryl thiosemicarbazone by oxidation with sodium nitrite, is treated with an alkyl isocyanate to form 3-2c. Treatment of 3-2c with a base such as sodium methoxide in methanol at room temperature (step b) results in cleavage of the urea bond and formation of a 2-(R^5)-4-(R^3)--5-imino-1,2,4-thiadiazolidin-3-one (3-3c). This imine may then be treated with an isocyanate under conditions equivalent to those described in Scheme 3a, step a, to form 3-4c.

Scheme 3c





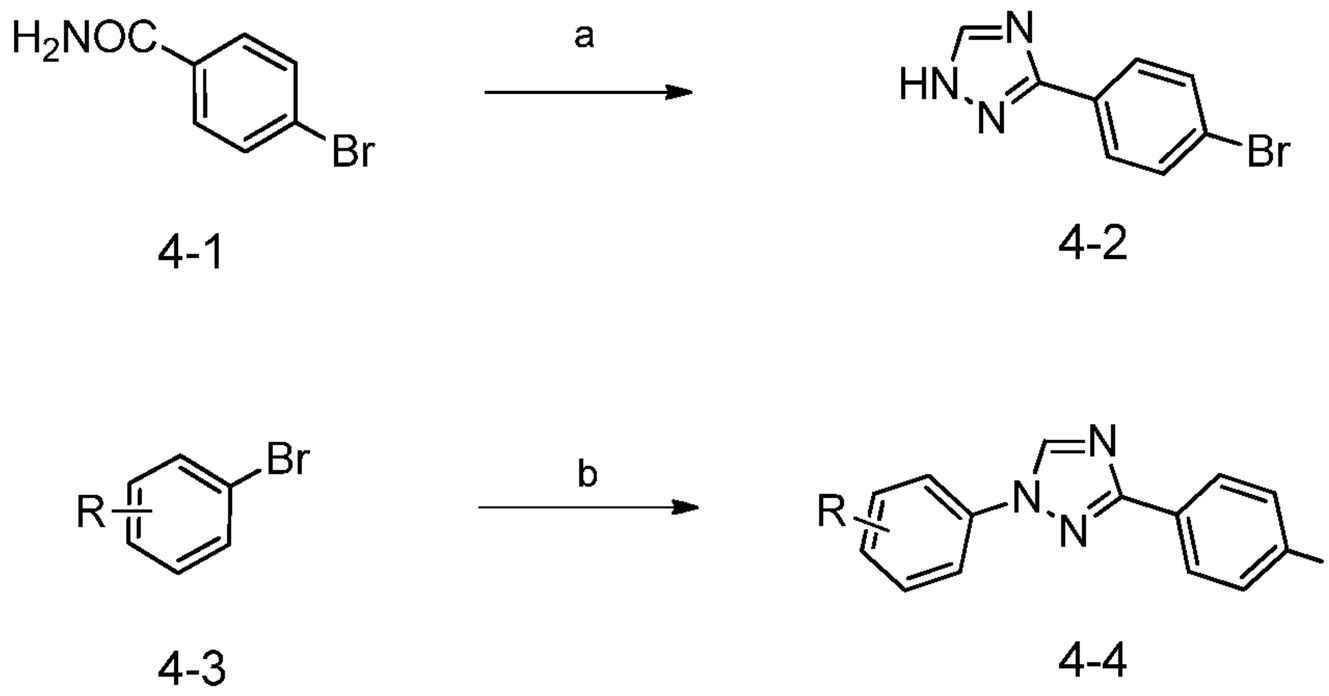
PREPARATION OF TRIARYL-INTERMEDIATES

Molecules of Formula One can be prepared by making a triaryl intermediate, Ar^1-Het-Ar^2, and then linking it to an appropriate intermediate to form a desired compound. A wide variety of triaryl intermediates can be used to prepare molecules of Formula One, provided that such triaryl intermediates contain a suitable functional group on Ar^2 to which the rest of the desired functional group can be attached. Suitable functional groups include an amino, isocyanate, carboxyl, or a halogen (preferably bromo or iodo). These triaryl intermediates can be prepared by methods previously described in the chemical literature, including Crouse, et al., WO2009102736 (the entire disclosure of which is hereby incorporated by reference).

The triaryl aldehydes used as precursors in preparation of the molecules of Formula One can be prepared according to procedures described in Crouse, et al., US 2012/0202688 A1. Some of the procedures described above require use of halo-aryl intermediates, Ar^1-Het-Ph-Br, which are novel intermediates. These may be prepared as described in Scheme 4. 3-(4-Bromophenyl)-1,2,4-triazole (4-2, step a) is prepared in two steps from 4-bromobenzamide (4-1) under conditions described previously (Crouse, et al., WO2009102736). This triazole can then be coupled to an aryl halide (R = C_1-C_6 haloalkoxy) such as 4-trifluoromethoxyphenyl bromobenzene, in the presence of cesium carbonate or potassium phosphate, in a polar aprotic solvent such as dimethylformamide. This reaction is catalyzed by a copper salt such as copper(I) iodide and a chelator such as 8-hydroxyquinoline, both present in about

0.05 to about 0.25 equivalents, at a temperature ranging between about 80 ºC and about 140 ºC, to form the 1-aryl-3-(4-bromophenyl) triazole (4-4, step b).

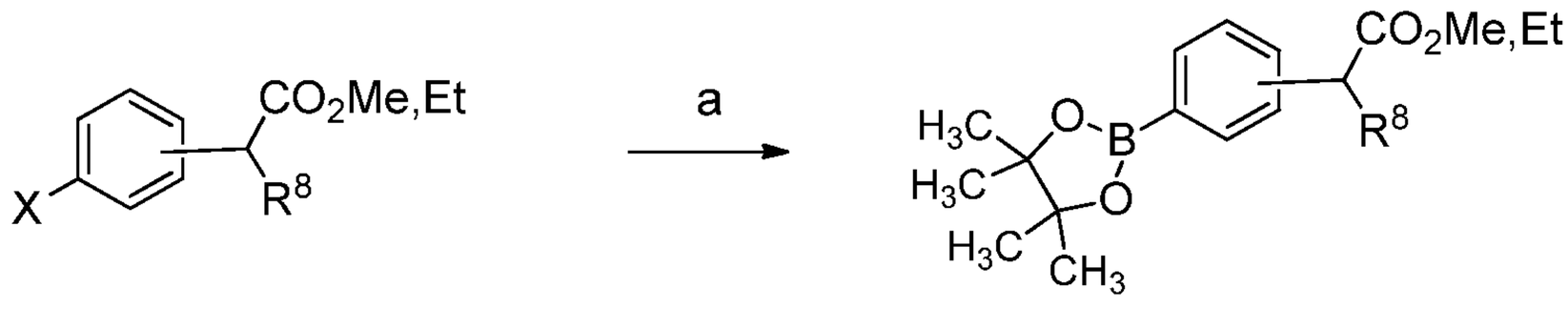
Scheme 4



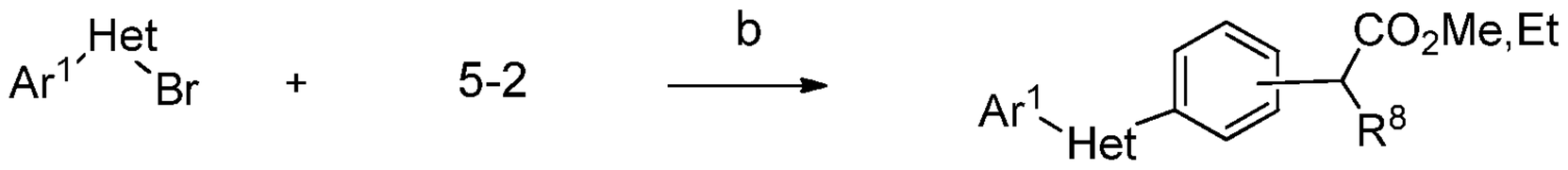
PREPARATION OF 1-ATOM LINKED INTERMEDIATES

Molecules of Formula One wherein L is a one-carbon linker, can be prepared from acid or amine intermediates described in Scheme 5 and Scheme 6, respectively. Acid precursors Ar^1-Het-Ar^2-L-CO_2H, unsubstituted or mono- or di-substituted with R^8; can be prepared as shown in the Scheme 5. Boronic esters (5-2, step a) can be prepared using Miyaura conditions from halophenyl esters (5-1). Coupling of the boronate esters with a bromo-heterocycle (5-3, step b) can be accomplished using a palladium catalyst and phosphine ligand, in the presence of a base, such as sodium bicarbonate, potassium phosphate, or cesium fluoride, in a suitable solvent system, such as dioxane/water, at temperatures from about 50 ºC to about 120 ºC to form triaryl ester intermediates (5-4, step c). Among palladium catalysts, tetrakis(triphenylphosphine) palladium(0) is preferred, although other well-known palladium catalysts may be used. Saponification of the ester may be achieved by using a strong base such as sodium hydroxide or lithium hydroxide in methanol or ethanol with or without tetrahydrofuran/water to furnish the desired carboxylic acid (5-5, step c).

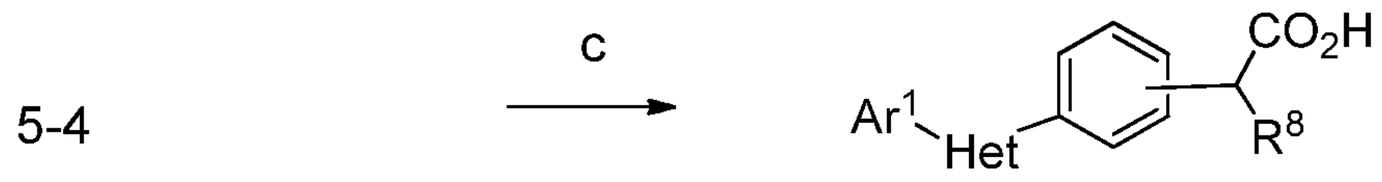
Scheme 5



5-1 5-2



5-3 5-4

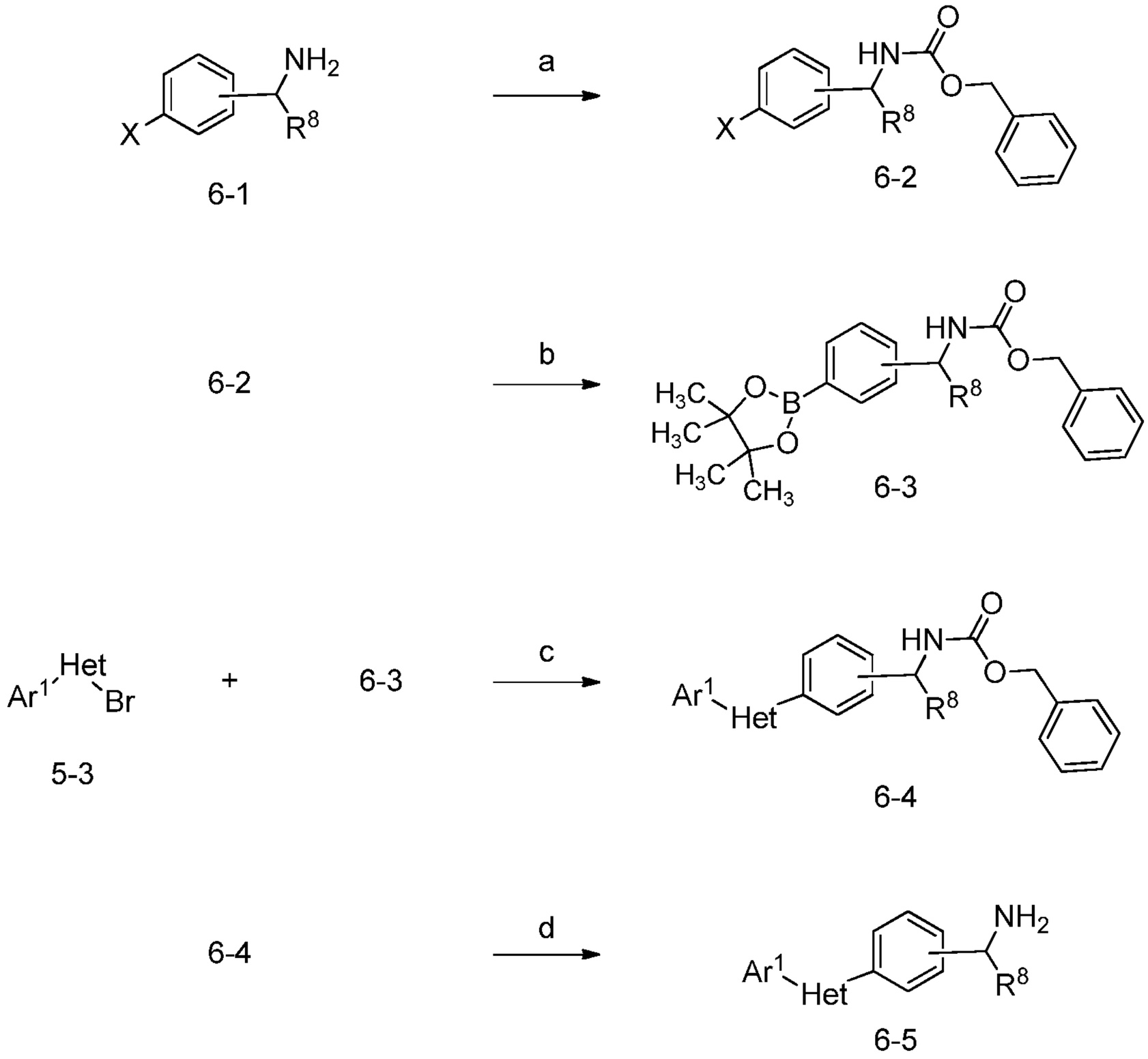


5-5

Amine precursors Ar^1-Het-Ar^2-L-NH_2, unsubstituted or mono- or di-substituted with R^8, can be prepared as shown in the Scheme 6. Halobenzyl amines (6-1) may be protected using benzyl chloroformate in the presence of a base such as triethylamine in an aprotic solvent such as dichloromethane at about -10 ºC to about 10 ºC to provide *N*-carboxybenzyl (Cbz) protected benzyl amines (6-2, step a). Alternatively, other *N*-protecting groups such as *tert*-butoxycarbonyl (BOC) or 9-fluorenylmethylcarbonyl (Fmoc) may be employed in step a using similar conditions described above for Cbz. The Cbz protected boronic ester 6-3 can be prepared using Miyaura conditions (step b). Coupling of the boronate esters with a bromo-heterocycle (5-3) can be accomplished using a palladium catalyst and phosphine ligand, in the presence of a base, such as sodium bicarbonate, potassium phosphate, or cesium fluoride, in a suitable solvent system, such as dioxane/water, at temperatures from about 50 ºC to about 120 ºC to form *N*-protected aminoalkylphenyl intermediates (6-4, step c). Deprotection of the Cbz group can be accomplished under acidic conditions with a strong acid such as hydrogen bromide, followed by free basing with a base such as sodium bicarbonate or sodium

hydroxide, to furnish the free amine precursors Ar^1-Het-Ar^2-L-NH_2 (6-5, step d). Similar methods could be applied to compounds wherein L is greater than 1–carbon.

Scheme 6



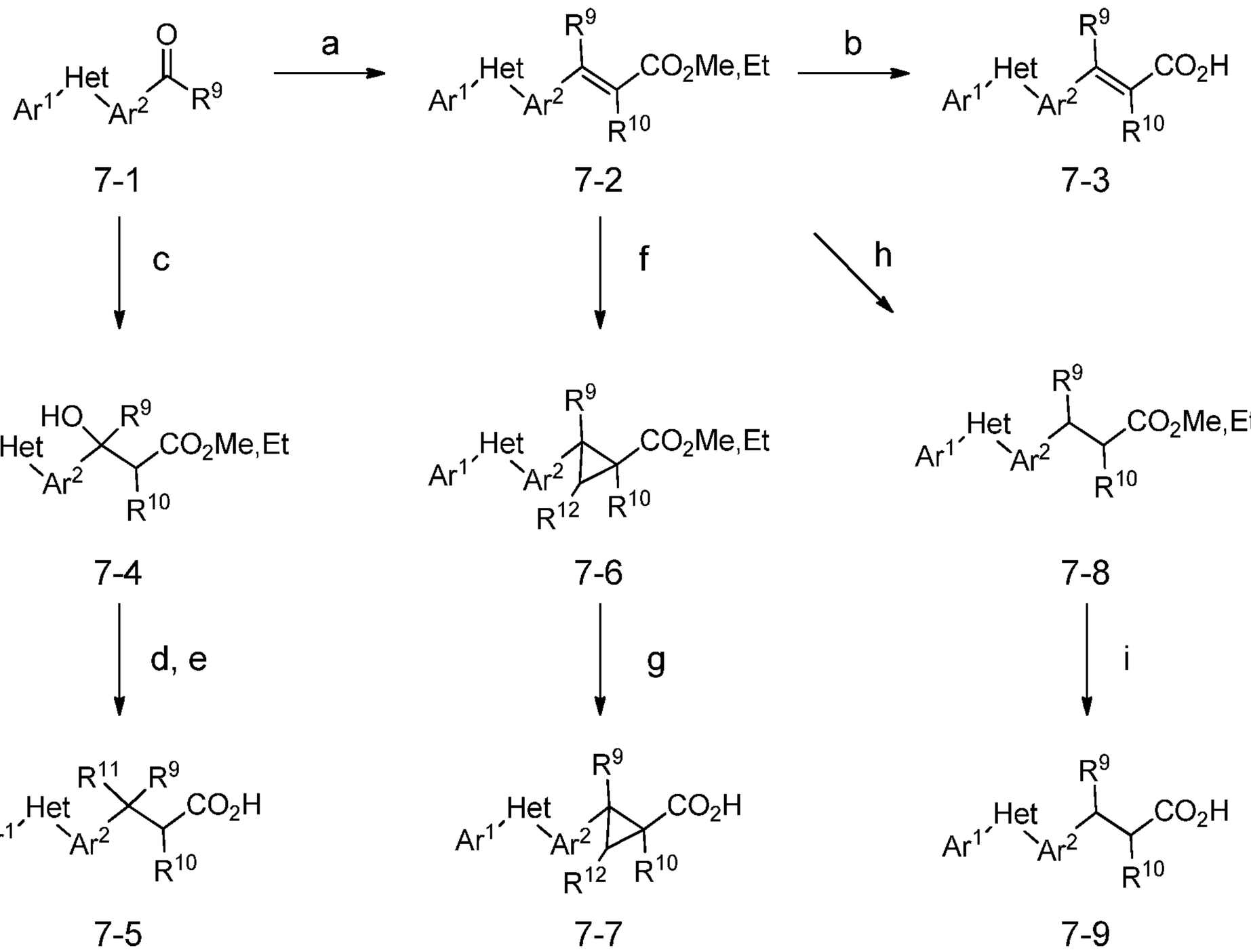
PREPARATION OF ETHYL LINKED INTERMEDIATES

Preparation of compounds wherein L is a two-atom group is described in Schemes 7 to Schemes 9. Condensation of the aldehyde (7-1, R^9 = H) (described in US 2012/0202688 A1) with reagents such as ethyl diethylphosphonoacetate or a Wittig reagent such as ethyl 2-(triphenylphosphoranylidene)propanoate) or α-substituted acetates such as ethyl 2-fluoroacetate or ethyl 2-cyanoacetate in the presence of a suitable base such as sodium hydride or *n*-butyl lithium in aprotic solvents such as tetrahydrofuran or diethyl ether at temperatures from about -78 ºC to about 20 ºC can be used to prepare acrylic esters (7-2, step a) unsubstituted or

mono-substituted with R^9 and R^{10}. Saponification of the resultant ester may be achieved by using a strong base such as sodium hydroxide in methanol or ethanol with or without tetrahydrofuran/water to furnish the vinyl carboxylic acid (7-3, step b). In some cases the partial condensation of aldehyde (7-1, R^9 = H) may result in the isolation of the alcohol intermediate (7-4, step c) especially when R^{10} is electron withdrawing. Substitution of this alcohol with nucleophilic reagents such as Deoxo-Fluor® (step d) followed by saponification as described above (step e) can generate highly substituted ethyl carboxylic acids (7-5) additionally substituted with R^{11}, wherein R^{11} is defined as R^8 above. When the saturated linkage is preferred, the acrylate ester (7-2) can be converted to the corresponding cyclopropane (7-6, step f) unsubstituted or mono- or di-substituted with R^{12}; with sulfur ylides such as those formed *in situ* from trimethyl sulfonium iodide in the presence of an inorganic base such as sodium hydride in a polar aprotic solvent such as dimethyl sulfoxide or tetrahydrofuran. Likewise the acrylate ester (7-2) can be reduced to the parent alkane (7-8, step h) using hydrogen gas and a palladium catalyst. Both the cyclopropane and the alkane can be hydrolyzed under basic conditions described above to generate the free carboxylic acids 7-7 (step g) and 7-9 (step i), respectively.

In a similar manner, condensation of the ketone (7-1, R^9 = Alkyl) (described in WO 2011017504 A1) with either ethyl diethylphosphonoacetate or a Wittig reagent such as ethyl 2-(triphenylphosphoranylidene)propanoate or α-substituted alkyl esters such as ethyl 2-fluoroacetate or ethyl 2-cyanoacetate under similar conditions described above may generate the α-alkyl acrylate esters 7-2 or alcohols 7-4. Subsequent treatment of 7-2 or 7-4 as described above for R^9 = H may lead to either the corresponding unsaturated (7-3) or saturated (7-5, 7-7, 7-9) carboxylic acids.

Scheme 7



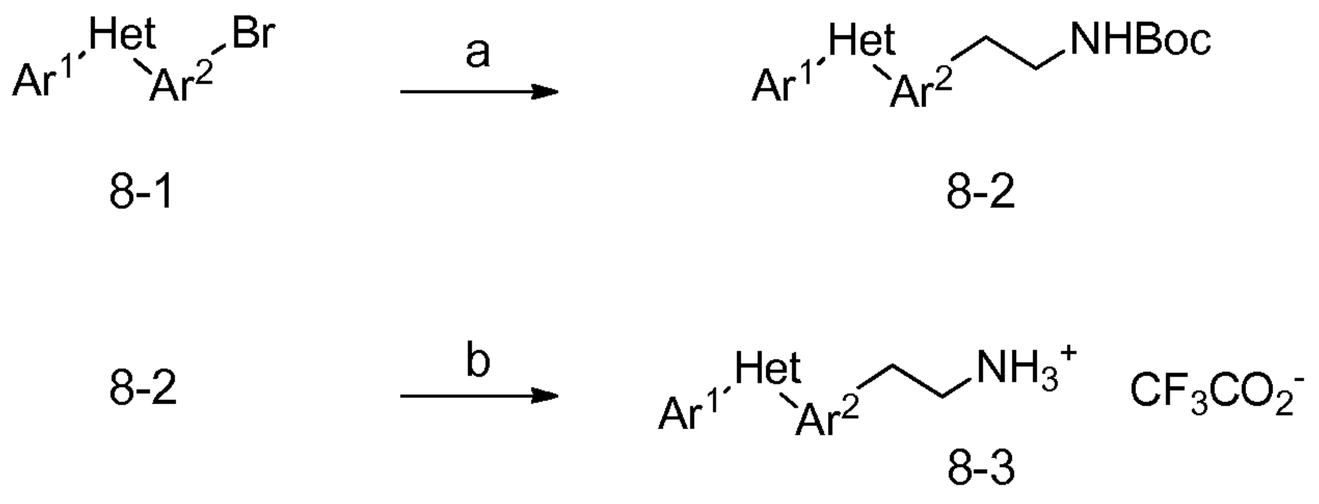
7-1 7-2 7-3

7-4 7-6 7-8

7-5 7-7 7-9

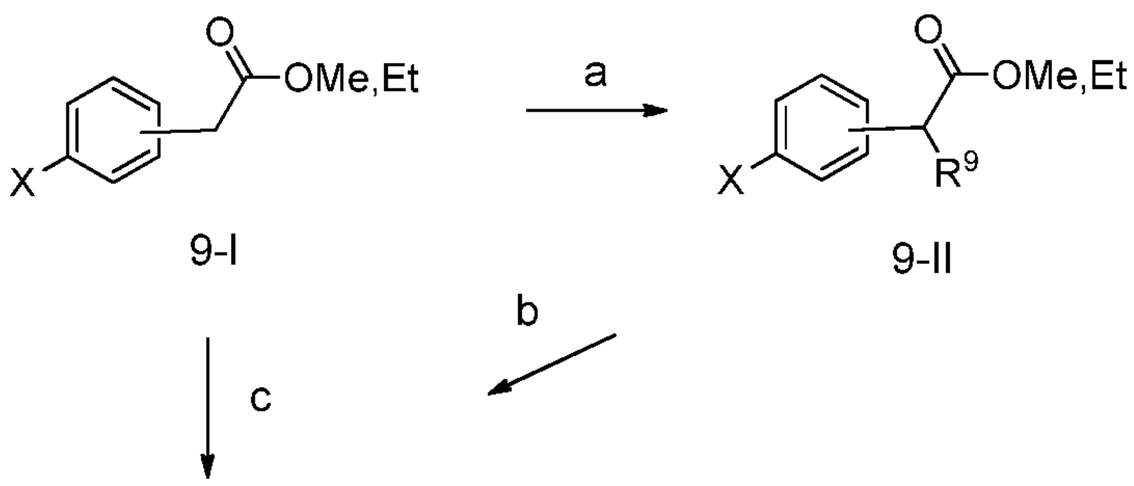
Alternatively, compounds wherein L is a 2-carbon linker may also be prepared as shown in Scheme 8. Using conditions first described by Molander et al. *Org. Lett.*, **2007**, *9* (2), pp 203–206, coupling of a bromide Ar^1-Het-Ar^2-Br (8-1, step a), with potassium (2-((*tert*-butoxycarbonyl)amino)ethyl)trifluoroborate in the presence of a palladium catalyst such as palladium(II) acetate, and a base such as cesium carbonate, at temperatures from about 80 ºC to about 120 ºC, results in the formation of the corresponding 2-(*tert*-butoxycarbonyl)amino)ethyl derivative 8-2. Further treatment of this material with from about 1 to about 5 equivalents of an acid such as trifluoroacetic acid or hydrogen chloride, in an aprotic solvent such as dichloromethane or dioxane at temperatures from about 0 ºC to about 50 ºC, results in the cleavage of the *tert*-butoxycarbonyl group and formation of the trifluoroacetic acid salt of the amine Ar^1-Het-Ar^2-L-NH_2 (8-3, step b).

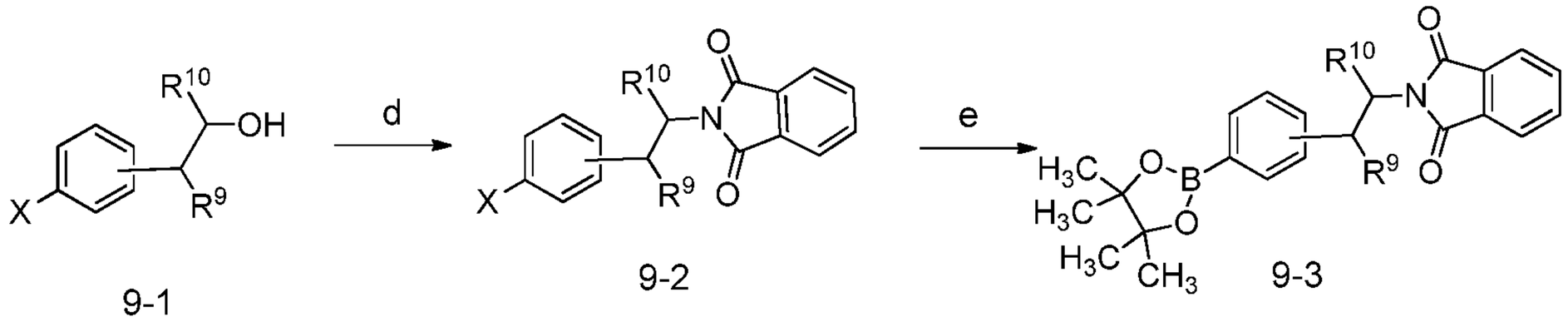
Scheme 8

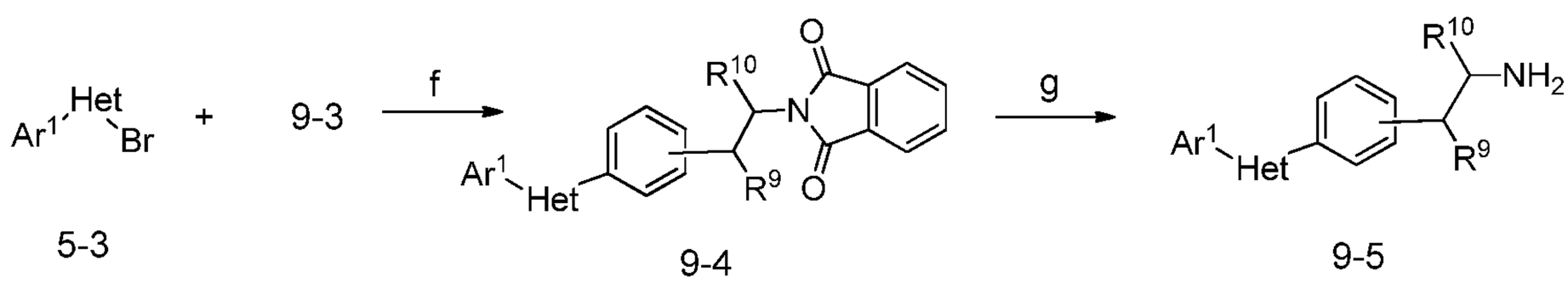


Aminoalkyl precursors Ar^1-Het-Ar^2-L-NH_2, wherein L is 2-carbon atoms, mono- or di-substituted with R^9, wherein R^9 is defined as above; and unsubstituted or mono-substituted with R^{10}, wherein R^{10} is defined as above, can be prepared as shown in Scheme 9. Halophenyl carbinols 9-1, wherein X can be selected from Cl, Br, or I, unsubstituted at R^9 and R^{10} are available commercially. Carbinols 9-1 that are mono- or di-substituted at R^9 can be prepared from the corresponding halophenyl acetate (9-I, step a) in similar fashion to that described by Shin et al. *Bioorg. Med. Chem. Lett.*, **2008**, *18*, pp 4424-4427 followed by reduction with a metal hydride such as lithium aluminum hydride in an ethereal solvent such as tetrahydrofuran or diethyl ether at temperatures at or below about 0 ºC. Both 9-I and 9-II may be further mono-substituted (step b or step c) with R^{10} *via* reduction to the corresponding aldehyde with a metal hydride such as diisobutylaluminum hydride and further treatment with a Grignard reagent in a similar fashion to that described by Brimble et al. *Org. Lett.*, **2012**, *14* (23), pp 5820-5823. Carbinols 9-1 can be treated with phthalimide under Mitsunobu conditions to generate *N*-phthalimido intermediates 9-2 (step d). The halide can be converted into a boronic ester under Miyaura conditions to form boronate esters (9-3, step e). Coupling of the boronate esters with a bromo-heterocycle can be accomplished using a palladium catalyst, such tetrakis(triphenylphosphine) palladium(0), in the presence of a base, such as sodium bicarbonate, in a suitable solvent system, such as dioxane/water, at temperatures from about 50 ºC to about 120 ºC to provide *N*-phthalimido intermediates 9-4 (step f). Deprotection using hydrazine and methanol or other suitable solvent can furnish the amine 9-5 (step g).

Scheme 9



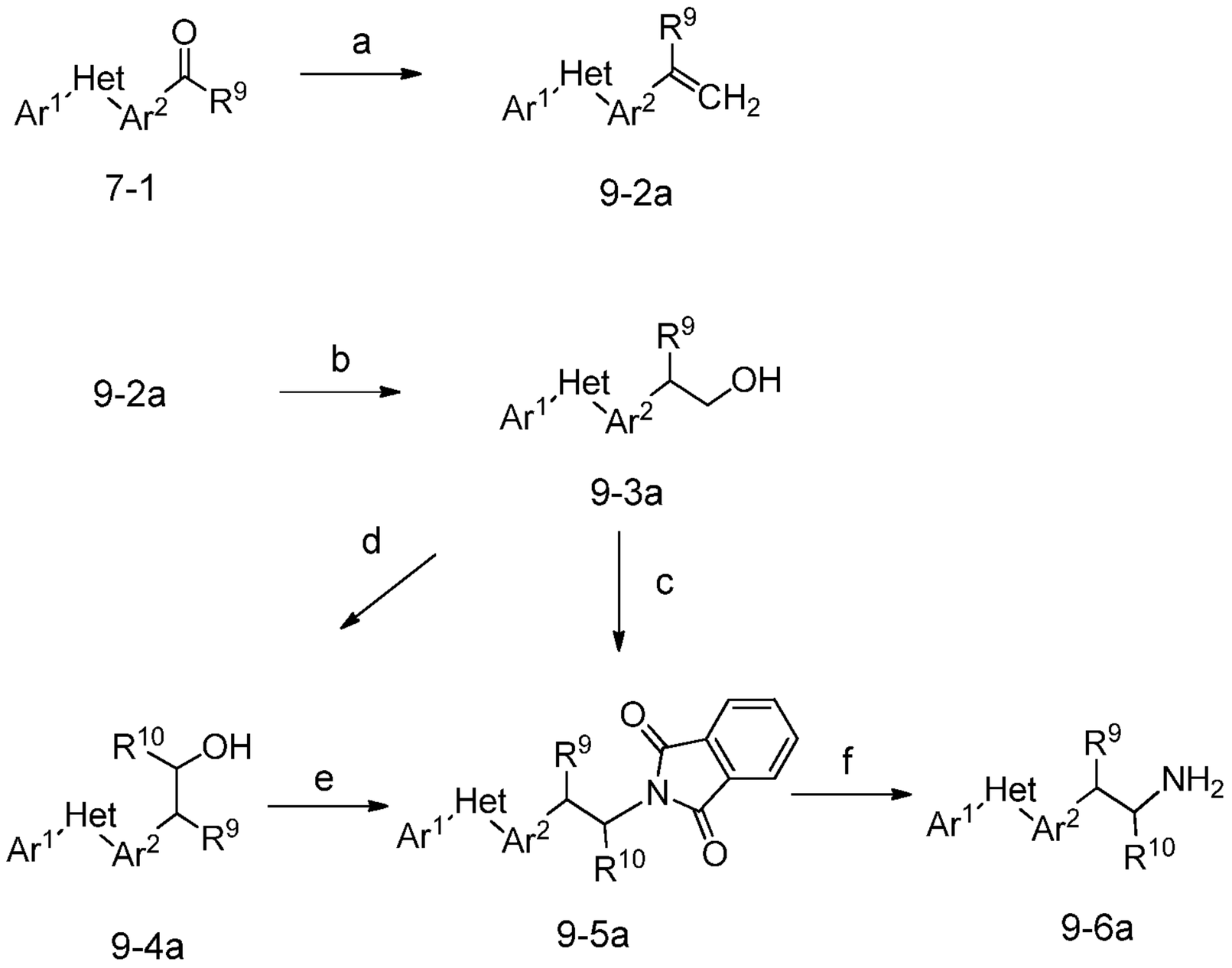




Alternatively, compounds wherein L is a 2-atom linker may also be prepared as shown in Scheme 9a. Olefination of aldehyde (7-1, R^9 = H, step a) may be achieved with methylenetriphenylphosphorane which can be prepared from methyl triphenylphosphonium iodide in the presence of a base such as sodium hydride or 1,8-diazabicycloundec-7-ene in an aprotic solvent such as tetrahydrofuran or dichloromethane at temperatures of about -78 ºC to about 40 ºC. Further treatment of this material (9-2a) with a hydroborating reagent such as 9-borabicyclo(3.3.1)nonane in an aprotic solvent such as tetrahydrofuran followed by oxidation with an oxidant such as hydrogen peroxide can generate ethyl alcohol 9-3a (step b). Carbinols 9-3a can be treated with phthalimide under Mitsunobu conditions to generate *N*-phthalimido intermediates 9-5a (step c), wherein R^{10} = H. Deprotection using hydrazine and methanol or other suitable solvent can furnish the amine 9-6a (step f). Additionally, 9-3a may be further mono-substituted (step d) with R^{10}, wherein R^{10} is defined as above, *via* oxidation to the corresponding aldehyde under Swern conditions followed by addition of a Grignard reagent such as described above (Scheme 9). Carbinols 9-4a can be further treated with phthalimide under Mitsunobu

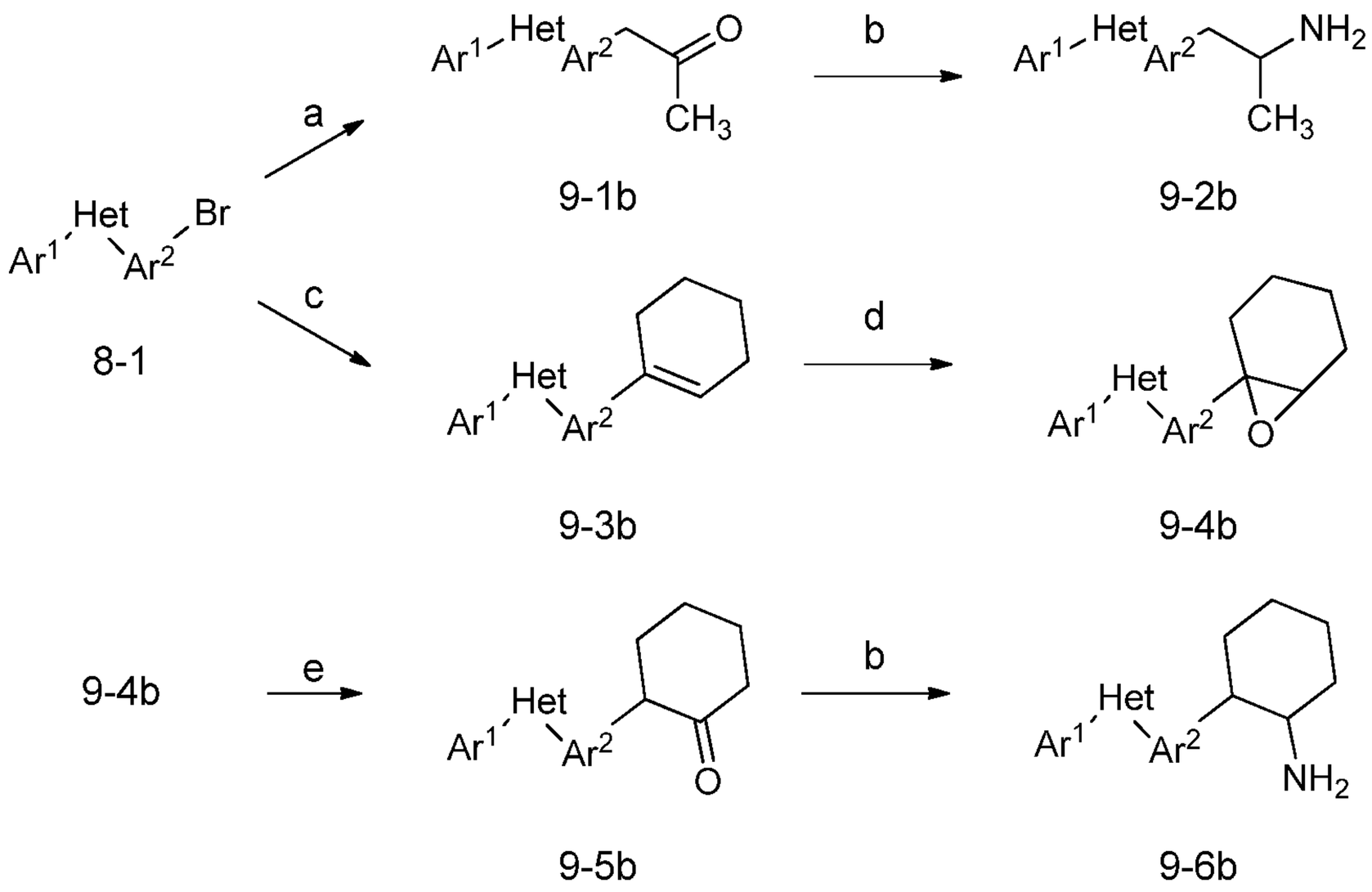
conditions to generate *N*-phthalimido intermediates 9-5a (step e). Deprotection using hydrazine and methanol or other suitable solvent can furnish the amine 9-6a (step f).

Scheme 9a



Scheme 9b outlines an alternative route for constructing analogs wherein the linker L is a two-atom linker. Copper-catalyzed arylation of 2,4-pantane-2,4-dione with 8-1 (*JACS*, **2010**, *132*, 8273.) may provide the substituted acetone intermediate 9-1b (step a). Reductive amination (step b), using any of a variety of conditions familiar to those skilled in the art, may generate amine 9-2b, which may be converted into the target molecules using conditions described previously in Scheme 2. When a linker contains a chiral center, such as with intermediate 9-2b, these intermediates may be separated into their pure isomeric forms either by means of a chiral column, or by fractional crystallization of the salt prepared from a chiral acid such as (+) and (-) tartaric acid.

Scheme 9b



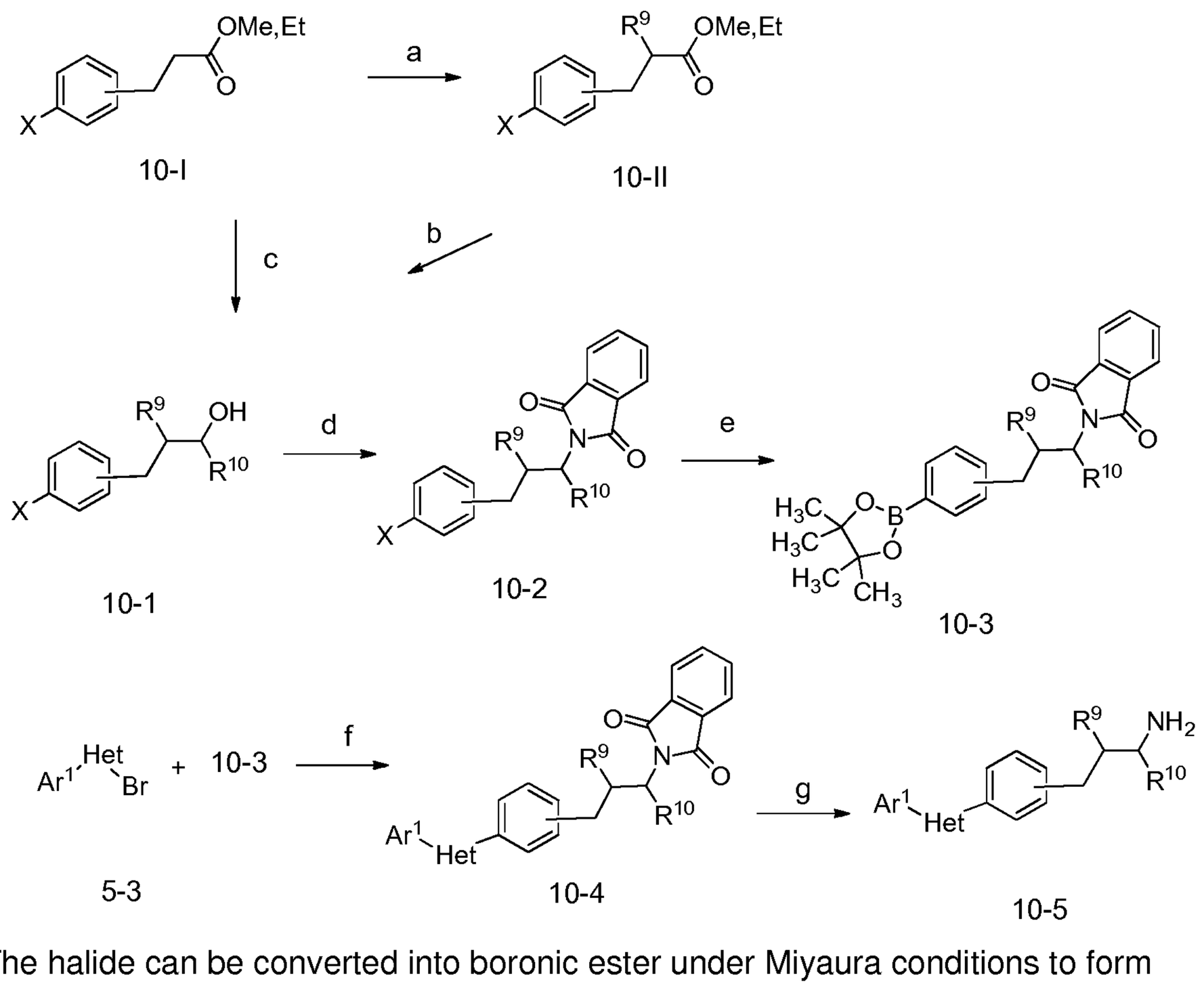
Construction of analogs wherein the ethyl linking group is part of a 6-membered ring is may also be accomplished starting from bromide 8-1. Coupling of 8-1 with 2-cyclohex-1-enyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Scheme 9b, step c) under standard Suzuki coupling conditions can lead to alkene 9-3b. Epoxidation with standard reagents, such as *meta*-chloroperoxybenzoic acid (step d), followed by acid-catalyzed rearrangement using indium trichloride (*J.Org.Chem.* **1998**, *63(23)*, 8212.) may generates ketone 9-5b. Reductive amination and conversion into the target molecules can be accomplished using conditions described above.

PREPARATION OF PROPYL LINKED INTERMEDIATES

Preparation of compounds wherein L is a three-atom group is described in Schemes 10 and 11. Aminoalkyl precursors Ar^1-Het-Ar^2-L-NH_2, wherein L is 3-carbon atoms, mono- or di-substituted with R^9, wherein R^9 is defined as above; and unsubstituted or mono-substituted with R^{10}, wherein R^{10} is defined as above; can be prepared as shown in Scheme 10. Halophenyl carbinol 10-1, wherein X is Br and R^9 and R^{10} are H, is available commercially. Carbinols 10-1 that are mono- or di-substituted at R^9 can be prepared from the corresponding halophenyl acetate (10-I, step a) in similar fashion to that described by Shin et al. *Bioorg. Med. Chem. Lett.*,

2008, *18*, pp 4424-4427, followed by reduction with a metal hydride such as lithium aluminum hydride in an ethereal solvent such as tetrahydrofuran at temperatures at or below about 0 ºC. Both 10-I and 10-II may be further mono-substituted (step b or step c) with R^{10} *via* reduction to the corresponding aldehyde with a metal hydride such as diisobutylaluminum hydride and further treatment with a Grignard reagent such as methylmagnesium bromide in a similar fashion to that described by Brimble et al. *Org. Lett.*, **2012**, *14* (23), pp 5820-5823; Carbinols 10-1 can be treated with phthalimide under Mitsunobu conditions to generate *N*-phthalimido intermediates 10-2 (step d).

Scheme 10

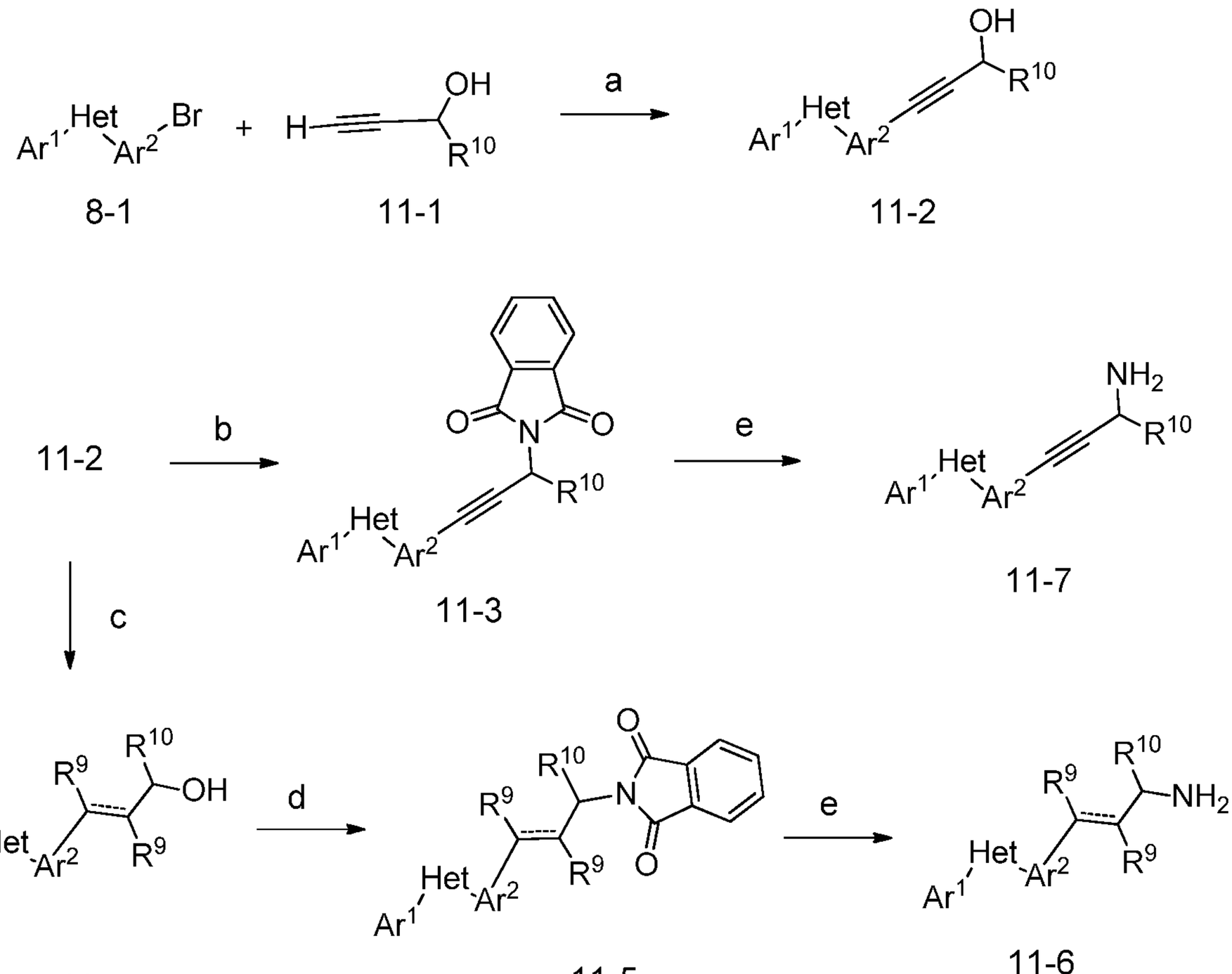


The halide can be converted into boronic ester under Miyaura conditions to form boronate esters (10-3, step e). Coupling of the boronate esters with a bromo-heterocycle can be accomplished using a palladium catalyst, such tetrakis(triphenylphosphine) palladium(0), in the presence of a base, such as sodium bicarbonate, in a suitable solvent system, such as dioxane/water, at temperatures

from about 50 ºC to about 120 ºC to provide *N*-phthalimido intermediates 10-4 (step f). Deprotection using hydrazine and methanol or other suitable solvent can furnish the amine 10-5 (step g).

Alternatively, compounds wherein L is a 3-atom linker may also be prepared as shown in Scheme 11. Bromide Ar^1-Het-Ar^2-Br (8-1) can be coupled with an appropriate alkynyl alcohol (11-1, step a) unsubstituted or mono-substituted with R^{10}, wherein R^{10} is defined as above; in the presence of a palladium catalyst such as bistriphenylphosphine dichloropalladium(II), copper(I) iodide, and a base such as triethylamine, at temperatures from about 50 ºC to about 120 ºC, to generate the corresponding alkynyl alcohol derivatives 11-2. The resultant carbinols 11-2 can be treated with phthalimide under Mitsunobu conditions to generate *N*-phthalimido intermediates 11-3 (step b) which can be converted to amine (11-7, step e) using hydrazine and methanol or other suitable solvent. Carbinols 11-2 can be reduced using a transition metal catalyst, such as palladium under an atmosphere of hydrogen to provide alkenyl or fully saturated alkyl carbinols 11-4 unsubstituted at R^{10}. Additionally, carbinols 11-2 can be treated with a metal hydride such as lithium aluminum hydride to provide the (*E*)- alkenyl carbinol 11-4. Likewise, carbinol 11-2 may be protected with a protecting group such as *tert*-butyl diphenyl silane, and treated with a hydrometallation reagent such as Schwartz' reagent followed by an electrophile quench, with, for example, elemental iodine or NBS. Alternatively, the carbinol 11-2 may be treated with a transmetallation reagent such as pinacol diboron for further use in transition metal-catalyzed coupling reactions, such as Suzuki or Negishi, to prepare carbinols 11-4 mono- or di-substituted with R^9, wherein R^9 is defined as above (step c). Following deprotection, the resultant carbinols 11-4 can be treated with phthalimide under Mitsunobu conditions to generate *N*-phthalimido intermediates 11-5 (step d) which can be converted to an amine (11-6, step e) using hydrazine and methanol or other suitable solvent.

Scheme 11

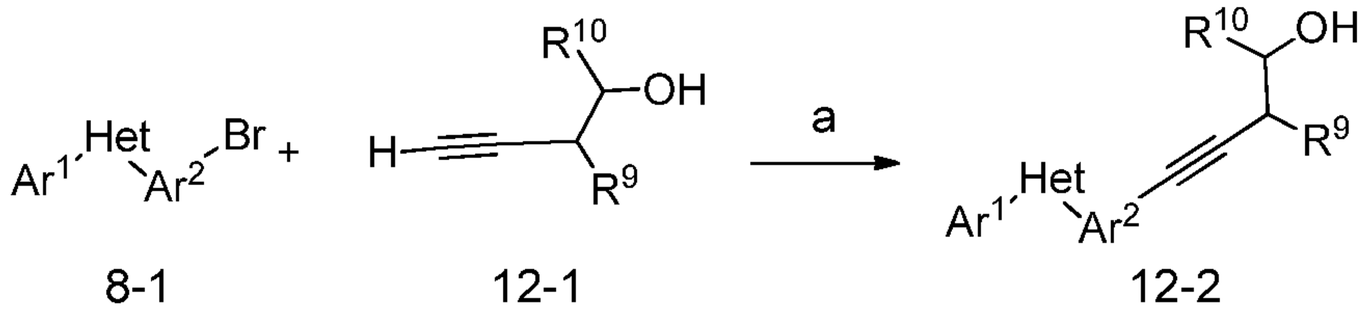


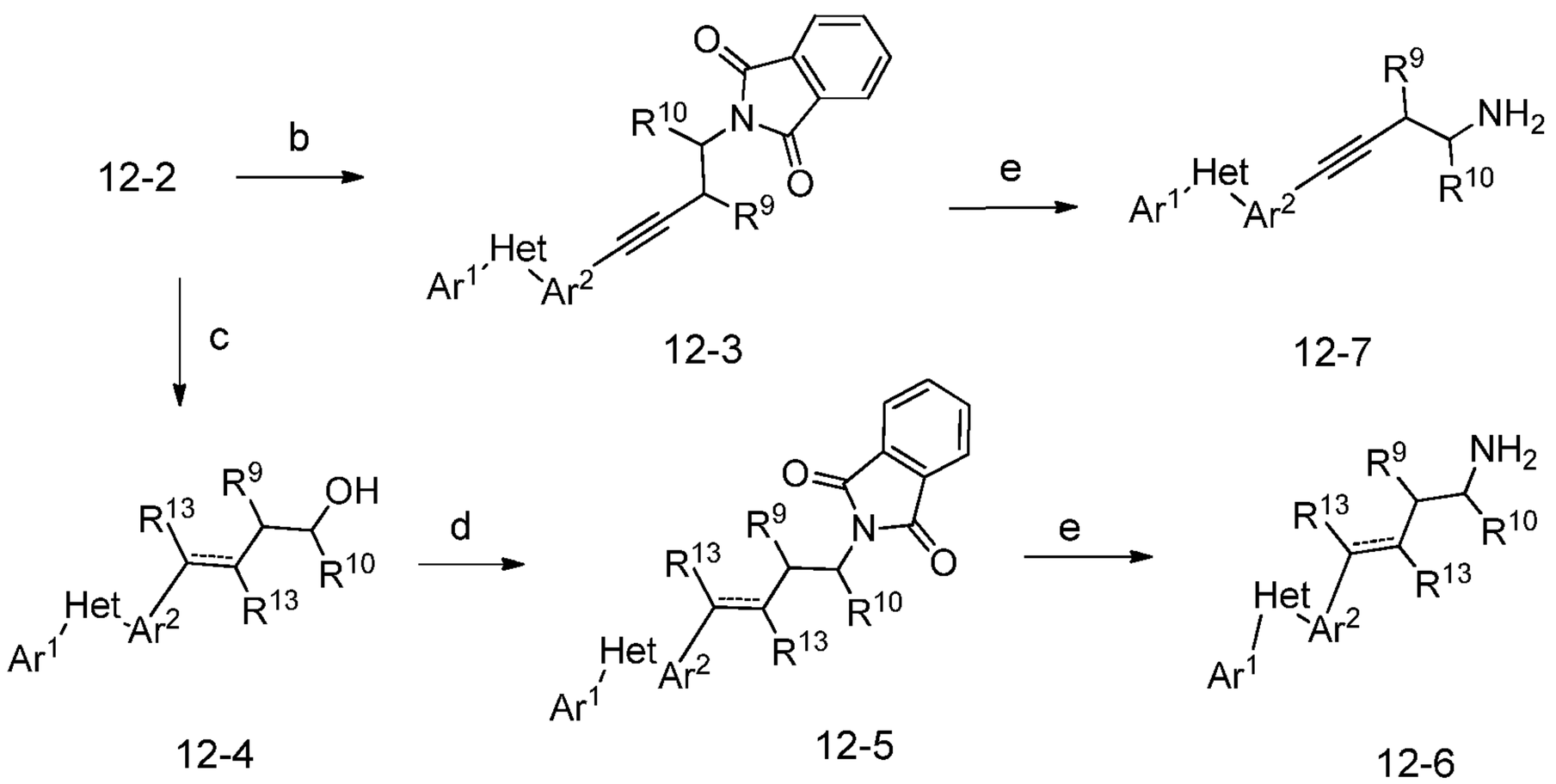
PREPARATION OF BUTYL LINKED INTERMEDIATES

Compounds wherein L is a 4-atom linker may be prepared as shown in Scheme 12. Bromide Ar^1-Het-Ar^2-Br (8-1) can be coupled with an appropriate alkynyl alcohol (12-1, step a) unsubstituted or mono-substituted with R^{10}, wherein R^{10} is defined as above; mono- or di-substituted with R^9, wherein R^9 is defined as above; in the presence of a palladium catalyst such as bistriphenylphosphine dichloropalladium, copper(I) iodide, and a base such as triethylamine, at temperatures from about 50 ºC to about 120 ºC, to generate the corresponding alkynyl alcohol derivatives 12-2. The resultant carbinols 12-2 can be treated with phthalimide under Mitsunobu conditions (step b) to generate *N*-phthalimido intermediates 12-3 which can be converted to an amine (12-7, step e) using hydrazine and methanol or other suitable solvents. Carbinols 12-2 can be reduced using a transition metal catalyst, such as palladium under an atmosphere of

hydrogen to provide alkenyl or fully saturated alkyl carbinols 12-4 (step c) unsubstituted at R^{13}. Additionally, carbinols 12-2 can be treated with a metal hydride such as lithium aluminum hydride to provide the (*E*)-alkenyl carbinols 12-4 (step c). Likewise, carbinol 12-2 may be protected with a protecting group such as *tert*-butyl diphenyl silane, and treated with a hydrometallation reagent such as Schwartz' reagent followed by an electrophile quench, with, for example, elemental iodine or NBS. Alternatively the carbinol 12-2 may be treated with a transmetallation reagent such as pinacol diboron for further use in transition metal-catalyzed coupling reactions, such as Suzuki or Negishi, to prepare carbinols 12-4 mono- or di-substituted with R^{13}, wherein R^{13} is defined as R^8 above (step c).

Scheme 12



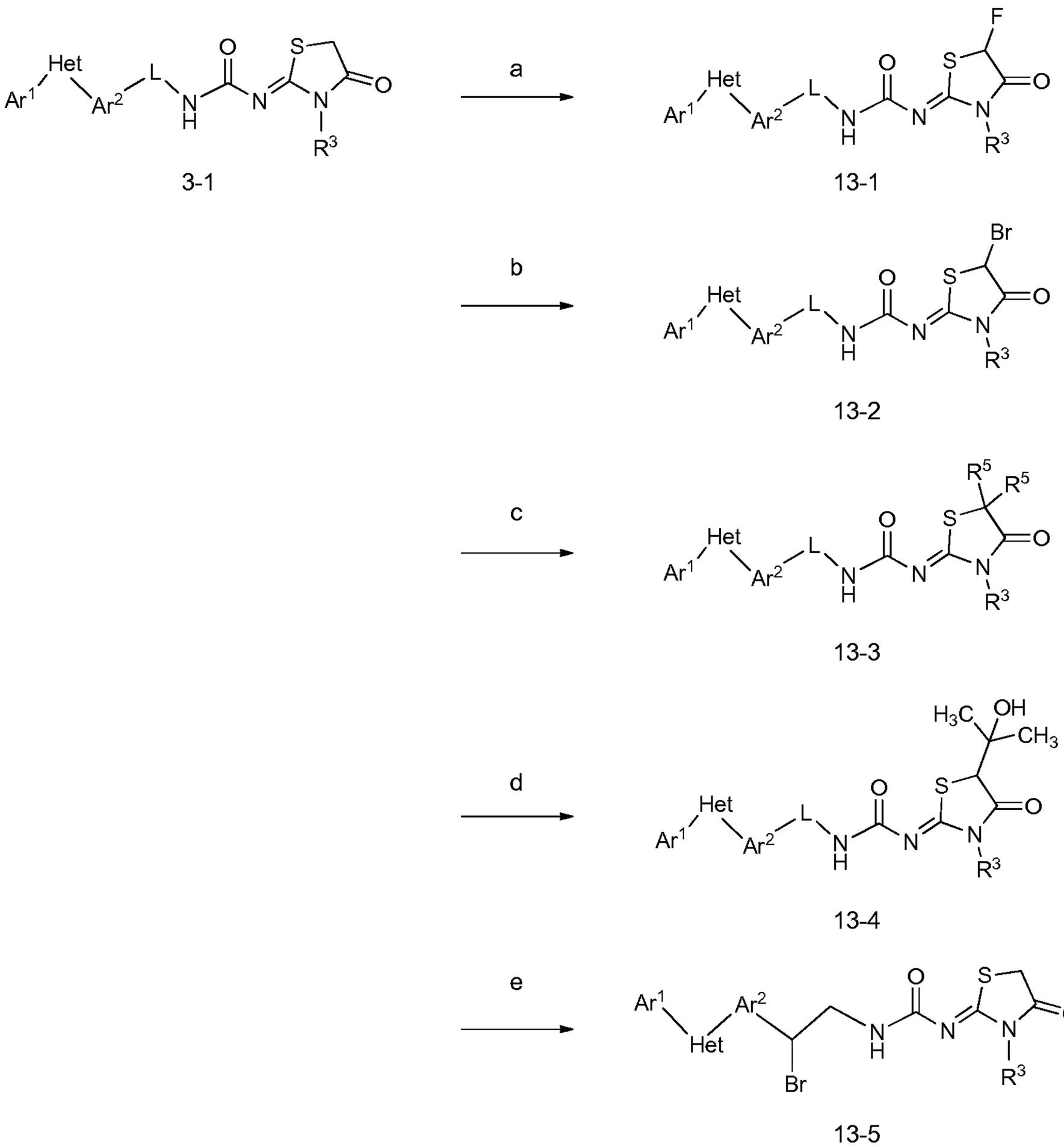


Following deprotection, the resultant carbinols 12-4 can be treated with phthalimide under Mitsunobu conditions (step d) to generate *N*-phthalimido intermediates 12-5 which can be converted to an amine (12-6, step e) using hydrazine and methanol or other suitable solvent.

PREPARATION OF SUBSTITUTED THIOBIURETS

2-Imino 1,3-thiazolin-4-ones (3-1) may be further functionalized using a variety of conditions. When treated with Selectfluor® and 9-fluorenone in anhydrous acetonitrile (*JACS*. **2013**, *135*, 17494.), molecules having the formula 3-1 may be converted into the mono-fluoro analogs (13-1).

Scheme 13



Treatment with molecular bromine in a non-protic solvent such as dichloromethane at from about 0 ºC to about 30 ºC (step b) may result in mono-bromination on the

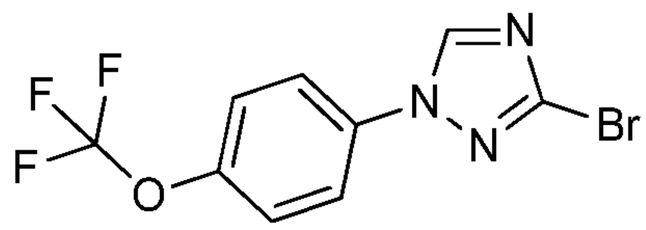
thiazolinone ring (13-2). Alkylation (step c), using at least 2 equivalents of an alkylating agent R^5-I and a strong base such as sodium hydride or lithium diisopropylamide in a polar aprotic solvent such as dimethylformamide or tetrahydrofuran may lead to a di-alkylated product (13-3). Treatment with a ketone or an aldehyde and an inorganic base such as potassium carbonate or cesium carbonate may result in the formation of a carbinol (13-4). For analogs of compounds of the formula 3-1 wherein L is a $-CH_2CH_2-$ group, free-radical bromination using *N*-bromosuccinimide and a free radical initiator such as azobis (isobutyronitrile) in carbon tetrachloride at about 30 ºC to about 77 ºC may lead to the mono-brominated product (13-5) wherein the bromine is incorporated into the ethyl linker.

EXAMPLES

These examples are for illustration purposes and are not to be construed as limiting the disclosure to only the embodiments disclosed in these examples.

Starting materials, reagents, and solvents that were obtained from commercial sources were used without further purification. Anhydrous solvents were purchased as Sure/Seal™ from Aldrich and were used as received. Melting points were obtained on a Thomas Hoover Unimelt capillary melting point apparatus or an OptiMelt Automated Melting Point System from Stanford Research Systems and are uncorrected. Examples using “room temperature” were conducted in climate controlled laboratories with temperatures ranging from about 20 °C to about 24 °C. Molecules are given their known names, named according to naming programs within ISIS Draw, ChemDraw or ACD Name Pro. If such programs are unable to name a molecule, the molecule is named using conventional naming rules. ^{1}H NMR spectral data are in ppm (δ) and were recorded at 300, 400 or 600 MHz, and ^{13}C NMR spectral data are in ppm (δ) and were recorded at 75, 100 or 150 MHz, unless otherwise stated.

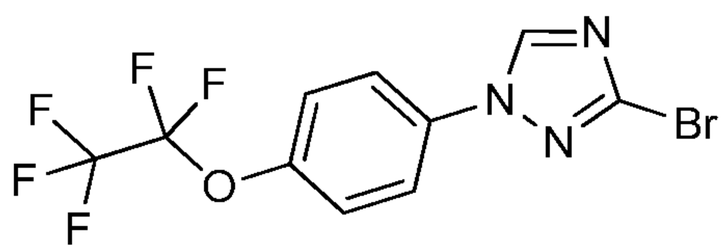
Example 1: Preparation of 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (C1)



To a 100 mL round bottomed flask, equipped with a stir bar, was added copper(I) iodide (0.397 g, 2.08 mmol), 3-bromo-1*H*-1,2,4-triazole (4.62 g, 31.2 mmol), and cesium carbonate (6.79 g, 20.83 mmol), as solids. These solids were diluted with anhydrous dimethyl sulfoxide (34.7 mL). Then 1-iodo-4-(trifluoromethoxy)benzene (1.65 mL, 10.4 mmol) was added as a liquid. The flask was placed under nitrogen atmosphere, and the suspension was heated to an internal temperature of 100 °C for 20 hours. The reaction mixture was allowed to cool to room temperature and filtered through a pad of Celite®, washing with excess ethyl acetate (200 mL). The filtrate was poured into a brine solution (200 mL), and the layers were partitioned. The aqueous phase was extracted with additional ethyl acetate (2 x 100 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* flash column chromatography using 10-50% ethyl acetate/hexanes as eluent to afford the title compound as a white solid (1.80 g, 54%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.35 (s, 1H), 7.97 (d, J = 8.9 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.06; ESIMS *m/z* 308, 310 ([M+H]$^+$).

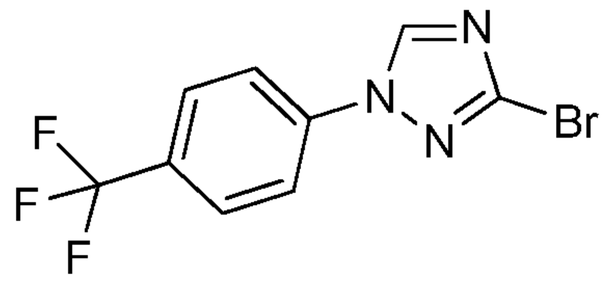
The following compounds were prepared in accordance to the procedure in Example 1.

Preparation of 3-bromo-1-(4-(pentafluoroethoxy)phenyl)-1*H*-1,2,4-triazole (C1a)



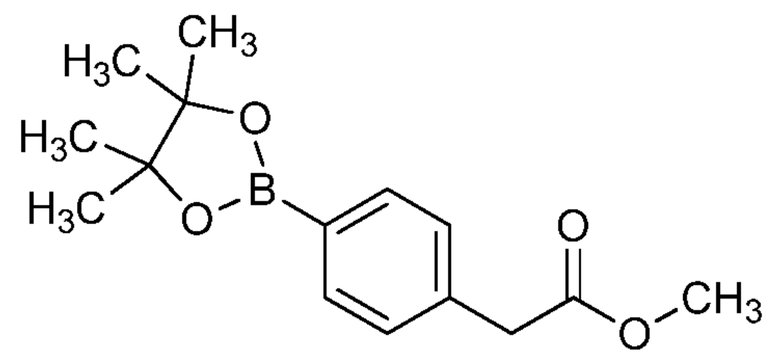
The title compound was prepared as described in Example 1 using 1-iodo-4-pentafluoroethoxybenzene and isolated as a white solid (1.60 g, 31%): mp 72–74 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.75 - 7.68 (m, 2H), 7.42 - 7.36 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.94, -87.92; ESIMS *m/z* 357, 359 ([M+H]$^+$).

Preparation of 3-bromo-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (C1b)



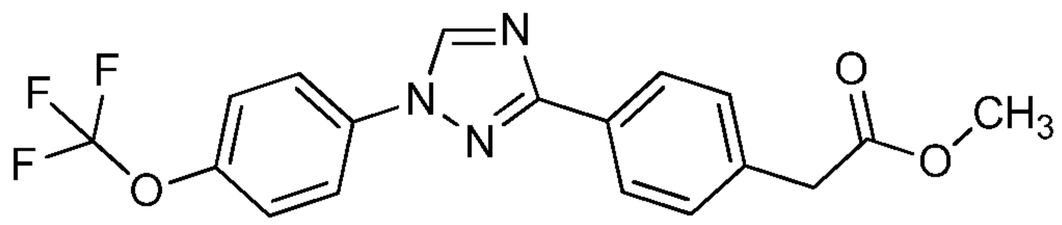
The title compound was prepared as described in Example 1 using 1-iodo-4-trifluoromethylbenzene and isolated as a white solid (2.32 g, 31%): mp 104–105 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.81 (s, 4H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.64; ESIMS *m/z* 292, 294 ($[M+H]^+$).

Example 2: Preparation of methyl 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (C2)



To a 200 mL round bottomed flask, equipped with a stir bar, was added [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.799 g, 1.09 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (6.65 g, 26.2 mmol), and potassium acetate (4.28 g, 43.7 mmol) as solids. These solids were diluted with dioxane (100 mL). The flask was sealed and pumped and purged with nitrogen atmosphere. Then methyl 2-(4-bromophenyl)acetate (5.00 g, 21.8 mmol) was added. The reaction mixture was then warmed to an internal temperature of 70 ℃ for 6 hours. The reaction mixture was allowed to cool to room temperature, and was poured into a brine solution and the layers were partitioned. The aqueous phase was extracted with ethyl acetate (3 x 125 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* flash column chromatography using 0-30% ethyl acetate/hexanes as eluent to afford the title compound as a clear liquid (4.93 g, 70%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68 - 7.58 (m, 2H), 7.35 - 7.23 (m, 2H), 3.71 (s, 2H), 3.61 (s, 3H), 1.29 (s, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.29, 137.72, 134.45, 128.86, 83.56, 82.79, 51.68, 40.23, 24.62; EIMS *m/z* 276 ($[M]^+$).

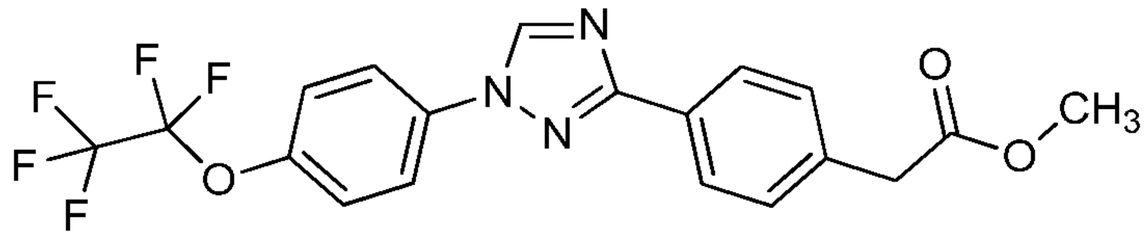
Example 3: Preparation of methyl 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (C3)



To a 200 mL round bottomed flask equipped with a magnetic stir bar was added 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) (3.45 g, 11.2 mmol), and methyl 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (**C2**) (3.71 g, 13.4 mmol). These reagents were diluted with dioxane (45.0 mL) and water (11.3 mL) and the resulting solution was sparged with nitrogen gas for 10 minutes. Tri-*tert*-butylphosphonium tetrafluoroborate (0.325 g, 1.12 mmol), palladium(II) acetate (0.126 g, 0.560 mmol) and cesium fluoride (3.40 g, 22.4 mmol) were added as solids. The flask was sealed and placed under nitrogen atmosphere. The reaction mixture was heated to an internal temperature of 60 °C. The reaction mixture was allowed to cool to room temperature, and was poured into a brine solution and the layers were partitioned. The aqueous phase was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* flash column chromatography using 0-10% ethyl acetate/hexanes as eluent to afford the title compound as an off-white solid (3.45 g, 82%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.11 - 8.04 (m, 4H), 7.63 (ddt, J = 7.9, 2.1, 1.1 Hz, 2H), 7.48 - 7.36 (m, 2H), 3.77 (s, 2H), 3.64 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.02; ESIMS *m/z* 378 ([M+H]$^+$).

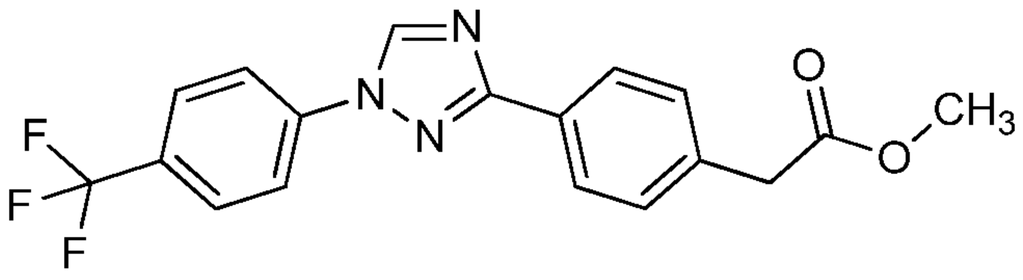
The following compounds were prepared in accordance to the procedure in Example 3.

Preparation of methyl 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (C4)



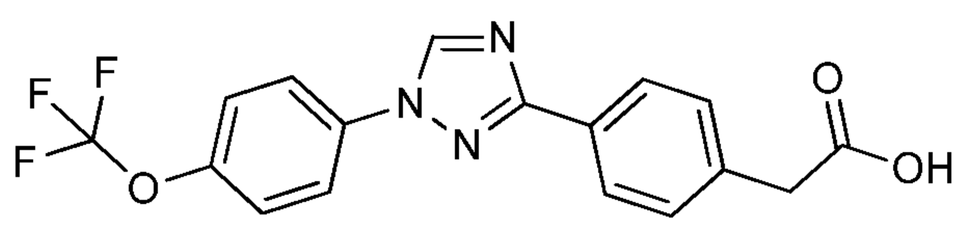
The title compound was prepared as described in Example 3 using 3-bromo-1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazole (**C1a**) and methyl 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (**C2**) and isolated as a white solid (3.57 g, 59%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (s, 1H), 8.18 - 8.04 (m, 4H), 7.68 - 7.58 (m, 2H), 7.48 - 7.38 (m, 2H), 3.78 (s, 2H), 3.65 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -85.20 (d, J = 2.9 Hz), -86.93; ESIMS *m/z* 428 ([M+H]$^+$).

Preparation of methyl 2-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (C5)



The title compound was prepared as described in Example 3 using 3-bromo-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (**C1b**) and methyl 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (**C2**) and isolated as a white solid (2.3 g, 81%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.53 (s, 1H), 8.23 - 8.16 (m, 2H), 8.08 (d, J = 8.2 Hz, 2H), 8.03 - 7.96 (m, 2H), 7.49 - 7.38 (m, 2H), 3.78 (s, 2H), 3.65 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.82; ESIMS *m/z* 362 ([M+H]$^{+}$).

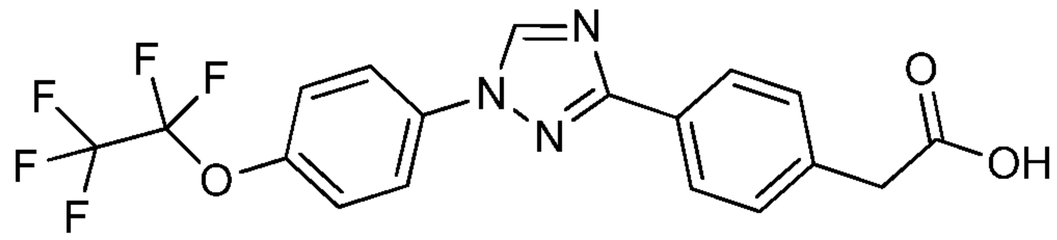
Example 4: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (C6)



To a 100 mL round bottomed flask, equipped with a magnetic stir bar, was added methyl 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (**C3**) (3.45 g, 9.14 mmol) and lithium hydroxide·hydrate (1.15 g, 27.4 mmol) as solids. These solids were diluted with tetrahydrofuran (24 mL), methanol (24 mL), and water (12 mL). The reaction was stirred at room temperature for 2 hours. The reaction mixture was then concentrated to dryness. The resulting solid was then diluted with water, and the resulting suspension was adjusted to pH 2.9. The subsequent precipitate was extracted with ethyl acetate (5 x 100 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated to afford the title compound as a white solid (3.27 g, 96%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 9.40 (s, 1H), 8.15 - 8.03 (m, 4H), 7.63 (dq, J = 7.9, 1.0 Hz, 2H), 7.49 - 7.36 (m, 2H), 3.66 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 364 ([M+H]$^{+}$).

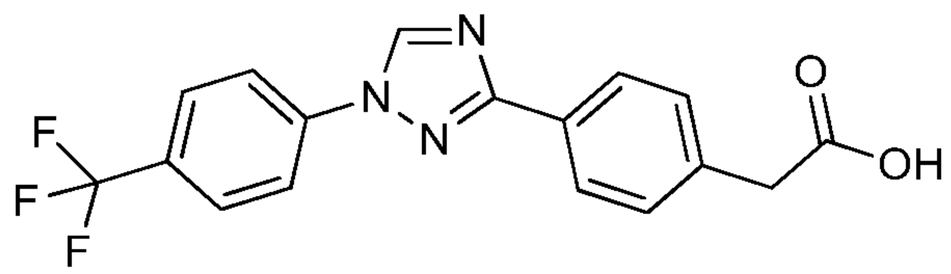
The following compounds were prepared in accordance to the procedure in Example 4.

Preparation of 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (C7)



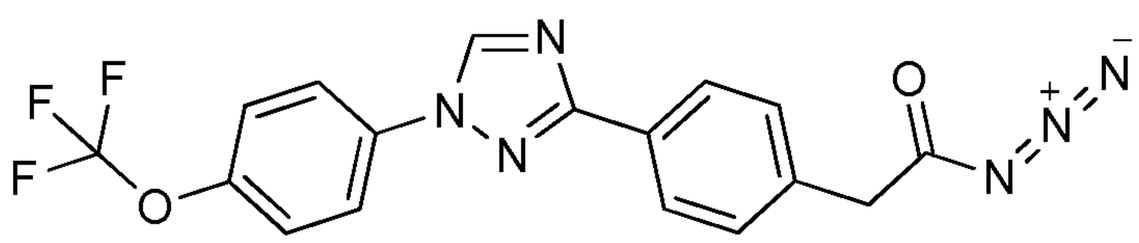
The title compound was prepared as described in Example 4 using methyl 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (**C4**) and isolated as a white solid (3.4 g, 94%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 9.41 (s, 1H), 8.15 - 8.02 (m, 4H), 7.67 - 7.58 (m, 2H), 7.47 - 7.37 (m, 2H), 3.66 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -85.20, -86.92; ESIMS *m/z* 414 ([M+H]$^+$).

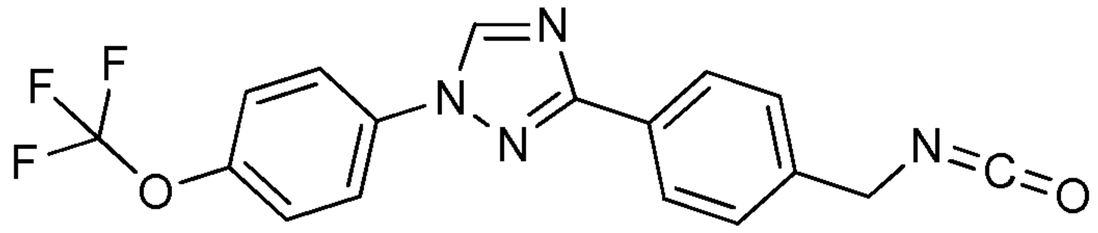
Preparation of 2-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (C8)



The title compound was prepared as described in Example 4 with methyl 2-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (**C5**) and isolated as a white solid (0.378 g, 98%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.42 (s, 1H), 9.53 (s, 1H), 8.25 - 8.16 (m, 2H), 8.11 - 8.04 (m, 2H), 7.99 (d, J = 8.6 Hz, 2H), 7.47 - 7.39 (m, 2H), 3.66 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.79; ESIMS *m/z* 348 ([M+H]$^+$).

Example 5: Preparation of (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (C9)

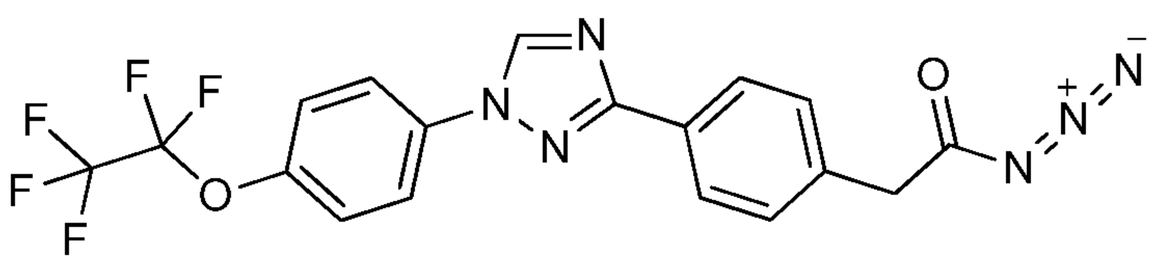


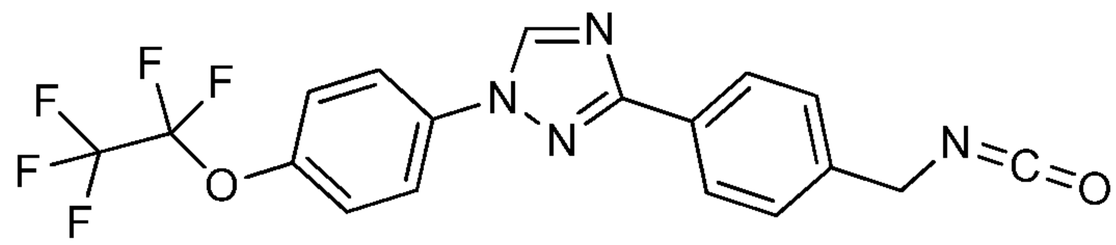


In a 100 mL round bottomed flask, equipped with a magnetic stir bar, 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (**C6**) (2.00 g, 5.51 mmol) was diluted with toluene (37 mL). Then triethylamine (0.767 mL, 5.51 mmol) and diphenyl phosphorazidate (1.19 mL, 5.51 mmol) were added. The reaction was allowed to stir for 2.5 hours at room temperature. The reaction was then poured in to water and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* flash column chromatography using 0-10% ethyl acetate/hexanes as eluent to afford the title compound as an off-white solid (0.800 g, 37%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (d, J = 5.9 Hz, 1H), 8.21 - 7.99 (m, 4H), 7.69 - 7.57 (m, 2H), 7.57 - 7.38 (m, 2H), 4.70 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.99 (d, J = 4.1 Hz); ESIMS *m/z* 361 ([M+H]$^+$) (methyl carbamate).

The following compounds were prepared in accordance to the procedure in Example 5. Physical properties indicate that the isolated products are often a mixture of the acyl azide and rearranged isocyanate.

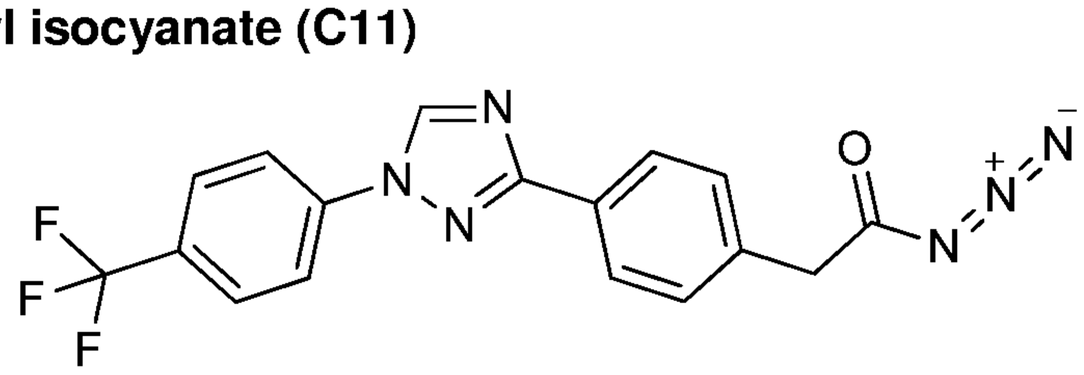
Preparation of 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (C10)

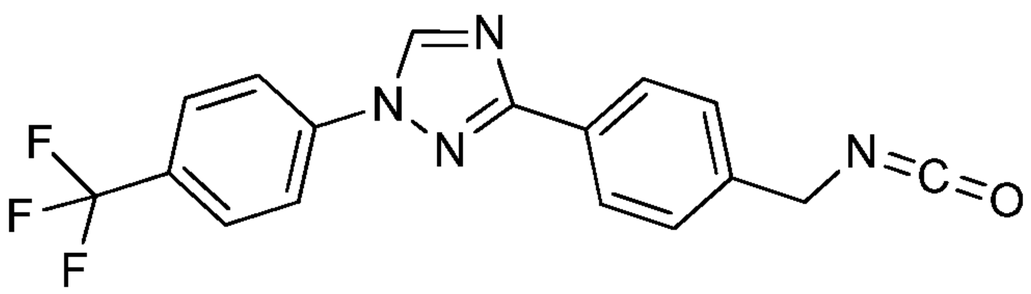




The title compound was prepared as described in Example 5 using 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (**C7**) and isolated as a white solid (1.45 g, 46%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 - 9.32 (m, 1H), 8.19 - 7.97 (m, 4H), 7.68 - 7.36 (m, 4H), 4.70 (s, 1H), 4.34 (d, J = 6.1 Hz, 1H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -85.23 (d, J = 9.8 Hz), -86.95 (d, J = 8.0 Hz); ESIMS *m/z* 442 ([M+H]$^{+}$) (methyl carbamate).

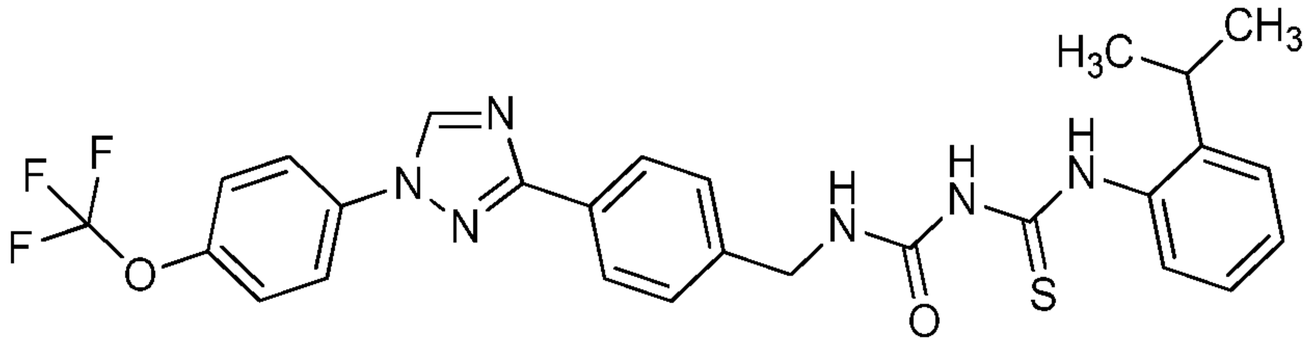
Preparation of 2-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(trifluromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (C11)





The title compound was prepared as described in Example 5 with 2-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (**C8**) and isolated as a white solid (0.082 g, 25%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.55 (s, 1H), 8.27 - 8.06 (m, 4H), 7.99 (d, J = 8.5 Hz, 2H), 7.56 - 7.49 (m, 1H), 7.44 (dd, J = 8.4, 6.9 Hz, 1H), 4.71 (s, 1H), 3.87 (s, 1H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.80 (d, J = 2.9 Hz); ESIMS *m/z* 345 ([M+H]$^{+}$).

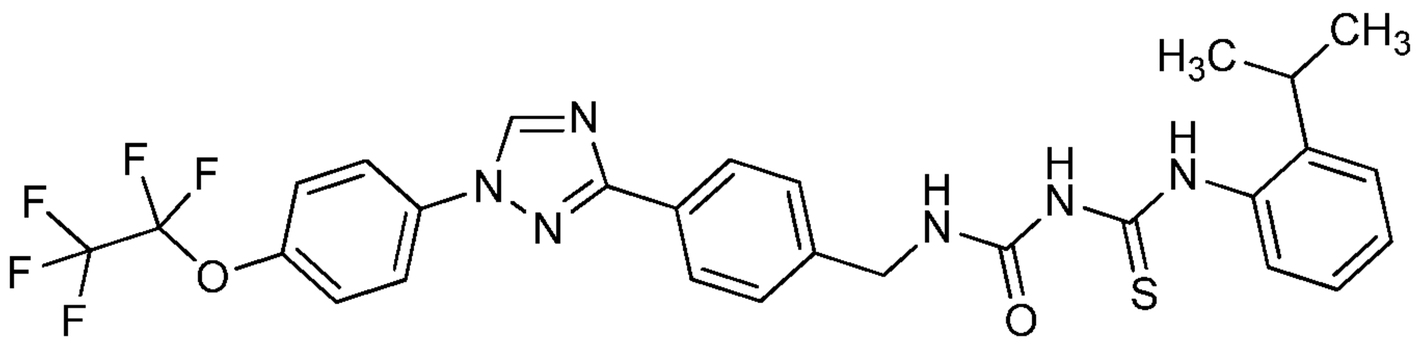
Example 6: Preparation of *N*-[2-(propan-2-yl)phenyl]-*N'*-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)dicarbonimidothioic diamide (F14)



In a 20 mL vial, equipped with a magnetic stir bar, (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (**C9**) (0.200 g, 0.515 mmol) was suspended in acetonitrile (3.3 mL). The vial was capped and the suspension was heated at 80 °C, for 3 hours. The suspension was cooled to room temperature and 1-(2-isopropylphenyl)thiourea (0.110 g, 0.567 mmol) and cesium carbonate (0.201 g, 0.618 mmol) were charged as solids. This suspension was stirred at room temperature for 18 hours. The reaction mixture was filtered through a glass-fritted funnel. The filtrate was concentrated and the resulting residue was purified *via* reverse-phase flash column chromatography (C_{18} column) using 5-100% acetonitrile/water as eluent to afford the title compound as a light yellow solid (0.104 g, 36%).

The following compounds were prepared in accordance to the procedure in Example 6.

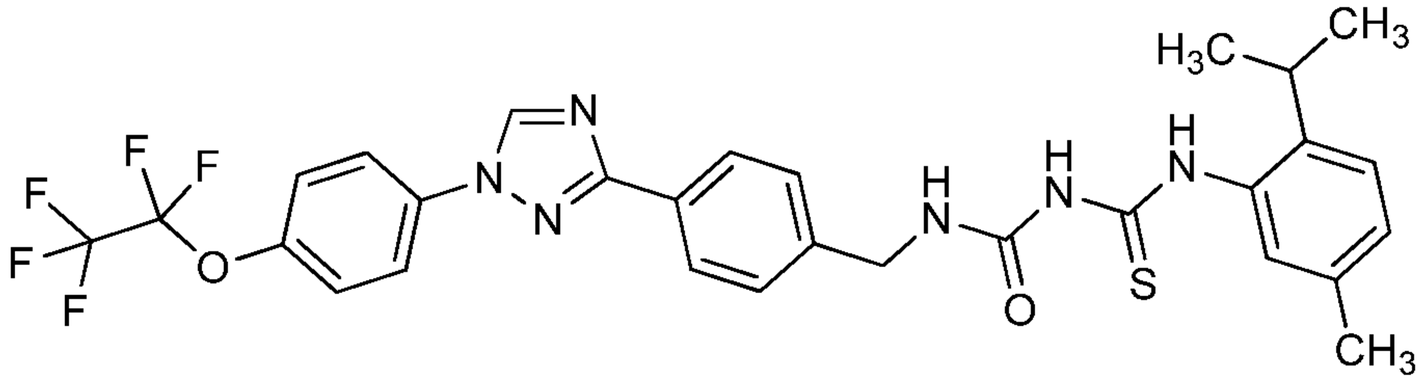
Preparation of *N*-(4-{1-[4-(pentafluoroethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)-*N'*-[2-(propan-2-yl)phenyl]dicarbonimidothioic diamide (F15)



The title compound was prepared as described in Example 6 using 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-

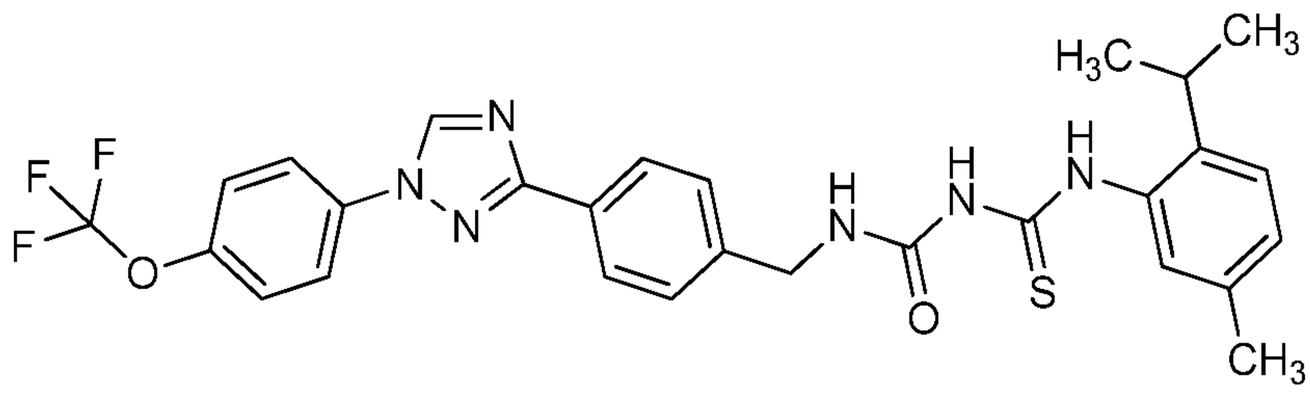
(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (**C10**) and 1-(2-isopropylphenyl)thiourea and isolated as a yellow solid (0.102 g, 36%).

Preparation of *N*-[5-methyl-2-(propan-2-yl)phenyl]-*N'*-(4-{1-[4-(pentafluoroethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)dicarbonimidothioic diamide (F16)



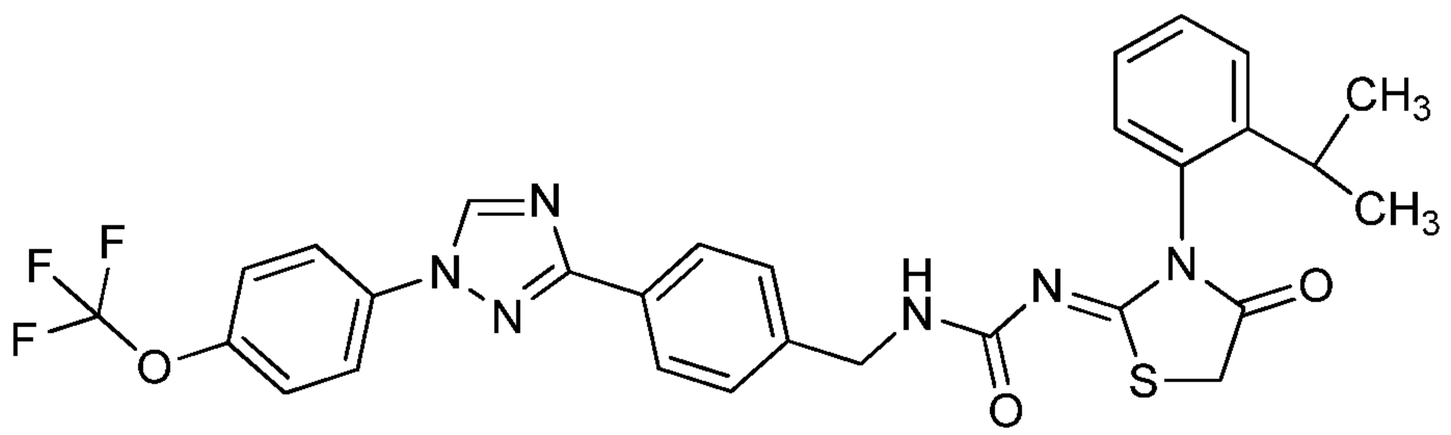
The title compound was prepared as describe in Example 6 using 2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (**C10**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a yellow solid (0.130 g, 44%).

Preparation of *N*-[5-methyl-2-(propan-2-yl)phenyl]-*N'*-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)dicarbonimidothioic diamide (F35)



The title compound was prepared as described in Example 6 using (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (**C9**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a yellow solid (0.043 g, 15%).

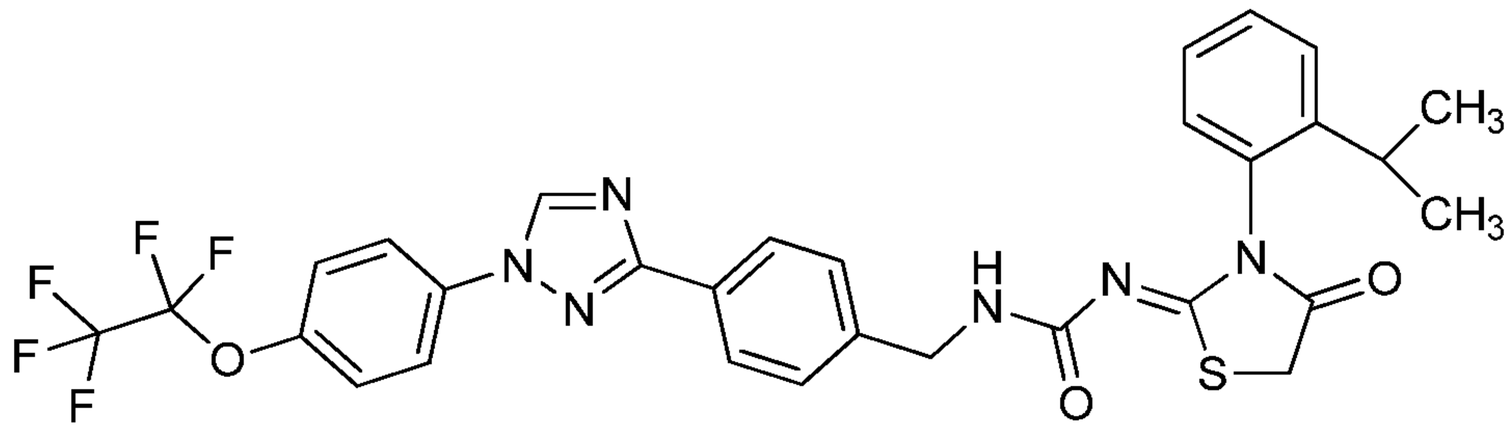
Example 7: Preparation of *(Z)*-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (F17)



In a 50 mL round bottomed flask, equipped with a magnetic stir bar, *N*-[2-(propan-2-yl)phenyl]-*N'*-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)dicarbonimidothioic diamide (**F14**) (0.067 g, 0.12 mmol) and sodium acetate (0.012 g, 0.15 mmol) was diluted with acetonitrile (1.2 mL), then methyl 2-bromoacetate (0.013 mL, 0.13 mmol) was added. The flask was fitted with a reflux condenser and the reaction mixture was heated at 70 °C. After 4 hours, an additional aliquot of methyl 2-bromoacetate (0.013 mL, 0.13 mmol) was added, and the reaction was allowed to heat for an additional 18 hours. An additional aliquot of methyl 2-bromoacetate (0.013 mL, 0.13 mmol) and sodium acetate (0.012 g, 0.15 mmol) was added, and the reaction was allowed to heat for an additional 4 hours. The reaction mixture was cooled and diluted with water and extracted with ethyl acetate (50 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* reverse-phase flash column (C_{18} column) chromatography using 5-100% acetonitrile/water as eluent to afford the title compound as a white solid (0.036 g, 49%).

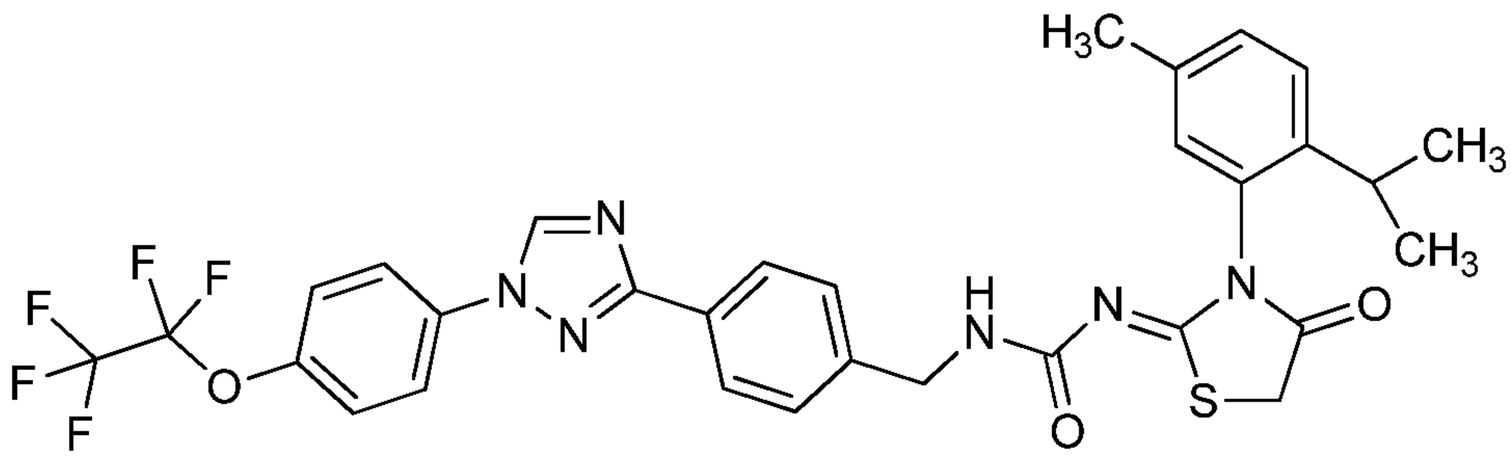
The following compounds were prepared in accordance to the procedure in Example 7.

Preparation of *(Z)*-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (F18)



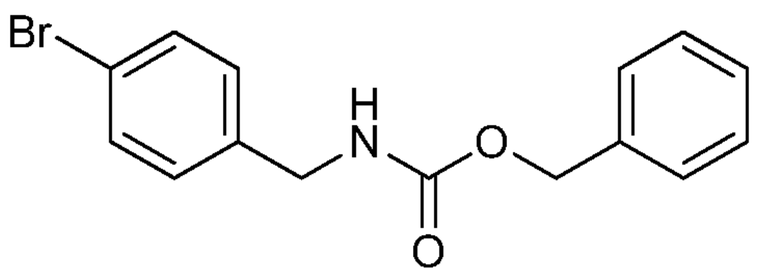
The title compound was prepared as described in Example 7 using *N*-(4-{1-[4-(pentafluoroethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)-*N'*-[2-(propan-2-yl)phenyl]dicarbonimidothioic diamide (**F15**) and isolated as an off-white solid (0.043 g, 47%).

Preparation of *(Z)*-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (F19)



The title compound was prepared as described in Example 7 using *N*-[5-methyl-2-(propan-2-yl)phenyl]-*N'*-(4-{1-[4-(pentafluoroethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)dicarbonimidothioic diamide (**F16**) and isolated as a white solid (0.056 g, 46%).

Example 8: Preparation of benzyl 4-bromobenzylcarbamate (C12)

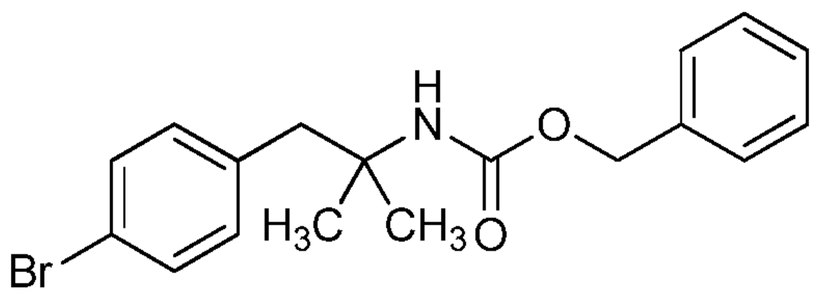


In a 500 mL round bottomed flask, equipped with a magnetic stir bar, (4-bromophenyl)methanaminium chloride (10.0 g, 44.9 mmol) and sodium hydroxide (4.00 g, 100 mmol) were dissolved in tetrahydrofuran (80 mL) and water (80 mL). The solution was cooled in an ice water bath, and benzyl chloroformate (7.06 mL, 49.4 mmol) was added dropwise. The reaction was allowed to stir for 1 hour. The reaction was poured into a brine solution and extracted with ethyl acetate (2 x 200 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated to afford the title compound as a white solid (14.8 g, 102%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (t, J = 6.0 Hz, 1H), 7.64 - 7.53 (m, 2H), 7.47 - 7.33 (m, 5H), 7.32 - 7.20 (m, 2H), 5.10 (s, 2H), 4.23 (d, J = 6.2 Hz, 2H); ^{13}C

NMR (101 MHz, DMSO-d_6) δ 156.33, 139.20, 137.05, 131.10, 129.22, 128.33, 127.72, 119.77, 65.42, 43.19; ESIMS *m/z* 320, 322 ($[M+H]^+$).

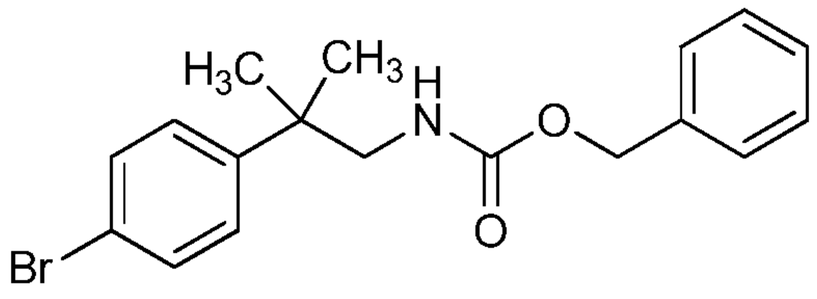
The following compounds were prepared in accordance to the procedure in Example 8.

Preparation of benzyl (1-(4-bromophenyl)-2-methylpropan-2-yl)carbamate (CB1)



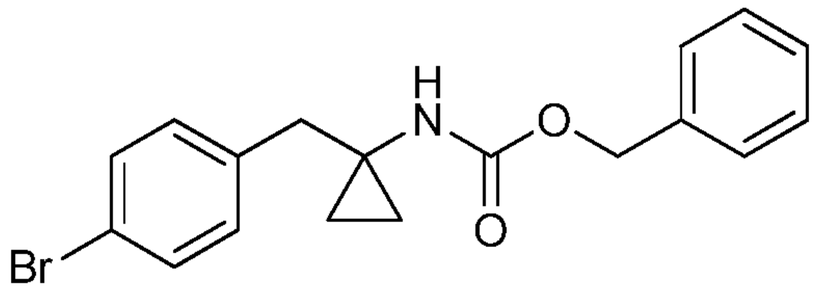
The title compound was prepared as described in Example 8 using 1-(4-bromophenyl)-2-methylpropan-2-amine and isolated as a off-white solid (6.67 g, 81%): mp 82-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 - 7.27 (m, 7H), 6.90 (d, *J* = 8.3 Hz, 2H), 5.09 (s, 2H), 4.47 (s, 1H), 2.94 (s, 2H), 1.27 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.02, 136.77, 132.13, 131.02, 130.49, 128.54, 128.23, 128.15, 120.32, 69.73, 66.09, 53.02, 27.41; ESIMS *m/z* 363 ($[M+H]^+$).

Preparation of benzyl (2-(4-bromophenyl)-2-methylpropyl)carbamate (CB2)



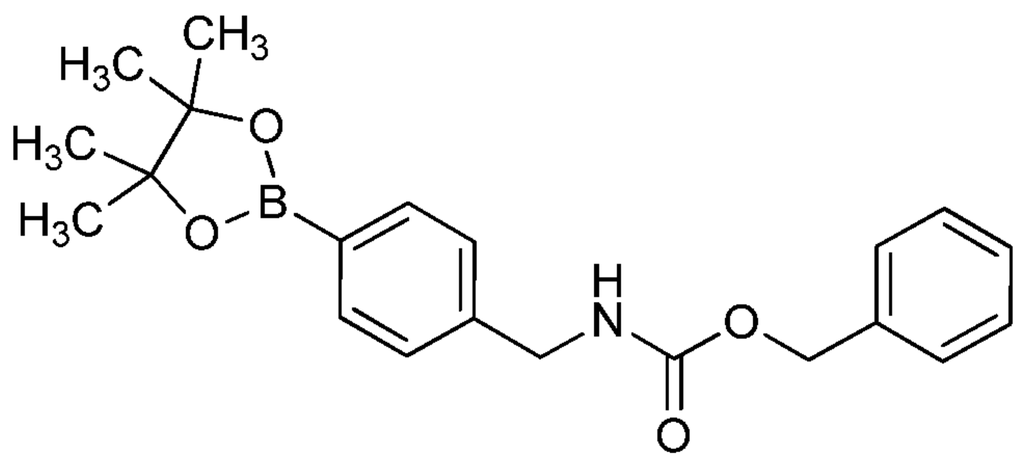
The title compound was prepared as described in Example 8 using 2-(4-bromophenyl)-2-methylpropan-1-amine and isolated as a tan oil (7.83 g, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 - 7.40 (m, 2H), 7.40 - 7.27 (m, 5H), 7.20 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 4.48 (t, *J* = 6.1 Hz, 1H), 3.38 (d, *J* = 6.3 Hz, 2H), 1.30 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.51, 145.44, 136.42, 131.54, 128.53, 128.17, 128.13, 127.87, 120.27, 66.77, 52.39, 38.86, 26.36; ESIMS *m/z* 363 ($[M+H]^+$).

Preparation of benzyl (1-(4-bromobenzyl)cyclopropyl)carbamate (CB3)



The title compound was prepared as described in Example 8 using 1-(4-bromobenzyl)cyclopropanamine (Ukrorgsyntez Ltd) and isolated as a pale yellow solid (3.33 g, 81%): mp 84-86 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 - 7.28 (m, 7H), 5.08 (s, 2H), 2.82 (s, 2H), 0.85 - 0.69 (m, 4H) (NH not observed); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.85, 136.52, 131.43, 131.07, 128.73, 128.57, 128.51, 128.14, 120.39, 66.47, 40.93, 34.36, 13.54; ESIMS *m/z* 362 ([M+2]$^{+}$).

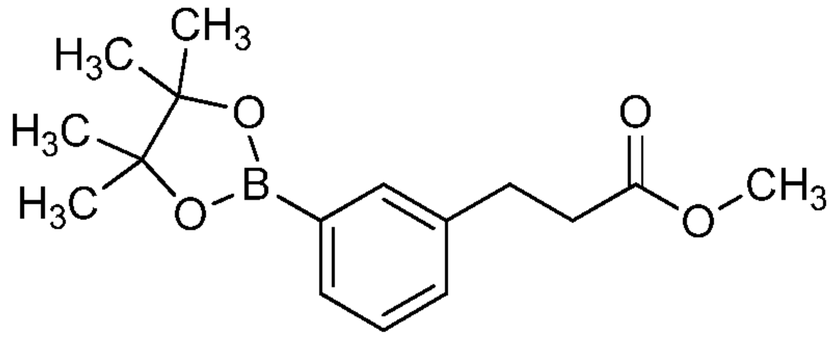
Example 9: Preparation of benzyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylcarbamate (C13)



In a 500 mL round bottomed flask, equipped with a magnetic stir bar, benzyl 4-bromobenzylcarbamate (**C12**) (14.3 g, 44.7 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (12.5 g, 49.1 mmol), and potassium acetate (8.77 g, 89.0 mmol) were diluted with dioxane (170 mL). The suspension was sparged with nitrogen gas for 10 minutes. The [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (1.63 g, 2.23 mmol) was added as a solid. The flask was placed under nitrogen atmosphere and the reaction mixture was warmed to an internal temperature of 70 ℃ for 18 hours. The reaction mixture was cooled to room temperature, poured into a brine solution and extracted with ethyl acetate (3 x 250 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* flash column chromatography using 0-10% ethyl acetate/B, where B = 1:1 dichloromethane:hexanes, as eluent to afford the title compound as an orange solid (11.8 g, 69%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (t, J = 6.2 Hz, 1H), 7.71 - 7.60 (m, 2H), 7.43 - 7.24 (m, 7H), 5.06 (s, 2H), 4.24 (d, J = 6.2 Hz, 2H), 1.29 (s, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 156.35, 143.18, 137.12, 134.45, 128.31, 127.69, 126.38, 83.51, 66.32, 65.37, 64.89, 43.83, 24.62; ESIMS *m/z* 368 ([M+H]$^{+}$).

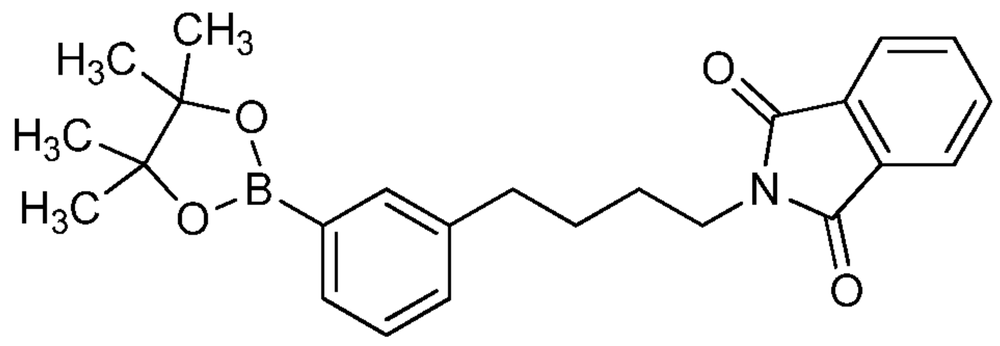
The following compounds were prepared in accordance to the procedure in Example 9.

Preparation of methyl 3-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoate (C13a)



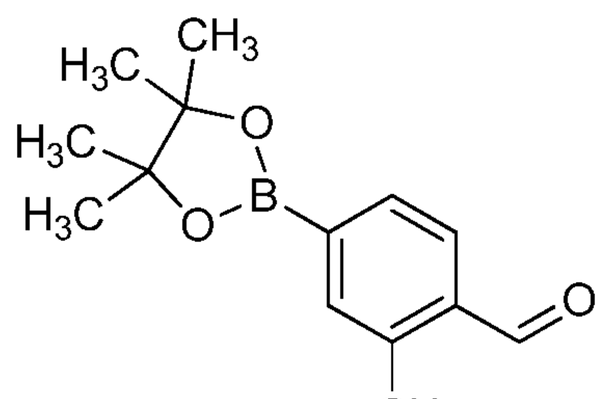
The title compound was prepared as described in Example 9 using methyl 3-(3-bromophenyl)propanoate and isolated as a tan solid (9.18 g, 75%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56 - 7.47 (m, 2H), 7.35 (dt, J = 7.7, 1.7 Hz, 1H), 7.33 - 7.23 (m, 1H), 3.57 (s, 3H), 2.86 (t, J = 7.6 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 1.29 (s, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.57, 139.91, 134.28, 132.18, 131.32, 127.86, 83.54, 51.20, 34.88, 30.10, 24.63; EIMS *m/z* 290.

Preparation of 2-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (C13b)



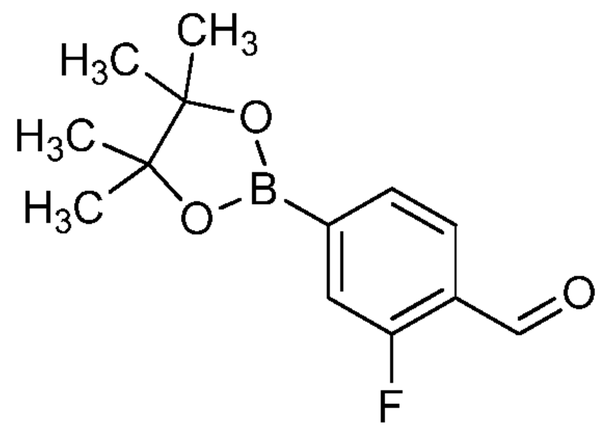
The title compound was prepared as described in Example 9 using 2-(4-(3-bromophenyl)butyl)isoindoline-1,3-dione (**C57a**) and isolated as a tan solid (5.50 g, 62%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.90 - 7.78 (m, 4H), 7.54 - 7.42 (m, 2H), 7.33 - 7.23 (m, 2H), 3.59 (t, J = 6.5 Hz, 2H), 2.60 (t, J = 7.2 Hz, 2H), 1.70 - 1.48 (m, 4H), 1.28 (s, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.90, 141.32, 134.33, 131.83, 131.56, 131.40, 127.76, 122.93, 83.50, 37.17, 34.52, 28.49, 27.67, 24.64; ESIMS *m/z* 406 ([M+H]$^{+}$).

Preparation of 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (CB4)



The title compound was prepared as described in Example 9 using 4-bromo-2-methylbenzaldehyde and isolated as a clear and colorless oil (0.623 g, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 7.78 (d, J = 0.8 Hz, 2H), 7.70 (s, 1H), 2.67 (s, 3H), 1.36 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.08, 139.40, 138.02, 135.89, 132.45, 130.86, 84.28, 24.87, 19.37; IR (thin film) cm^{-1} 2978, 2927, 2728,1700, 1355, 1194.

Preparation of 2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (CB5)

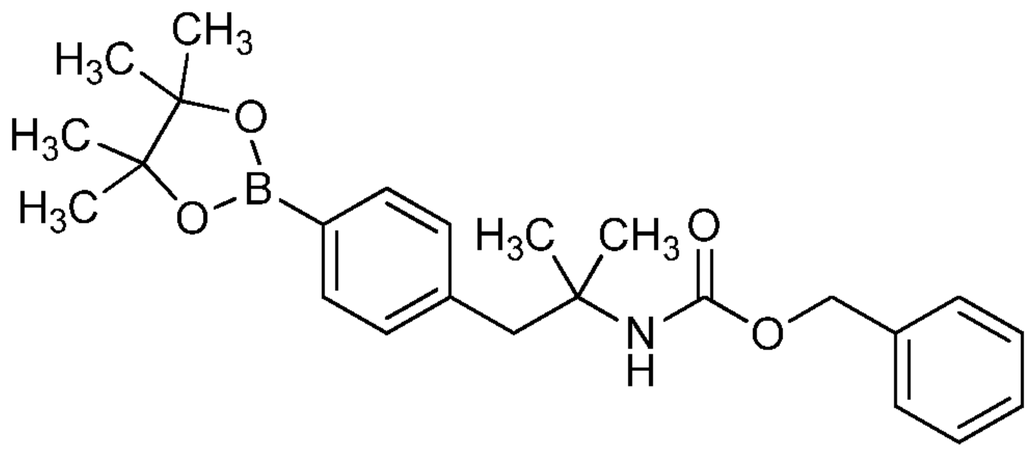


The title compound was prepared as described in Example 9 using 4-bromo-2-fluorobenzaldehyde and isolated as a white solid (4.1 g, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (d, J = 0.8 Hz, 1H), 7.84 (dd, J = 7.6, 6.7 Hz, 1H), 7.67 (dt, J = 7.6, 0.8 Hz, 1H), 7.58 (dd, J = 10.7, 0.9 Hz, 1H), 1.36 (s, 12H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.56.

Preparation of methyl 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (CB6)

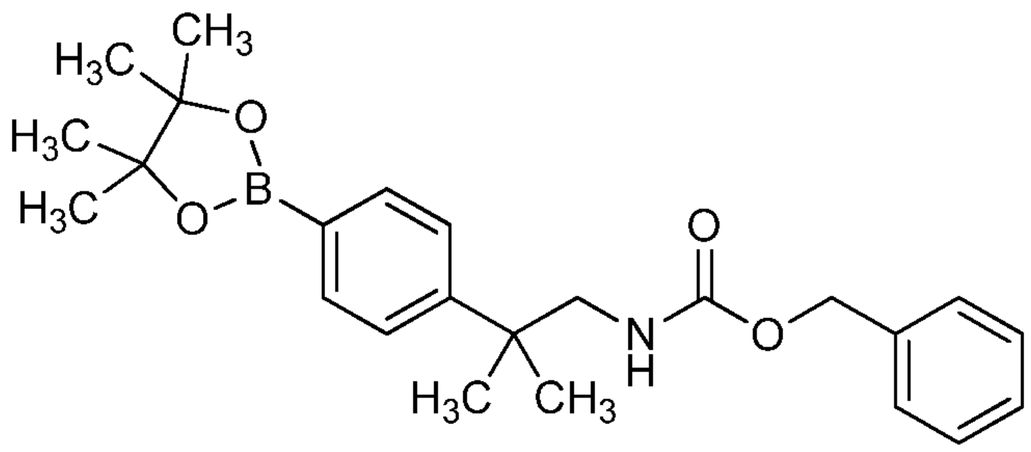
The title compound was prepared as described in Example 9 using methyl 2-(3-bromophenyl)acetate and isolated as a white solid (14.68 g, 97%, 80% pure): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (dt, J = 8.4, 1.7 Hz, 2H), 7.44 - 7.28 (m, 2H), 3.71 (s, 2H), 3.62 (s, 3H), 1.30 (s, 12H); ESIMS m/z 276 ([M]$^+$).

Preparation of benzyl (2-methyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-yl)carbamate (CB7)



The title compound was prepared as described in Example 9 using benzyl (1-(4-bromophenyl)-2-methylpropan-2-yl)carbamate (**CB1**) and isolated as a clear oil (6.12 g, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 7.9 Hz, 2H), 7.38 (d, J = 5.6 Hz, 5H), 7.10 (d, J = 7.9 Hz, 2H), 5.09 (s, 2H), 4.51 (s, 1H), 3.00 (s, 2H), 1.34 (s, 12H), 1.29 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.73, 141.11, 136.77, 134.45, 129.95, 128.52, 128.10, 128.06, 83.71, 66.09, 54.47, 53.21, 27.43, 24.88; ESIMS m/z 410 ([M+H]$^+$).

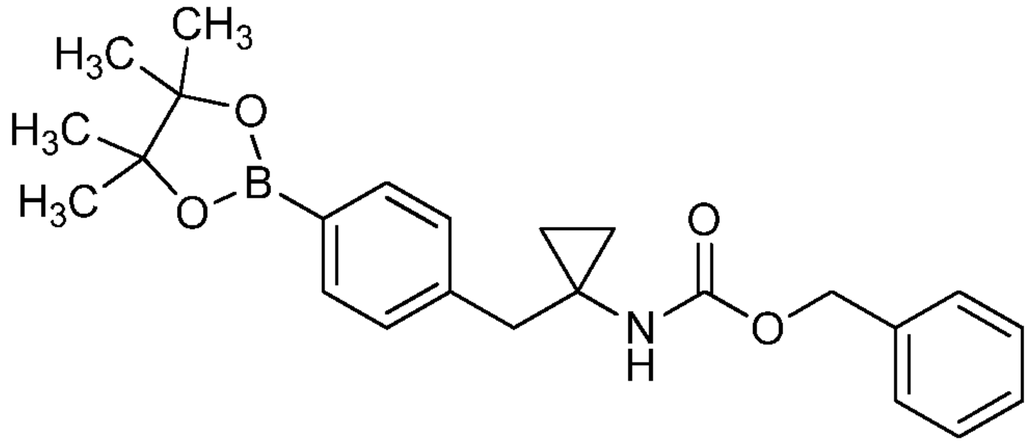
Preparation of benzyl (2-methyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propyl)carbamate (CB8)



The title compound was prepared as described in Example 9 using benzyl (2-(4-bromophenyl)-2-methylpropyl)carbamate (**CB2**) and isolated as a pale yellow oil (8.47 g, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 - 7.73 (m, 2H), 7.32 (dtd, J = 14.5, 7.4, 6.8, 2.7 Hz, 7H), 5.04 (s, 2H), 4.50 - 4.37 (m, 1H), 3.41 (d, J = 6.3 Hz, 2H), 1.34 (s, 12H), 1.33 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.56, 149.64, 136.52, 135.07,

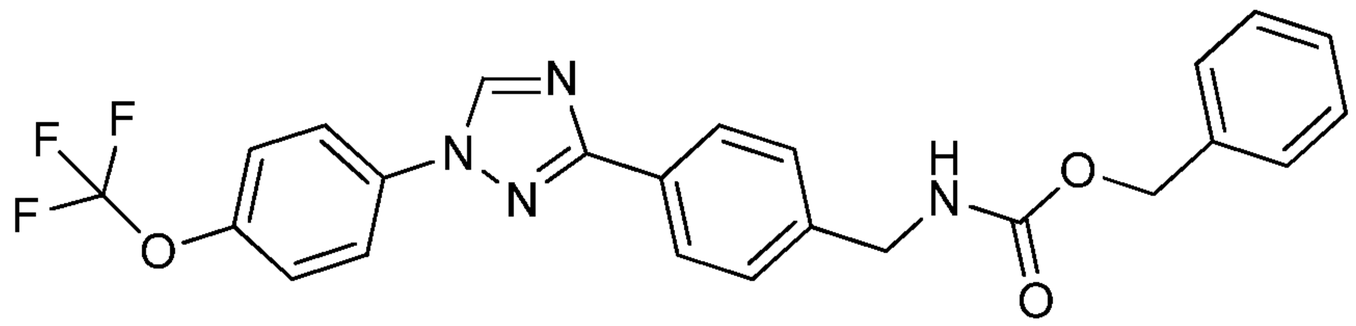
131.54, 128.48, 128.06, 127.87, 125.34, 83.77, 66.66, 52.46, 39.15, 26.36, 24.86; ESIMS *m/z* 410 ($[M+H]^+$).

Preparation of benzyl (1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)cyclopropyl)carbamate (CB9)



The title compound was prepared as described in Example 9 using benzyl (1-(4-bromobenzyl)cyclopropyl)carbamate (**CB3**) and purified using ethyl acetate/hexanes as eluent; isolated as a white solid (2.53 g, 67%): mp 102-104 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 - 7.63 (m, 2H), 7.51 - 7.28 (m, 5H), 7.16 (d, *J* = 7.5 Hz, 2H), 5.08 (s, 2H), 4.90 (s, 1H), 2.89 (s, 2H), 1.34 (s, 12H), 0.80 (s, 4H); ESIMS *m/z* 408 ($[M+H]^+$).

Example 10: Preparation of benzyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylcarbamate (C14)

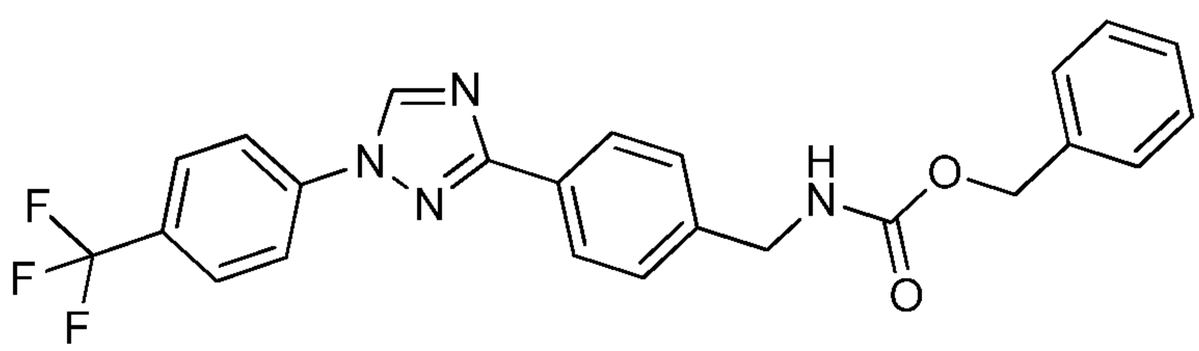


In a 50 mL round bottomed flask, equipped with a magnetic stir bar, 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) (1.0 g, 3.3 mmol), benzyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylcarbamate (**C13**) (1.3 g, 3.6 mmol), bistriphenylphosphine dichloropalladium(II) (0.120 g, 0.171 mmol), and potassium phosphate (1.38 g, 6.49 mmol) were charged as solids. The flask was sealed and placed under nitrogen atmosphere. Dioxane (17.3 mL) and water (4.3 mL) were added. The reaction was warmed to an internal temperature of 65 ℃ for 18 hours. The reaction mixture was cooled to room temperature, poured into a brine solution and extracted with ethyl acetate (3 x 75 mL). The combined organic layers

were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified *via* flash column chromatography using 0-50% ethyl acetate/hexanes as eluent to afford the title compound as a white solid (0.850 g, 56%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.17 - 8.00 (m, 4H), 7.91 (t, J = 6.2 Hz, 1H), 7.72 - 7.59 (m, 2H), 7.46 - 7.12 (m, 7H), 5.07 (s, 2H), 4.29 (d, J = 6.1 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 469 ([M+H]$^+$).

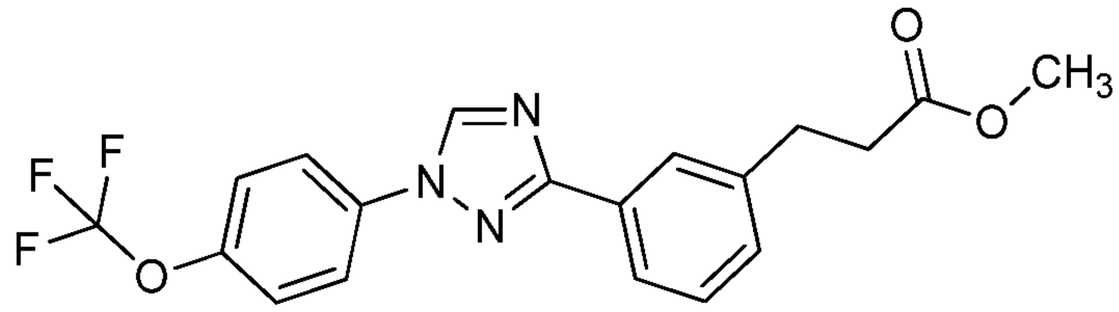
The following compounds were prepared in accordance to the procedure in Example 10.

Preparation of benzyl 4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylcarbamate (C15)



The title compound was prepared as described in Example 10 using 3-bromo-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (**C1b**), benzyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylcarbamate (C13), tri-*tert*-butylphosphonium tetrafluoroborate, palladium(II) acetate, and cesium fluoride and isolated as a white solid (0.846 g, 36%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.53 (s, 1H), 8.28 - 8.14 (m, 2H), 8.16 - 8.04 (m, 2H), 8.04 - 7.95 (m, 2H), 7.92 (t, J = 6.2 Hz, 1H), 7.49 - 7.13 (m, 7H), 5.07 (s, 2H), 4.29 (d, J = 6.2 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.79; ESIMS *m/z* 453 ([M+H]$^+$).

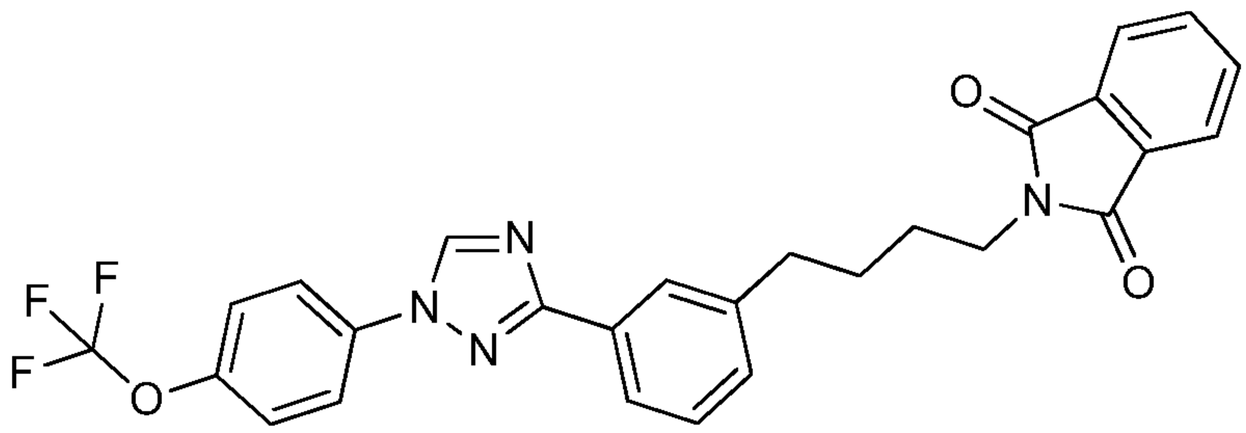
Preparation of methyl 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (CA1)



The title compound was prepared as described in Example 10 using 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**), methyl 3-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoate (**C13a**), and [1,1′-bis(di-*tert*-

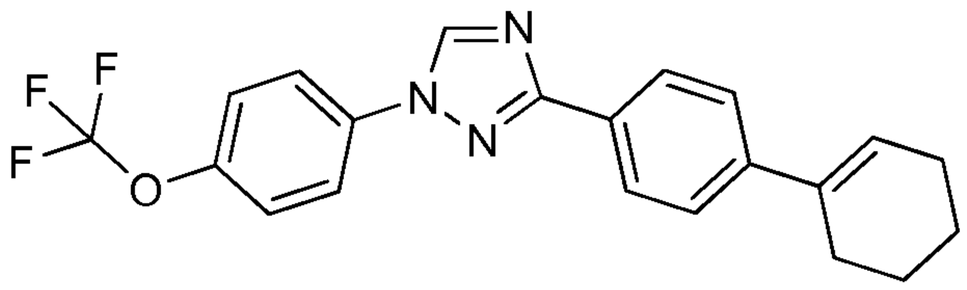
butylphosphino)ferrocene]dichloropalladium(II) at 80 ºC and isolated as a dark orange solid (9.86 g, 91%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.12 - 8.03 (m, 2H), 8.01 - 7.91 (m, 2H), 7.66 - 7.58 (m, 2H), 7.49 - 7.40 (m, 1H), 7.34 (dt, J = 7.8, 1.6 Hz, 1H), 3.59 (s, 3H), 2.95 (t, J = 7.5 Hz, 2H), 2.70 (t, J = 7.6 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.01; ESIMS *m/z* 392 ([M+H]$^+$).

Preparation of 2-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)isoindoline-1,3-dione (CA2)



The title compound was prepared as described in Example 10 using 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**), 2-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (**C13b**), and [1,1′-bis(di-*tert*-butylphosphino)ferrocene]dichloropalladium(II) at 75 ºC and isolated as a dark orange solid (5.48 g, 82%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 8.13 - 8.04 (m, 2H), 7.96 - 7.89 (m, 2H), 7.88 - 7.77 (m, 4H), 7.67 - 7.57 (m, 2H), 7.45 - 7.38 (m, 1H), 7.31 (dt, J = 7.7, 1.5 Hz, 1H), 3.69 - 3.53 (m, 2H), 2.70 (t, J = 6.8 Hz, 2H), 1.64 (dq, J = 6.6, 3.1 Hz, 4H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 507 ([M+H]$^+$).

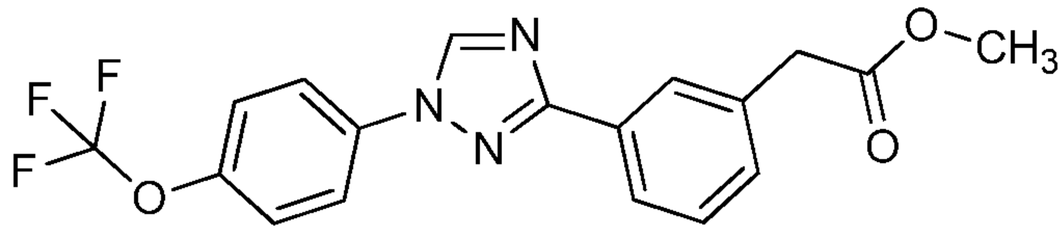
Preparation of 3-(2',3',4',5'-tetrahydro-[1,1'-biphenyl]-4-yl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (CB10)



The title compound was prepared as described in Example 10 using 3-(4-bromophenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C52**) with tetrakis(triphenylphosphine)palladium(0) as catalyst, sodium carbonate as base and heating to 100 ºC for 3 hours; isolated as an orange solid (2.18 g, 57%, 79% pure):

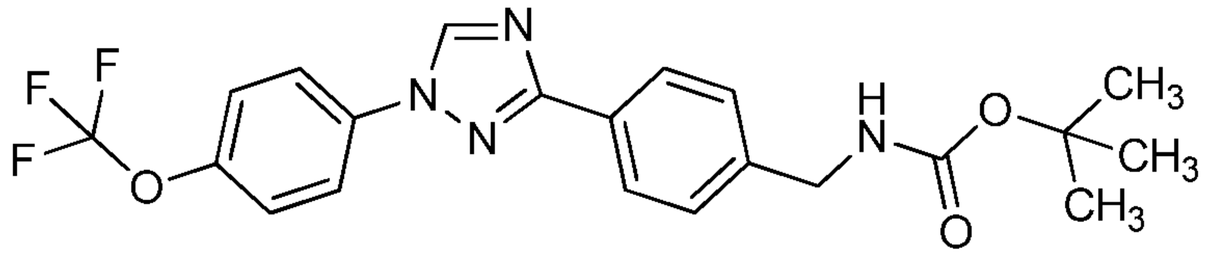
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.15 - 8.06 (m, 2H), 7.80 (dd, *J* = 9.0, 2.3 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.39 (ddd, *J* = 8.0, 2.5, 1.3 Hz, 2H), 6.28 - 6.21 (m, 1H), 2.46 (ddt, *J* = 6.3, 4.1, 2.0 Hz, 2H), 2.24 (dtd, *J* = 6.3, 3.8, 1.8 Hz, 2H), 1.85 - 1.75 (m, 2H), 1.71 - 1.63 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -58.03; ESIMS *m/z* 386 ($[M+H]^+$).

Preparation of methyl 2-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (CB11)



The title compound was prepared as described in Example 10 using methyl 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetate (**CB6**) using [1,1′-bis(di-*tert*-butylphosphino)ferrocene]dichloropalladium(II) as catalyst, sodium carbonate as base and heating to 75 ºC for 30 hours; isolated as a pink solid (4.96 g, 72%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.12 - 8.05 (m, 2H), 8.05 - 7.98 (m, 2H), 7.61 (ddt, *J* = 7.9, 2.0, 1.0 Hz, 2H), 7.47 (td, *J* = 7.6, 0.6 Hz, 1H), 7.38 (ddd, *J* = 7.6, 2.0, 1.2 Hz, 1H), 3.81 (s, 2H), 3.64 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.06; ESIMS *m/z* 378 ($[M+H]^+$).

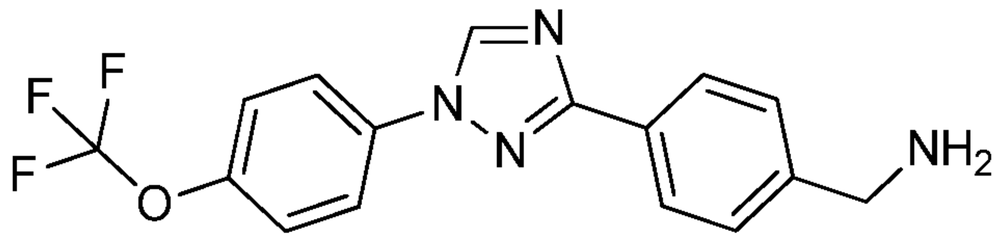
Example 10a: Preparation of *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylcarbamate (C15a)



In a 20 mL vial (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetyl azide/2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methyl isocyanate (**C9**) (0.205 g, 0.528 mmol) was diluted with *tert*-butanol (10.0 mL, 105 mmol). The solution was heated to 80 ℃ overnight. The reaction was cooled and poured into a brine solution and extracted with ethyl acetate (4x). The combined organics were dried over magnesium sulfate, filtered, and concentrated. The resulting residue was purified by flash column chromatography using 0-40%

ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided the title compound as a white solid (0.0890 g, 39%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.15 - 8.01 (m, 4H), 7.63 (dp, J = 7.9, 1.0 Hz, 2H), 7.47 (t, J = 6.1 Hz, 1H), 7.42 - 7.35 (m, 2H), 4.20 (d, J = 6.2 Hz, 2H), 1.41 (s, 9H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 435 ([M+H]$^+$).

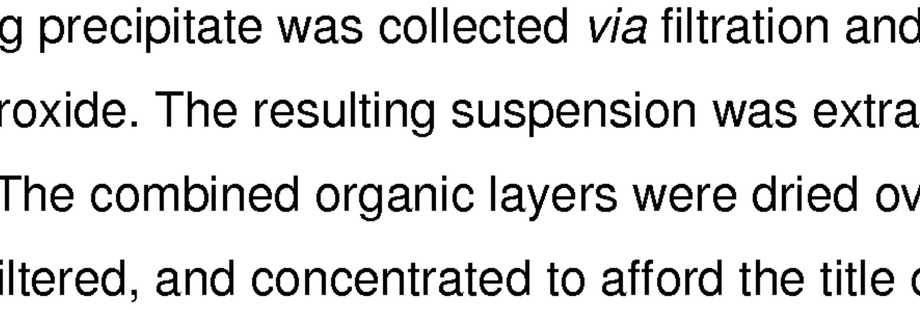
Example 11: Preparation of (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (C16)



In a 200 mL round bottomed flask equipped with a magnetic stir bar, benzyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylcarbamate (**C14**) (0.850 g, 1.82 mmol) was diluted with a solution of hydrogen bromide in acetic acid (33 wt %, 15.0 mL, 1.82 mmol). The suspension was allowed to stir for 1 hour. Diethyl ether (150 mL) was added, and the reaction mixture was stirred for an additional 30 minutes. The resulting precipitate was collected *via* filtration and treated with aqueous sodium hydroxide. The resulting suspension was extracted with ethyl acetate (3 x 75 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated to afford the title compound as a white solid (0.448 g, 74%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 8.07 (dd, J = 10.6, 8.6 Hz, 4H), 7.69 - 7.56 (m, 2H), 7.48 (d, J = 8.2 Hz, 2H), 3.79 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESMIS *m/z* 318 ([M+H]$^+$) (-NH_2).

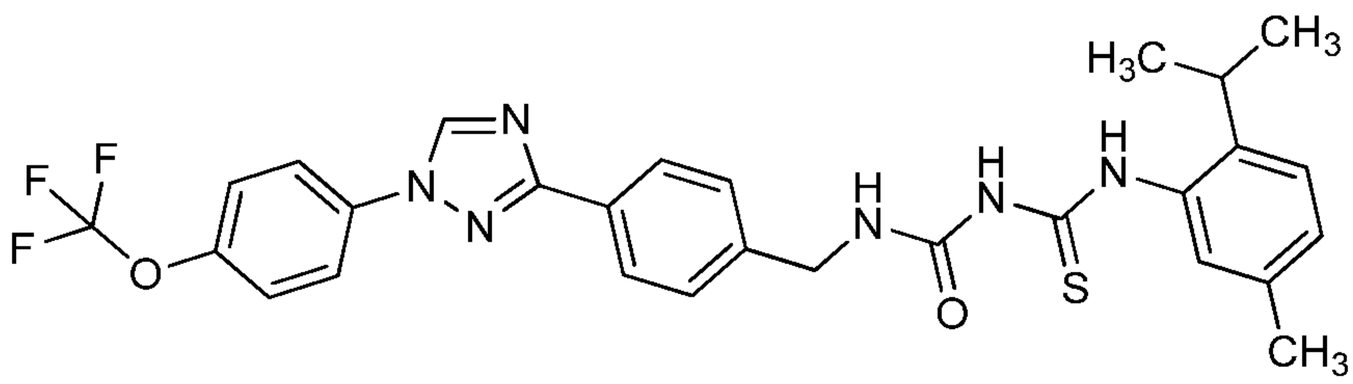
The following compounds were prepared in accordance to the procedure in Example 11.

Preparation of (4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (CA3)



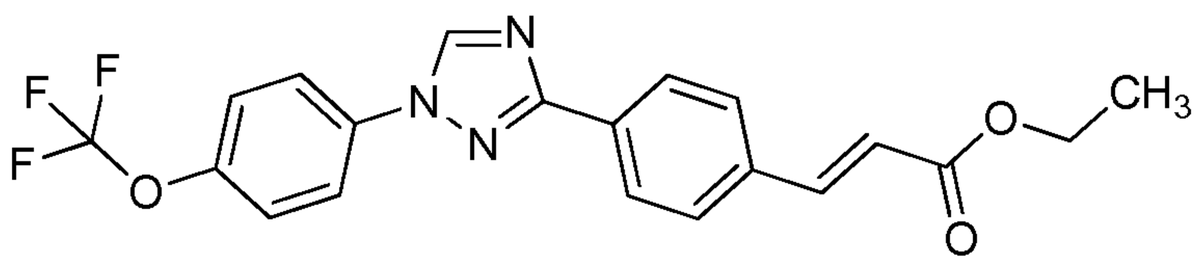
The title compound was prepared as described in Example 11 from benzyl 4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylcarbamate (**C15**) and isolated as a tan solid (4.67 g, 79%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 8.21 (d, J = 8.3 Hz, 2H), 8.09 (d, J = 7.9 Hz, 2H), 8.00 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 7.9 Hz, 2H), 3.82 (s, 2H).

Example 12: Preparation of *N*-[5-methyl-2-(propan-2-yl)phenyl]-*N'*-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}benzyl)dicarbonimidothioic diamide (F35)



In a 200 mL round bottomed flask equipped with a magnetic stir bar, (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) (0.448 g, 1.34 mmol) was diluted with tetrahydrofuran (9.0 mL). To the suspension was added triphosgene (0.398 g, 1.34 mmol) and triethylamine (0.374 mL, 2.68 mmol). The resulting suspension was stirred for 1hour at room temperature. UPLC analysis of a methanol-quenched aliquot shows a mixture of the methyl carbamate and the isocyanate. To the reaction mixture 1-(2-isopropyl-5-methylphenyl)thiourea (0.279 g, 1.34 mmol) and cesium carbonate (0.480 g, 1.47 mmol) were added. The reaction mixture was allowed to stir at room temperature for 18 hours. An additional portion of 1-(2-isopropyl-5-methylphenyl)thiourea (0.279 g, 1.34 mmol) and cesium carbonate (0.480 g, 1.47 mmol) were added and the reaction mixture was warmed to an internal temperature of 60 ℃ for 1 hour. The reaction mixture was poured into water and extracted with ethyl acetate (3 x 75 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting residue was purified by reverse-phase flash column (C_{18} column) chromatography using 5-100% acetonitrile/water as eluent followed by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent to give the title compound as a white solid (0.007 g, 0.9%).

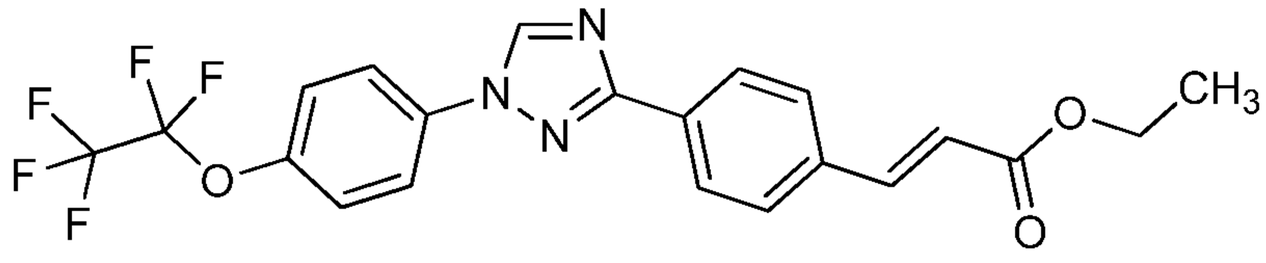
Example 13: Preparation of (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (C17)



To an oven-dried 2 L three-necked round bottomed flask equipped with a stirring bar was added sodium hydride (60% oil immersion, 7.20 g, 180 mmol) as a solid that was pre-weighed into a 25-mL vial. This was diluted with anhydrous tetrahydrofuran (1 L) under nitrogen, and the solution was stirred in an ice bath. Ethyl 2-(diethoxyphosphoryl)acetate (30.0 mL, 151 mmol) was added dropwise in portions over 20 minutes, and the reaction was stirred at 0 ℃ for an additional 2 hours. 4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (50.0. g, 150 mmol) was added in solid portions over 20 minutes, and the reaction turned orange. After stirring for 30 minutes, the ice bath was removed and the reaction was warmed to room temperature over 1 hour. The reaction was quenched with slow addition of saturated aqueous ammonium chloride (500 mL) and allowed to stand at room temperature overnight. The biphasic reaction mixture was diluted with water and extracted with 1:1 ethyl acetate/hexanes (3x). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to afford the title compound as an orange solid (61.4 g, 100%): mp 135–137 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 2H), 7.85 - 7.77 (m, 2H), 7.73 (d, *J* = 16.0 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 6.51 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 404 ($[M+H]^+$).

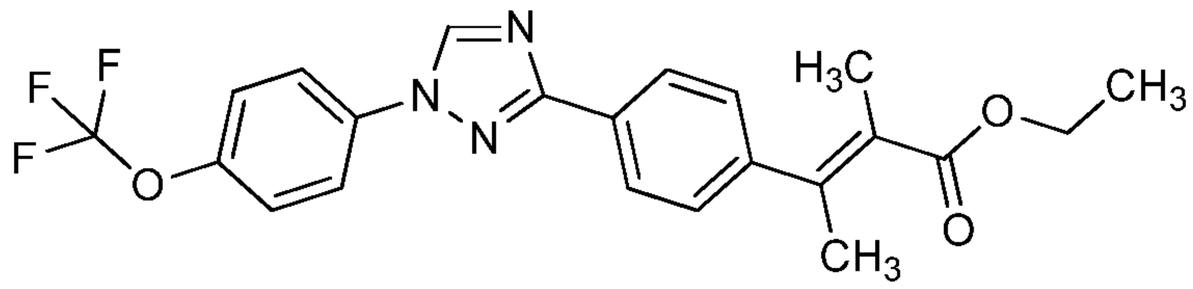
The following compounds were prepared in accordance to the procedure in Example 13.

Preparation of (*E*)-ethyl 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (C18)



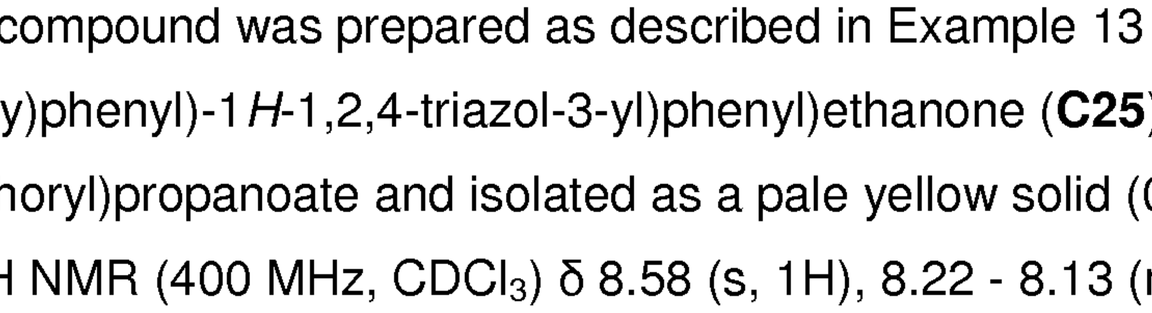
The title compound was prepared as described in Example 13 from 4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde and isolated as a white solid (2.08 g, 100%): mp 149–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.32 - 8.16 (m, 2H), 7.89 - 7.77 (m, 2H), 7.73 (d, *J* = 16.0 Hz, 1H), 7.68 - 7.58 (m, 2H), 7.47 - 7.35 (m, 2H), 6.51 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.89, -87.85, -87.86; ESIMS *m/z* 454 ($[M+H]^+$).

Preparation of (*E*)-ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoate (CA4)



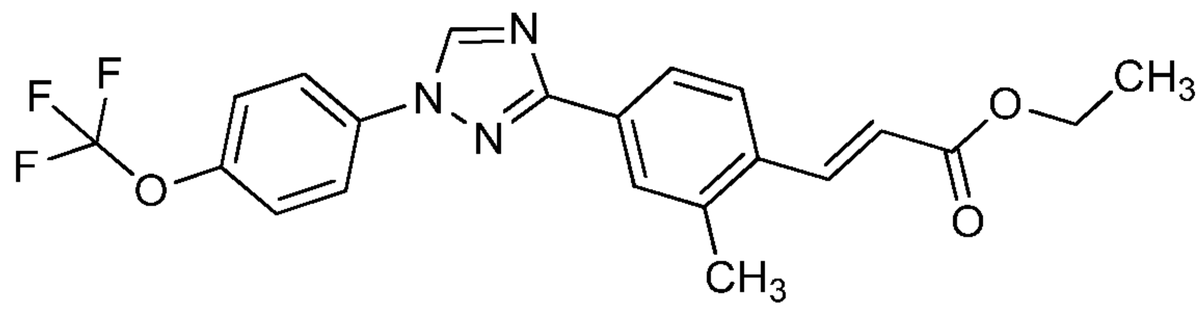
The title compound was prepared as described in Example 13 from 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanone (**C25**) and ethyl 2-(diethoxyphosphoryl)propanoate and isolated as a pale yellow solid (0.480 g, 27%): mp 68-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.22 - 8.13 (m, 2H), 7.86 - 7.77 (m, 2H), 7.40 (dt, *J* = 8.0, 1.0 Hz, 2H), 7.31 - 7.25 (m, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.29 (q, *J* = 1.5 Hz, 3H), 1.80 (q, *J* = 1.5 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.91, 163.24, 148.37, 144.86, 144.66, 141.54, 135.56, 129.10, 127.77, 126.57, 125.32, 122.42, 121.18, 60.45, 22.94, 17.45, 14.32; ESIMS *m/z* 432 ($[M+H]^+$).

Preparation of (*E*)- ethyl 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (CA5)



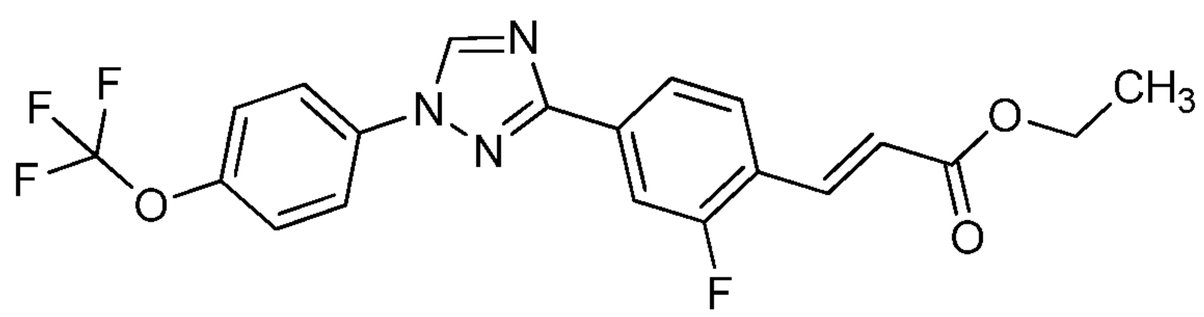
The title compound was prepared as described in Example 13 from 4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde and isolated as a pale yellow solid (4.02 g, 100%): mp 135-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.23 (d, *J* = 8.3 Hz, 2H), 7.95 - 7.88 (m, 2H), 7.81 (dt, *J* = 8.3, 0.7 Hz, 2H), 7.73 (d, *J* = 16.0 Hz, 1H), 7.69 - 7.56 (m, 2H), 6.51 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.41 - 1.31 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.50; ESIMS *m/z* 388 ($[M+H]^+$).

Preparation of (*E*)-ethyl 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (CB12)



The title compound was prepared as described in Example 13 from 2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (**CB35**) and isolated as a white solid (1.16 g, 98%): mp 157-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.10 - 7.96 (m, 3H), 7.84 - 7.76 (m, 2H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.40 (dt, *J* = 8.1, 1.0 Hz, 2H), 6.44 (d, *J* = 15.9 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.53 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 418 ($[M+H]^+$).

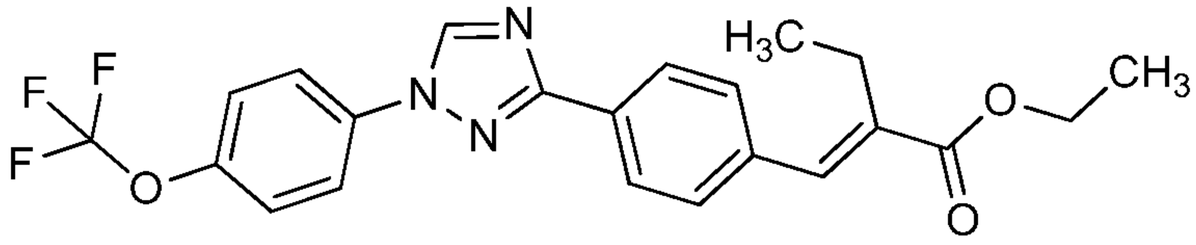
Preparation of (*E*)-ethyl 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (CB13)



The title compound was prepared as described in Example 13 from 2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (**CB36**) and isolated as a light orange solid (1.1 g, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.03 - 7.91 (m, 2H), 7.80 (d, *J* = 9.0 Hz, 2H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.40 (dt, *J*

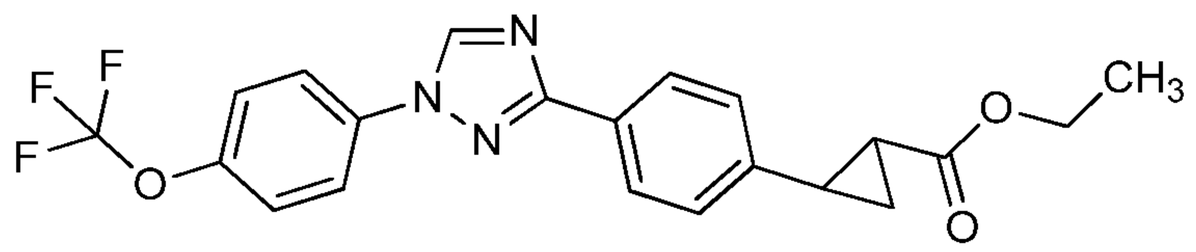
= 8.1, 1.0 Hz, 2H), 6.63 (s, 1H), 6.59 (s, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ESIMS *m/z* 422 ([M+H]$^+$).

Preparation of (*E/Z*)-ethyl 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylidene)butanoate (CB14)



The title compound was prepared as described in Example 13 from 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde and ethyl 2-(diethoxyphosphoryl)butanoate; isolated as a yellow solid (4.36 g, 102%) as mixture of *E* and *Z* isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.53 (m, 1H), 8.29 – 8.10 (m, 2H), 7.86 – 7.66 (m, 3H), 7.58 – 7.48 (m, 2H), 7.44 – 7.31 (m, 2H), 4.23 (dq, *J* = 53.7, 7.1 Hz, 2H), 2.70 – 2.42 (m, 2H), 1.42 – 1.09 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 432 ([M+H]$^+$).

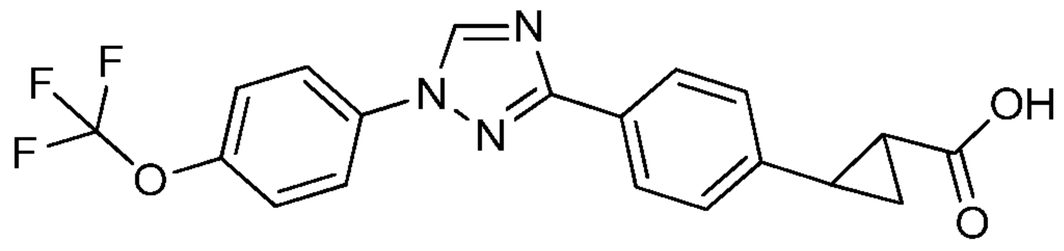
Example 14: Preparation of ethyl 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarboxylate (C19)



To an oven-dried round bottomed flask was added sodium hydride (60% oil immersion, 0.380 g, 9.50 mmol) and anhydrous dimethyl sulfoxide (30 mL). Gas evolution occurred, and the solution was stirred at room temperature for 15 minutes. Trimethylsulfoxonium iodide (2.10 g, 9.54 mmol) was added, the flask neck was rinsed with anhydrous dimethyl sulfoxide (5 mL), and the reaction was stirred for 15 minutes. To the reaction was added (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**C17**) (3.22 g, 7.98 mmol) as a solid. The reaction was stirred at room temperature for 30 minutes, and then quenched with water and extracted with 1:1 ethyl acetate/hexanes (2x). The combined organic layers were washed with water (3x), dried over anhydrous sodium sulfate, filtered, and concentrated to afford the title compound as a yellow oil (1.50 g, 41%): ^{1}H NMR

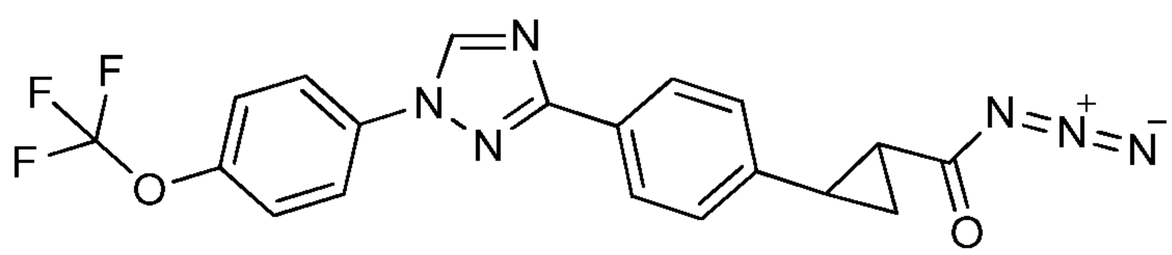
(400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 9.1 Hz, 2H), 7.39 (dd, *J* = 6.6, 5.9 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 4.19 (dt, *J* = 14.0, 7.0 Hz, 2H), 2.64 - 2.52 (m, 2H), 1.97 (ddd, *J* = 8.5, 5.3, 4.2 Hz, 1H), 1.71 - 1.61 (m, 1H), 1.42 - 1.32 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 418 ($[M+H]^+$).

Example 15: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarboxylic acid (C20)



To ethyl 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)-cyclopropane-carboxylate (**C19**) (1.50 g, 3.59 mmol) in methanol (24 mL) was added sodium hydroxide (2 N, 7.20 mL, 14.4 mmol) and stirred at room temperature for 4 hours. The reaction was acidified with hydrogen chloride (2 N) and the methanol was evaporated off under vacuum. The aqueous solution was extracted with ethyl acetate (2x), dried over anhydrous sodium sulfate, filtered, and concentrated to afford the title compound as a yellow oil (1.62 g, 98%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.13 - 8.08 (m, 2H), 7.83 - 7.77 (m, 3H), 7.40 (t, *J* = 5.9 Hz, 4H), 7.22 (d, *J* = 8.3 Hz, 2H), 2.65 (ddd, *J* = 6.7, 5.3, 2.8 Hz, 2H), 2.03 - 1.95 (m, 1H), 1.76 - 1.66 (m, 2H), 1.47 (ddd, *J* = 8.4, 6.6, 4.7 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 390 ($[M+H]^+$).

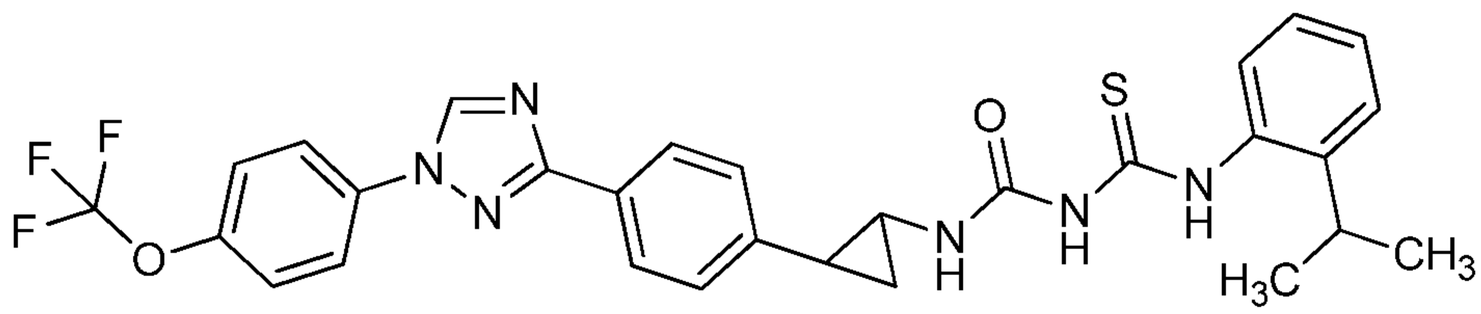
Example 16: Preparation 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (C21)



To 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)-cyclopropanecarboxylic acid (**C20**) (2.49 g, 6.40 mmol) in toluene (30 mL) was added triethylamine (2.20 mL, 16.0 mmol), followed by diphenyl phosphorazidate (1.70 mL, 8.00 mmol). The yellow solution was stirred overnight at room temperature. The

reaction was quenched with water and saturated aqueous sodium bicarbonate, extracted with 1:1 ethyl acetate/hexanes (2x), dried over anhydrous sodium sulfate, and filtered. The crude compound was adsorbed onto silica gel and purified by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent to afford the title compound as a yellow oil (1.94 g, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.16 - 8.03 (m, 2H), 7.83 - 7.72 (m, 2H), 7.44 - 7.34 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 2.70 (ddd, *J* = 9.3, 6.8, 4.1 Hz, 1H), 1.98 (ddd, *J* = 8.4, 5.3, 4.1 Hz, 1H), 1.78 (dt, *J* = 9.4, 5.0 Hz, 1H), 1.53 (ddd, *J* = 8.3, 6.8, 4.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03.

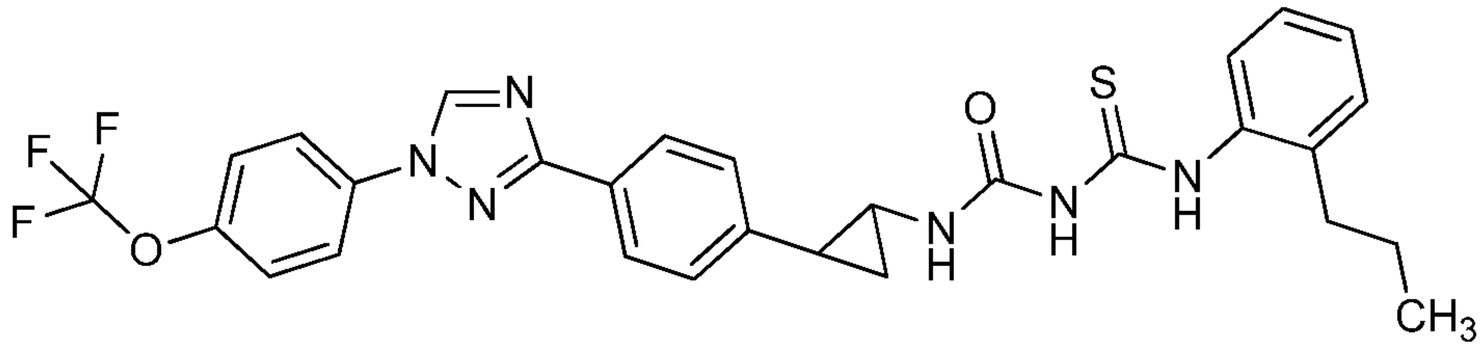
Example 17: Preparation of *N*-[2-(propan-2-yl)phenyl]-*N'*-,2-(4-{1-[4-(trifluoro methoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (F22)



A solution of (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) (0.250 g, 0.600 mmol) in 1,2-dichloroethane (3 mL) was heated at 80 °C for 3 hours. The reaction was cooled and 2-(isopropylphenyl)thiourea (0.129 g, 0.660 mmol) and cesium carbonate (0.443 g, 1.36 mmol) were added. The reaction mixture was stirred at room temperature overnight, and then diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated. The crude compound was loaded onto a Celite® cartridge with dichloromethane and purified by flash column chromatography using 0-40% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as a white solid (0.108 g, 31%).

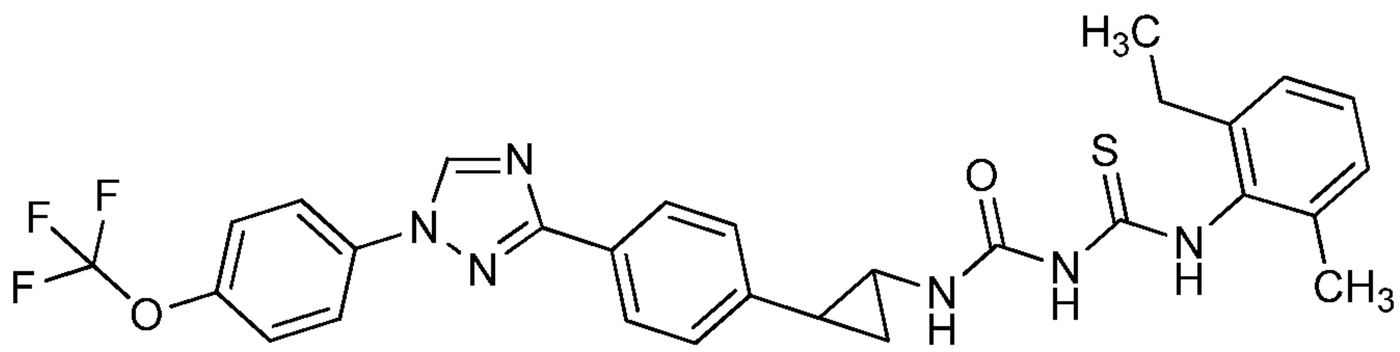
The following compounds were prepared in accordance to the procedure in Example 17.

Preparation of *N*-(2-propylphenyl)-*N'*-[(2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (F23)



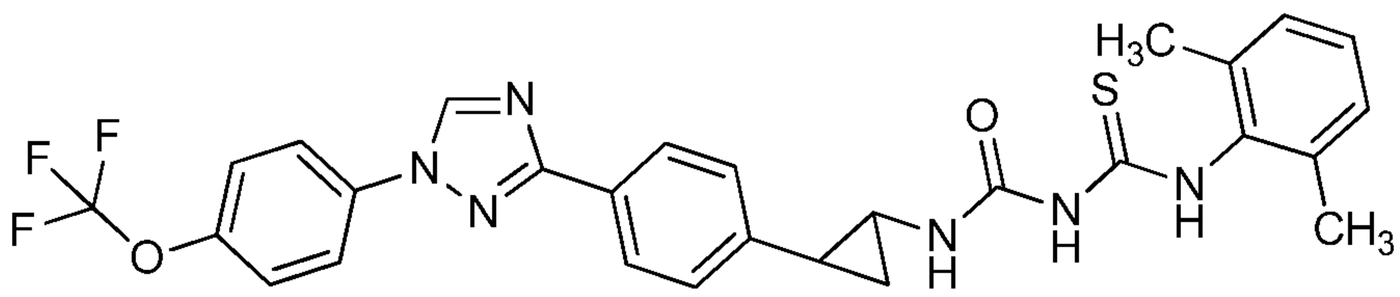
The title compound was prepared as described in Example 17 using (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) and 1-(2-propylphenyl)thiourea and isolated as an off-white solid (0.059 g, 18%).

Preparation of *N*-(2-ethyl-6-methylphenyl)-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (F24)



The title compound was prepared as described in Example 17 using (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) and isolated as a white solid (0.105 g, 33%).

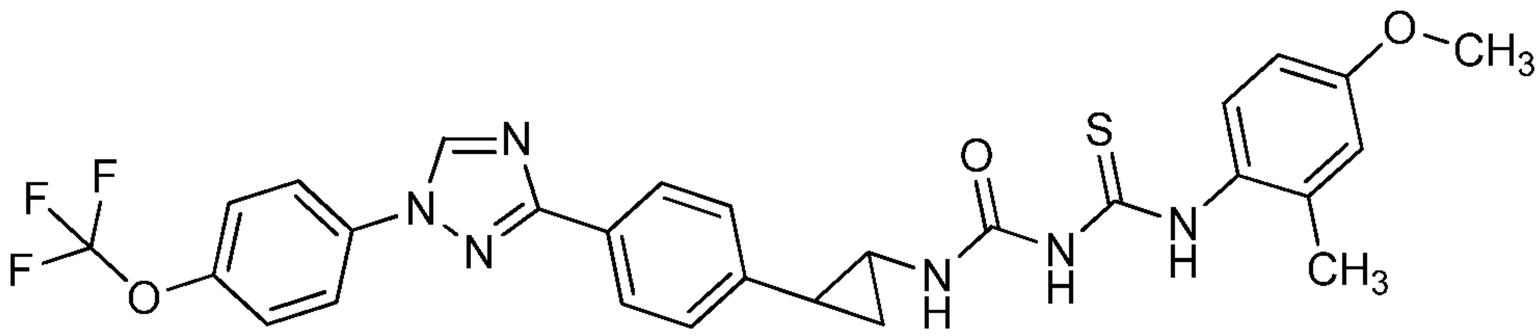
Preparation of *N*-(2,6-dimethylphenyl)-*N'*-[(2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (F25)



The title compound was prepared as described in Example 17 using (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) and 1-(2,6-dimethylphenyl)thiourea and isolated as a white solid (0.105 g, 29%).

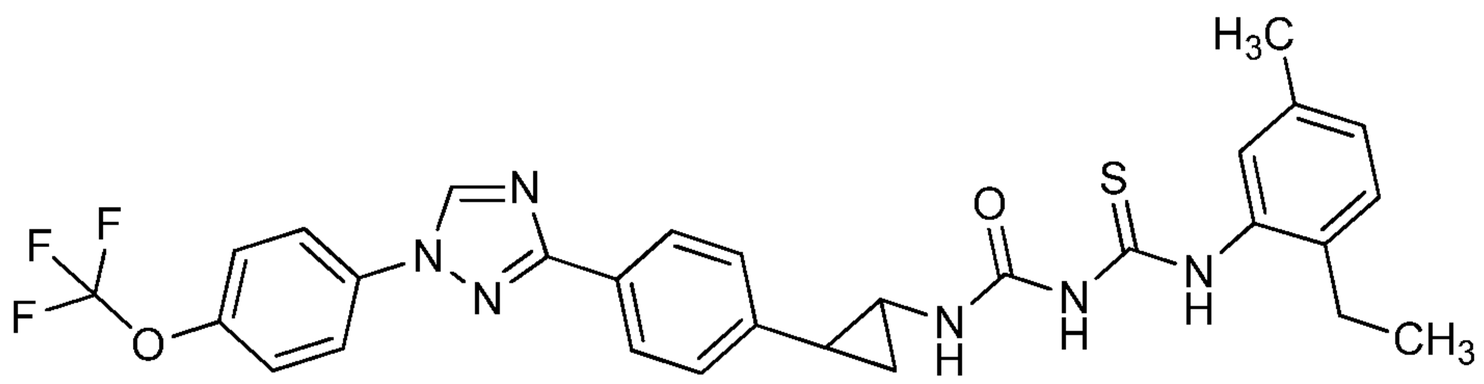
Preparation of *N*-(4-methoxy-2-methylphenyl)-*N'*-[(2-(4-{1-[4-(trifluoromethoxy)

phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (F26)



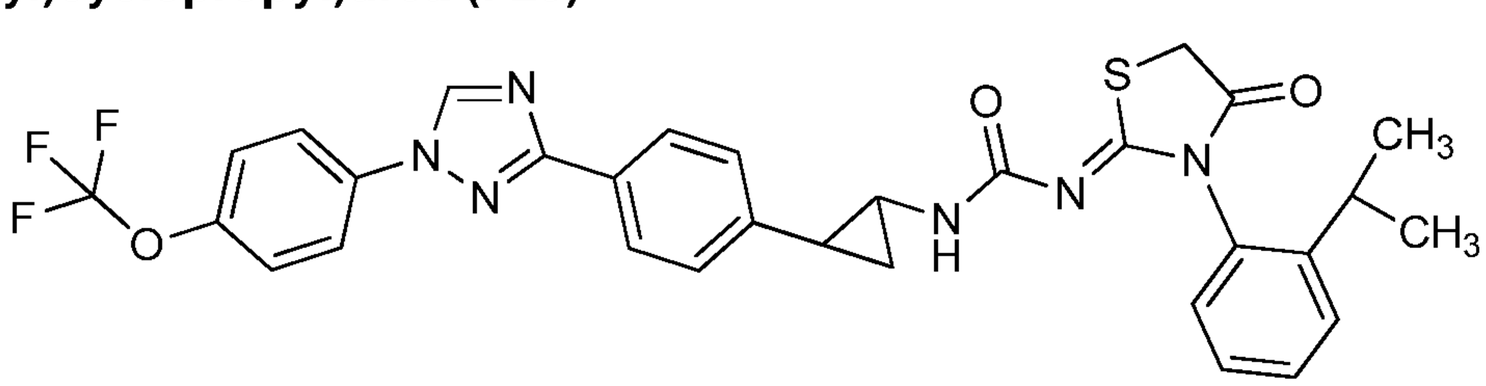
The title compound was prepared as described in Example 17 using (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as a white oily solid (0.009 g, 3%).

Preparation of *N*-(2-ethyl-5-methylphenyl)-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (F27)



The title compound was prepared as described in Example 17 using (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) and 1-(2-ethyl-5-methylphenyl)thiourea (**CA41**) and isolated as an off-white solid (0.069 g, 22%).

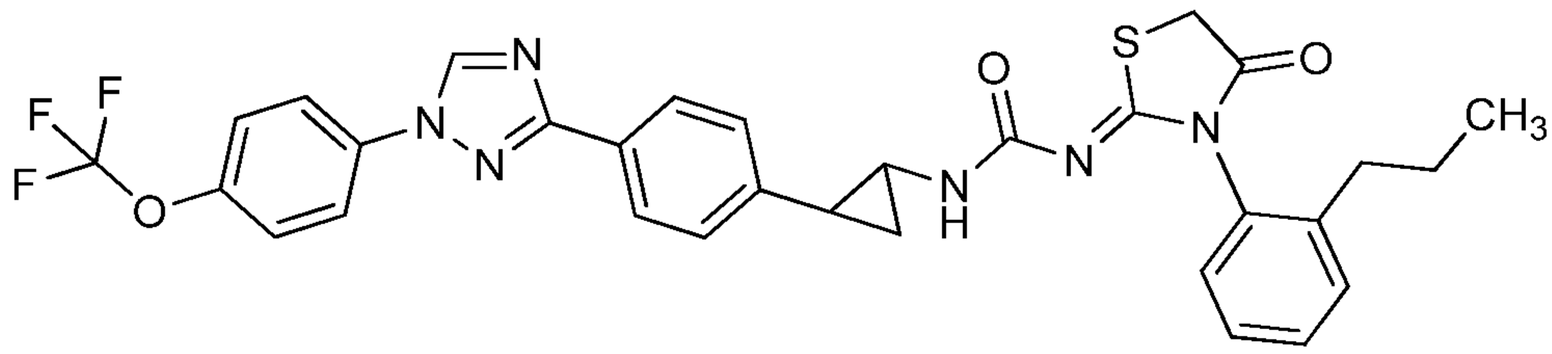
Example 18: Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropyl)urea (F29)



A solution of *N*-[2-(propan-2-yl)phenyl]-*N'*-,2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (**F22**) (0.082 g, 0.14 mmol), methyl 2-bromoacetate (0.020 mL, 0.21 mmol), and sodium acetate (0.027 g, 0.33 mmol) in ethanol (1.8 mL) was heated at 65 °C overnight. The reaction was cooled, loaded onto a Celite® cartridge, and purified by flash column chromatography using 0-40% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as an off-white solid (0.061 g, 68%).

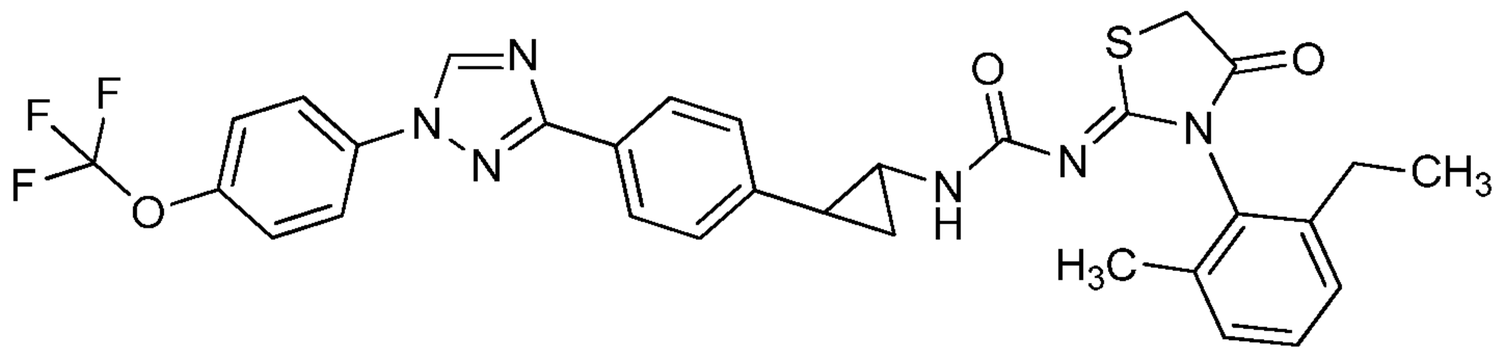
The following compounds were prepared in accordance to the procedure in Example 18.

Preparation of (*Z*)-1-(4-oxo-3-(2-propylphenyl)thiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropyl)urea (F30)



The title compound was prepared as described in Example 18 from *N*-(2-propylphenyl)-*N'*-[(2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (**F23**) and isolated as an off-white oily solid (0.026 g, 68%).

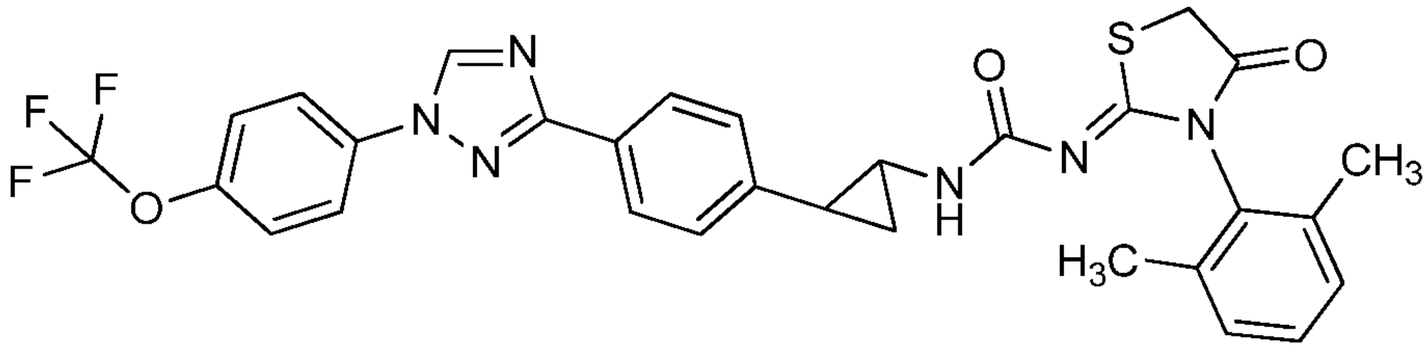
Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropyl)urea (F31)



The title compound was prepared as described in Example 18 from *N*-(2-ethyl-6-methylphenyl)-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-

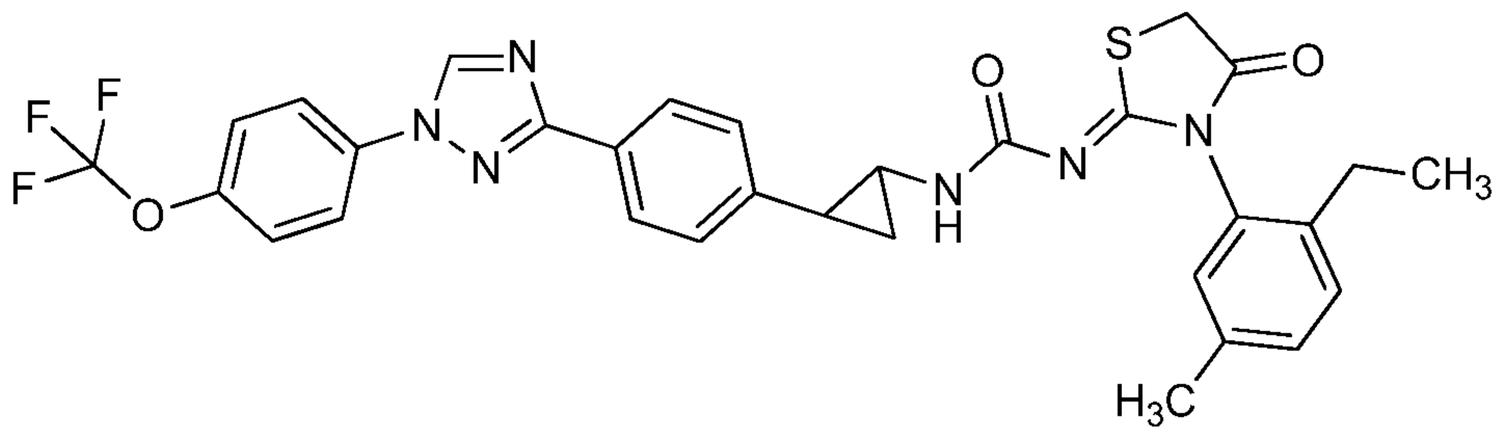
yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (**F24**) and isolated as an oil (0.006 g, 8%).

Preparation of (*Z*)-1-(3-(2,6-dimethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropyl)urea (F32)



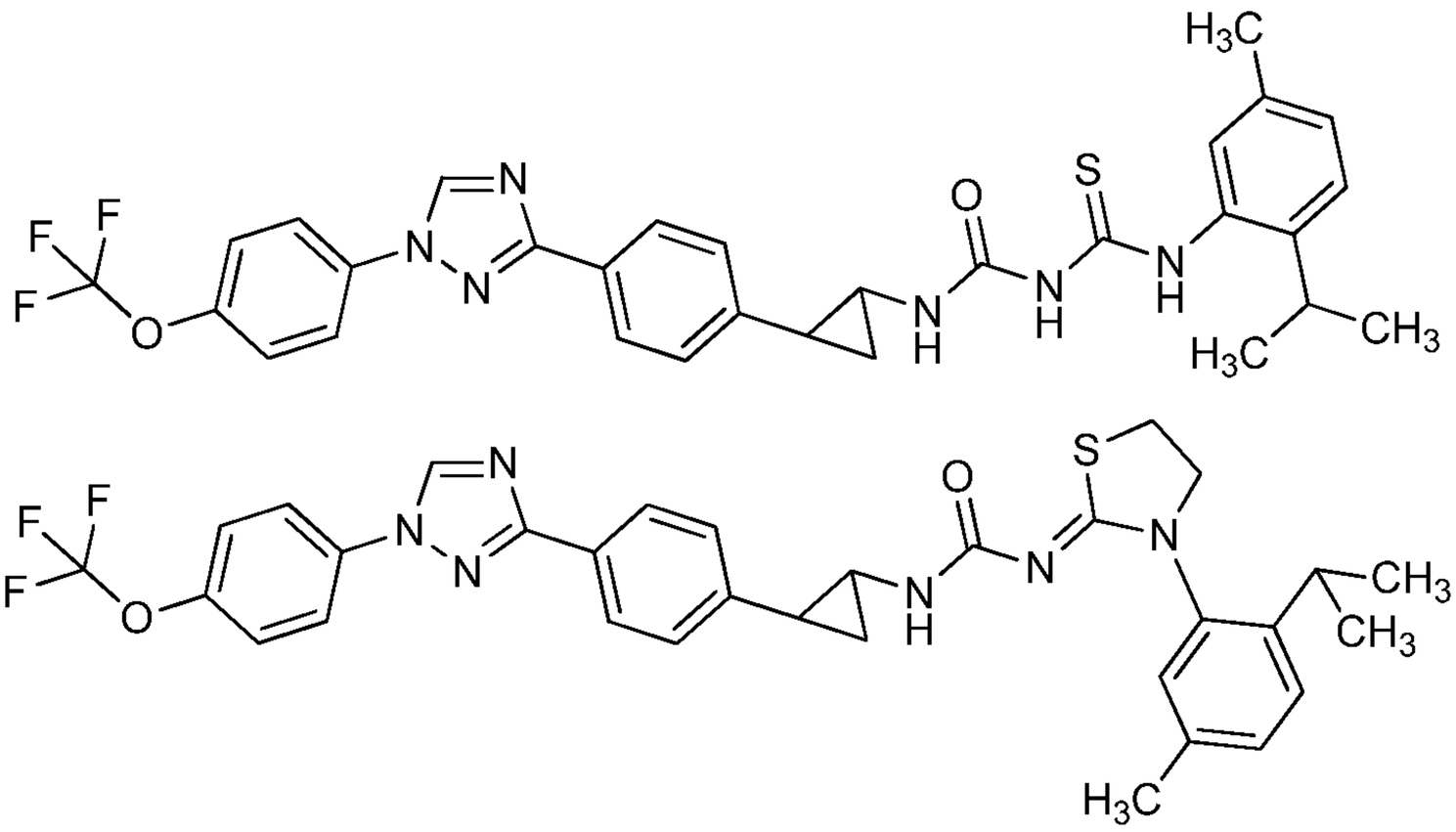
The title compound was prepared as described in Example 18 from *N*-(2,6-dimethylphenyl)-*N'*-[(2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (**F25**) and isolated as an oil (0.006 g, 7%).

Preparation of (*Z*)-1-(3-(2-ethyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropyl)urea (F33)



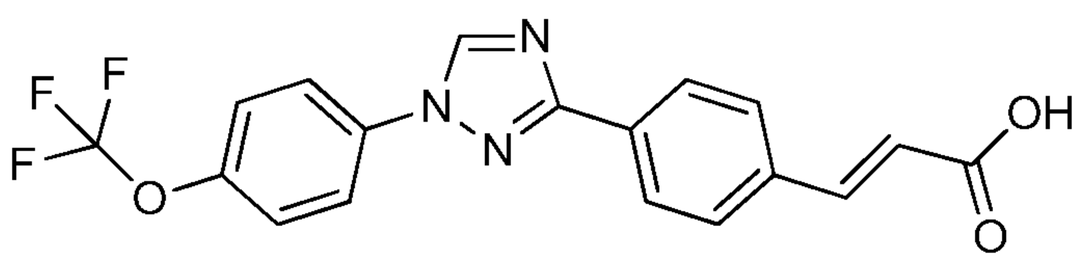
The title compound was prepared as described in Example 18 from *N*-(2-ethyl-5-methylphenyl)-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl]dicarbonimidothioic diamide (**F27**) and isolated as a yellow solid (0.035 g, 71%).

Example 19: Preparation of *N*-[5-methyl-2-(propan-2-yl)phenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)cyclopropyl] dicarbonimidothioic diamide (F28) and (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)thiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)-phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropyl)urea (F34)



A solution of (2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclopropanecarbonyl azide (**C21**) (0.210 g, 0.510 mmol) in 1,2-dichloroethane (2.5 mL) was heated at 80 °C for 3 hours. The reaction was cooled to room temperature and 1-(2-isopropyl-5-methylphenyl)thiourea (0.127 g, 0.610 mmol) and cesium carbonate (0.345 g, 1.06 mmol) were added. The reaction mixture was stirred at room temperature overnight. The reaction was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate (2x), the organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge with dichloromethane and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound (**F28**) as a white solid (0.025 g, 8%) and the title compound (**F34**) as a yellow oil (0.028 g, 8%).

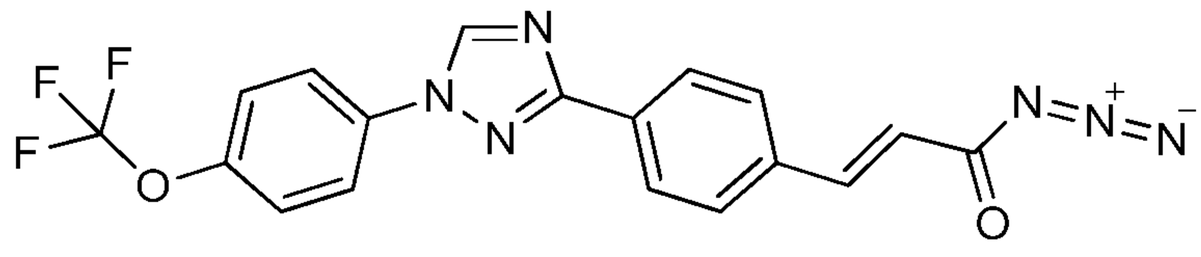
Example 20: Preparation of (*E*)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylic acid (C22)



To (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**C17**) (1.95 g, 4.83 mmol) in methanol (25 mL) was added sodium hydroxide (2 N, 10 mL, 20.0 mmol) and the solution was stirred at room temperature

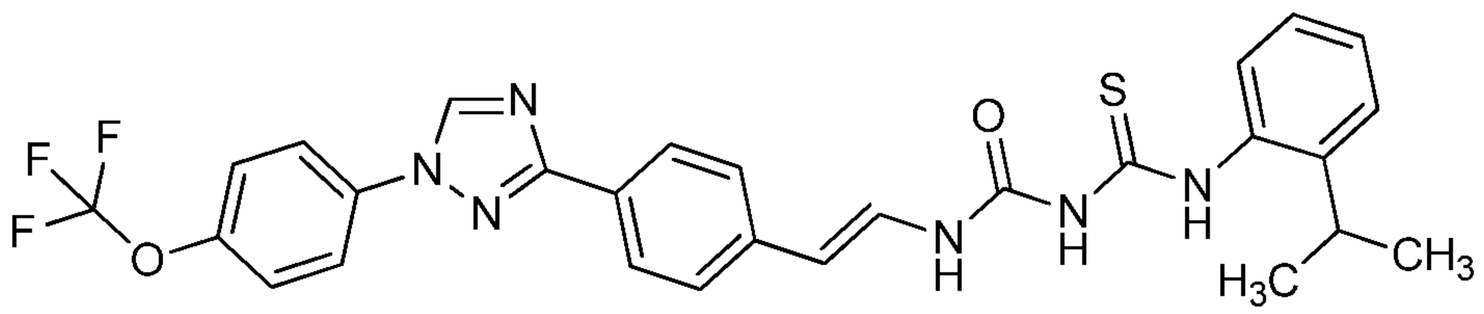
overnight. The methanol was evaporated off under reduced pressure, the reagents were diluted with acetonitrile, and additional sodium hydroxide (2 N, 20 mL, 40.0 mmol) was added. The reaction was stirred at room temperature for 5 hours and then acidified with hydrogen chloride (2 N). The white precipitate was vacuum-filtered to afford the title compound as a white solid (1.72 g, 94%): mp 239–241 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 9.44 (s, 1H), 8.14 (d, J = 8.4 Hz, 2H), 8.12 - 8.05 (m, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.69 - 7.59 (m, 3H), 6.61 (d, J = 16.0 Hz, 1H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS m/z 376 ([M+H]$^+$).

Example 21: Preparation of (*E*)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acryloyl azide (C23)



To (*E*)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylic acid (**C22**) (1.72 g, 4.59 mmol) in isopropanol (15.3 mL) was diphenyl phosphorazidate (1.3 mL, 6.03 mmol) and triethylamine (0.96 mL, 6.89 mmol) and stirred at room temperature for 6 hours. The white precipitate for filtered, rinsed with isopropanol, and dried to afford the title compound as a white solid (1.46 g, 78%): mp 106 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.24 (d, J = 8.4 Hz, 2H), 7.86 - 7.73 (m, 3H), 7.66 (d, J = 8.3 Hz, 2H), 7.40 (d, J = 8.3 Hz, 2H), 6.52 (t, J = 14.6 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS m/z 401 ([M+H]$^+$).

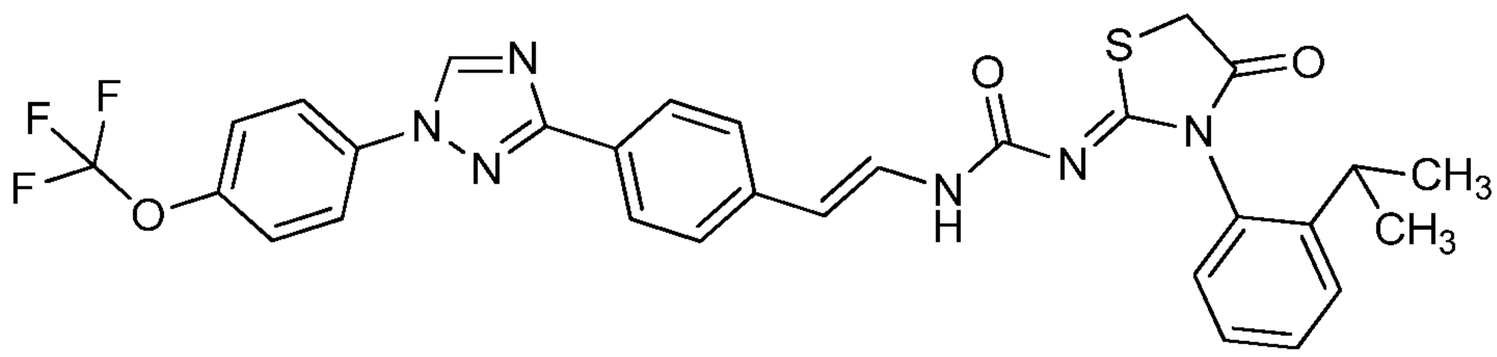
Example 22: Preparation of *N*-[2-(propan-2-yl)phenyl]-*N'*-[(*E*)-2-(4-{1-[4-(trifluoro methoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethenyl]dicarbonimidothioic diamide (F11)



(*E*)-3-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acryloyl azide (**C23**) (0.175 g, 0.440 mmol) in anhydrous acetonitrile (2.2 mL) was heated at 80 °C for 2 hours. The reaction was cooled and 1-(2-isopropylphenyl)thiourea (0.110

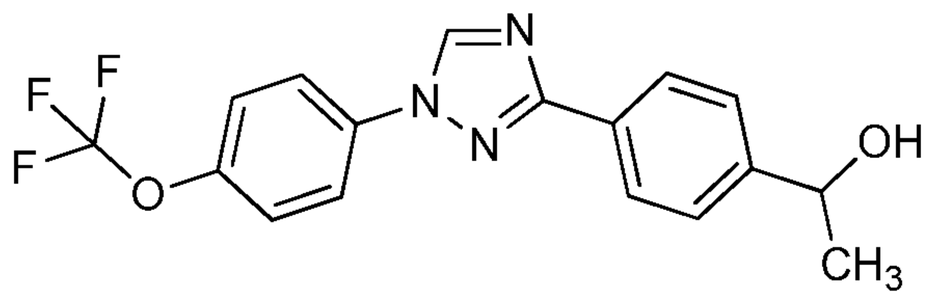
g, 0.570 mmol) and cesium carbonate (0.214 g, 0.660 mmol) were added. The reaction mixture was stirred at room temperature overnight, and then diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-40% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as a yellow solid (0.0800 g, 32%).

Example 23: Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-((*E*)-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)styryl)urea (F12)



To *N*-[2-(propan-2-yl)phenyl]-*N'*-[(*E*)-2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethenyl]dicarbonimidothioic diamide (**F11**) (0.056 g, 0.099 mmol) and sodium acetate (0.020 g, 0.24 mmol) in ethanol (0.86 mL) was added methyl 2-bromoacetate (0.012 mL, 0.12 mmol), and the solution was heated at 65 °C for 2 hours. The reaction mixture was loaded directly onto a Celite® cartridge and purified by flash column chromatography using 0-50% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as an orange solid (0.052 g, 84%).

Example 24: Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanol (C24)

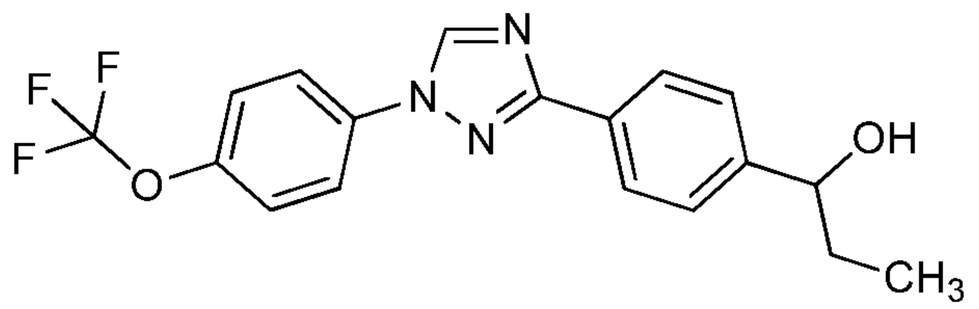


To 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (8.49 g, 25.5 mmol) in anhydrous tetrahydrofuran (102 mL) in dry ice/acetone bath was added methylmagnesium bromide (1 M in butyl ether, 25.5 mL, 25.5 mmol). The

solution was then warmed to room temperature and stirred overnight. The reaction was acidified with hydrogen chloride (2 N, 10 mL) until pH 2, diluted with water, and extracted with ethyl acetate (2x). The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to afford the title compound as an orange liquid (8.80 g, 94%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.27 - 8.11 (m, 2H), 7.90 - 7.68 (m, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 4.98 (q, *J* = 6.5 Hz, 1H), 1.54 (d, *J* = 6.5 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 350 ($[M+H]^+$).

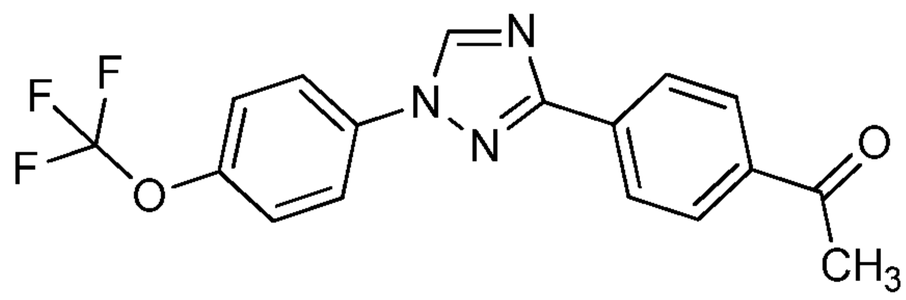
The following compounds were prepared in accordance to the procedure in Example 24.

Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-ol (CA6)



The title compound was prepared as described in Example 24 from 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde and ethylmagnesium bromide and isolated as a yellow oil (5.00 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.20 - 8.12 (m, 2H), 7.85 - 7.76 (m, 2H), 7.50 - 7.44 (m, 2H), 7.39 (dq, *J* = 8.0, 1.0 Hz, 2H), 4.68 (t, *J* = 6.5 Hz, 1H), 1.93 - 1.75 (m, 2H), 1.59 (s, 1H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 364 ($[M+H]^+$).

Example 25: Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanone (C25)

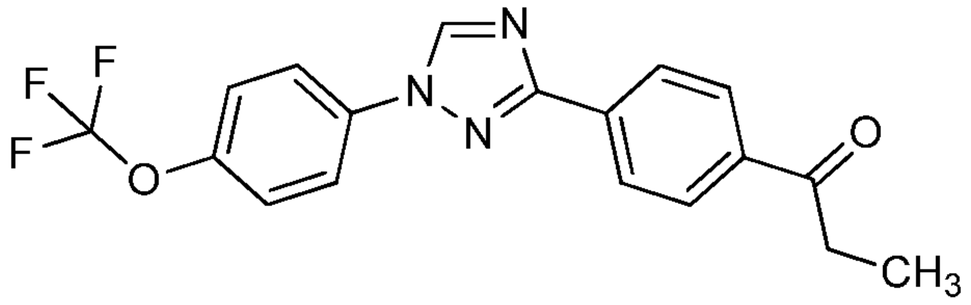


To 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanol (**C24**) (8.80 g, 25.2 mmol) in dichloromethane (168 mL) and dimethyl sulfoxide (84 mL) was added triethylamine (17 mL) and stirred in an ice bath. Pyridine·sulfur

trioxide (16.0 g, 101 mmol) was added in two portions. The reaction was warmed to room temperature over 3 hours, diluted with dichloromethane, and washed with water. The aqueous layer was extracted one additional time with dichloromethane. The combined dichloromethane layers were washed with water, dried over anhydrous sodium sulfate, filtered, and adsorbed onto silica gel. Purification by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent provided the title compound as a white solid (6.71 g, 73%): mp 140–141.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.33 - 8.27 (m, 2H), 8.11 - 8.05 (m, 2H), 7.85 - 7.78 (m, 2H), 7.41 (dd, *J* = 9.0, 0.8 Hz, 2H), 2.66 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.01; ESIMS *m/z* 348 ($[M+H]^+$).

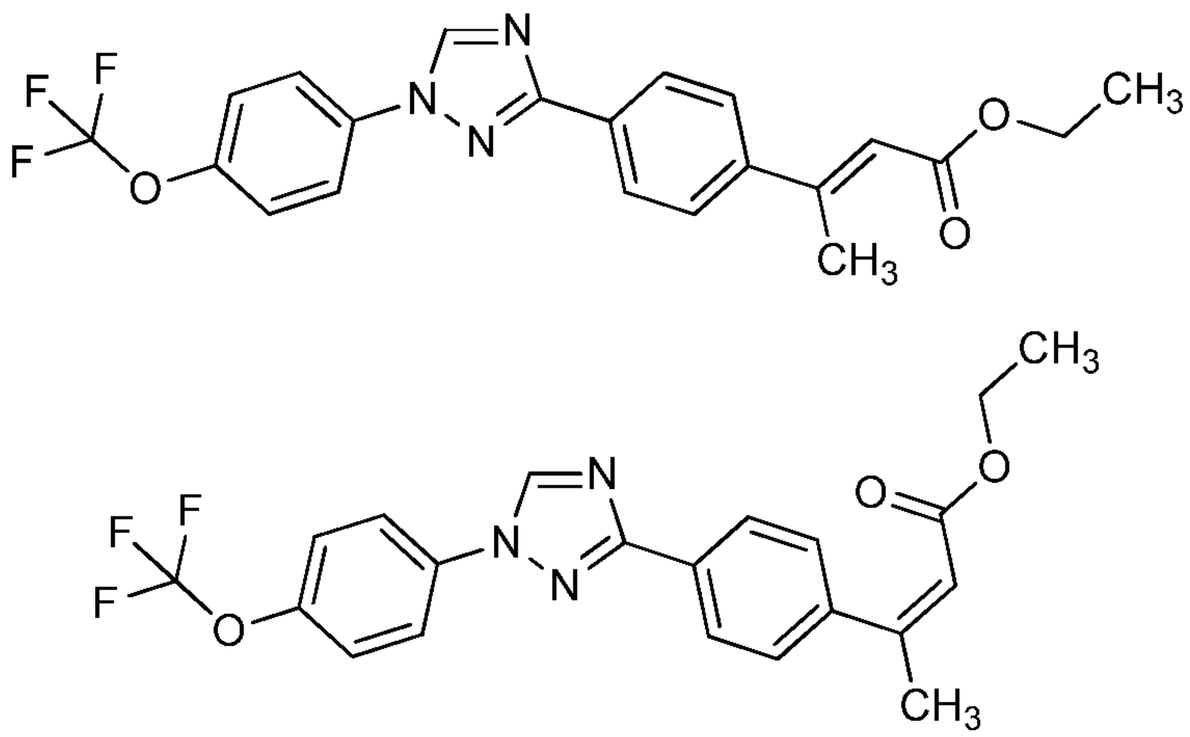
The following compounds were prepared in accordance to the procedure in Example 25.

Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-one (CA7)



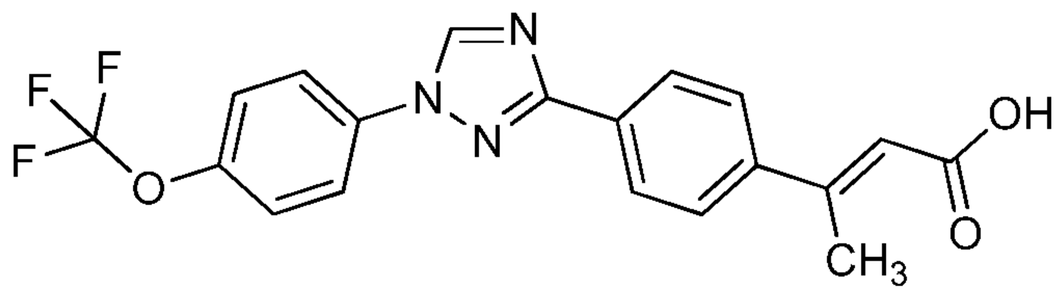
The title compound was prepared from 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-ol (**CA6**) and isolated as a white solid (4.1 g, 63%, 75% pure): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.32 - 8.25 (m, 2H), 8.11 - 8.05 (m, 2H), 7.82 (dd, *J* = 8.9, 1.9 Hz, 2H), 7.41 (dt, *J* = 8.1, 1.0 Hz, 2H), 3.06 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 362 ($[M+H]^+$).

Example 26: Preparation of (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoate (C26) and (*Z*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoate (C27)



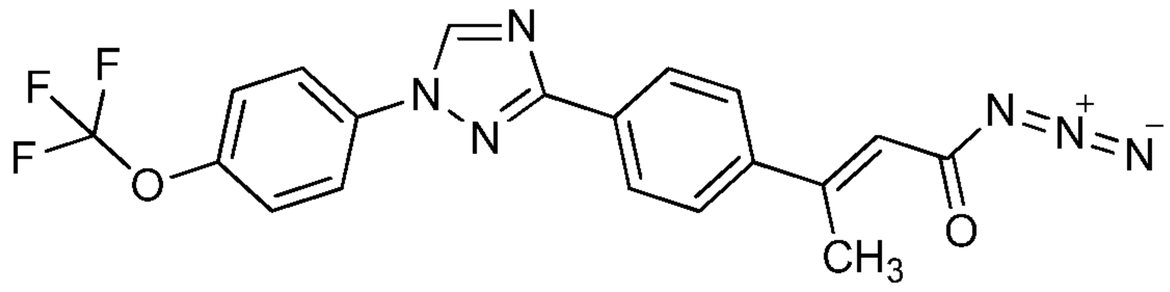
To an oven-dried round bottomed flask was added sodium hydride (60% oil suspension, 0.880 g, 1.53 mmol) and anhydrous tetrahydrofuran (36 mL) and the solution was stirred under nitrogen in an ice bath. Ethyl 2-(diethoxyphosphoryl)acetate (3.4 mL, 17.3 mmol) was added dropwise and stirred for 30 minutes in an ice bath. 1-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanone (**C25**) (5.00 g, 14.4 mmol) was added in solid portions to the solution, in which the solution turned yellow. The reaction was warmed to room temperature overnight, quenched with saturated aqueous ammonium chloride, and extracted with diethyl ether (2x). The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge with dichloromethane, and the cartridge was dried in vacuum oven. Purification by reverse-phase flash column chromatography using 0-100% acetonitrile/water as eluent afforded title compound (**C26**) as a white solid (4.06 g, 67%): mp 109–110.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.28 - 8.16 (m, 2H), 7.88 - 7.77 (m, 2H), 7.66 - 7.55 (m, 2H), 7.45 - 7.34 (m, 2H), 6.22 (d, *J* = 1.3 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.62 (d, *J* = 1.3 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 418 ($[M+H]^+$), and title compound (**C27**) as a white solid (1.08 g, 18%): mp 83–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.22 - 8.15 (m, 2H), 7.86 - 7.76 (m, 2H), 7.39 (dd, *J* = 9.0, 0.8 Hz, 2H), 7.36 - 7.31 (m, 2H), 5.95 (d, *J* = 1.4 Hz, 1H), 4.02 (q, *J* = 7.1 Hz, 2H), 2.22 (d, *J* = 1.4 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 418 ($[M+H]^+$).

Example 27: Preparation of (*E*)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoic acid (C28)



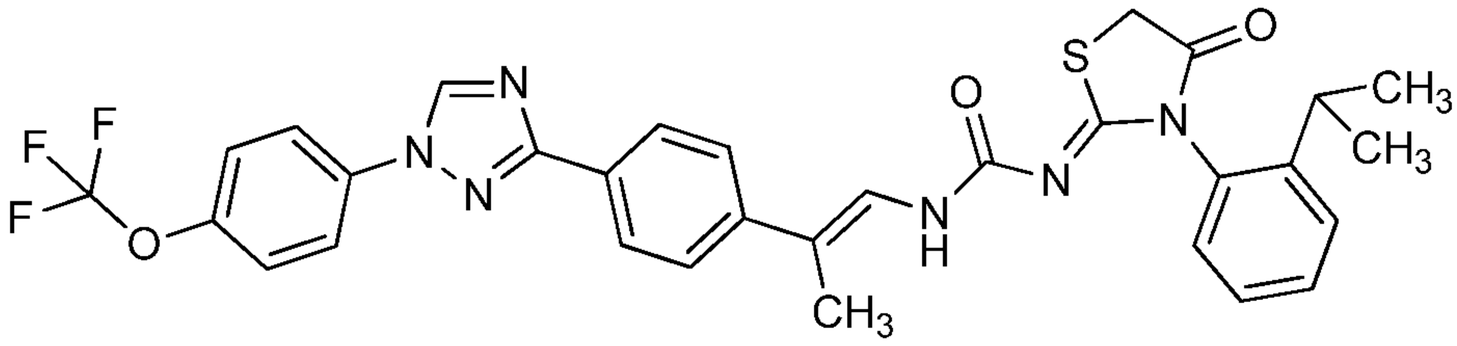
To (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoate (**C26**) (1.30 g, 3.10 mmol) in methanol (10 mL) was added sodium hydroxide (2 N, 12.3 mL, 24.6 mmol) and stirred at room temperature overnight. Additional sodium hydroxide (2 N) was added and the reaction was heated to 50 °C for 3 days. The reaction was acidified with hydrogen chloride (2 N) and the white precipitate was collected by vacuum filtration to afford the title compound as a white solid (1.16 g, 95%): mp 234–238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.32 (s, 1H), 9.43 (s, 1H), 8.14 (d, J = 8.6 Hz, 2H), 8.09 (d, J = 9.1 Hz, 2H), 7.73 (d, J = 8.6 Hz, 2H), 7.68 - 7.53 (m, 2H), 6.22 (d, J = 1.3 Hz, 1H), 2.54 (d, J = 1.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 390 ([M+H]$^{+}$).

Example 28: Preparation of (*E*)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoyl azide (C29)



To (*E*)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoic acid (**C28**) (1.14 g, 2.93 mmol) in isopropanol (9.8 mL) was added triethylamine (0.53 mL, 3.81 mmol) and diphenyl phosphorazidate (0.68 mL, 3.23 mmol). The reaction was stirred at room temperature overnight. The white precipitate was vacuum-filtered and dried in a vacuum oven to afford the title compound as a white solid (0.978 g, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.25 - 8.19 (m, 2H), 7.85 - 7.78 (m, 2H), 7.65 - 7.58 (m, 2H), 7.44 - 7.37 (m, 2H), 6.16 (d, J = 1.3 Hz, 1H), 2.68 (d, J = 1.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 387 ([M+H]$^{+}$) (isocyanate).

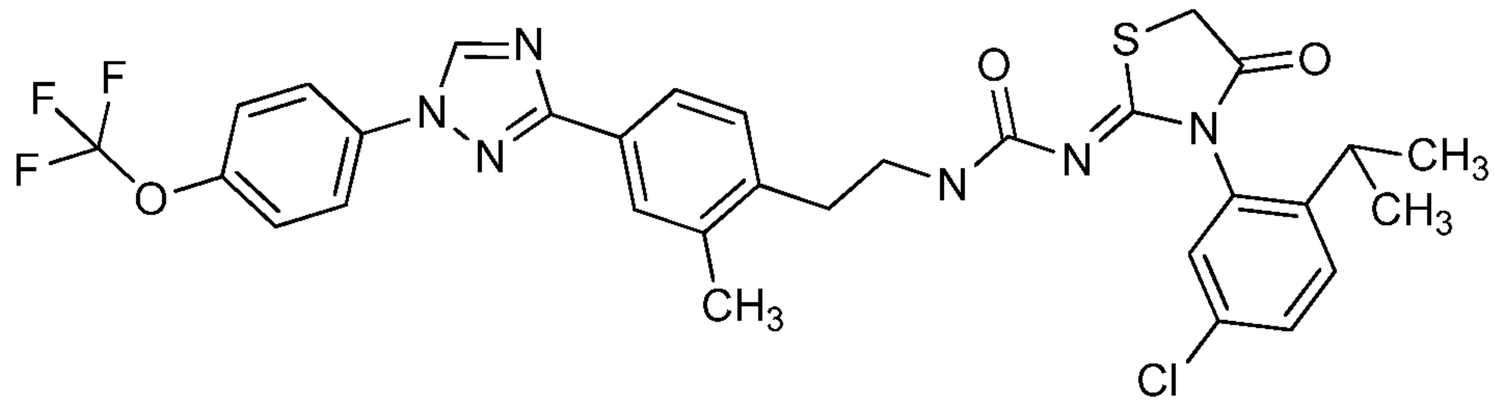
Example 29: Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-((*E*)-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)prop-1-en-1-yl)urea (F13)



(*E*)-3-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoyl azide (**C29**) (0.28 g, 0.68 mmol) in acetonitrile (3.4 mL) was heated at 80 °C for 3 hours. The reaction was cooled and 1-(2-isopropylphenyl)thiourea (0.14 g, 0.74 mmol) and cesium carbonate (0.28 g, 0.86 mmol) were added. The reaction was stirred at room temperature overnight, diluted with ethyl acetate and washed with water. The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to provide an orange foam. To the crude material (0.39 g) was added sodium acetate (0.082 g, 1.0 mmol), ethanol (3.4 mL), and methyl 2-bromoacetate (0.10 mL, 1.0 mmol). The reaction mixture was heated at 65 °C for 3 hours. The reaction was cooled, diluted with ethyl acetate, and washed with water. The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude compound was loaded onto a Celite® cartridge with dichloromethane and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as an orange sticky gum (0.16 g, 37%).

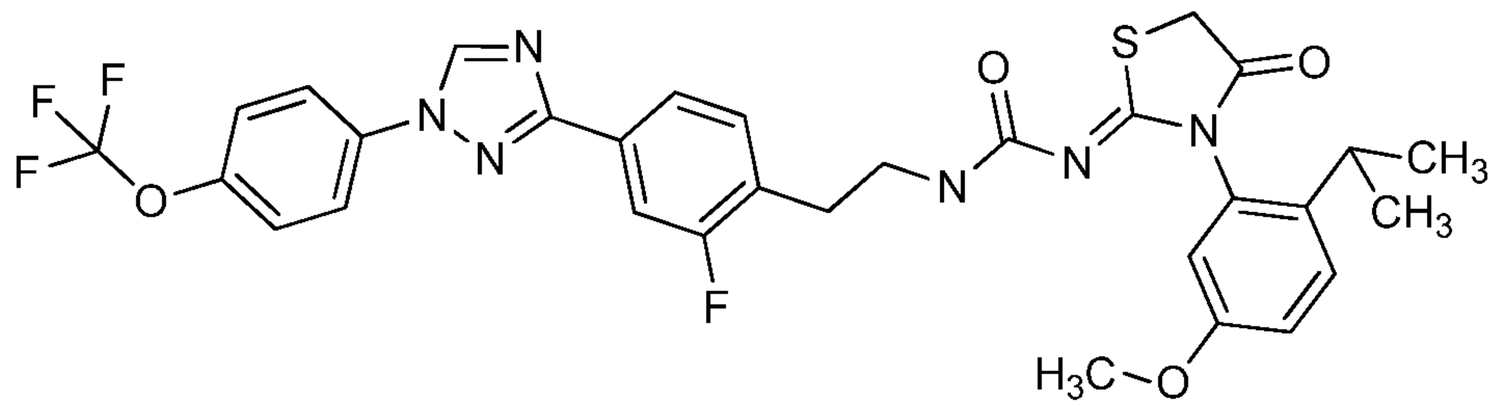
The following compounds were prepared in accordance to the procedure in Example 29.

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB7)



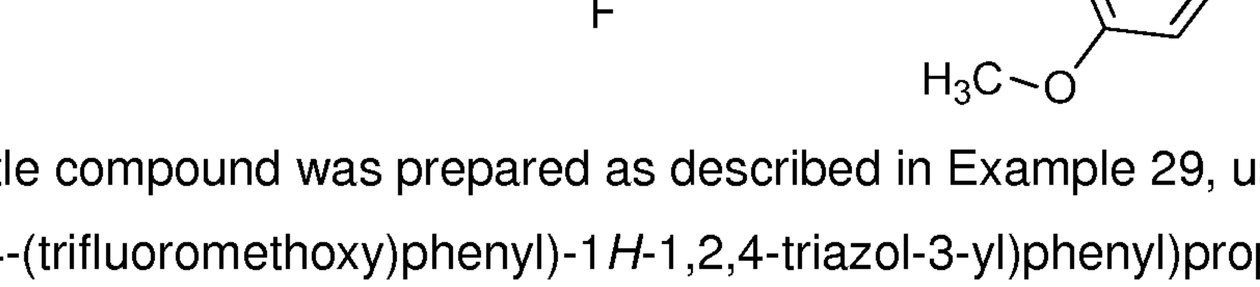
The title compound was prepared as described in Example 29, using 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**CB20**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and heating to a temperature of 60 ºC after methyl 2-bromoacetate was added; purified via reverse phase chromatography and isolated as a pink solid (0.033 g, 17%).

Preparation of (*Z*)-1-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)-3-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)urea (FB9)



The title compound was prepared as described in Example 29, using 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**CB21**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and heating to a temperature of 60 ºC when methyl 2-bromoacetate added; purified via reverse phase chromatography and isolated as a pink solid (0.023 g, 11%).

Example 30: Preparation of ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (C30)

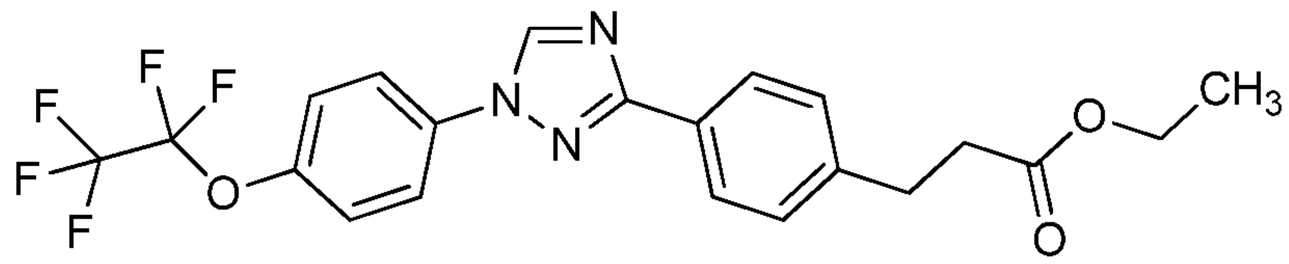


A mixture of (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**C17**) (1.08 g, 2.68 mmol) and palladium on carbon (10%, 0.285 g,

0.270 mmol) in ethyl acetate (10.7 mL) was stirred at room temperature. The reaction flask was evacuated under vacuum, backfilled with nitrogen, evacuated under vacuum again, and then backfilled with hydrogen by balloon (~1 atm). The reaction was stirred at room temperature overnight and then filtered through a pad of Celite® and concentrated to afford the title compound as a gray oil that solidified to a wax upon standing at room temperature (0.999 g, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.14 - 8.07 (m, 2H), 7.80 (d, *J* = 9.1 Hz, 2H), 7.42 - 7.36 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.02 (t, *J* = 7.8 Hz, 2H), 2.67 (t, *J* = 7.8 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 406 ($[M+H]^+$).

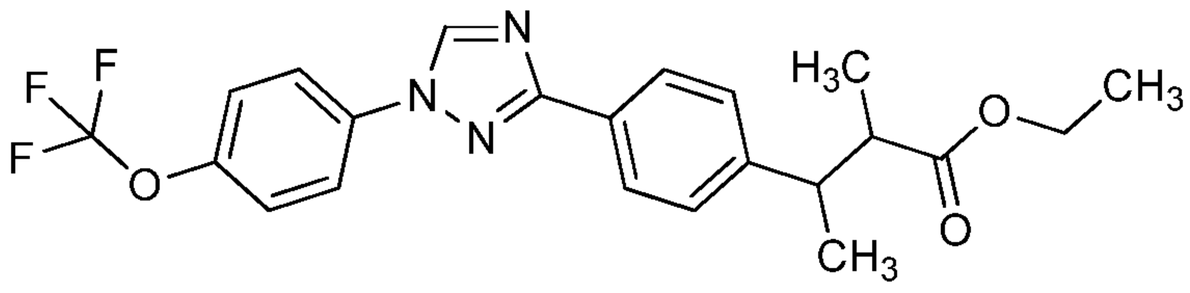
The following compounds were prepared in accordance to the procedure in Example 30.

Preparation of ethyl 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (C31)



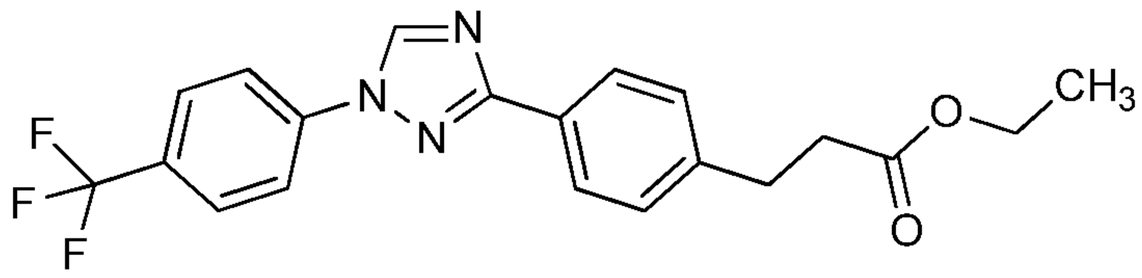
The title compound was prepared from (*E*)-ethyl 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**C18**) and isolated as an off-white fluffy solid (2.00 g, 97%): mp 109–110.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 1.3 Hz, 1H), 8.14 - 8.08 (m, 2H), 7.84 - 7.77 (m, 2H), 7.42 - 7.36 (m, 2H), 7.35 - 7.29 (m, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.02 (t, *J* = 7.8 Hz, 2H), 2.67 (dd, *J* = 8.3, 7.2 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.90, -87.85; ESIMS *m/z* 456 ($[M+H]^+$).

Preparation of ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoate (CA8)



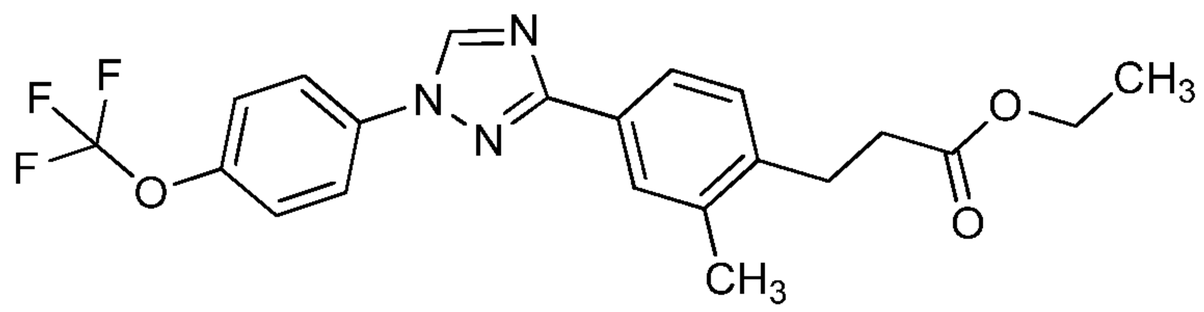
The title compound was prepared from (*E*)-ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoate (**CA4**) and isolated as a yellow oil (0.495 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.12 - 8.05 (m, 2H), 7.83 - 7.73 (m, 2H), 7.38 (dq, *J* = 8.0, 1.1 Hz, 2H), 7.34 - 7.29 (m, 2H), 3.94 (q, *J* = 7.1 Hz, 2H), 3.11 (dq, *J* = 8.8, 7.1 Hz, 1H), 2.69 (dd, *J* = 8.6, 6.9 Hz, 1H), 1.31 (d, *J* = 7.1 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 434 ($[M+H]^+$).

Preparation of ethyl 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (CA9)



The title compound was prepared from (*E*)-ethyl 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**CA5**) and isolated as a white solid (3.88 g, 96%): mp 81-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.12 (d, *J* = 8.2 Hz, 2H), 7.91 (dt, *J* = 8.2, 0.8 Hz, 2H), 7.83 - 7.74 (m, 2H), 7.33 (dd, *J* = 8.0, 0.7 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.02 (t, *J* = 7.8 Hz, 2H), 2.67 (dd, *J* = 8.3, 7.2 Hz, 2H), 1.35 (td, *J* = 7.1, 0.6 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.50; ESIMS *m/z* 390 ($[M+H]^+$).

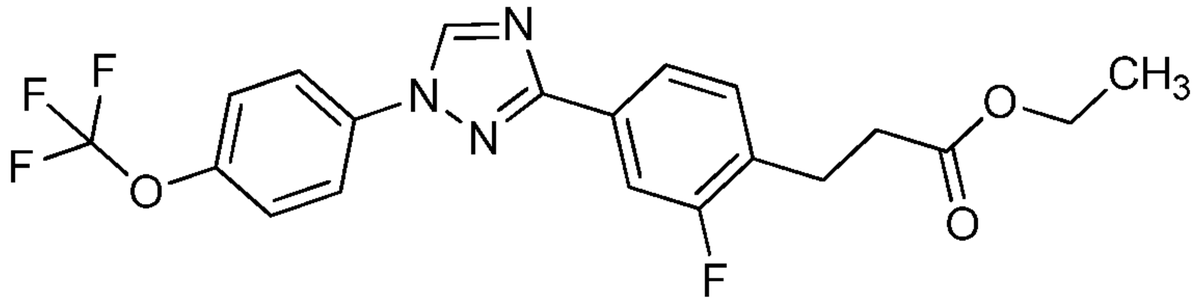
Preparation of ethyl 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (CB15)



The title compound was prepared from (*E*)-ethyl 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**CB12**) and isolated as a gray solid (1.14 g, 98%): mp 109-111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.99 (d, *J* = 1.8 Hz, 1H), 7.95 (ddd, *J* = 7.8, 2.0, 0.7 Hz, 1H), 7.83 - 7.77 (m, 2H), 7.38 (dq, *J* = 7.9, 1.0 Hz, 2H), 7.26 (s, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.00 (dd, *J*

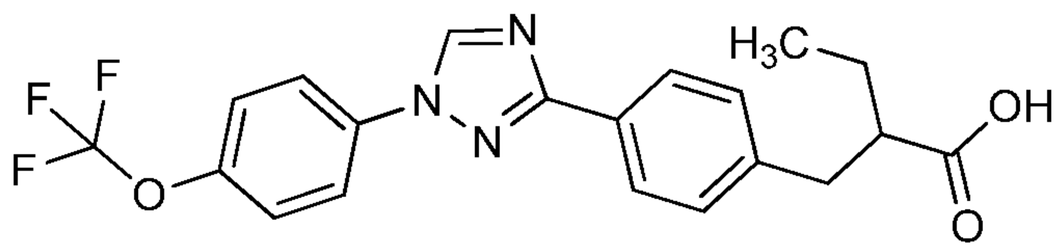
= 8.9, 7.0 Hz, 2H), 2.69 - 2.55 (m, 2H), 2.41 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 420 ($[M+H]^+$).

Preparation of ethyl 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (CB16)



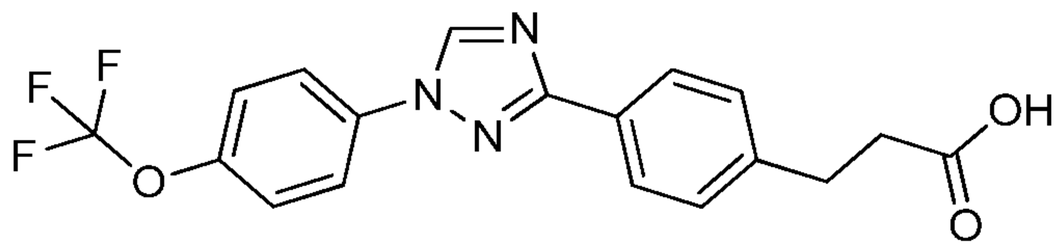
The title compound was prepared from (*E*)-ethyl 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**CB13**) using palladium hydroxide on carbon and ethanol as solvent; isolated as a tan solid (0.871 g, 67%, 85% pure): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.92 - 7.82 (m, 2H), 7.79 (d, *J* = 9.0 Hz, 2H), 7.43 - 7.36 (m, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.03 (t, *J* = 7.7 Hz, 2H), 2.67 (dd, *J* = 8.2, 7.2 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).; ^{19}F NMR (376 MHz, $CDCl_3$) δ (376 MHz, $CDCl_3$) δ -58.03, -117.98; ESIMS *m/z* 423 ($[M]^+$).

Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)butanoic acid (CB17)



The title compound was prepared from (*E/Z*)-ethyl 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzylidene)butanoate (**CB14**) and isolated as a brown solid (1.15 g, 28%): mp 149-150 °C; ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.58 (s, 1H), 8.13 - 8.02 (m, 2H), 7.82 - 7.74 (m, 2H), 7.38 (dq, *J* = 8.9, 0.9 Hz, 2H), 7.35 - 7.28 (m, 2H), 3.04 (dd, *J* = 13.7, 8.3 Hz, 1H), 2.85 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.75 - 2.61 (m, 1H), 1.77 - 1.60 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H) (O<u>H</u> not observed); ^{19}F NMR (376 MHz, $CDCl_3$) δ (376 MHz, $CDCl_3$) δ -58.03, -117.98; ESIMS *m/z* 406 ($[M+H]^+$).

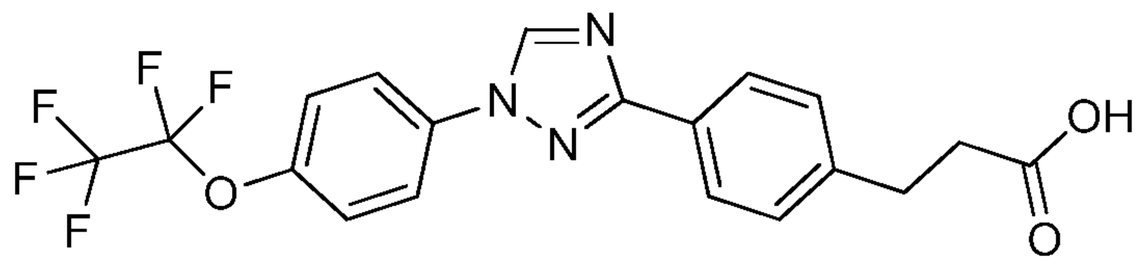
Example 31: Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (C32)



To ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl) propanoate (**C30**) (0.975 g, 2.41 mmol) in methanol (60 mL) was added sodium hydroxide (2 N, 12.0 mL, 24.1 mmol) and the solution was stirred at room temperature overnight. The methanol was concentrated under vacuum, and the residue was acidified with hydrogen chloride (2 N). The white precipitate was vacuum filtered and dried to afford the title compound as a white solid (0.945 g, 99%): mp 145 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 8.04 (dd, J = 21.4, 8.7 Hz, 4H), 7.62 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 2.89 (t, J = 7.6 Hz, 2H), 2.59 (t, J = 7.6 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 378 ([M+H]$^+$).

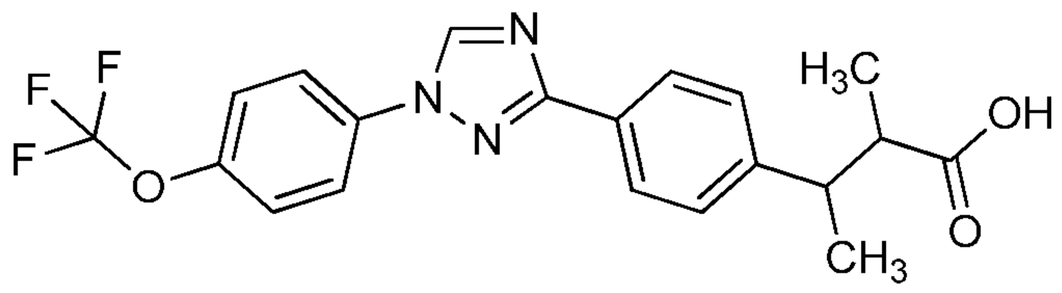
The following compounds were prepared in accordance to the procedure in Example 31.

Preparation of 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl) propanoic acid (C33)



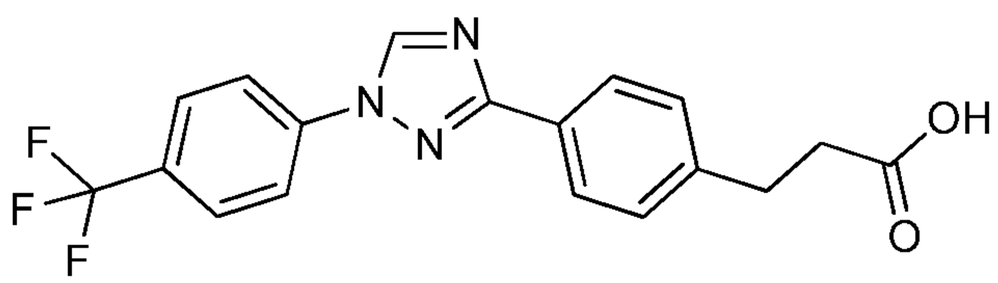
The title compound was prepared from ethyl 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (**C31**) and isolated as a white solid (2.25 g, 100%): mp 142–144 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.05 (dd, J = 24.5, 8.6 Hz, 4H), 7.62 (d, J = 8.9 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 2.89 (t, J = 7.6 Hz, 2H), 2.59 (t, J = 7.6 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.86, -85.19, -86.92; ESIMS *m/z* 428 ([M+H]$^+$).

Preparation of 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoic acid (CA10)



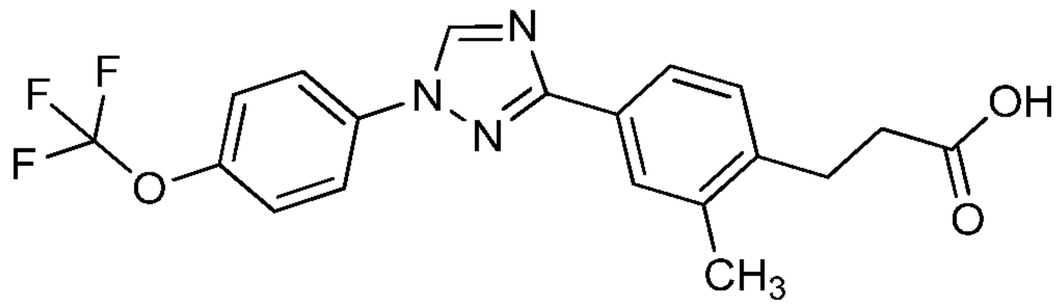
The title compound was prepared from ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoate (**CA8**) and isolated as a yellow oil (0.370 g, 33%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.0 Hz, 1H), 8.15 - 8.03 (m, 2H), 7.83 - 7.73 (m, 2H), 7.40 - 7.27 (m, 4H), 3.18 (p, *J* = 7.2 Hz, 1H), 2.76 (dq, *J* = 8.3, 7.0 Hz, 1H), 1.35 - 1.29 (m, 3H), 1.23 (d, *J* = 6.9 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 406 ($[M+H]^+$).

Preparation of 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (CA11)



The title compound was prepared from ethyl 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (**CA9**) and isolated as a white solid (2.85 g, 79%): mp 155-157 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.17 (s, 1H), 9.52 (s, 1H), 8.26 - 8.12 (m, 2H), 8.12 - 7.86 (m, 3H), 7.39 (d, *J* = 8.2 Hz, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.79; ESIMS *m/z* 362 ($[M+H]^+$).

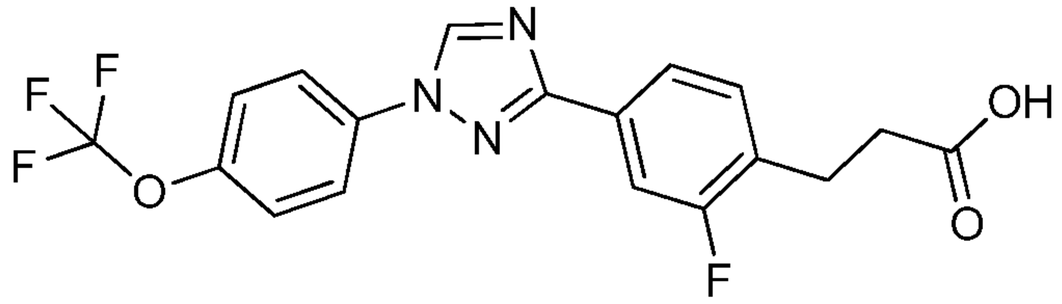
Preparation of 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (CB18)



The title compound was prepared from ethyl 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (**CB15**) and isolated as a white solid (1.039 g, 96%): ^{1}H NMR (400 MHz, CD_3OD) δ 9.13 (s, 1H), 8.06 - 7.99 (m, 2H), 7.94 (d, *J* = 1.8 Hz, 1H), 7.89 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.54 -

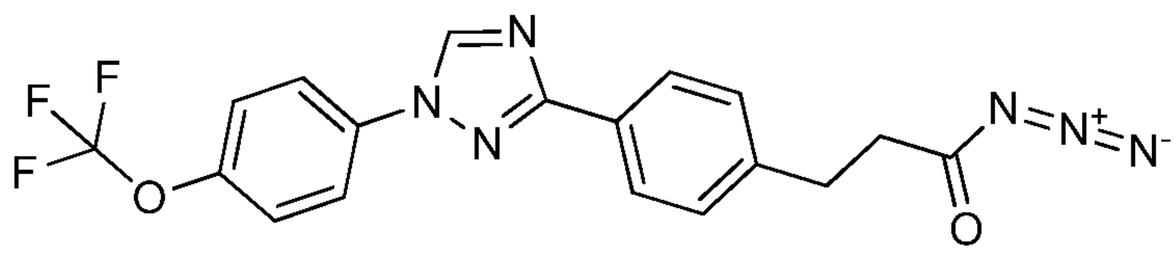
7.46 (m, 2H), 7.30 (d, *J* = 7.9 Hz, 1H), 2.99 (t, *J* = 7.9 Hz, 2H), 2.61 (dd, *J* = 8.5, 7.2 Hz, 2H), 2.42 (s, 3H); ^{19}F NMR (376 MHz, CD_3OD) δ -59.68; ESIMS *m/z* 391 ($[M]^+$).

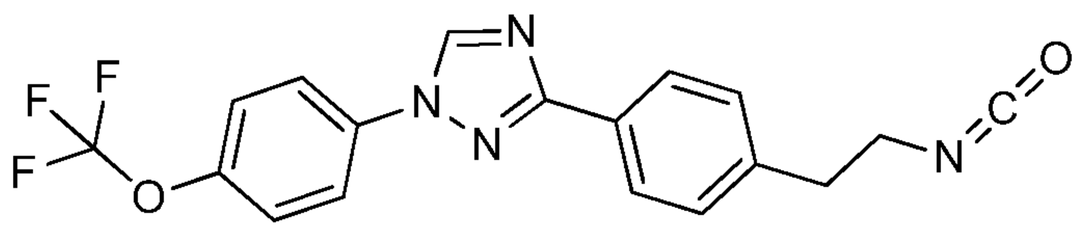
Preparation of 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (CB19)



The crude title compound was prepared from ethyl 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (**CB16**) and isolated as a white solid and used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.01 (d, *J* = 9.0 Hz, 2H), 7.93 - 7.83 (m, 1H), 7.80 (dd, *J* = 11.4, 1.6 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 1H), 3.00 (t, *J* = 7.7 Hz, 2H), 2.64 (t, *J* = 7.6 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -55.72, -116.16; ESIMS *m/z* 395 ($[M]^+$).

Example 32: Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (34) and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (C34a)



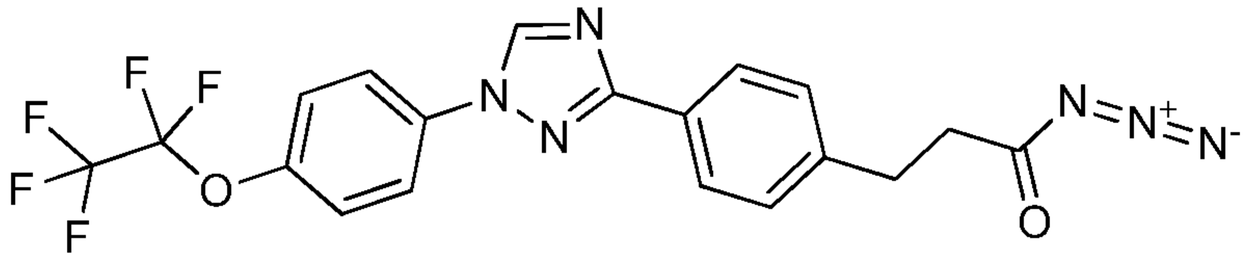


To 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**C32**) (0.70 g, 1.9 mmol) in anhydrous toluene (12 mL) was added triethylamine (0.26 mL, 1.9 mmol) and diphenyl phosphorazidate (0.40 mL, 1.9 mmol). The reaction mixture was stirred at room temperature for 2 hours, loaded directly onto a Celite® cartridge, and purified by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent affording the title compound as a white solid (0.37 g,

50%). ^{1}H NMR is consistent with a mixture of the acyl azide (**34**) and the rearranged isocyanate (**34a**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (two singlets, total = 1H), 8.20 - 8.07 (m, 2H), 7.80 (m, 2H), 7.44 - 7.27 (m, 4H), 3.59 (t, *J* = 6.9 Hz, 1H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.72 (d, *J* = 7.2 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 403 ($[M+H]^+$) (acyl azide).

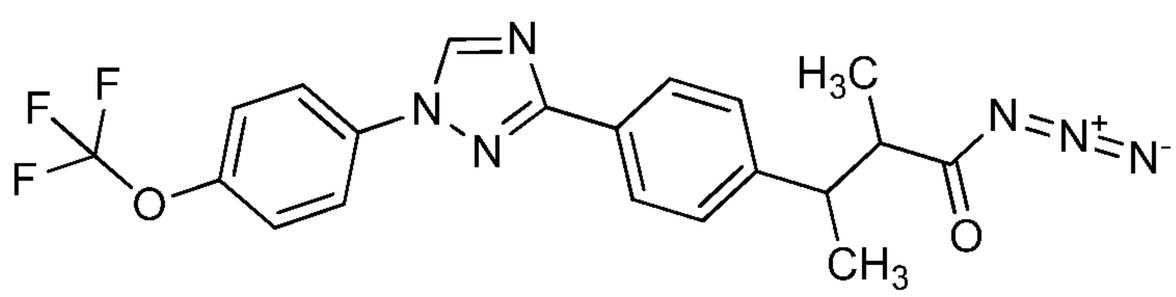
The following compounds were prepared in accordance to the procedure in Example 32.

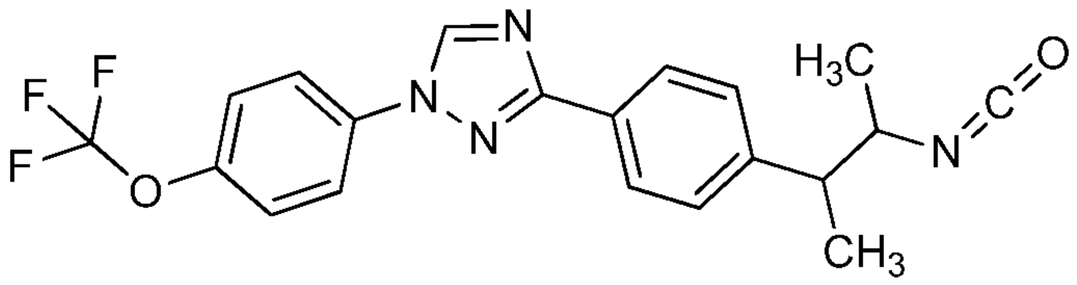
Preparation of 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl) propanoyl azide (C35)



The title compound was prepared from 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**C33**) and was isolated as a white solid (0.416 g, 57%): mp 68 °C (dec.): ^{1}H NMR is consistent with a mixture of the acyl azide and the rearranged isocyanate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 - 8.53 (m, 1H), 8.23 - 8.06 (m, 2H), 7.85 - 7.75 (m, 2H), 7.39 (m, 2H), 7.36 - 7.28 (m, 2H), 3.59 (t, *J* = 6.8 Hz, 1H), 3.00 (t, *J* = 7.3 Hz, 2H), 2.70 (d, *J* = 7.2 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.90, -87.85; ESIMS *m/z* 453 ($[M+H]^+$).

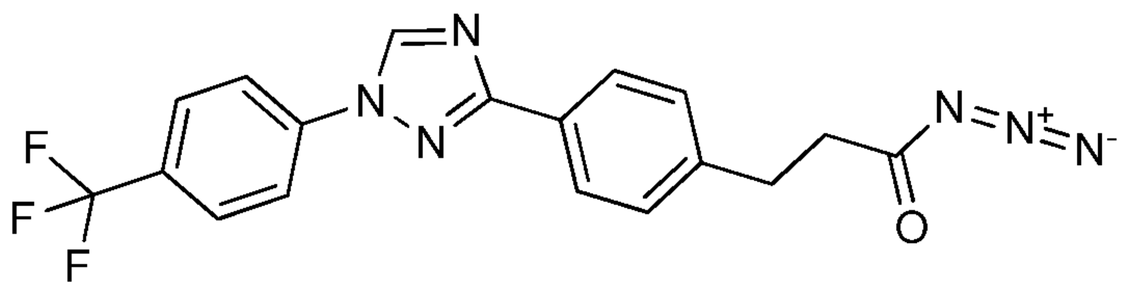
Preparation of 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide/3-(4-(3-isocyanatobutan-2-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (C35a)

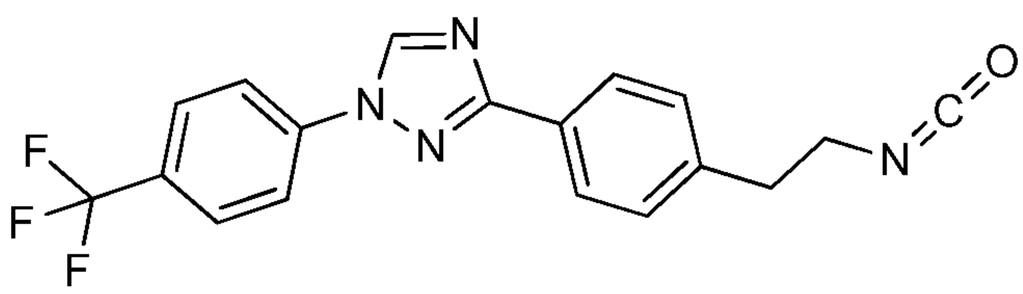




The title compounds were prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoic acid (**CA10**) and isolated as a clear oil (3:1 azide:isocyanate, 0.246 g, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.20 - 8.10 (m, 2H), 7.83 - 7.73 (m, 2H), 7.42 - 7.28 (m, 4H), 3.77 (m, 1H), 2.86 (m, 1H), 1.39 (two d, J = 7.0 Hz, 3H), 1.25 (two d, J = 6.5 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 431 ($[M+H]^+$).

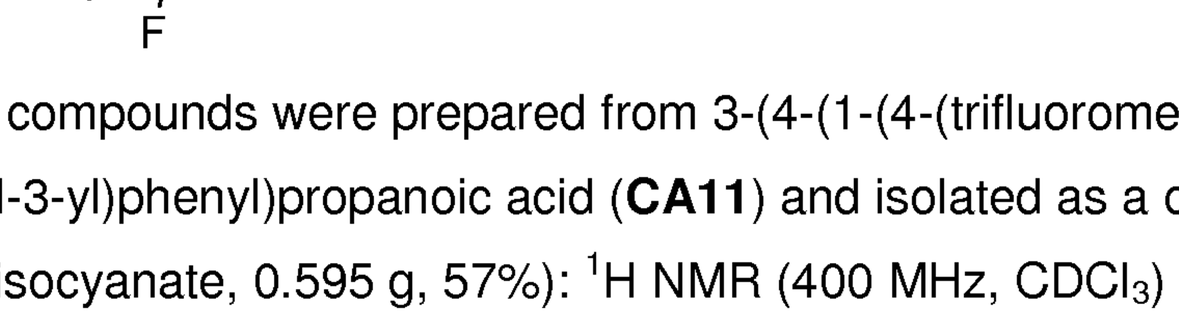
Preparation of 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl) propanoyl azide/3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (C35b)





The title compounds were prepared from 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**CA11**) and isolated as a clear oil (mixture azide:isocyanate, 0.595 g, 57%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 2.8 Hz, 1H), 8.21 - 8.10 (m, 2H), 7.91 (m, 2H), 7.80 (m, 2H), 7.38 - 7.29 (m, 2H), 3.59 (t, J = 6.9 Hz, 1H), 3.00 (t, J = 7.2 Hz, 2H), 2.72 (d, J = 7.2 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49.

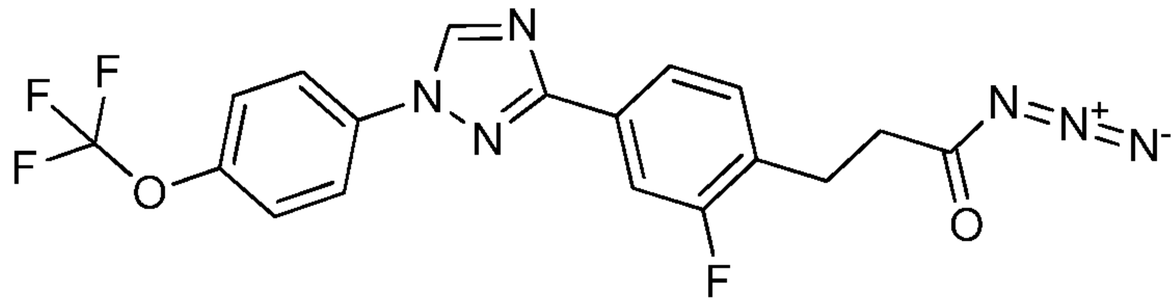
Preparation of 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (CB20)



The title compound was prepared from 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**CB18**) using

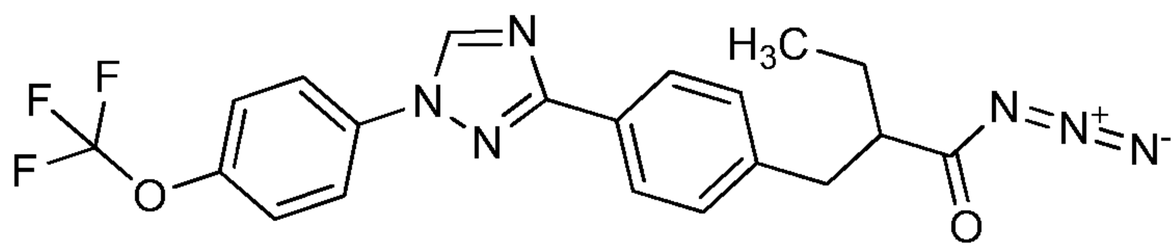
acetonitrile as co-solvent and was isolated as a white solid (0.636 g, 57%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.00 (d, *J* = 1.8 Hz, 1H), 7.98 - 7.94 (m, 1H), 7.84 - 7.75 (m, 2H), 7.39 (ddt, *J* = 7.9, 2.0, 1.0 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 1H), 3.06 - 2.90 (m, 2H), 2.75 - 2.59 (m, 2H), 2.41 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.04; ESIMS *m/z* 389 ($[M+H]-N_2^+$).

Preparation of 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (CB21)



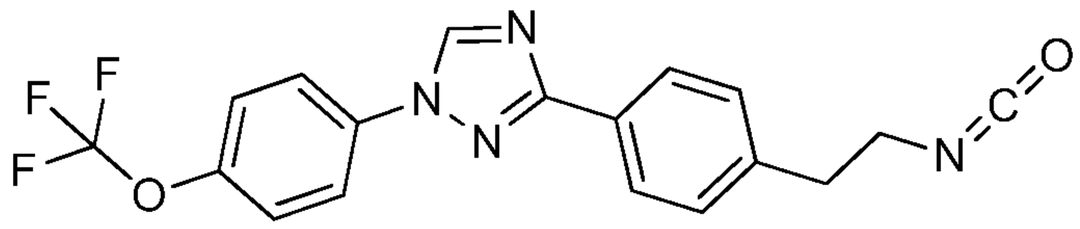
The title compound was prepared from 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**CB19**) using acetonitrile as co-solvent and was isolated as a white solid (0.084 g, 29%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.94 - 7.83 (m, 2H), 7.83 - 7.75 (m, 2H), 7.39 (ddd, *J* = 7.7, 1.9, 0.9 Hz, 2H), 7.35 - 7.29 (m, 1H), 3.10 - 2.96 (m, 2H), 2.81 - 2.66 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03, -117.86.

Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)butanoyl azide (CB22)



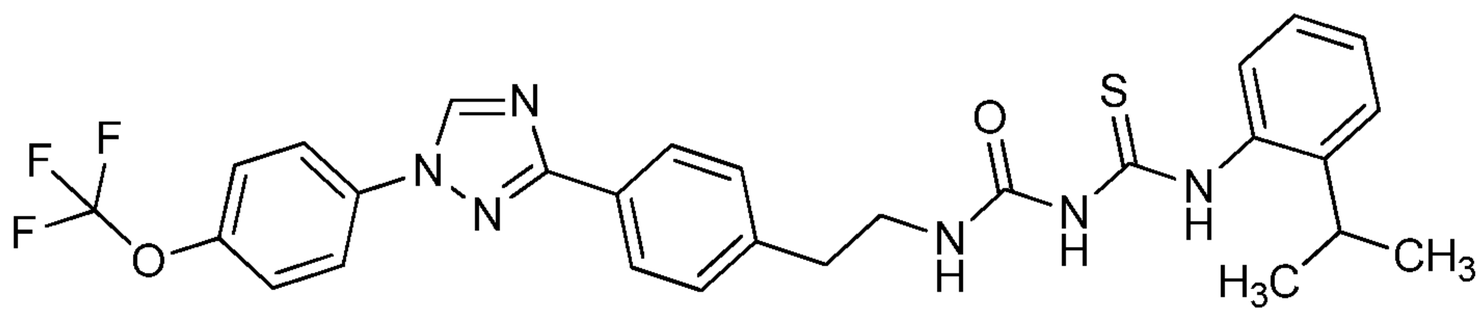
The title compound was prepared from 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)butanoic acid (**CB17**) and was isolated as a clear oil (0.512 g, 56%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.20 - 8.10 (m, 2H), 7.84 - 7.74 (m, 2H), 7.39 (dt, *J* = 8.0, 1.0 Hz, 2H), 7.36 - 7.29 (m, 2H), 3.68 (tdd, *J* = 8.3, 5.3, 4.4 Hz, 1H), 2.98 - 2.77 (m, 2H), 1.76 - 1.64 (m, 1H), 1.61 - 1.51 (m, 1H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03, -117.86; ESIMS *m/z* 431 ($[M+H]^+$).

Example 32a: Preparation of 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoro methoxy)phenyl)-1*H*-1,2,4-triazole (C34a)



A 1 L three-neck round bottomed flask was equipped with mechanic stirrer, thermocouple, and condenser. Tetrahydrofuran (120 mL) was added. After it was cooled to -3 °C, ethyl carbonochloridate (3.16 mL, 33.2 mmol) and triethylamine (4.64 mL, 33.2 mmol) were added. 3-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**C32**) (11.4g, 30.2 mmol) was added in portions, keeping the reaction temperature below 0 °C. The reaction mixture turned into white suspension quickly. LC-MS showed no starting material left after 1 hr. A solution of sodium azide (2.16 g, 33.2 mmol) in water (44 mL) was added slowly, keeping the reaction temperature below -2 °C. The reaction mixture was stirred at -2 °C for 2 hours. Cold water (200 mL) was added to the reaction mixture very slowly while stirring at 0 °C. It was stirred at 0 °C for 30 minutes after the addition. The white solid that formed was filtered while it was cold. The solid was dried in vacuum under a stream of nitrogen at room temperature for 48 hours to afford the isocyanate as a tan solid (10.5 g, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.20 – 8.11 (m, 2H), 7.85 – 7.76 (m, 2H), 7.47 – 7.30 (m, 4H), 3.59 (t, *J* = 6.9 Hz, 2H), 2.97 (t, *J* = 6.9 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 375.2 ($[M+H]^+$).

Example 33: Preparation of *N*-[2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (F2)

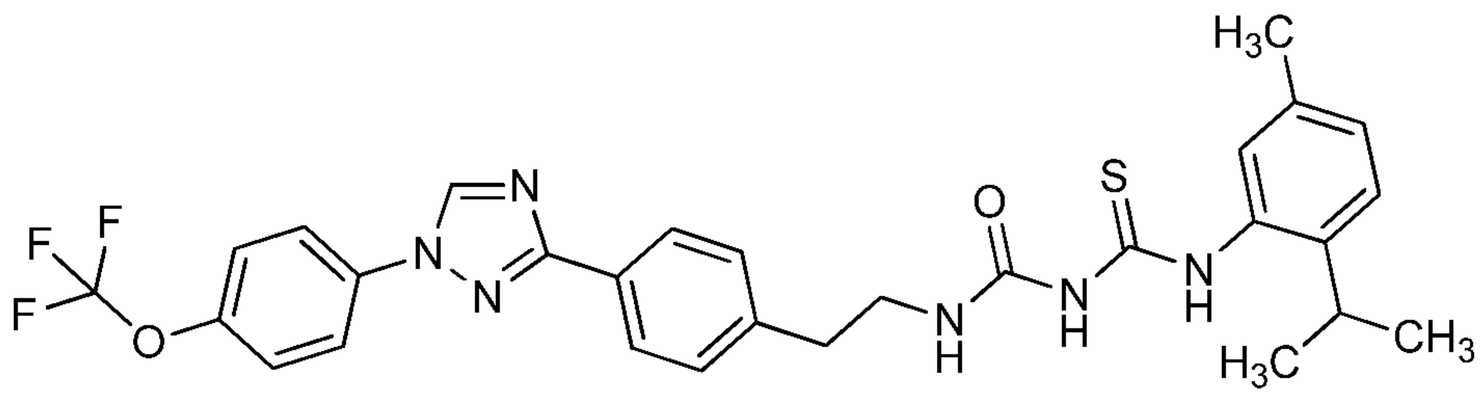


3-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) (0.19 g, 0.46 mmol) in acetonitrile (2.3 mL) was heated at 80 °C for 2 hours. The reaction mixture was cooled and 1-(2-isopropylphenyl)thiourea (0.11 g, 0.55 mmol) and cesium carbonate (0.20 g, 0.60 mmol) were added. The reaction was stirred at room temperature for 4 hours, and then quenched with water and

extracted with ethyl acetate (2x). The organic layers were dried over anhydrous sodium sulfate, filtered, concentrated, and loaded onto a Celite® cartridge with dichloromethane. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent afforded the title compound as a white powder (0.097 g, 36%).

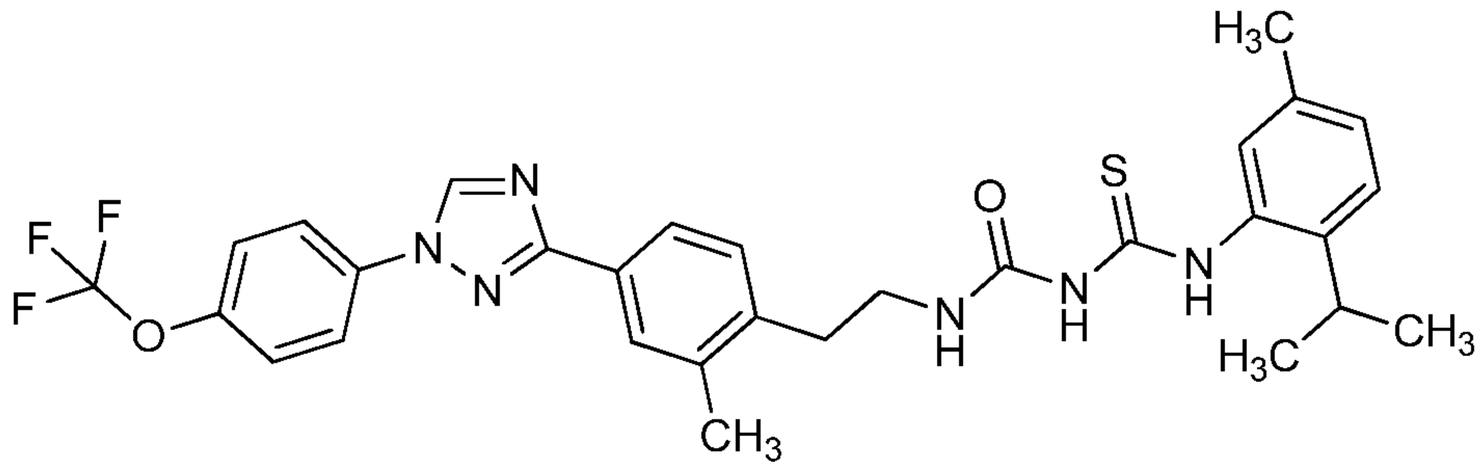
The following compounds were prepared in accordance to the procedure in Example 33.

Preparation of *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (F3)



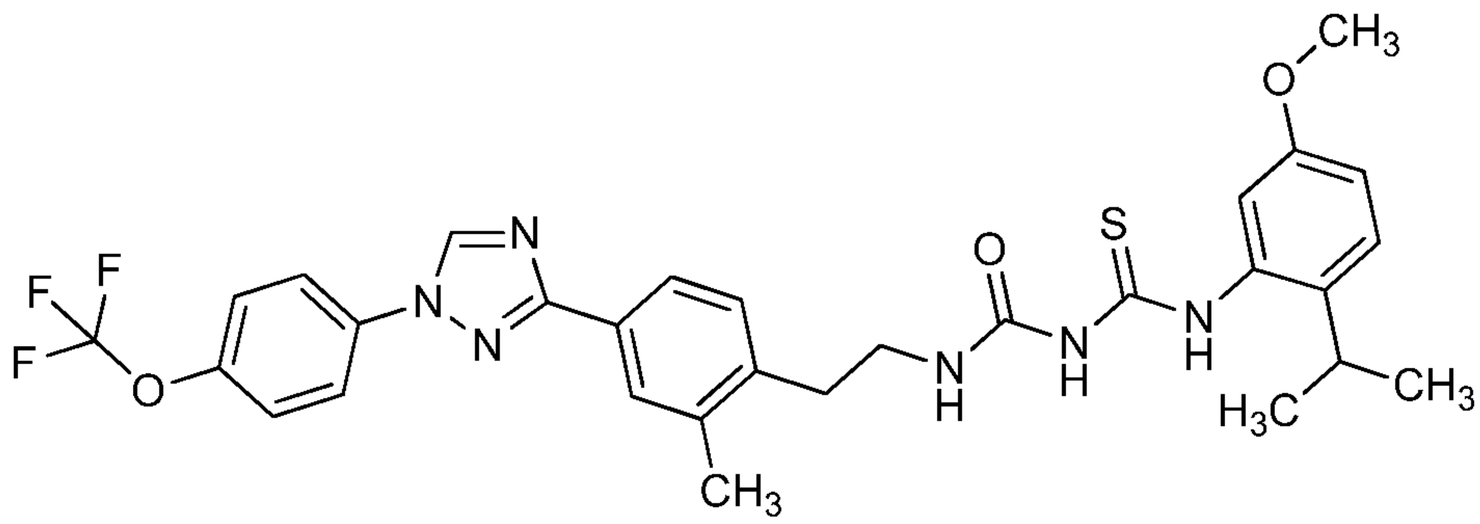
The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C3**4) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a white solid (0.158 g, 43%).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[2-[2-methyl-4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (FB1)



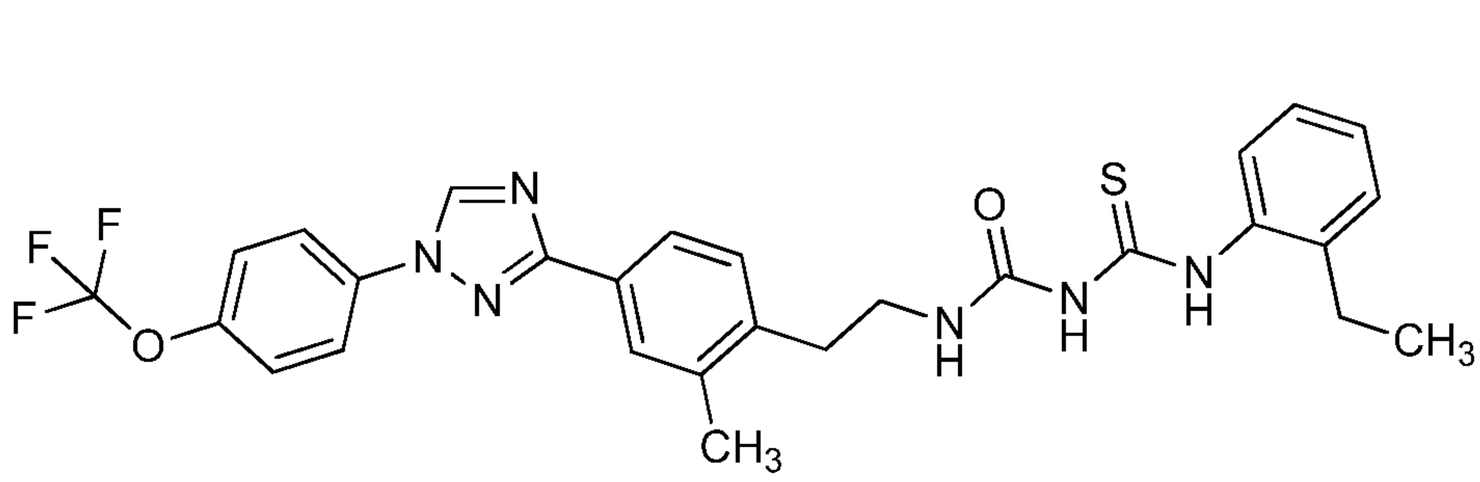
The title compound was prepared from 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**CB20**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated, without purification, as a white solid (0.180 g, 79%, 88% pure).

Preparation of 1-[(2-isopropyl-5-methoxy-phenyl)carbamothioyl]-3-[2-[2-methyl-4-[1-[4-(trifluoromethoxy)phenyl] -1*H* -1,2,4-triazol-3-yl]phenyl]ethyl]urea (FB2)



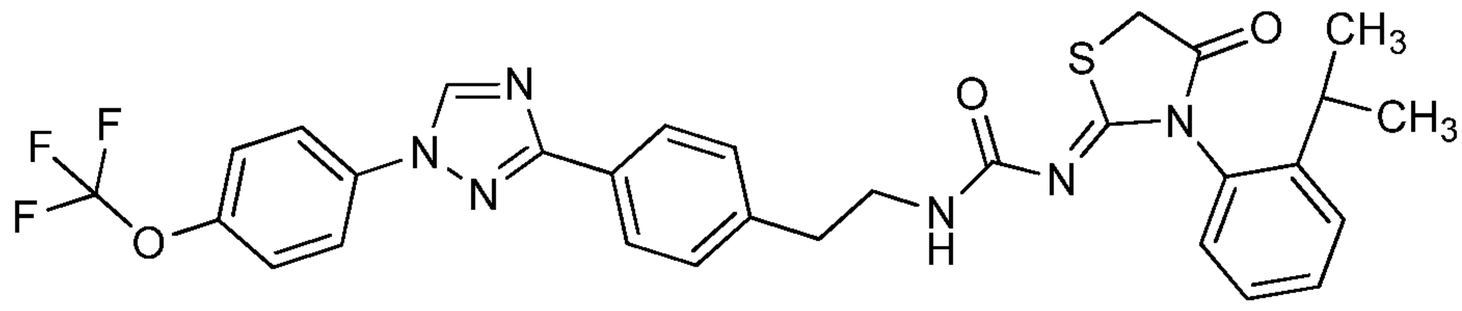
The title compound was prepared from 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**CB20**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated, without purification, as a yellow solid (0.165 g, 75%).

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[2-[2-methyl-4-[1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (FB5)



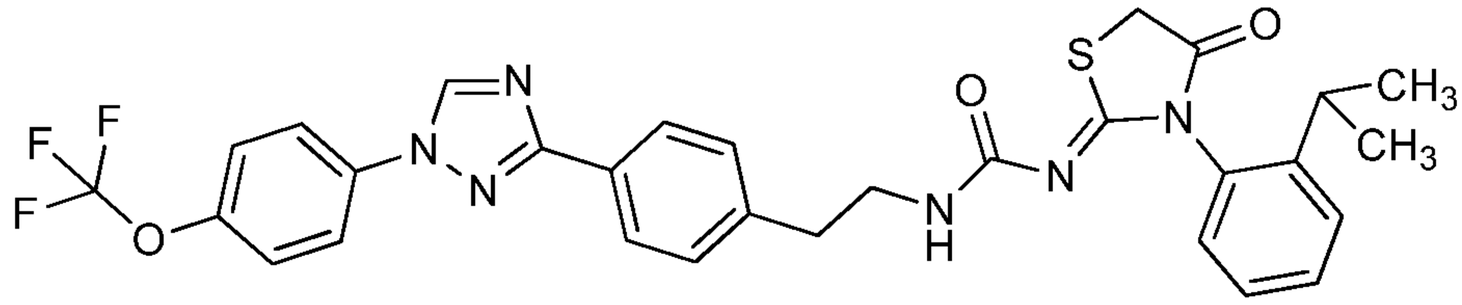
The title compound was prepared from 3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**CB20**) and 1-(2-ethylphenyl)thiourea and isolated, without purification, as a yellow solid (0.144 g, 83%).

Example 34: Preparation of *(Z)*-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F1), Method A



To *N*-[2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F2**) (0.030 g, 0.053 mmol) and sodium acetate (0.016 g, 0.20 mmol) in ethanol (0.5 mL) was added methyl 2-bromoacetate (0.01 mL, 0.10 mmol) and the solution was heated at 65 °C for 1.5 hours. The reaction was cooled and loaded directly onto a Celite® cartridge. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes as eluent afforded the title compound as a clear oil (0.016 g, 49%).

Example 35: Preparation of *(Z)*-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F1), Method B

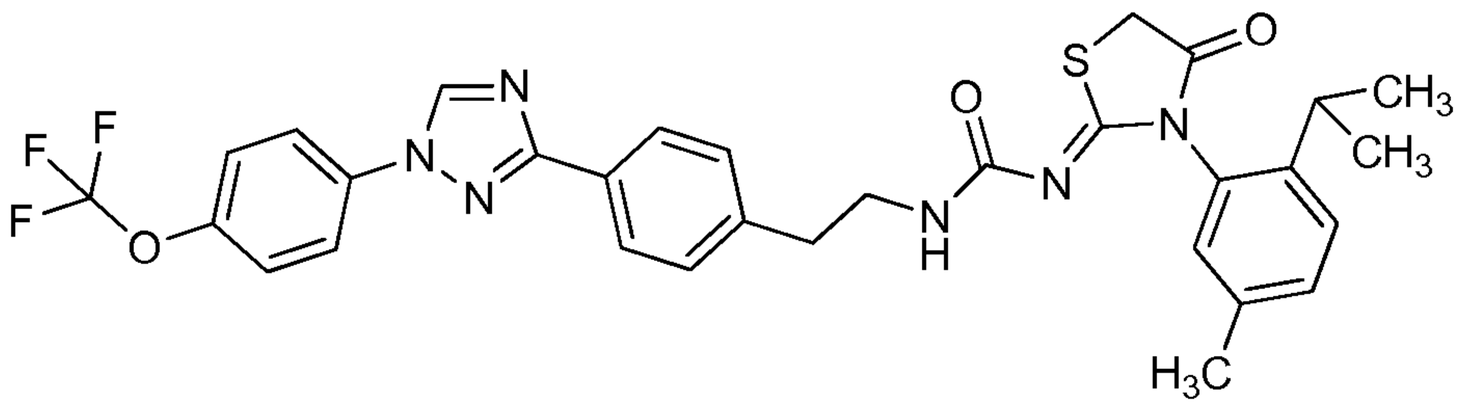


3-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) (0.24 g, 0.59 mmol) in acetonitrile (2.9 mL) was heated at 80 °C for 2 hours. The reaction was cooled and cesium carbonate (0.29 g, 0.88 mmol) and 1-(2-isopropylphenyl)thiourea (0.14 g, 0.70 mmol) were added. The reaction was stirred at room temperature overnight. LC/MS showed formation of the thiobiuret was complete. The reaction mixture was diluted with ethanol (2.9 mL) and sodium acetate (0.19 g, 2.4 mmol) and methyl 2-bromoacetate (0.12 mL, 1.2 mmol) were added. The solution was heated at 65 °C for 2 hours. The reaction was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulfate, filtered, concentrated, and loaded onto a Celite® cartridge with dichloromethane. Purification by flash column chromatography using 0-100% ethyl

acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent afforded the title compound as a tan oil (0.22 g, 62%).

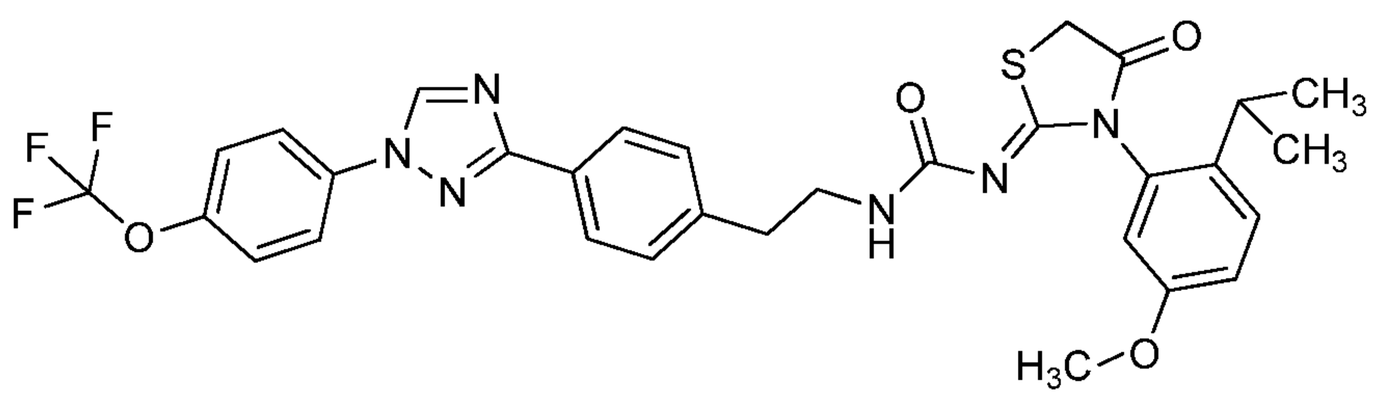
The following compounds were prepared in accordance to the procedure in Examples 34 or 35.

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F5)



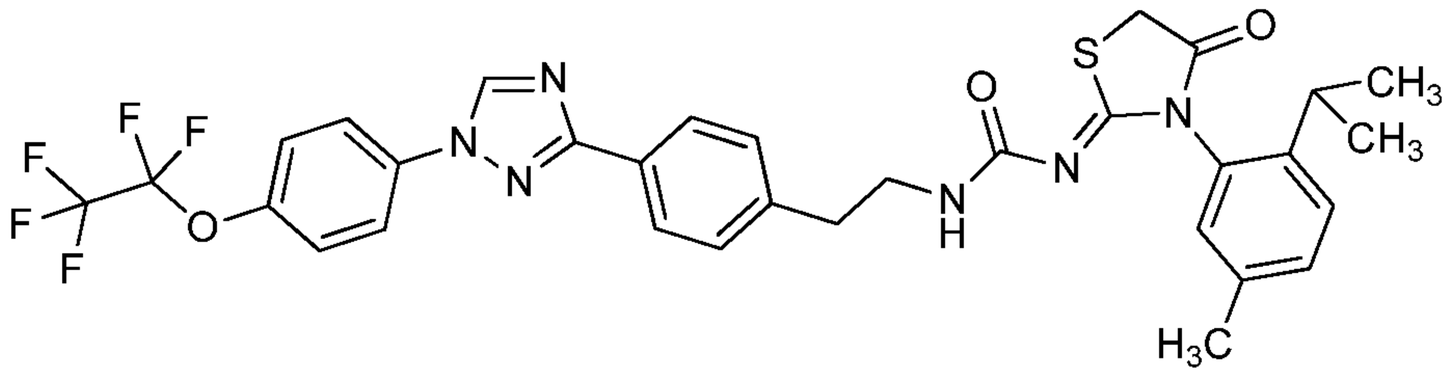
The title compound was prepared as described in Example 34 using *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a pale pink solid (0.114 g, 29%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F6)



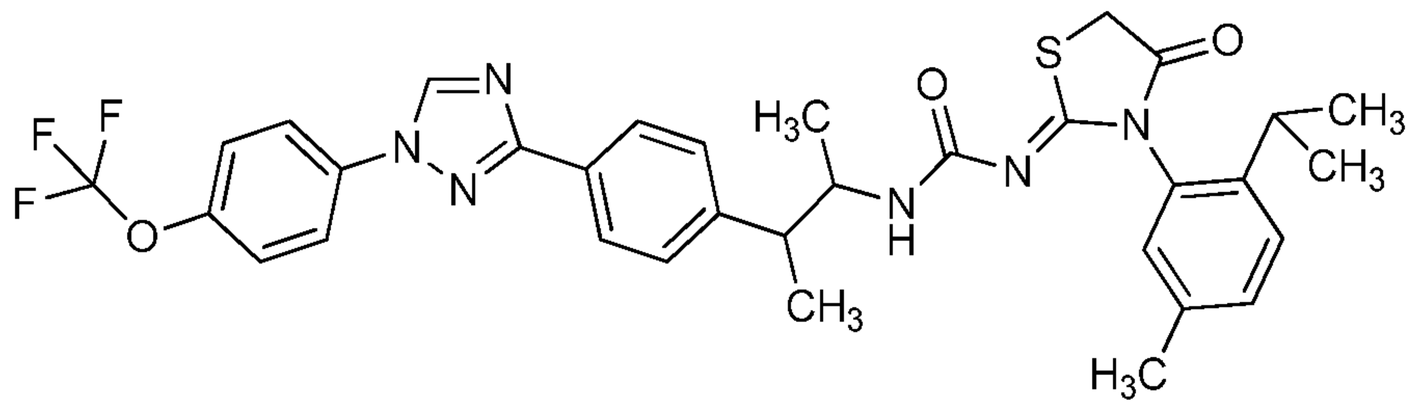
The title compound was prepared as described in Example 35 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated as an orange solid (0.075 g, 35%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F9)



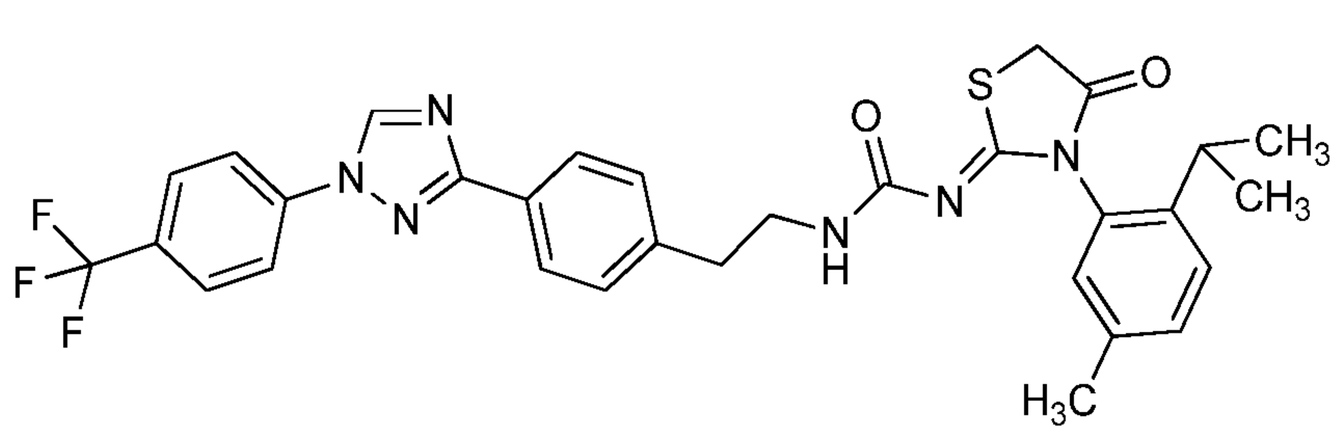
The title compound was prepared as described in Example 35 using 1-(2-isopropyl-5-methylphenyl)thiourea and 3-(4-(1-(4-(perfluoroethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)-propanoyl azide (**C35**) and isolated as a brown gum (0.146 g, 43%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-2-yl)urea (P66, P353)



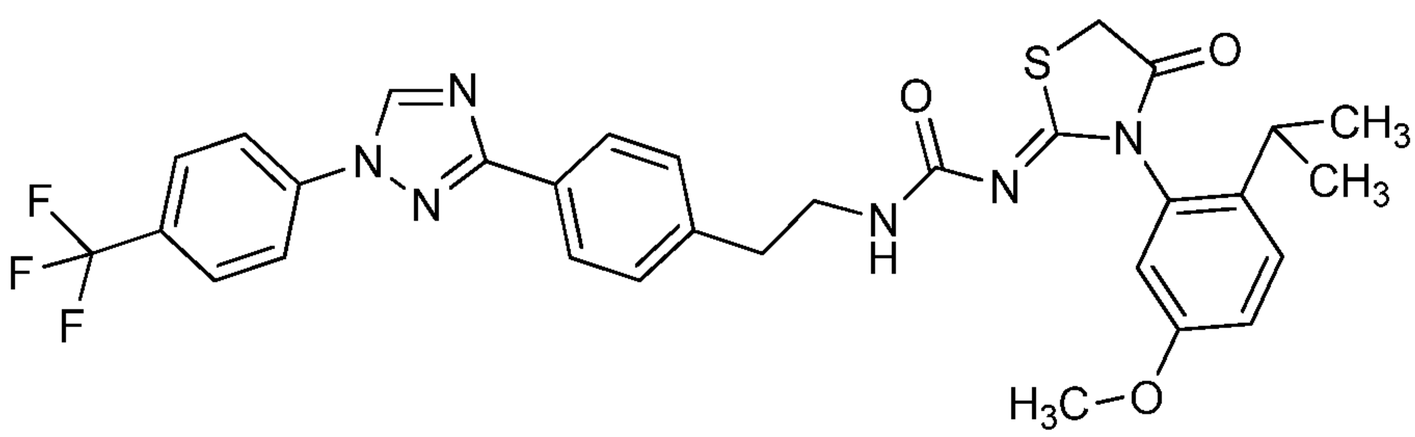
The title compound was prepared as described in Example 35 using 1-(2-isopropyl-5-methylphenyl)thiourea and 2-methyl-3-(4-(1-(4-(trifluoromethoxy) phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide/3-(4-(3-isocyanatobutan-2-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C35a**) and isolated as an off-white powder (0.146 g, 39%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P52)



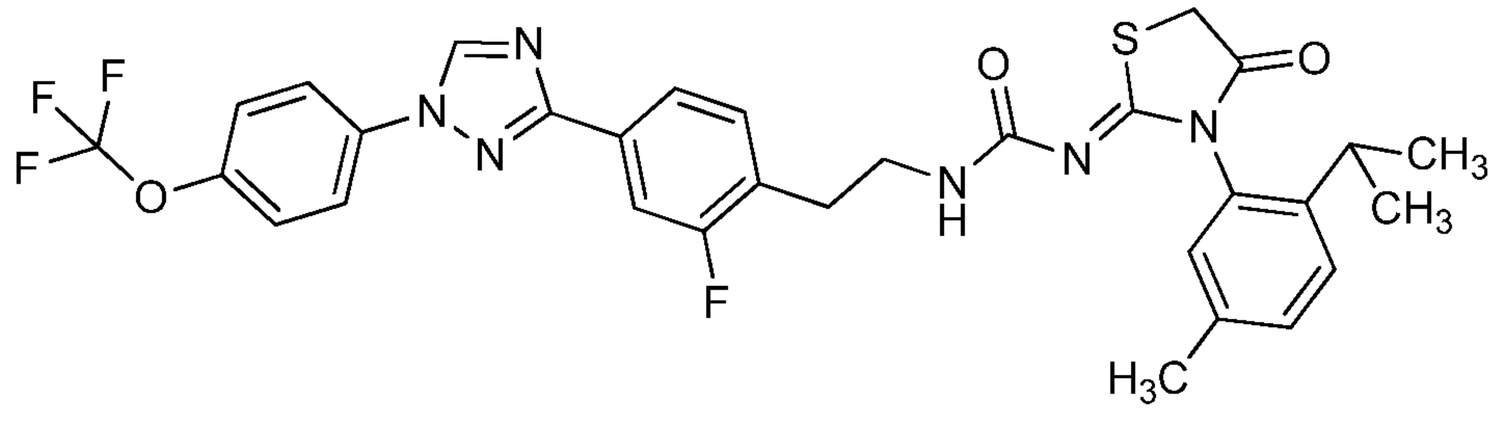
The title compound was prepared as described in Example 35 using 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide/3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (**C35b**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a tan glassy foam (0.132 g, 46%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P53)



The title compound was prepared as described in Example 35 using 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide/3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (**C35b**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (CA40) and isolated as a brown foam (0.040 g, 30%).

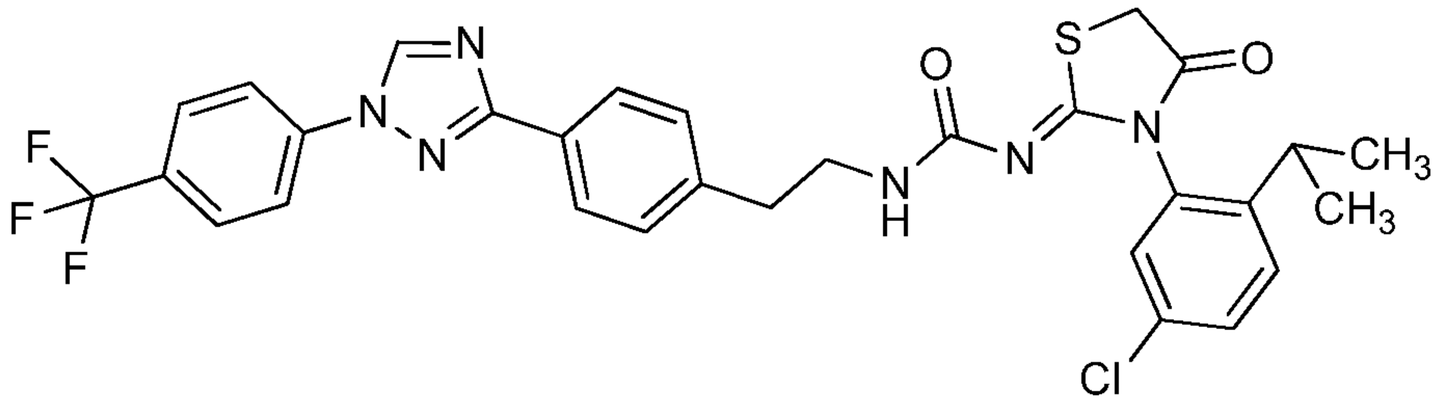
Preparation of (*Z*)-1-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)-3-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)urea (FB8)



The title compound was prepared as described in Example 35 using 3-(2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**CB21**) and 1-(2-isopropyl-5-methylphenyl)thiourea at a temperature of 60 ºC and

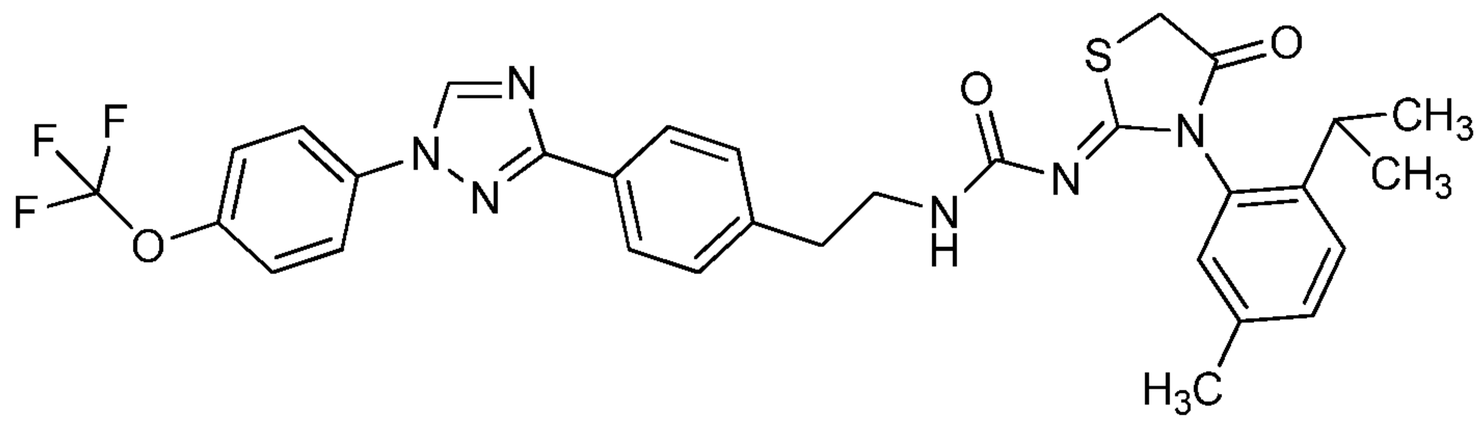
followed by reverse phase chromatography; isolated as an orange oil (0.028 g, 13%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB50)



The title compound was prepared as described in Example 35 using 3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide/3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (**C35b**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) at a temperature of 60 ºC; isolated as a clear oil (0.019 g, 12%).

Example 35a: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F5)

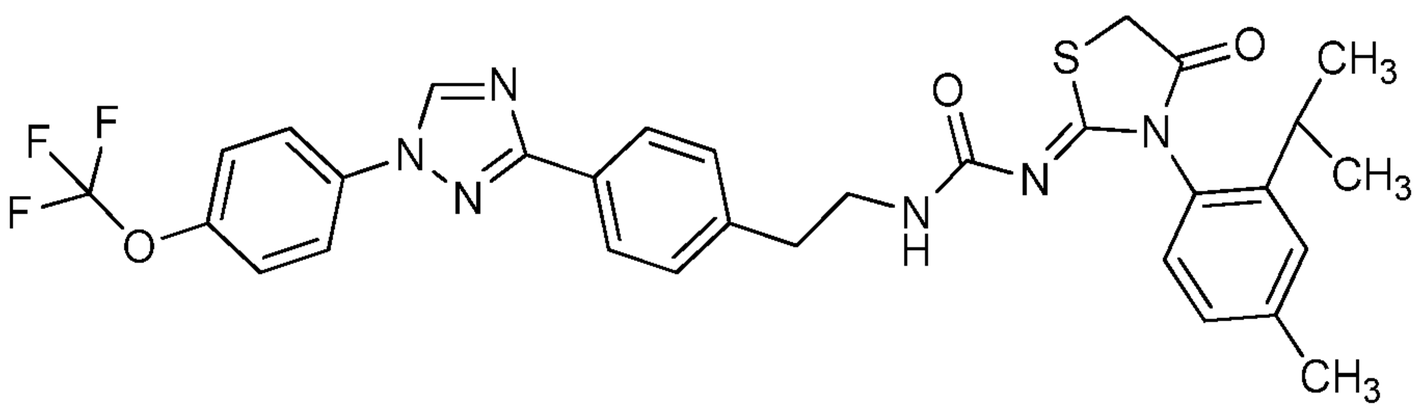


To a 250 mL round bottomed flask was added acetonitrile (100 mL). 3-(4-(2-Isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**34a**) (11.0 g, 29.4 mmol) was added in one portion. 1-(2-Isopropyl-5-methylphenyl)thiourea (6.73 g, 32.3 mmol) and cesium carbonate (9.57 g, 29.4 mmol) were added to the above solution. The reaction mixture was stirred at room temperature under nitrogen overnight. Ethanol (100 mL) was added to the mixture. Methyl 2-bromoacetate (8.99 g, 58.8 mmol) and sodium acetate (9.64 g, 118 mmol) were then added. The reaction mixture was stirred at 60 ºC for 2 hours, forming an orange suspension. The reaction mixture was cooled and filtered through a filter paper, and the solids were

washed with ethyl acetate (2 x 100 mL). The orange filtrate was concentrated. The solid residue was purified by flash column chromatography using 10-20% dichloromethane/B, where B = 1:1 ethyl acetate/acetone, as eluent to afford the title compound as a slightly orange foam (8.60 g, 45%).

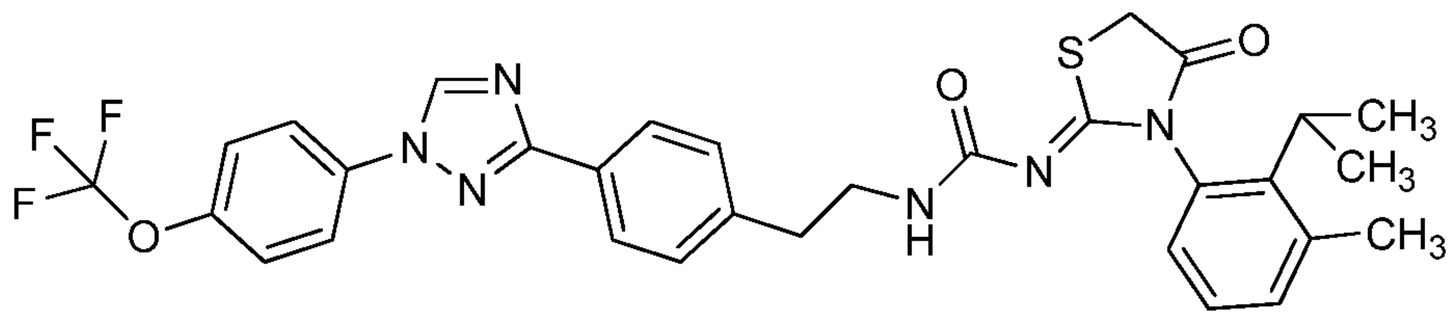
The following compounds were prepared in accordance to the procedure in Example 35a.

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P26)



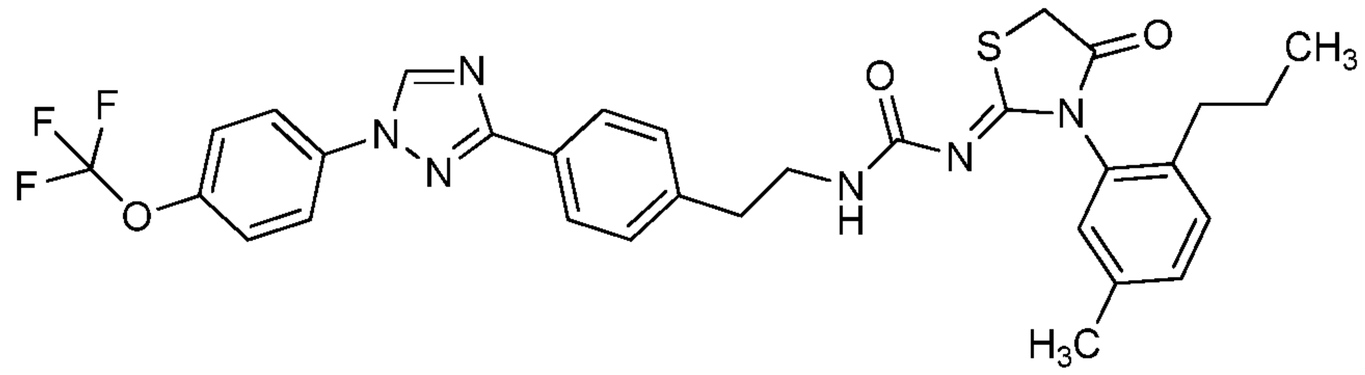
The title compound was prepared from 1-(2-isopropyl-4-methylphenyl)thiourea and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a brown oil (0.121 g, 47%).

Preparation of (*Z*)-1-(3-(2-isopropyl-3-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P27)



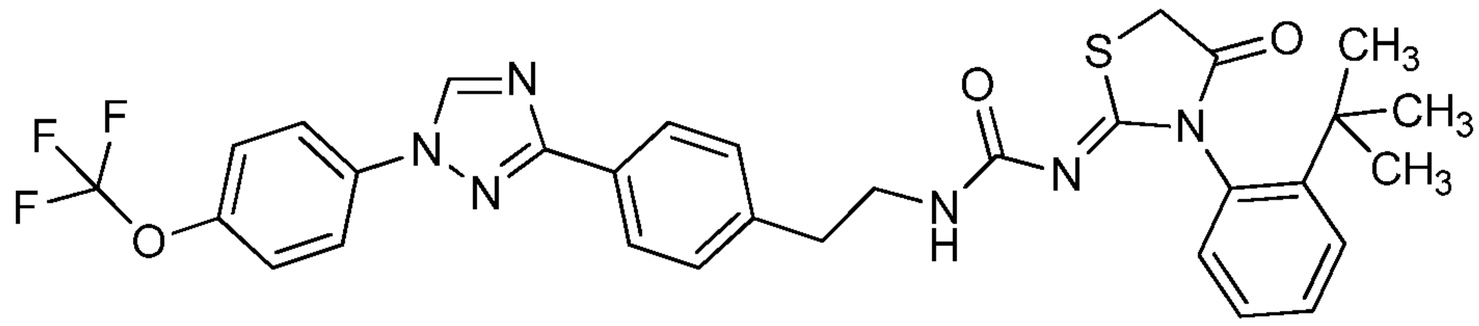
The title compound was prepared from 1-(2-isopropyl-3-methylphenyl)thiourea and 3-(4-(2-Isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a yellow oil (0.075 g, 31%).

Preparation of (*Z*)-1-(3-(5-methyl-2-propylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P29)



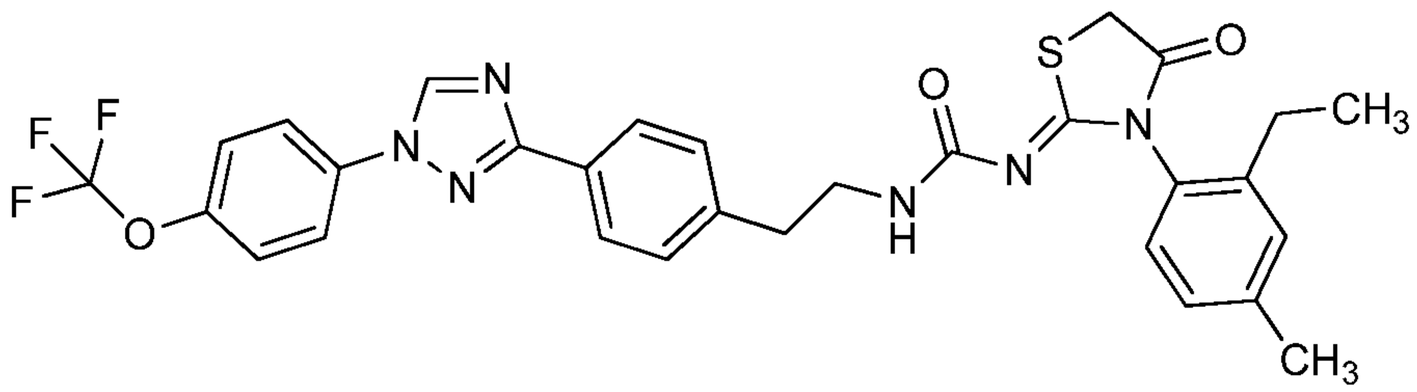
The title compound was prepared from 1-(5-methyl-2-propylphenyl)thiourea (**CA38**) and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a pale pink solid (0.113 g, 43%).

Preparation of (*Z*)-1-(3-(2-(*tert*-butyl)phenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P30)



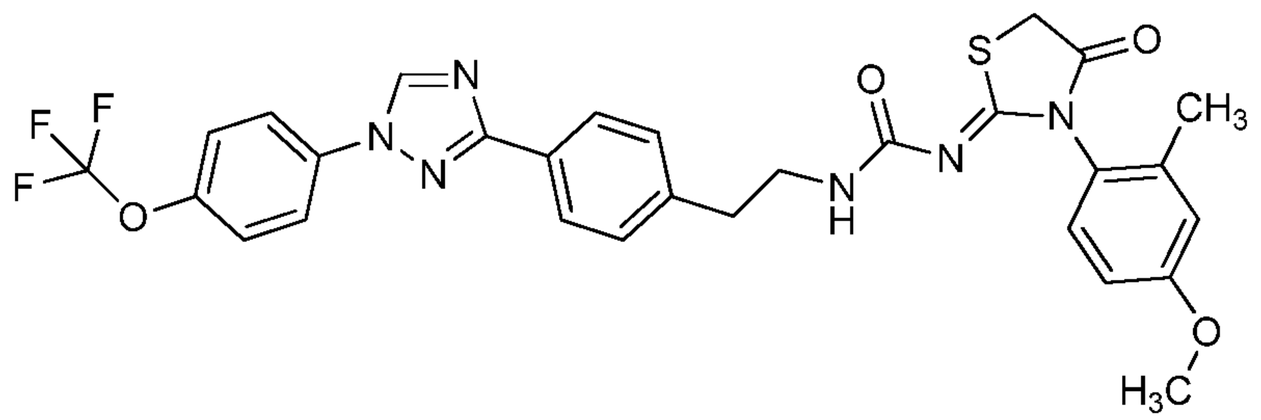
The title compound was prepared from 1-(2-(*tert*-butyl)phenyl)thiourea and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a pink solid (0.076 g, 31%).

Preparation of (*Z*)-1-(3-(2-ethyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P31)



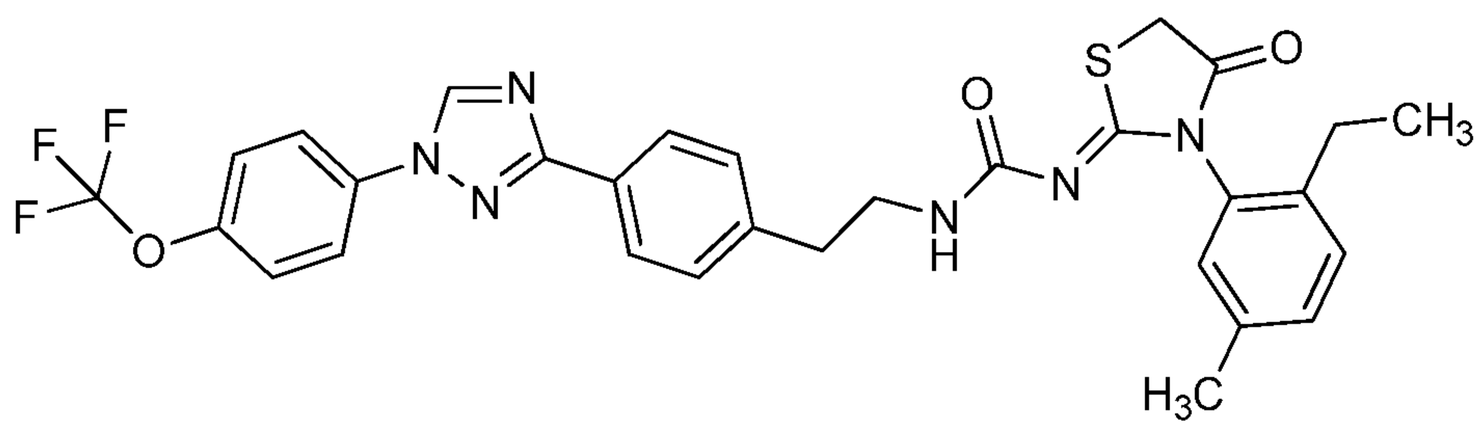
The title compound was prepared from 1-(2-ethyl-4-methylphenyl)thiourea (**CA42**) and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a pink solid (0.114 g, 47%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P44)



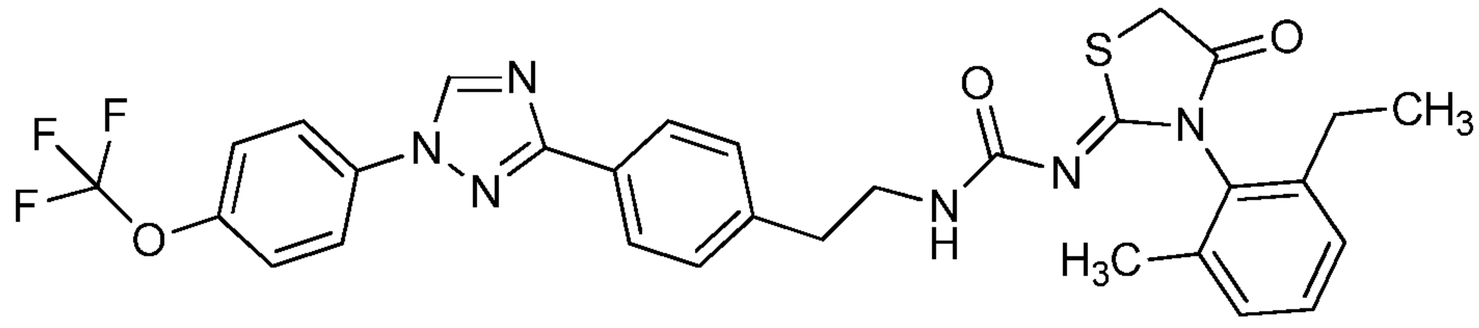
The title compound was prepared as described in Example 35a using 1-(4-methoxy-2-methylphenyl)thiourea and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a yellow solid (0.120 g, 49%).

Preparation of (*Z*)-1-(3-(2-ethyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P49)



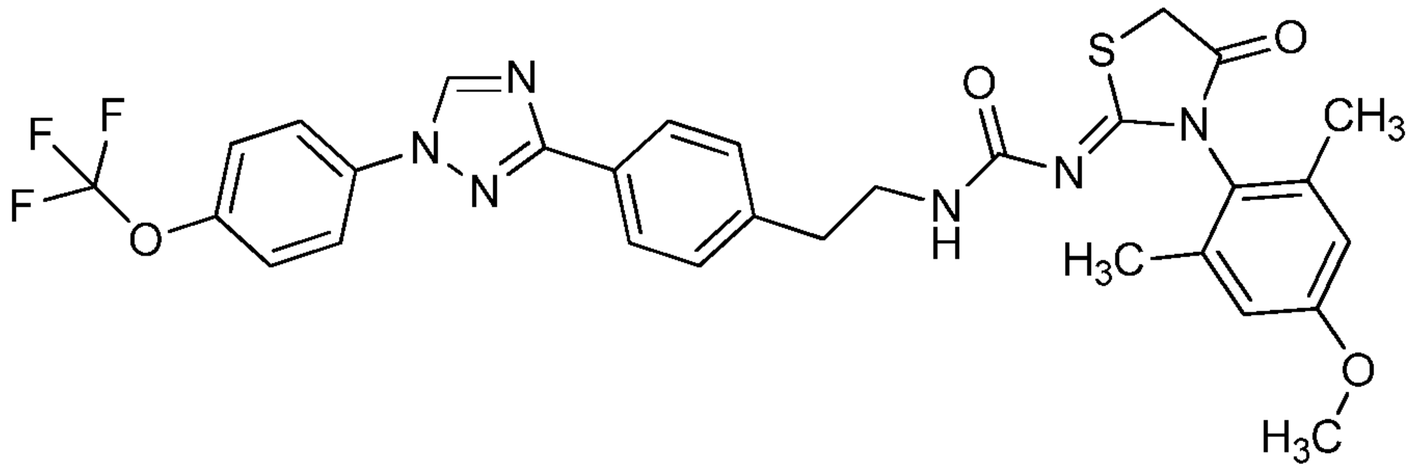
The title compound was prepared from 1-(2-ethyl-5-methylphenyl)thiourea (CA41) and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a pink solid (0.099 g, 43%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P50)



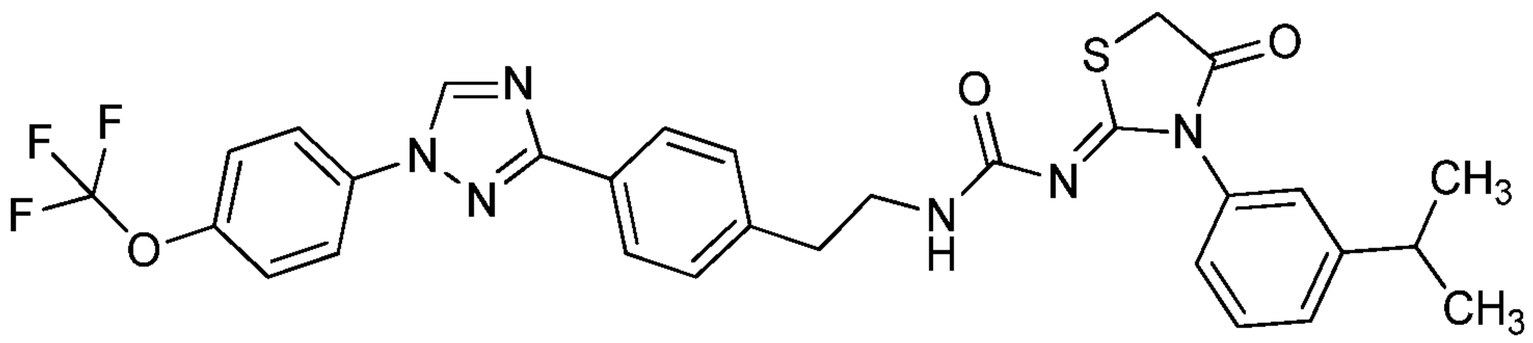
The title compound was prepared from 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as an off-white solid (0.076 g, 33%).

Preparation of (*Z*)-1-(3-(4-methoxy-2,6-dimethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P47)



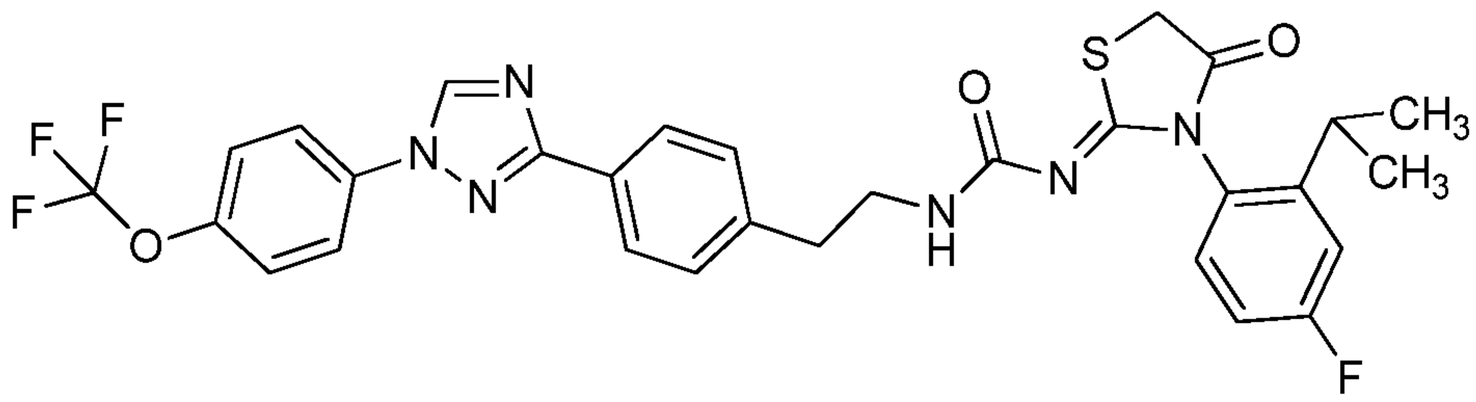
The title compound was prepared from1-(4-methoxy-2,6-dimethylphenyl)thiourea and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a yellow oil (0.055 g, 23%).

Preparation of (*Z*)-1-(3-(3-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P51)



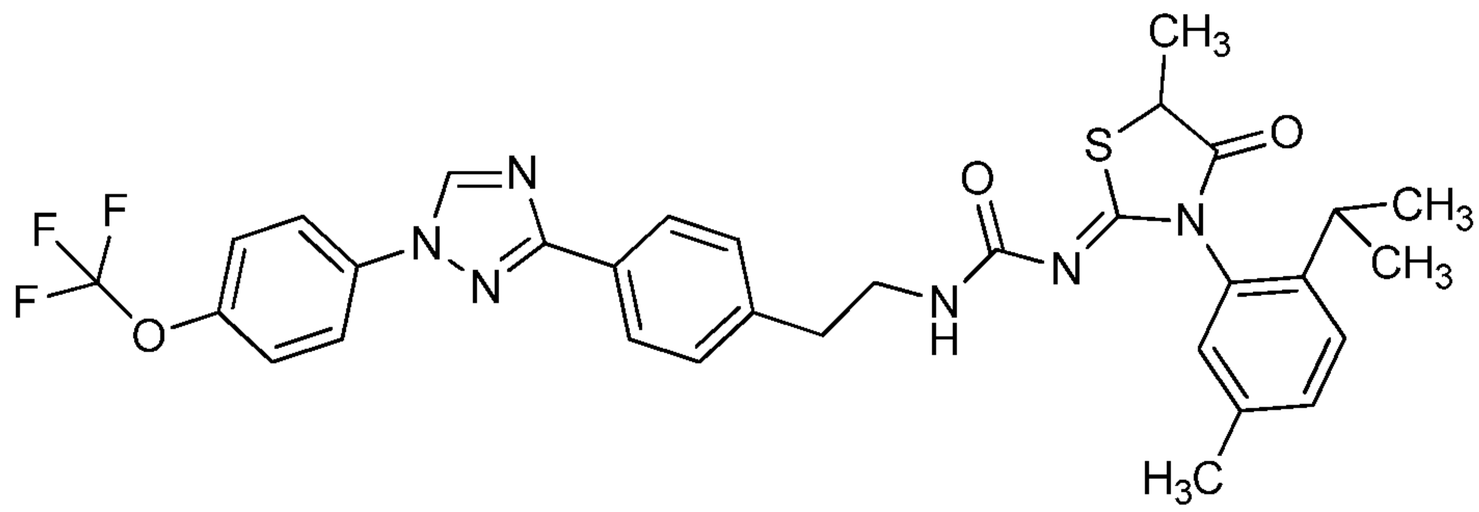
The title compound was prepared from 1-(3-isopropylphenyl)thiourea and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a dark brown oil (0.094 g, 37%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P28)



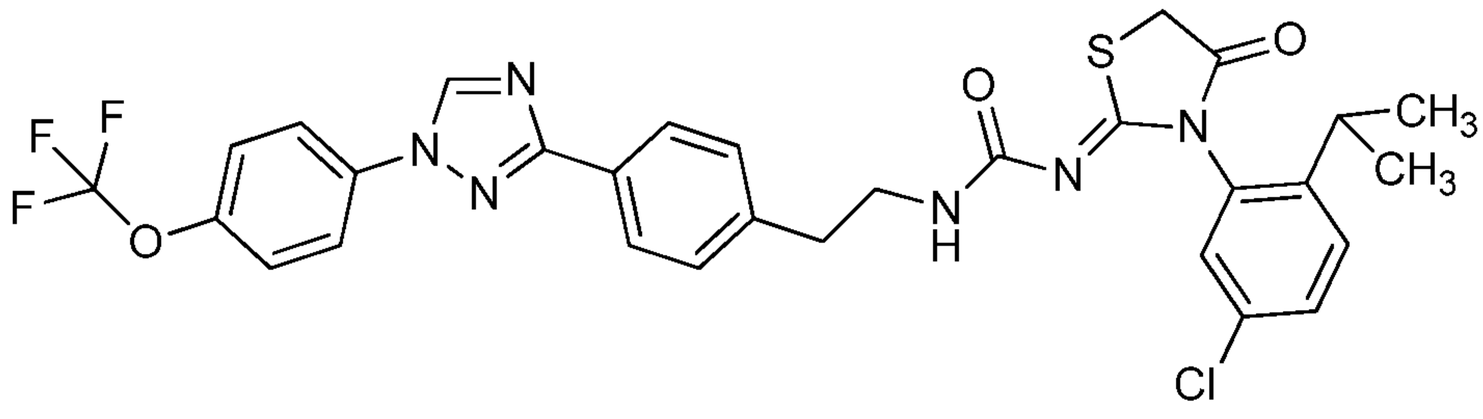
The title compound was prepared from 1-(4-fluoro-2-isopropylphenyl)thiourea and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a brown foam (0.151 g, 37%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-5-methyl-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P57)



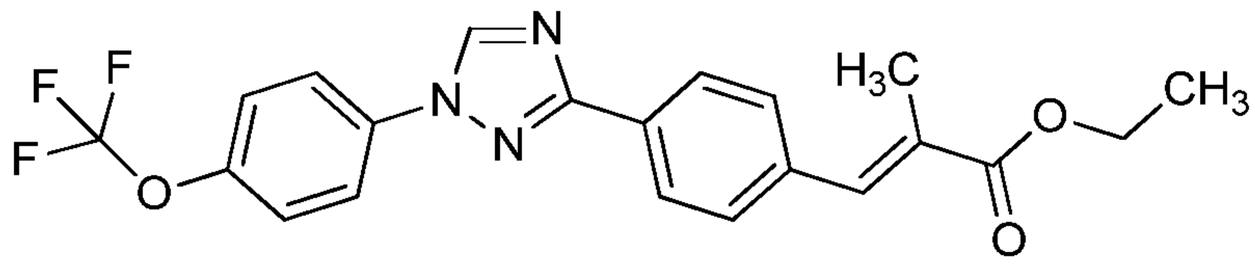
The title compound was prepared from 1-(2-isopropyl-5-methylphenyl)thiourea, 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**), and methyl 2-brompropanoate and isolated as a clear sticky oil (0.192 g, 49%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB40)



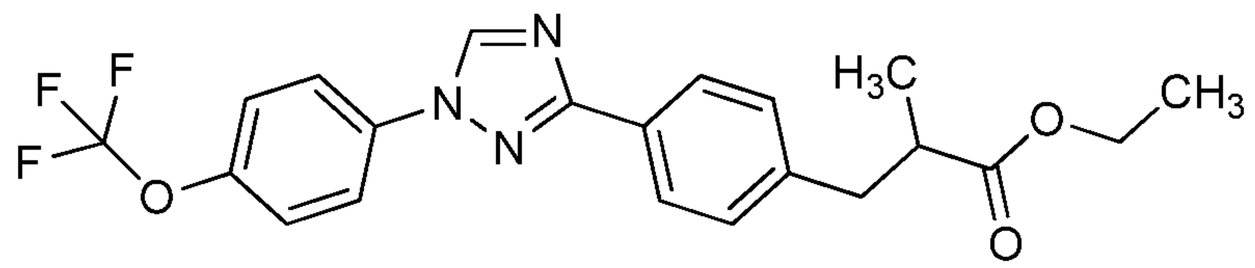
The title compound was prepared from 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and isolated as a brown glassy foam (0.173 g, 48%).

Example 36: Preparation of (*E*)-ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (C36)



4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (7.56 g, 22.7 mmol) and ethyl 2-(triphenylphosphoranylidene)propanoate (9.87 g, 27.2 mmol) in anhydrous toluene (30 mL) was heated at 110 °C for 16 hours. Additional ethyl 2-(triphenylphosphoranylidene)propanoate (2.40 g, 6.06 mmol) was then added, and the reaction was heated at 110 °C for 4 hours. The reaction was cooled, concentrated under vacuum, and loaded onto silica gel. Purification by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent followed by reverse-phase flash column chromatography using 0-100% acetonitrile/water as eluent afforded the title compound as a white solid (5.92 g, 62%): mp 126–127.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.27 - 8.17 (m, 2H), 7.84 - 7.78 (m, 2H), 7.73 (s, 1H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.17 (d, *J* = 1.5 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 418 ($[M+H]^+$).

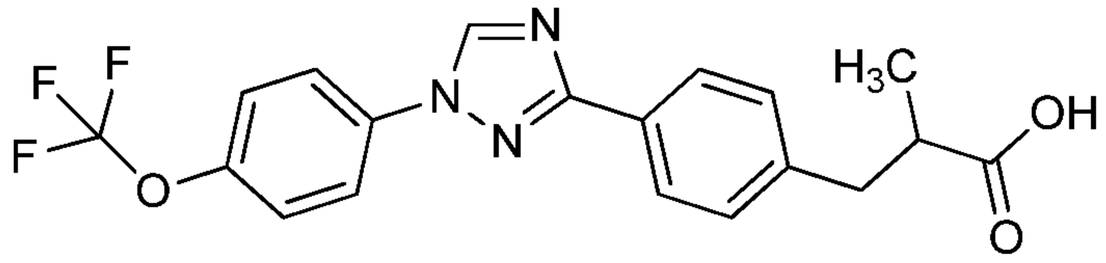
Example 37: Preparation of ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (C37)



A flask containing (*E*)-ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**C36**) (0.96 g, 2.3 mmol) and palladium on carbon (10 wt%, 0.24 g, 0.23 mmol) in ethyl acetate (10 mL) was evacuated under vacuum, filled with nitrogen, evacuated under vacuum, and then placed under hydrogen by balloon (~1 atm). After stirring at room temperature for 20 hours, the reaction was filtered through a pad of Celite® and concentrated to afford the title compound as a white solid (1.0 g, 100%): mp 73–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.14 - 8.07 (m, 2H), 7.86 - 7.76 (m, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz,

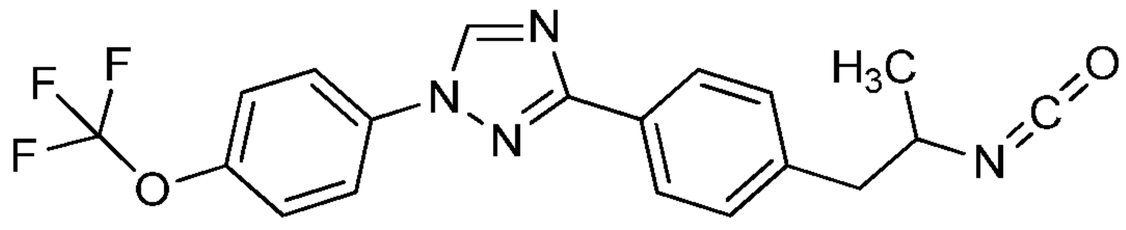
2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.22 - 2.99 (m, 1H), 2.75 (dq, *J* = 13.3, 7.5 Hz, 2H), 1.24 - 1.15 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 420 ($[M+H]^+$).

Example 38: Preparation of 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (C38)



To ethyl 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (**C37**) (0.986 g, 2.35 mmol) in methanol (7.8 mL) was added sodium hydroxide (2 N, 5.9 mL, 11.8 mmol) and the solution was stirred at room temperature for 4 hours. The reaction was acidified with hydrogen chloride (2 N), and the white precipitate was vacuum-filtered to afford the title compound as a white solid (0.865 g, 93%): mp 142–144 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.19 (s, 1H), 9.39 (s, 1H), 8.14 - 7.95 (m, 4H), 7.71 - 7.55 (m, 2H), 7.42 - 7.27 (m, 2H), 3.04 - 2.89 (m, 1H), 2.75 - 2.62 (m, 2H), 1.07 (d, *J* = 6.2 Hz, 3H). ^{19}F NMR (376 MHz, acetone-D_6) δ -58.03; ESIMS *m/z* 392 ($[M+H]^+$).

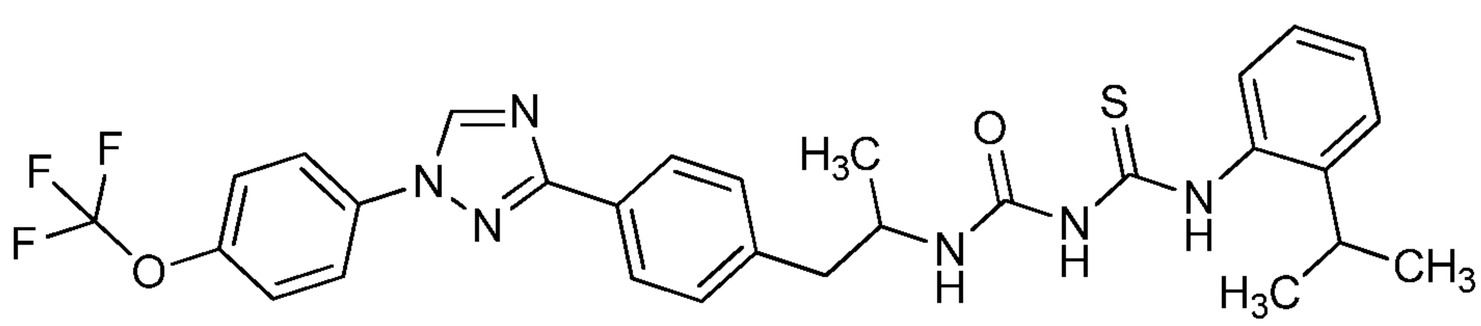
Example 39: Preparation of 3-(4-(2-isocyanatopropyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (C39)



To 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)-propanoic acid (0.84 g, 2.2 mmol) in toluene (21.6 mL) was added triethylamine (0.33 mL, 2.4 mmol) and diphenyl phosphorazidate (0.47 mL, 2.2 mmol) and the solution was stirred at room temperature for 2 hours. The reaction was diluted with ethyl acetate and water and the layers separated. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as a white solid (0.53 g, 58%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.21 - 8.11 (m, 2H), 7.88 - 7.77 (m, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.4 Hz,

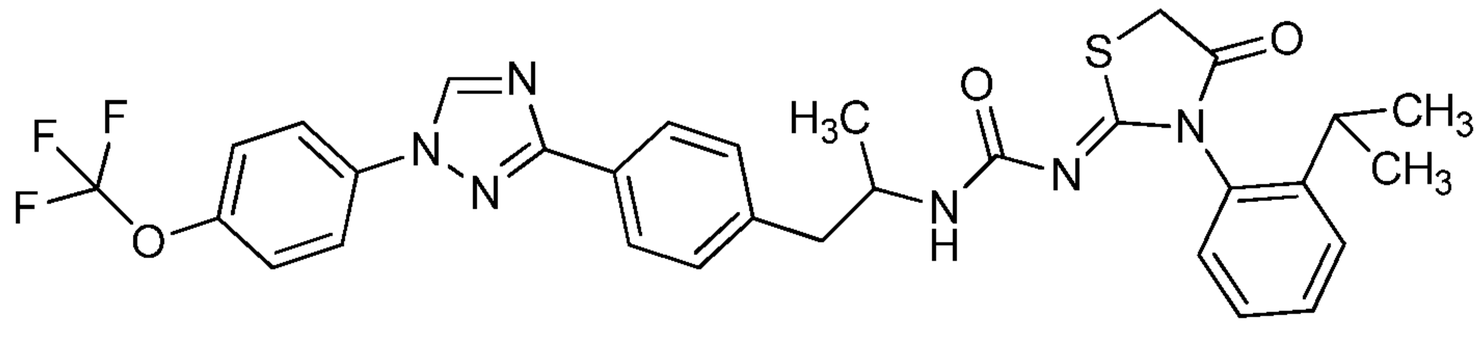
2H), 3.94 - 3.80 (m, 1H), 2.87 (d, *J* = 6.8 Hz, 2H), 1.35 (d, *J* = 6.5 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 389 ($[M+H]^+$).

Example 40: Preparation of *N*-[2-(propan-2-yl)phenyl]-*N'*-[1-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)propan-2-yl]dicarbonimidothioic diamide (F4)



3-(4-(2-Isocyanatopropyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C39**) (0.17 g, 0.41 mmol) in acetonitrile (2.1 mL) was heated at 80 °C for 2 hours to ensure complete conversion to the isocyanate. The reaction was cooled and 1-(2-isopropylphenyl)thiourea (0.83 g, 0.43 mmol) and cesium carbonate (0.17 g, 0.53 mmol) were added and stirred at room temperature overnight. The reaction was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to afford the title compound as a white solid (0.25 g, 95%).

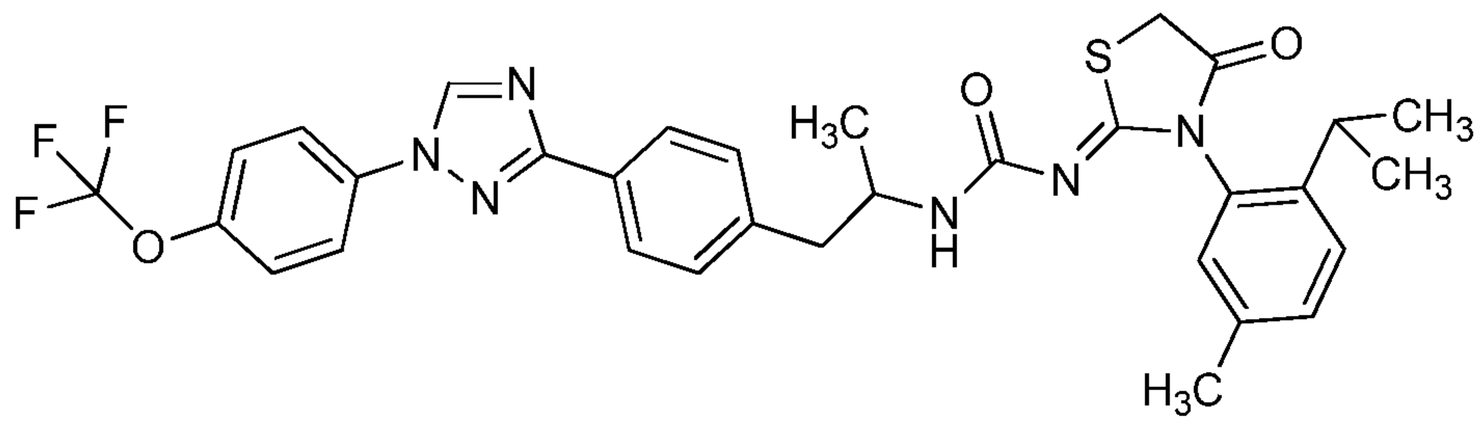
Example 41: Preparation of *(Z)*-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (F7)



To *N*-[2-(propan-2-yl)phenyl]-*N'*-[1-(4-{1-[4-(trifluoromethoxy)phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)propan-2-yl]dicarbonimidothioic diamide (**F4**) (0.20 g, 0.34 mmol) and sodium acetate (0.056 g, 0.68 mmol) in ethanol (2.3 mL) was added methyl 2-bromoacetate (0.05 mL, 0.51 mmol), and the reaction was heated at 65 °C for 2 hours. The reaction was cooled and diluted with water and extracted with ethyl acetate (2x). The organic layers were dried over anhydrous sodium sulfate, filtered,

and concentrated. The crude material was loaded onto a silica gel cartridge with dichloromethane and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as a white solid (0.070 g, 33%).

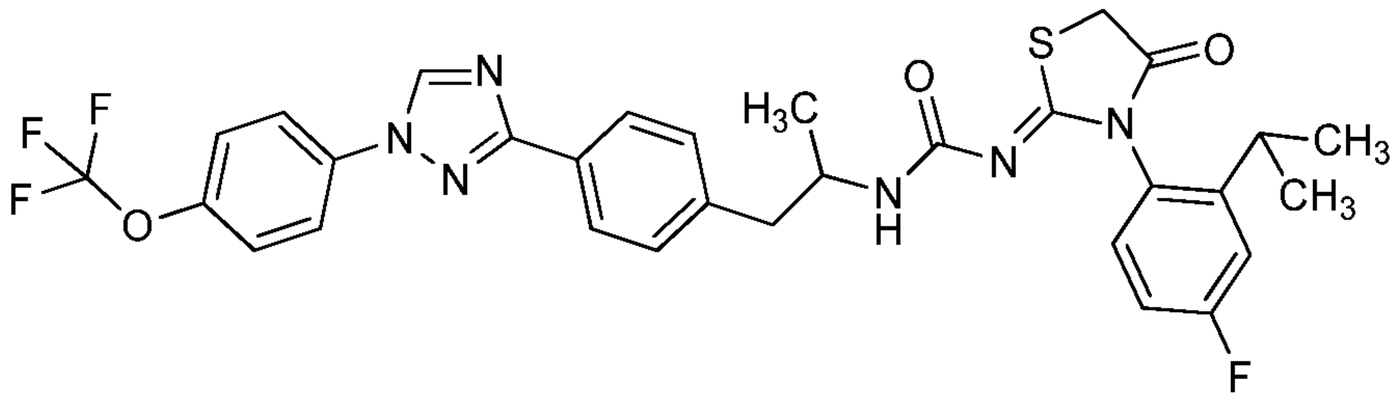
Example 42: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (F8)



3-(4-(2-Isocyanatopropyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C39**) (0.17 g, 0.41 mmol) in acetonitrile (2 mL) was heated at 80 °C for 2 hours to ensure complete conversion to the isocyanate. The reaction was cooled and 1-(2-isopropyl-5-methylphenyl)thiourea (0.095 g, 0.46 mmol) and cesium carbonate (0.20 g, 0.60 mmol) were added. The reaction was stirred at room temperature for 3 days. The reaction was diluted with ethanol (2.5 mL) and sodium acetate (0.064 g, 0.78 mmol) and methyl 2-bromoacetate (0.05 mL, 0.53 mmol) were added. The reaction was heated at 65 °C for 2.5 hours. The reaction mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted an additional time with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as an off-white solid (0.054 g, 20%).

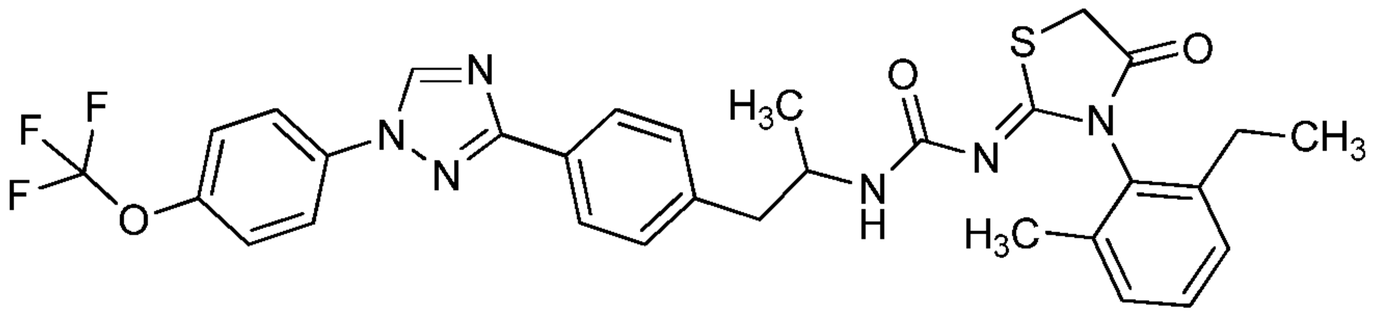
The following compounds were prepared in accordance to the procedure in Example 42.

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (P33)



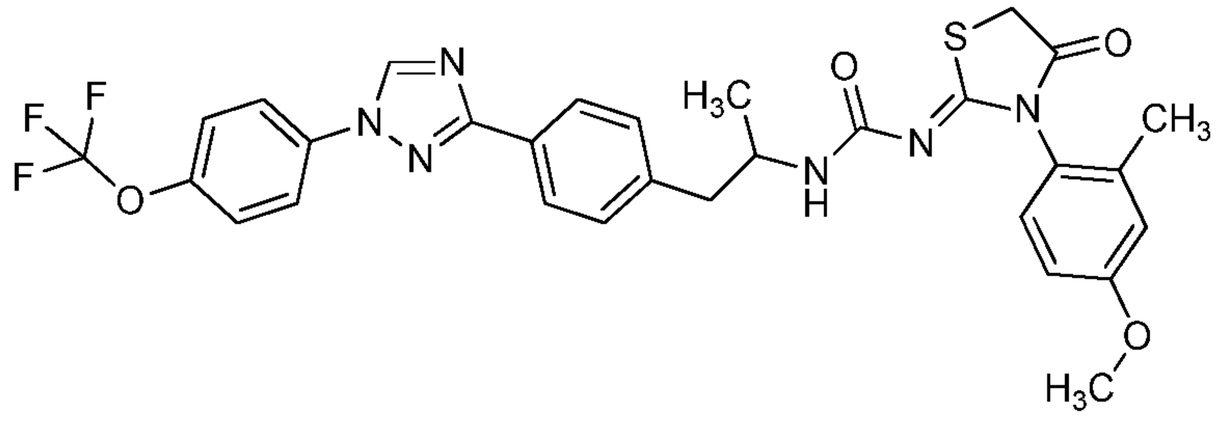
The title compound was prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C39**) and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as a brown solid (0.183 g, 60%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (P42)



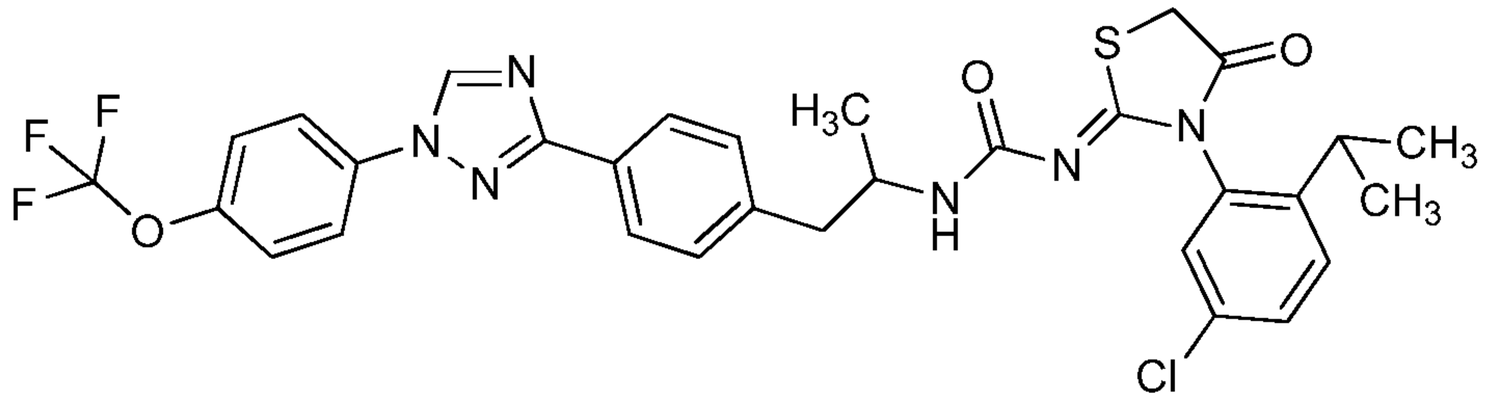
The title compound was prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C39**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) and isolated as an off-white solid (0.117 g, 39%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (P45)



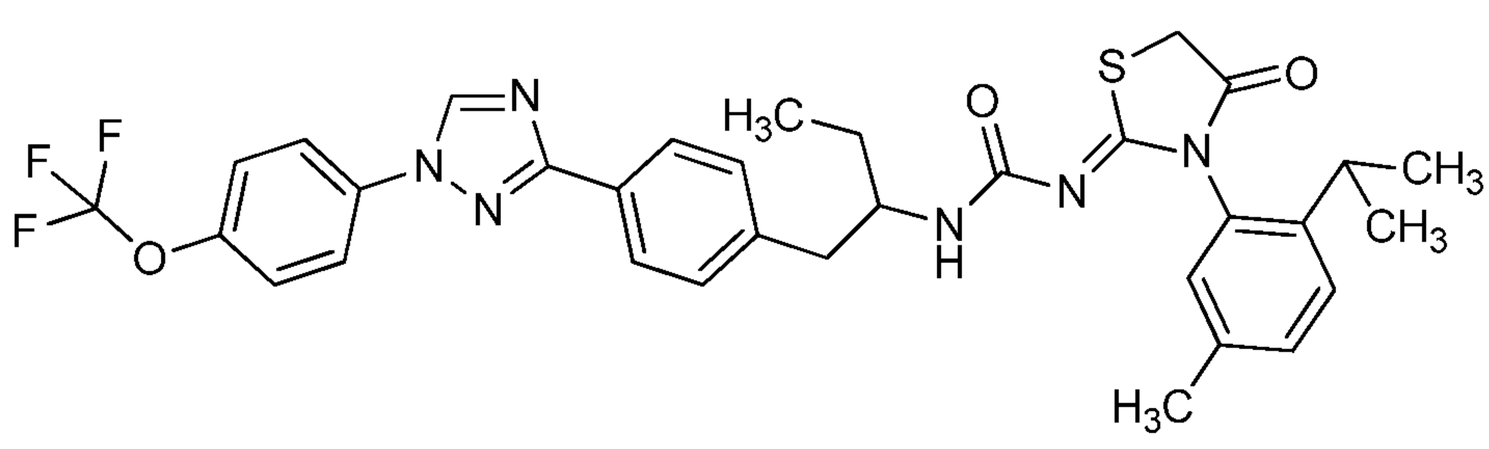
The title compound was prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C39**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as a brown solid (0.224 g, 65%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (FB42)



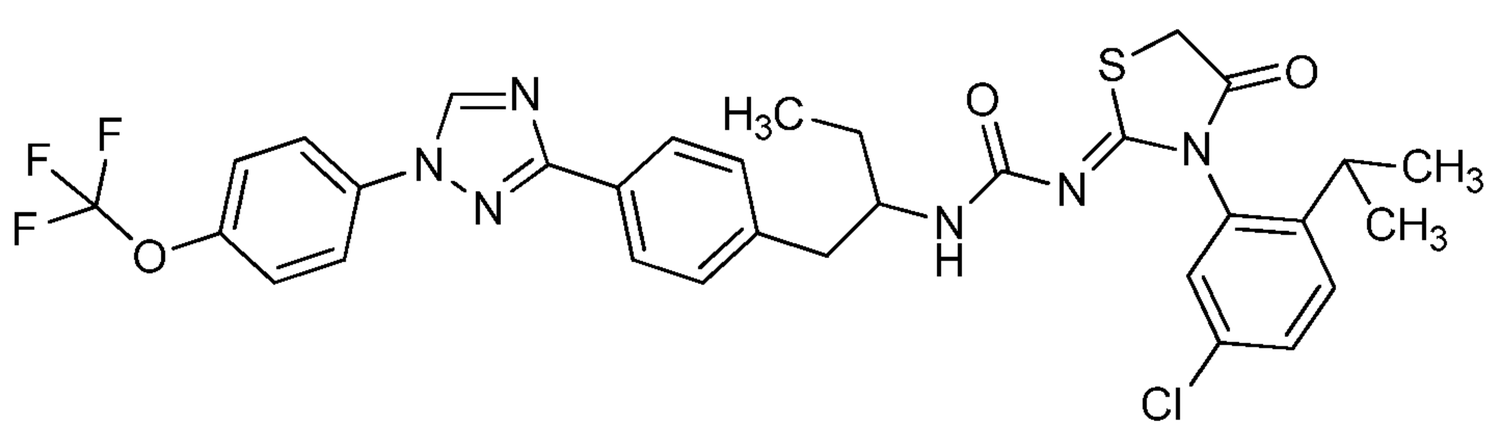
The title compound was prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C39**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and isolated as a brown oil (0.110 g, 46%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-2-yl)urea (FB43) 12412827



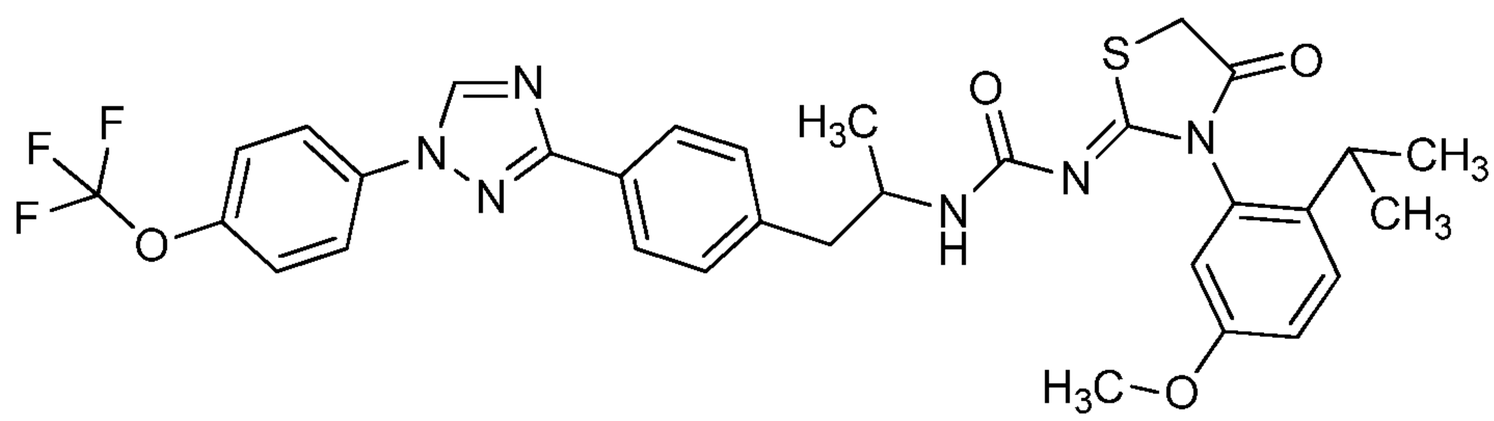
The title compound was prepared from 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)butanoyl azide (**CB22**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a peach glassy foam (0.122 g, 53%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-2-yl)urea (FB44)



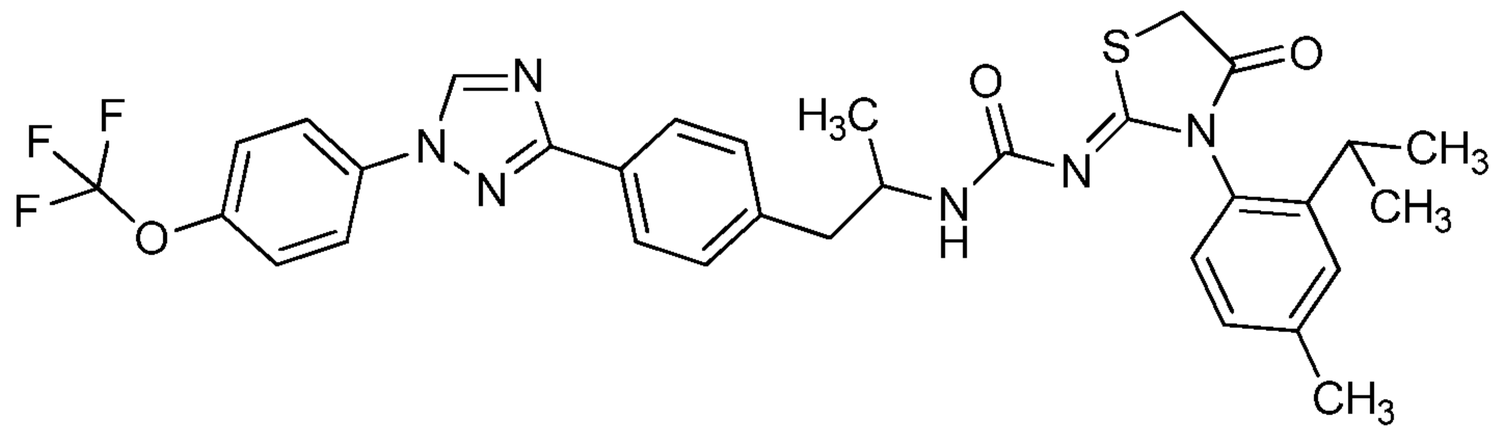
The title compound was prepared from 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)butanoyl azide (**CB22**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and isolated as a tan glassy foam (0.132 g, 60%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (FB47)



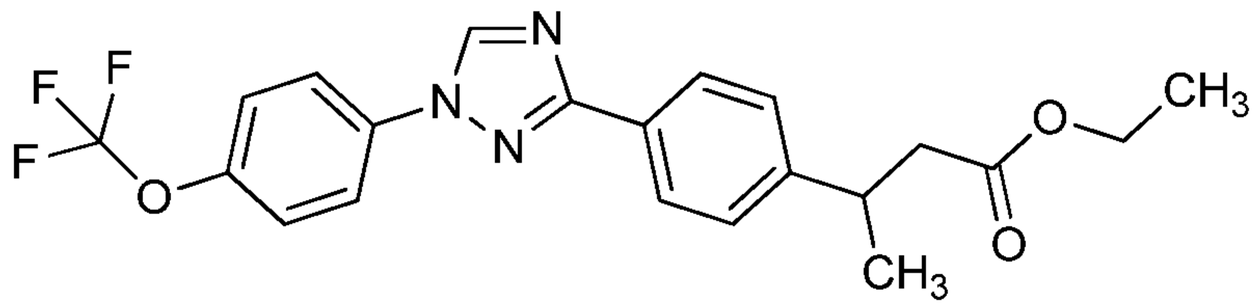
The title compound was prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C39**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated as a brown oil (0.146 g, 42%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (FB48)



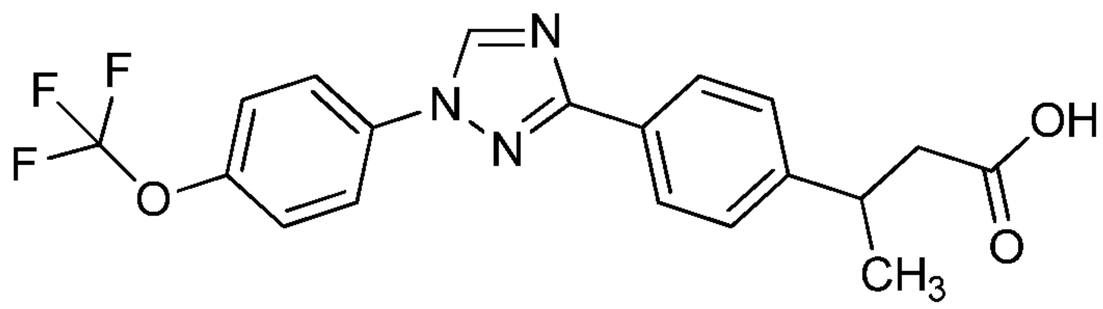
The title compound was prepared from 2-methyl-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C39**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as a brown oil (0.130 g, 47%).

Example 43: Preparation of ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoate (C40)



A flask containing (*E*)-ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-2-enoate (**C26**) (1.80 g, 4.31 mmol) and palladium on carbon (10 wt %, 0.46 g, 0.43 mmol) in ethyl acetate (14.5 mL) was evacuated and backfilled with nitrogen, and then evacuated and placed under hydrogen by balloon (~1atm). The reaction was stirred at room temperature overnight, and then filtered through Celite® and concentrated to afford the title compound as a tan liquid (1.79 g, 98%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.17 - 8.07 (m, 2H), 7.87 - 7.75 (m, 2H), 7.38 (d, *J* = 9.1 Hz, 2H), 7.36 - 7.31 (m, 2H), 4.08 (qd, *J* = 7.1, 0.8 Hz, 2H), 3.35 (dd, *J* = 14.6, 7.2 Hz, 1H), 2.62 (qd, *J* = 15.1, 7.6 Hz, 2H), 1.34 (d, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 420 ($[M+H]^+$).

Example 44: Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoic acid (C41)

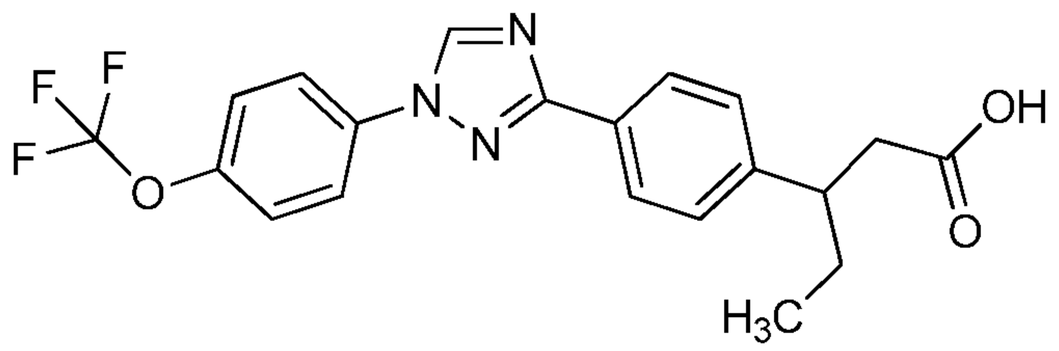


To ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl) butanoate (**C40**) (1.78 g, 4.24 mmol) in methanol (14 mL) was added sodium hydroxide (2 N, 12.7 mL, 25.4 mmol) and stirred at room temperature for 4 hours. The reaction acidified with hydrogen chloride (2 N), and the methanol was concentrated off under vacuum. The aqueous solution was extracted with ethyl acetate (3x). The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to afford the title compound as a clear gum (0.470 g, 28%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (s, 1H), 8.11 - 8.05 (m, 2H), 8.02 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 3.21 (dd, *J* = 14.4, 7.1 Hz,

1H), 2.56 (d, *J* = 7.4 Hz, 2H), 1.26 (d, *J* = 7.0 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 392 ($[M+H]^+$).

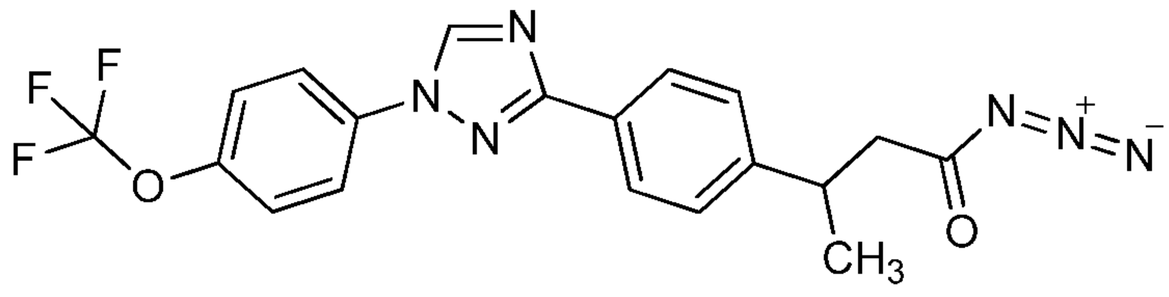
The following compounds were prepared in accordance to the procedure in Example 44.

Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoic acid (CA12)



The title compound was prepared from ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoate (**CA4**8) and isolated as a white solid (0.927 g, 36%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 9.39 (s, 1H), 8.17 - 7.94 (m, 4H), 7.73 - 7.51 (m, 2H), 7.46 - 7.25 (m, 2H), 2.96 (ddd, *J* = 14.7, 8.7, 6.0 Hz, 1H), 2.64 (dd, *J* = 15.5, 6.6 Hz, 1H), 2.55 - 2.49 (m, 1H), 1.79 - 1.49 (m, 2H), 0.74 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.99; ESIMS *m/z* 406 ($[M+H]^+$).

Example 45: Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide (C42)

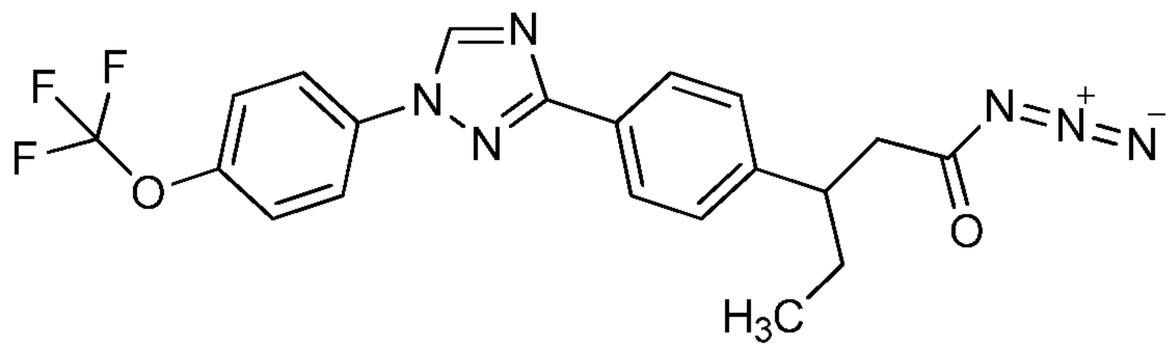


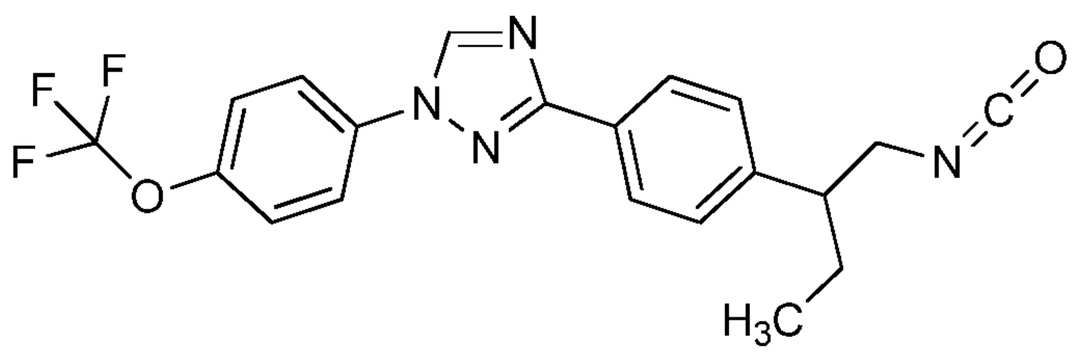
To 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoic acid (**C41**) (1.77 g, 4.52 mmol) in toluene (18 mL) was added triethylamine (0.82 mL, 5.88 mol) and diphenyl phosphorazidate (1.05 mL, 4.98 mmol) and the solution was stirred at room temperature for 3 hours. The reaction was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1

dichloromethane/hexanes, as eluent to afford the title compound as a clear oil (0.223 g, 12% yield): ^{1}H NMR is consistent with a mixture of carbonyl azide and isocyanate. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.28 - 8.03 (m, 2H), 7.88 - 7.66 (m, 2H), 7.48 - 7.30 (m, 4H), 3.60 - 3.40 (m, 2H), 3.08 (q, *J* = 6.9 Hz, 1H), 2.81 - 2.49 (m, 1H), 1.37 (dd, *J* = 10.4, 7.0 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 417 ($[M+H]^+$)

The following compounds were prepared in accordance to the procedure in Example 45.

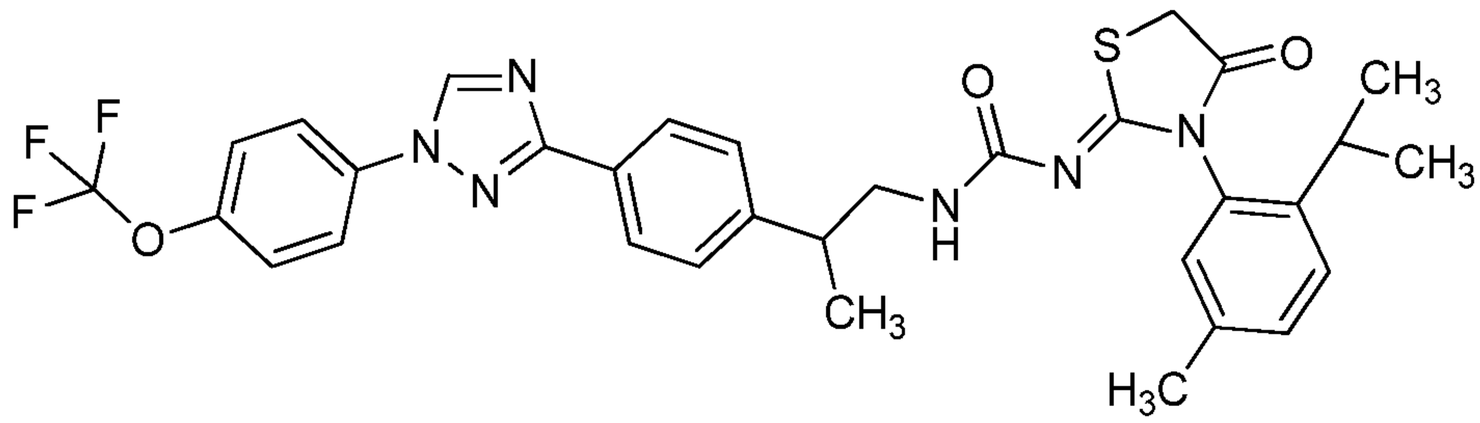
Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoyl azide/3-(4-(1-isocyanatobutan-2-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (C42a)





The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoic acid (**CA12**) to furnish a mixture of azide and isocyanate, 0.723 g, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (two s, 1H), 8.20 – 8.15 (m, 2H), 7.85 – 7.74 (m, 2H), 7.39 (dt, *J* = 9.0, 1.0 Hz, 2H), 7.34 – 7.29 (m, 2H), 3.62 – 3.38 (m, 2H), 2.77 – 2.59 (m, 1H), 1.93 – 1.59 (m, 2H), 0.94 – 0.83 (m, 3H).

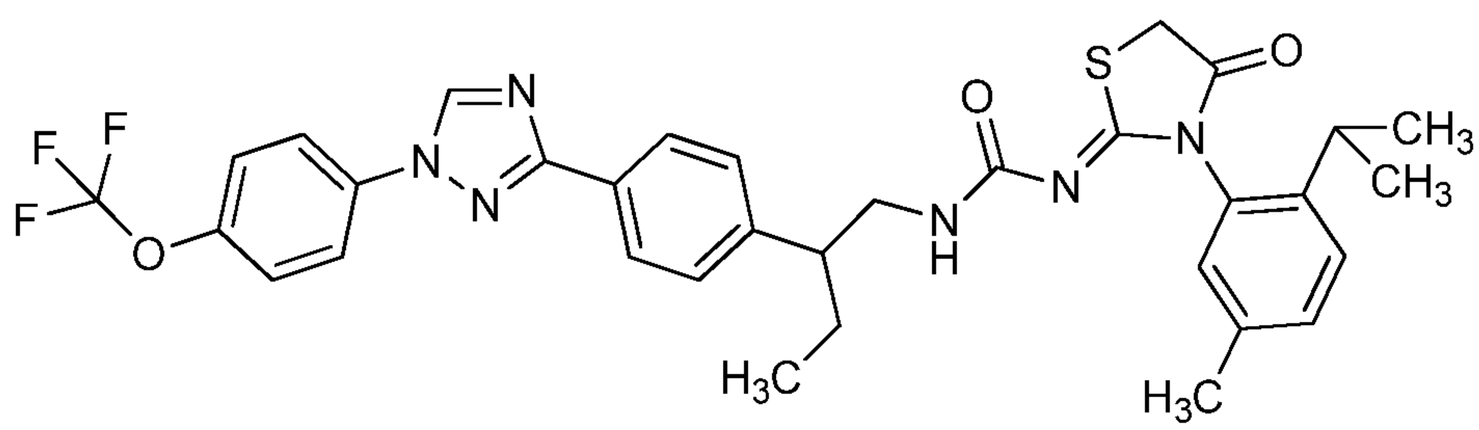
Example 46: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (F10)



3-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide (**C42**) (0.22 g, 0.52 mmol) in acetonitrile (2.6 mL) was heated at 80 °C for 2 hours. The reaction was cooled and 1-(2-isopropyl-5-methylphenyl)thiourea (0.12 g, 0.57 mmol) and cesium carbonate (0.20 g, 0.61 mmol) were added. The reaction was stirred at room temperature for 18 hours. Sodium acetate (0.093 g, 1.1 mmol), methyl 2-bromoacetate (0.07 mL, 0.78 mmol) and ethanol (2.6 mL) were added, and the reaction mixture was heated at 65 °C for 3 hours. The reaction was cooled, diluted with ethyl acetate, and washed with water. The aqueous layer was extracted once more with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to afford the title compound as an orange solid (0.12 g, 35%).

The following compounds were prepared in accordance to the procedure in Example 46.

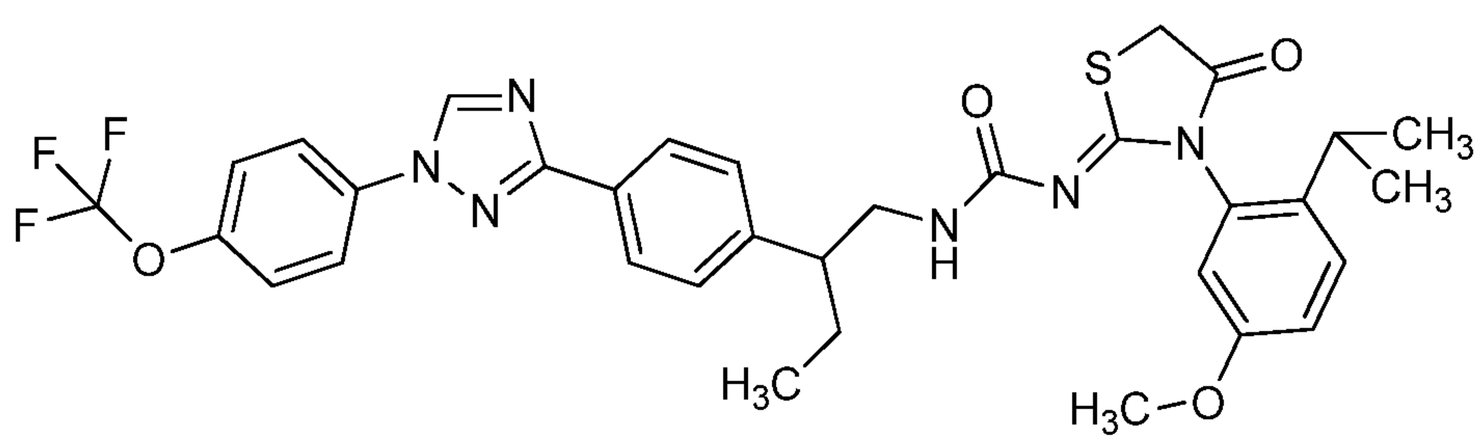
Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P364)



The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoyl azide/3-(4-(1-isocyanatobutan-2-yl)phenyl)-1-

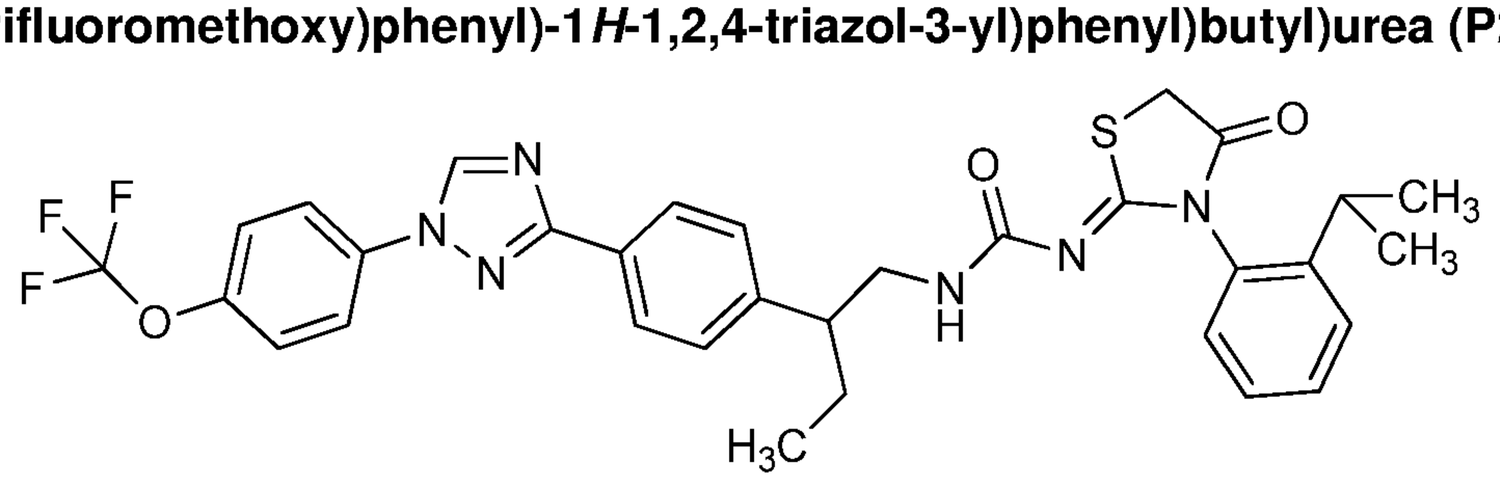
(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C42a**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a pink solid (0.110 g, 43%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P683)



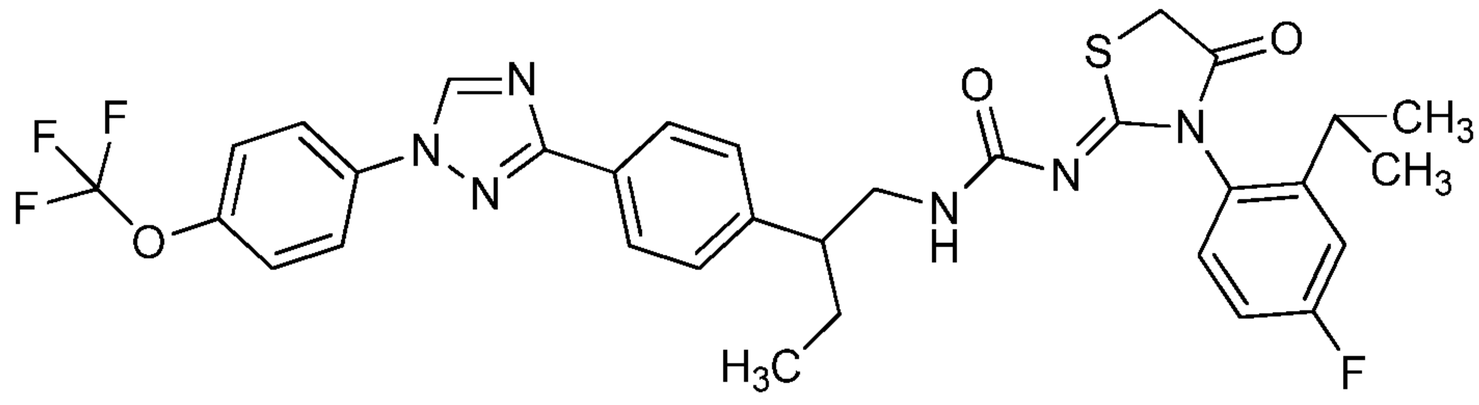
The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoyl azide/3-(4-(1-isocyanatobutan-2-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C42a**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated as a brown foam (0.091 g, 47%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P209)



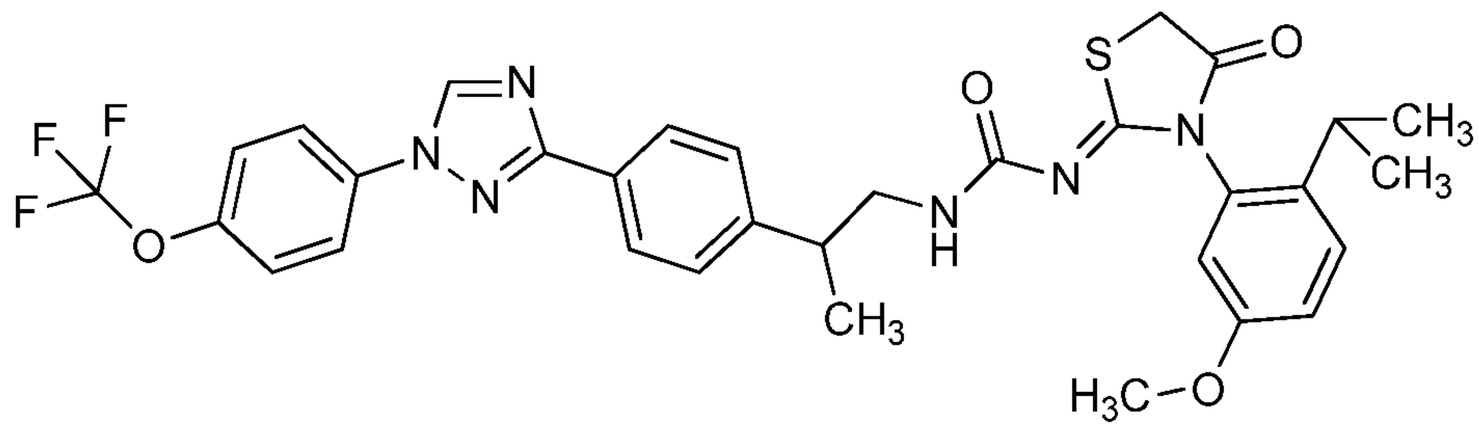
The title compound was prepared from3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoyl azide/3-(4-(1-isocyanatobutan-2-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C42a**) and 1-(2-isopropylphenyl)thiourea and isolated as a brown foam (0.041 g, 30%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P1163)



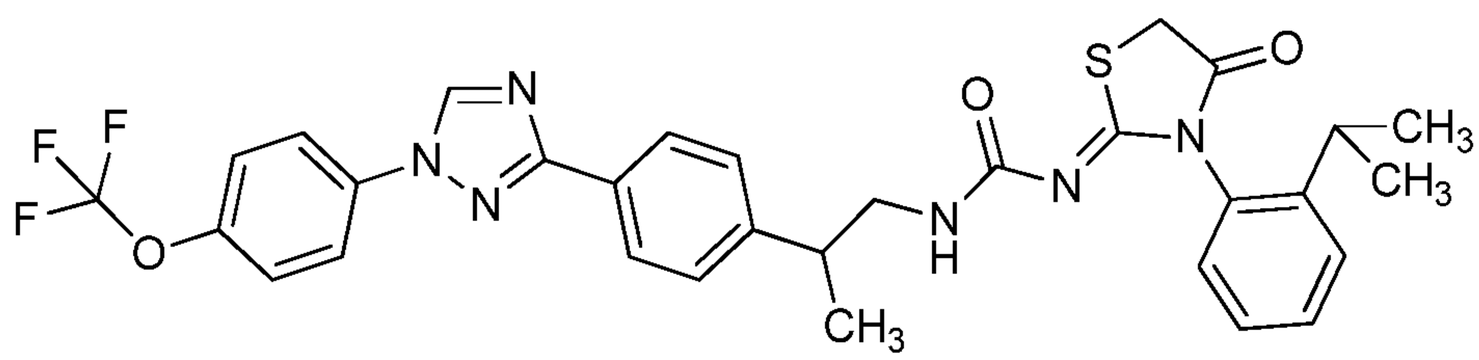
The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoyl azide/3-(4-(1-isocyanatobutan-2-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C42a**) and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as a brown foam (0.072 g, 30%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P679)



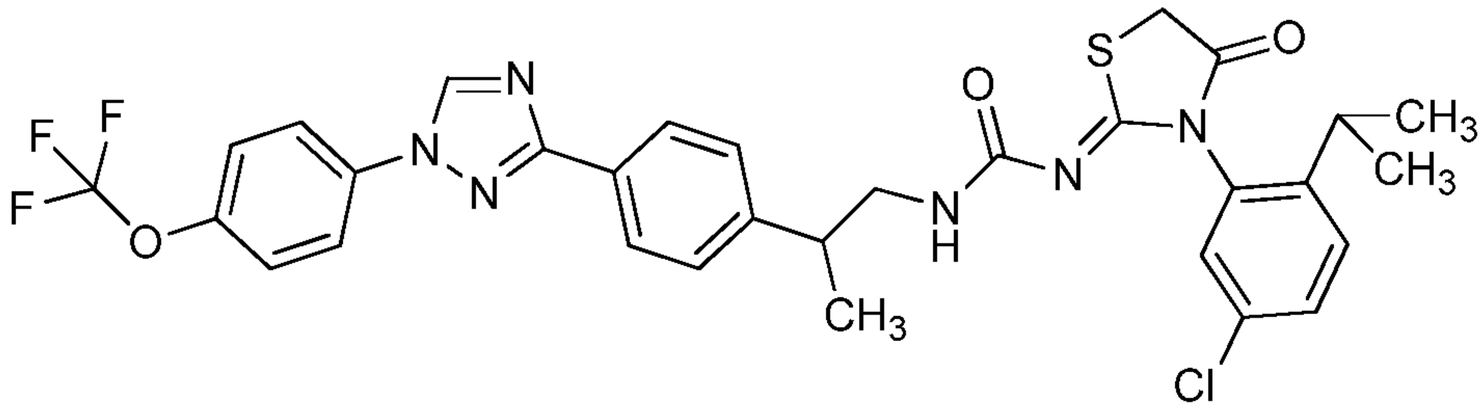
The title compound was prepared as described in Example 46 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide (C42) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated as a brown solid (0.118 g, 54%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P205)



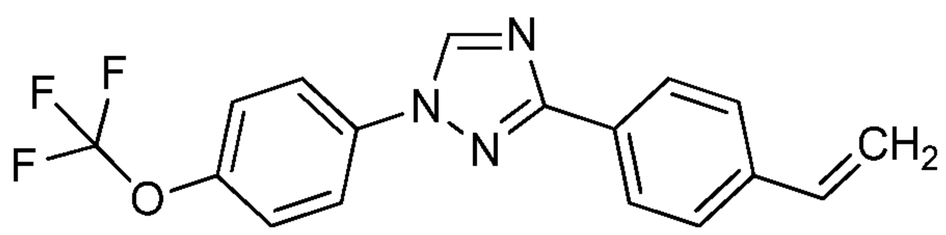
The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide (**C42**) and 1-(2-isopropylphenyl)thiourea and isolated as a brown solid (0.105 g, 43%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (FB49)



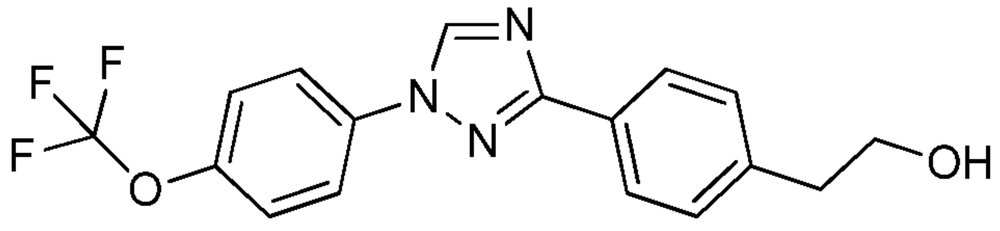
The title compound was prepared from 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butanoyl azide (**C42**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and isolated as a brown oil (0.055 g, 22%).

Example 47: Preparation of 1-(4-(trifluoromethoxy)phenyl)-3-(4-vinylphenyl)-1*H*-1,2,4-triazole (C43)



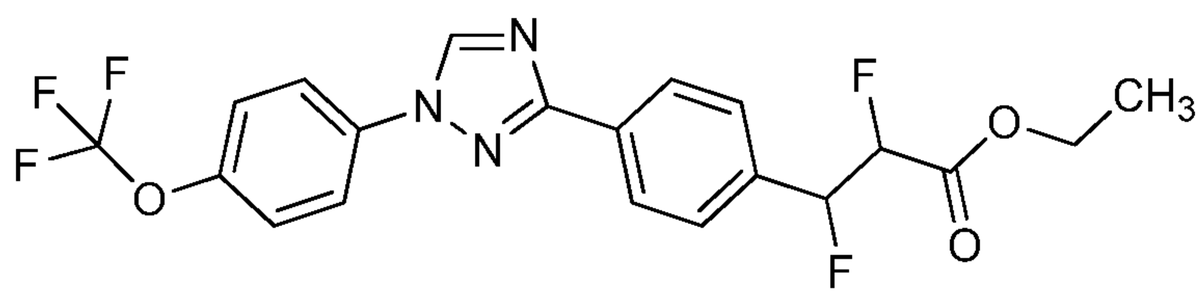
Methyltriphenylphosphonium bromide (32.2 g, 90.0 mmol) and 1,8-diazabicycloundec-7-ene (14.9 mL, 99.0 mmol) were dissolved in tetrahydrofuran (260 mL) and refluxed for 30 minutes. 4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (15.0 g, 45.0 mmol) was added, and the reaction was heated at 65 °C for 5 hours. The solution was cooled and stirred at room temperature overnight. The reaction mixture was poured into water and extracted with hexanes. The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude compound was purified by flash column chromatography using 0-70% ethyl acetate/hexanes as eluent to afford the title compound as a white solid (10.4 g, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.16 (d, *J* = 8.3 Hz, 2H), 7.80 (d, *J* = 9.0 Hz, 2H), 7.58 - 7.47 (m, 2H), 7.39 (d, *J* = 9.1Hz, 2H), 6.77 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.84 (dd, *J* = 17.6, 0.8 Hz, 1H), 5.32 (dd, *J* = 10.9, 0.8 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 332 ($[M+H]^+$).

Example 48: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanol (C44)



To 1-(4-(trifluoromethoxy)phenyl)-3-(4-vinylphenyl)-1*H*-1,2,4-triazole (**C43**) (2.0 g, 6.0 mmol) in tetrahydrofuran (50 mL) was added 9-borabicyclo(3.3.1)nonane (24 mL, 12.1 mmol), and the reaction was stirred at room temperature for 4.5 hours. Sodium hydroxide (3 N, 4.0 mL, 12.0 mmol) was added, followed by hydrogen peroxide (30% wt, 1.5 mL, 15.1 mmol). The light green solution was stirred at room temperature overnight. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to give a light green oil. The crude compound was purified by flash column chromatography using 0-50% ethyl acetate/hexanes as eluent to afford the title compound as a white solid (1.5 g, 69%): mp 85–98 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (s, 1H), 8.06 (d, J = 9.0 Hz, 2H), 8.01 (d, J = 8.1 Hz, 2H), 7.61 (dd, J = 9.2, 1.0 Hz, 2H), 7.41 - 7.30 (m, 2H), 4.69 (t, J = 5.2 Hz, 1H), 3.65 (td, J = 7.0, 5.1 Hz, 2H), 2.79 (t, J = 6.9 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.18, 147.08, 143.70, 141.45, 135.72, 129.39, 128.23, 127.93, 125.96, 122.57, 121.10, 61.90, 61.90; ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 349 ([M+H]$^{+}$).

Example 49: Preparation of ethyl 2,3-difluoro-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (C45)

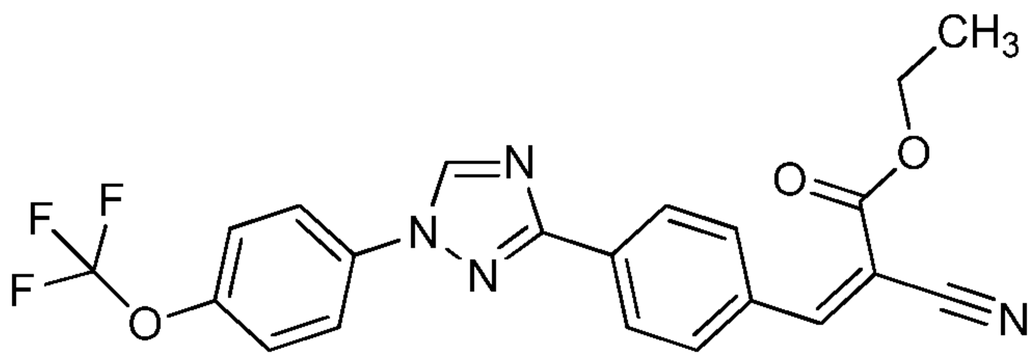


Step 1. Sodium hydride (60% oil immersion, 0.48 g, 12 mmol) was added to a dry, oven-dried round bottomed flask and placed under nitrogen. Diethyl ether (9 mL) was added, followed by absolute ethanol (0.05 mL), and the reaction was cooled in an ice bath. Ethyl 2-fluoroacetate (0.87 mL, 9.0 mmol) was added dropwise. The reaction was stirred for 15 minutes in ice bath (gas evolution ceased). 4-(1-(4-

(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (2.2 g, 6.5 mmol) was added in solid portions. The solution slowly turned color to a golden yellow. The ice bath was removed after 1 hour and warmed to room temperature, stirring for an additional 2 hours until the reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether, and stirred at room temperature for 3 days. The biphasic solution was diluted with brine and extracted with ethyl acetate (2x). The organic layers were dried organic over anhydrous sodium sulfate, filtered, and concentrated to give an orange liquid. The crude material was purified by reverse-phase flash column chromatography using 0-100% acetonitrile/water as eluent to afford the intermediate ethyl 2-fluoro-3-hydroxy-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate as a crude compound (0.11 g).

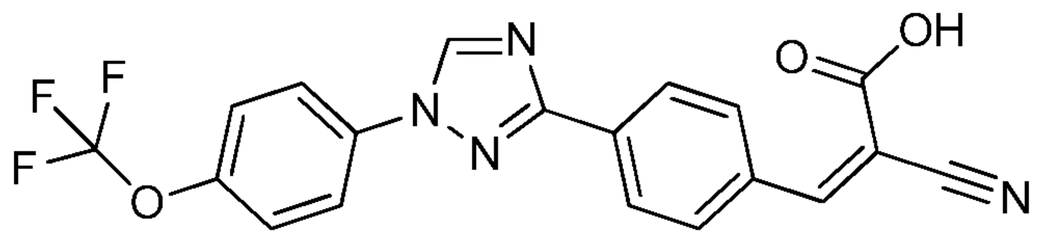
Step 2. To the crude ethyl 2-fluoro-3-hydroxy-3-(4-(1-(4-(trifluoromethoxy) phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (0.11 g, 0.26 mmol) in dichloromethane (1.7 mL) at 0 °C was added Deoxo-fluor® (0.05 mL, 0.28 mmol) and stirred for 30 minutes. The reaction mixture was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-60% ethyl acetate/hexanes as eluent to afford the title compound as a yellow oil (0.054 g, 47%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 1.9 Hz, 1H), 8.32 - 8.14 (m, 2H), 7.87 - 7.73 (m, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 6.11 - 5.76 (m, 1H), 5.52 - 4.90 (m, 1H), 4.27 (dqd, *J* = 23.6, 7.1, 2.1 Hz, 2H), 1.27 (dt, *J* = 19.4, 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.04, -187.64, -187.68, -192.41, -192.44, -202.56, -202.60, -204.97, -205.00; ESIMS *m/z* 442 ($[M+H]^+$).

Example 50: Preparation of (*Z*)-ethyl 2-cyano-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (C46)



To 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (3.0 g, 9.0 mmol) in ethanol (11.5 mL) was added ethyl 2-cyanoacetate (0.95 mL, 8.9 mmol) and pyrrolidine (0.97 mL, 12 mmol). A yellow precipitate formed immediately and additional ethanol (10 mL) was added. The reaction was stirred at room temperature for 18 hours and then concentrated onto Celite®. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes as eluent afforded the title compound as a white solid (2.1 g, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.36 - 8.31 (m, 2H), 8.29 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.85 - 7.79 (m, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.46, 162.24, 154.18, 141.89, 135.36, 134.76, 132.41, 131.53, 127.22, 122.47, 121.33, 115.51, 103.28, 62.82, 14.19; ESIMS *m/z* 429 ($[M+H]^+$).

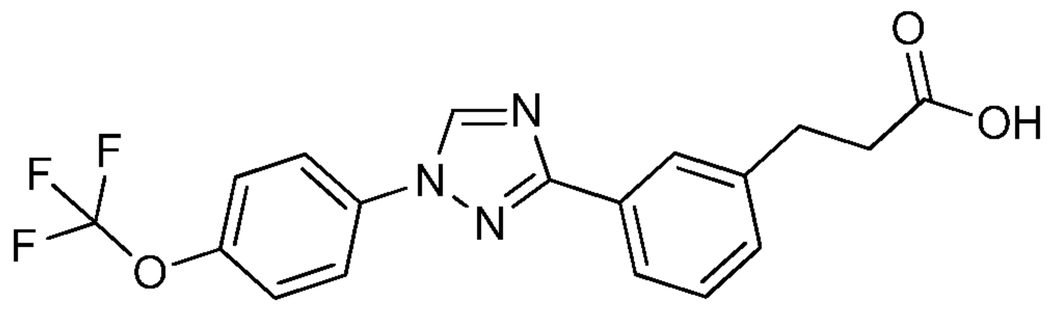
Example 51: Preparation of (*Z*)-2-cyano-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylic acid (C47)



To (*Z*)-ethyl 2-cyano-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acrylate (**C46**) (2.5 g, 5.8 mmol) in tetrahydrofuran/methanol/water (3:2:1, 42 mL) was added lithium hydroxide (2.5 mL, 7.5 mmol) and stirred at room temperature for 18 hours. The reaction mixture was concentrated under vacuum, cooled in an ice bath, and acidified with hydrogen chloride (2 N). The precipitate was filtered and washed with cold water to afford the title compound as a brown solid (2.2 g, 82%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.49 (s, 1H), 8.39 (s, 1H), 8.28 (d, *J* = 8.5 Hz, 2H), 8.18 (d, *J* = 8.5 Hz, 2H), 8.13 – 8.08 (m, 2H), 7.64 (d, *J* = 8.4 Hz, 2H); ESIMS *m/z* 401 ($[M+H]^+$).

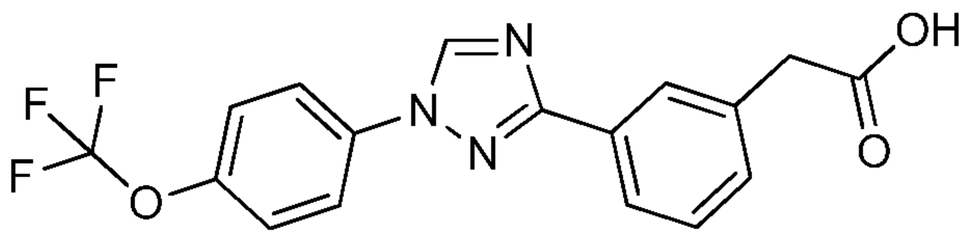
The following compounds were prepared in accordance to the procedure in Example 51.

Preparation of 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (CA13)



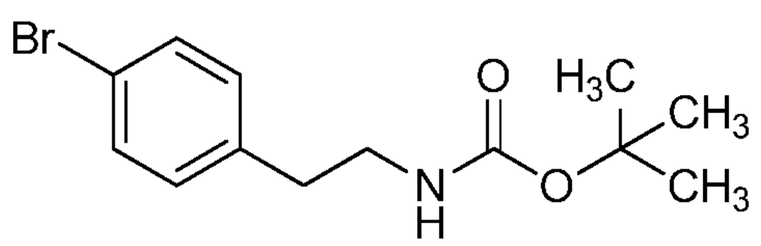
The title compound was prepared from methyl 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoate (**CA1**) and isolated as a tan solid (9.09 g, 94%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.13 - 8.04 (m, 2H), 7.98 (t, J = 1.7 Hz, 1H), 7.94 (dt, J = 7.7, 1.4 Hz, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.35 (dt, J = 7.7, 1.4 Hz, 1H), 2.93 (t, J = 7.5 Hz, 2H), 2.61 (t, J = 7.5 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.99; ESIMS *m/z* 378 ([M+H]$^+$), 376 ([M-H]$^-$).

Preparation of 2-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (CB23)



The title compound was prepared from methyl 2-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetate (**CB11**) and isolated as a light brown solid (4.28 g, 88%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (s, 1H), 9.42 (s, 1H), 8.13 - 8.06 (m, 2H), 8.06 - 7.96 (m, 2H), 7.63 (dq, J = 8.0, 1.0 Hz, 2H), 7.47 (td, J = 7.6, 0.6 Hz, 1H), 7.38 (dt, J = 7.7, 1.5 Hz, 1H), 3.70 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 364 ([M+H]$^+$), 362 ([M-H]$^-$).

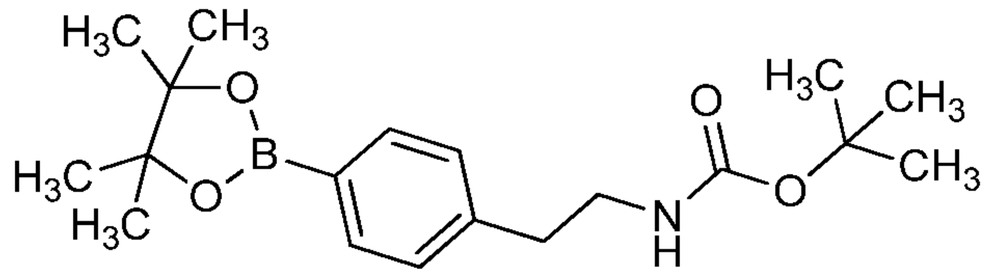
Example 52: Preparation of *tert*-butyl 4-bromophenethylcarbamate (C48)



To a stirring solution of 4-dimethylaminopyridine (0.19 g, 1.5 mmol) and di-*tert*-butyl dicarbonate (2.6 g, 12 mmol) in dichloromethane (40 mL) was added 4-bromophenethylamine (1.6 mL, 10 mmol) and stirring was continued at room temperature for 48 hours. The reaction mixture directly adsorbed onto silica gel and purified by flash column chromatography using 0-40% ethyl acetate/hexanes as

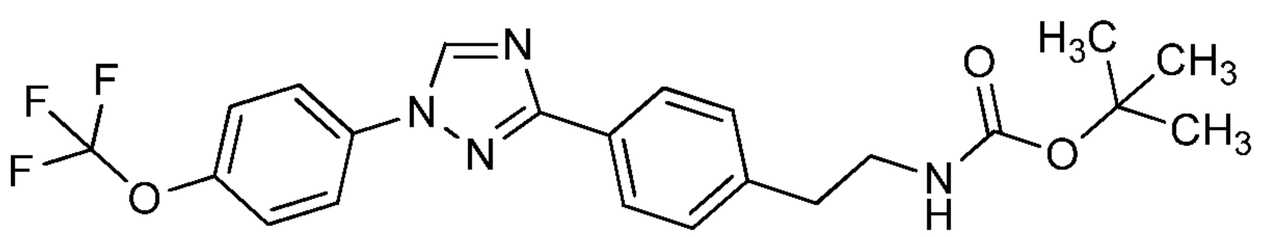
eluent to afford the title compound as a white solid (0.68 g, 22%): mp 58–59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 4.51 (s, 1H), 3.43 - 3.27 (m, 2H), 2.75 (t, *J* = 7.0 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.79, 137.97, 131.62, 130.55, 120.25, 77.21, 41.58, 35.65, 28.39; EIMS *m/z* 301 ($[M]^+$).

Example 53: Preparation of *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenethylcarbamate (C49)



A mixture of *tert*-butyl 4-bromophenethylcarbamate (**C48**) (0.68 g, 2.3 mmol), bis(pinacolato)diborane (0.89 g, 3.5 mmol), potassium acetate (0.69 g, 7.0 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.10 g, 0.14 mmol), and 1,1′-bis(diphenylphosphino)ferrocene (0.075 g, 0.14 mmol) in anhydrous dioxane (7 mL) was heated at 80 °C for 18 hours. The reaction was cooled, diluted with ethyl acetate, and washed with water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated. The crude compound was adsorbed onto silica gel and purified by flash column chromatography using 0-60% ethyl acetate/hexanes as eluent to afford the title compound as a clear oil (0.86 g, 104%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.9 Hz, 2H), 7.23 - 7.17 (m, 2H), 4.51 (s, 1H), 3.46 - 3.28 (m, 2H), 2.81 (t, *J* = 7.1 Hz, 2H), 1.43 (s, 9H), 1.34 (s, 12H); ESIMS *m/z* 348 ($[M+H]^+$).

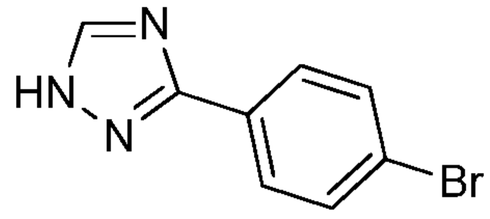
Example 54: Preparation of *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (C50)



A mixture of 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) (0.55 g, 1.8 mmol), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenethyl carbamate (**C49**) (0.63 g, 1.8 mmol),

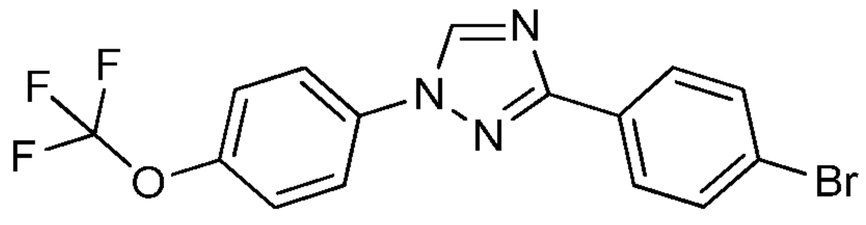
tetrakis(triphenylphosphine)palladium(0) (0.21 g, 0.18 mmol), and sodium bicarbonate (0.33 g, 3.9 mmol) in dioxane/water (16 mL, 3:1) in a 20 mL vial was capped and heated at 140 ºC for 30 minutes in a Biotage Initiator® microwave reactor with external IR-sensor temperature monitoring from the side of the vessel. The reaction was diluted with ethyl acetate and washed with water. The aqueous layers were extracted with ethyl acetate (2x), and the combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The crude material was loaded onto a Celite® cartridge and purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/ hexanes, as eluent to provide the title compound as a white solid (0.48 g, 60%): mp 149 – 151 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.13 (d, *J* = 8.1 Hz, 2H), 7.84 - 7.76 (m, 2H), 7.42 - 7.35 (m, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 4.55 (s, 1H), 3.51 - 3.34 (m, 2H), 2.87 (t, *J* = 7.0 Hz, 2H), 1.44 (s, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 449 ($[M+H]^+$).

Example 55: Preparation of 3-(4-bromophenyl)-1*H*-1,2,4-triazole (C51)



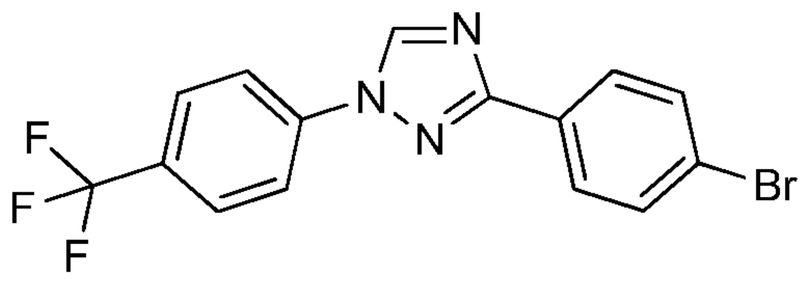
4-Bromo benzamide (28.0 g, 0.140 mol) was suspended in 1,1-dimethoxy-*N,N*-dimethylmethanamine (50 mL, 420 mmol) and the solution was stirred and heated to 90 ℃ for 2 hours. The solution was then cooled to ambient temperature and diethyl ether (150 mL) was added. The solution was cooled to 0 ℃ overnight and filtered to give (*E*)-4-bromo-*N*-((dimethylamino)methylene)benzamide as a colorless solid (25.6 g). This material was then dissolved in acetic acid (50 mL) and hydrazine (3.50 g, 110 mmol) was added slowly (exotherm) to the stirred solution, which solidified. The mixture was heated to 90 ℃ and a stir bar was added. The solid slowly dissolved over 8 hours and was then cooled to ambient temperature and the solution was diluted with water (35 mL). The resulting white solid was filtered and dried *in vacuo* to furnish the title compound as a colorless solid (19.8 g, 88%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.91 (s, 1H), 8.51 (s, 1H), 8.01 - 7.93 (m, 2H), 7.73 - 7.67 (m, 2H; ESIMS *m/z* 224, 226 ($[M+H]^+$).

Example 56: Preparation of 3-(4-bromophenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (C52)



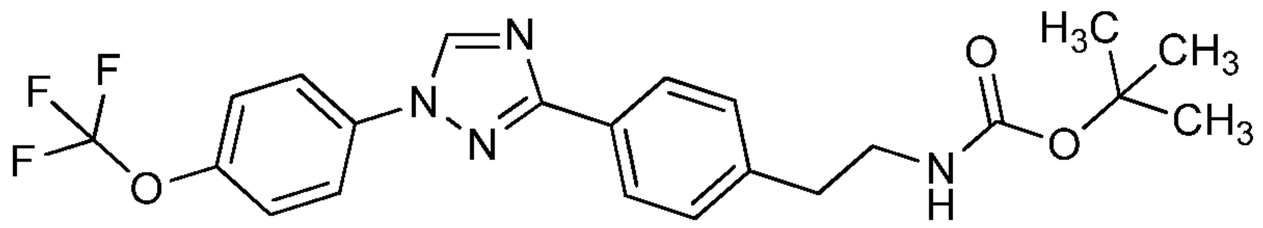
To a solution of 1-iodo-4-(trifluoromethoxy)benzene (15.0 g, 52.0 mmol) in dimethylformamide (90 mL) and water (10 mL) was added 3-(4-bromophenyl)-1*H*-1,2,4-triazole (C51) (11.0 g, 49.0 mmol), cesium carbonate (34.0 g, 104 mmol), copper(I) iodide (2.80 g, 14.7 mmol), and 8-hydroxyquinoline (2.20 g, 15.0 mmol), and the solution was heated at 140 ºC for 8 hours. The cooled solution was decanted from a layer of solid, diluted with a ammonium hydroxide (1 N, 100 mL) solution, and extracted with of diethyl ether (2 x 100 mL). The combined organic layer was dried and concentrated, and the brown solid was eluted through a short silica gel column using 20% ethyl acetate/hexanes as eluent to give the title compound as a light tan solid (9.50 g, 50%): mp 111–113 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.07 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 2H); ESIMS *m/z* 384 ($[M+H]^+$).

Preparation of 3-(4-bromophenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (C53)



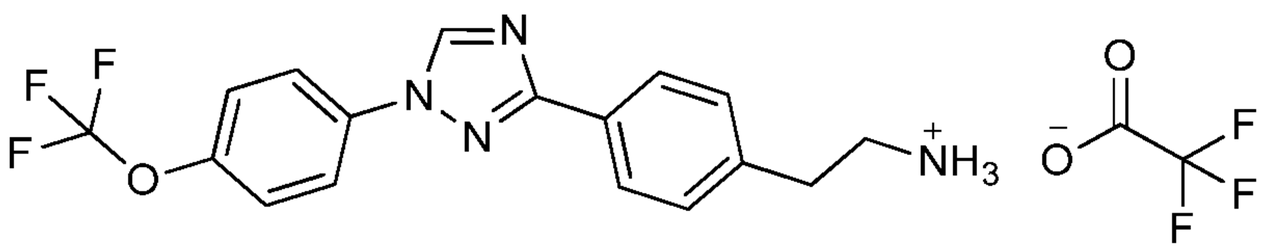
The title compound was prepared as described in Example 56 using 1-iodo-4-(trifluoromethyl)benzene to furnish the title compound as a white solid (3.21 g, 64%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.06 (d, *J* = 8.6 Hz, 2H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H); ESIMS *m/z* 368, 370 ($[M+H]^+$).

Example 57: Preparation of *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (C50)



To a solution of 3-(4-bromophenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C52**) (0.13 g, 0.32 mmol) in toluene (4 mL) and water (1 mL) was added potassium (2-((*tert*-butoxycarbonyl)amino)ethyl)trifluoroborate (0.082 g, 0.33 mmol), palladium(II) acetate (0.027 g, 0.027 mmol), cesium carbonate (0.33 g, 1.0 mmol), and dicyclohexyl(2',6'-diisopropoxy-[1,1'-biphenyl]-2-yl)phosphine (0.016 g, 0.034 mmol), and the solution was stirred under nitrogen and heated to 95 ºC for 8 hours. The solution was then cooled and diluted with diethyl ether (5 mL) and adsorbed onto a silica gel pre-column. Flash column chromatography using 0-50% ethyl acetate/hexanes as eluent furnished the title compound as a light tan solid (0.095 g, 63%): mp 149–153 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.18 – 8.10 (m, 2H), 7.84 – 7.77 (m, 2H), 7.43 – 7.35 (m, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 4.58 (d, *J* = 8.1 Hz, 1H), 3.49 – 3.34 (m, 1H), 2.87 (t, *J* = 7.0 Hz, 1H),1.44 (s, 9H); ESIMS *m/z* 449 ($[M+H]^+$).

Example 58: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (C55)

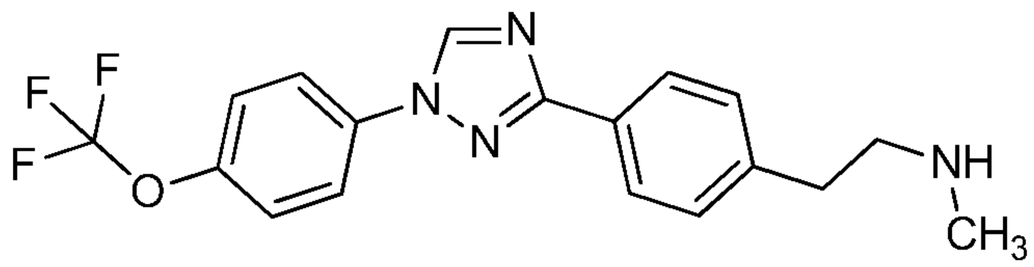


To a stirred and cooled (0 ºC) solution of tert-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1H-1,2,4-triazol-3-yl)phenethylcarbamate (C50) (0.35 g, 0.77 mmol) in dichloromethane (2.6 mL) was added trifluoroacetic acid (0.060 mL, 0.78 mmol), and the solution was allowed to warm slowly to ambient temperature. After 18 hours, an additional amount of trifluoroacetic acid (0.060 mL, 0.78 mmol) was added. After 24 hours a third aliquot of trifluoroacetic acid (0.060 mL, 0.78 mmol) was added. After an additional 24 hours, the solution was concentrated to give the title compound as a tan solid (0.325 g, 88%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.08 (dd, *J* = 8.8, 2.6 Hz, 4H), 7.87 (s, 2H), 7.63 (d, *J* = 8.3 Hz, 2H),

7.43 (d, *J* = 8.3 Hz, 2H), 3.17 - 3.06 (m, 2H), 2.99 - 2.89 (m, 2H); ESIMS m/z 349 ([M+H]+).

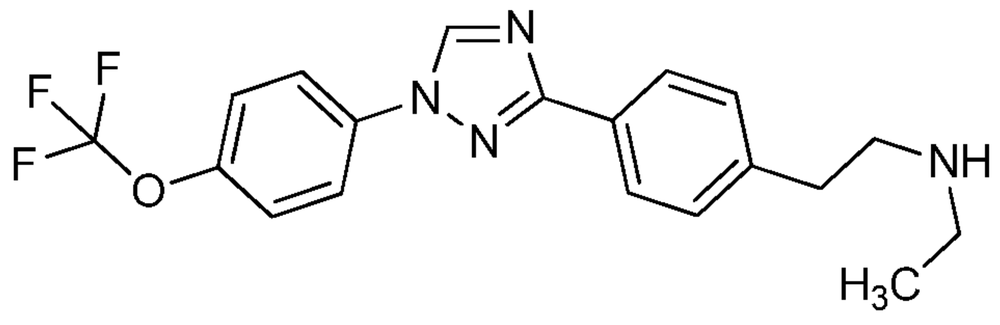
The following compounds were prepared in accordance to the procedure in Example 58.

Preparation of *N*-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (CB24)



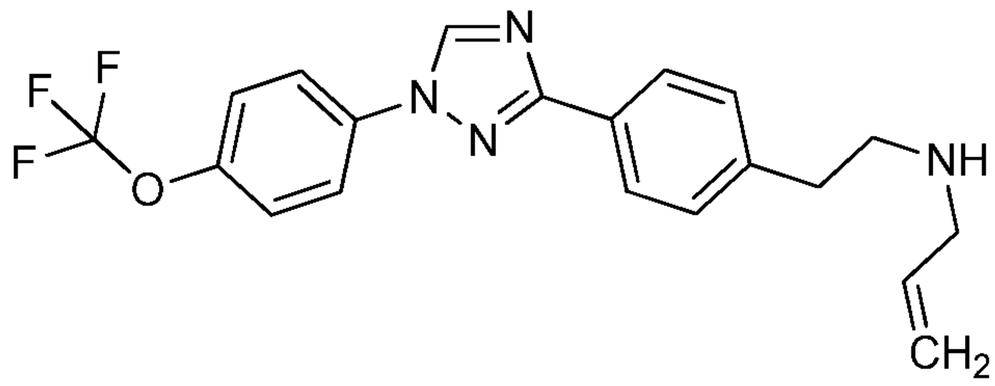
The title compound was prepared from *tert*-butyl methyl(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (**CB63**), neutralized with aqueous sodium bicarbonate, and isolated as a yellow waxy solid with excess trifluoroacetic acid (5.73 g, 111%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.12 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 9.0 Hz, 2H), 7.37 (dd, *J* = 9.0, 1.0 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 3.23 - 3.12 (m, 2H), 3.05 (dd, *J* = 9.4, 6.3 Hz, 2H), 2.67 (s, 3H), 1.29 - 1.22 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.04, -75.71; ESIMS *m/z* 363 ($[M+H]^+$).

Preparation of *N*-ethyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (CB25)



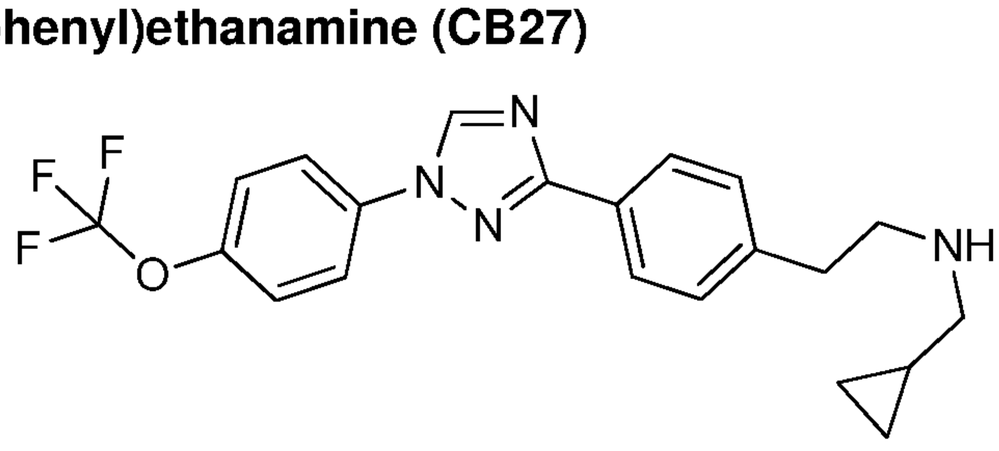
The title compound was prepared from *tert*-butyl ethyl(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (**CB64**), neutralized with aqueous sodium bicarbonate, and isolated as an orange solid (0.167 g, 98%, 80% pure): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.17 - 8.06 (m, 2H), 7.87 - 7.63 (m, 2H), 7.37 (dt, *J* = 8.0, 1.0 Hz, 2H), 7.34 - 7.28 (m, 2H), 3.21 (s, 2H), 3.14 - 2.97 (m, 4H), 1.84 (s, 1H), 0.87 (ddd, *J* = 12.0, 8.9, 6.6 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.04; ESIMS *m/z* 377 ($[M+H]^+$).

Preparation of *N*-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)prop-2-en-1-amine (CB26)



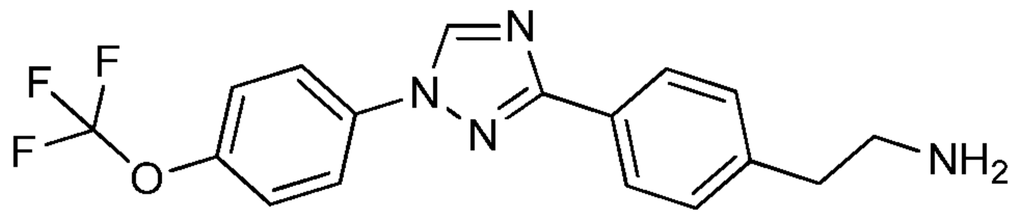
The title compound was prepared from *tert*-butyl allyl(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (**CB65**), neutralized with aqueous sodium bicarbonate, and isolated as a yellow solid (0.124 g, 90%): mp 110-120 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.14 - 8.07 (m, 2H), 7.81 - 7.73 (m, 2H), 7.42 - 7.34 (m, 2H), 7.34 - 7.28 (m, 2H), 5.92 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.43 - 5.22 (m, 2H), 3.49 (dt, *J* = 6.6, 1.2 Hz, 2H), 3.19 - 2.92 (m, 5H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.04; ESIMS *m/z* 389 ($[M+H]^+$).

Preparation of *N*-(cyclopropylmethyl)-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (CB27)



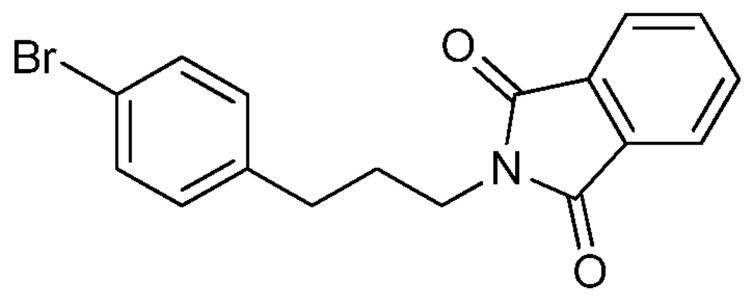
The title compound was prepared from *tert*-butyl (cyclopropylmethyl)(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (**CB66**), neutralized with aqueous sodium bicarbonate, and isolated as a white solid (0.125 g, 100%): mp 162-166 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.15 - 8.09 (m, 2H), 7.81 - 7.75 (m, 2H), 7.38 (dq, *J* = 8.9, 0.9 Hz, 2H), 7.34 - 7.29 (m, 2H), 3.22 (dd, *J* = 10.2, 6.0 Hz, 2H), 3.09 (dd, *J* = 10.0, 6.1 Hz, 2H), 2.84 (d, *J* = 7.3 Hz, 2H), 1.11 (ddd, *J* = 12.7, 8.1, 4.8 Hz, 1H), 0.86 (dd, *J* = 12.8, 5.8 Hz, 1H), 0.69 - 0.58 (m, 2H), 0.37 - 0.29 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 403 ($[M+H]^+$).

Example 58a: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (CA51)



To a stirred and cooled (0 ºC) solution of *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (C50) (0.10 g, 0.22 mmol) in dichloromethane (1.6 mL) was added trifluoroacetic acid (0.19 mL, 0.25 mmol), and the solution was allowed to warm slowly to ambient temperature and stirred overnight. The reaction mixture was concentrated, taken up in hexanes, and concentrated until a solid was obtained. The solid was dissolved in dichloromethane and washed with saturated sodium bicarbonate. The aqueous layer was extracted with dichloromethane (2x). The combined organic layers were washed with saturated sodium bicarbonate. The organic layers were dried over magnesium sulfate, filtered, and concentrated to give the title compound as a white solid (0.075 g, 97%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.18 – 8.07 (m, 2H), 7.83 – 7.74 (m, 2H), 7.41 – 7.29 (m, 4H), 3.02 (t, *J* = 6.8 Hz, 2H), 2.81 (t, *J* = 6.8 Hz, 2H), 1.45 – 1.29 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.04.

Example 59: Preparation of 2-(3-(4-bromophenyl)propyl)isoindoline-1,3-dione (C56)

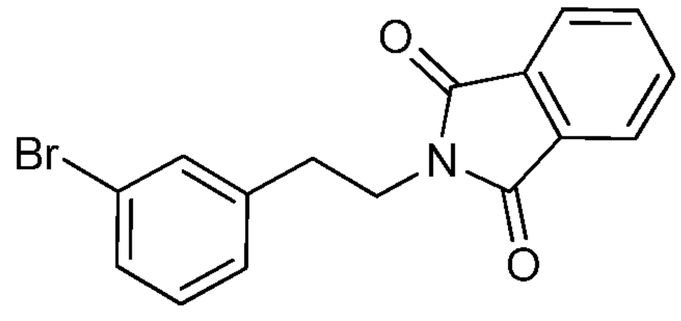


To 3-(4-bromophenyl)propan-1-ol (4.70 g, 21.9 mmol), isoindoline-1,3-dione (3.54 g, 24.0 mmol) and triphenylphosphine (6.88 g, 26.2 mmol) in a 500 mL round bottomed flask equipped with a stir bar, nitrogen, and addition funnel, and cooled in an ice water bath was added diisopropyl azodicarboxylate (5.10 mL, 26.2 mmol). The reaction was allowed to warm to room temperature over the weekend. The reaction mixture was adsorbed onto Celite®. Purification by flash column chromatography using 5-20% ethyl acetate/hexanes as eluent provided a solid which was dried overnight at 50 ºC *in vacuo* to afford the title compound as a white solid (6.51 g, 87%): mp 88–90 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 - 7.79 (m, 2H), 7.71

(dd, *J* = 5.5, 3.0 Hz, 2H), 7.38 - 7.32 (m, 2H), 7.11 - 7.04 (m, 2H), 3.73 (t, *J* = 7.1 Hz, 2H), 2.68 - 2.59 (m, 2H), 2.07 - 1.96 (m, 2H); ESIMS *m/z* 346 [$(M+2)^+$].

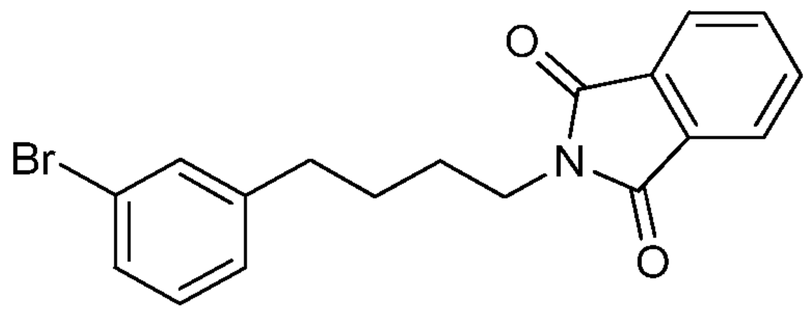
The following compounds were prepared in accordance to the procedure in Example 59.

Preparation of 2-(3-bromophenethyl)isoindoline-1,3-dione (C57)



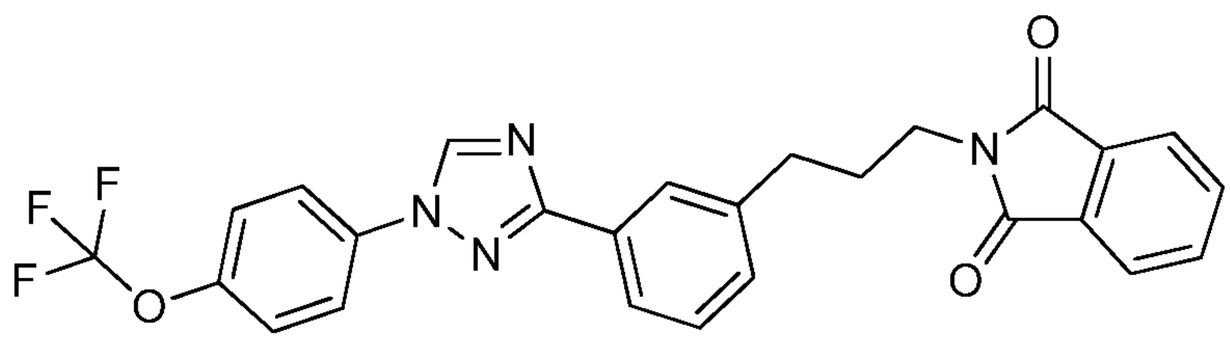
The title compound was prepared from 2-(3-bromophenyl)ethanol to afford the title compound as a white solid (3.92 g, 81%): mp 100–104 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 - 7.81 (m, 2H), 7.76 - 7.69 (m, 2H), 7.43 - 7.39 (m, 1H), 7.35 (dt, *J* = 7.4, 1.8 Hz, 1H), 7.22 - 7.13 (m, 2H), 3.94 - 3.87 (m, 2H), 2.99 - 2.92 (m, 2H); ESIMS *m/z* 332 ([M+2]$^+$).

Preparation of 2-(4-(3-bromophenyl)butyl)isoindoline-1,3-dione (C57a)



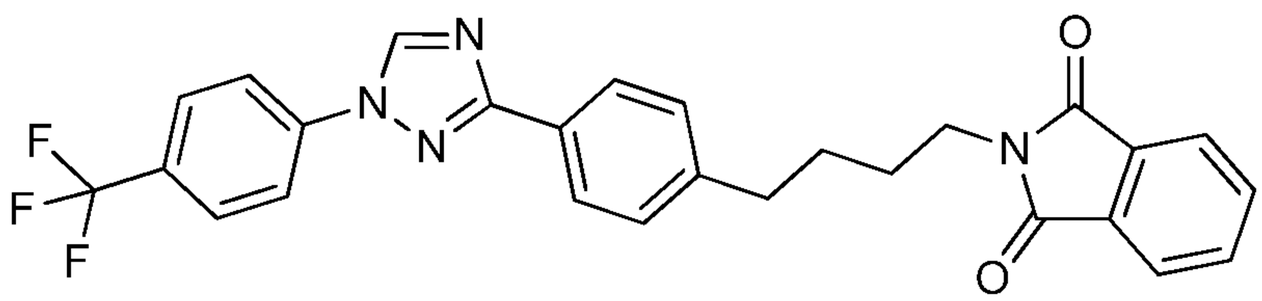
The title compound was prepared from 4-(3-bromophenyl)butan-1-ol (**C86**) to afford the title compound as a white solid (7.68 g, 62%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.91 - 7.78 (m, 4H), 7.40 (t, *J* = 1.9 Hz, 1H), 7.35 (dt, *J* = 7.2, 2.0 Hz, 1H), 7.28 - 7.15 (m, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 1.72 - 1.45 (m, 4H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.92, 144.86, 134.30, 131.57, 131.00, 130.34, 128.57, 127.41, 122.94, 121.55, 37.10, 34.08, 28.08, 27.50; EIMS *m/z* 357,359.

Preparation of 2-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)isoindoline-1,3-dione (CA14)



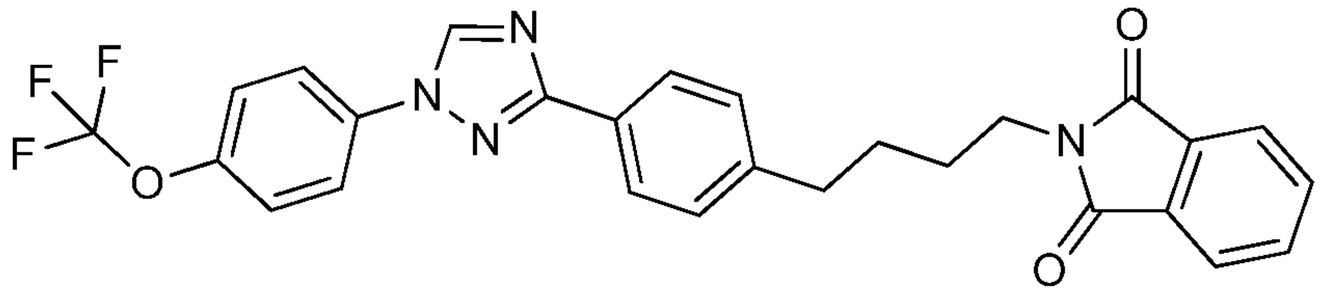
The title compound was prepared from 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-ol (**CA45**) and isolated as a light yellow solid (4.49 g, 81%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 8.18 - 8.02 (m, 2H), 7.96 (t, J = 1.7 Hz, 1H), 7.89 (dt, J = 7.7, 1.5 Hz, 1H), 7.87 - 7.76 (m, 4H), 7.62 (d, J = 8.5 Hz, 2H), 7.40 (t, J = 7.6 Hz, 1H), 7.34 (dt, J = 7.7, 1.5 Hz, 1H), 3.65 (t, J = 7.0 Hz, 2H), 2.73 (t, J = 7.7 Hz, 2H), 1.97 (p, J = 7.5 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 493 ([M+H]$^+$).

Preparation of 2-(4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)isoindoline-1,3-dione (CA15)



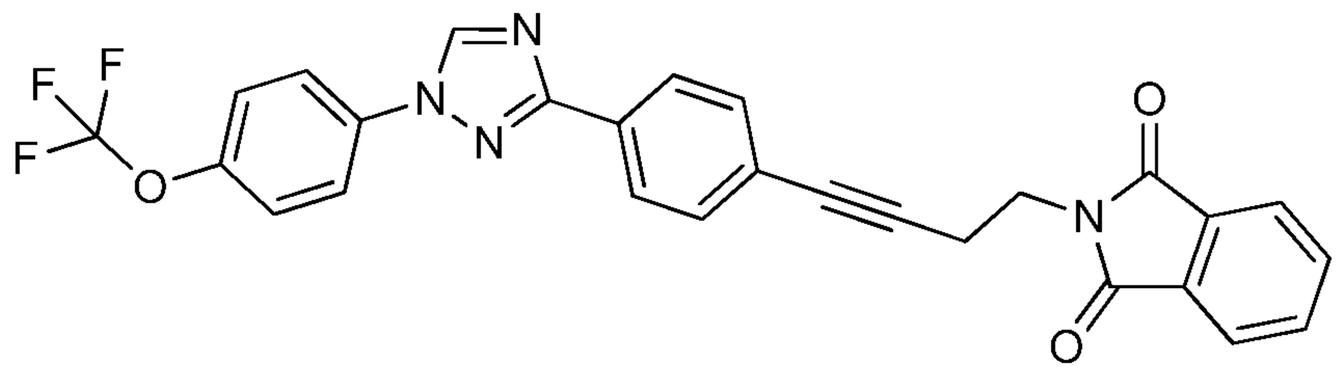
The title compound was prepared from 4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-ol (**CA24**), further purified by trituration with diethyl ether/hexanes and isolated as a white solid (0.372 g, 76%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.15 - 8.06 (m, 2H), 7.94 - 7.87 (m, 2H), 7.87 - 7.81 (m, 2H), 7.81 - 7.77 (m, 2H), 7.71 (dd, J = 5.5, 3.0 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 3.73 (t, J = 6.7 Hz, 2H), 2.73 (t, J = 7.1 Hz, 2H), 1.82 - 1.65 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48; ESIMS *m/z* 491 ([M+H]$^+$).

Preparation of 2-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)isoindoline-1,3-dione (CA16)



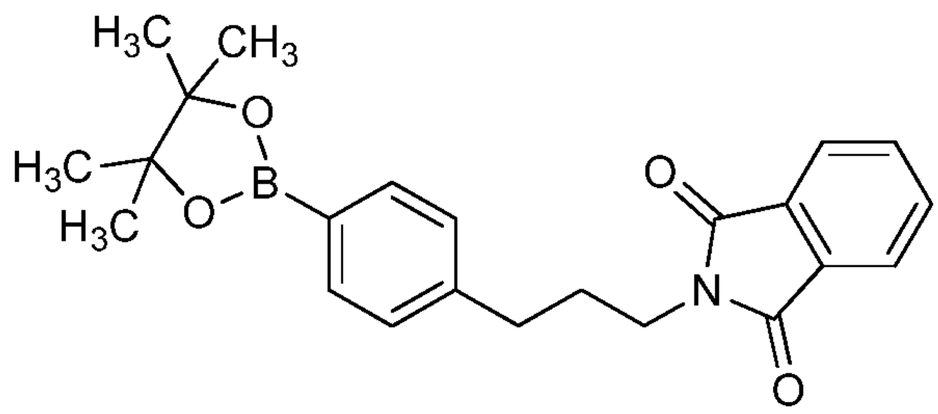
The title compound was prepared from 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-ol (**CA25**) and isolated as a white solid (2.39 g, 59%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.12 - 8.06 (m, 2H), 7.84 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.83 - 7.77 (m, 2H), 7.75 - 7.66 (m, 2H), 7.38 (dd, *J* = 9.2, 1.0 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 3.73 (t, *J* = 6.7 Hz, 2H), 2.72 (t, *J* = 7.1 Hz, 2H), 1.85 - 1.61 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 507 ($[M+H]^+$).

Preparation of 2-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-yl)isoindoline-1,3-dione (CA17)



The title compound was prepared from 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-ol (**CA23**) and isolated as a white solid (0.393 g, 74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.09 (d, *J* = 8.3 Hz, 2H), 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 4.00 (t, *J* = 7.0 Hz, 2H), 2.86 (t, *J* = 7.0 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 503 ($[M+H]^+$).

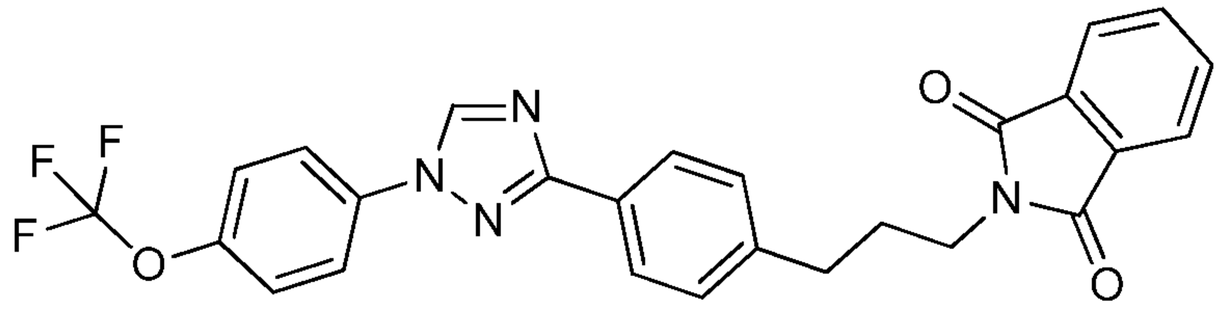
Example 60: Preparation of 2-(3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propyl)isoindoline-1,3-dione (C58)



To 2-(3-(4-bromophenyl)propyl)isoindoline-1,3-dione (**C56**) (6.46 g, 18.8 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (7.15 g, 28.2 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.831 g, 1.13 mmol), and 1,1′-bis(diphenylphosphino)ferrocene (0.624 g, 1.13 mmol) in a 200 mL round bottomed flask equipped with a stir bar and nitrogen was added potassium(II)

acetate (5.53 g, 56.3 mmol) followed by dioxane (56.9 mL). The reaction mixture was evacuated and purged with nitrogen. The reaction was heated to 80 ºC overnight. The reaction was cooled. The reaction was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using 5-20% ethyl acetate/hexanes as eluent provided the title compound as a yellow oil (7.41 g, 101%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.72 - 7.67 (m, 4H), 7.23 - 7.17 (m, 2H), 3.74 (t, *J* = 7.2 Hz, 2H), 2.75 - 2.65 (m, 2H), 2.08 - 1.97 (m, 2H), 1.33 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.38, 144.40, 134.93, 133.84, 132.09, 127.73, 123.17, 83.62, 60.40, 37.81, 33.42, 29.71, 24.85; ESIMS *m/z* 392 ($[M+H]^+$).

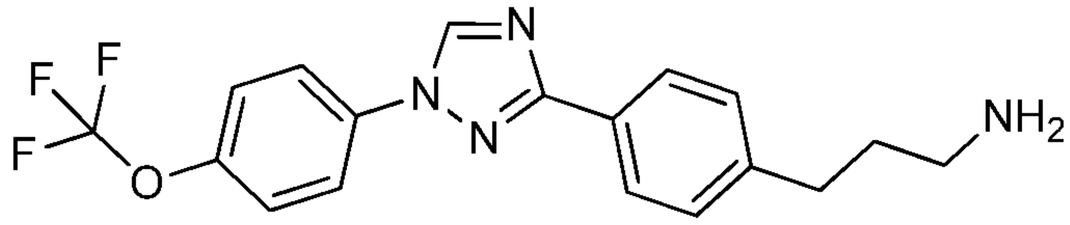
Example 61: Preparation of 2-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)isoindoline-1,3-dione (C59)



To 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) (0.50 g, 1.6 mmol), 2-(3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propyl)isoindoline-1,3-dione (**C58**) (0.64 g, 1.6 mmol), sodium bicarbonate (0.27 g, 3.3 mmol), and tetrakis(triphenylphosphine)palladium(0) (0.19 g, 0.16 mmol) in a 10-20 mL microwave vial equipped with a stir bar was added dioxane (12 mL) and water (4.1 mL). The reaction was capped and heated at 140 ºC for 30 minutes in a Biotage Initiator® microwave reactor with external IR-sensor temperature monitoring from the side of the vessel. The mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using 0-30% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided a solid which was dried under house vacuum overnight. The title compound was obtained as a

white solid (0.42 g, 53%): mp 145–148 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 0.8 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 2H), 7.84 (ddd, *J* = 5.5, 3.0, 0.8 Hz, 2H), 7.82 - 7.77 (m, 2H), 7.69 (ddd, *J* = 5.5, 3.0, 0.8 Hz, 2H), 7.38 (dt, *J* = 9.0, 1.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.78 (t, *J* = 7.2 Hz, 2H), 2.79 - 2.71 (m, 2H), 2.08 (p, *J* = 7.5 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 493 ($[M+H]^+$).

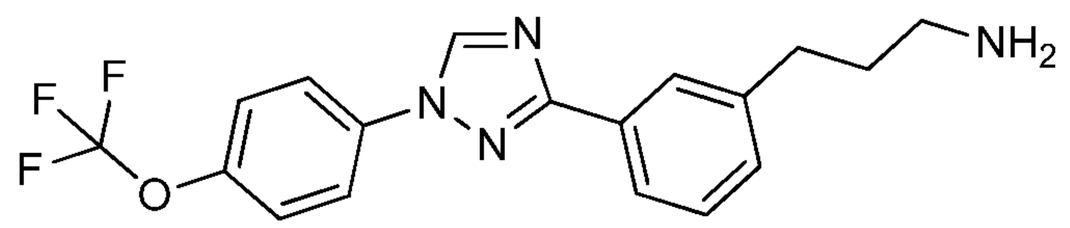
Example 62: Preparation of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (C60)



To 2-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)isoindoline-1,3-dione (**C59**) (0.373 g, 0.758 mmol) in a 25 mL vial equipped with a stir bar, Vigreux column, and nitrogen was added methanol (7.58 mL) followed by hydrazine monohydrate (0.110 mL, 2.27 mmol). The reaction was heated to 50 ºC until determined to be complete by LCMS. The reaction mixture was cooled to room temperature and diluted with dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane (2x). The organic layers were washed with sodium hydroxide (1 N, 4x), poured through a phase separator and concentrated. The resultant solid was dried *in vacuo* over 72 hours at 50 ºC to provide the title compound as an off-white solid (0.262 g, 95%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (s, 1H), 8.10 - 8.04 (m, 2H), 8.04 - 7.98 (m, 2H), 7.66 - 7.59 (m, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.69 - 2.63 (m, 2H), 2.56 (t, *J* = 6.9 Hz, 2H), 1.74 - 1.59 (m, 2H), (NH_2 not observed); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 363 ($[M+H]^+$).

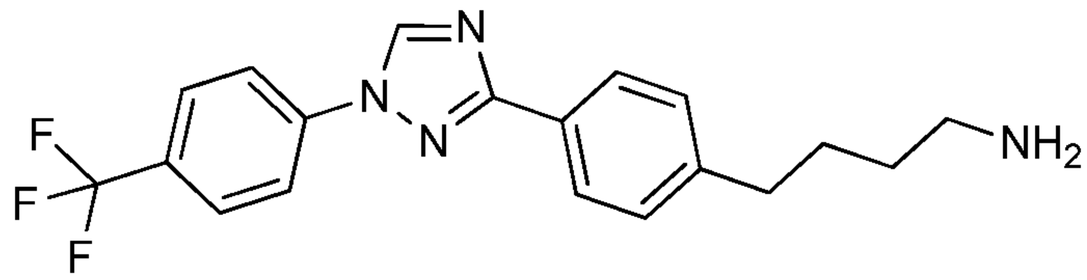
The following compounds were prepared in accordance to the procedure in Example 62.

Preparation of 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (CA18)



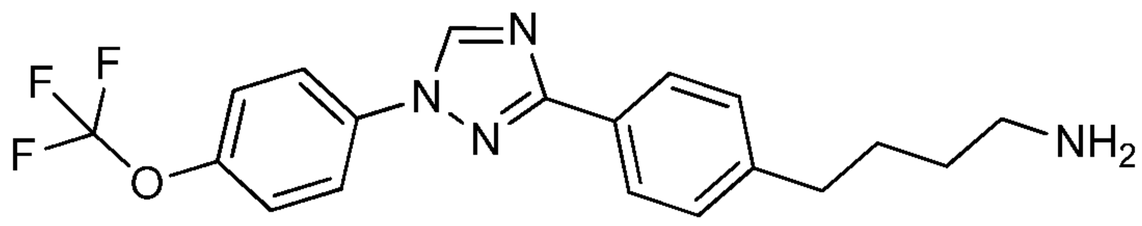
The title compound was prepared as described in Example 62 using 2-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)isoindoline-1,3-dione (**CA14**) and isolated as a clear oil (3.49 g, 100%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.12 - 8.04 (m, 2H), 8.00 - 7.88 (m, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.31 (dt, J = 7.7, 1.5 Hz, 1H), 2.71 (q, J = 9.0, 7.9 Hz, 2H), 2.57 (t, J = 6.8 Hz, 2H), 1.74 - 1.62 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.01; ESIMS *m/z* 364 ([M+H]$^+$).

Preparation of 4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (CA19)



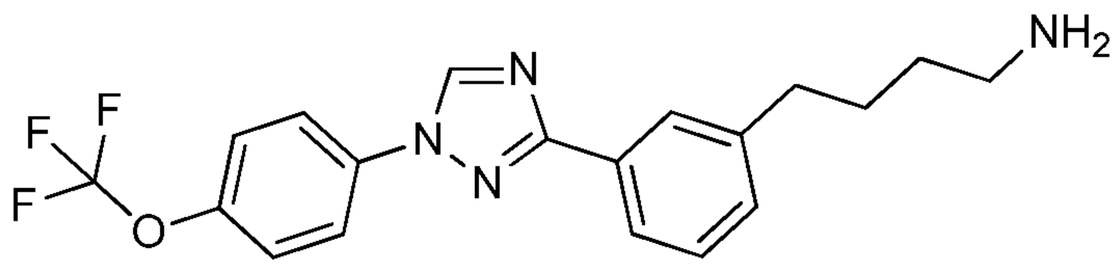
The title compound was prepared as described in Example 62 using 2-(4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)isoindoline-1,3-dione (**CA15**), further purified with an SCX column and isolated as a yellow solid (0.215 g, 79%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.11 (d, J = 8.2 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 2.70 (t, J = 7.6 Hz, 2H), 1.82 - 1.65 (m, 6H), 1.54 (d, J = 8.1 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48; ESIMS *m/z* 361 ([M+H]$^+$).

Preparation of 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (CA20)



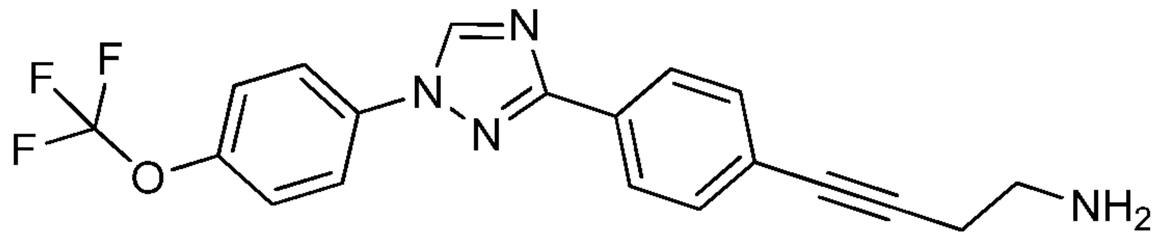
The title compound was prepared as described in Example 62 using 2-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)isoindoline-1,3-dione (**CA16**) and isolated as a white solid (1.76 g, 99%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.10 (d, J = 8.2 Hz, 2H), 7.84 - 7.77 (m, 2H), 7.38 (dt, J = 8.1, 1.0 Hz, 2H), 7.33 - 7.27 (m, 2H), 2.78 - 2.65 (m, 4H), 1.76 - 1.64 (m, 2H), 1.58 - 1.45 (m, 2H), 1.08 (bs, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 377 ([M+H]$^+$).

Preparation of 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (CA21)



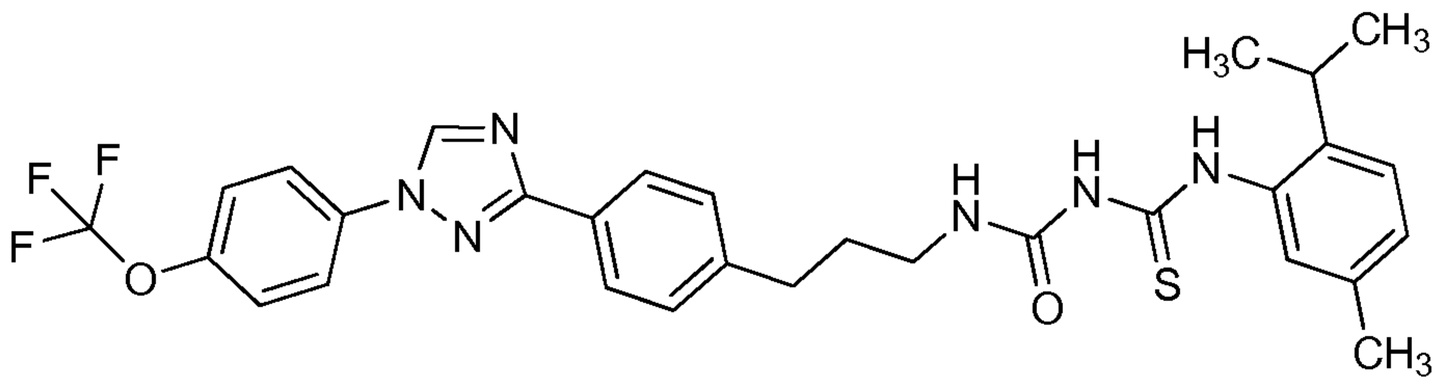
The title compound was prepared as described in Example 62 using 2-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)isoindoline-1,3-dione (**CA2**) and isolated as a light brown residue (1.94 g, 47%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.13 - 8.05 (m, 2H), 7.98 - 7.89 (m, 2H), 7.67 - 7.56 (m, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.31 (dt, J = 7.8, 1.5 Hz, 1H), 2.67 (t, J = 7.7 Hz, 2H), 2.57 (t, J = 6.9 Hz, 2H), 1.64 (tt, J = 9.2, 6.8 Hz, 2H), 1.40 (p, J = 7.1 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 378 ([M+H]$^{+}$).

Preparation of 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-amine (CA22)



The title compound was prepared as described in Example 62 using 2-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-yl)isoindoline-1,3-dione (**CA17**), further purified using an SCX column and isolated as a yellow solid (0.304 g, 104%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.16 - 8.09 (m, 2H), 7.84 - 7.76 (m, 2H), 7.56 - 7.48 (m, 2H), 7.44 - 7.34 (m, 2H), 2.95 (t, J = 6.3 Hz, 2H), 2.59 (t, J = 6.3 Hz, 2H), (NH_2 not observed); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 373 ([M+H]$^{+}$).

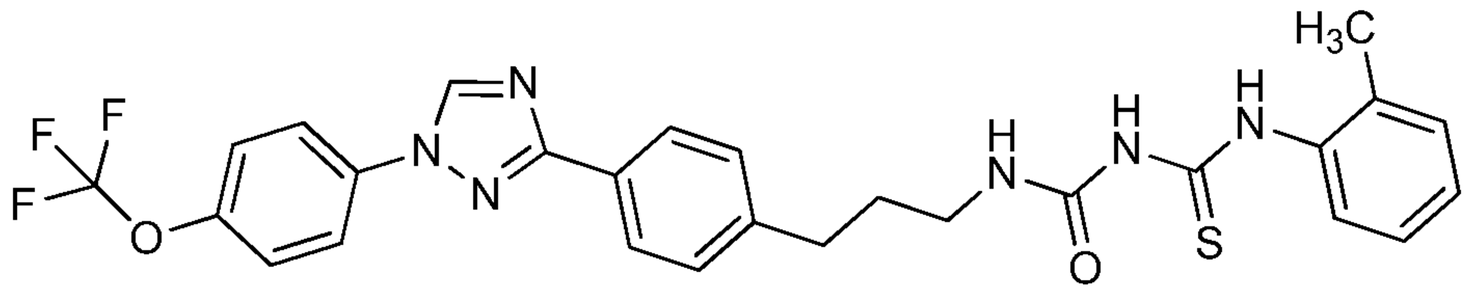
Example 63: Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (F21)



To 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) (0.231 g, 0.639 mmol) in a 25 mL vial equipped with a stir bar and nitrogen was added dichloromethane (4.3 mL), water (2.1 mL), and sodium bicarbonate (0.161 g, 1.92 mmol). Triphosgene (0.0760 g, 0.255 mmol) was added in one portion and the reaction was stirred vigorously until the conversion of the starting material was observed by LCMS. The reaction mixture was diluted with dichloromethane, poured through a phase separator and concentrated. The resultant solid was suspended in acetonitrile (6.0 mL) in a 100 mL round bottomed flask equipped with a stir bar and nitrogen. To this was added cesium carbonate (0.229 g, 0.702 mmol) and 1-(2-isopropyl-5-methylphenyl)thiourea (0.133 g, 0.639 mmol). The reaction was stirred overnight at room temperature. The mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated. Purification by flash column chromatography using 0-30% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided mixed fractions. The fractions were combined and re-purified by flash column chromatography using 0-30% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and the resultant solid was dried *in vacuo* at 50 ºC overnight to afford the title compound as a white solid (0.145 g, 38%).

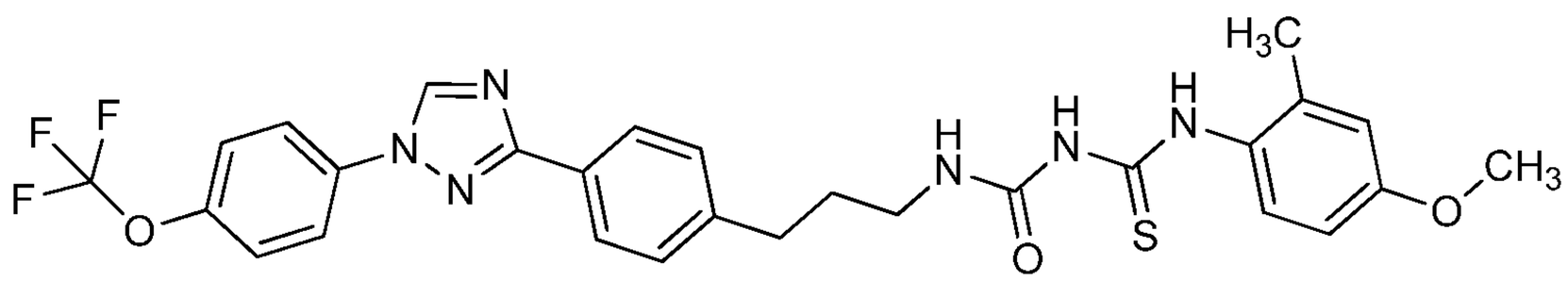
The following compounds were prepared in accordance to the procedure in Example 63.

Preparation of 1-(*o*-tolylcarbamothioyl)-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC92)



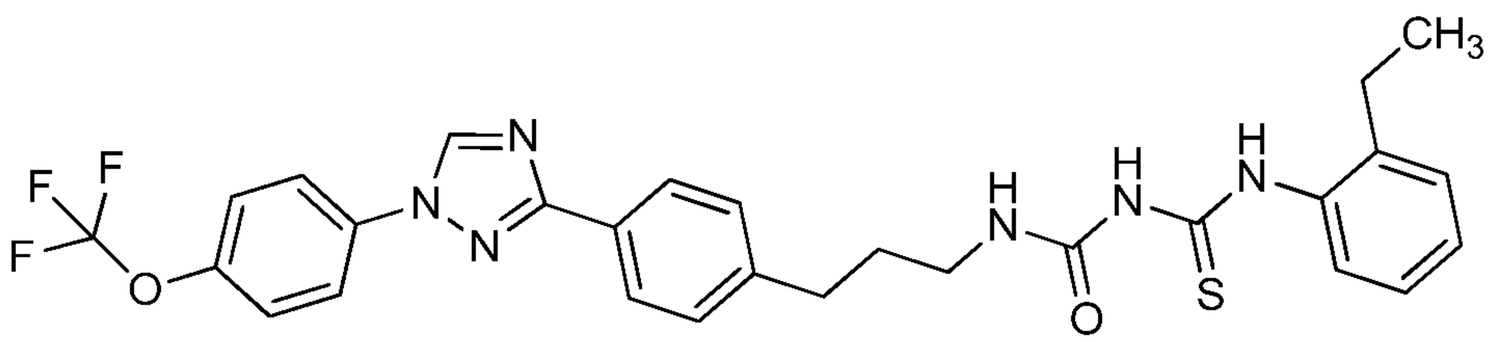
The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(o-tolyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.061 g, 21%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 10.06 (s, 1H), 9.39 (s, 1H), 8.14 - 7.99 (m, 3H), 7.63 (dt, *J* = 7.3, 1.3 Hz, 3H), 7.45 - 7.35 (m, 2H), 7.33 - 7.14 (m, 4H), 7.09 (t, *J* = 5.6 Hz, 1H), 3.17 (q, *J* = 6.6 Hz, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.21 (s, 3H), 1.92 - 1.74 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 555 ([M+H]$^{+}$), 553 ([M-H]$^{-}$).

Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC105)



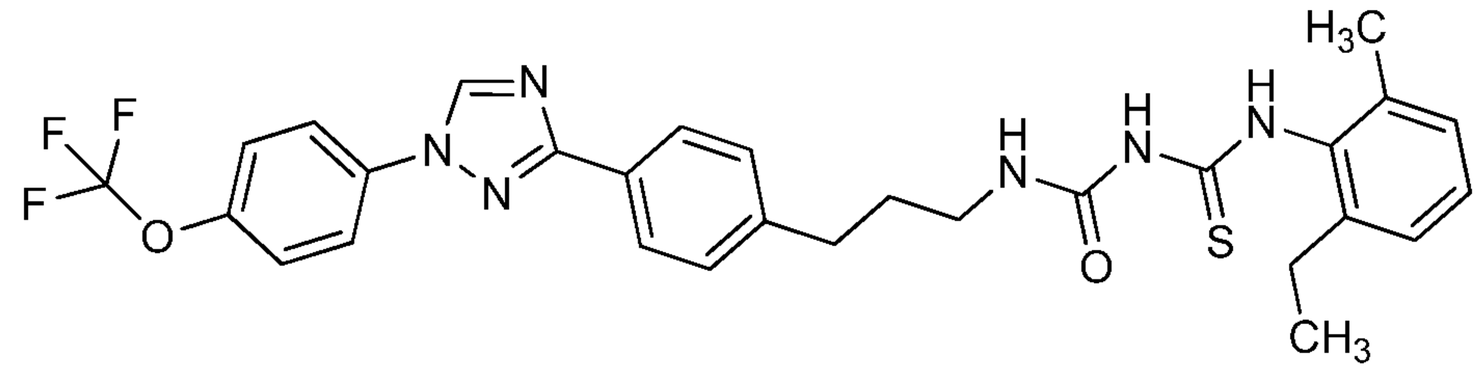
The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(4-methoxy-2-methylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.119 g, 38%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.79 (s, 1H), 10.00 (s, 1H), 9.39 (s, 1H), 8.16 - 7.98 (m, 4H), 7.70 - 7.57 (m, 2H), 7.38 (dd, *J* = 8.4, 1.9 Hz, 3H), 7.08 (t, *J* = 5.7 Hz, 1H), 6.84 (d, *J* = 2.9 Hz, 1H), 6.77 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.75 (s, 3H), 3.16 (q, *J* = 6.5 Hz, 2H), 2.70 (dd, *J* = 8.5, 6.7 Hz, 2H), 2.17 (s, 3H), 1.81 (p, *J* = 7.2 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 585 ([M+H]$^{+}$), 583 ([M-H]$^{-}$).

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC93)



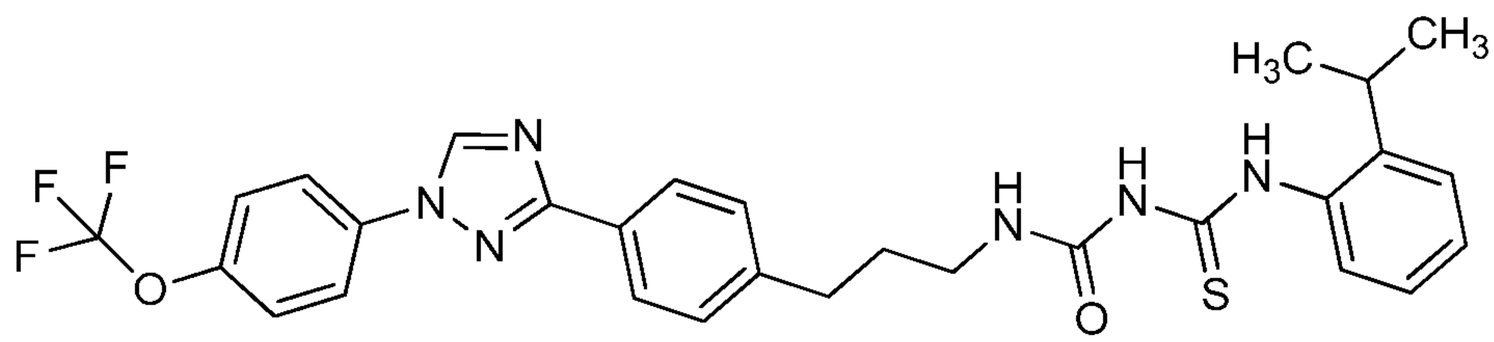
The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(2-ethylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.112 g, 37%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 10.07 (s, 1H), 9.39 (s, 1H), 8.16 - 7.98 (m, 4H), 7.66 - 7.59 (m, 2H), 7.59 - 7.52 (m, 1H), 7.43 - 7.35 (m, 2H), 7.31 - 7.19 (m, 3H), 7.10 (t, *J* = 5.6 Hz, 1H), 3.17 (q, *J* = 6.5 Hz, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.55 (q, *J* = 7.6 Hz, 2H), 1.91 - 1.71 (m, 2H), 1.17 - 1.11 (m, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 569 ([M+H]$^{+}$), 567 ([M-H]$^{-}$).

Preparation of 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC101)



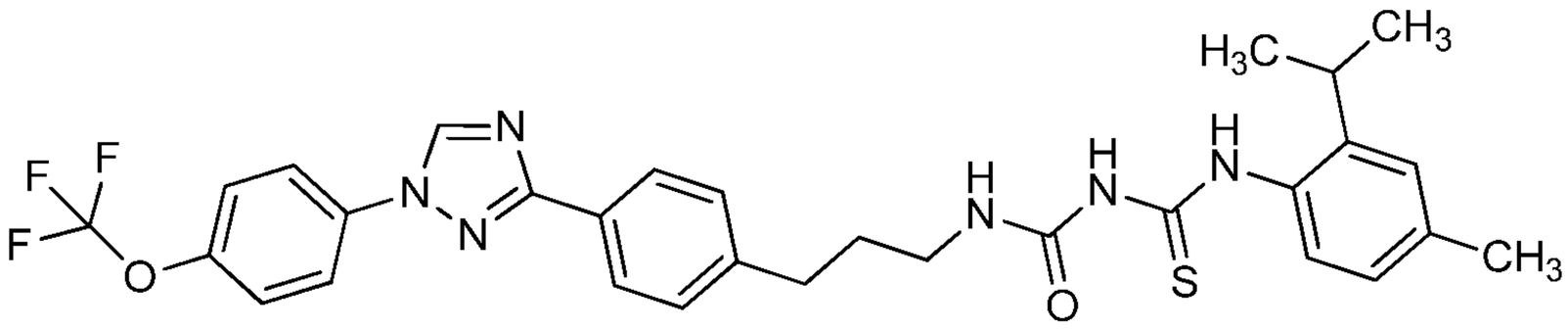
The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (C60) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**). Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.146 g, 47%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.59 (s, 1H), 10.07 (s, 1H), 9.39 (s, 1H), 8.14 - 8.00 (m, 4H), 7.68 - 7.59 (m, 2H), 7.45 - 7.33 (m, 2H), 7.23 - 7.02 (m, 4H), 3.17 (q, *J* = 6.6 Hz, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.51 (p, *J* = 1.9 Hz, 2H), 2.18 (s, 3H), 1.90 - 1.73 (m, 2H), 1.12 (t, *J* = 7.5 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 583 ([M+H]$^{+}$), 581 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC94)



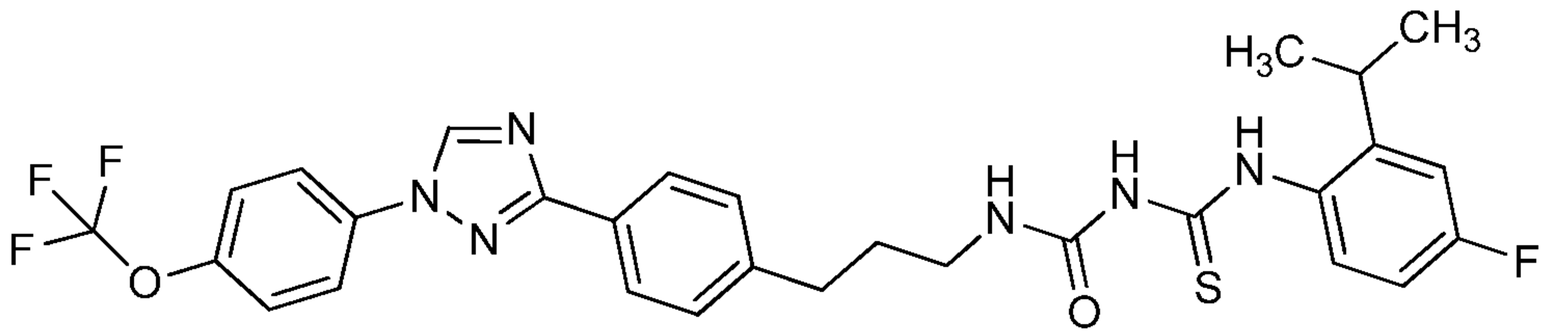
The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(2-isopropylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.161 g, 31%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 10.08 (s, 1H), 9.39 (s, 1H), 8.13 - 7.99 (m, 4H), 7.68 - 7.58 (m, 2H), 7.49 - 7.31 (m, 4H), 7.24 (dtd, *J* = 24.9, 7.4, 1.6 Hz, 2H), 7.09 (t, *J* = 5.4 Hz, 1H), 3.17 (q, *J* = 6.5 Hz, 2H), 3.01 (p, *J* = 6.8 Hz, 1H), 2.70 (t, *J* = 7.7 Hz, 2H), 1.82 (p, *J* = 7.3 Hz, 2H), 1.17 (d, *J* = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 583 ([M+H]$^{+}$), 581 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H* -1,2,4-triazol-3-yl]phenyl]propyl]urea (PC102)



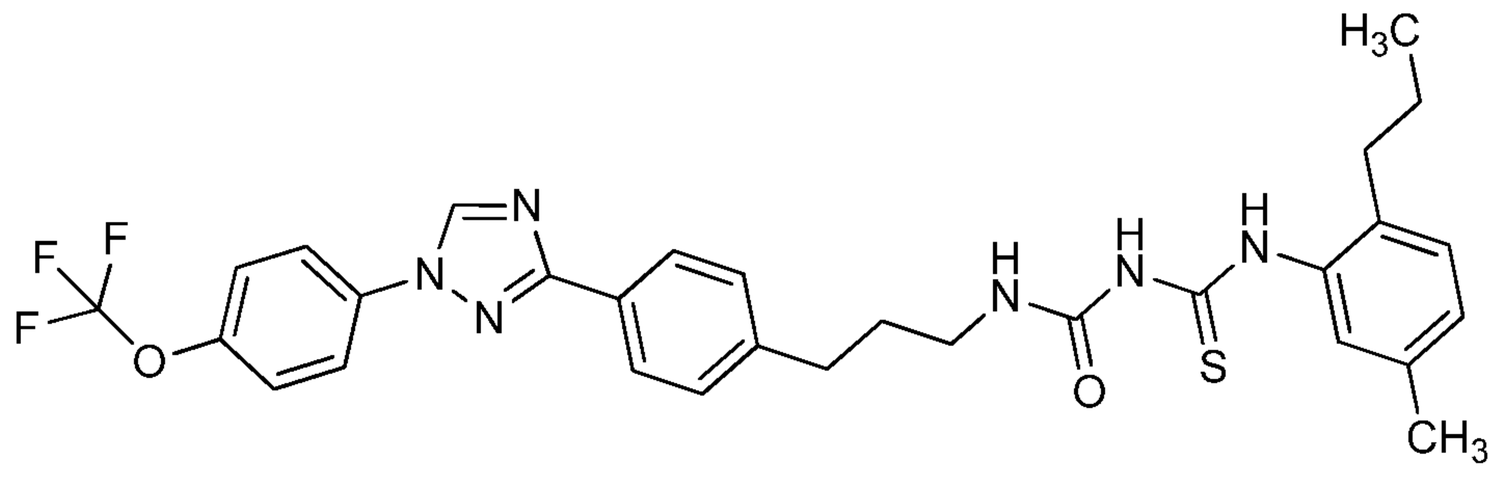
The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(2-isopropyl-4-methylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.101 g, 32%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (s, 1H), 10.04 (s, 1H), 9.39 (s, 1H), 8.14 - 7.99 (m, 4H), 7.71 - 7.55 (m, 2H), 7.46 - 7.33 (m, 2H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 2.0 Hz, 1H), 7.08 (t, *J* = 5.6 Hz, 1H), 7.04 - 6.95 (m, 1H), 3.17 (d, *J* = 5.2 Hz, 2H), 2.96 (p, *J* = 6.8 Hz, 1H), 2.70 (dd, *J* = 8.6, 6.6 Hz, 2H), 2.31 (s, 3H), 1.81 (p, *J* = 7.3 Hz, 2H), 1.16 (d, *J* = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 597 ([M+H]$^{+}$), 595 ([M-H]$^{-}$).

Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC103)



The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(4-fluoro-2-isopropylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.116 g, 36%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H), 10.11 (s, 1H), 9.39 (s, 1H), 8.15 - 7.97 (m, 4H), 7.63 (dd, J = 8.7, 1.5 Hz, 2H), 7.39 (dd, J = 8.5, 5.7 Hz, 3H), 7.16 (dd, J = 10.4, 3.0 Hz, 1H), 7.12 - 6.97 (m, 2H), 3.26 - 3.11 (m, 2H), 3.05 - 2.89 (m, 1H), 2.70 (dd, J = 8.6, 6.7 Hz, 2H), 1.92 - 1.71 (m, 2H), 1.16 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97 , -114.39; ESIMS *m/z* 601 ([M+H]$^{+}$), 599 ([M-H]$^{-}$).

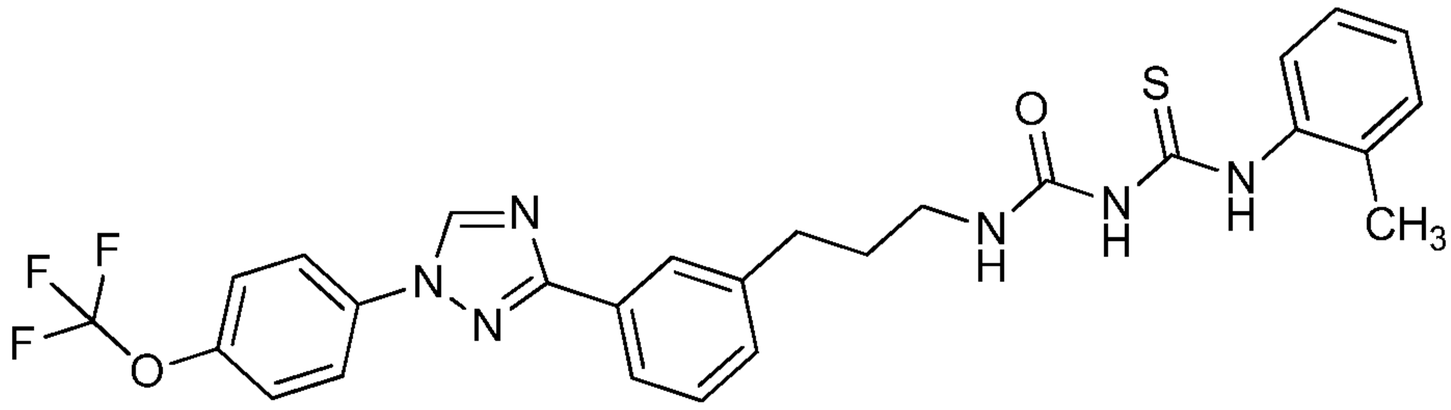
Preparation of 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC99)



The title compound was prepared as described in Example 63 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**C60**) and 1-(5-methyl-2-propylphenyl)thiourea (**CA38**). Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.111 g, 35%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 10.04 (s, 1H), 9.39 (s, 1H), 8.14 - 7.98 (m, 4H), 7.62 (d, J = 8.6 Hz, 2H), 7.45 - 7.33 (m, 3H), 7.14 (d, J = 7.8 Hz, 1H), 7.09 (t, J = 5.7 Hz, 1H), 7.05 - 6.98 (m, 1H), 3.17 (q, J = 6.5 Hz, 2H), 2.70 (t, J = 7.6 Hz, 2H), 2.49 - 2.41 (m, 2H), 2.27 (s, 3H), 1.81 (dt, J = 13.7, 6.7 Hz, 2H), 1.50 (q,

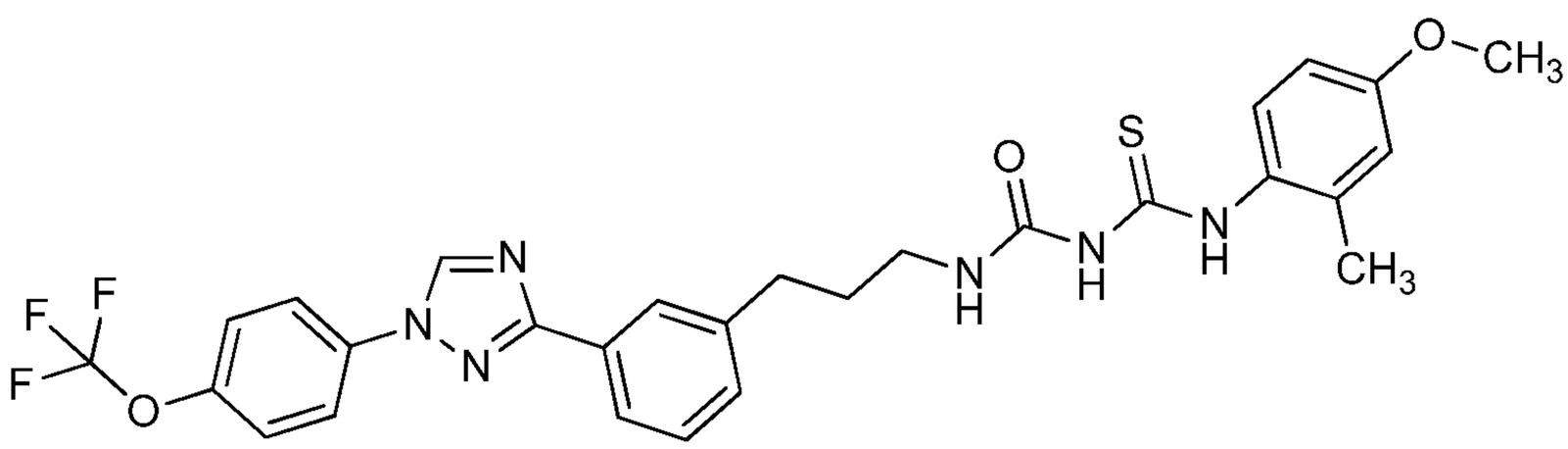
J = 7.4 Hz, 2H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 597 ($[M+H]^+$), 595 ($[M-H]^-$).

Preparation of 1-(*o*-tolylcarbamothioyl)-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC118)



The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(*o*-tolyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.075 g, 24%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 10.05 (s, 1H), 9.40 (s, 1H), 8.12 - 8.04 (m, 2H), 8.01 - 7.92 (m, 2H), 7.68 - 7.57 (m, 3H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.36 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.29 - 7.24 (m, 1H), 7.24 - 7.13 (m, 2H), 7.10 (t, *J* = 5.7 Hz, 1H), 3.18 (q, *J* = 6.5 Hz, 2H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.93 - 1.74 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 555 ($[M+H]^+$), 553 ($[M-H]^-$).

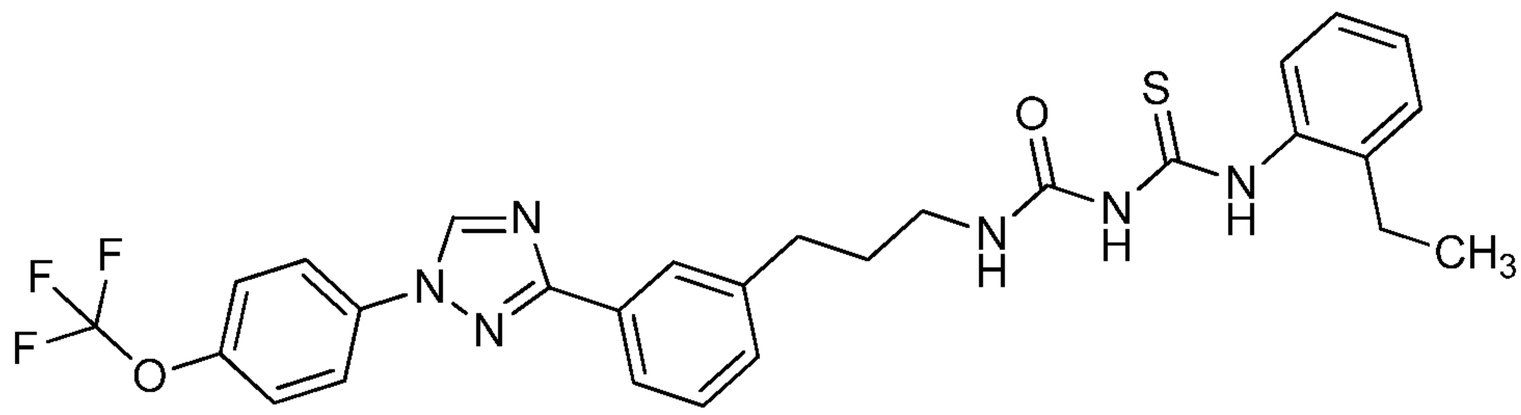
Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC131)



The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(4-methoxy-2-methylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.103 g, 31%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.80 (s, 1H), 10.00 (s, 1H), 9.40 (s, 1H), 8.13 - 8.04

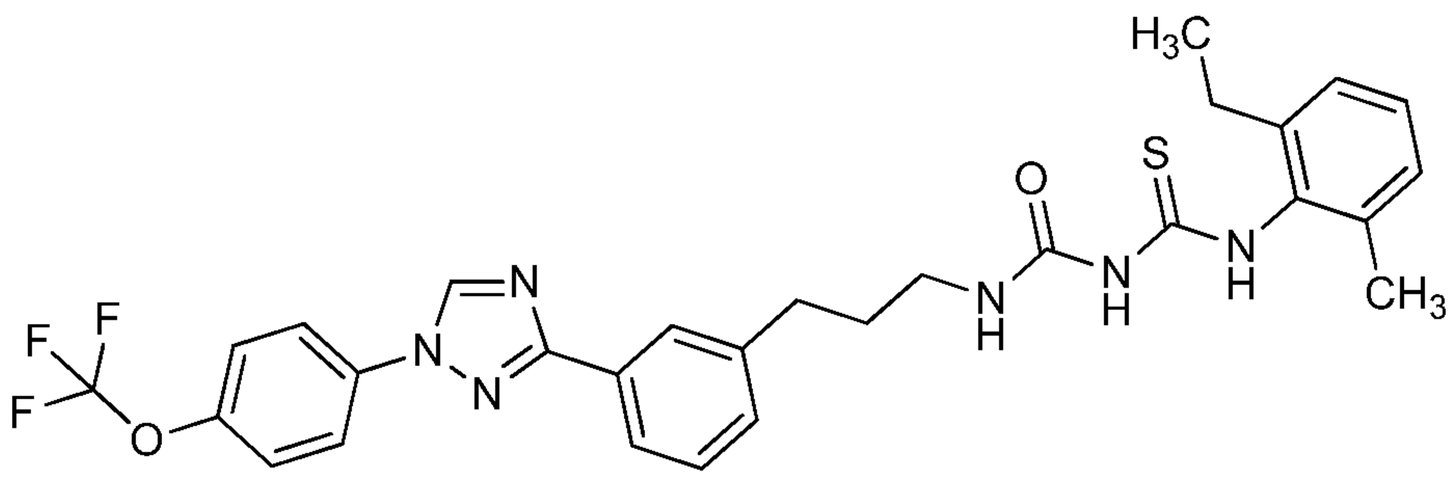
(m, 2H), 8.02 - 7.92 (m, 2H), 7.67 - 7.57 (m, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.42 - 7.30 (m, 2H), 7.08 (t, *J* = 5.6 Hz, 1H), 6.83 (d, *J* = 2.9 Hz, 1H), 6.76 (dd, *J* = 8.7, 2.9 Hz, 1H), 3.74 (s, 3H), 3.17 (q, *J* = 6.5 Hz, 2H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.16 (s, 3H), 1.93 - 1.72 (m, 2H); ^{19}F NMR (376 MHz, DMSO-*d*$_6$) δ -56.97; ESIMS *m/z* 585 ([M+H]$^+$), 583 ([M-H]$^-$).

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC119)



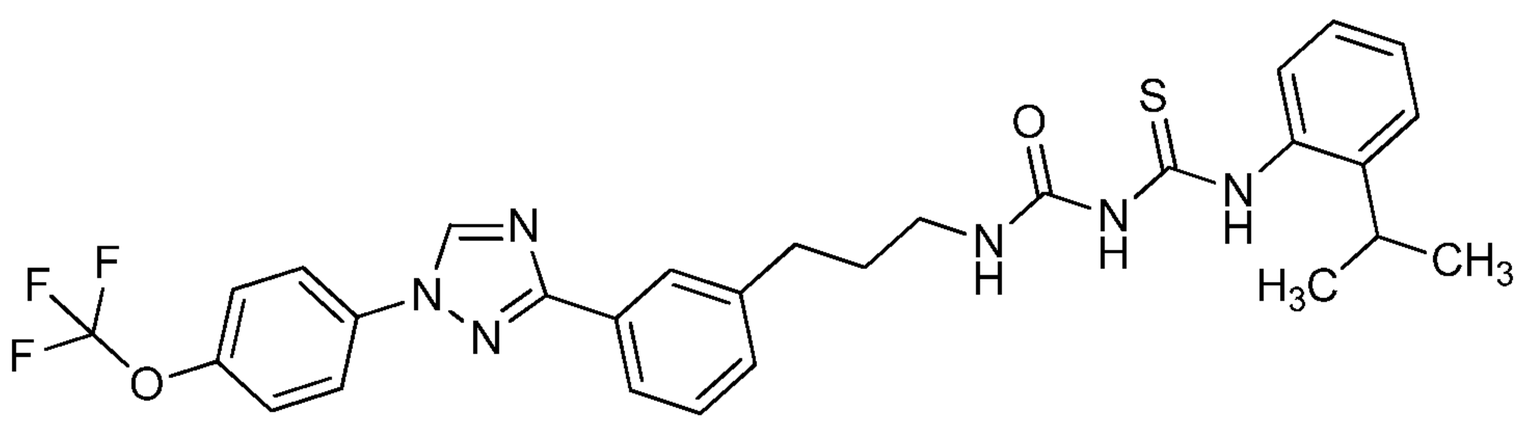
The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(2-ethylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.175 g, 55%): ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 12.04 (s, 1H), 10.07 (s, 1H), 9.40 (s, 1H), 8.13 - 8.04 (m, 2H), 8.02 - 7.93 (m, 2H), 7.65 - 7.59 (m, 2H), 7.55 (dt, *J* = 6.5, 3.7 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.36 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.31 - 7.24 (m, 1H), 7.21 (dd, *J* = 5.8, 3.5 Hz, 2H), 7.15 - 7.06 (m, 1H), 3.18 (q, *J* = 6.5 Hz, 2H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 1.90 - 1.74 (m, 2H), 1.12 (t, *J* = 7.5 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-*d*$_6$) δ -56.98; ESIMS *m/z* 569 ([M+H]$^+$), 567 ([M-H]$^-$).

Preparation of 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC127)



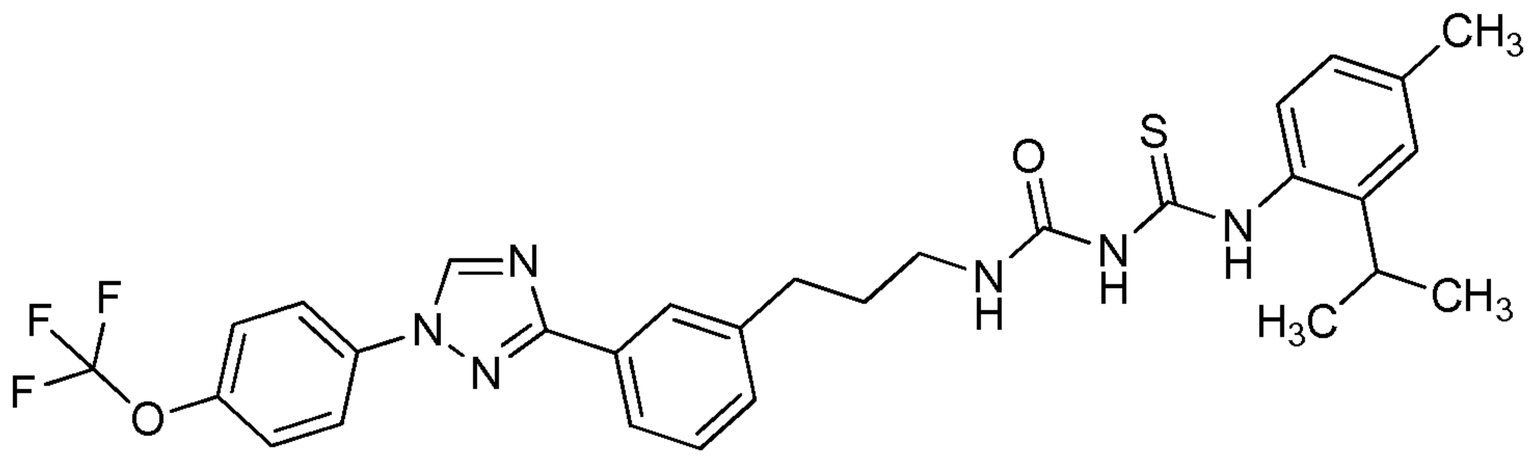
The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**). Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.154 g, 47%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.59 (s, 1H), 10.07 (s, 1H), 9.41 (s, 1H), 8.13 - 8.05 (m, 2H), 8.03 - 7.92 (m, 2H), 7.62 (dt, *J* = 7.8, 1.1 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.36 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.21 - 7.14 (m, 1H), 7.14 - 7.04 (m, 3H), 3.18 (q, *J* = 6.6 Hz, 2H), 2.83 - 2.67 (m, 2H), 2.48 (d, *J* = 2.6 Hz, 2H), 2.17 (s, 3H), 1.92 - 1.76 (m, 2H), 1.11 (t, *J* = 7.6 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 583 ([M+H]$^{+}$), 581 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC120)



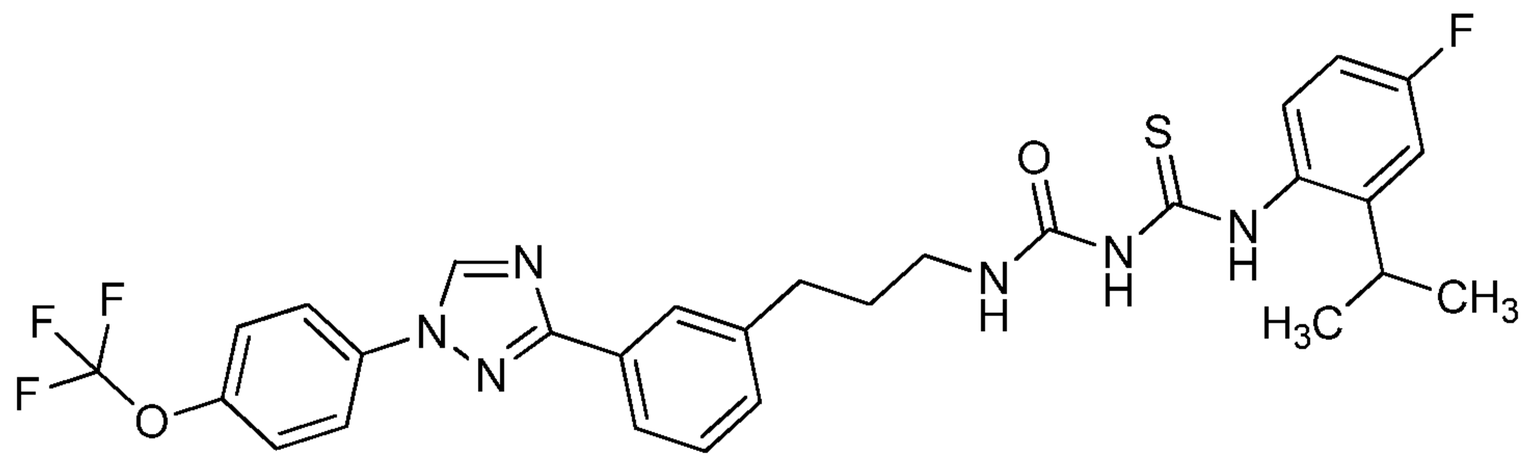
The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(2-isopropylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.131 g, 40%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 10.07 (s, 1H), 9.41 (s, 1H), 8.13 - 8.04 (m, 2H), 8.01 - 7.93 (m, 2H), 7.62 (ddd, *J* = 7.9, 2.0, 1.0 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.39 - 7.32 (m, 2H), 7.27 (td, *J* = 7.5, 1.5 Hz, 1H), 7.20 (td, *J* = 7.5, 1.7 Hz, 1H), 7.11 (t, *J* = 5.6 Hz, 1H), 3.18 (q, *J* = 6.5 Hz, 2H), 3.00 (hept, *J* = 6.8 Hz, 1H), 2.73 (t, *J* = 7.7 Hz, 2H), 1.93 - 1.75 (m, 2H), 1.16 (d, *J* = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 583 ([M+H]$^{+}$), 581 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC128)



The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(2-isopropyl-4-methylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.123 g, 37%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (s, 1H), 10.04 (s, 1H), 9.41 (s, 1H), 8.12 - 8.04 (m, 2H), 8.02 - 7.91 (m, 2H), 7.61 (ddd, J = 7.9, 2.0, 1.0 Hz, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.36 (dt, J = 7.7, 1.4 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 1.9 Hz, 1H), 7.09 (t, J = 5.6 Hz, 1H), 7.04 - 6.97 (m, 1H), 3.17 (q, J = 6.5 Hz, 2H), 2.95 (hept, J = 7.0 Hz, 1H), 2.82 - 2.64 (m, 2H), 2.30 (s, 3H), 1.91 - 1.77 (m, 2H), 1.14 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 597 ([M+H]$^{+}$), 595 ([M-H]$^{-}$).

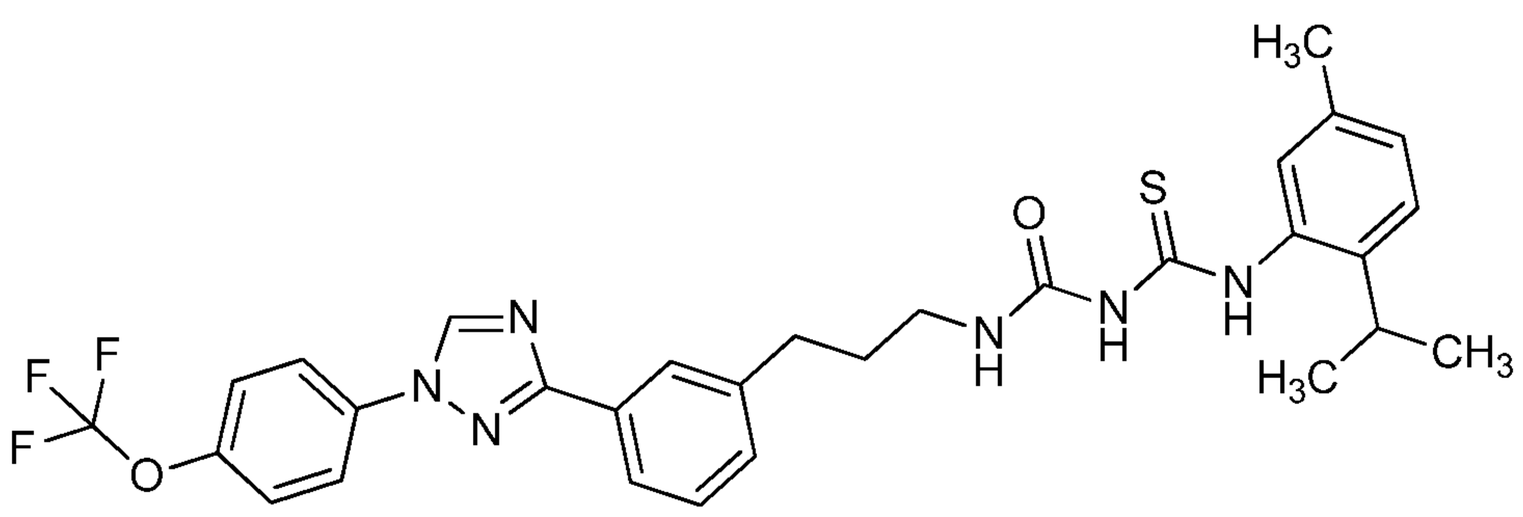
Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC129)



The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(4-fluoro-2-isopropylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.140 g, 41%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H), 10.11 (s, 1H), 9.41 (s, 1H), 8.13 - 8.04 (m, 2H), 8.02 - 7.92 (m, 2H), 7.61 (dq, J = 7.8, 1.0 Hz, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.43 - 7.31 (m, 2H), 7.15 (dd, J = 10.4, 3.0 Hz, 1H), 7.10 (t, J = 5.6 Hz, 1H), 7.03 (td,

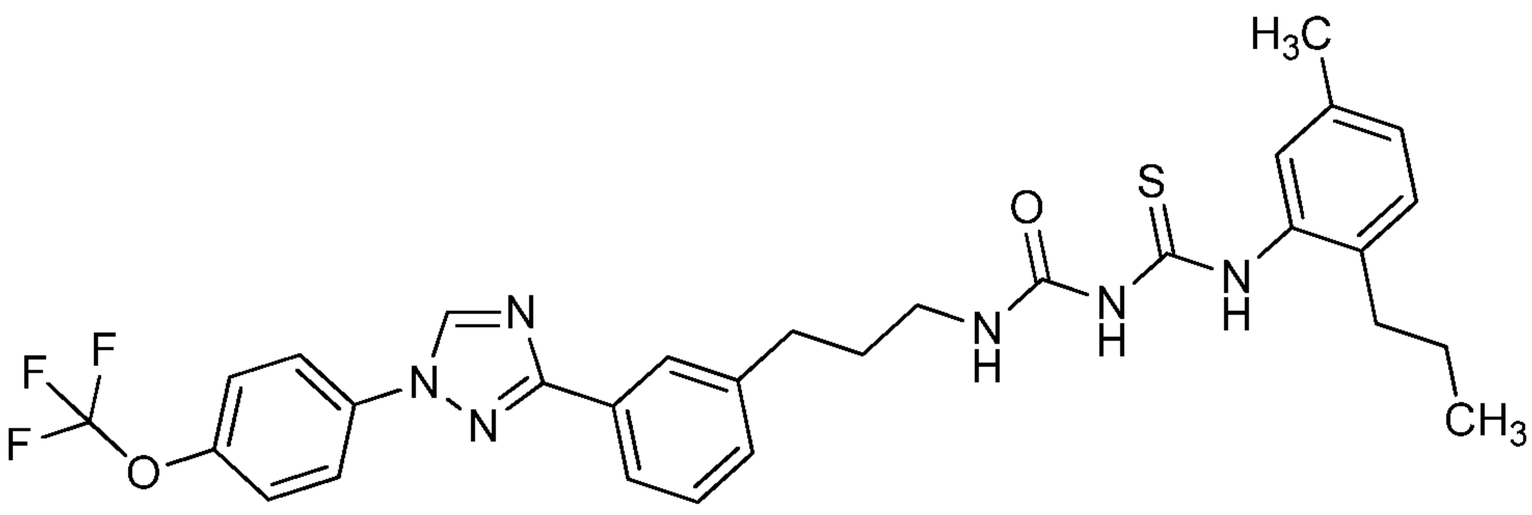
J = 8.5, 3.0 Hz, 1H), 3.26 - 3.10 (m, 2H), 2.97 (pd, *J* = 6.9, 1.6 Hz, 1H), 2.73 (dd, *J* = 8.5, 6.7 Hz, 2H), 1.90 - 1.76 (m, 2H), 1.15 (d, *J* = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97 , -114.41; ESIMS *m/z* 601 ($[M+H]^+$), 599 ($[M-H]^-$).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC124)



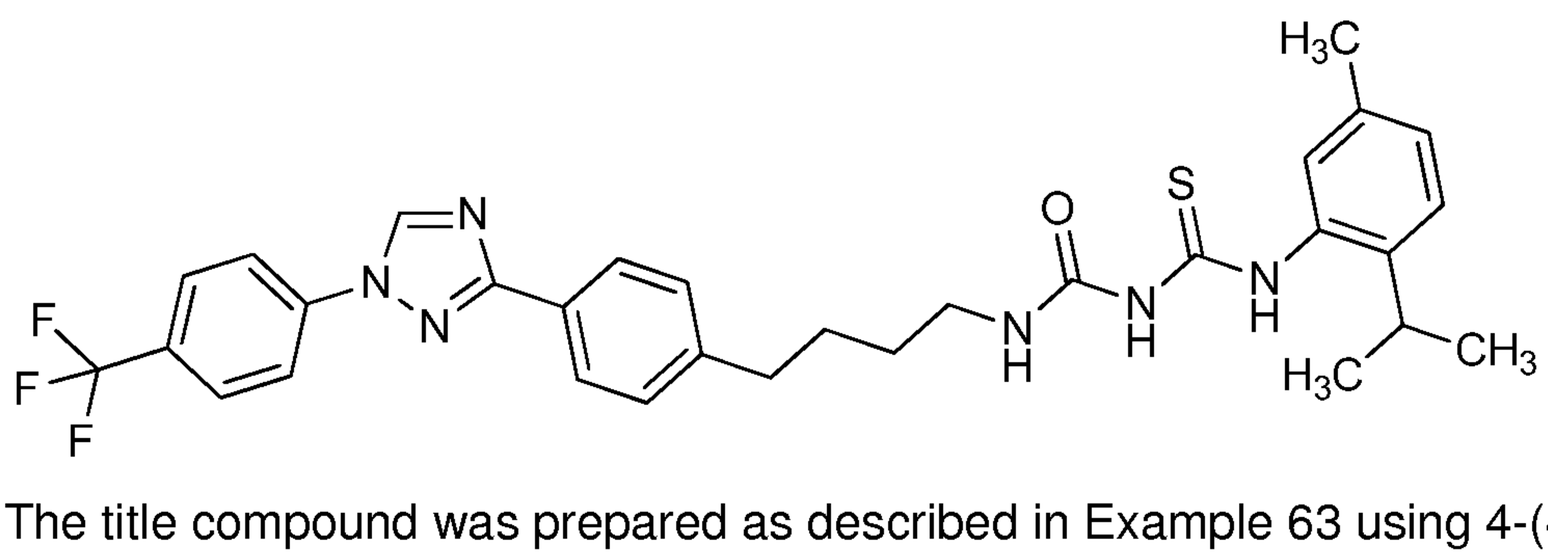
The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(2-isopropyl-5-methylphenyl)thiourea. Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.118 g, 35%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.91 (s, 1H), 10.05 (s, 1H), 9.40 (s, 1H), 8.13 - 8.04 (m, 2H), 8.03 - 7.93 (m, 2H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.36 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.21 (dd, *J* = 4.9, 3.0 Hz, 2H), 7.15 - 7.03 (m, 2H), 3.18 (q, *J* = 6.5 Hz, 2H), 2.95 (hept, *J* = 6.7 Hz, 1H), 2.73 (t, *J* = 7.7 Hz, 2H), 2.25 (s, 3H), 1.90 - 1.76 (m, 2H), 1.13 (d, *J* = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 597 ($[M+H]^+$), 595 ($[M-H]^-$).

Preparation of 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]propyl]urea (PC125)



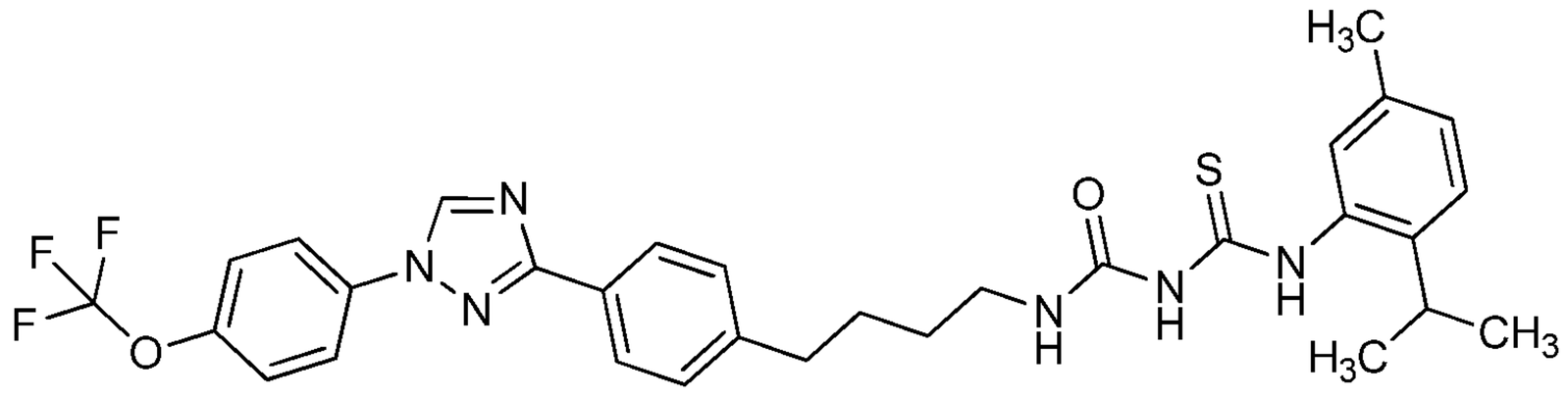
The title compound was prepared as described in Example 63 using 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CA18**) and 1-(5-methyl-2-propylphenyl)thiourea (**CA38**). Sodium acetate was used in place of sodium bicarbonate. The title compound was isolated as a white solid (0.134 g, 40%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 10.04 (s, 1H), 9.40 (s, 1H), 8.14 - 8.04 (m, 2H), 8.03 - 7.92 (m, 2H), 7.68 - 7.57 (m, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.42 - 7.32 (m, 2H), 7.11 (t, *J* = 7.1 Hz, 2H), 7.01 (ddd, *J* = 7.9, 1.7, 0.8 Hz, 1H), 3.18 (q, *J* = 6.5 Hz, 2H), 2.73 (dd, *J* = 8.7, 6.6 Hz, 2H), 2.45 (dd, *J* = 8.6, 6.6 Hz, 2H), 2.26 (s, 3H), 1.91 - 1.75 (m, 2H), 1.55 - 1.41 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.98; ESIMS *m/z* 597 ([M+H]$^{+}$), 595 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethyl)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC159)



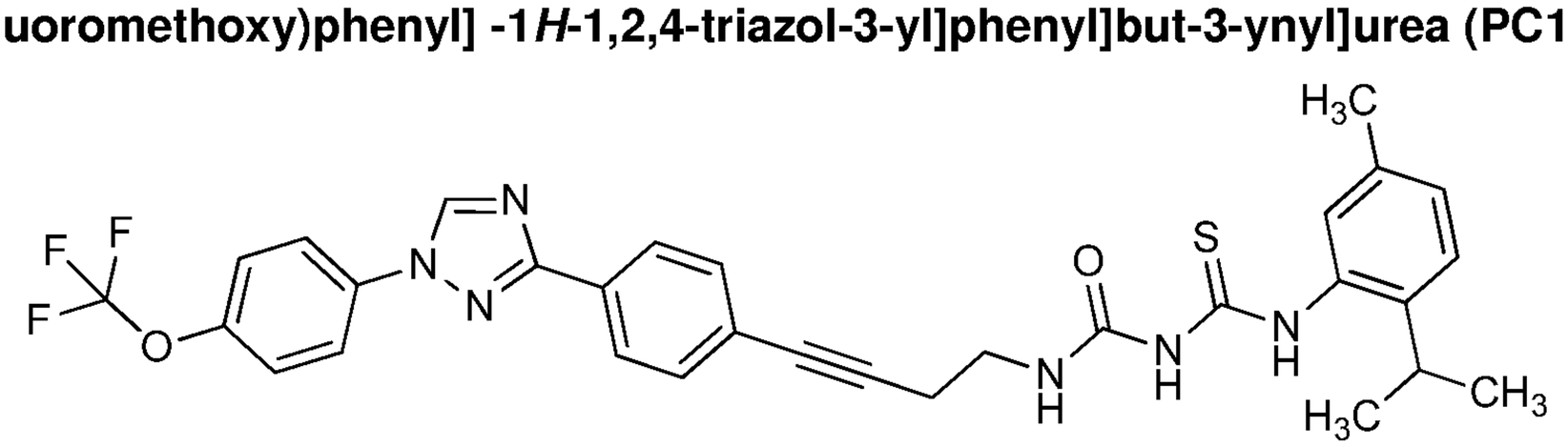
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA19**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a white solid (0.101 g, 37%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.86 (bs, 1H), 9.77 (bs, 1H), 8.65 (s, 1H), 8.19 - 8.03 (m, 2H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.85 - 7.72 (m, 2H), 7.40 - 7.20 (m, 5H), 5.68 (bs, 1H), 3.29 (d, *J* = 17.5 Hz, 2H), 3.13 - 2.94 (m, 1H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 1.69 (s, 2H), 1.56 (s, 2H), 1.21 (d, *J* = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48; ESIMS *m/z* 595 ([M+H]$^{+}$).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC150)



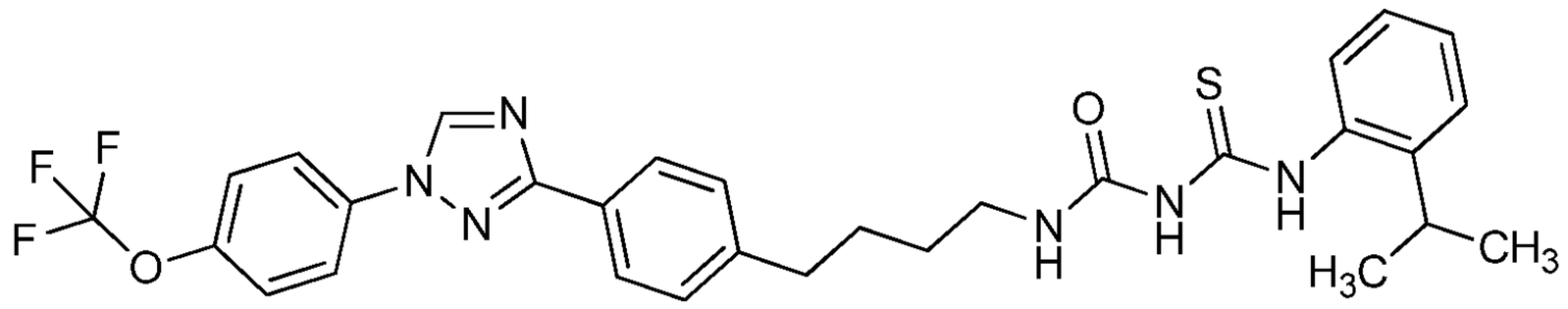
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a white solid (0.153 g, 38%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.91 (s, 1H), 10.01 (s, 1H), 9.38 (s, 1H), 8.11 - 8.00 (m, 4H), 7.67 - 7.59 (m, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 7.12 - 7.05 (m, 1H), 7.05 - 6.98 (m, 1H), 3.17 (q, J = 6.5 Hz, 2H), 2.94 (hept, J = 6.7 Hz, 1H), 2.75 - 2.64 (m, 2H), 2.25 (s, 3H), 1.73 - 1.59 (m, 2H), 1.58 - 1.43 (m, 2H), 1.13 (d, J = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 611 ([M+H]$^{+}$).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]but-3-ynyl]urea (PC160)



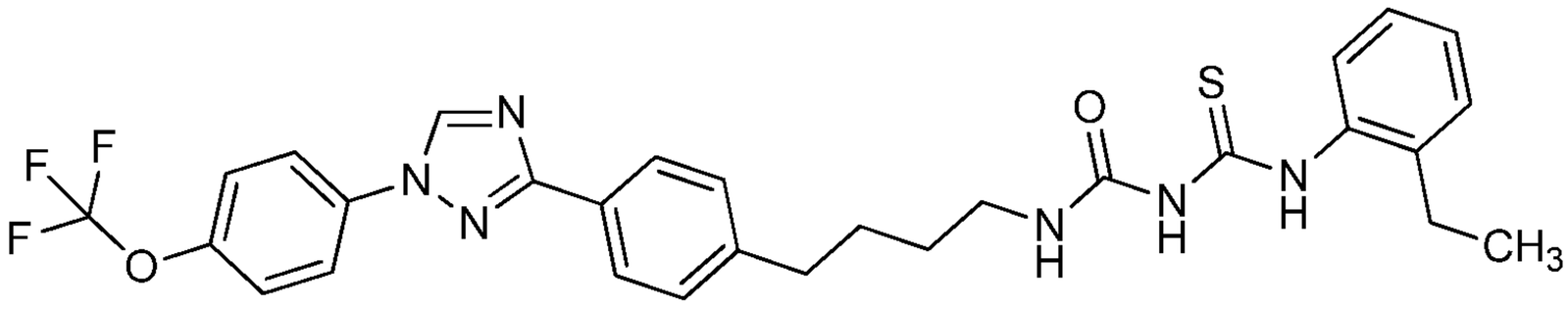
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-amine (**CA22**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a white solid (0.183 g, 39%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.90 (s, 1H), 10.27 (s, 1H), 9.43 (s, 1H), 8.09 (m, 4H), 7.66 - 7.60 (m, 2H), 7.60 - 7.55 (m, 2H), 7.25 - 7.18 (m, 3H), 7.09 (d, J = 7.7 Hz, 1H), 3.40 (q, J = 6.4 Hz, 2H), 2.96 (hept, J = 6.7 Hz, 1H), 2.68 (t, J = 6.6 Hz, 2H), 2.26 (s, 3H), 1.14 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 607 ([M+H]$^{+}$).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC146)



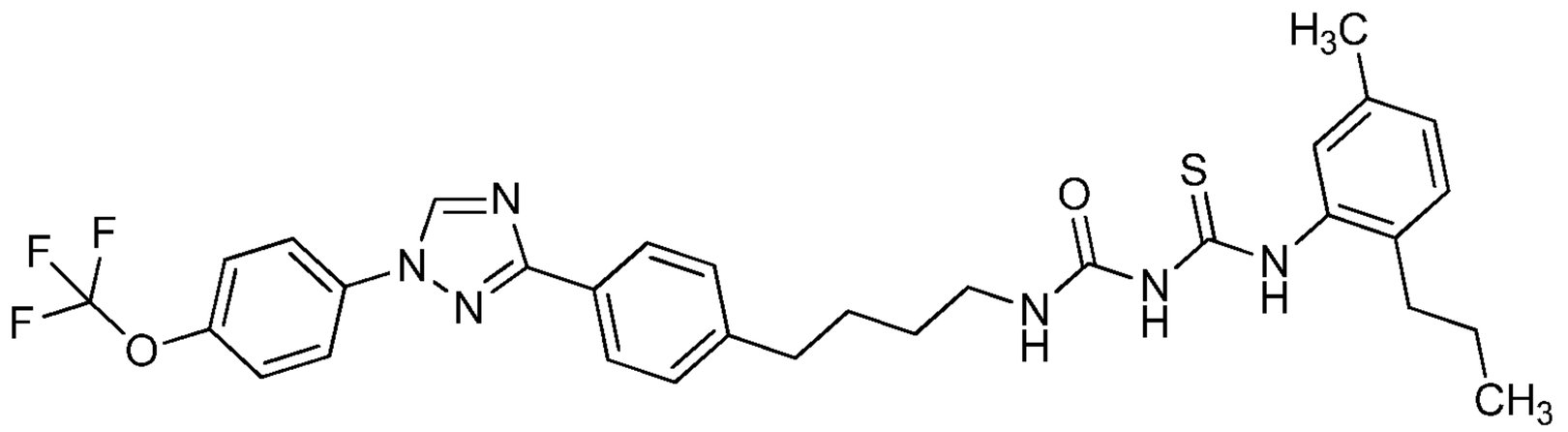
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2-isopropylphenyl)thiourea and isolated as a white solid (0.091 g, 38%): ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.95 (s, 1H), 10.02 (s, 1H), 9.37 (s, 1H), 8.10 - 7.97 (m, 4H), 7.61 (d, J = 8.6 Hz, 2H), 7.44 - 7.29 (m, 4H), 7.29 - 7.14 (m, 2H), 7.01 (s, 1H), 3.23 - 3.11 (m, 2H), 3.04 - 2.90 (m, 1H), 2.67 (t, J = 7.4 Hz, 2H), 1.71 - 1.56 (m, 2H), 1.56 - 1.42 (m, 2H), 1.14 (d, J = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 597 ([M+H]$^{+}$).

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy) phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC145)



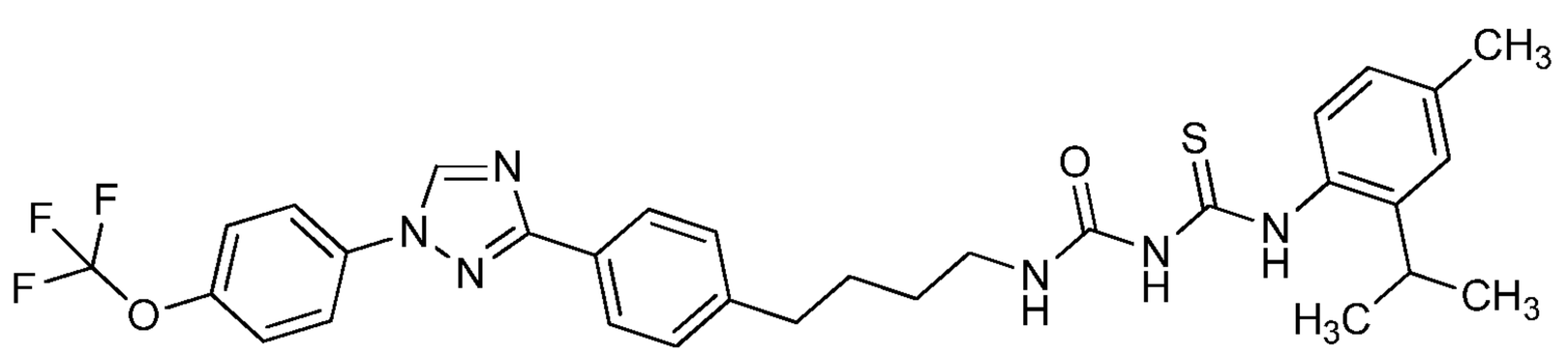
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2-ethylphenyl)thiourea and isolated as a white solid (0.111 g, 48%): ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.01 (s, 1H), 10.01 (s, 1H), 9.37 (s, 1H), 8.09 - 7.98 (m, 4H), 7.61 (d, J = 8.6 Hz, 2H), 7.53 (dd, J = 5.6, 3.7 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.30 - 7.23 (m, 1H), 7.19 (dd, J = 5.8, 3.5 Hz, 2H), 7.01 (s, 1H), 3.22 - 3.11 (m, 2H), 2.73 - 2.63 (m, 2H), 2.52 (d, J = 7.6 Hz, 2H), 1.63 (m, 2H), 1.49 (m, 2H), 1.15 - 1.04 (m, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 583 ([M+H]$^{+}$).

Preparation of 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC151)



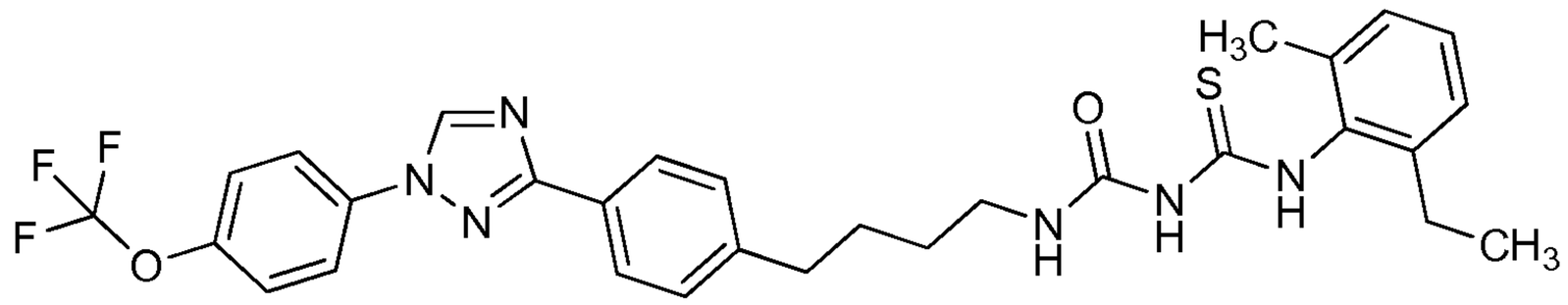
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(5-methyl-2-propylphenyl)thiourea (**CA38**) and isolated as a white solid (0.110 g, 45%): ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.98 (s, 1H), 9.97 (s, 1H), 9.36 (s, 1H), 8.03 (m, 4H), 7.60 (d, J = 8.7 Hz, 2H), 7.35 (m, 3H), 7.11 (d, J = 7.8 Hz, 1H), 7.05 - 6.92 (m, 2H), 3.16 (q, J = 6.3 Hz, 2H), 2.66 (t, J = 7.5 Hz, 2H), 2.42 (t, J = 7.6 Hz, 2H), 2.24 (s, 3H), 1.72 - 1.56 (m, 2H), 1.56 - 1.38 (m, 4H), 0.82 (t, J = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 611 ([M+H]$^{+}$).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC154)



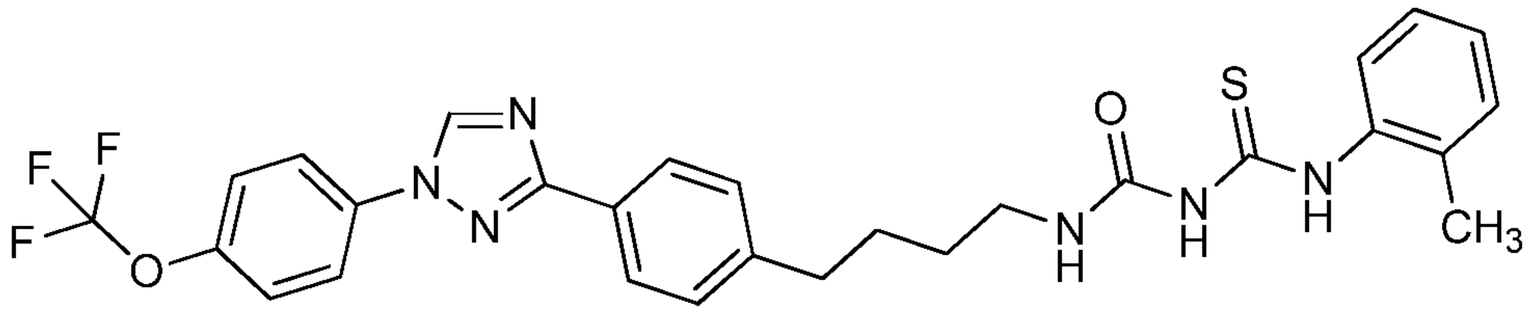
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as a white solid (0.100 g, 41%): ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.84 (s, 1H), 9.97 (s, 1H), 9.36 (s, 1H), 8.11 - 7.96 (m, 4H), 7.60 (d, J = 8.5 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.11 (s, 1H), 6.98 (d, J = 8.0 Hz, 2H), 3.15 (q, J = 6.3 Hz, 2H), 3.00 - 2.83 (m, 1H), 2.66 (t, J = 7.6 Hz, 2H), 2.28 (s, 3H), 1.72 - 1.55 (m, 2H), 1.55 - 1.42 (m, 2H), 1.12 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 611 ([M+H]$^{+}$).

Preparation of 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC153)



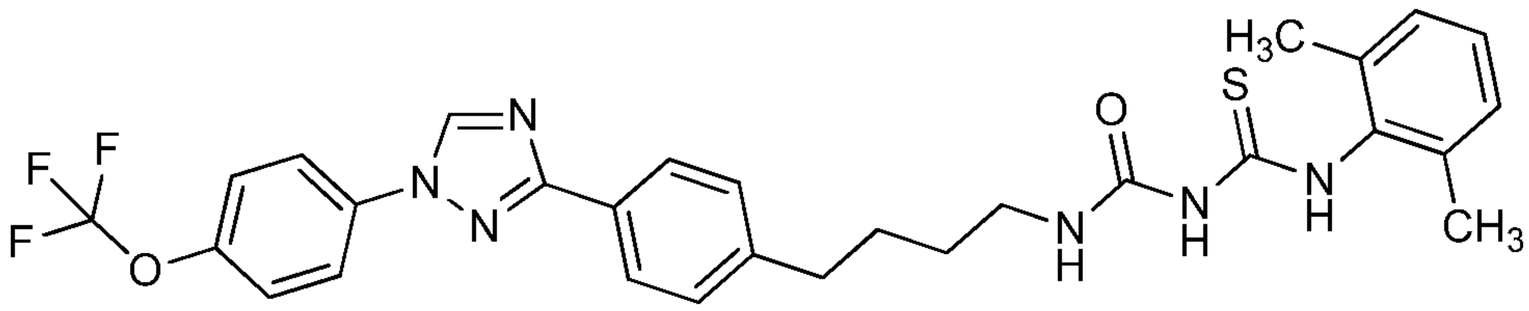
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) and isolated as a white solid (0.141 g, 59%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.59 (s, 1H), 10.00 (s, 1H), 9.37 (s, 1H), 8.12 - 7.98 (m, 4H), 7.66 - 7.54 (m, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.24 - 7.13 (m, 1H), 7.11 (d, J = 2.9 Hz, 2H), 7.00 (d, J = 5.7 Hz, 1H), 3.18 (q, J = 6.5 Hz, 2H), 2.75 - 2.61 (m, 2H), 2.49 - 2.44 (m, 2H), 2.16 (s, 3H), 1.65 (q, J = 7.7 Hz, 2H), 1.52 (q, J = 7.3 Hz, 2H), 1.11 (t, J = 7.6 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 597 ([M+H]$^{+}$).

Preparation of 1-(*o*-tolylcarbamothioyl)-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC144)



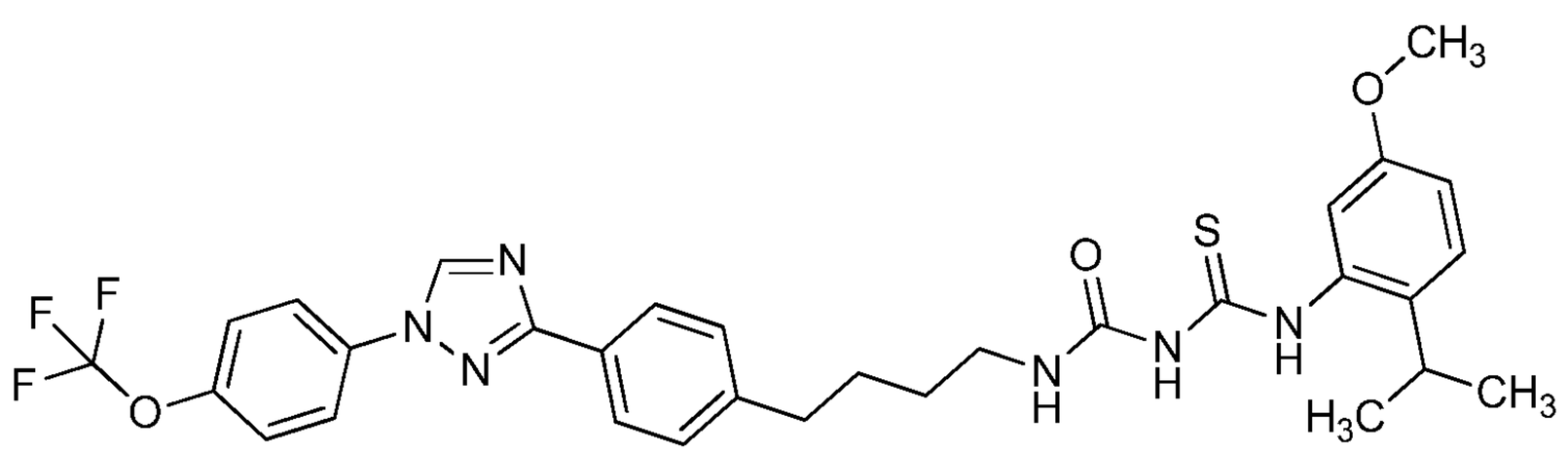
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(*o*-tolyl)thiourea and isolated as a white solid (0.097 g, 43%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 9.98 (s, 1H), 9.37 (s, 1H), 8.14 - 7.90 (m, 4H), 7.66 - 7.54 (m, 3H), 7.37 (d, J = 8.1 Hz, 2H), 7.31 - 7.23 (m, 1H), 7.23 - 7.14 (m, 2H), 7.02 (s, 1H), 3.23 - 3.12 (m, 2H), 2.68 (t, J = 7.5 Hz, 2H), 2.20 (s, 3H), 1.70 - 1.59 (m, 2H), 1.57 - 1.44 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 569 ([M+H]$^{+}$).

Preparation of 1-[(2,6-dimethylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoro methoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC152)



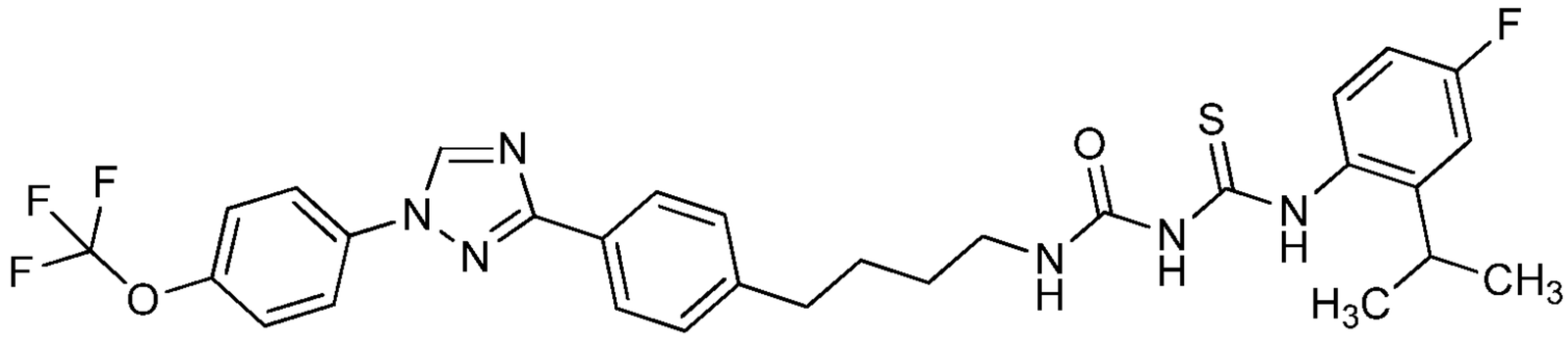
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2,6-dimethylphenyl)thiourea and isolated as a white solid (0.122 g, 53%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.53 (s, 1H), 9.98 (s, 1H), 9.37 (s, 1H), 8.11 - 8.00 (m, 4H), 7.66 - 7.58 (m, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.09 (q, J = 5.2 Hz, 3H), 6.99 (t, J = 5.7 Hz, 1H), 3.18 (q, J = 6.5 Hz, 2H), 2.69 (t, J = 7.6 Hz, 2H), 2.15 (s, 6H), 1.66 (p, J = 7.5 Hz, 2H), 1.51 (p, J = 6.9 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 583 ([M+H]$^{+}$).

Preparation of 1-[(2-isopropyl-5-methoxy-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC156)



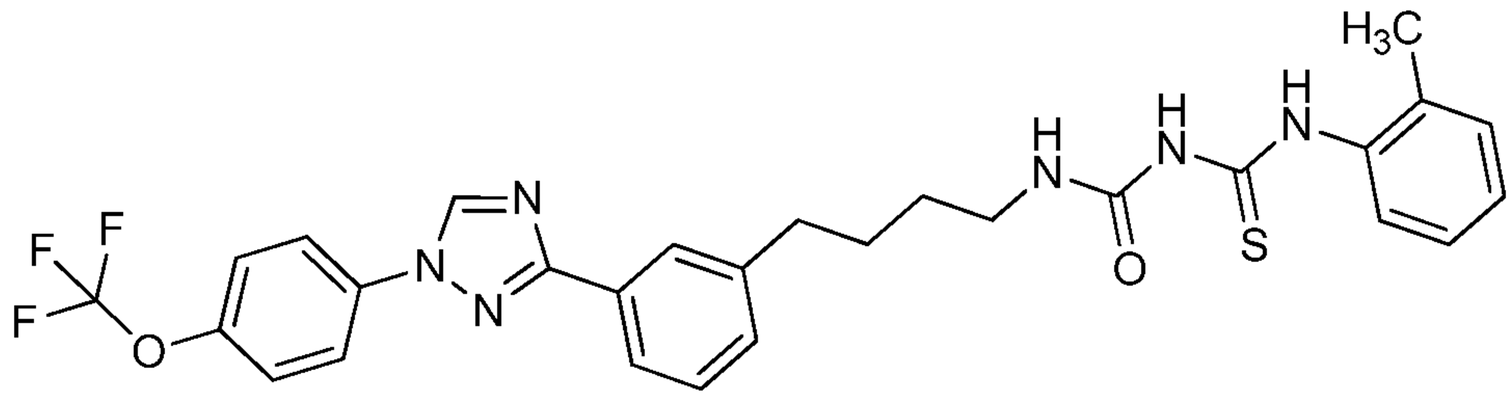
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated as a white solid (0.114 g, 46%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 10.01 (s, 1H), 9.36 (s, 1H), 8.13 - 7.97 (m, 4H), 7.68 - 7.56 (m, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.7 Hz, 1H), 7.11 (d, J = 2.7 Hz, 1H), 7.01 (d, J = 5.9 Hz, 1H), 6.84 (dd, J = 8.6, 2.8 Hz, 1H), 3.71 (s, 3H), 3.18 (q, J = 6.5 Hz, 2H), 2.92 (hept, J = 6.9 Hz, 1H), 2.68 (t, J = 7.6 Hz, 2H), 1.65 (p, J = 7.6 Hz, 2H), 1.51 (q, J = 7.2 Hz, 2H), 1.13 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 627 ([M+H]$^{+}$).

Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC155)



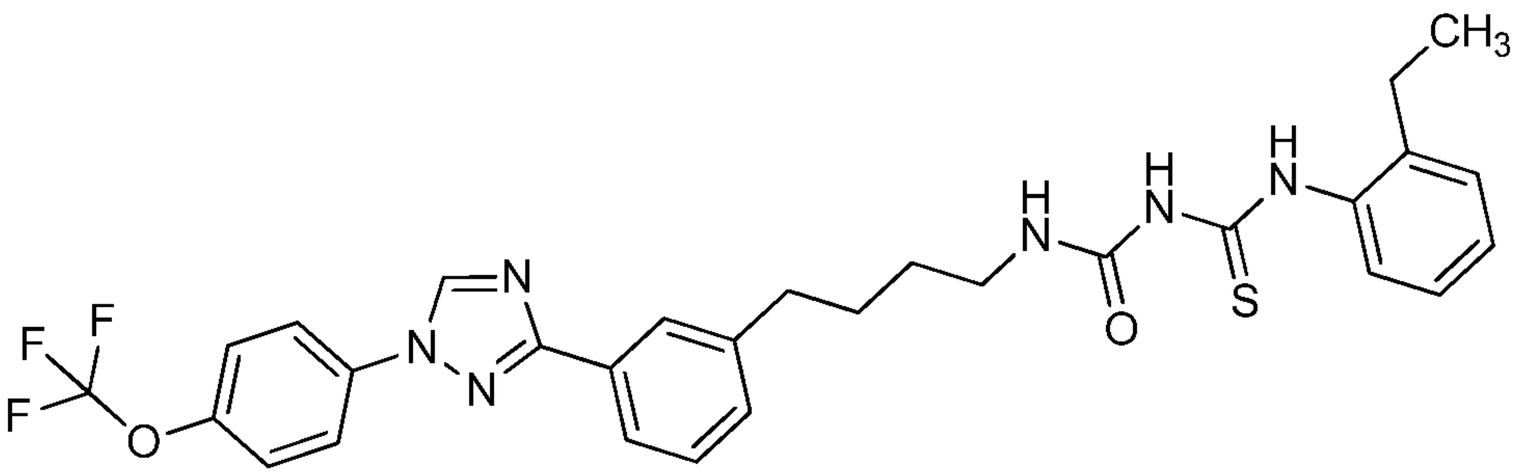
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as a white solid (0.089 g, 36%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H), 10.04 (s, 1H), 9.37 (s, 1H), 8.11 - 7.99 (m, 4H), 7.61 (d, J = 8.8 Hz, 2H), 7.44 - 7.31 (m, 3H), 7.14 (dd, J = 10.4, 2.9 Hz, 1H), 7.09 - 6.96 (m, 2H), 3.18 (q, J = 6.5 Hz, 2H), 3.03 - 2.90 (m, 1H), 2.68 (t, J = 7.5 Hz, 2H), 1.70 - 1.58 (m, 2H), 1.56 - 1.44 (m, 2H), 1.15 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97, -114.40; ESIMS *m/z* 615 ([M+H]$^{+}$).

Preparation of 1-(*o*-tolylcarbamothioyl)-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC170)



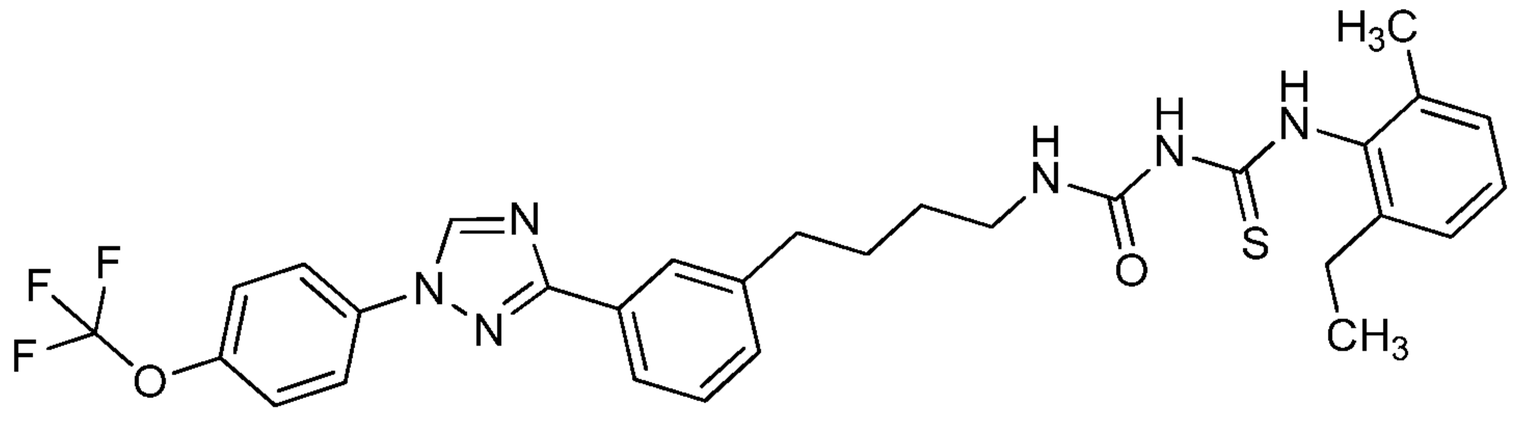
The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(*o*-tolyl)thiourea and isolated as a white solid (0.102 g, 35%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 10.01 (s, 1H), 9.39 (s, 1H), 8.11 - 8.05 (m, 2H), 7.98 (t, J = 1.7 Hz, 1H), 7.94 (dt, J = 7.7, 1.4 Hz, 1H), 7.67 - 7.57 (m, 3H), 7.44 (t, J = 7.6 Hz, 1H), 7.34 (dt, J = 7.7, 1.5 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.23 - 7.13 (m, 2H), 7.03 (t, J = 5.7 Hz, 1H), 3.19 (q, J = 6.5 Hz, 2H), 2.72 (t, J = 7.6 Hz, 2H), 2.19 (s, 3H), 1.74 - 1.60 (m, 2H), 1.52 (p, J = 6.9 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 569 ([M+H]$^{+}$).

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy) phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC171)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(2-ethylphenyl)thiourea and isolated as a white solid (0.113 g, 38%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 10.04 (s, 1H), 9.41 (s, 1H), 8.13 - 8.06 (m, 2H), 8.00 (d, J = 1.7 Hz, 1H), 7.96 (dt, J = 7.7, 1.4 Hz, 1H), 7.69 - 7.60 (m, 2H), 7.56 (dd, J = 5.6, 3.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.36 (dt, J = 7.7, 1.5 Hz, 1H), 7.31 - 7.26 (m, 1H), 7.26 - 7.19 (m, 2H), 7.05 (t, J = 5.6 Hz, 1H), 3.21 (q, J = 6.5 Hz, 2H), 2.74 (t, J = 7.6 Hz, 2H), 2.59 - 2.53 (m, 2H), 1.69 (tt, J = 9.0, 6.6 Hz, 2H), 1.54 (p, J = 6.9 Hz, 2H), 1.12 (t, J = 7.5 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 583 ([M+H]$^{+}$).

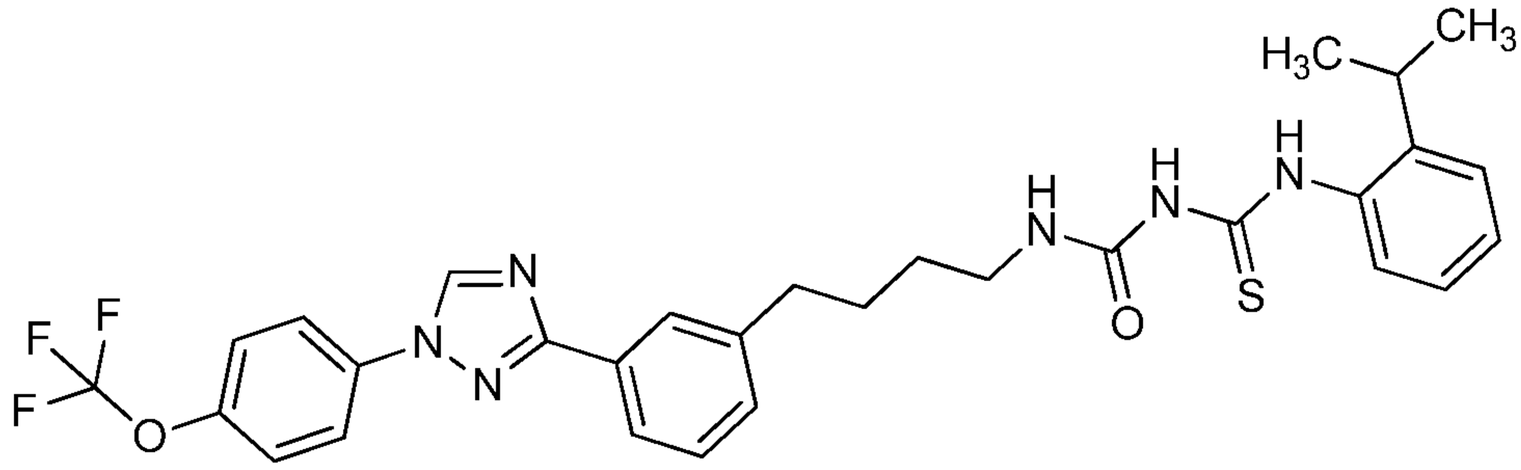
Preparation of 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC179)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) and isolated as a white solid (0.143 g, 47%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.62 (s, 1H), 10.04 (s, 1H), 9.40 (s, 1H), 8.12 - 8.06 (m, 2H), 8.00 (t, J = 1.6 Hz, 1H), 7.96 (dt, J = 7.7, 1.4 Hz, 1H), 7.64 (ddt, J = 7.8, 1.9, 0.9 Hz, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.36 (dt, J = 7.7, 1.4 Hz, 1H), 7.22 - 7.15 (m, 1H), 7.10 (dq, J = 6.3, 1.8 Hz, 2H), 7.02 (t, J = 5.7 Hz, 1H), 3.21 (q, J = 6.5 Hz, 2H), 2.74 (t, J = 7.6 Hz, 2H), 2.48 (td, J = 7.5, 1.9 Hz, 2H), 2.17 (s, 3H), 1.69 (p,

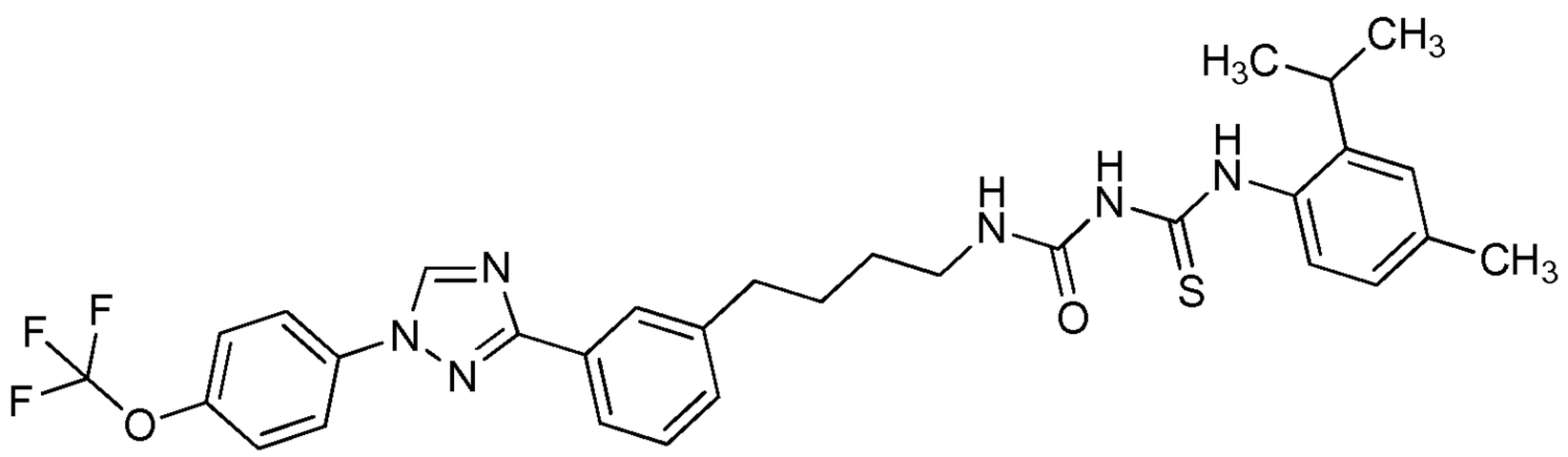
J = 7.6 Hz, 2H), 1.62 - 1.48 (m, 2H), 1.11 (t, J = 7.6 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS m/z 597 ([M+H]$^+$).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC172)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(2-isopropylphenyl)thiourea and isolated as a white solid (0.072 g, 24%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.99 (s, 1H), 10.05 (s, 1H), 9.41 (s, 1H), 8.13 - 8.07 (m, 2H), 8.00 (t, J = 1.7 Hz, 1H), 7.96 (dt, J = 7.8, 1.4 Hz, 1H), 7.64 (dq, J = 7.7, 1.0 Hz, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.42 (dd, J = 7.9, 1.5 Hz, 1H), 7.36 (ddd, J = 7.8, 3.3, 1.6 Hz, 2H), 7.28 (td, J = 7.5, 1.5 Hz, 1H), 7.21 (td, J = 7.5, 1.7 Hz, 1H), 7.05 (t, J = 5.7 Hz, 1H), 3.21 (q, J = 6.4 Hz, 2H), 3.00 (p, J = 6.9 Hz, 1H), 2.74 (t, J = 7.6 Hz, 2H), 1.69 (p, J = 7.8 Hz, 2H), 1.54 (p, J = 7.0 Hz, 2H), 1.16 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS m/z 597 ([M+H]$^+$).

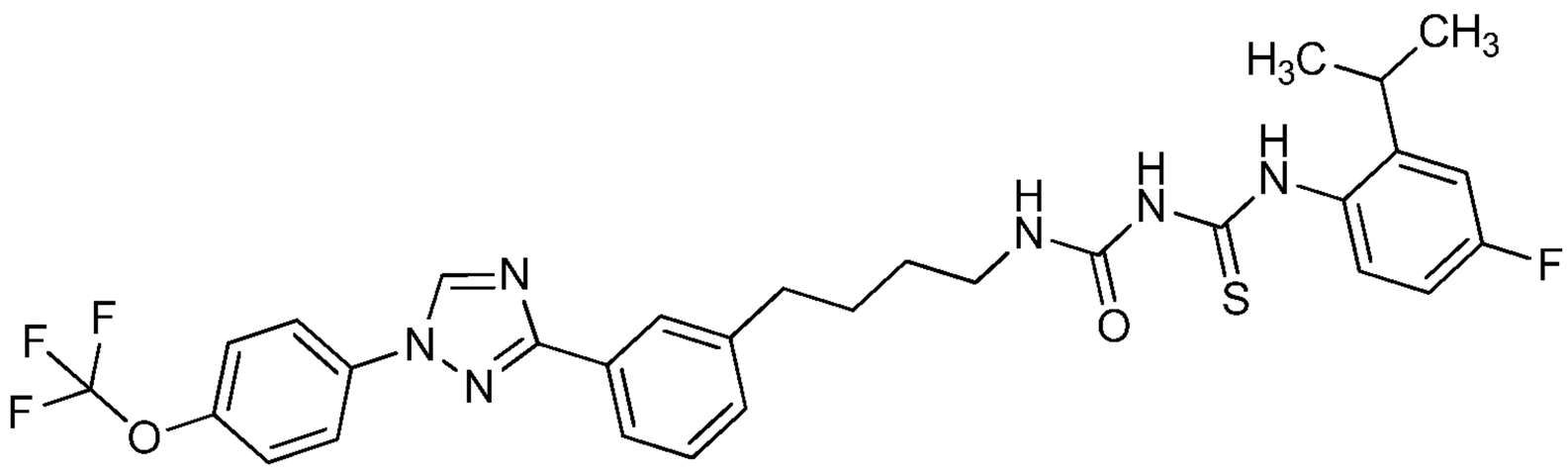
Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC180)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as a white solid (0.139 g, 45%):

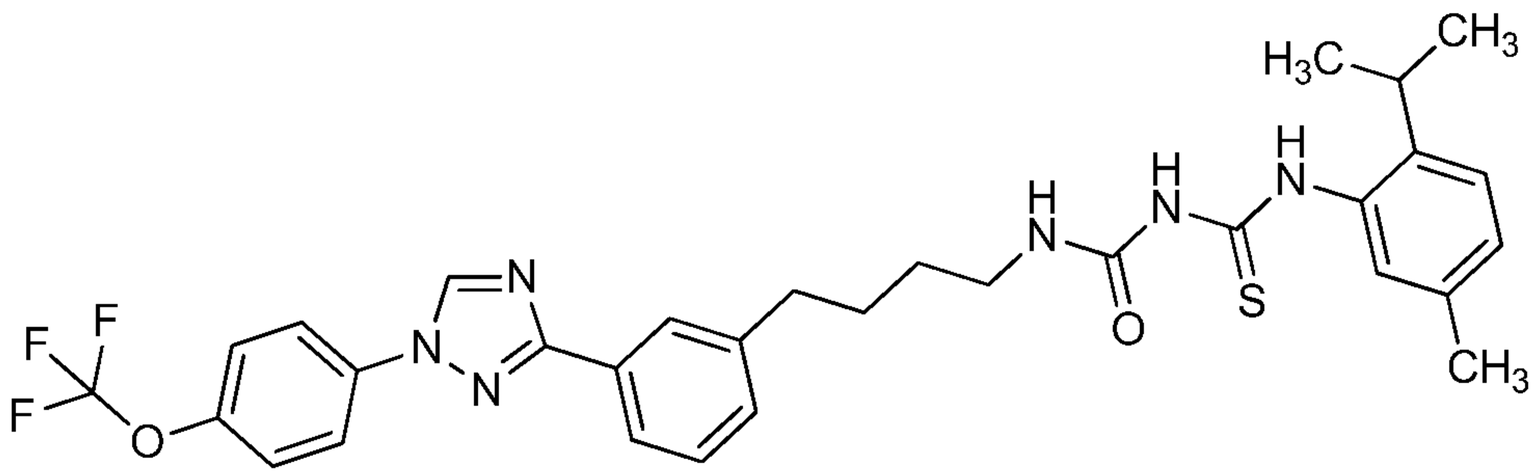
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 10.01 (s, 1H), 9.40 (s, 1H), 8.13 - 8.07 (m, 2H), 8.00 (d, J = 1.7 Hz, 1H), 7.96 (dt, J = 7.7, 1.4 Hz, 1H), 7.64 (dq, J = 7.8, 1.0 Hz, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.36 (dt, J = 7.7, 1.4 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.15 (dd, J = 2.0, 0.9 Hz, 1H), 7.07 - 6.97 (m, 2H), 3.20 (q, J = 6.5 Hz, 2H), 2.95 (p, J = 6.9 Hz, 1H), 2.74 (t, J = 7.6 Hz, 2H), 2.32 (s, 3H), 1.68 (p, J = 7.3 Hz, 2H), 1.61 - 1.47 (m, 2H), 1.15 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS m/z 611 ([M+H]$^+$).

Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC181)



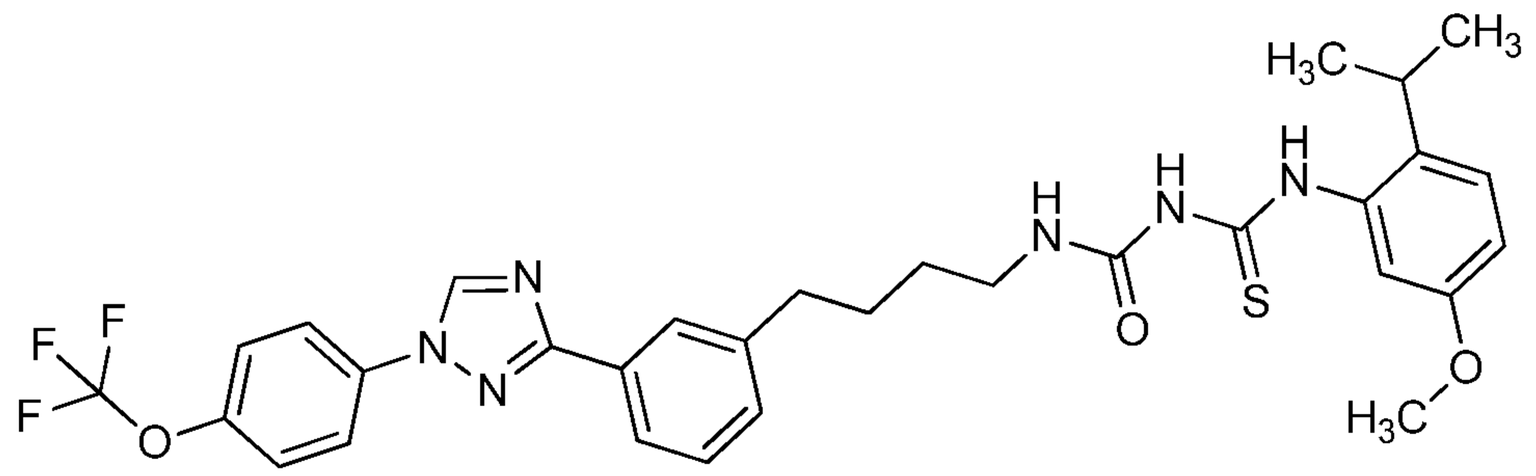
The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as a white solid (0.114 g, 36%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (s, 1H), 10.09 (s, 1H), 9.41 (s, 1H), 8.13 - 8.07 (m, 2H), 8.00 (t, J = 1.6 Hz, 1H), 7.96 (dt, J = 7.7, 1.4 Hz, 1H), 7.69 - 7.61 (m, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.43 - 7.33 (m, 2H), 7.16 (dd, J = 10.4, 3.0 Hz, 1H), 7.05 (td, J = 8.3, 2.9 Hz, 2H), 3.20 (q, J = 6.5 Hz, 2H), 3.05 - 2.90 (m, 1H), 2.74 (t, J = 7.6 Hz, 2H), 1.76 - 1.62 (m, 2H), 1.61 - 1.48 (m, 2H), 1.15 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96 , -114.42; ESIMS m/z 615 ([M+H]$^+$).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC176)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as a white solid (0.119 g, 38%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.93 (s, 1H), 10.03 (s, 1H), 9.41 (s, 1H), 8.13 - 8.07 (m, 2H), 8.00 (t, J = 1.7 Hz, 1H), 7.96 (dt, J = 7.6, 1.4 Hz, 1H), 7.68 - 7.61 (m, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.36 (dt, J = 7.6, 1.5 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.13 - 7.07 (m, 1H), 7.04 (t, J = 5.5 Hz, 1H), 3.20 (q, J = 6.5 Hz, 2H), 2.95 (p, J = 6.9 Hz, 1H), 2.74 (t, J = 7.6 Hz, 2H), 2.27 (s, 3H), 1.78 - 1.62 (m, 2H), 1.61 - 1.46 (m, 2H), 1.14 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 611 ([M+H]$^{+}$).

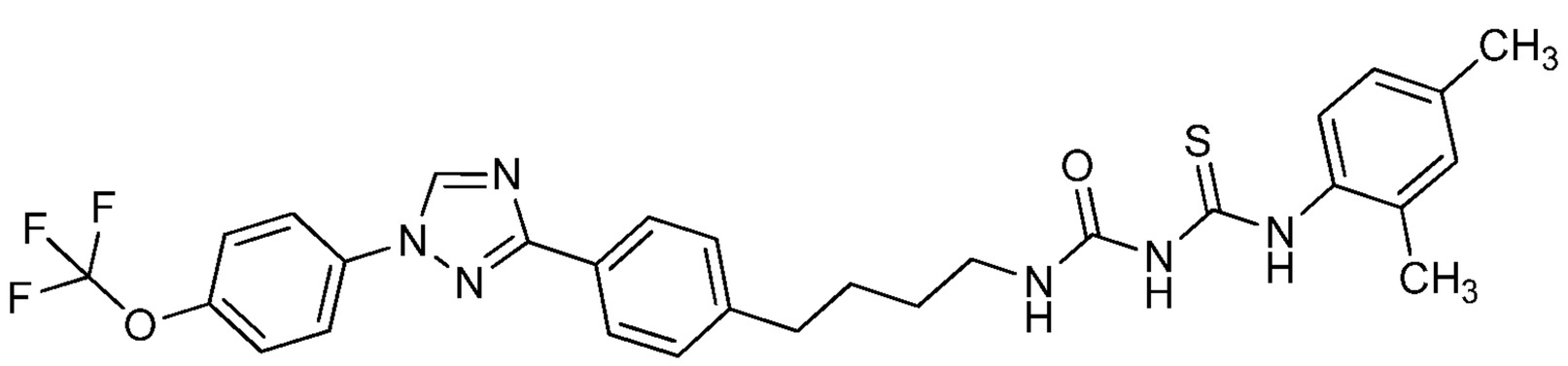
Preparation of 1-[(2-isopropyl-5-methoxy-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (PC182)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(2-isopropyl-5-methoxyphenyl)thiourea (**CA40**) and isolated as a white solid (0.141 g, 44%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 10.03 (s, 1H), 9.39 (s, 1H), 8.12 - 8.04 (m, 2H), 7.98 (t, J = 1.6 Hz, 1H), 7.94 (dt, J = 7.7, 1.4 Hz, 1H), 7.62 (ddd, J = 7.7, 1.9, 1.0 Hz, 2H), 7.45 (t, J = 7.6 Hz, 1H), 7.34 (dt, J = 7.7, 1.5 Hz, 1H), 7.23 (d, J = 8.7 Hz, 1H), 7.10 (d, J = 2.7 Hz, 1H), 7.03 (t, J = 5.6 Hz, 1H), 6.84 (dd, J =

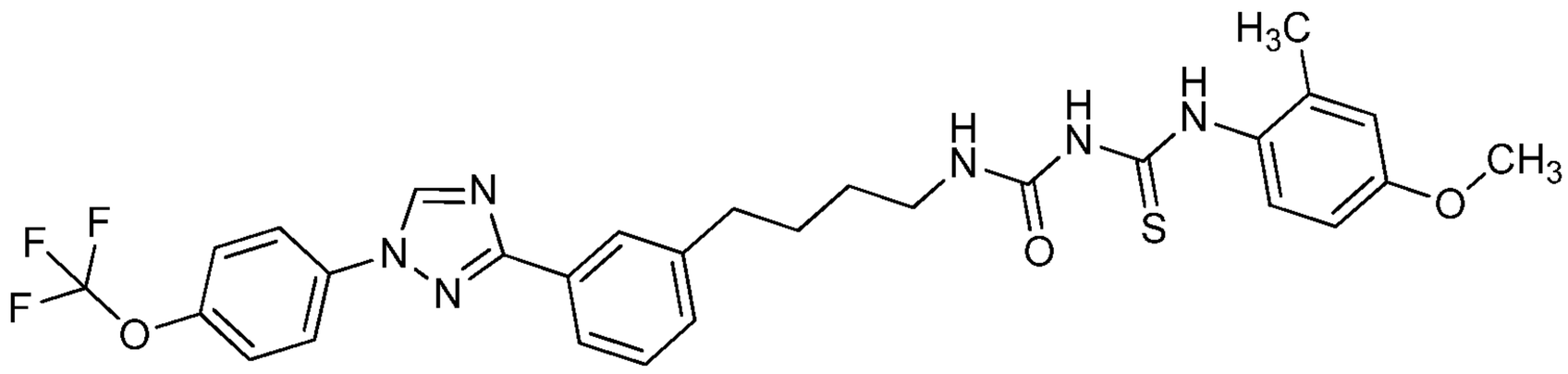
8.7, 2.8 Hz, 1H), 3.71 (s, 3H), 3.18 (q, *J* = 6.4 Hz, 2H), 2.91 (p, *J* = 6.8 Hz, 1H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.67 (p, *J* = 7.7 Hz, 2H), 1.52 (p, *J* = 6.9 Hz, 2H), 1.12 (d, *J* = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 627 ([M+H]$^+$).

Preparation of 1-[(2,4-dimethylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (FB16)



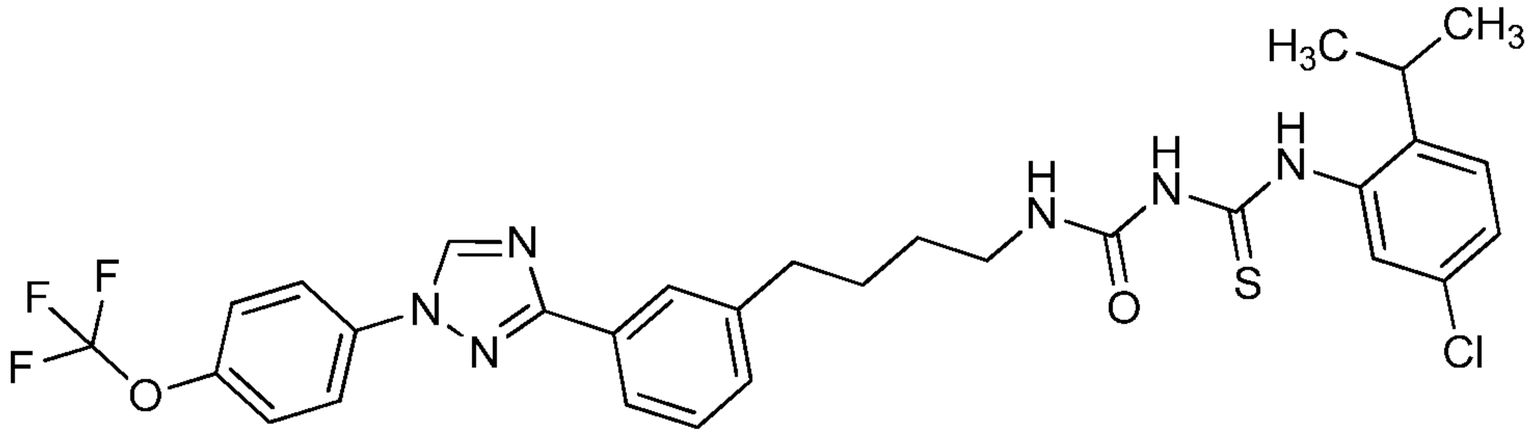
The title compound was prepared as described in Example 63 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA20**) and 1-(2,4-dimethylphenyl)thiourea and isolated as a white solid (0.106 g, 46%).

Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (FB36)



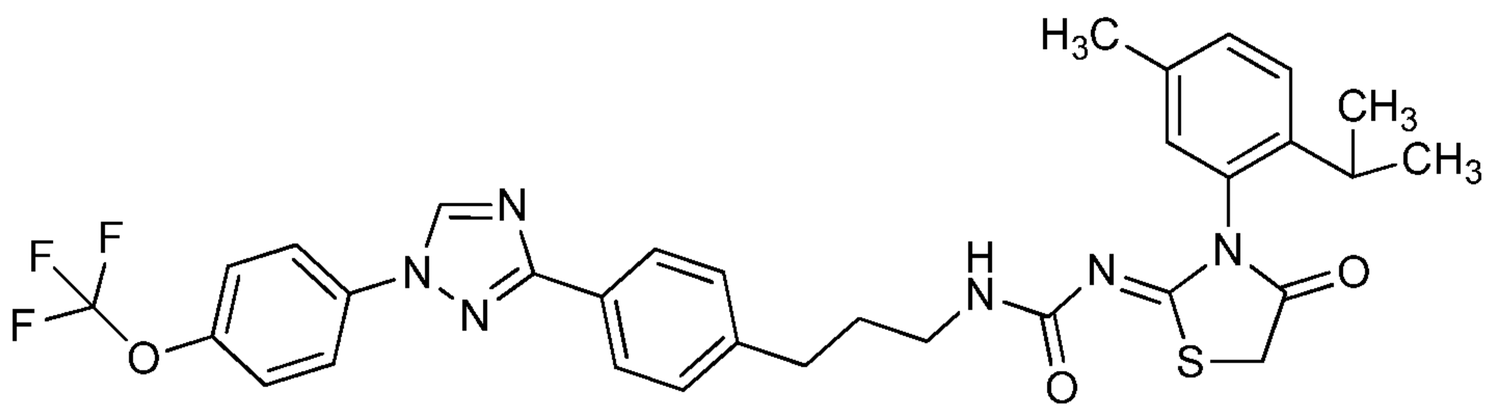
The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as a white solid (0.082 g, 27%).

Preparation of 1-[(5-chloro-2-isopropyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (FB37)



The title compound was prepared as described in Example 63 using 4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-amine (**CA21**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and isolated as a white solid (0.098 g, 31%).

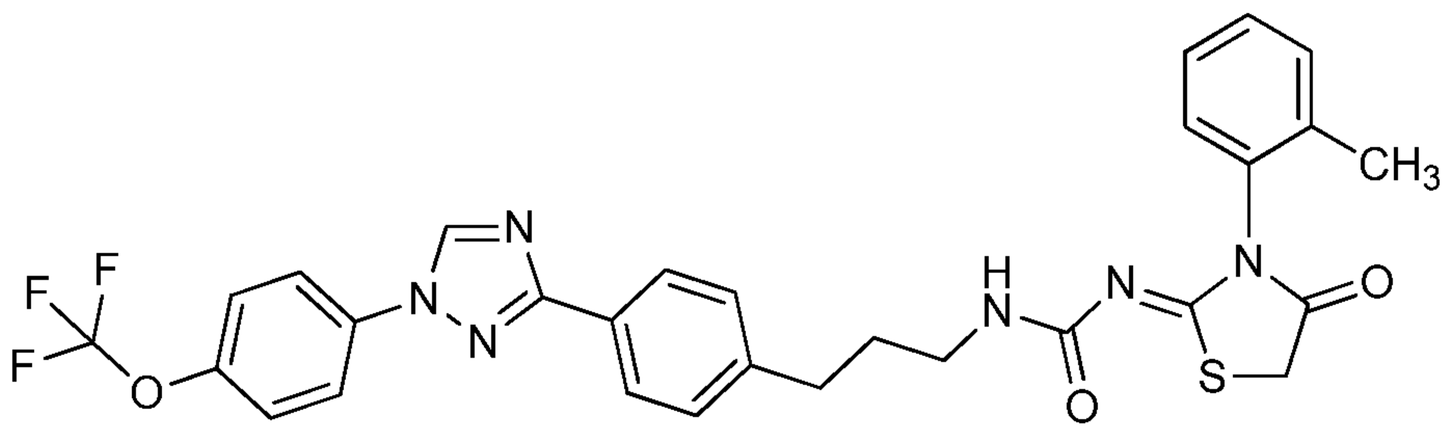
Example 64: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (F20)



To 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**F21**) (0.110 g, 0.184 mmol) in a 25 mL vial equipped with a stir bar and Vigreux column was added sodium acetate (0.0600 g, 0.735 mmol), ethanol (2 mL) and methyl bromoacetate (0.0250 mL, 0.276 mmol). The reaction was heated to 70 ºC overnight. The reaction was cooled and diluted with dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane. The organic layers were poured through a phase separator and concentrated. Purification by flash column chromatography using 0-30% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided a solid which was dried overnight at 50 ºC *in vacuo* to afford the title compound as a white solid (0.0791 g, 68%).

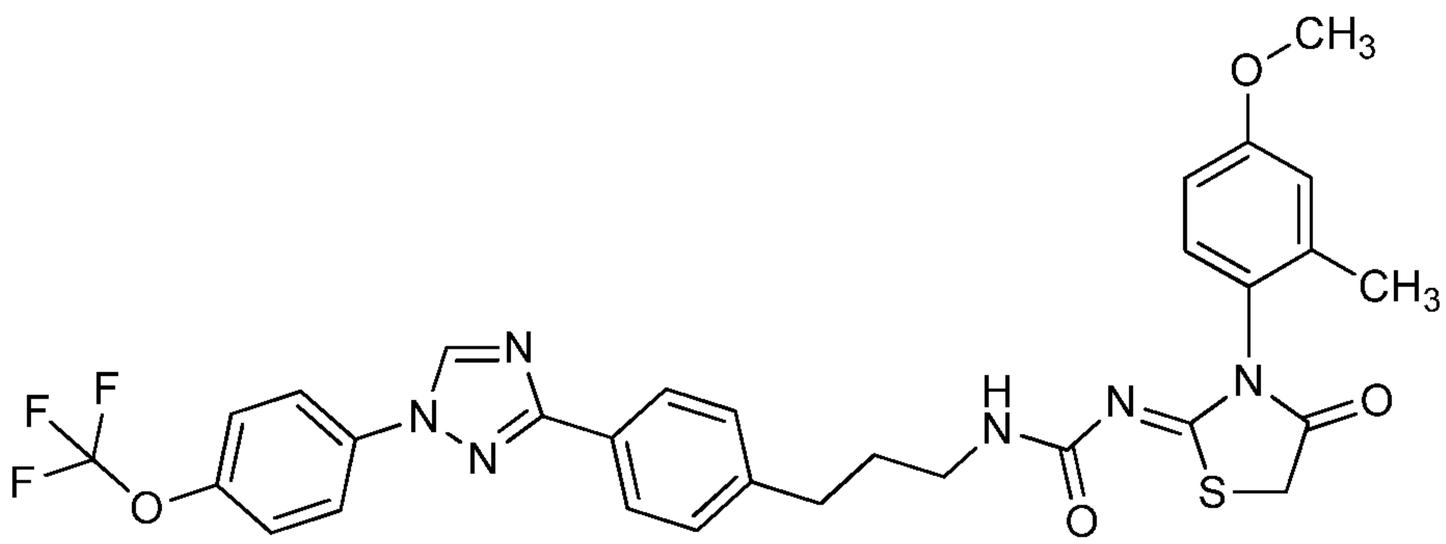
The following compounds were prepared in accordance to the procedure in Example 64.

Preparation of (*Z*)-1-(4-oxo-3-(o-tolyl)thiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P92)



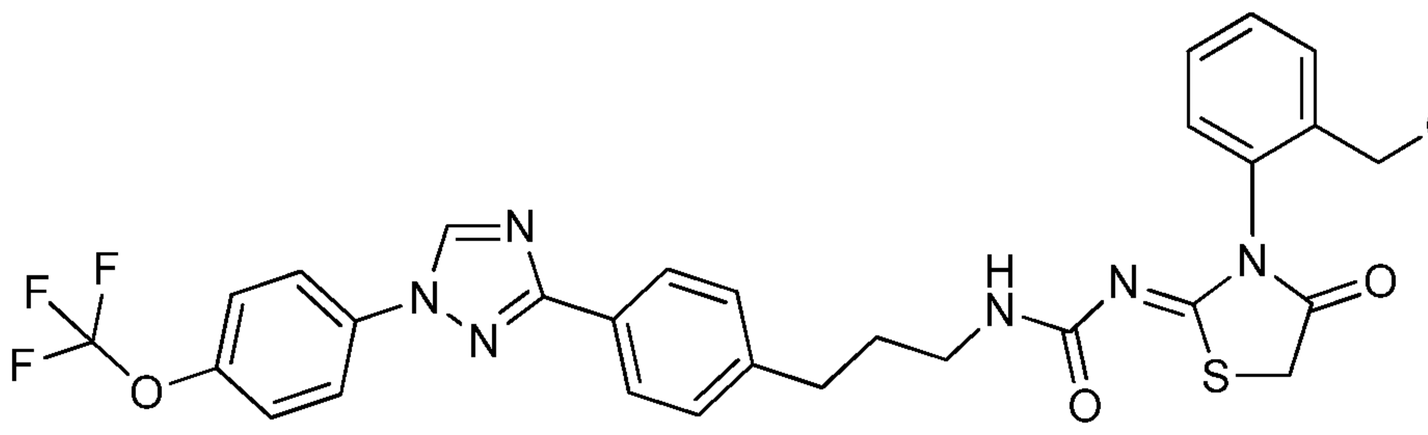
The title compound was prepared as described in Example 64 using 1-(*o*-tolylcarbamothioyl)-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC92**) and isolated as a light yellow solid (0.036 g, 72%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P105)



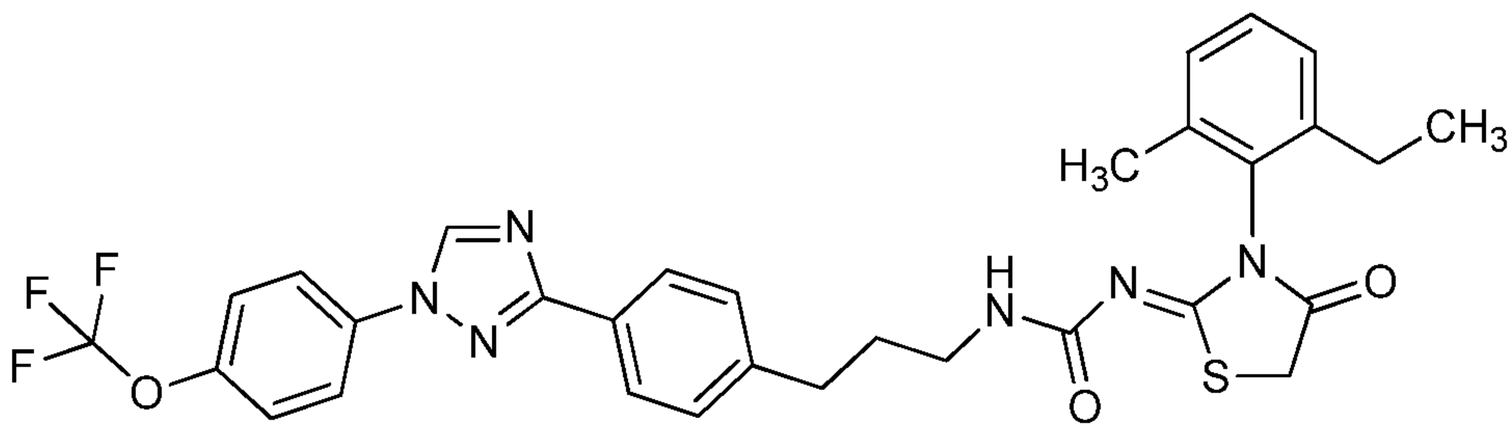
The title compound was prepared as described in Example 64 using 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC105**) and isolated as a light yellow solid (0.085 g, 75%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P93, P510)



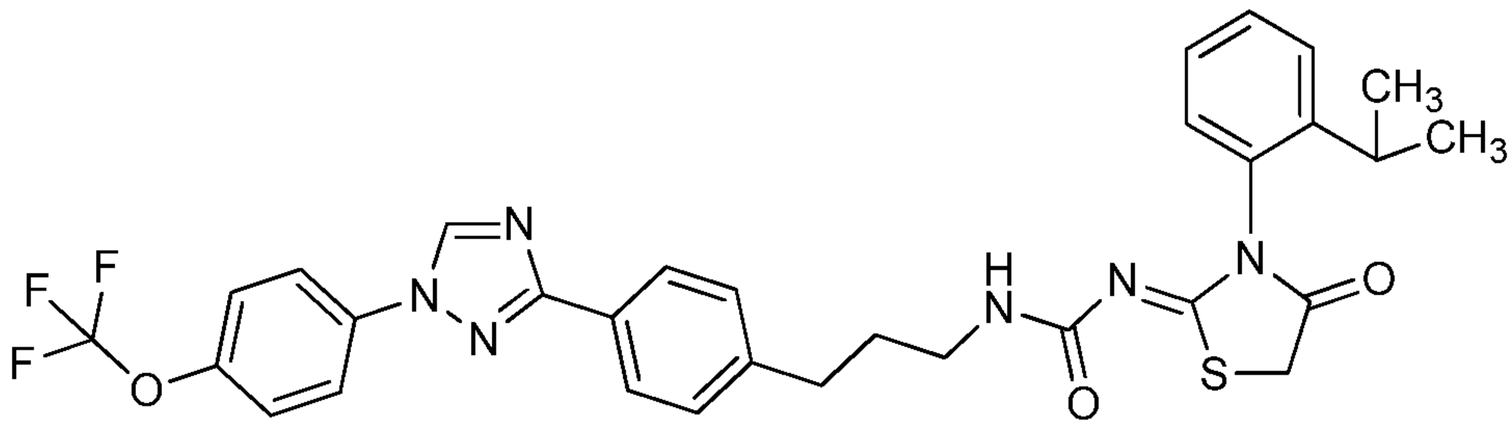
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC93**) and isolated as a light yellow solid (0.057 g, 54%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P101)



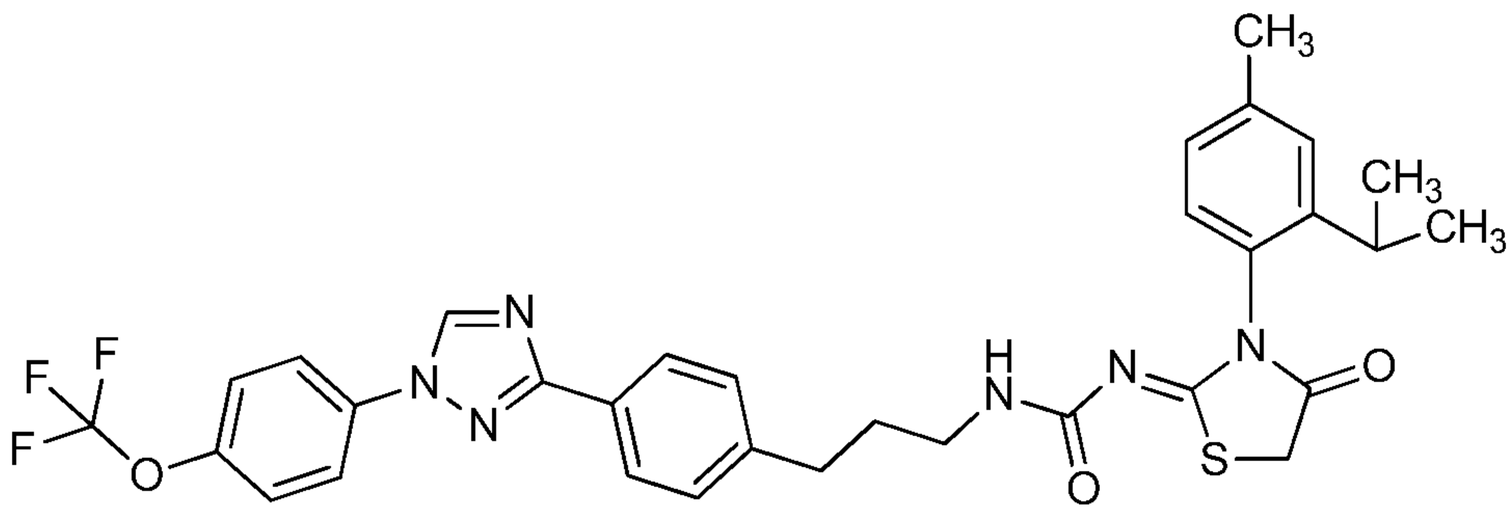
The title compound was prepared as described in Example 64 using 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC101**) and isolated as a light yellow solid (0.059 g, 41%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P94, P197)



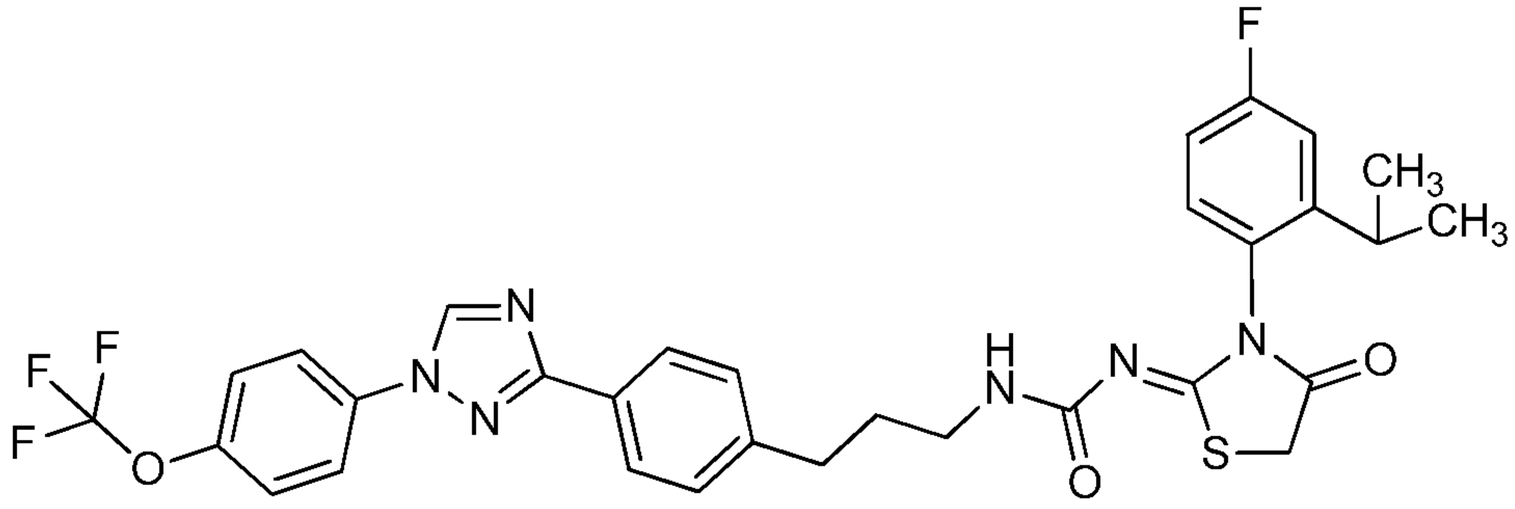
The title compound was prepared as described in Example 64 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC94**) and isolated as a light yellow solid (0.071 g, 80%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P102)



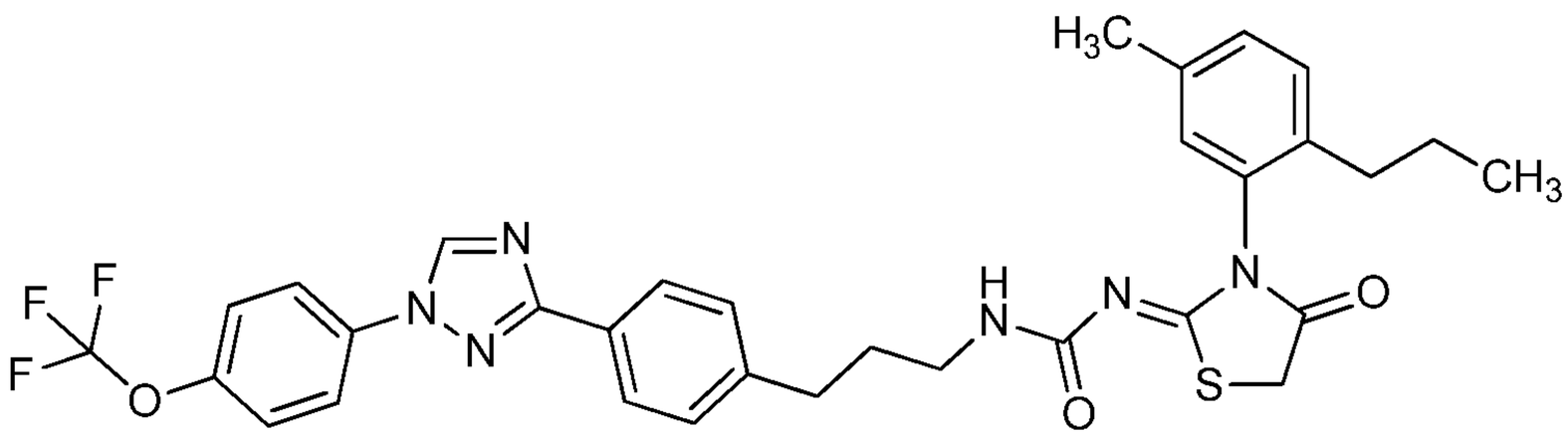
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC102**) and isolated as a light yellow solid (0.070 g, 75%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P103, P1150)



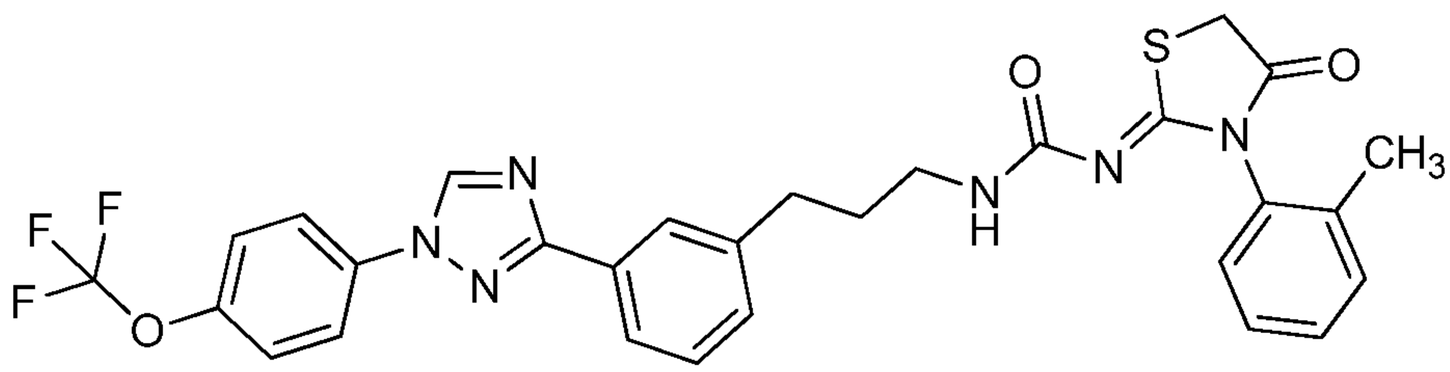
The title compound was prepared as described in Example 64 using 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC103**) and isolated as a light yellow solid (0.084 g, 77%).

Preparation of (*Z*)-1-(3-(5-methyl-2-propylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P99, P830)



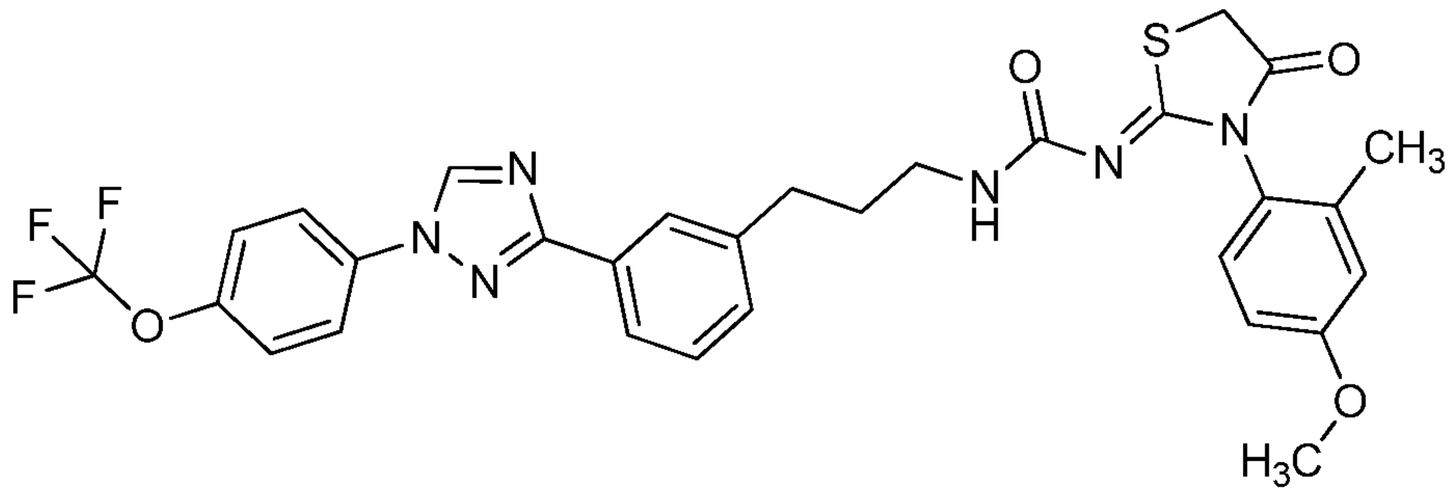
The title compound was prepared as described in Example 64 using 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[3-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC99**) and isolated as a light yellow solid (0.075 g, 72%).

Preparation of (*Z*)-1-(4-oxo-3-(*o*-tolyl)thiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P118)



The title compound was prepared as described in Example 64 using 1-(*o*-tolylcarbamothioyl)-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC118**) and isolated as an off-white solid (0.051 g, 80%).

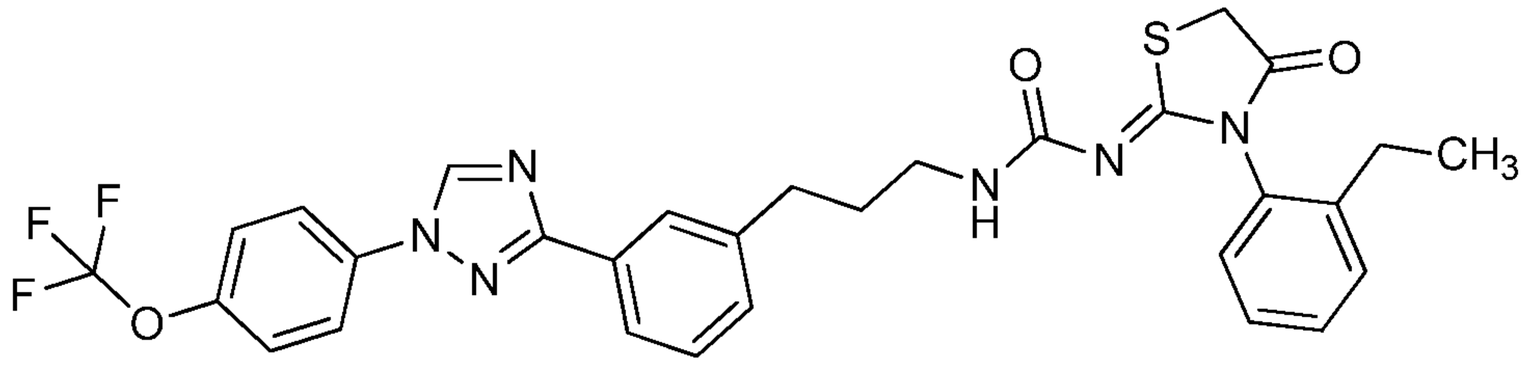
Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P131)



The title compound was prepared as described in Example 64 using 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-

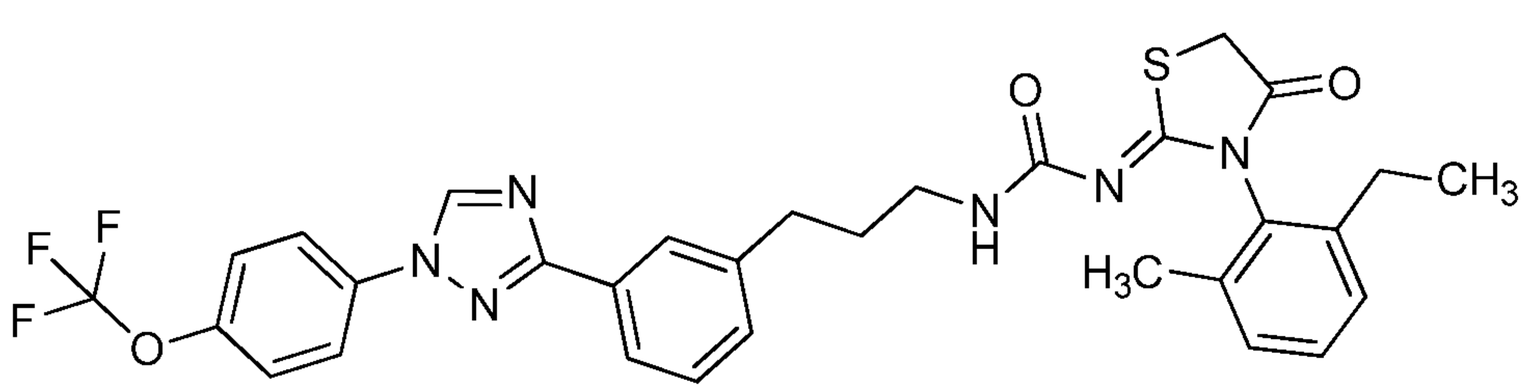
1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC131**) and isolated as an off-white solid (0.074 g, 89%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P119)



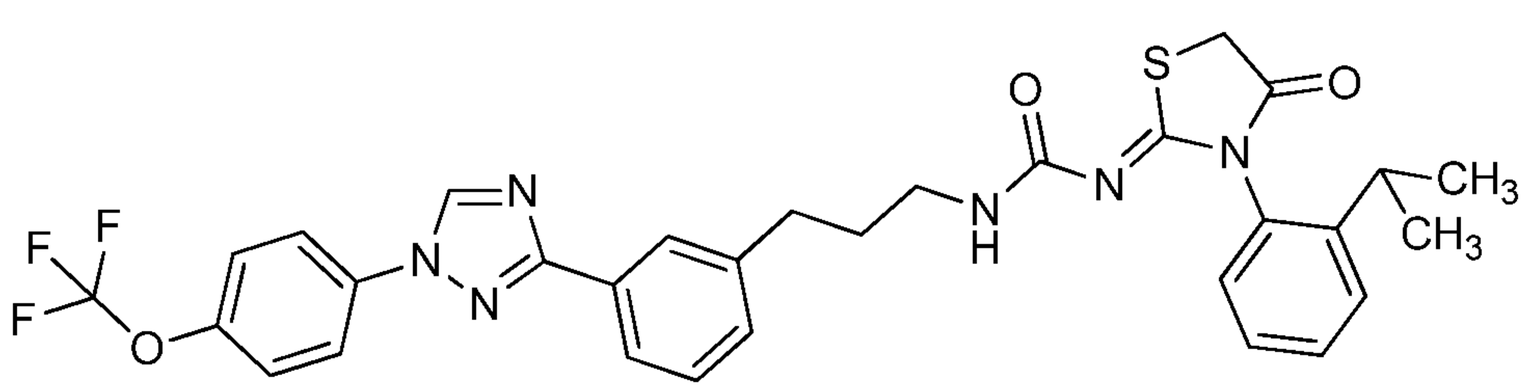
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC119**) and isolated as an off-white solid (0.071 g, 83%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P127)



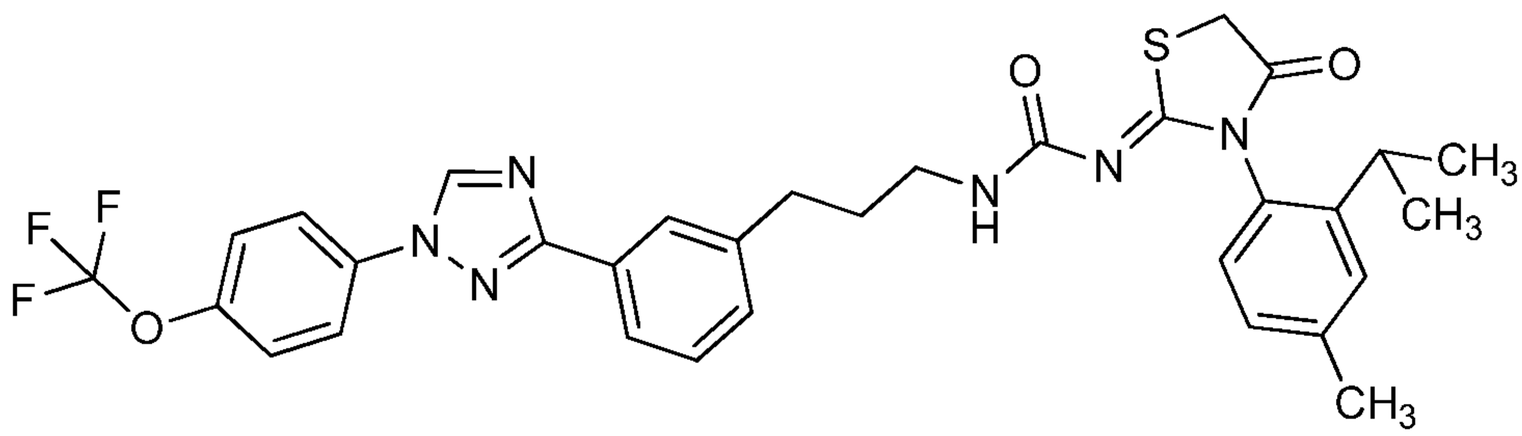
The title compound was prepared as described in Example 64 using 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC127**) and isolated as an off-white solid (0.061 g, 43%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P120)



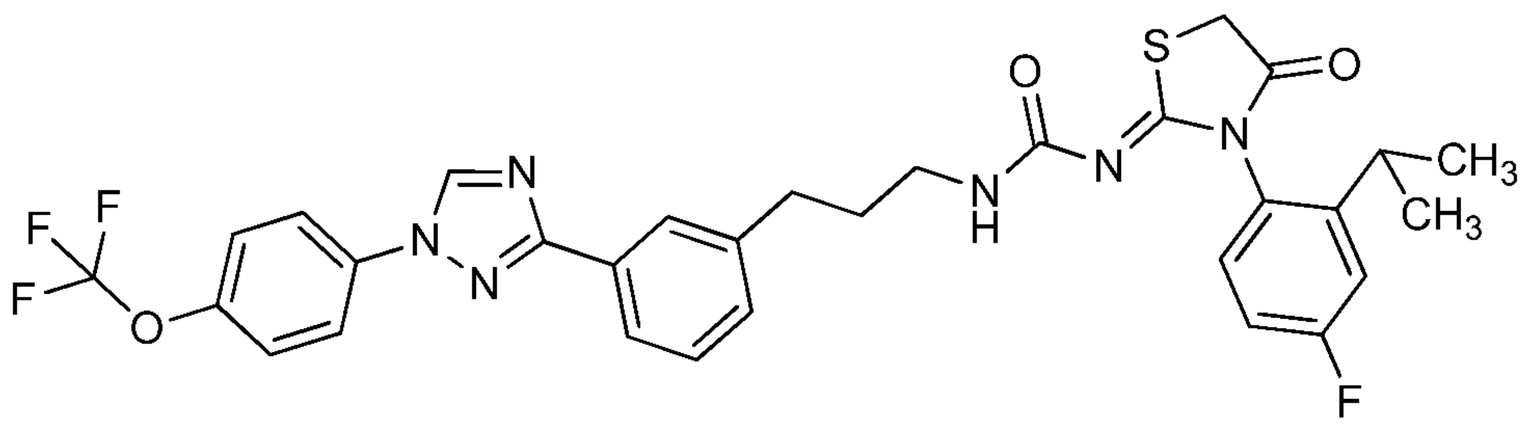
The title compound was prepared as described in Example 64 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC120**) and isolated as an off-white solid (0.091 g, 80%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P128)



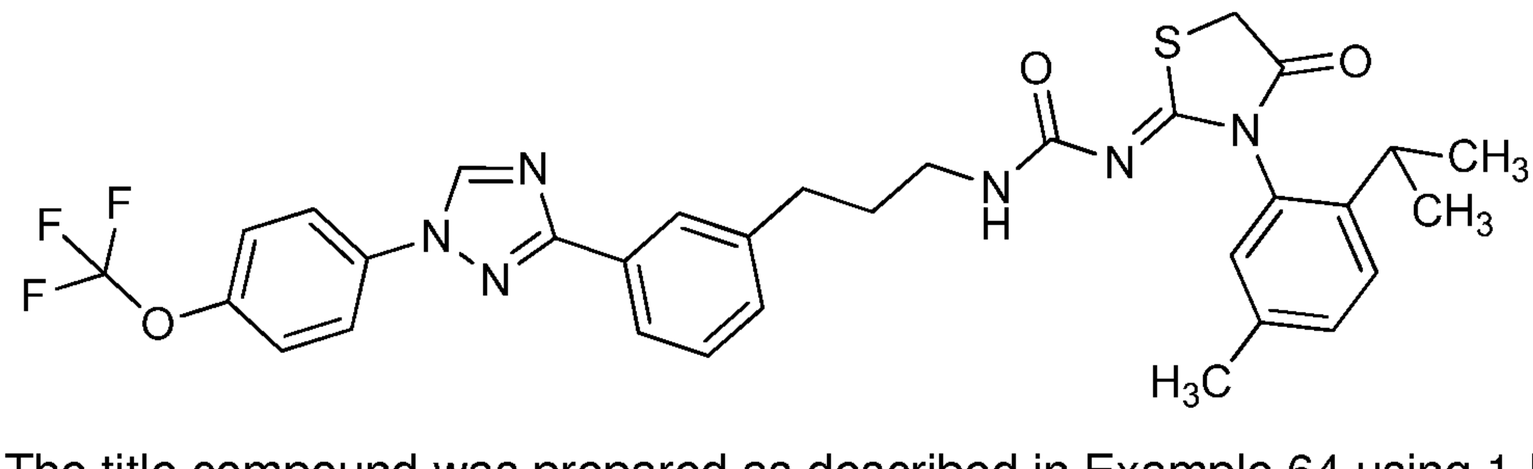
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC128**) and isolated as an off-white solid (0.091 g, 84%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P129)



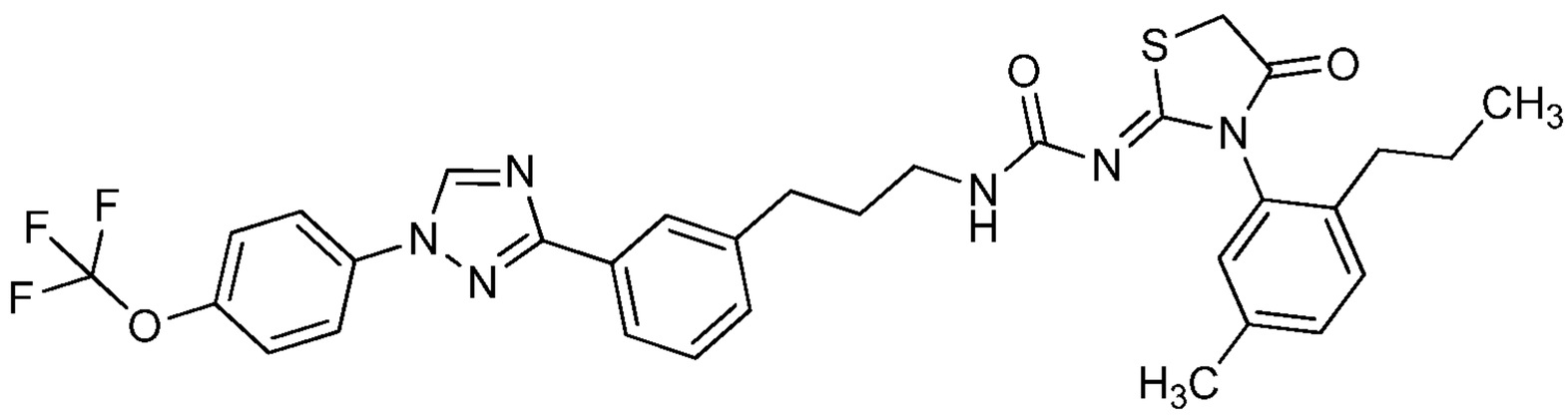
The title compound was prepared as described in Example 64 using 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC129**) and isolated as an off-white solid (0.095 g, 81%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P124)



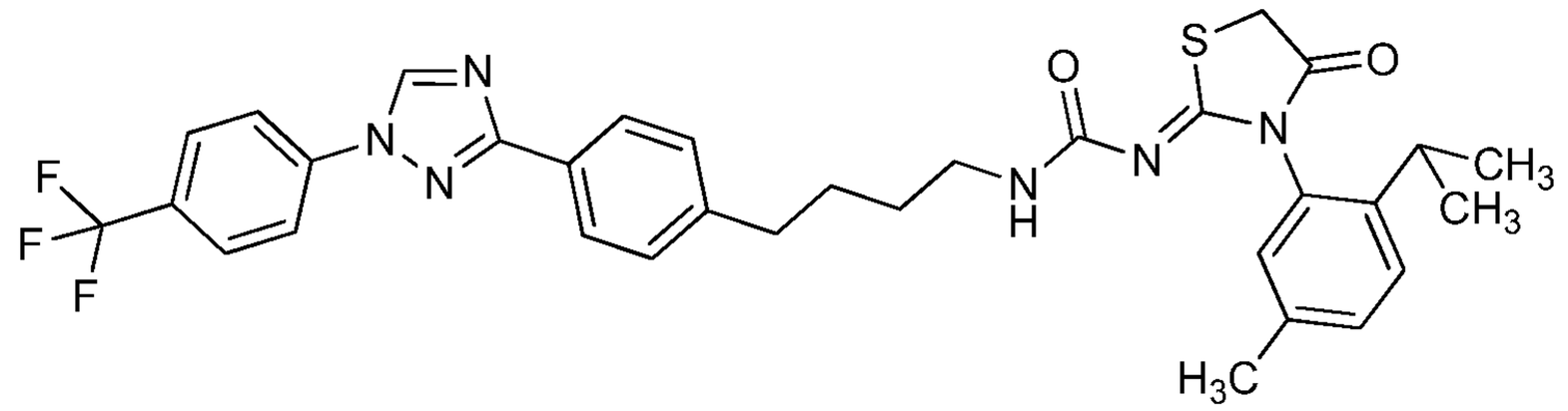
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC124**) and isolated as an off-white solid (0.077 g, 80%).

Preparation of (*Z*)-1-(3-(5-methyl-2-propylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (P125)



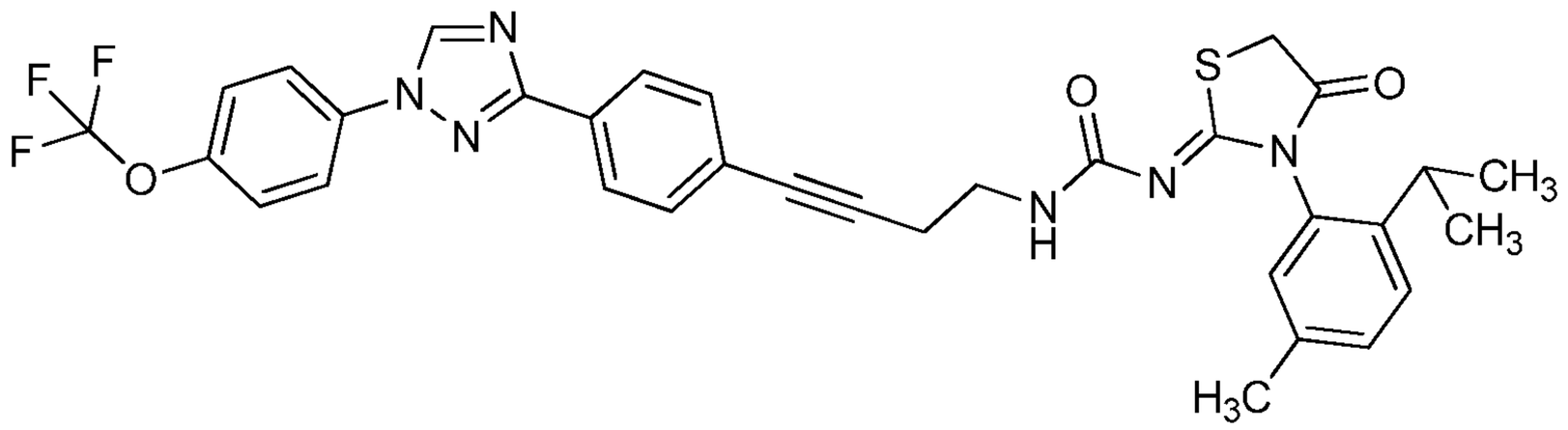
The title compound was prepared as described in Example 64 using 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[3-[3-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]propyl]urea (**PC125**) and isolated as an off-white solid (0.097 g, 86%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P159)



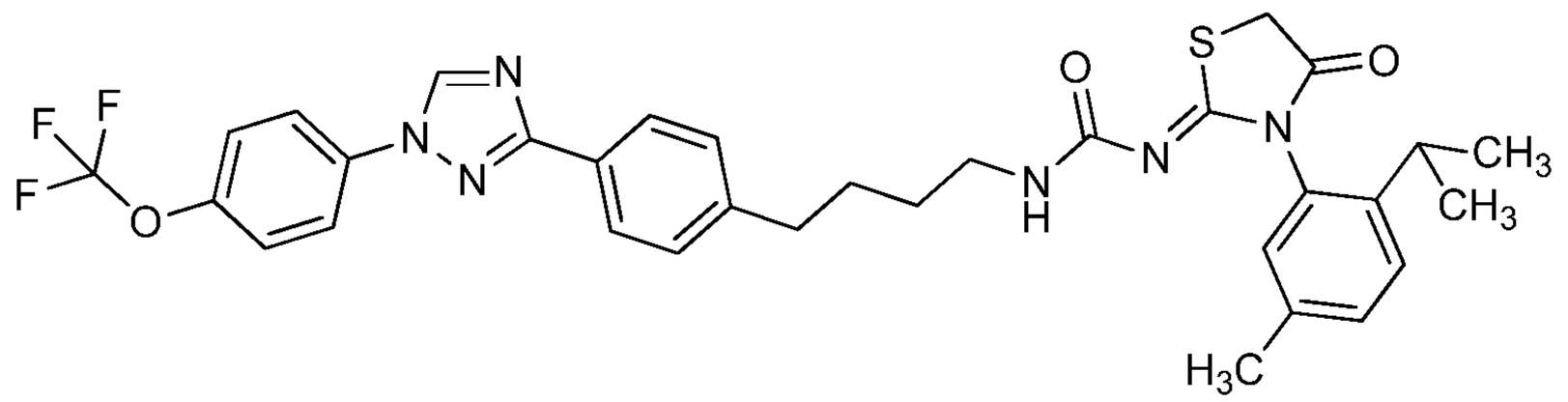
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethyl)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC159**) and isolated as a white solid (0.063 g, 70%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-yl)urea (P160)



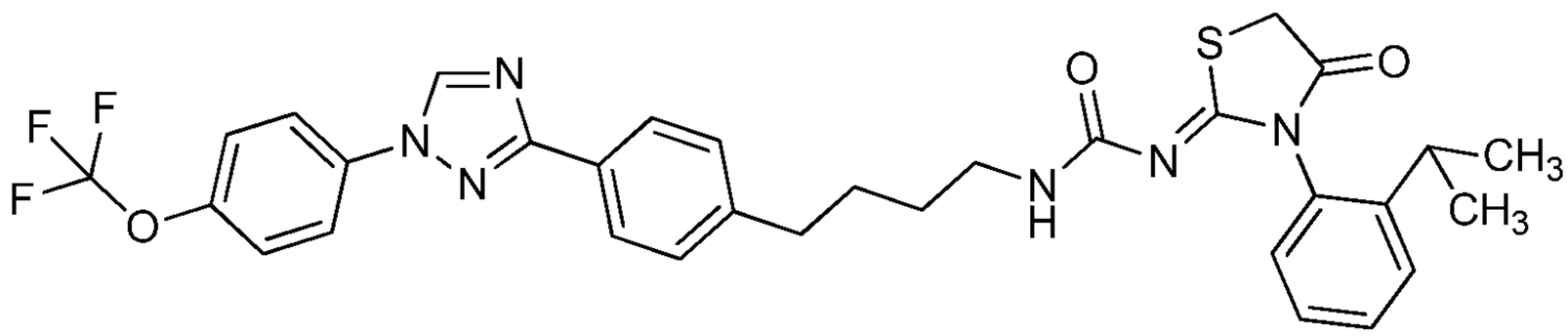
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]but-3-ynyl]urea (**PC160**) and isolated as a yellow solid (0.122 g, 74%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P150, P363)



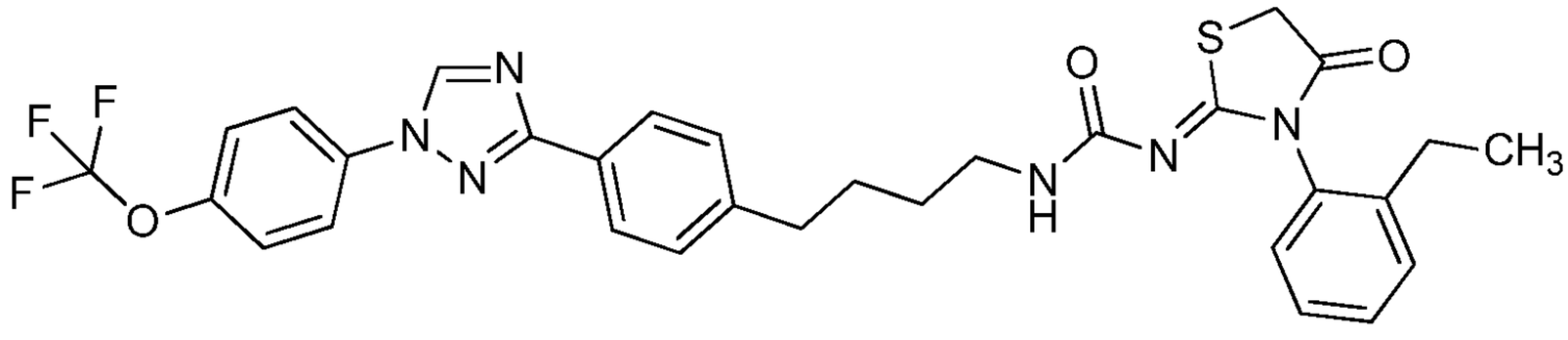
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC150**) and isolated as a white solid (0.068 g, 78%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P146, P208)



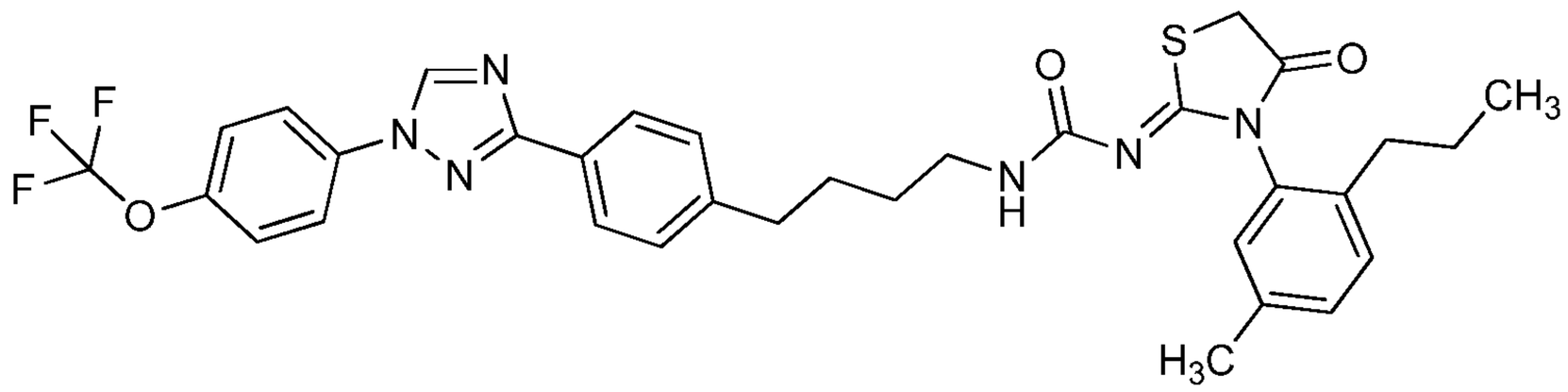
The title compound was prepared as described in Example 64 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC146**) isolated as a white solid (0.063 g, 80%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P145, P522)



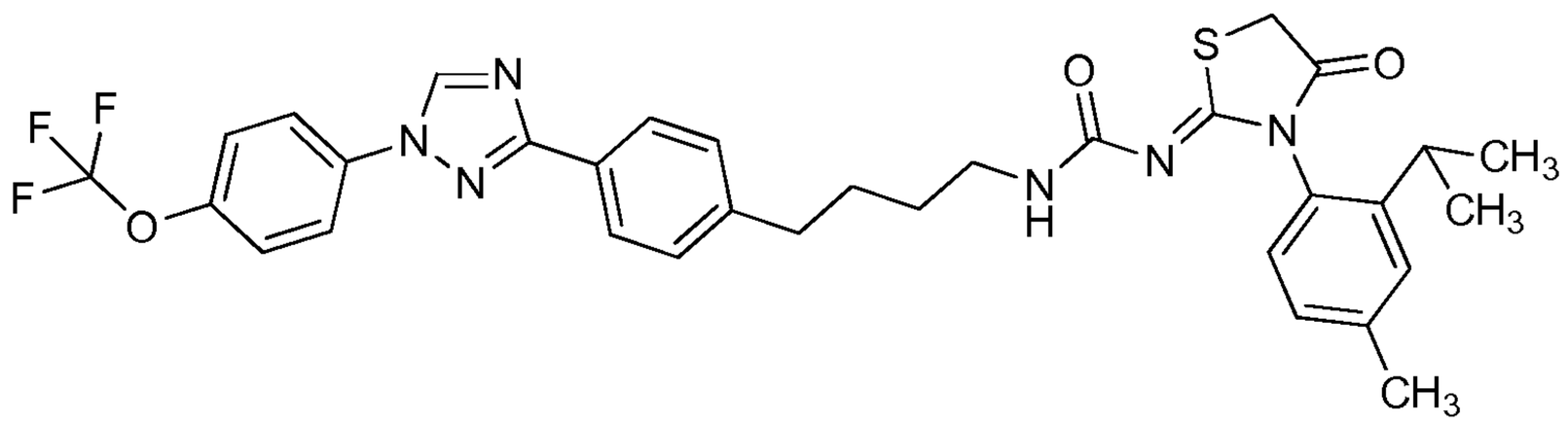
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC145**) and isolated as a white solid (0.084 g, 83%).

Preparation of (*Z*)-1-(3-(5-methyl-2-propylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P151, P842)



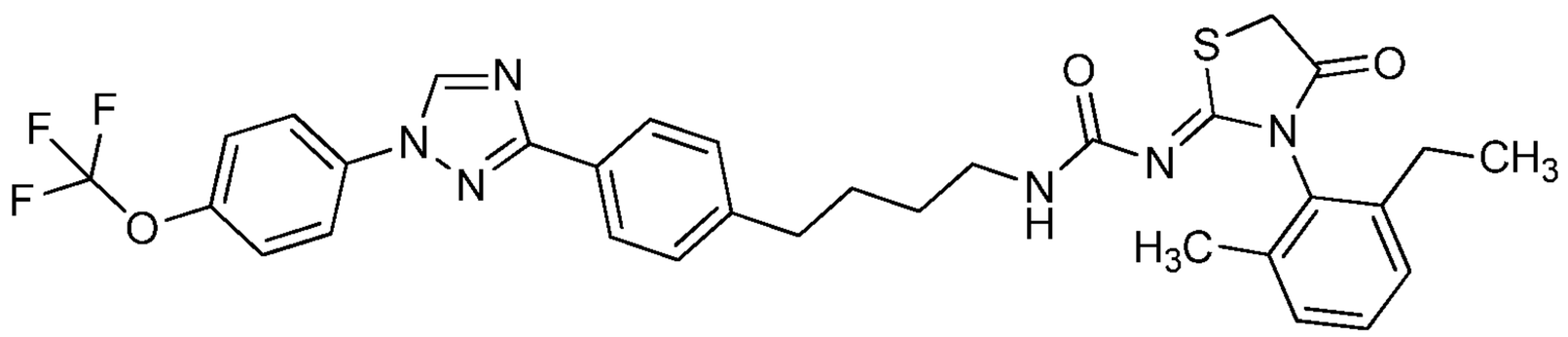
The title compound was prepared as described in Example 64 using 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC151**) and isolated as a white solid (0.081 g, 81%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P154)



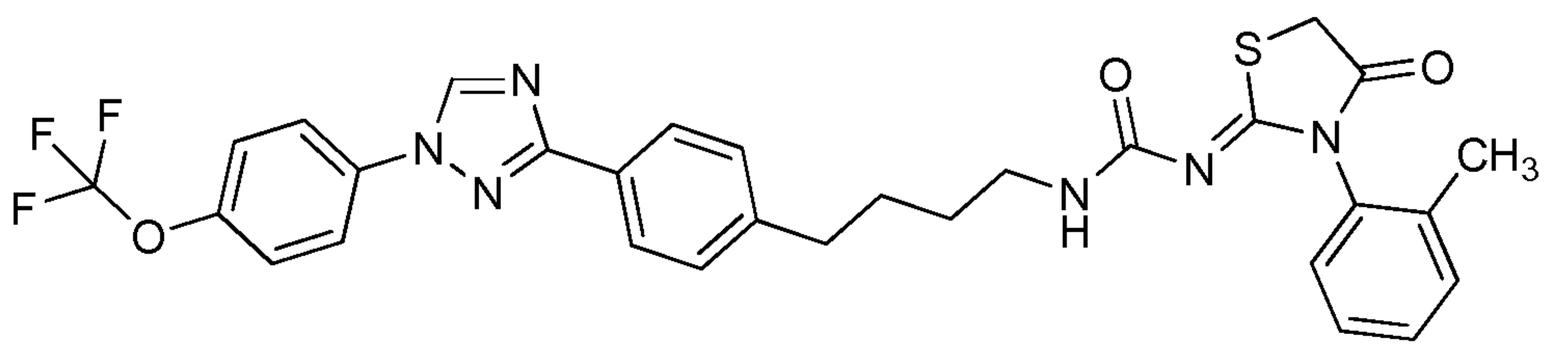
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC154**) and isolated as a white solid (0.070 g, 82%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P153)



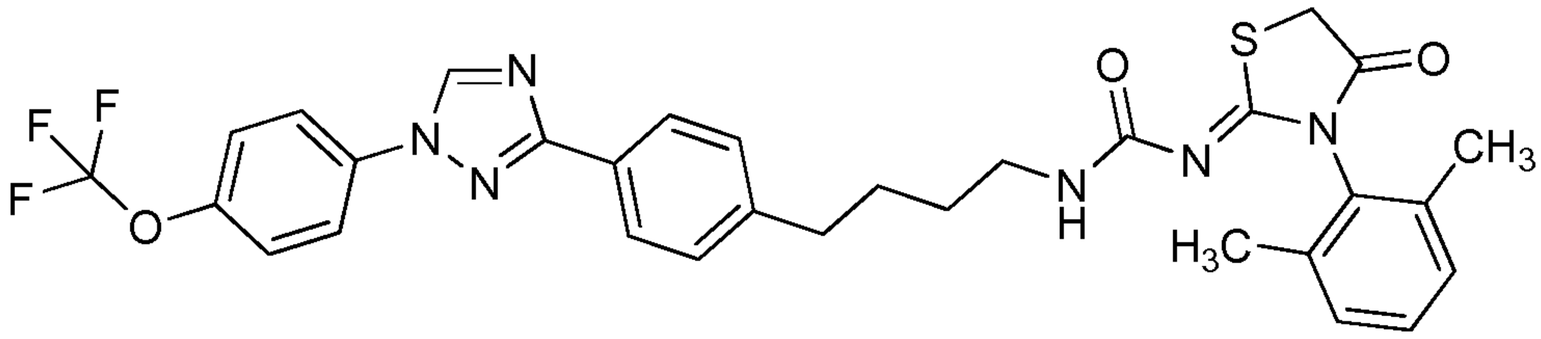
The title compound was prepared as described in Example 64 using 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC153**) and isolated as a white foam (0.059 g, 52%).

Preparation of (*Z*)-1-(4-oxo-3-(o-tolyl)thiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P144)



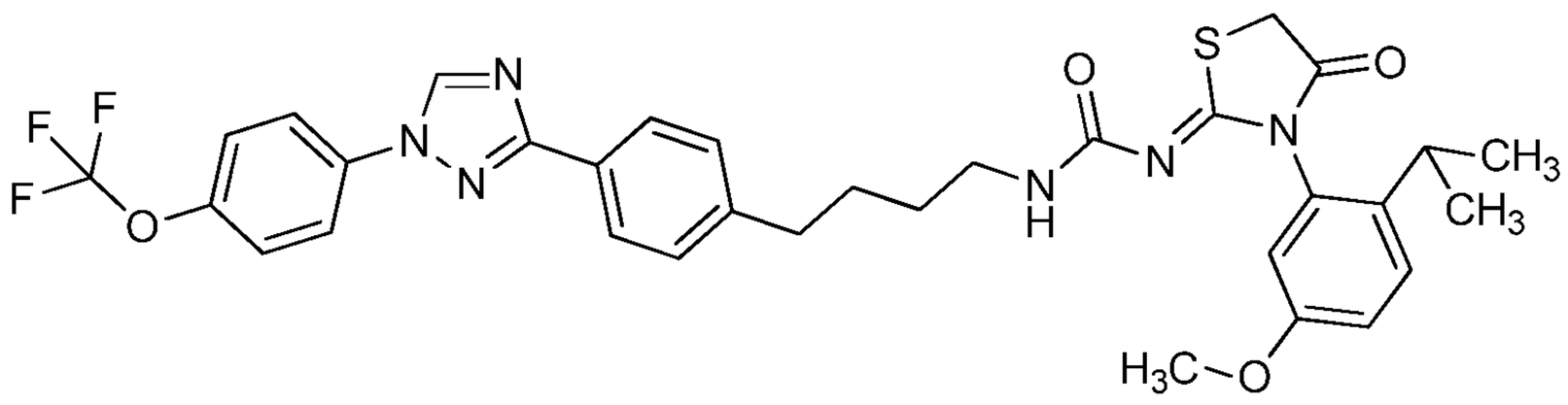
The title compound was prepared as described in Example 64 using 1-(*o*-tolylcarbamothioyl)-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC144**) and isolated as a white foam (0.070 g, 76%).

Preparation of (*Z*)-1-(3-(2,6-dimethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P152, P1481)



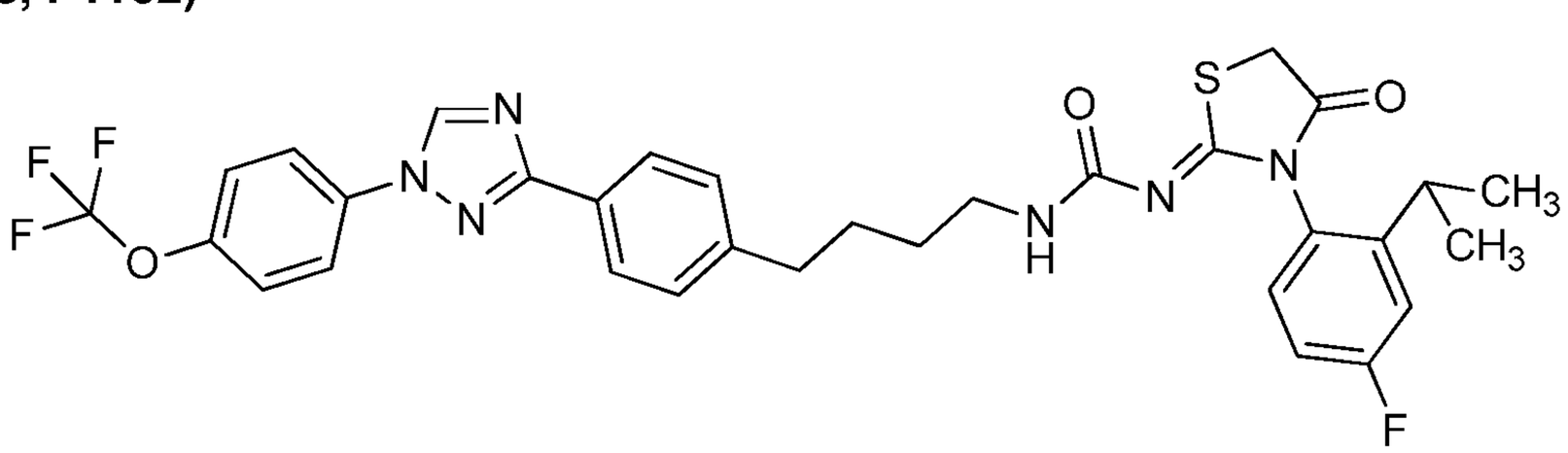
The title compound was prepared as described in Example 64 using 1-[(2,6-dimethylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC152**) and isolated as a white solid (0.078 g, 72%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P156, P682)



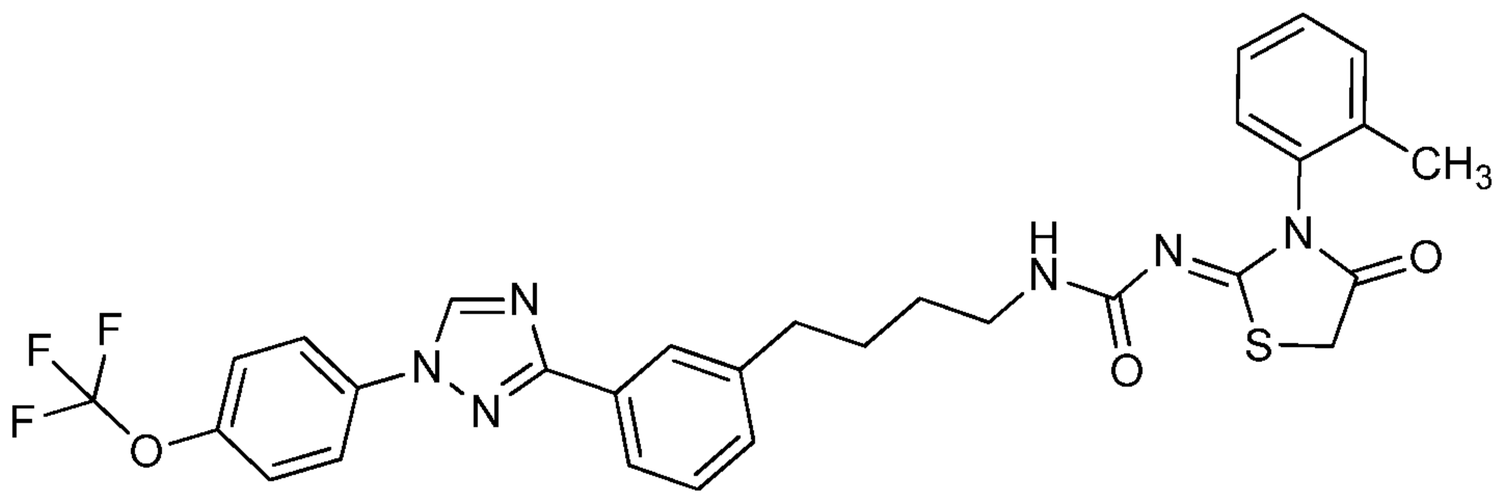
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methoxy-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC156**) and isolated as a white solid (0.089 g, 82%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P155, P1162)



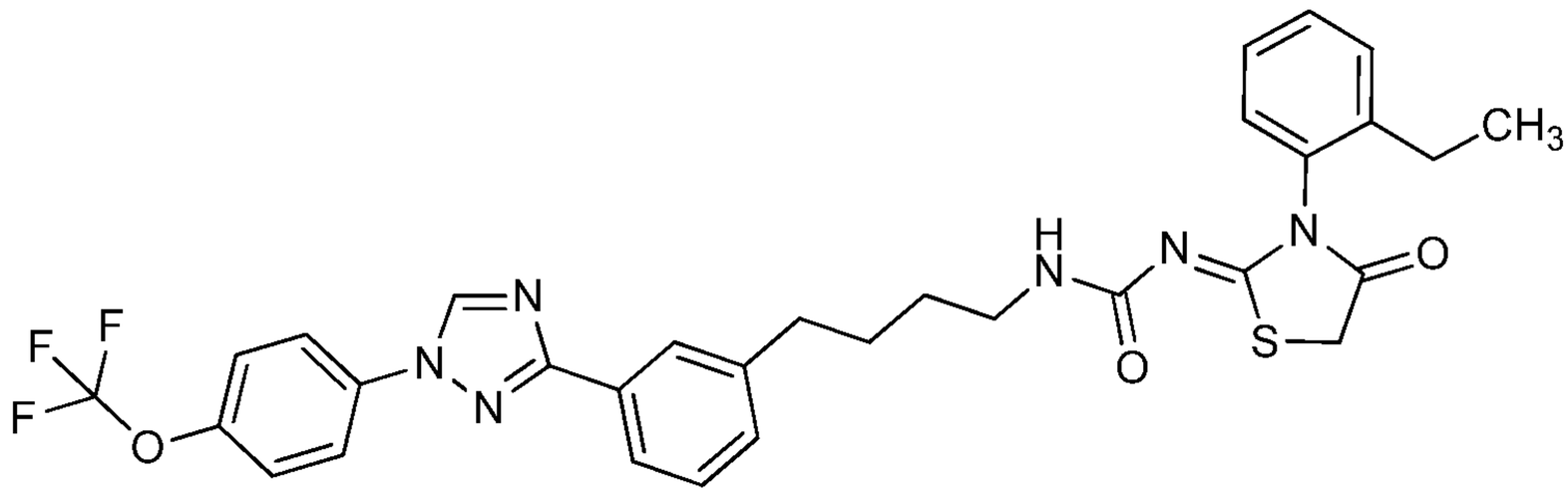
The title compound was prepared as described in Example 64 using 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl]-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC155**) and isolated as a white foam (0.075 g, 88%).

Preparation of (*Z*)-1-(4-oxo-3-(o-tolyl)thiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P170)



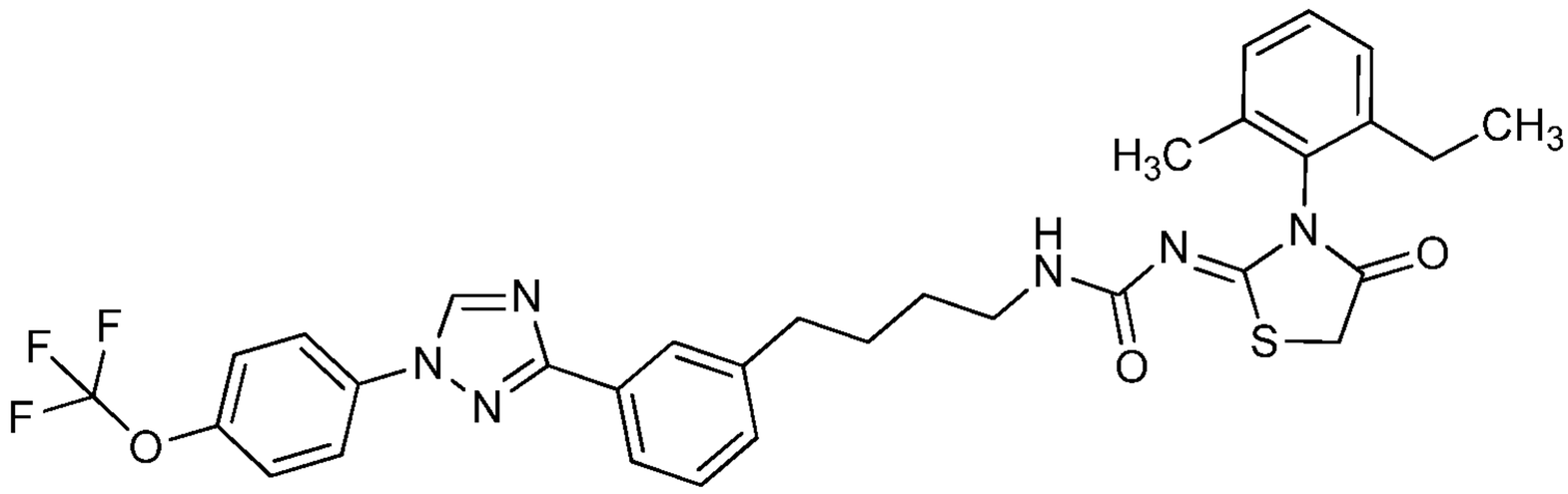
The title compound was prepared as described in Example 64 using 1-(*o*-tolylcarbamothioyl)-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl])-1*H* -1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC170**) and isolated as a white solid (0.061 g, 72%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P171)



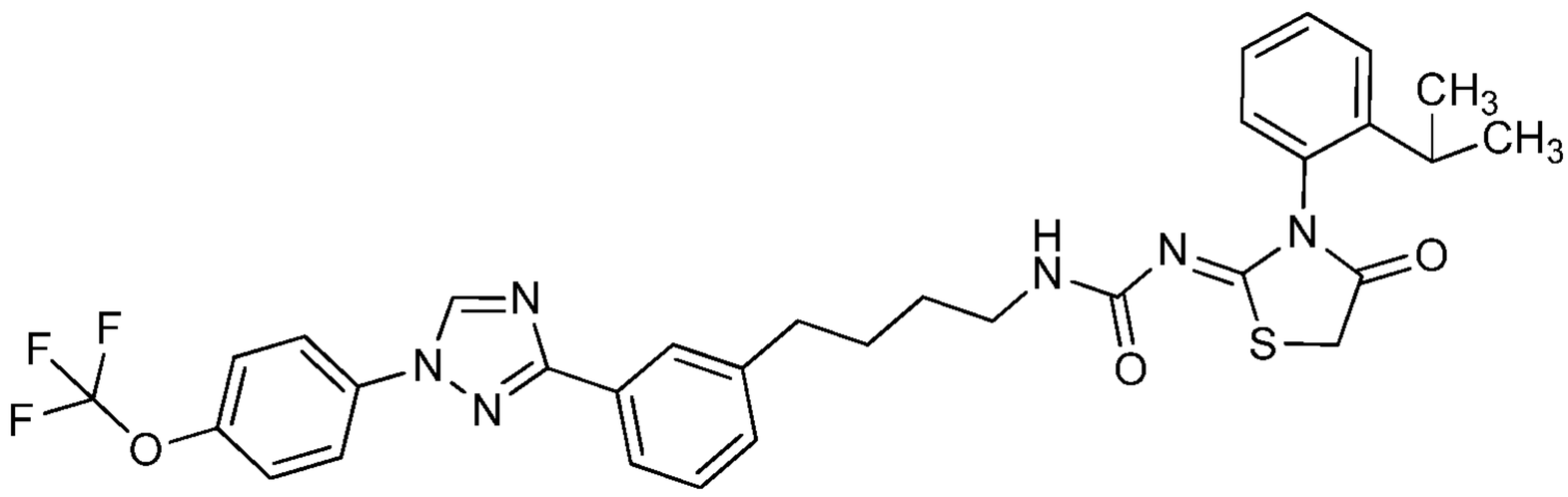
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC171**) and isolated as a white solid (0.078 g, 77%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P179)



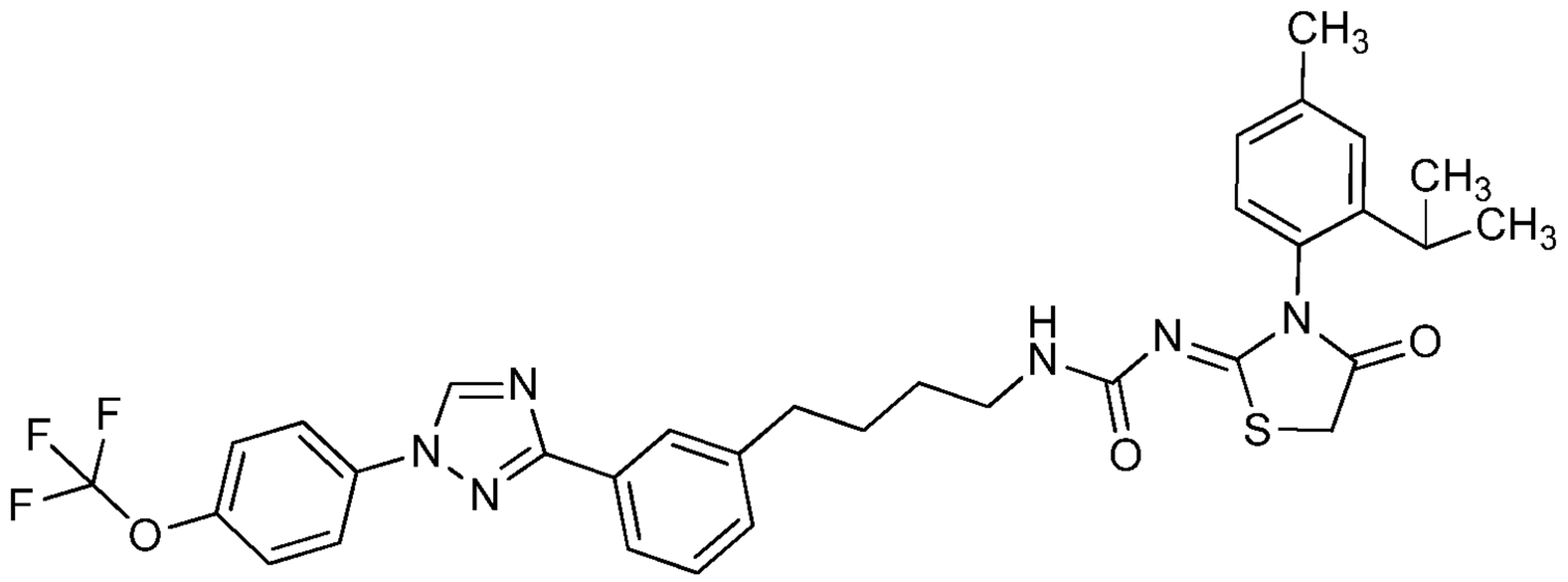
The title compound was prepared as described in Example 64 using 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC179**) and isolated as a white solid (0.048 g, 37%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P172)



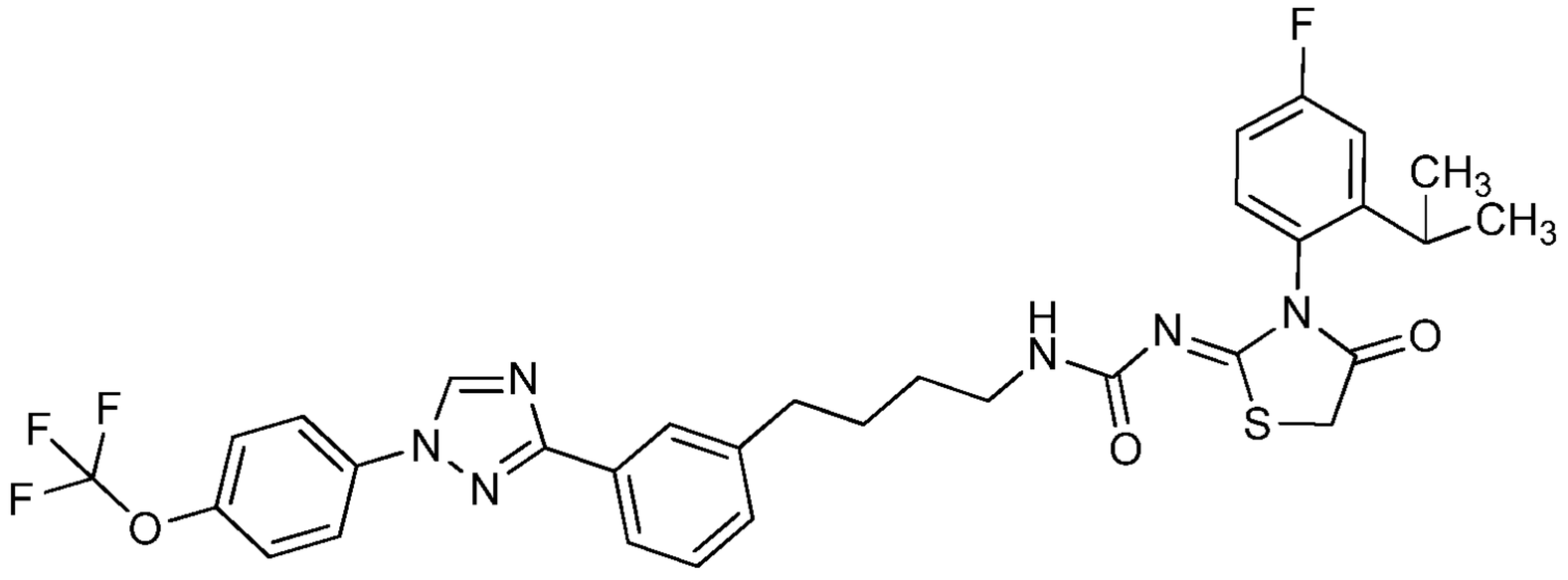
The title compound was prepared as described in Example 64 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC172**) and isolated as a white solid (0.048 g, 80%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P180)



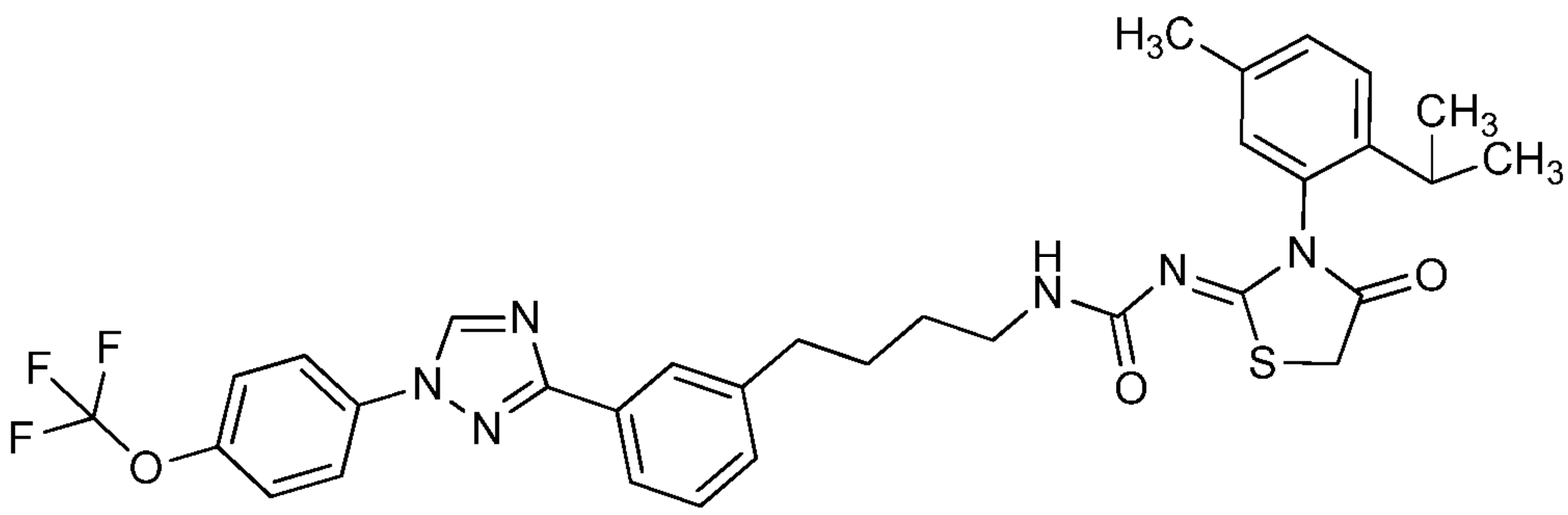
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC180**) and isolated as a white solid (0.086 g, 66%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P181)



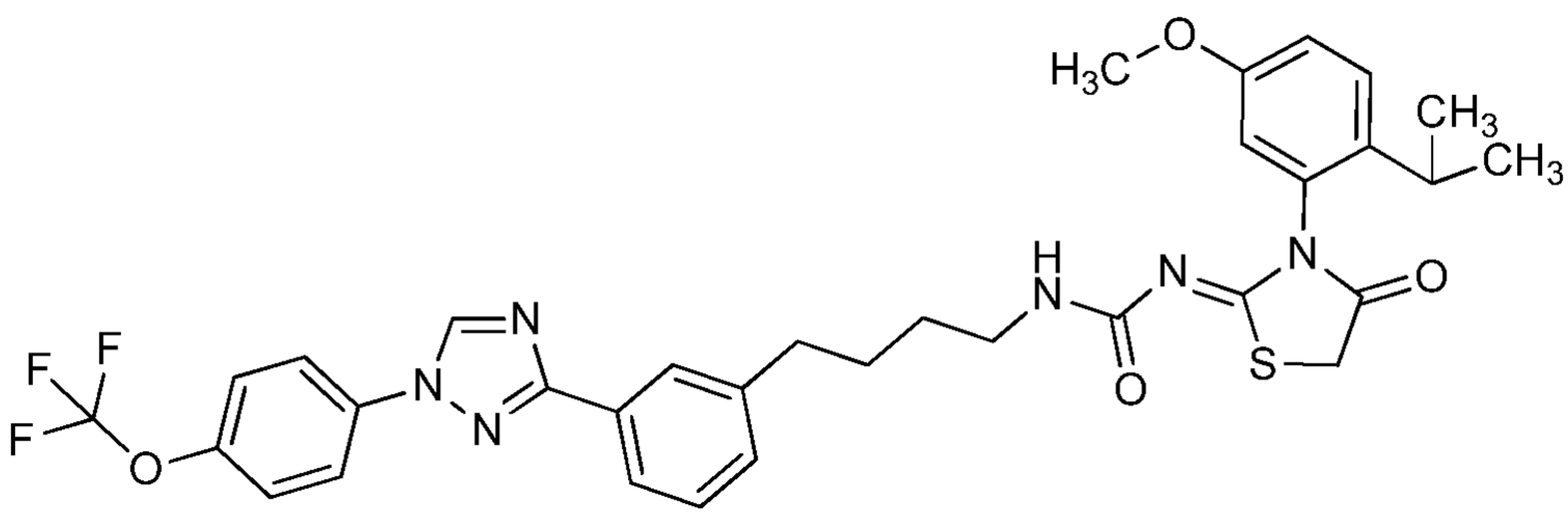
The title compound was prepared as described in Example 64 using 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC181**) and isolated as a white solid (0.058 g, 57%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P176)



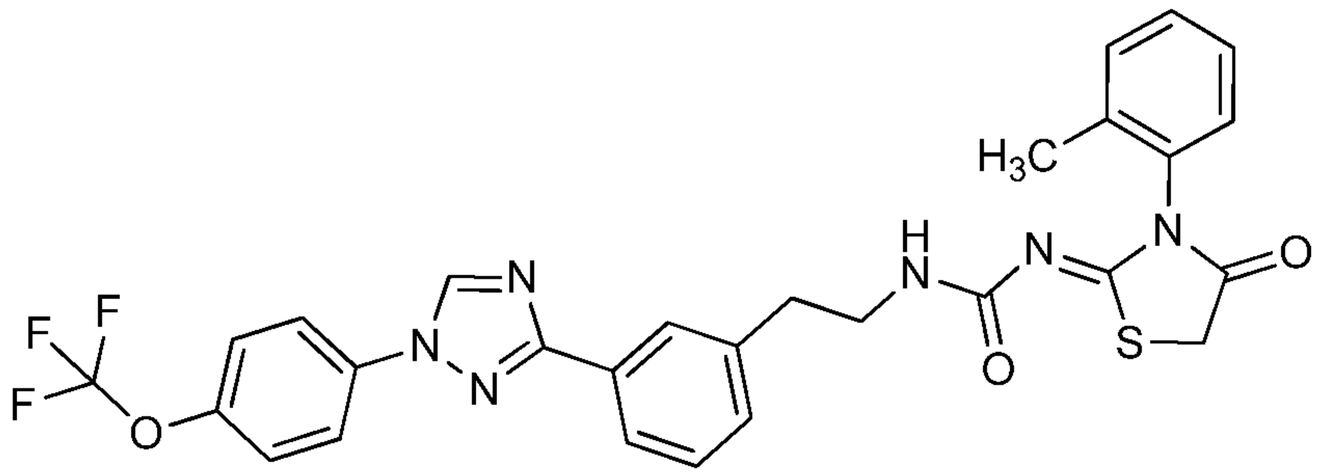
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC176**) and isolated as a white solid (0.076 g, 74%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (P182)



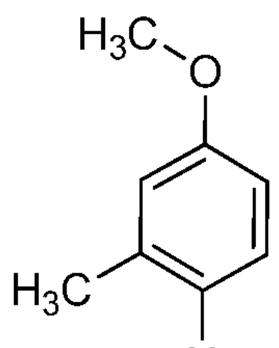
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methoxy-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**PC182**) and isolated as a white solid (0.064 g, 58%).

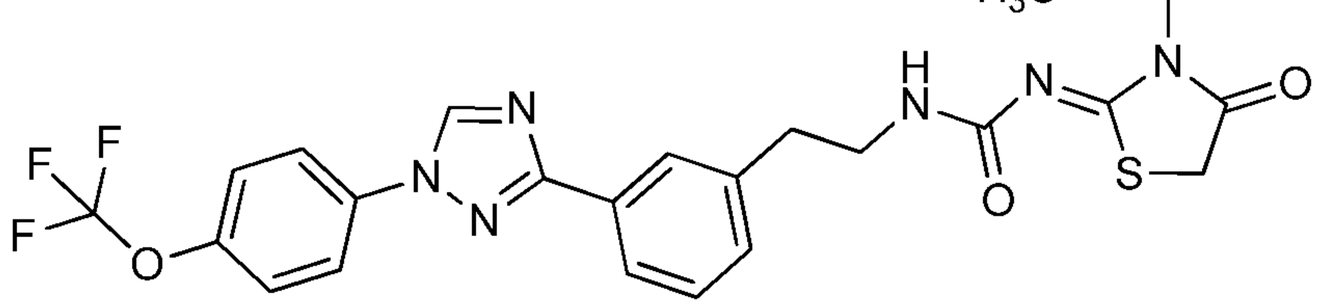
Preparation of (*Z*)-1-(4-oxo-3-(o-tolyl)thiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P74)



The title compound was prepared as described in Example 64 using 1-(*o*-tolylcarbamothioyl)-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC74**) and isolated as a white solid (0.076 g, 77%).

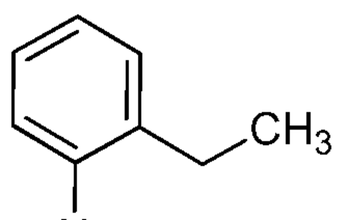
Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P87)

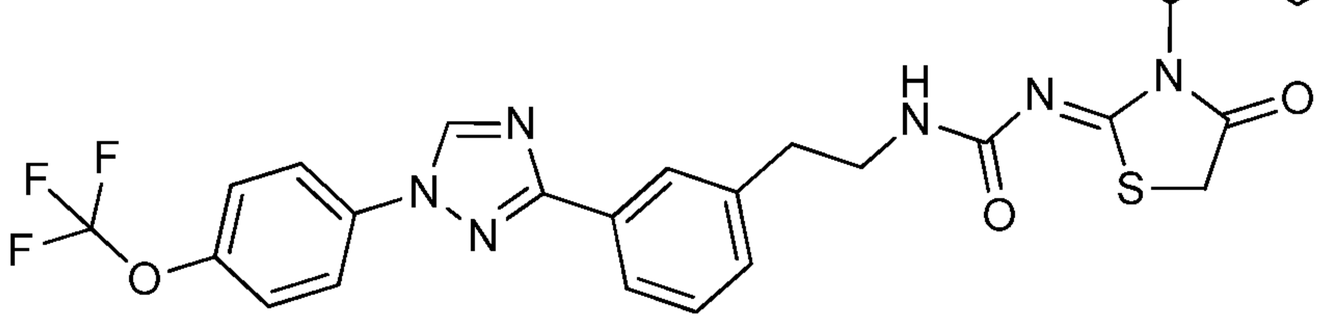




The title compound was prepared as described in Example 64 using 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC87**) and isolated as a white solid (0.079 g, 84%).

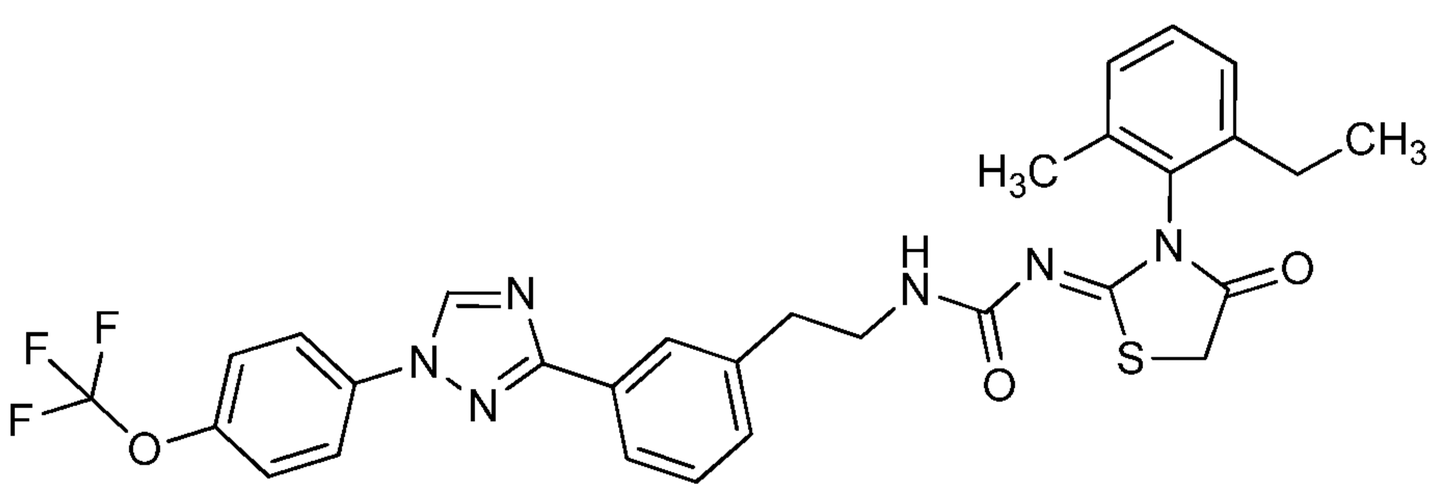
Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P75)





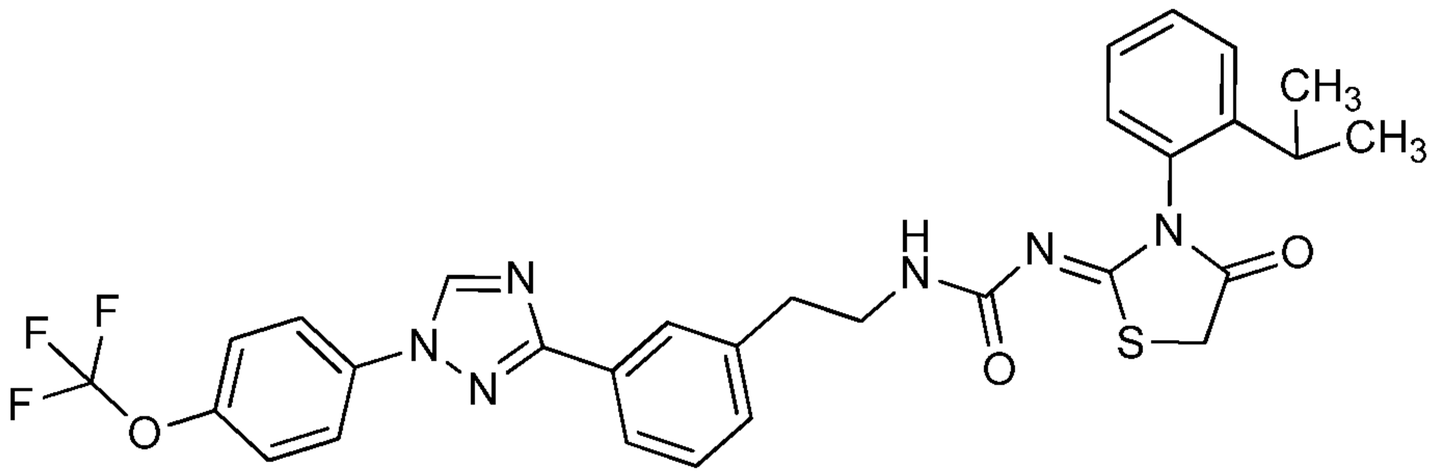
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC75**) and isolated as a white solid (0.071 g, 73%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P83)



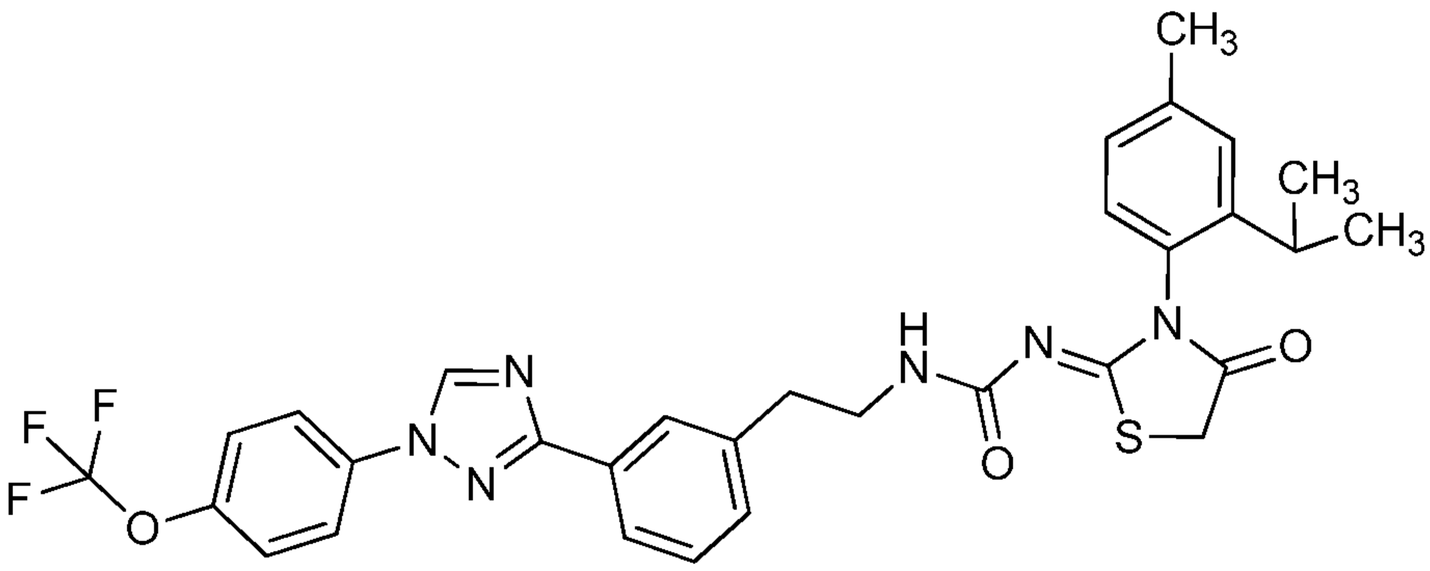
The title compound was prepared as described in Example 64 using 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC83**) and isolated as a white solid (0.042 g, 34%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P76)



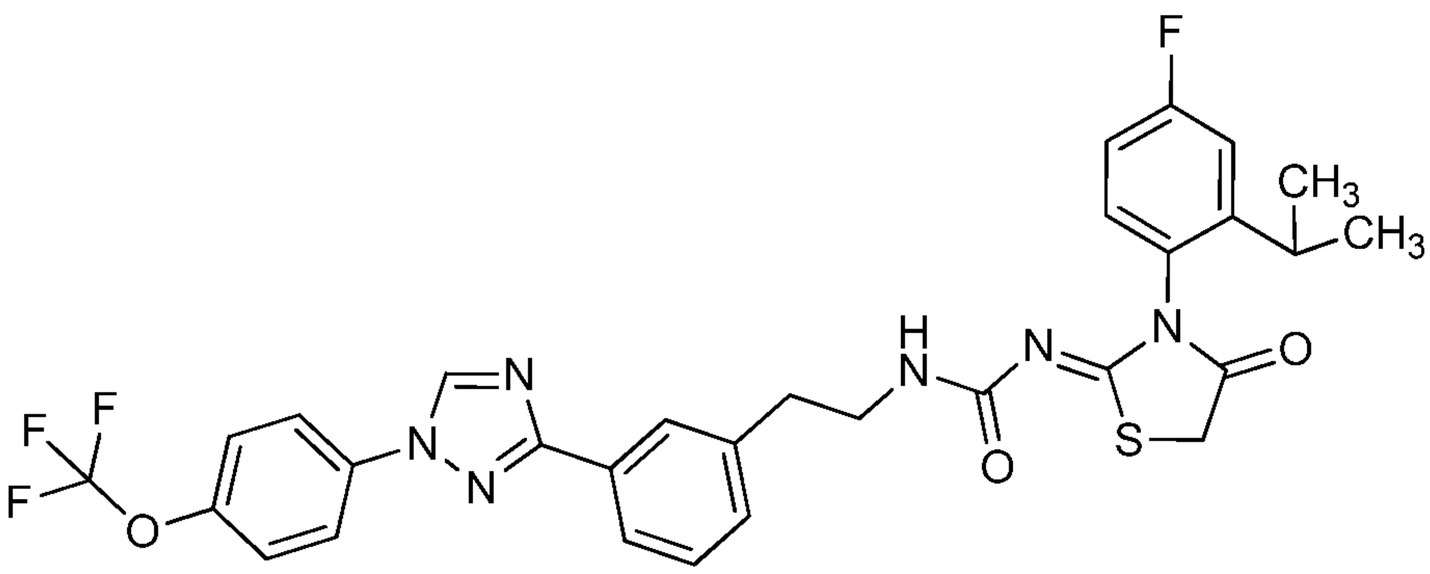
The title compound was prepared as described in Example 64 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC76**) and isolated as a white solid (0.026 g, 72%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P84)



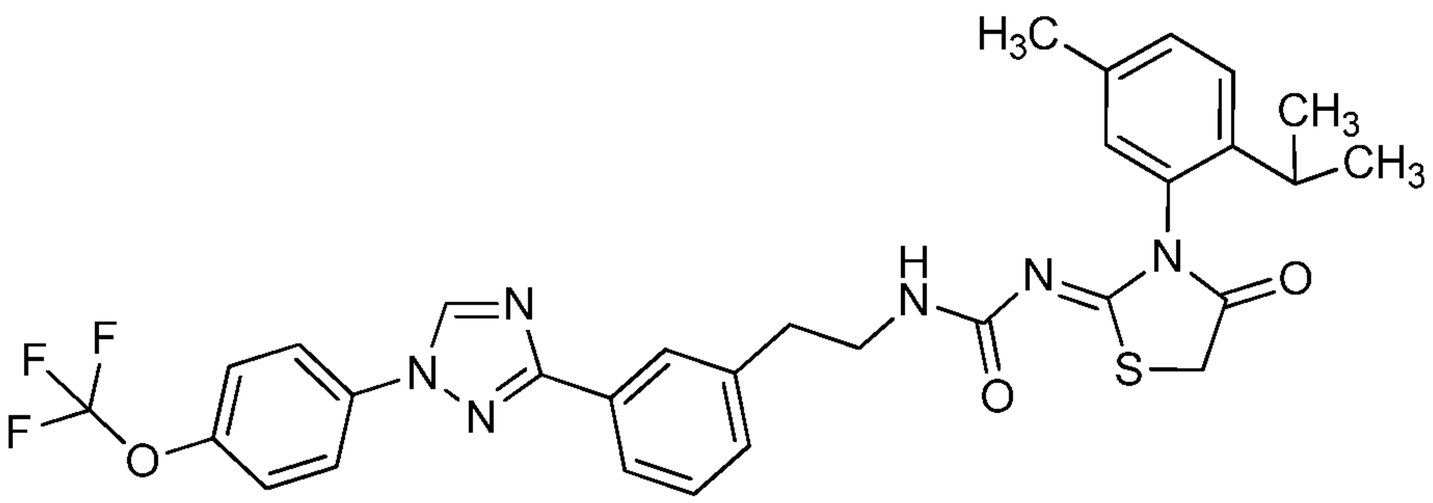
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC84**) and isolated as a white solid (0.056 g, 77%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P85)



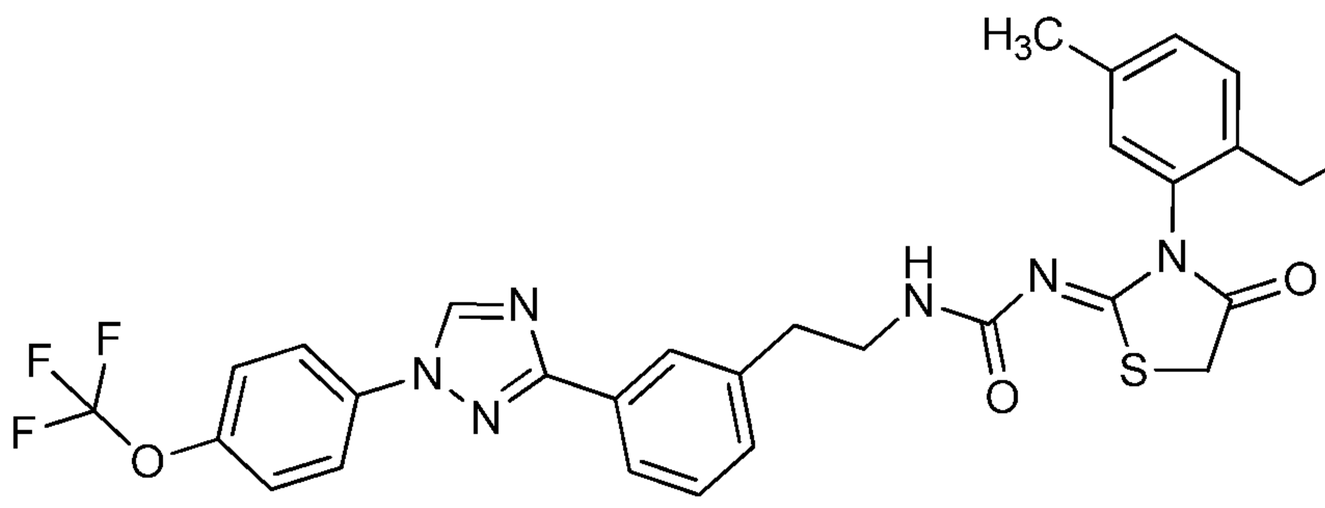
The title compound was prepared as described in Example 64 using 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC85**) and isolated as a white solid (0.063 g, 77%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P81)



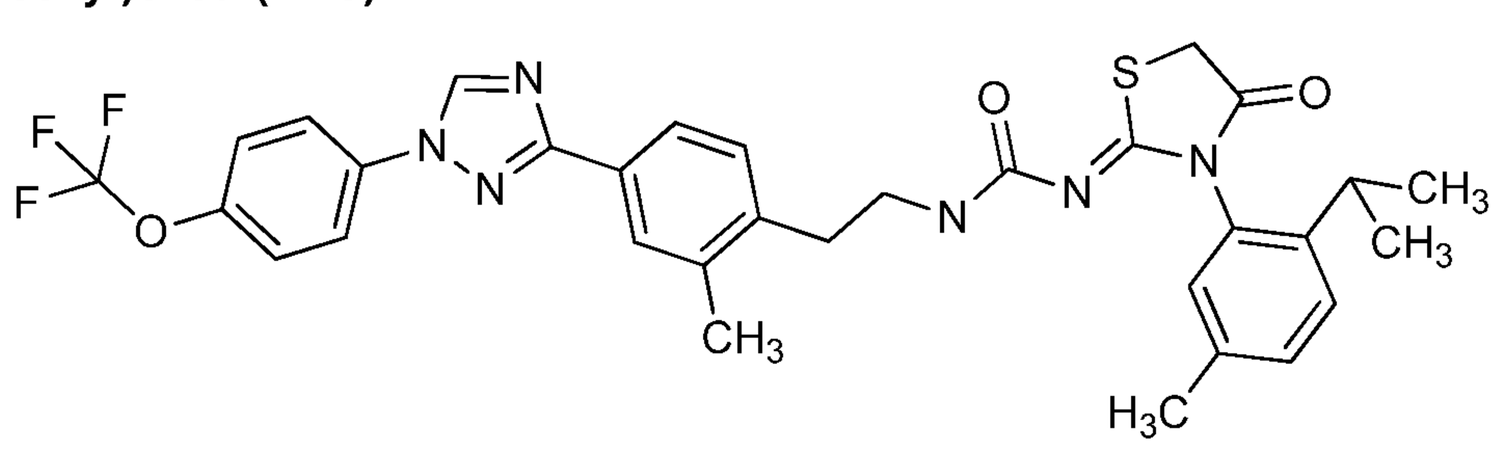
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC81**) and isolated as a yellow solid (0.014 g, 68%).

Preparation of (*Z*)-1-(3-(5-methyl-2-propylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P80)



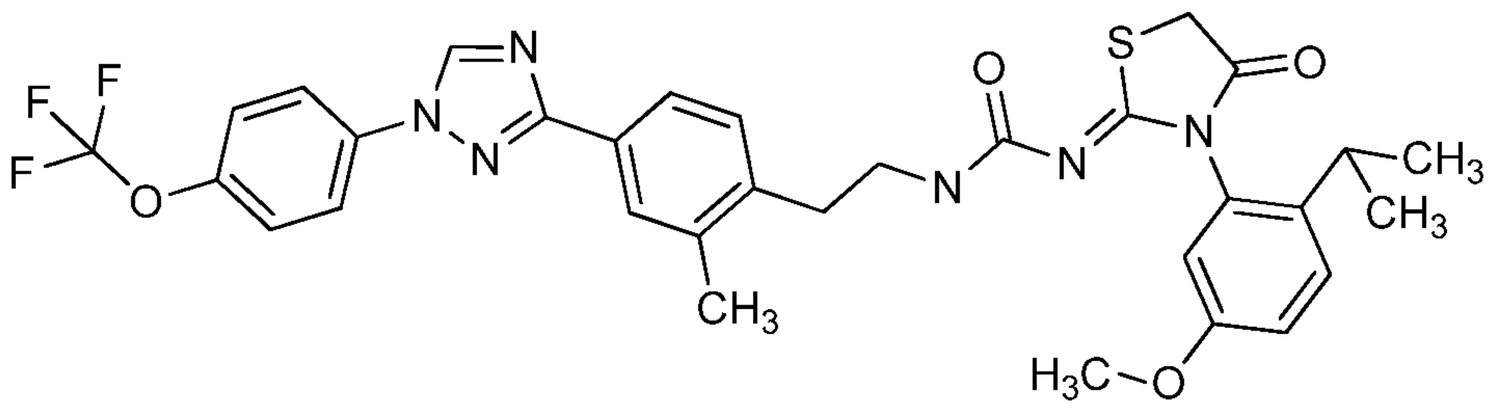
The title compound was prepared as described in Example 64 using 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**PC80**) and isolated as a white solid (0.076 g, 74%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB3)



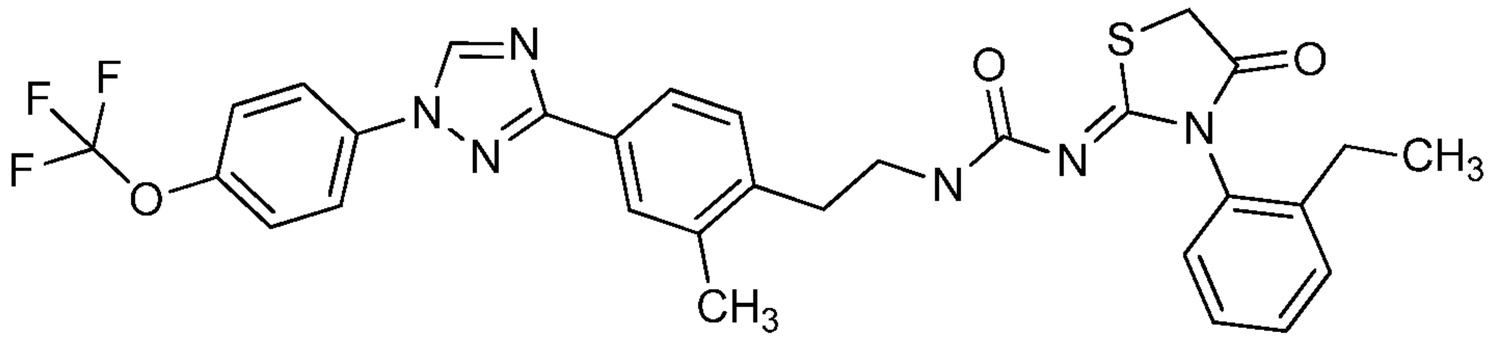
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[2-[2-methyl-4-[1-[4-(trifluoromethoxy)phenyl] **-1*H*** -1,2,4-triazol-3-yl]phenyl]ethyl]urea (**FB1**) at a temperature of 60 ºC and followed by reverse phase chromatography; isolated as a yellow wax (0.016 g, 10%).

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methoxyphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB4)



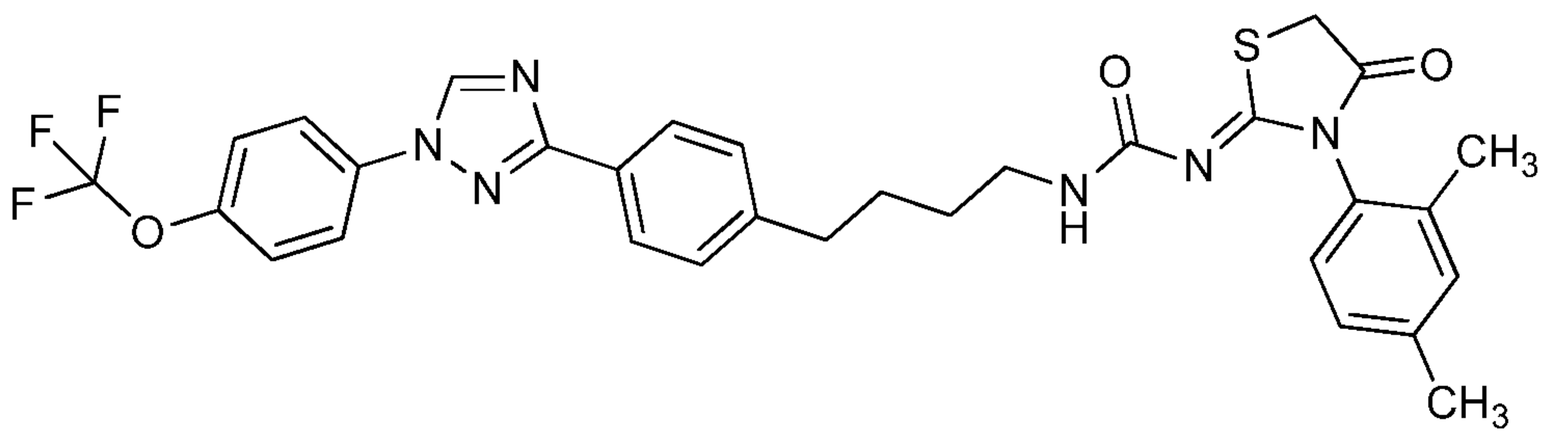
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methoxy-phenyl)carbamothioyl]-3-[2-[2-methyl-4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**FB2**) at a temperature of 60 ºC and followed by reverse phase chromatography isolated as a light yellow solid (0.034 g, 19%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB6)



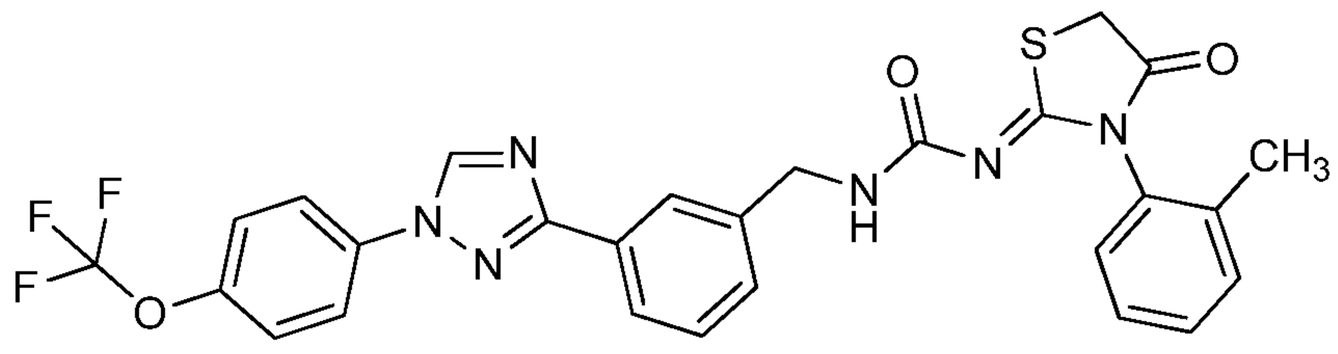
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[2-[2-methyl-4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (**FB5**) at a temperature of 60 ºC and followed by reverse phase chromatography; isolated as a pink solid (0.010 g, 7%).

Preparation of (*Z*)-1-(3-(2,4-dimethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (FB17)



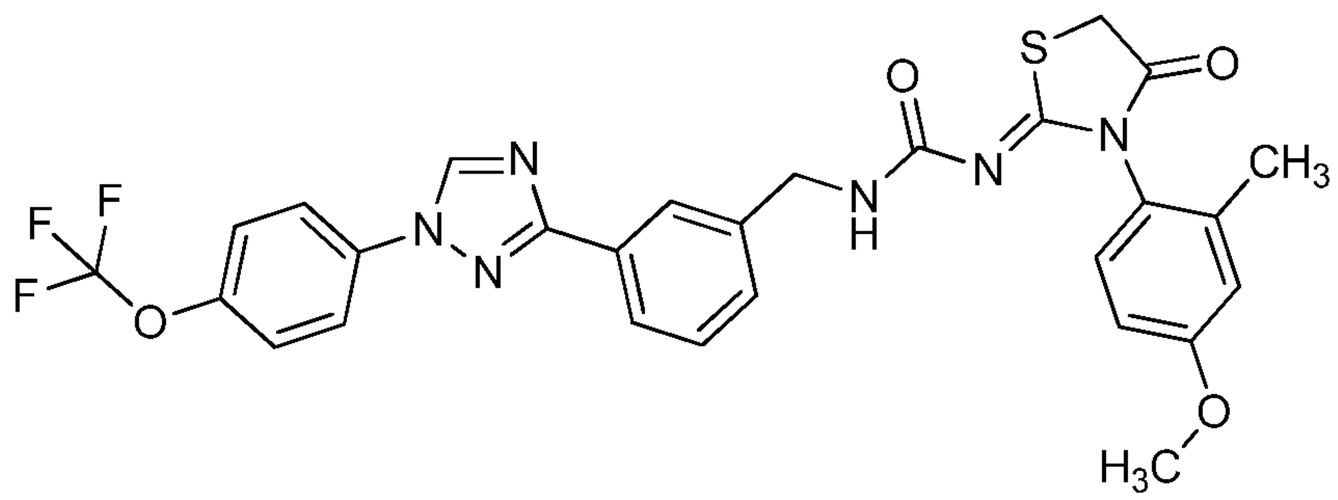
The title compound was prepared as described in Example 64 using 1-[(2,4-dimethylphenyl)carbamothioyl]-3-[4-[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**FB16**) and isolated as a white foam (0.078 g, 83%).

Preparation of (*Z*)-1-(4-oxo-3-(*o*-tolyl)thiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB27)



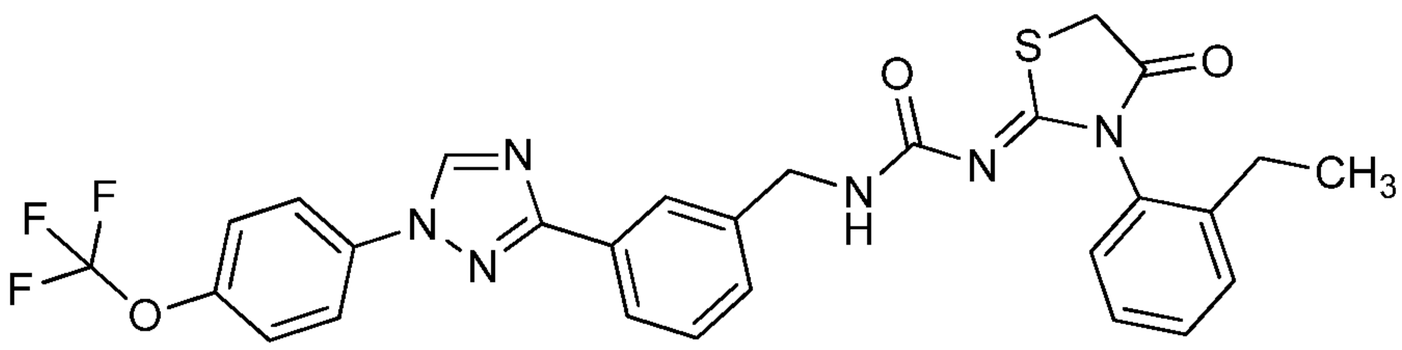
The title compound was prepared as described in Example 64 using 1-(*o*-tolylcarbamothioyl)-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H* -1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB18**) and isolated as an off-white solid (0.090 g, 68%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB28)



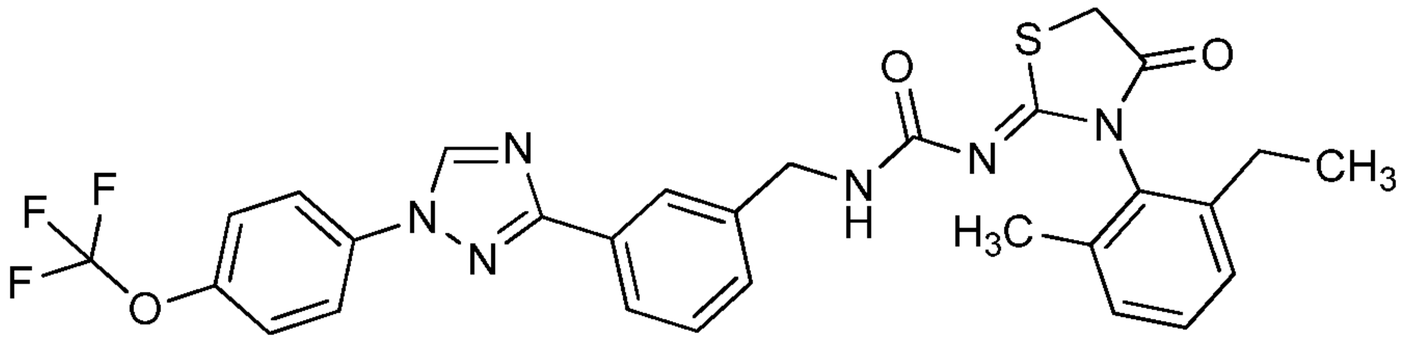
The title compound was prepared as described in Example 64 using 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB19**) and isolated as a light orange solid (0.042 g, 88%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB29)



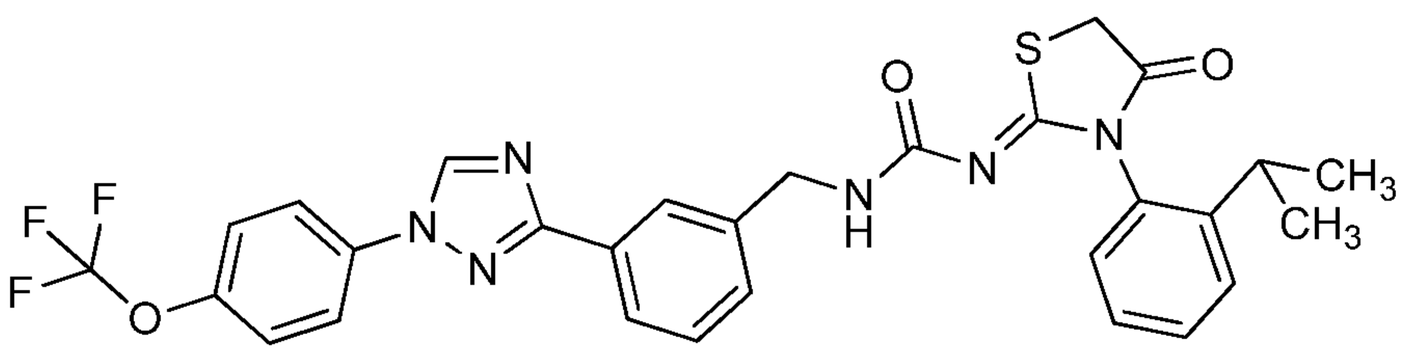
The title compound was prepared as described in Example 64 using 1-[(2-ethylphenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB20**) and isolated as a white solid (0.078 g, 57%).

Preparation of (*Z*)-1-(3-(2-ethyl-6-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB30)



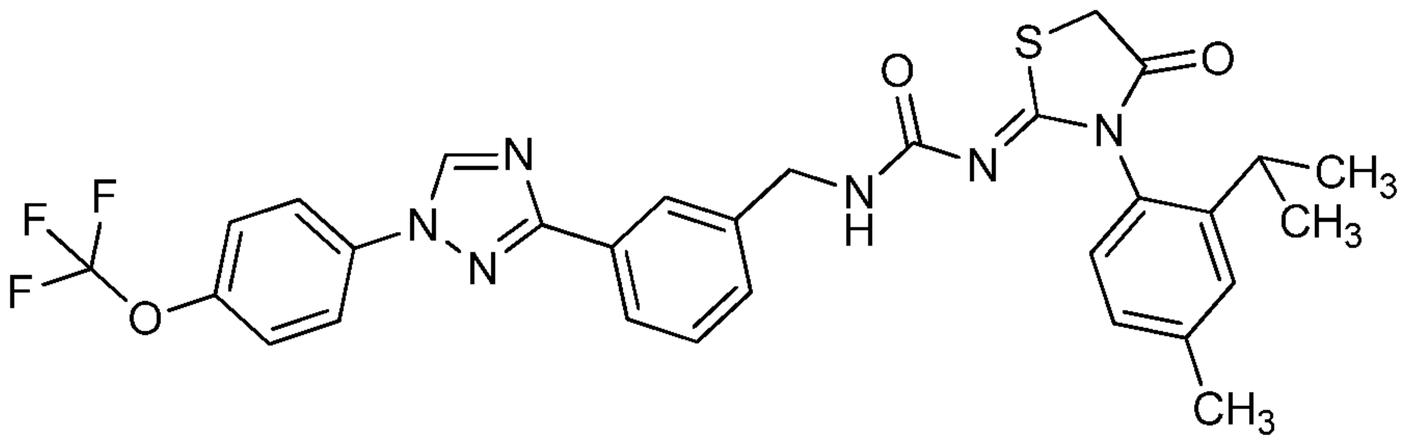
The title compound was prepared as described in Example 64 using 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FA21**) and isolated as a white solid (0.035 g, 17%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB31)



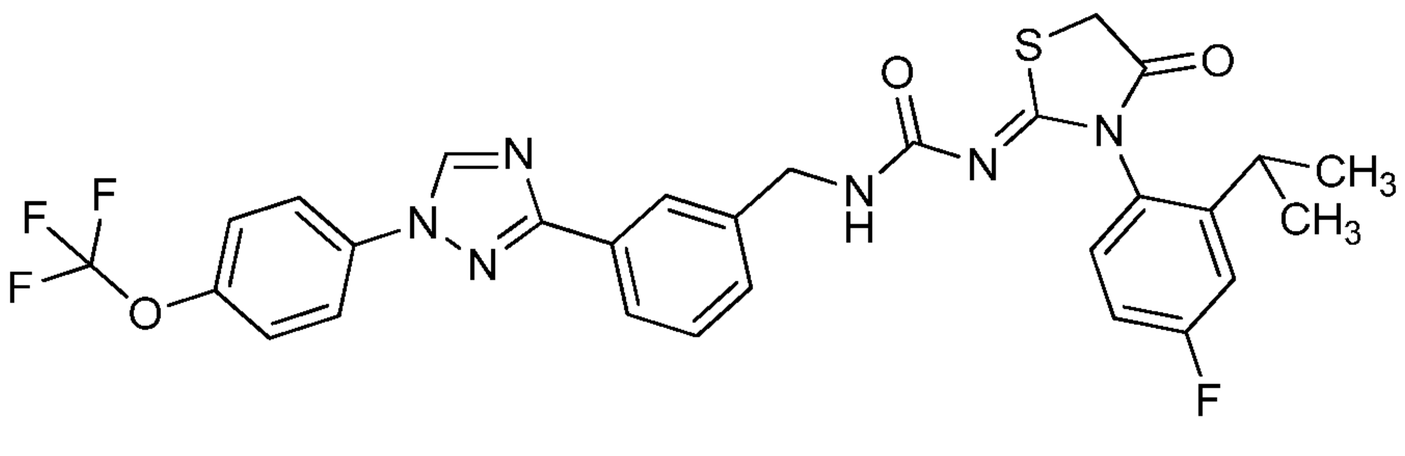
The title compound was prepared as described in Example 64 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FA22**) and isolated as a light yellow solid (0.115 g, 57%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB32)



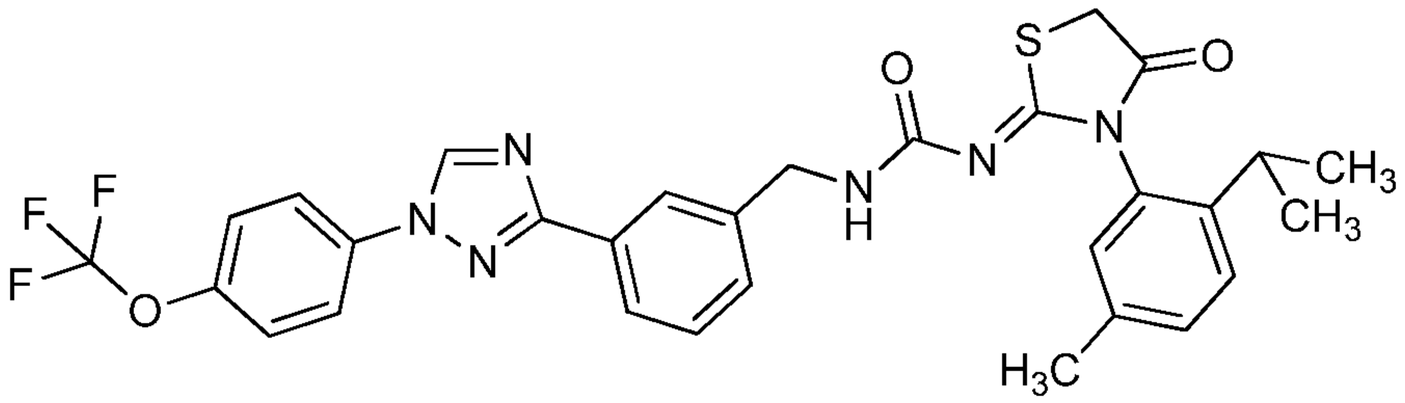
The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB23**) and isolated as a light orange solid (0.144 g, 70%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB33)



The title compound was prepared as described in Example 64 using 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB24**) and isolated as an off-white solid (0.097 g, 44%).

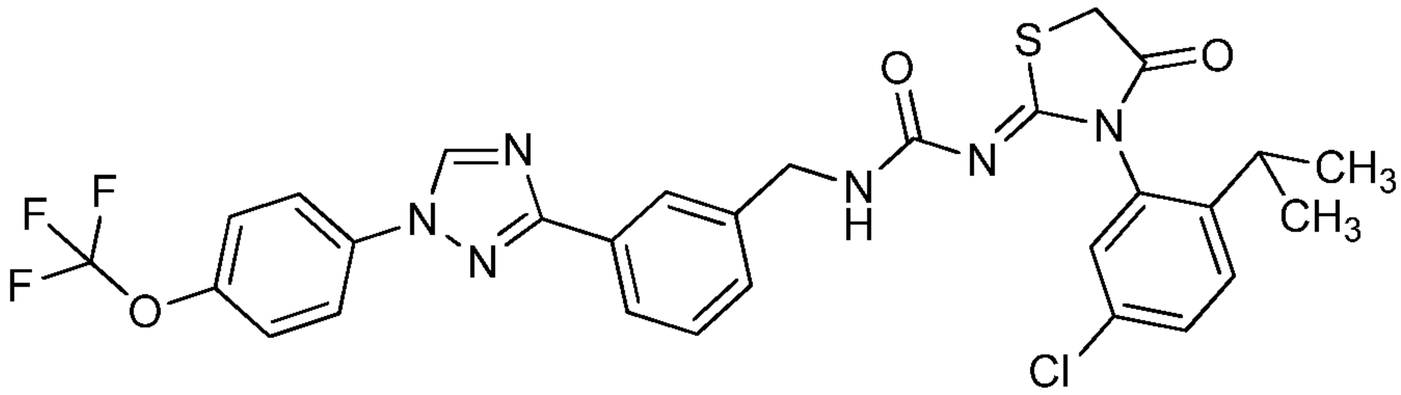
Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB34)



The title compound was prepared as described in Example 64 using 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-

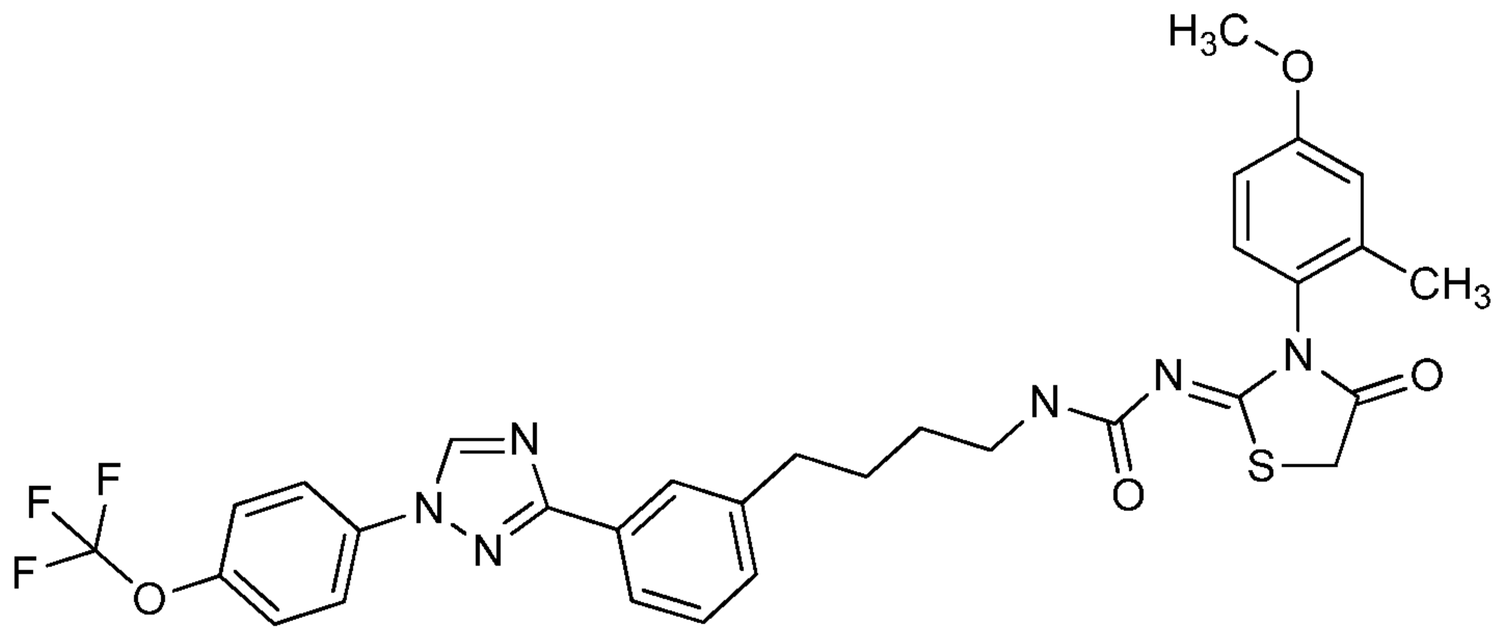
1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB25**) and isolated as an off-white solid (0.091 g, 56%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (FB35)



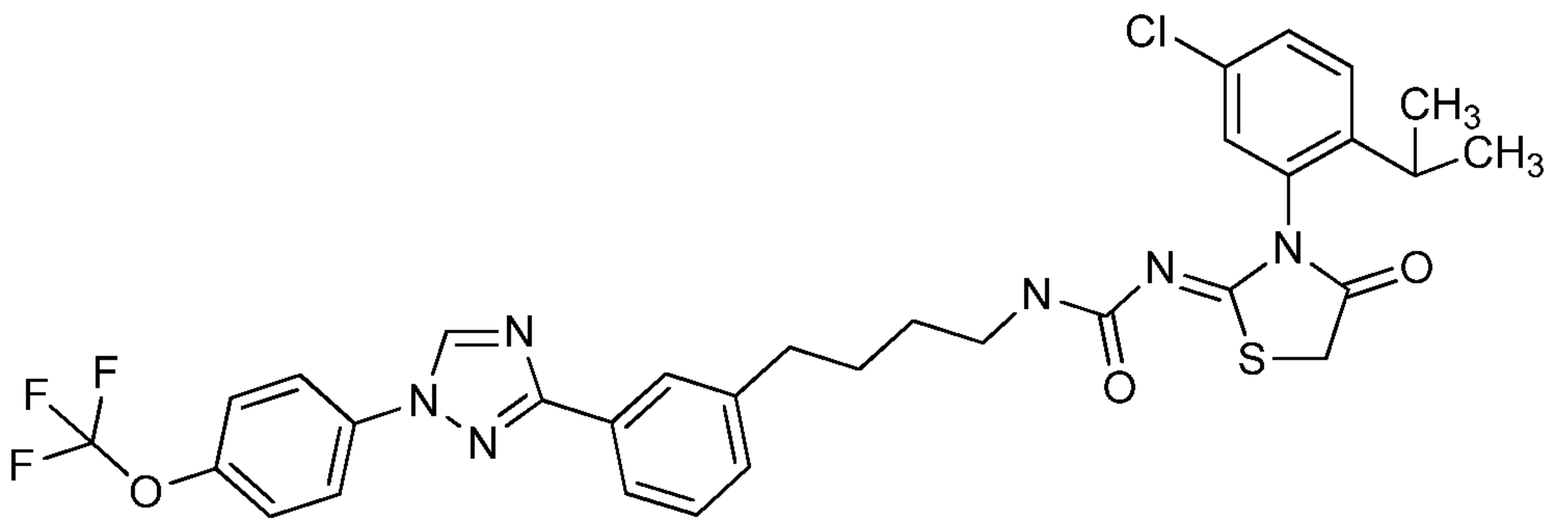
The title compound was prepared as described in Example 64 using 1-[(5-chloro-2-isopropyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**FB26**) and isolated as a light yellow solid (0.095 g, 62%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (FB38)



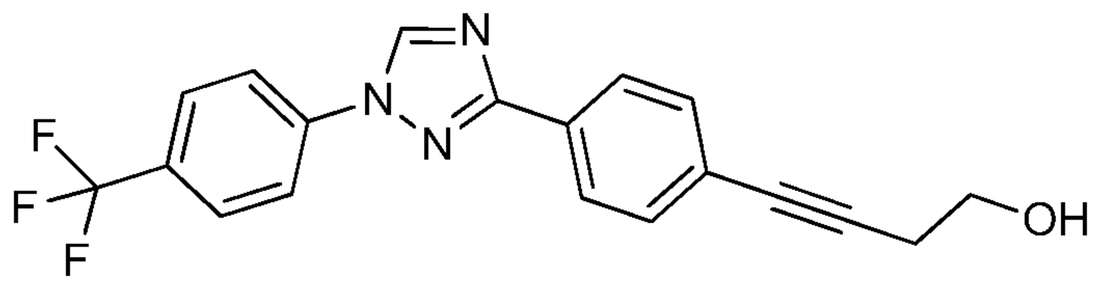
The title compound was prepared as described in Example 64 using 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**FB36**) and isolated as a white solid (0.048 g, 67%).

Preparation of (*Z*)-1-(3-(5-chloro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butyl)urea (FB39)



The title compound was prepared as described in Example 64 using 1-[(5-chloro-2-isopropyl-phenyl)carbamothioyl]-3-[4-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]butyl]urea (**FB37**) and isolated as a white solid (0.060 g, 58%).

Example 65: Preparation of 4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-ol (C61)

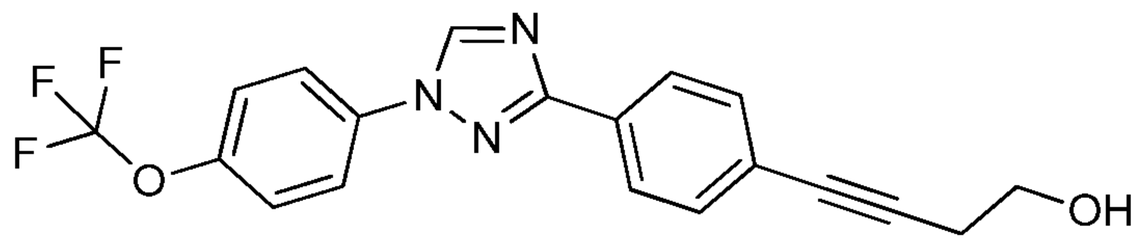


To 3-(4-bromophenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (**C53**) (0.50 g, 1.4 mmol) in a 25 mL vial equipped with a stir bar and cap with septa was added bis(triphenylphosphine)palladium(II) chloride (0.019 g, 0.027 mmol), copper(I) iodide (0.0026 g, 0.014 mmol) and triethylamine (8.5 mL) followed by but-3-yn-1-ol (0.12 mL, 1.6 mmol). The reaction was heated to 60 ºC overnight. The reaction was stopped and cooled to room temperature. The reaction mixture was treated with 50% ethyl acetate/water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water. The organic layer was dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using 0-50% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided a solid which was dried overnight at 50 ºC *in vacuo* to afford the title compound as a tan solid. It was calculated based on ^{1}H NMR to be mixed with the starting butynol (8%), (0.38 g, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.20 - 8.11 (m, 2H), 7.94 - 7.88 (m, 2H), 7.83 - 7.76 (m,

2H), 7.56 - 7.50 (m, 2H), 3.85 (q, *J* = 6.3 Hz, 2H), 2.74 (t, *J* = 6.2 Hz, 2H), 1.83 (t, *J* = 6.3 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.51; ESIMS *m/z* 358 ($[M+H]^+$).

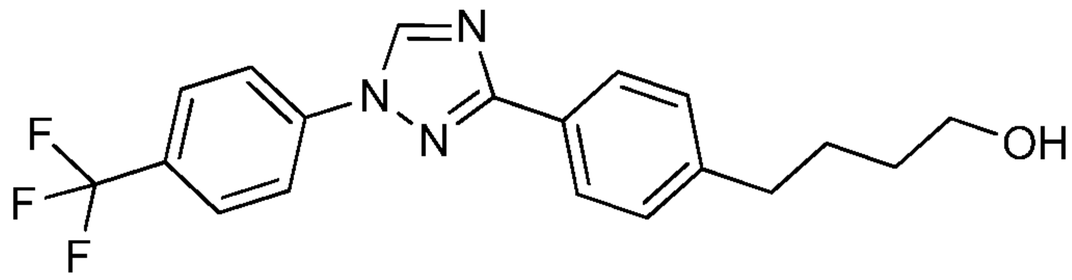
The following compounds were prepared in accordance to the procedure in Example 65.

Preparation of 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-ol (CA23)



The title compound was prepared as described in Example 65 using 3-(4-bromophenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C52**), further purified by trituration with diethyl ether/hexanes and isolated as a white solid (5.46 g, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.19 - 8.08 (m, 2H), 7.84 - 7.76 (m, 2H), 7.57 - 7.49 (m, 2H), 7.39 (dq, *J* = 8.8, 0.9 Hz, 2H), 3.85 (q, *J* = 6.3 Hz, 2H), 2.73 (t, *J* = 6.3 Hz, 2H), 1.83 (t, *J* = 6.3 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 374 ($[M+H]^+$).

Example 66: Preparation of 4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-ol (CA24)

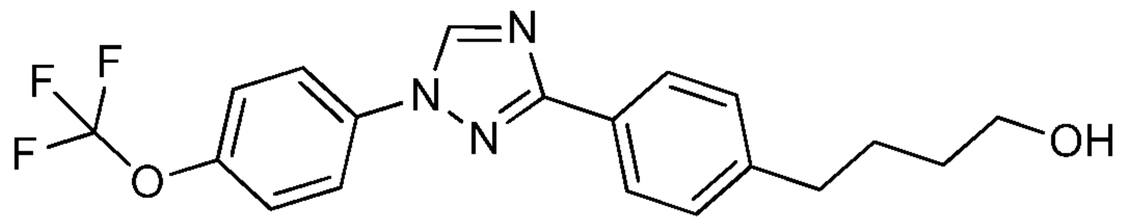


To 4-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-ol (**C61**) (0.376 g, 0.967 mmol) in a 100 mL round bottomed flask equipped with a stir bar and septa was added ethyl acetate (9.67 mL) followed by palladium on carbon (0.103 g, 0.0970 mmol). The reaction mixture was evacuated with vacuum and purged with hydrogen (balloon) (2x) and stirred at room temperature overnight. The reaction mixture was filtered through Celite®, washed with ethyl acetate and concentrated to provide the title compound as a white solid (0.363 g, 104%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.15 - 8.08 (m, 2H), 7.94 - 7.88 (m, 2H), 7.80 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.34 - 7.28 (m, 2H), 3.74 - 3.66 (m, 2H), 3.66 - 3.60 (m,

1H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.81 - 1.71 (m, 2H), 1.69 - 1.60 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48; ESIMS *m/z* 362 ($[M+H]^+$).

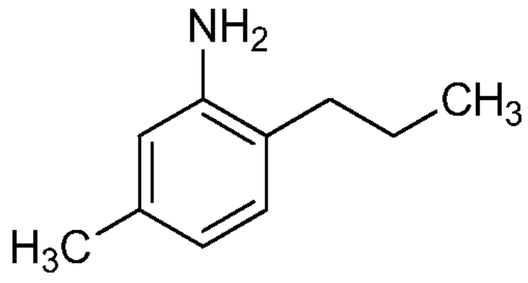
The following compounds were prepared in accordance to the procedure in Example 66.

Preparation of 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)butan-1-ol (CA25)



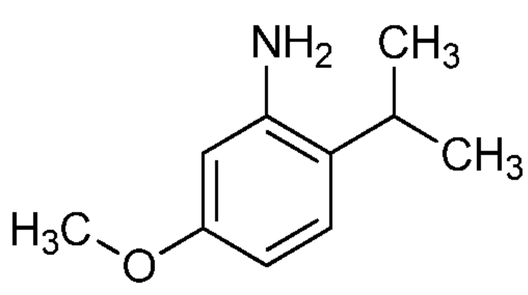
The title compound was prepared as described in Example 66 using 4-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)but-3-yn-1-ol (**CA23**) and isolated as a white solid (3.03 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.10 (d, *J* = 8.2 Hz, 2H), 7.86 - 7.76 (m, 2H), 7.39 (dq, *J* = 9.0, 0.9 Hz, 2H), 7.33 - 7.27 (m, 2H), 3.73 - 3.59 (m, 3H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.82 - 1.70 (m, 2H), 1.70 - 1.59 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 378 ($[M+H]^+$).

Preparation of 5-methyl-2-propylaniline (CA26)



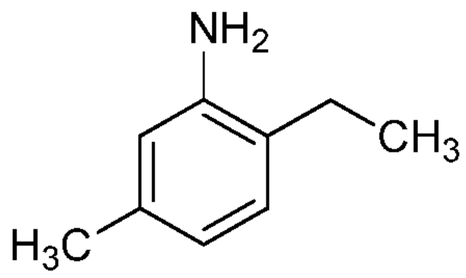
The title compound was prepared as described in Example 66 using 1-allyl-4-methyl-2-nitrobenzene (**CA30**) and isolated as a yellow liquid (1.39 g, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 6.51 (s, 1H), 3.55 (s, 2H), 2.47 - 2.37 (m, 2H), 2.24 (s, 3H), 1.69 - 1.53 (m, 2H), 0.99 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.91, 136.52, 129.46, 123.83, 119.49, 116.29, 33.05, 22.10, 21.05, 14.19; EIMS *m/z* 149 ($[M]^+$).

Preparation of 2-isopropyl-5-methoxyaniline (CA27)



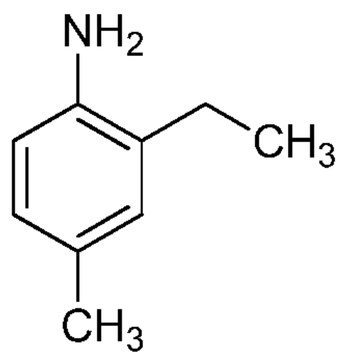
The title compound was prepared as described in Example 66 using 4-methoxy-2-nitro-1-(prop-1-en-2-yl)benzene (**CA43**) and isolated as a yellow liquid (2.23 g, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J = 8.4 Hz, 1H), 6.35 (dd, J = 8.5, 2.6 Hz, 1H), 6.25 (d, J = 2.6 Hz, 1H), 3.75 (s, 3H), 3.65 (s, 2H), 2.83 (p, J = 6.8 Hz, 1H), 1.24 (d, J = 6.8 Hz, 6H); EIMS *m/z* 165 ($[M]^+$).

Preparation of 2-ethyl-5-methylaniline (CA28)



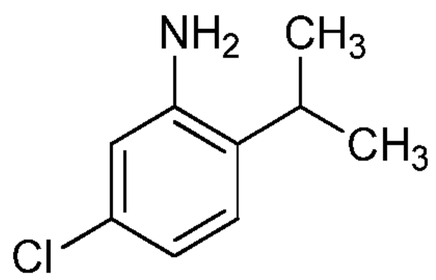
The title compound was prepared as described in Example 66 using 4-methyl-2-nitro-1-vinylbenzene (**CA31**) and isolated as a yellow liquid (0.926 g, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, J = 7.6 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 6.52 (s, 1H), 3.56 (s, 2H), 2.48 (q, J = 7.5 Hz, 2H), 2.25 (s, 3H), 1.23 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.80, 136.48, 128.32, 125.22, 119.59, 116.15, 23.67, 21.03, 13.24; EIMS *m/z* 135 ($[M]^+$).

Preparation of 2-ethyl-4-methylaniline (CA29)



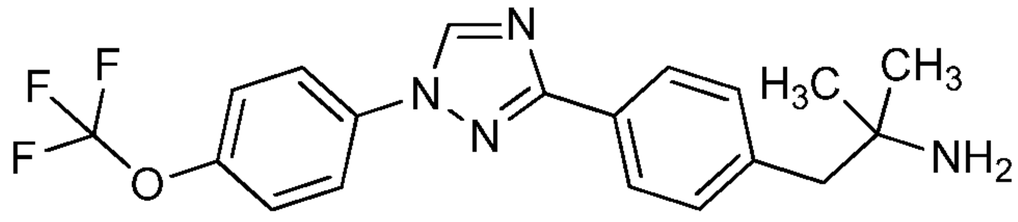
The title compound was prepared as described in Example 66 using 5-methyl-2-nitro-1-vinylbenzene (**CA32**) and isolated as a brown liquid (1.07 g, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (s, 1H), 6.86 - 6.82 (m, 1H), 6.60 (d, J = 7.9 Hz, 1H), 3.55 (s, 2H), 2.50 (q, J = 7.5 Hz, 2H), 2.24 (s, 3H), 1.24 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.35, 129.09, 128.25, 128.01, 127.19, 115.56, 24.05, 20.55, 13.17; EIMS *m/z* 135 ($[M]^+$).

Preparation of 5-chloro-2-isopropylaniline (CB27)



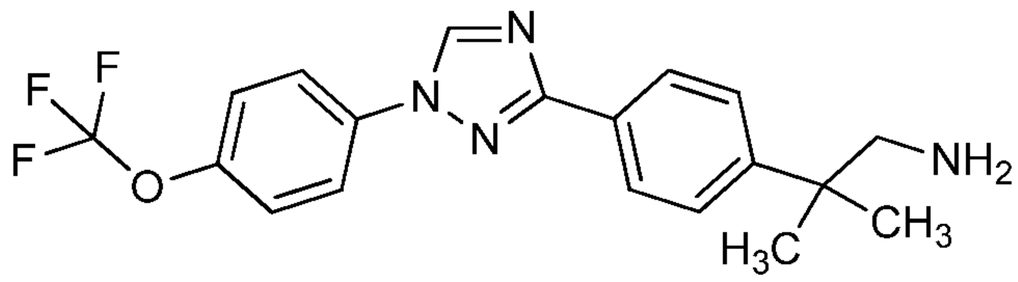
The title compound was prepared as described in Example 66 using 4-chloro-2-nitro-1-(prop-1-en-2-yl)benzene (**CB33**) and isolated as a brown liquid (1.82 g, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.31 (m, 1H), 7.22 - 7.16 (m, 1H), 7.07 (d, *J* = 8.1 Hz, 1H), 6.83 - 6.77 (m, 2H), 2.90 (p, *J* = 6.8 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 126.91, 126.83, 126.51, 121.34, 120.07, 116.37, 27.44, 22.34; EIMS *m/z* 169 ($[M]^+$).

Preparation of 2-methyl-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (CB28)



The title compound was prepared as described in Example 66 using benzyl (2-methyl-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)carbamate (**CB67**) and methanol as solvent; isolated as a yellow gum (0.775 g, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.13 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.39 (dd, *J* = 9.1, 1.0 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 2.74 (s, 2H), 2.05 (s, 2H), 1.16 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 377 ($[M+H]^+$).

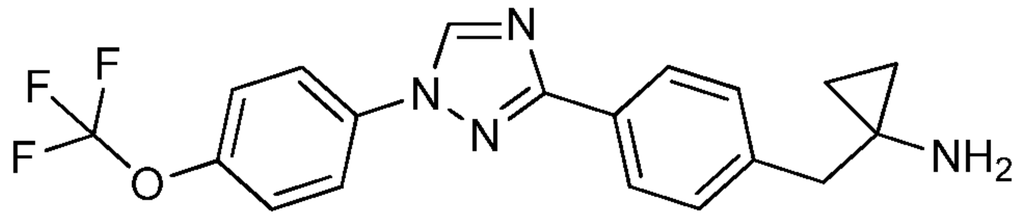
Preparation of 2-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (CB29)



The title compound was prepared as described in Example 66 using benzyl (2-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)carbamate (**CB68**) and methanol as solvent; isolated as a clear oil (0.427 g, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 2H),

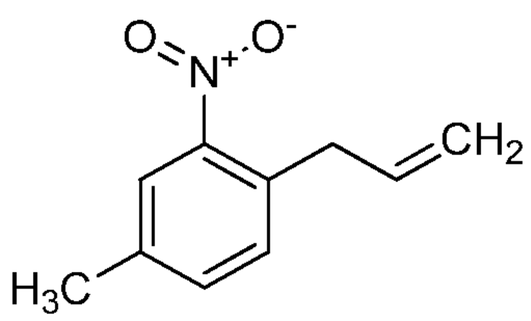
7.84 - 7.77 (m, 2H), 7.49 - 7.42 (m, 2H), 7.39 (dt, *J* = 7.9, 1.0 Hz, 2H), 2.85 (s, 2H), 1.78 (s, 2H), 1.36 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 377 ($[M+H]^+$).

Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)cyclopropanamine (CB30)



The title compound was prepared as described in Example 66 using benzyl (1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)cyclopropyl)carbamate (**CB69**) and isolated as a tan oil (0.392 g, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 - 8.49 (m, 1H), 8.19 - 8.06 (m, 2H), 7.84 - 7.72 (m, 2H), 7.44 - 7.29 (m, 4H), 3.49 (s, 2H), 2.17 (s, 3H), 0.73 - 0.59 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 375 ($[M+H]^+$).

Example 67: Preparation of 1-allyl-4-methyl-2-nitrobenzene (CA30)

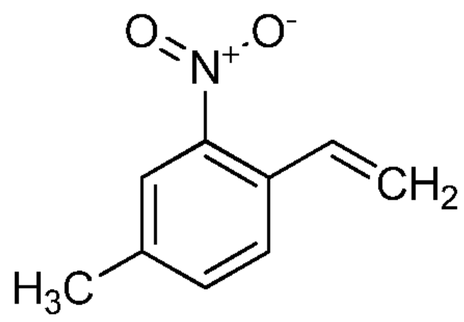


To 1-chloro-4-methyl-2-nitrobenzene (2.00 g, 11.7 mmol), allyltributylstannane (5.79 g, 17.5 mmol) and bis(triphenylphosphine)palladium(II) dichloride (0.818 g, 1.17 mmol) in two 25-mL reaction vials was added 1,2-dichloroethane (20 mL). The vials were capped and heated at 120 ºC for 45 minutes in a Biotage Initiator® microwave reactor with an external IR-sensor temperature monitoring from the side of the vessel. The reaction mixture was loaded onto a Celite® cartridge. The crude material was purified by flash column chromatography using 0-50% ethyl acetate/hexanes as eluent followed by reverse-phase flash column chromatography using 0-100% acetonitrile/water as eluent. The combined acetonitrile/water fractions were concentrated, extracted with ethyl acetate, dried over sodium sulfate, filtered, concentrated, and dried in a vacuum oven to provide the title compound as a yellow liquid (1.76 g, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 0.9 Hz, 1H), 7.34 (dd,

J = 7.8, 1.2 Hz, 1H), 7.24 (d, J = 7.8 Hz, 1H), 5.96 (ddt, J = 16.6, 10.1, 6.4 Hz, 1H), 5.08 (ddq, J = 18.5, 17.0, 1.5 Hz, 2H), 3.64 (d, J = 6.4 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.09, 137.62, 135.35, 133.81, 131.81, 131.72, 124.94, 116.81, 36.62, 20.72; EIMS *m/z* 176 ($[M]^+$).

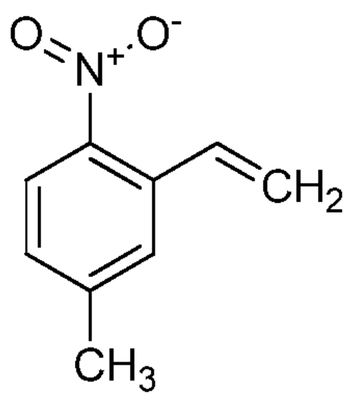
The following compounds were prepared in accordance to the procedure in Example 67.

Preparation of 4-methyl-2-nitro-1-vinylbenzene (CA31)



The title compound was prepared as described in Example 67 using 1-chloro-4-methyl-2-nitrobenzene and tributyl(vinyl)stannane, further purified by flash column chromatography and reverse phase chromatography and isolated as a yellow liquid (1.26 g, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 0.8 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.46 - 7.35 (m, 1H), 7.13 (dd, J = 17.3, 11.0 Hz, 1H), 5.71 (dd, J = 17.3, 0.9 Hz, 1H), 5.43 (dd, J = 11.0, 0.9 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.71, 138.91, 133.92, 132.31, 130.52, 128.22, 124.63, 118.10, 20.88; EIMS *m/z* 163 ($[M]^+$).

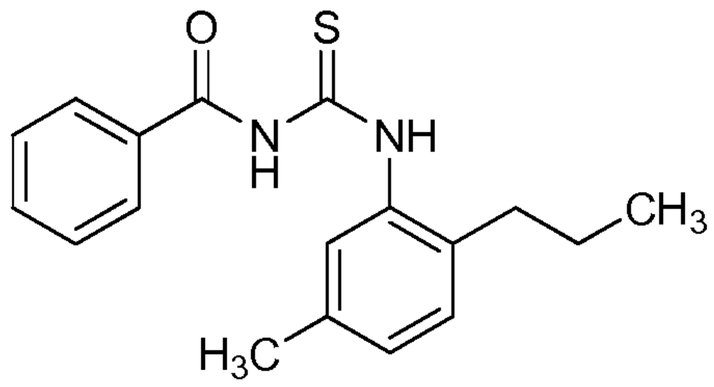
Preparation of 5-methyl-2-nitro-1-vinylbenzene (CA32)



The title compound was prepared as described in Example 67 using 1-chloro-4-methyl-2-nitrobenzene and tributyl(vinyl)stannane, further purified by flash column chromatography and reverse phase chromatography and isolated as a yellow liquid (1.46 g, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.3 Hz, 1H), 7.40 (d, J = 1.2 Hz, 1H), 7.21 (ddd, J = 11.0, 9.9, 8.2 Hz, 2H), 5.71 (dd, J = 17.3, 1.0 Hz, 1H), 5.46 (dd, J = 11.0, 1.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.56,

144.31, 133.64, 133.05, 129.08, 128.98, 124.68, 118.52, 21.49; EIMS *m/z* 163 ($[M]^+$).

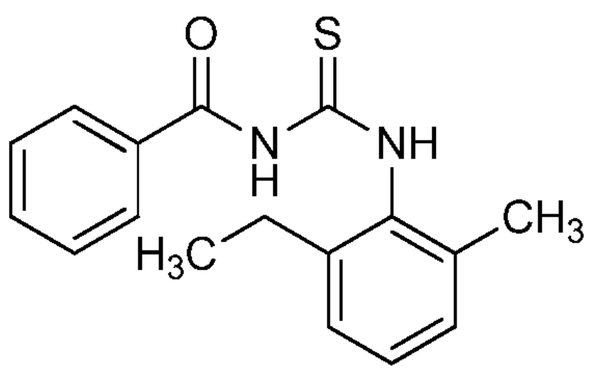
Example 68: Preparation of *N*-((5-methyl-2-propylphenyl)carbamothioyl)benzamide (CA33)



To 5-methyl-2-propylaniline (CA26) (1.38 g, 9.22 mmol) and benzoyl isothiocyanate (1.24 mL, 9.22 mmol) was added acetone (13 mL). The reaction was heated at 60 °C for 4 h. The reaction was cooled and concentrated. The resulting oil was dried in a vacuum oven overnight providing the title compound as a brown oil (3.26 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.20 (s, 1H), 9.15 (s, 1H), 7.92 (dt, *J* = 8.5, 1.7 Hz, 2H), 7.71 - 7.60 (m, 1H), 7.55 (m, 3H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.09 (dd, *J* = 7.8, 1.1 Hz, 1H), 2.66 - 2.55 (m, 2H), 2.36 (s, 3H), 1.72 - 1.57 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.64, 166.90, 136.22, 135.72, 134.57, 133.74, 131.68, 129.79, 129.22, 128.64, 127.55, 127.24, 33.28, 23.58, 21.01, 13.98; ESIMS *m/z* 313 ($[M+H]^+$).

The following compounds were prepared in accordance to the procedure in Example 68.

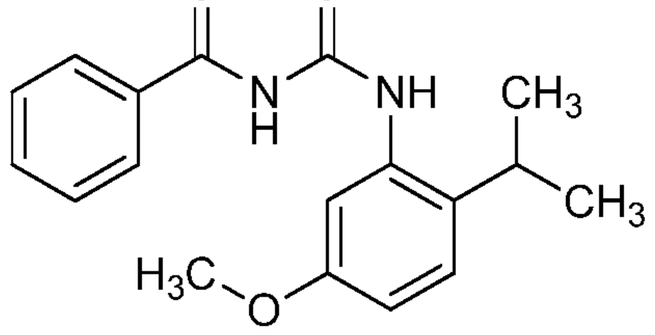
Preparation of *N*-((2-ethyl-6-methylphenyl)carbamothioyl)benzamide (CA34)



The title compound was prepared as described in Example 68 using 2-ethyl-6-methylaniline and isolated as a yellow liquid (6.41 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H), 9.21 (s, 1H), 8.02 - 7.85 (m, 2H), 7.73 - 7.63 (m, 1H), 7.62 -

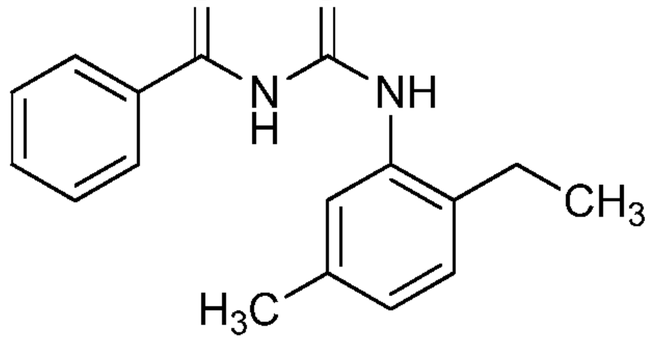
7.50 (m, 2H), 7.29 - 7.23 (m, 1H), 7.20 - 7.14 (m, 2H), 2.75 - 2.57 (m, 2H), 2.33 (s, 3H), 1.25 (t, J = 7.6 Hz, 3H); ESIMS *m/z* 299 ($[M+H]^+$).

Preparation of *N*-((2-isopropyl-5-methoxyphenyl)carbamothioyl)benzamide (CA35)



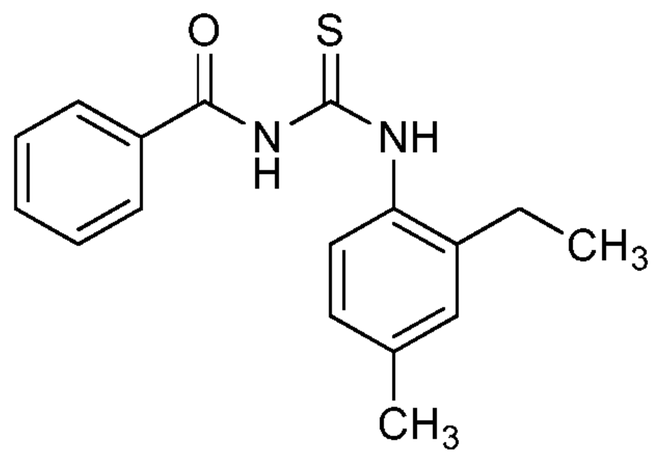
The title compound was prepared as described in Example 68 using 2-isopropyl-5-methoxyaniline (**CA27**) and isolated as a yellow liquid (4.63 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.23 (s, 1H), 9.13 (s, 1H), 7.98 - 7.82 (m, 2H), 7.74 - 7.61 (m, 1H), 7.61 - 7.51 (m, 2H), 7.32 - 7.26 (m, 2H), 6.89 (dd, J = 8.7, 2.7 Hz, 1H), 3.81 (s, 3H), 3.10 (p, J = 6.9 Hz, 1H), 1.26 (d, J = 6.8 Hz, 6H); ESIMS *m/z* 329 ($[M+H]^+$).

Preparation of *N*-((2-ethyl-5-methylphenyl)carbamothioyl)benzamide (CA36)



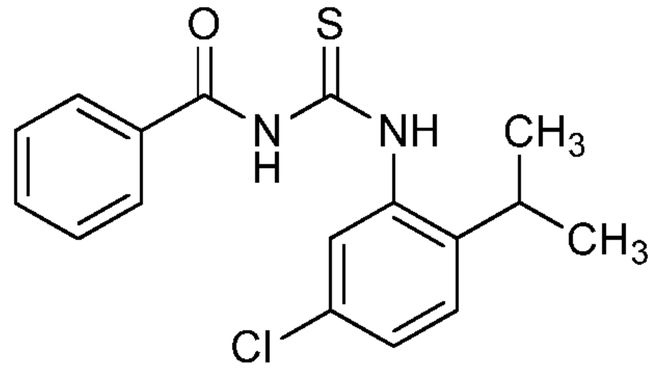
The title compound was prepared as described in Example 68 using 2-ethyl-5-methylaniline (**CA28**) and isolated as an orange solid (2.10 g, 97%): mp 105-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.18 (s, 1H), 9.14 (s, 1H), 7.92 (dt, J = 8.6, 1.7 Hz, 2H), 7.73 - 7.60 (m, 1H), 7.59 - 7.53 (m, 2H), 7.50 (s, 1H), 7.21 (d, J = 7.8 Hz, 1H), 7.11 (dd, J = 7.8, 1.1 Hz, 1H), 2.71 - 2.59 (m, 2H), 2.37 (s, 3H), 1.24 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.72, 166.94, 136.22, 136.13, 135.53, 133.75, 131.65, 129.23, 128.88, 128.86, 127.53, 127.23, 24.26, 20.98, 14.56; ESIMS *m/z* 299 ($[M+H]^+$).

Preparation of *N*-((2-ethyl-4-methylphenyl)carbamothioyl)benzamide (CA37)



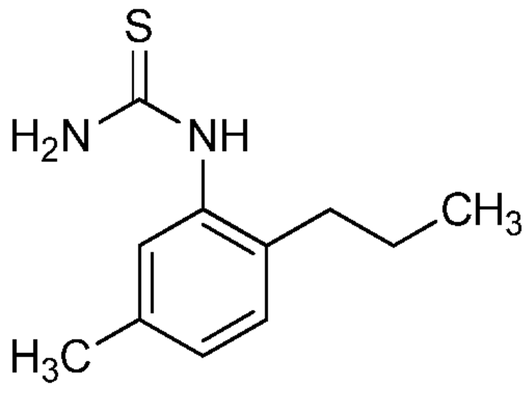
The title compound was prepared as described in Example 68 using 2-ethyl-4-methylaniline (**CA29**) and isolated as an orange solid (2.46 g, 100%): mp 103 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.16 (s, 1H), 9.18 (s, 1H), 7.95 - 7.86 (m, 2H), 7.68 - 7.60 (m, 1H), 7.60 - 7.51 (m, 4H), 7.15 - 7.05 (m, 2H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.37 (s, 3H), 1.25 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.89, 166.97, 138.94, 137.88, 133.75, 133.20, 131.67, 129.77, 129.23, 127.55, 127.15, 126.71, 24.63, 21.27, 14.52; ESIMS *m/z* 299 ($[M+H]^+$).

Preparation of *N*-((5-chloro-2-isopropylphenyl)carbamothioyl)benzamide (CB31)



The title compound was prepared as described in Example 68 using 5-chloro-2-isopropylaniline (**CB27**) followed by purification by flash column chromatography and isolated as a light yellow solid (16.3 g, 98%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.32 (s, 1H), 11.76 (s, 1H), 8.07 - 7.95 (m, 2H), 7.72 - 7.63 (m, 1H), 7.60 - 7.50 (m, 3H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.37 (dd, *J* = 8.5, 2.2 Hz, 1H), 3.08 (hept, *J* = 6.9 Hz, 1H), 1.19 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, DMSO) δ 181.12, 168.37, 142.95, 137.03, 133.18, 131.93, 129.67, 128.75, 128.40, 127.61, 127.55, 127.52, 27.63, 22.84; ESIMS *m/z* 333 ($[M+H]^+$).

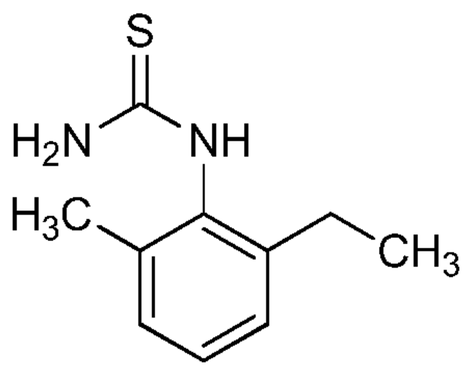
Example 69: Preparation of 1-(5-methyl-2-propylphenyl)thiourea (CA38)



To *N*-((5-methyl-2-propylphenyl)carbamothioyl)benzamide (**C72**) (3.21 g, 10.3 mmol) in methanol (80 mL) was added sodium hydroxide (2 N, 10.3 mL, 20.5 mmol) and heated at 50 °C for 2 hours and then stirred at room temperature over the weekend. The reaction was concentrated, diluted with water, extracted with dichloromethane, filtered through a phase separator, concentrated, and dried in a vacuum oven to provide the title compound as a tan solid (1.80 g, 83%): mp 143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.12 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.04 (s, 1H), 5.99 (d, *J* = 254.5 Hz, 2H), 2.57 (d, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 1.59 (dq, *J* = 14.8, 7.4 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.96, 137.53, 136.74, 134.00, 130.69, 129.72, 127.85, 32.90, 23.66, 20.80, 13.93; ESIMS *m/z* 209 ($[M+H]^+$).

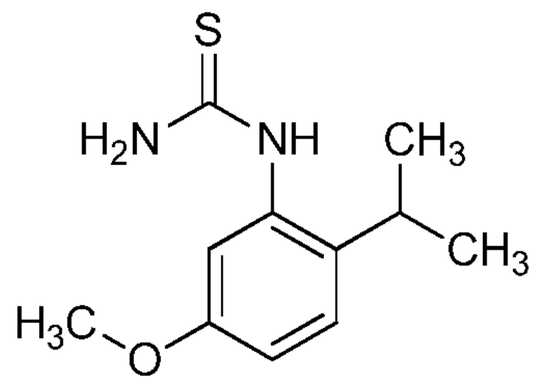
The following compounds were prepared in accordance to the procedure in Example 69.

Preparation of 1-(2-ethyl-6-methylphenyl)thiourea (CA39)



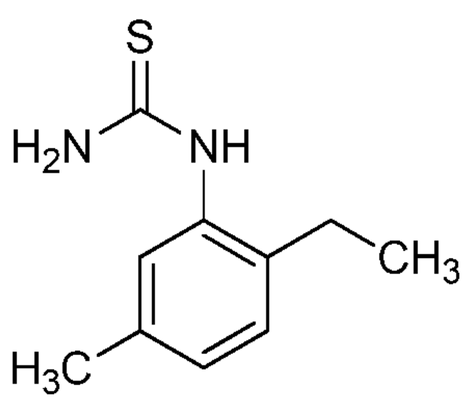
The title compound was prepared as described in Example 69 using *N*-((2-ethyl-6-methylphenyl)carbamothioyl)benzamide (**CA34**), further purified by trituration with water and isolated as a white solid (3.46 g, 83%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.25 (d, *J* = 7.9 Hz, 1H), 7.22 - 7.11 (m, 2H), 6.13 (bs, 1H), 5.33 (bs, 1H), 2.77 - 2.55 (m, 2H), 2.31 (s, 3H), 1.21 (t, *J* = 7.6 Hz, 3H); ESIMS *m/z* 195 ($[M+H]^+$).

Preparation of 1-(2-isopropyl-5-methoxyphenyl)thiourea (CA40)



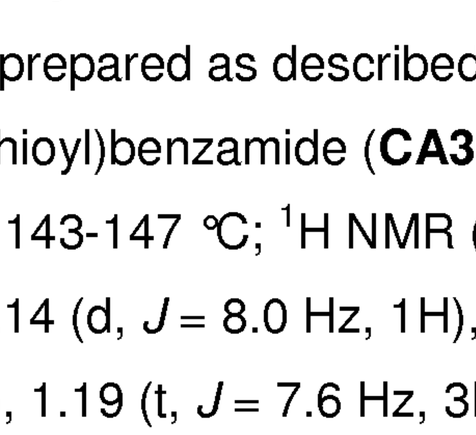
The title compound was prepared as described in Example 69 using *N*-((2-isopropyl-5-methoxyphenyl)carbamothioyl)benzamide (**CA35**) and isolated as an orange solid (2.65 g, 83%): mp 134-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.30 (d, *J* = 8.7 Hz, 1H), 6.93 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.75 (d, *J* = 2.7 Hz, 1H), 5.88 (s, 2H), 3.79 (s, 3H), 3.10 (p, *J* = 6.9 Hz, 1H), 1.19 (d, *J* = 6.9 Hz, 6H); ESIMS *m/z* 225 ($[M+H]^+$).

Preparation of 1-(2-ethyl-5-methylphenyl)thiourea (CA41)



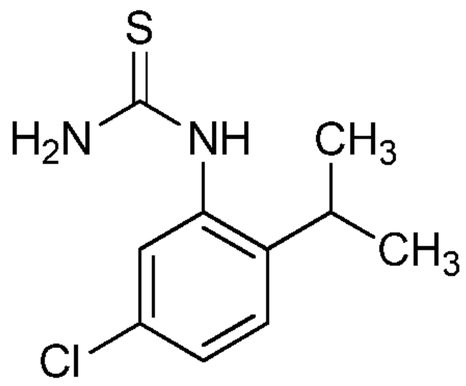
The title compound was prepared as described in Example 69 using *N*-((2-ethyl-5-methylphenyl)carbamothioyl)benzamide (**CA36**) and isolated as a pale orange solid (1.26 g, 94%): mp 143-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.04 (s, 1H), 5.86 (s, 2H), 2.61 (q, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.13, 138.27, 137.53, 133.74, 129.95, 129.93, 127.84, 24.00, 20.79, 14.77; ESIMS *m/z* 195 ($[M+H]^+$).

Preparation of 1-(2-ethyl-4-methylphenyl)thiourea (CA42)



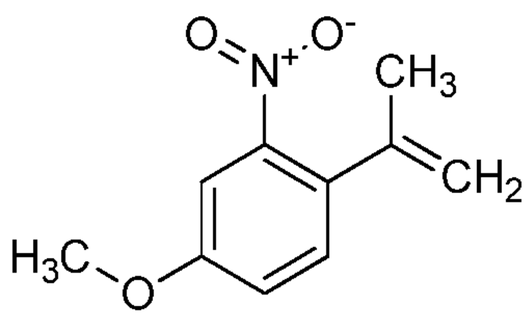
The title compound was prepared as described in Example 69 using *N*-((2-ethyl-4-methylphenyl)carbamothioyl)benzamide (**CA37**) and isolated as a tan solid (1.40 g, 86%): mp 153-155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.14 (d, *J* = 0.5 Hz, 1H), 7.08 (dt, *J* = 8.1, 4.8 Hz, 2H), 5.85 (d, *J* = 184.3 Hz, 2H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.35 (s, 3H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.32, 141.33, 139.33, 131.29, 130.75, 128.15, 127.36, 24.36, 21.18, 14.74; ESIMS *m/z* 195 ([M+H]$^+$).

Preparation of 1-(5-chloro-2-isopropylphenyl)thiourea (CB32)



The title compound was prepared as described in Example 69 using *N*-((5-chloro-2-isopropylphenyl)carbamothioyl)benzamide (**CB31**) and isolated as a brown sticky gum (1.38 g, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.34 (d, *J* = 1.4 Hz, 2H), 7.24 (t, *J* = 1.3 Hz, 1H), 5.97 (s, 2H), 3.27 - 3.10 (m, 1H), 1.21 (d, *J* = 6.8 Hz, 6H); ESIMS *m/z* 229 ([M+H]$^+$).

Example 70: Preparation of 4-methoxy-2-nitro-1-(prop-1-en-2-yl)benzene (CA43)

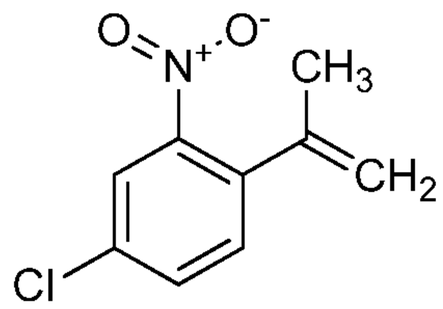


To 1-chloro-4-methoxy-2-nitrobenzene (5.03 g, 26.8 mmol), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (5.41 g, 32.2 mmol), bis(triphenylphosphine)palladium(II) chloride (1.50 g, 2.15 mmol), and sodium carbonate (3.41 g, 32.2 mmol) was added dioxane/water (4:1, 100 mL:25 mL). The reaction was heated at 80 °C for 5 hours. The reaction was cooled to room temperature overnight. The reaction mixture was diluted with water, extracted with ethyl acetate (3x), dried over sodium sulfate, filtered, and concentrated. Purification

by flash column chromatography using 0-5% ethyl acetate/hexanes as eluent followed by drying in vacuum oven provided the title compound as an orange oil (2.74 g, 53%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 2.7 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.08 (dd, *J* = 8.5, 2.6 Hz, 1H), 5.24 - 4.75 (m, 2H), 3.86 (s, 3H), 2.19 - 1.88 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.79, 148.61, 142.53, 131.41, 131.32, 119.24, 115.20, 108.64, 55.84, 23.38; EIMS *m/z* 193 ($[M]^+$).

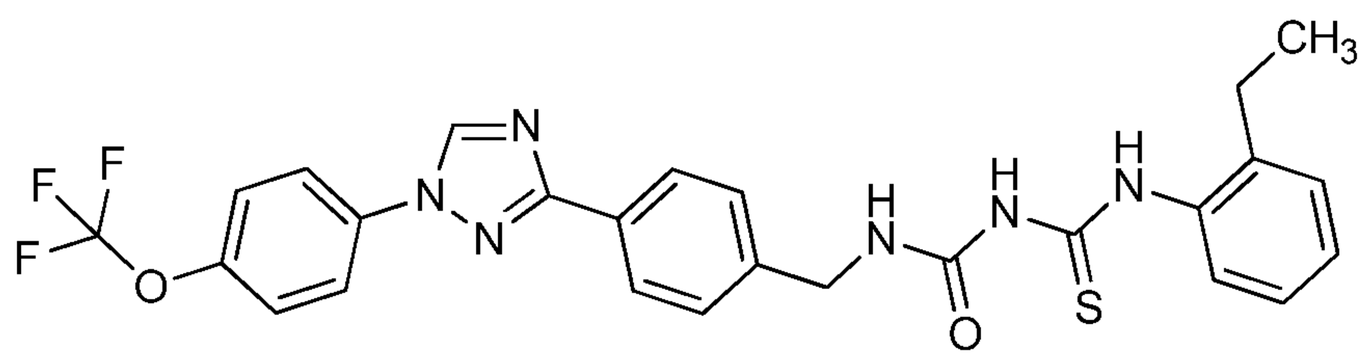
The following compounds were prepared in accordance to the procedure in Example 70.

Preparation of 4-chloro-2-nitro-1-(prop-1-en-2-yl)benzene (CB33)



The title compound was prepared as described in Example 70 using 1-bromo-4-chloro-2-nitrobenzene heated overnight and isolated as a light orange liquid (10.73 g, 84%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04 (d, *J* = 2.2 Hz, 1H), 7.76 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 5.24 (p, *J* = 1.5 Hz, 1H), 4.95 (p, *J* = 1.0 Hz, 1H), 2.07 (dd, *J* = 1.5, 0.9 Hz, 3H); ^{13}C NMR (101 MHz, DMSO) δ 148.37, 140.83, 136.10, 132.62, 132.45, 131.63, 123.50, 115.98, 22.60; EIMS *m/z* 197 ($[M]^+$).

Example 71: Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC2)**

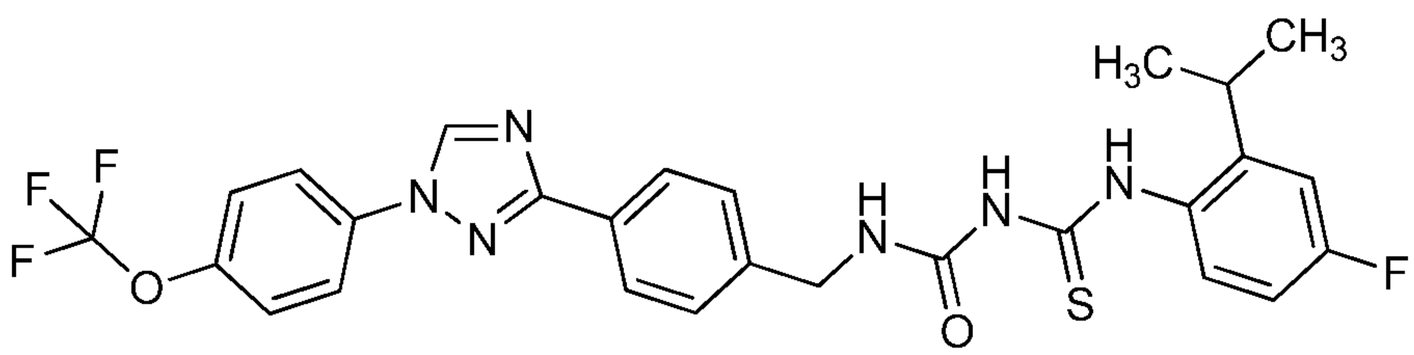


A fine suspension of (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) (0.300 g, 0.897 mmol) in dichloromethane (4.0 mL) was added, in a slow dropwise fashion, to a biphasic solution of bis(trichloromethyl) carbonate (0.107 g, 0.359 mmol) and sodium acetate (0.221 g, 2.69 mmol) in dichloromethane (4.0 mL) and water (2.0 mL). The reaction was allowed to stir for 30 minutes. The reaction was passed through a phase separator, washing with

additional dichloromethane and the organic layer was concentrated. The resulting residue was diluted with acetonitrile (4.0 mL), and 1-(2-ethylphenyl)thiourea (0.178 g, 0.987 mmol) and cesium carbonate (0.351 g, 1.08 mmol) were added as solids. The reaction was allowed to stir at room temperature overnight. The reaction mixture was diluted with dichloromethane and water and passed through a phase separator. The organic layer was concentrated on to Celite® and purified by reverse phase flash column chromatography (C_{18}) using 20-100% acetonitrile/water as eluent providing the title compound as a white solid (0.100 g, 16%) contaminated with ~20% of the dimer urea: ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.99 (s, 1H), 10.24 (s, 1H), 9.41 (s, 1H), 9.40 (d, J = 1.0 Hz, 1H), 8.18 - 8.03 (m, 6H), 7.63 (dddd, J = 9.2, 4.3, 2.0, 1.0 Hz, 3H), 7.54 (ddd, J = 12.1, 7.0, 4.8 Hz, 2H), 7.50 - 7.38 (m, 3H), 7.35 - 7.26 (m, 1H), 7.26 - 7.20 (m, 2H), 4.44 (d, J = 5.8 Hz, 2H), 2.56 (q, J = 7.6 Hz, 2H), 1.14 (t, J = 7.6 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS m/z 541 ([M+H]$^+$), 539 ([M-H]$^-$)

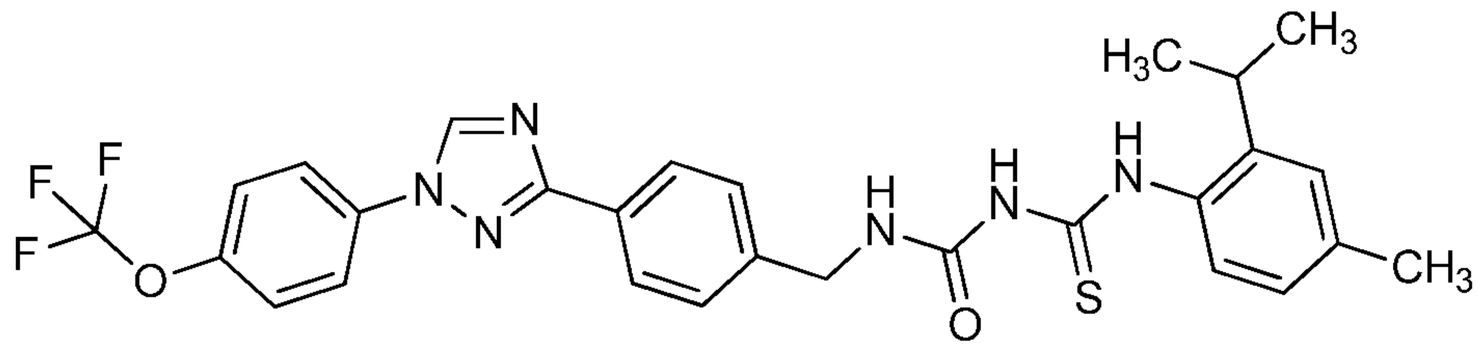
The following compounds were prepared in accordance to the procedure in Example 71.

Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC3)**



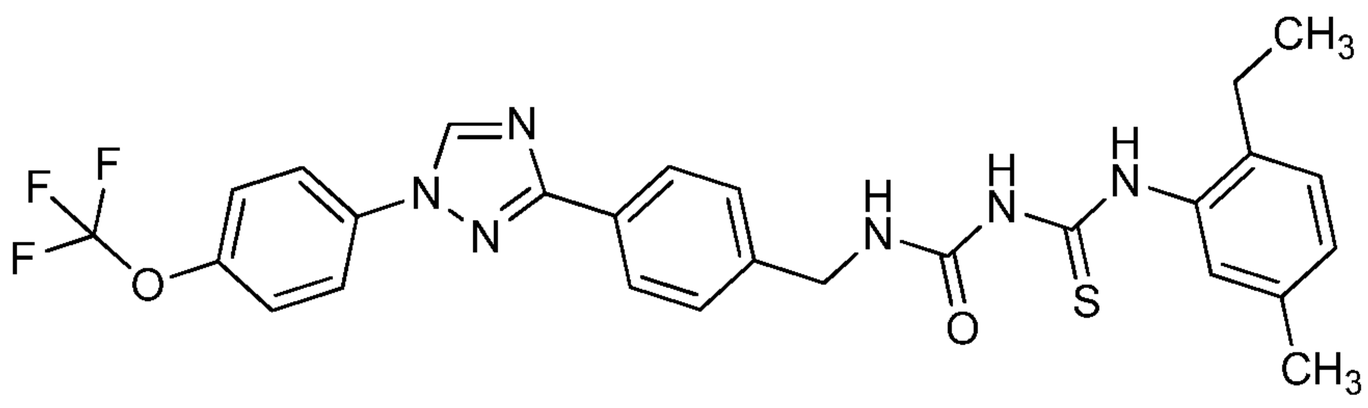
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as a white solid (0.157 g, 30%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.81 (s, 1H), 10.26 (s, 1H), 9.41 (s, 1H), 8.15 - 8.03 (m, 4H), 7.63 (ddt, J = 7.8, 1.9, 0.9 Hz, 2H), 7.58 - 7.44 (m, 3H), 7.39 (dd, J = 8.8, 5.6 Hz, 1H), 7.17 (dd, J = 10.3, 3.0 Hz, 1H), 7.05 (td, J = 8.5, 3.0 Hz, 1H), 4.44 (d, J = 5.8 Hz, 2H), 3.05 - 2.93 (m, 1H), 1.16 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96 , -114.33; ESIMS m/z 573 ([M+H]$^+$), 571 ([M-H]$^-$).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC5)**



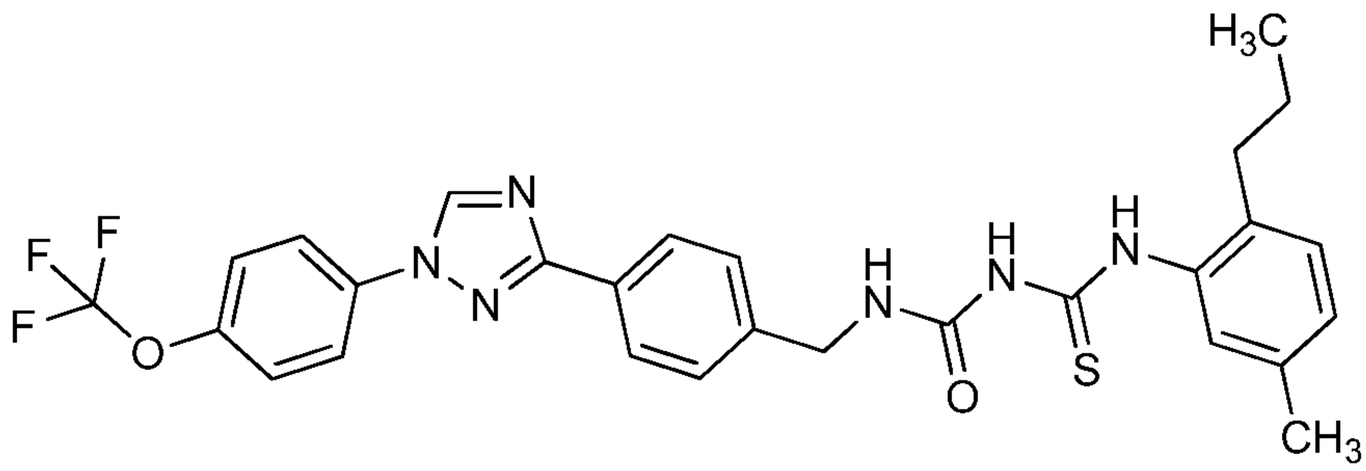
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as a white solid (0.110 g, 21%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 10.21 (s, 1H), 9.41 (s, 1H), 8.17 - 8.05 (m, 4H), 7.63 (dq, J = 8.9, 0.9 Hz, 2H), 7.56 - 7.44 (m, 3H), 7.26 (d, J = 8.0 Hz, 1H), 7.15 (d, J = 2.0 Hz, 1H), 7.06 - 6.98 (m, 1H), 4.44 (d, J = 5.8 Hz, 2H), 2.97 (hept, J = 6.7 Hz, 1H), 2.31 (s, 3H), 1.16 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 569 ([M+H]$^{+}$), 567 ([M-H]$^{-}$).

Preparation of 1-[(2-ethyl-5-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC7)**



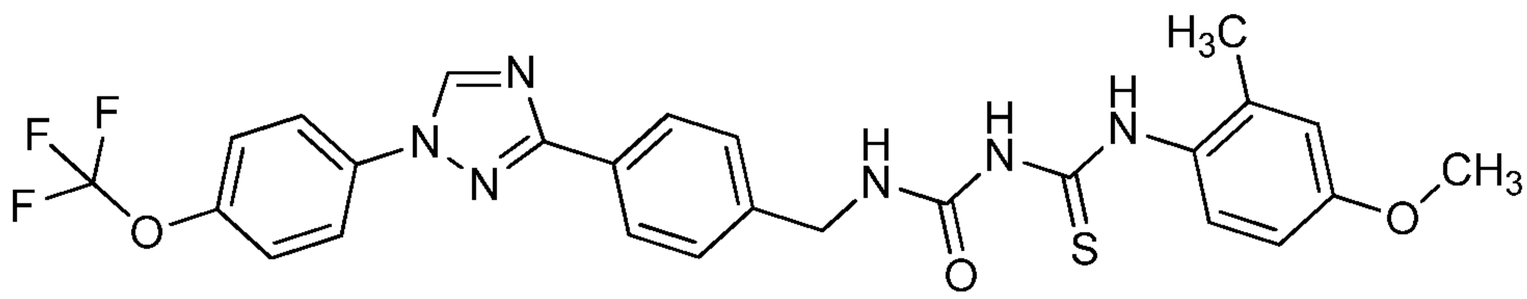
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) and 1-(2-ethyl-5-methylphenyl)thiourea (**CA41**) and isolated as an off white solid (0.092 g, 18%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 10.22 (s, 1H), 9.41 (d, J = 0.8 Hz, 1H), 8.18 - 8.04 (m, 4H), 7.63 (d, J = 8.7 Hz, 2H), 7.57 - 7.44 (m, 3H), 7.39 - 7.31 (m, 1H), 7.17 (d, J = 7.7 Hz, 1H), 7.04 (dd, J = 8.0, 1.7 Hz, 1H), 4.44 (d, J = 5.8 Hz, 2H), 2.51 (dt, J = 3.6, 1.9 Hz, 2H), 2.27 (s, 3H), 1.14 - 1.08 (m, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 555 ([M+H]$^{+}$), 553 ([M-H]$^{-}$).

Preparation of 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC8)**



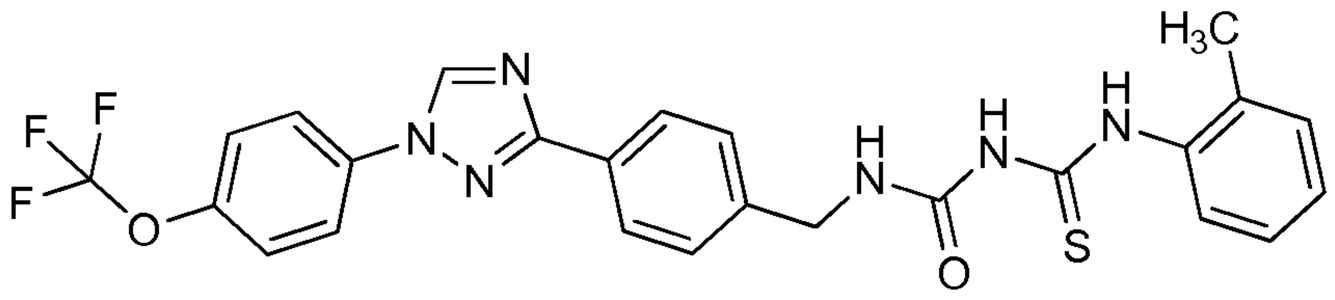
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) and 1-(5-methyl-2-propylphenyl)thiourea (**CA38**) and isolated as an off white solid (0.079 g, 15%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.98 (s, 1H), 10.22 (s, 1H), 9.41 (s, 1H), 8.14 - 8.06 (m, 4H), 7.69 - 7.61 (m, 2H), 7.56 - 7.44 (m, 3H), 7.39 (s, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 7.08 - 6.99 (m, 1H), 4.44 (d, *J* = 5.8 Hz, 2H), 2.49 - 2.43 (m, 2H), 2.27 (s, 3H), 1.50 (h, *J* = 7.3 Hz, 2H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 569 ([M+H]$^{+}$), 567 ([M-H]$^{-}$).

Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC6)**



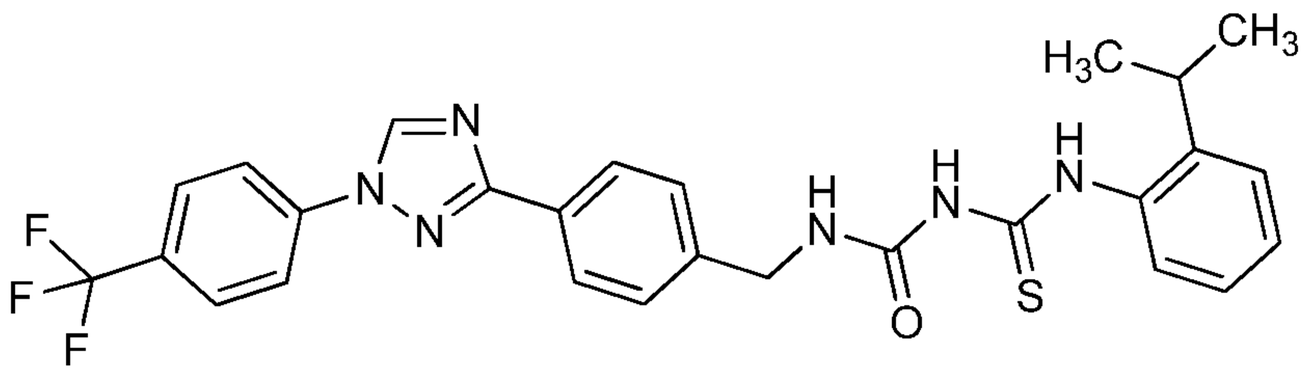
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as a white solid (0.076 g, 15%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (s, 1H), 10.18 (s, 1H), 9.41 (s, 1H), 8.11 - 8.04 (m, 5H), 7.69 - 7.58 (m, 3H), 7.58 - 7.35 (m, 5H), 6.90 - 6.82 (m, 1H), 6.77 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.43 (d, *J* = 5.8 Hz, 2H), 3.75 (s, 3H), 2.18 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESMIS *m/z* 557 ([M+H]$^{+}$), 555 ([M-H]$^{-}$).

Preparation of 1-(*o*-tolylcarbamothioyl)-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC1)**



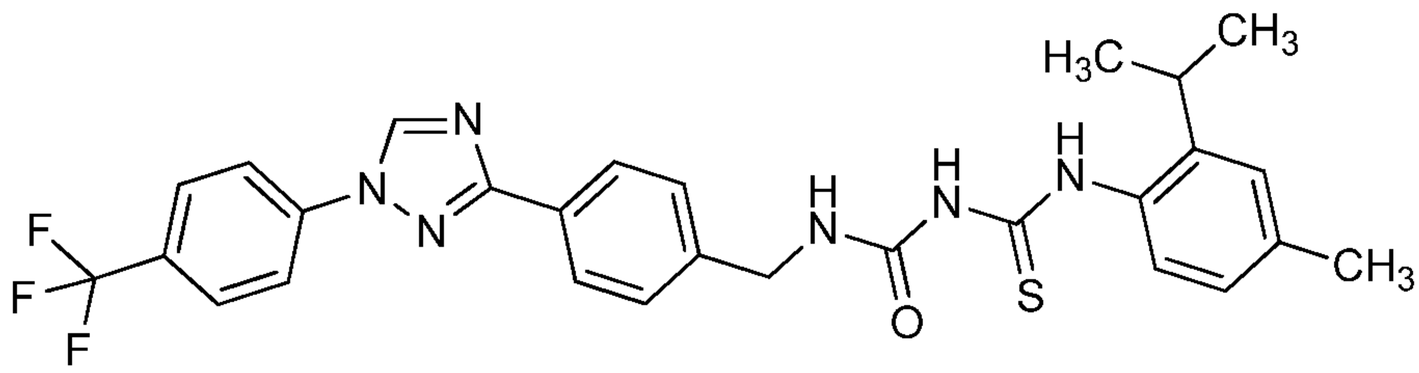
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**C16**) and 1-(*o*-tolyl)thiourea and isolated as a white solid (0.116 g, 24%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.00 (s, 1H), 10.22 (s, 1H), 9.41 (s, 1H), 8.18 - 8.06 (m, 4H), 7.64 (dp, J = 7.8, 0.9 Hz, 3H), 7.55 (t, J = 5.9 Hz, 1H), 7.52 - 7.46 (m, 2H), 7.32 - 7.28 (m, 1H), 7.27 - 7.17 (m, 2H), 4.46 (d, J = 5.8 Hz, 2H), 2.25 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 527 ([M+H]$^+$), 525 ([M-H]$^-$).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethyl)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC14)**



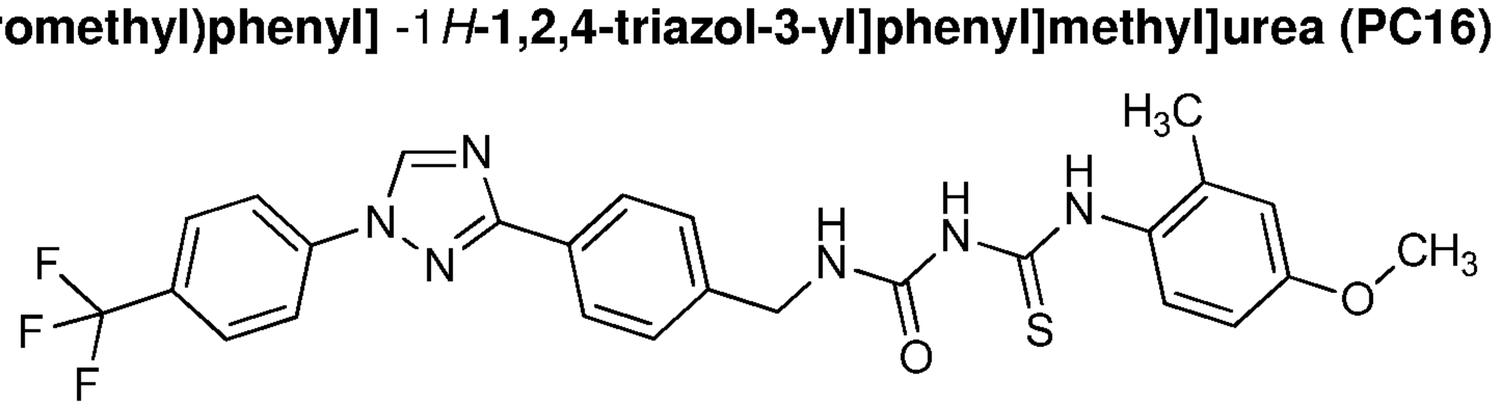
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**CA3**) and 1-(2-isopropylphenyl)thiourea and isolated as a white solid (0.088 g, 17%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 10.24 (s, 1H), 9.55 (s, 1H), 8.22 (d, J = 8.5 Hz, 2H), 8.19 - 8.13 (m, 2H), 8.01 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 5.9 Hz, 1H), 7.53 - 7.48 (m, 2H), 7.45 (dd, J = 7.8, 1.5 Hz, 1H), 7.38 (dd, J = 7.7, 1.6 Hz, 1H), 7.30 (td, J = 7.5, 1.5 Hz, 1H), 7.24 (td, J = 7.6, 1.7 Hz, 1H), 4.47 (d, J = 5.8 Hz, 2H), 3.05 (hept, J = 7.0 Hz, 1H), 1.20 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.79; ESIMS *m/z* 539 ([M+H]$^+$), 537 ([M-H]$^-$).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethyl)phenyl]-1,2,4-triazol-3-yl]phenyl]methyl]urea (PC15)



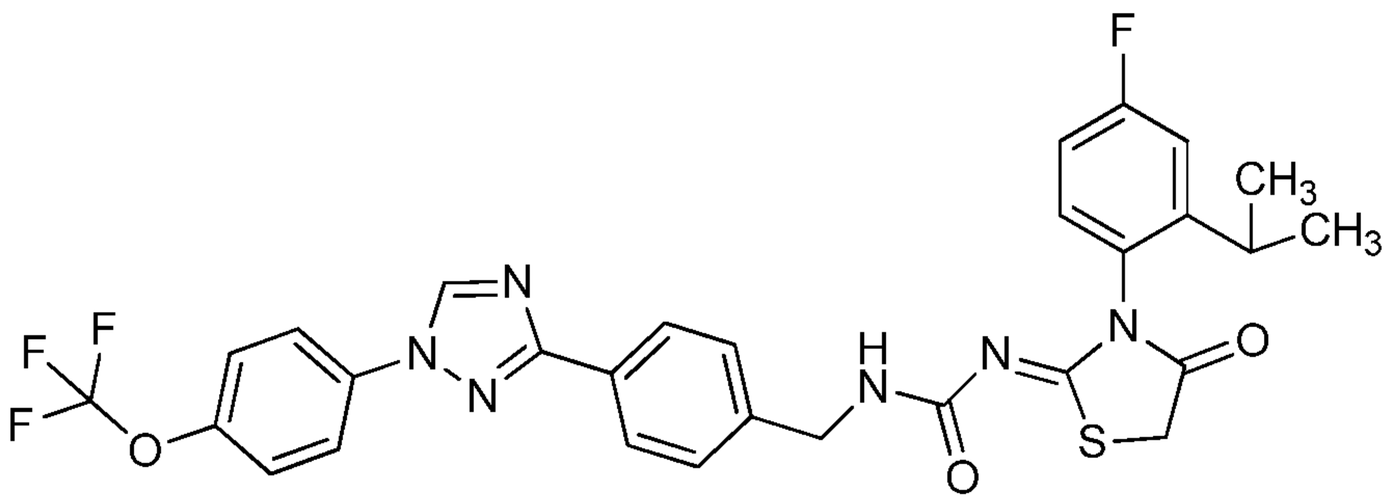
The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**CA3**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as a white solid (0.073 g, 14%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (s, 1H), 10.21 (s, 1H), 9.55 (s, 1H), 8.22 (d, J = 8.4 Hz, 2H), 8.19 - 8.12 (m, 2H), 8.01 (d, J = 8.5 Hz, 2H), 7.54 (t, J = 6.0 Hz, 1H), 7.52 - 7.47 (m, 2H), 7.29 (d, J = 8.0 Hz, 1H), 7.17 (d, J = 2.0 Hz, 1H), 7.07 - 7.01 (m, 1H), 4.47 (d, J = 5.8 Hz, 2H), 3.00 (hept, J = 6.9 Hz, 1H), 2.33 (s, 3H), 1.19 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.79; ESIMS m/z 553 ([M+H]$^{+}$), 551 ([M-H]$^{-}$).

Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethyl)phenyl] -1*H*-**1,2,4-triazol-3-yl]phenyl]methyl]urea (PC16)**



The title compound was prepared as described in Example 71 using (4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)methanamine (**CA3**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as a white solid (0.033 g, 6%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.17 (s, 1H), 9.53 (s, 1H), 9.18 (s, 1H), 8.22 (d, J = 8.4 Hz, 2H), 8.15 - 8.06 (m, 2H), 8.01 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.6 Hz, 1H), 7.07 (t, J = 6.0 Hz, 1H), 6.92 (d, J = 2.9 Hz, 1H), 6.88 (dd, J = 8.6, 2.9 Hz, 1H), 4.29 (dd, J = 5.9, 2.9 Hz, 2H), 3.82 (s, 3H), 2.11 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.79; ESIMS m/z 541 ([M+H]$^{+}$), 539 ([M-H]$^{-}$).

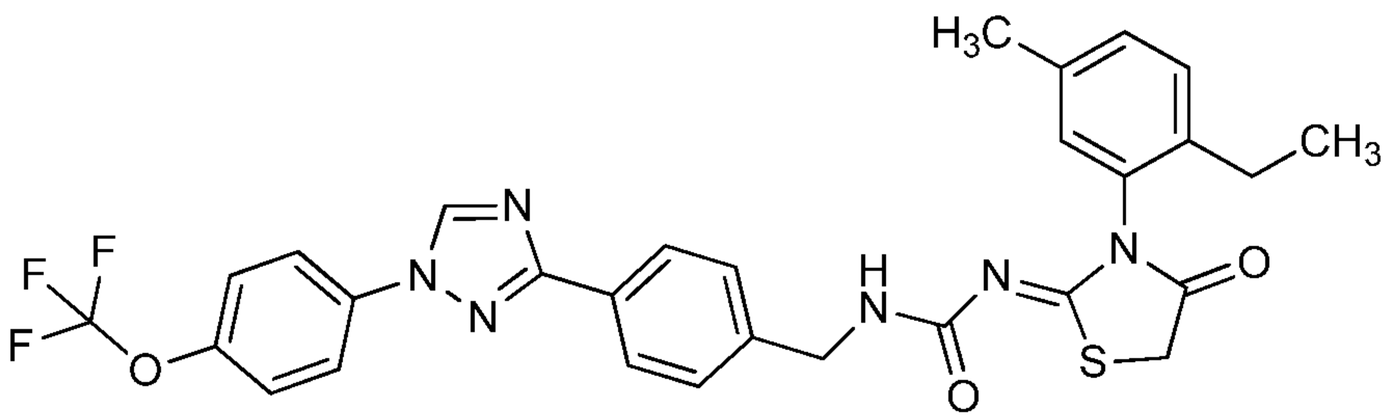
Example 72: Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P3, P1172)



To a 20 mL vial was added 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC3**) (0.092 g, 0.16 mmol), sodium acetate (0.040 g, 0.48 mmol), methyl 2-bromoacetate (0.084 mL, 0.80 mmol) and acetonitrile (2.0 mL). The vial was sealed and the reaction was heated overnight at 65 °C. The reaction mixture was diluted with brine solution and dichloromethane and passed through a phase separator. The organic layer was concentrated and the resulting residue was purified by flash column chromatography using 10-80% ethyl acetate/hexanes as eluent providing the title compound as a white solid (0.058 g, 58%).

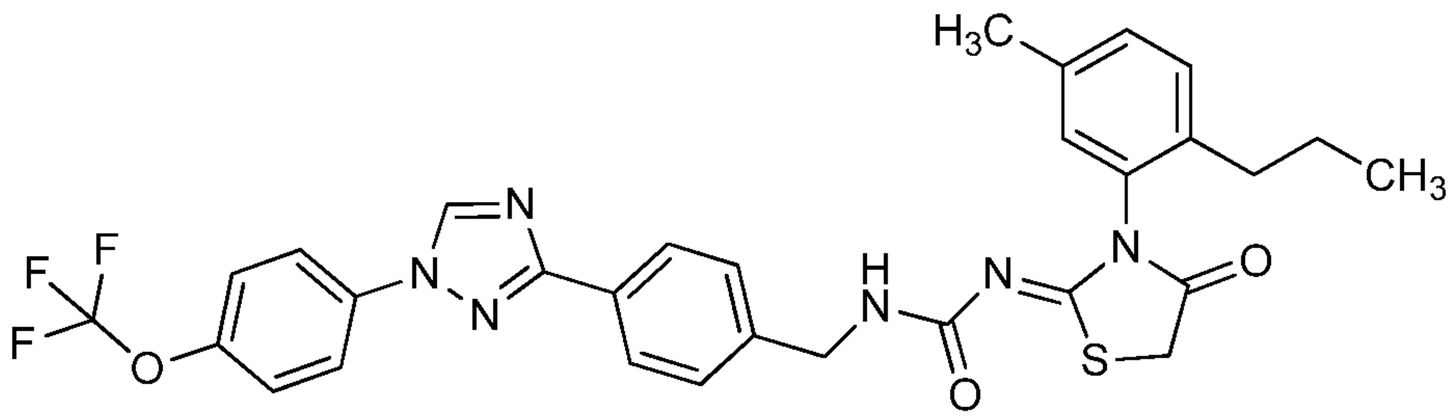
The following compounds were prepared in accordance to the procedure in Example 72.

Preparation of (*Z*)-1-(3-(2-ethyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P7)



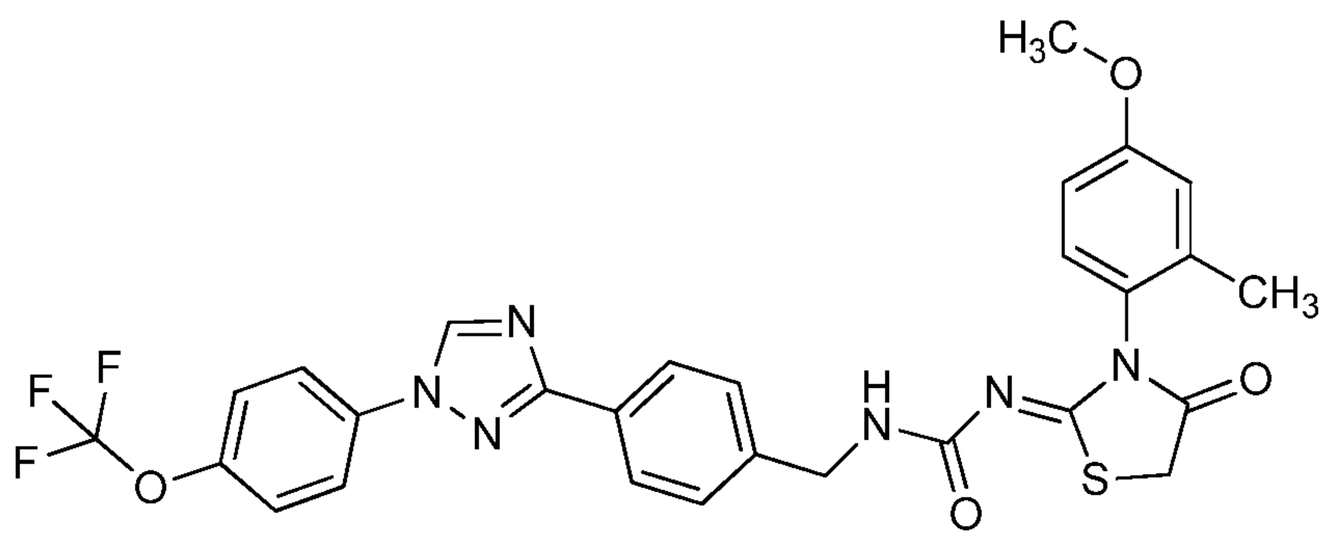
The title compound was prepared as described in Example 72 using 1-[(2-ethyl-5-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC7**) and isolated as an off-white solid (0.034 g, 44%).

Preparation of (*Z*)-1-(3-(5-methyl-2-propylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P8, P852)



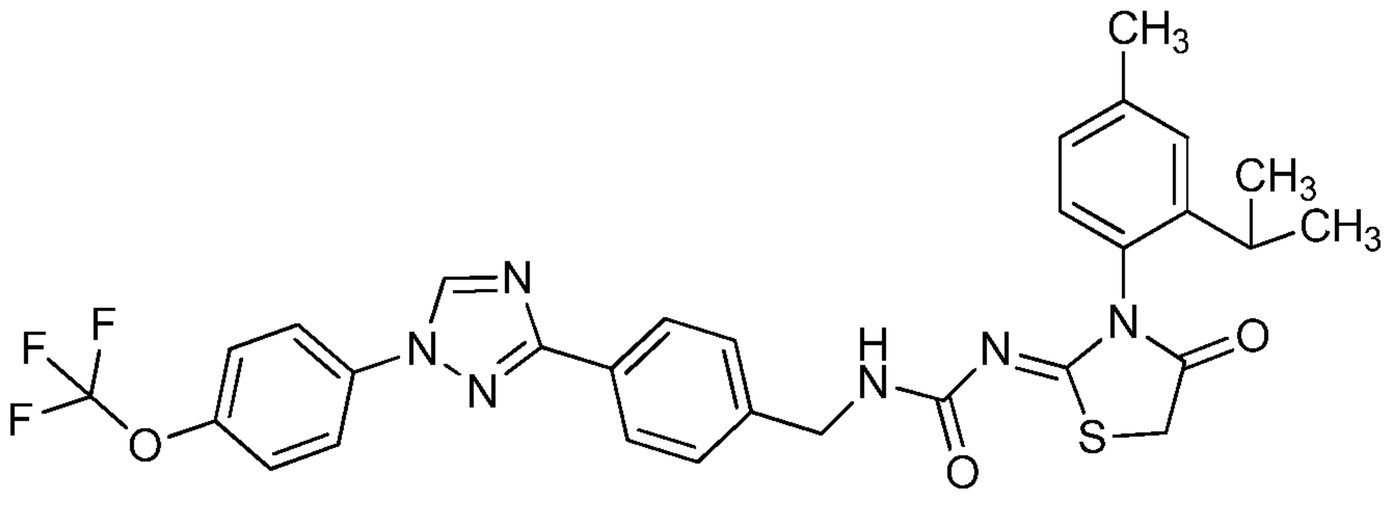
The title compound was prepared as described in Example 72 using 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC8**) and isolated as an off-white solid (0.018 g, 25%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P6)



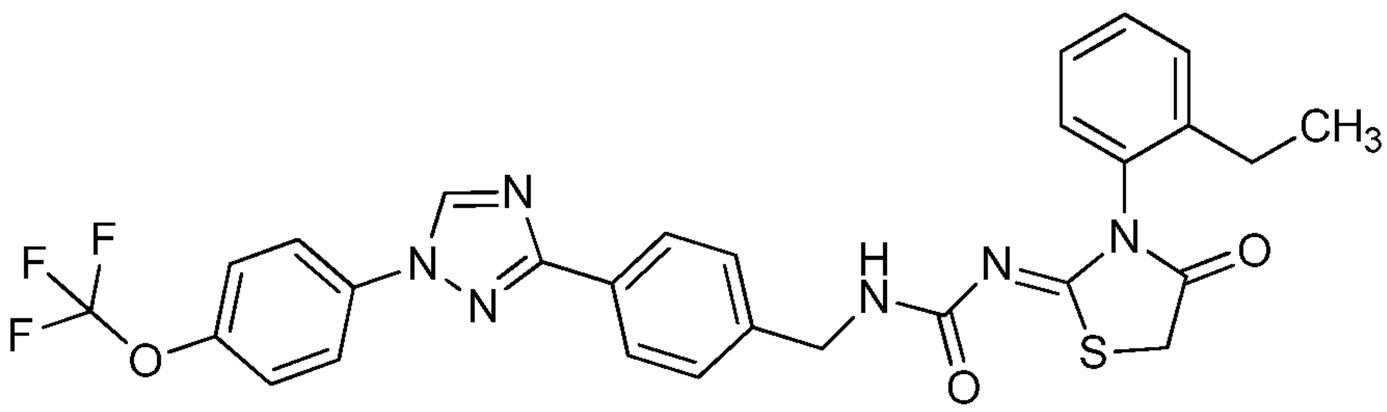
The title compound was prepared as described in Example 72 using 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC6**) and isolated as an off-white solid (0.041 g, 46%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P5)



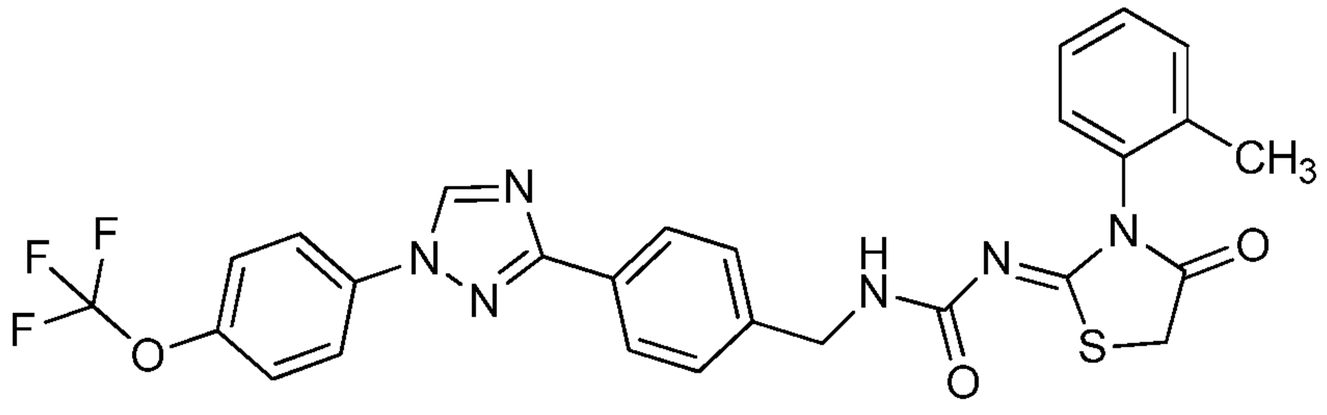
The title compound was prepared as described in Example 72 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC5**) and isolated as an off-white solid (0.012 g, 25%).

Preparation of (*Z*)-1-(3-(2-ethylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P2, P532)



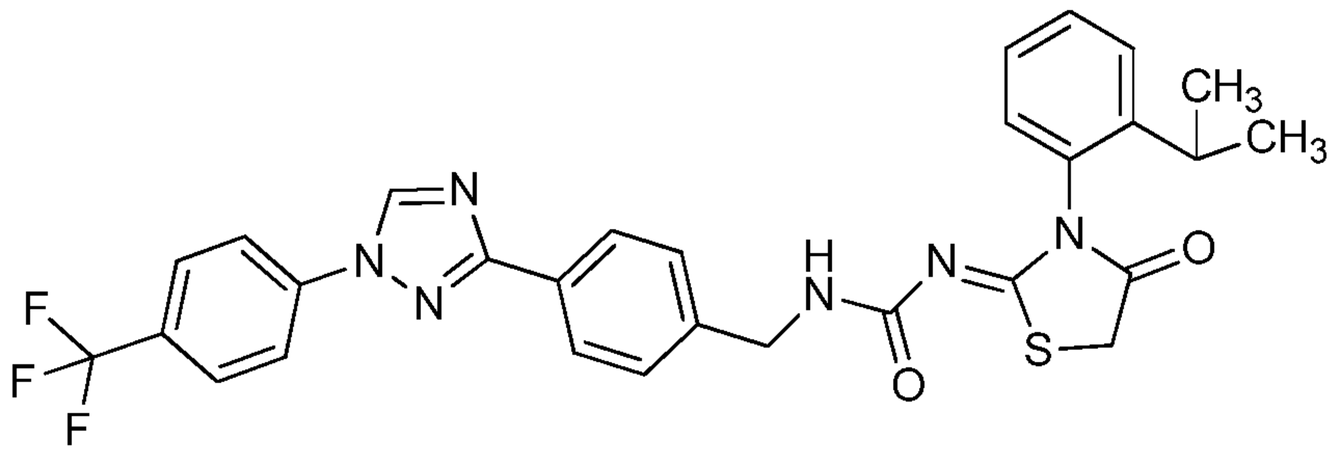
The title compound was prepared as described in Example 72 using 1-[(2-ethylphenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC2**) and isolated as a white solid (0.031 g, 28%).

Preparation of (*Z*)-1-(4-oxo-3-(*o*-tolyl)thiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P1)



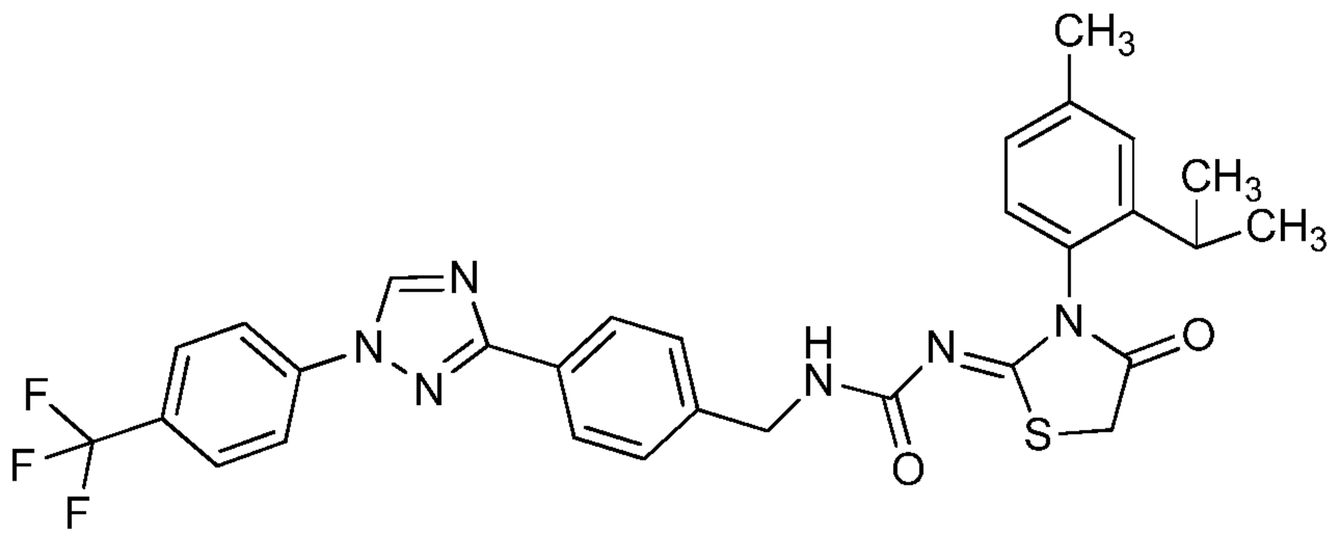
The title compound was prepared as described in Example 72 using 1-(*o*-tolylcarbamothioyl)-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC1**) and ethanol as solvent and isolated as a white solid (0.086 g, 79%).

Preparation of (*Z*)-1-(3-(2-isopropylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P14)



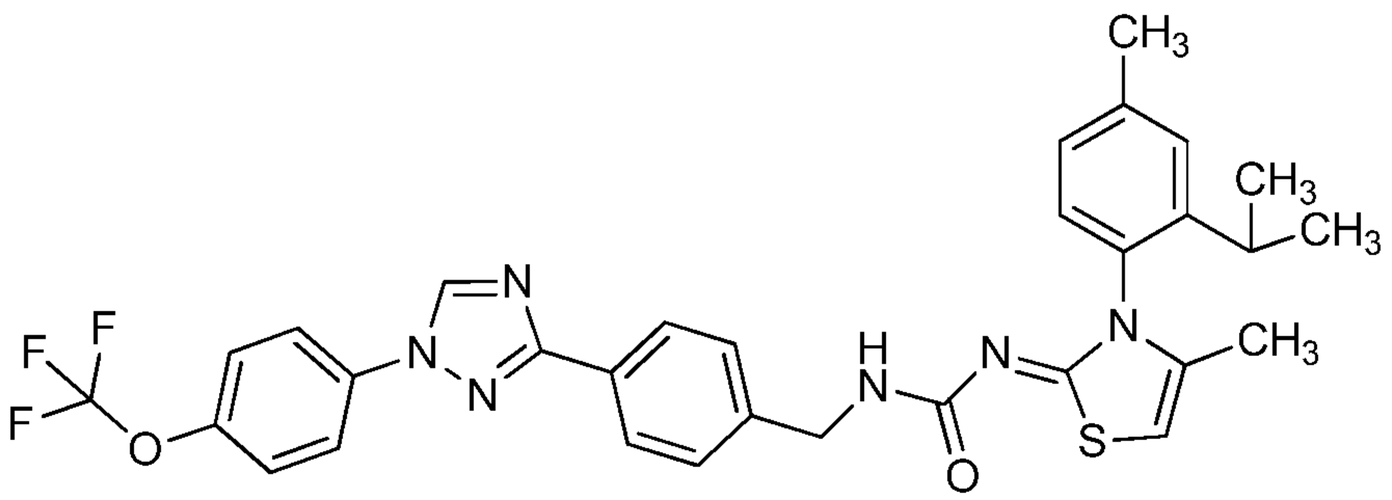
The title compound was prepared as described in Example 72 using 1-[(2-isopropylphenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethyl)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC14**) and ethanol as solvent and isolated as a white solid (0.055 g, 69%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P15)



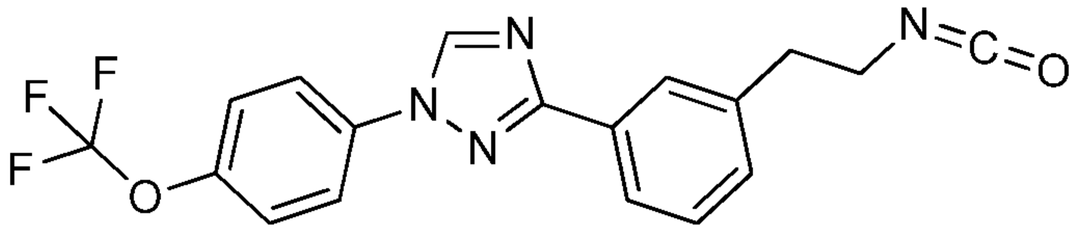
The title compound was prepared as described in Example 72 using 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethyl)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC15**) and ethanol as solvent and isolated as a white solid (0.049 g, 80%).

Example 73: Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-methylthiazol-2(3*H*)-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)urea (P20)



To a 20 mL vial was added 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[4-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (**PC5**) (0.044 g, 0.077 mmol), sodium acetate (0.019 g, 0.23 mmol), 1-chloropropan-2-one (0.0092 mL, 0.12 mmol) and acetonitrile (1.5 mL). The vial was sealed and heated overnight at 65 °C. The reaction mixture was diluted with brine solution and dichloromethane and passed through a phase separator. The organic layer was concentrated and the resulting residue was purified by flash column chromatography using 10-80% ethyl acetate/hexanes as eluent providing the title compound as an off-white solid (0.010 g, 21%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (s, 1H), 8.14 - 8.01 (m, 4H), 7.70 (s, 1H), 7.62 (dq, J = 7.7, 1.0 Hz, 2H), 7.45 - 7.35 (m, 2H), 7.34 - 7.27 (m, 1H), 7.15 (t, J = 1.3 Hz, 2H), 6.66 (q, J = 0.9 Hz, 1H), 4.47 - 4.28 (m, 2H), 2.73 - 2.62 (m, 1H), 2.39 (s, 3H), 2.10 (d, J = 1.1 Hz, 3H), 1.10 (d, J = 6.8 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 607 ([M+H]$^+$).

Example 74: Preparation of 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (CA44)

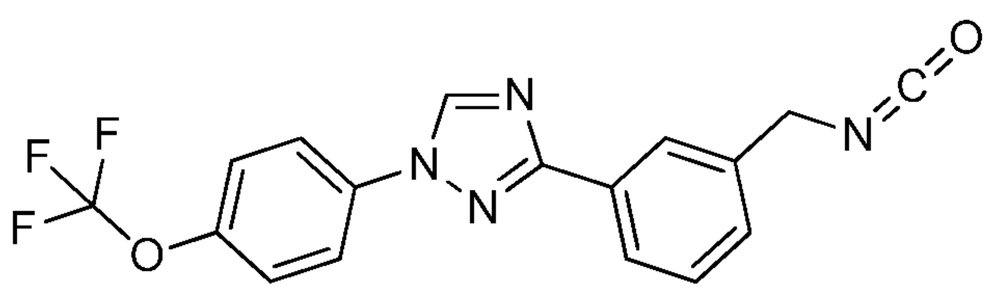


To a suspension of 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**CA13**) (3.0 g, 8.0 mmol) and triethylamine (1.1 mL, 8.0 mmol) in toluene (80 mL) in a 200 mL round bottomed flask was added diphenyl phosphorazidate (1.7 mL, 8.0 mmol). The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated on to Celite®. Purification by flash column chromatography using 0-50% ethyl acetate/hexanes as

eluent provided a pale yellow oil (1.8 g) which was stored overnight. The oil, which was determined by ^{1}H NMR to be a mixture of acyl azide and isocyanate solidified over time and was stored an additional night under vacuum. The resultant solid was dissolved in 1,2-dichloroethane (50 mL) 1,2-dichloroethane and heated at 60 °C for 3 hours. The solvent was concentrated to give the title compound (1.8 g, 59%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 8.13 - 8.06 (m, 2H), 8.06 - 7.98 (m, 2H), 7.63 (dq, J = 7.9, 1.0 Hz, 2H), 7.49 (td, J = 7.6, 0.6 Hz, 1H), 7.41 (dt, J = 7.7, 1.3 Hz, 1H), 3.66 (t, J = 6.6 Hz, 2H), 2.99 (t, J = 6.7 Hz, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97.

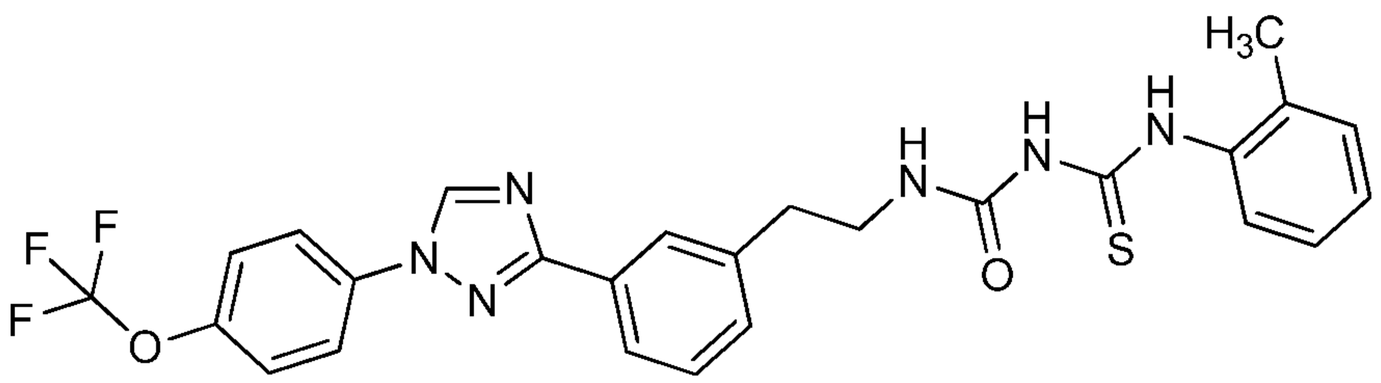
The following compounds were prepared in accordance to the procedure in Example 74.

Preparation of 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (CB34)



The title compound was prepared as described in Example 74 using 2-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)acetic acid (**CB23**) and isolated as a white solid (2.41 g, 48%, 85% pure): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.43 (s, 1H), 8.17 - 8.03 (m, 4H), 7.65 - 7.44 (m, 4H), 4.73 (s, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.00; ESIMS *m/z* 361 ([M+H]$^+$).

Example 75: Preparation of 1-(*o*-tolylcarbamothioyl)-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H* -1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC74)

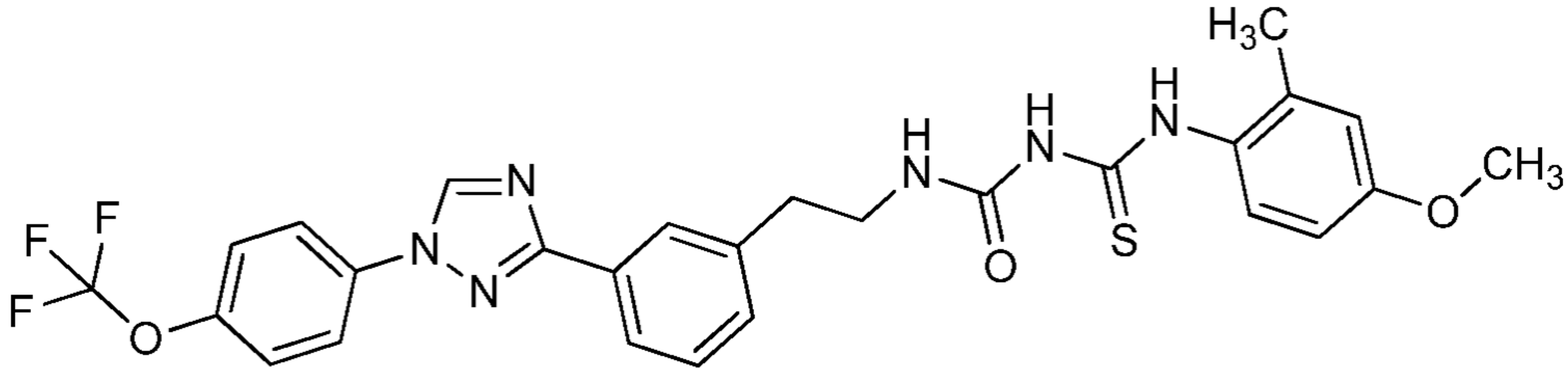


To a 20 mL vial, 1-(*o*-tolyl)thiourea (0.096 g, 0.58 mmol) and cesium carbonate (0.22 g, 0.68 mmol) were charged as solids. Then 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**)

(0.20 g, 0.52 mmol) in acetonitrile (4.0 mL) was added. The reaction was allowed to stir at room temperature overnight. The reaction mixture was diluted with dichloromethane and filtered through a phase separator. The filtrate was purified by flash column chromatography using 0-50% ethyl acetate/hexanes as eluent followed by flash column chromatography using 10-50% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent to provide the title compound as a white solid (0.11 g, 37%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 10.12 (s, 1H), 9.42 (s, 1H), 8.13 - 8.05 (m, 2H), 8.04 - 7.96 (m, 2H), 7.66 - 7.54 (m, 3H), 7.54 - 7.46 (m, 1H), 7.39 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.29 - 7.24 (m, 1H), 7.24 - 7.14 (m, 2H), 7.03 (t, *J* = 5.6 Hz, 1H), 3.46 (q, *J* = 6.6 Hz, 2H), 2.96 - 2.84 (m, 2H), 2.20 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 541 ([M+H]$^+$), 539 ([M-H]$^-$).

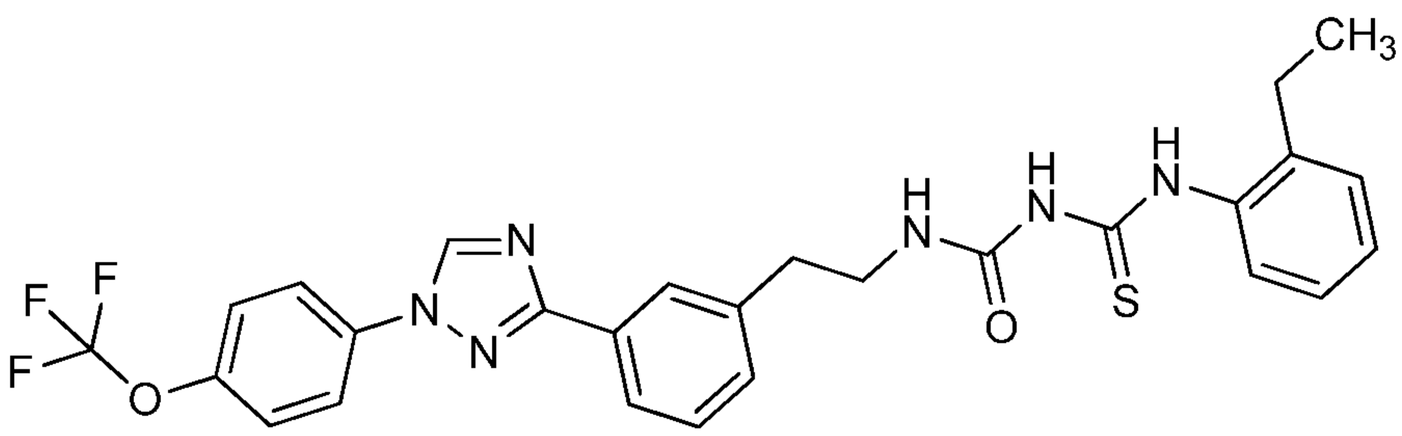
The following compounds were prepared in accordance to the procedure in Example 75.

Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC87)



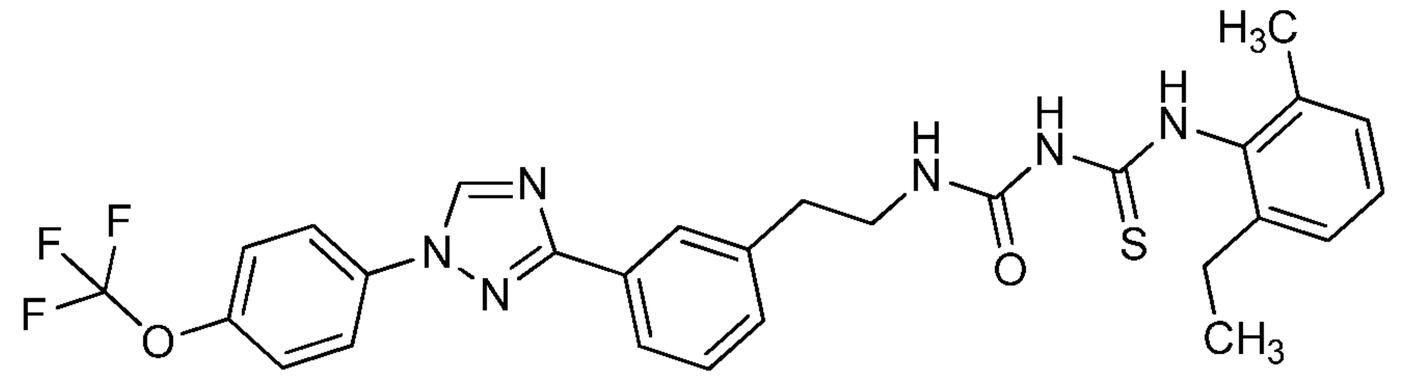
The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(4-methoxy-2-methylphenyl)thiourea isolated as a white solid (0.105 g, 34%):^{1}H NMR (400 MHz, DMSO-d_6) δ 11.78 (s, 1H), 10.07 (s, 1H), 9.42 (s, 1H), 8.13 - 8.05 (m, 2H), 8.04 - 7.96 (m, 2H), 7.66 - 7.57 (m, 2H), 7.53 - 7.45 (m, 1H), 7.42 - 7.32 (m, 2H), 7.01 (t, *J* = 5.7 Hz, 1H), 6.85 - 6.81 (m, 1H), 6.76 (dd, *J* = 8.7, 2.9 Hz, 1H), 3.74 (s, 3H), 3.45 (q, *J* = 6.6 Hz, 2H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.15 (s, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 517 ([M+H]$^+$), 569 [(M-H)$^+$].

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC75)



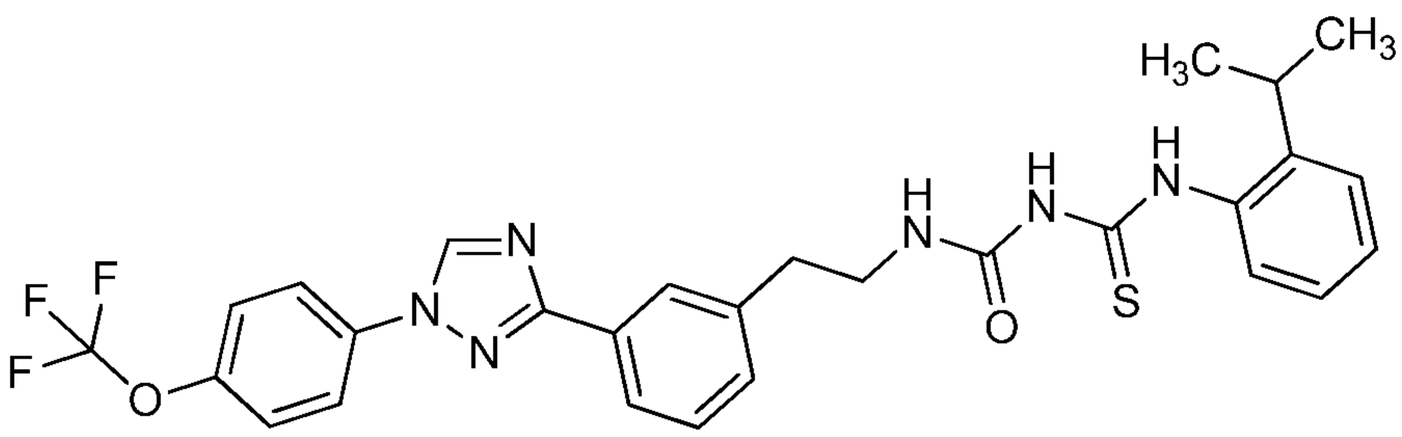
The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(2-ethylphenyl)thiourea isolated as a white solid (0.104 g, 35%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 10.13 (s, 1H), 9.42 (s, 1H), 8.15 - 8.05 (m, 2H), 8.05 - 7.96 (m, 2H), 7.67 - 7.57 (m, 2H), 7.56 - 7.45 (m, 2H), 7.39 (dt, J = 7.7, 1.4 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.25 - 7.17 (m, 2H), 7.09 - 6.96 (m, 1H), 3.47 (q, J = 6.5 Hz, 2H), 2.89 (t, J = 6.9 Hz, 2H), 2.58 - 2.51 (m, 2H), 1.11 (t, J = 7.5 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 555 ([M+H]$^{+}$), 553 ([M-H]$^{-}$).

Preparation of 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC83)



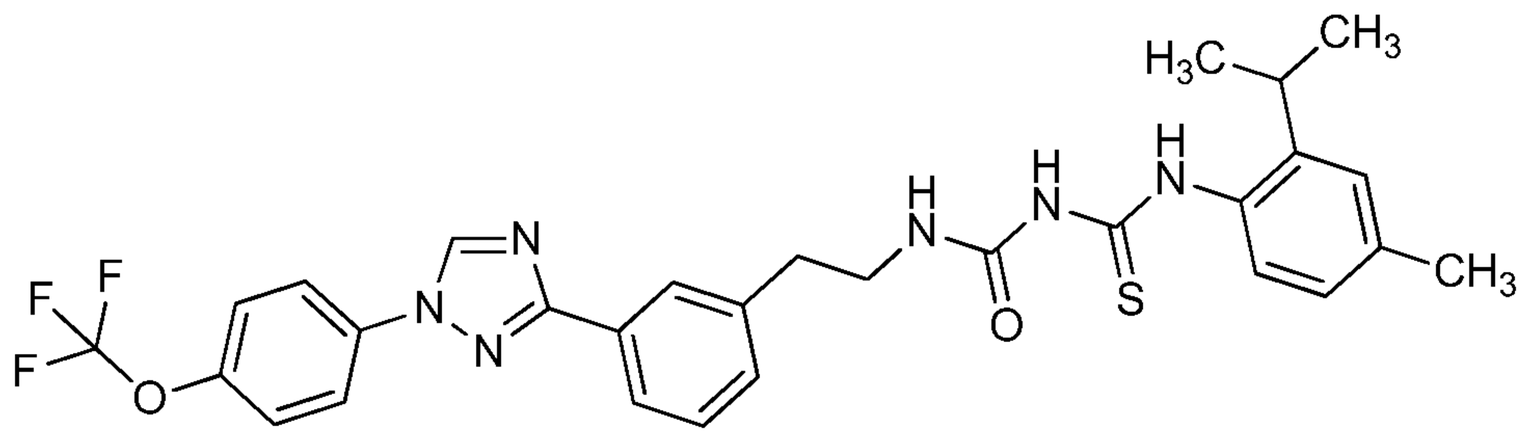
The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) isolated as a white solid (0.137 g, 45%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.58 (s, 1H), 10.13 (s, 1H), 9.42 (s, 1H), 8.16 - 8.05 (m, 2H), 8.05 - 7.96 (m, 2H), 7.62 (ddd, J = 7.9, 2.0, 1.0 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.39 (dt, J = 7.7, 1.4 Hz, 1H), 7.21 - 7.12 (m, 1H), 7.13 - 7.05 (m, 2H), 7.00 (t, J = 5.7 Hz, 1H), 3.47 (q, J = 6.7 Hz, 2H), 2.90 (t, J = 6.9 Hz, 2H), 2.47 (dd, J = 7.6, 2.9 Hz, 2H), 2.14 (s, 3H), 1.14 - 1.08 (m, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 569 ([M+H]$^{+}$), 567 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC76)



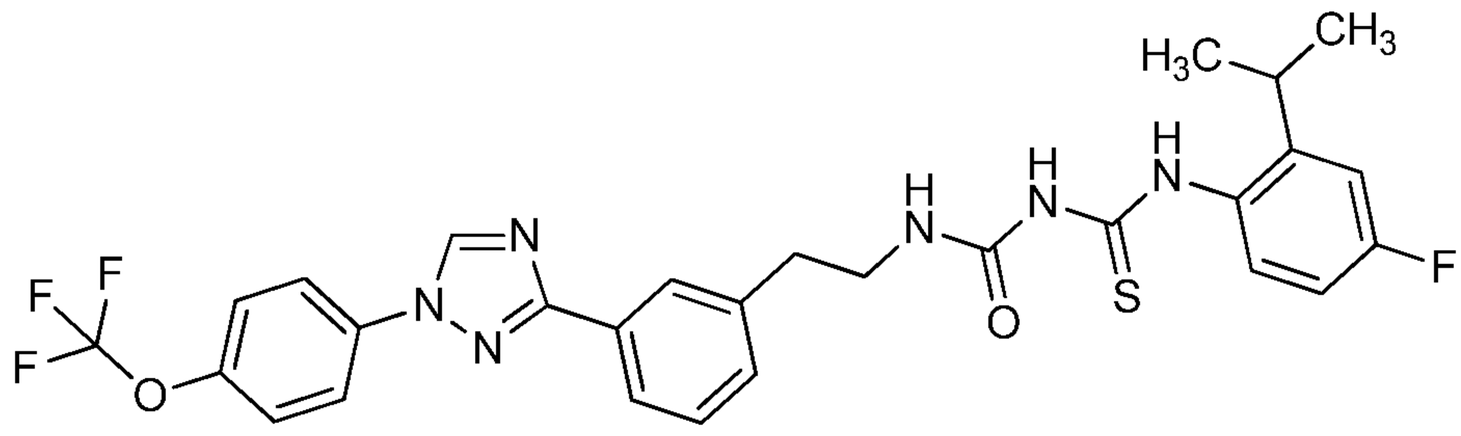
The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(2-isopropylphenyl)thiourea isolated as a white solid (0.033 g, 11%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 10.14 (s, 1H), 9.42 (s, 1H), 8.14 - 8.05 (m, 2H), 8.05 - 7.94 (m, 2H), 7.68 - 7.57 (m, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.39 (dq, J = 7.8, 1.5 Hz, 2H), 7.34 (dd, J = 7.8, 1.6 Hz, 1H), 7.26 (td, J = 7.5, 1.5 Hz, 1H), 7.20 (td, J = 7.5, 1.6 Hz, 1H), 7.03 (t, J = 5.7 Hz, 1H), 3.47 (q, J = 6.6 Hz, 2H), 2.98 (p, J = 6.9 Hz, 1H), 2.89 (t, J = 6.9 Hz, 2H), 1.15 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 569 ([M+H]$^{+}$), 567 ([M-H]$^{-}$).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC84)



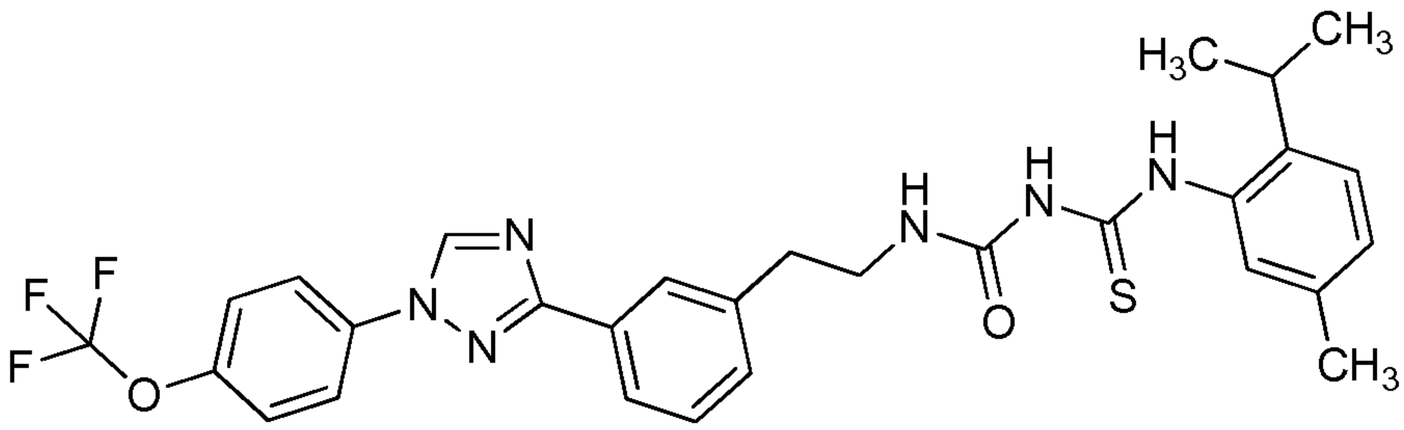
The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(2-isopropyl-4-methylphenyl)thiourea isolated as a white solid (0.077 g, 25%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H), 10.10 (s, 1H), 9.42 (s, 1H), 8.15 - 8.05 (m, 2H), 8.04 - 7.96 (m, 2H), 7.61 (ddd, J = 7.9, 2.0, 1.0 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.39 (dt, J = 7.7, 1.4 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.16 - 7.11 (m, 1H), 7.05 - 6.96 (m, 2H), 3.46 (q, J = 6.7 Hz, 2H), 2.91 (dt, J = 17.9, 6.9 Hz, 3H), 2.30 (s, 3H), 1.14 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 583 ([M+H]$^{+}$), 581 ([M-H]$^{-}$).

Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC85)



The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(4-fluoro-2-isopropylphenyl)thiourea isolated as a white solid (0.085 g, 27%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 10.17 (s, 1H), 9.42 (s, 1H), 8.14 - 8.05 (m, 2H), 8.05 - 7.95 (m, 2H), 7.68 - 7.58 (m, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.43 - 7.31 (m, 2H), 7.15 (dd, J = 10.3, 3.0 Hz, 1H), 7.03 (td, J = 8.3, 2.9 Hz, 2H), 3.47 (q, J = 6.6 Hz, 2H), 3.01 - 2.82 (m, 3H), 1.14 (d, J = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97 , -114.40; ESIMS m/z 587 ([M+H]$^{+}$), 585 ([M-H]$^{-}$).

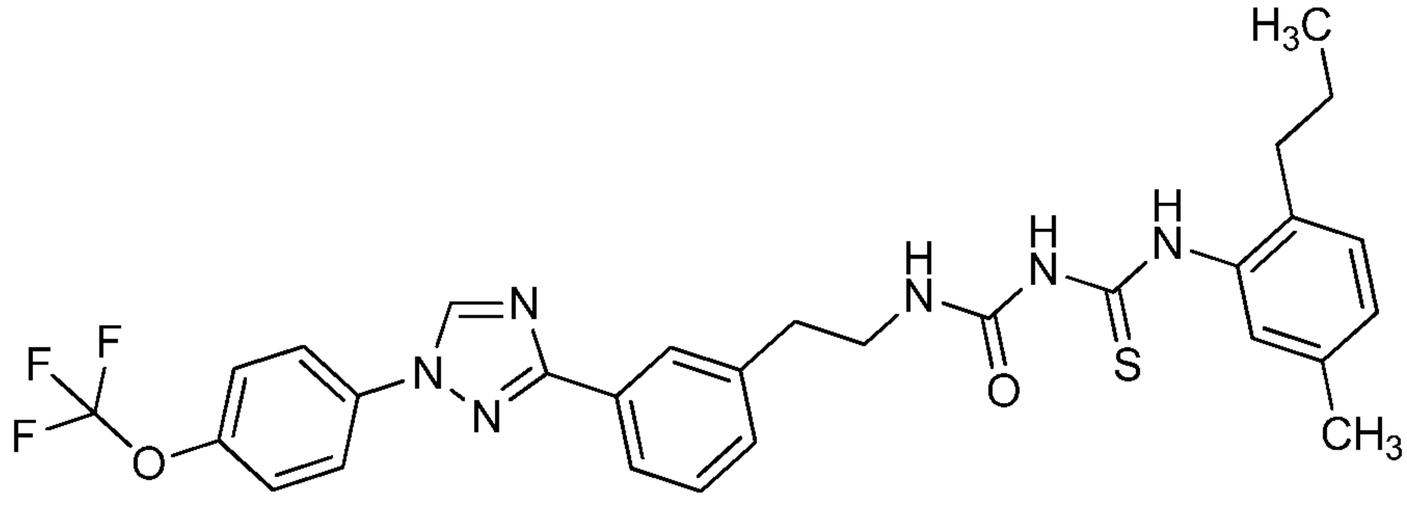
Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC81)



The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(2-isopropyl-5-methylphenyl)thiourea isolated as an off-white solid (0.019 g, 6%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 10.12 (s, 1H), 9.42 (s, 1H), 8.14 - 8.05 (m, 2H), 8.05 - 7.96 (m, 2H), 7.62 (ddd, J = 7.8, 1.9, 0.9 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.39 (dt, J = 7.7, 1.5 Hz, 1H), 7.24 - 7.17 (m, 2H), 7.12 - 7.05 (m, 1H), 7.02 (t, J = 5.8 Hz, 1H), 3.52 - 3.42 (m, 2H), 2.91 (dt, J = 14.1, 6.9 Hz, 3H), 2.25 (s, 3H),

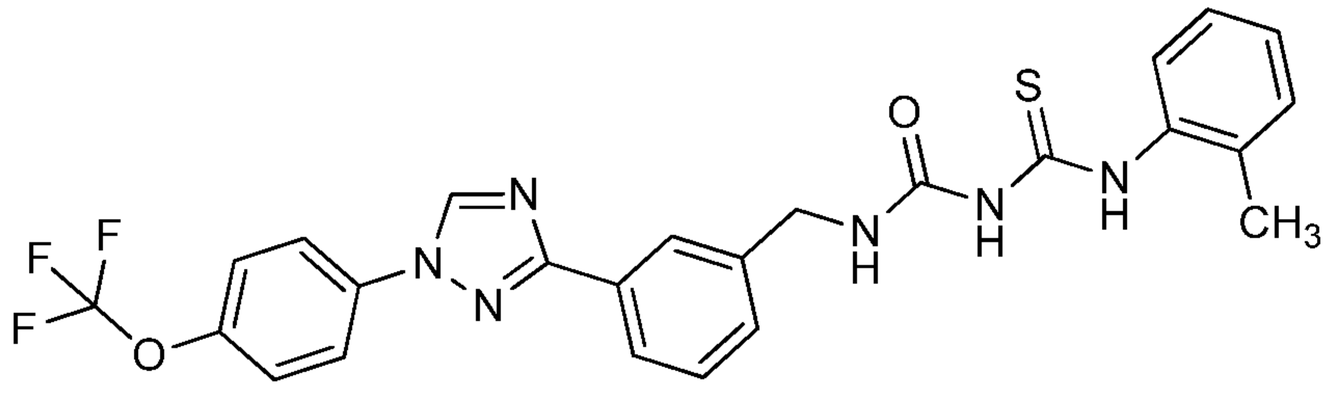
1.13 (d, *J* = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 583($[M+H]^+$), 581 ($[M-H]^-$).

Preparation of 1-[(5-methyl-2-propyl-phenyl)carbamothioyl]-3-[2-[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]ethyl]urea (PC80)



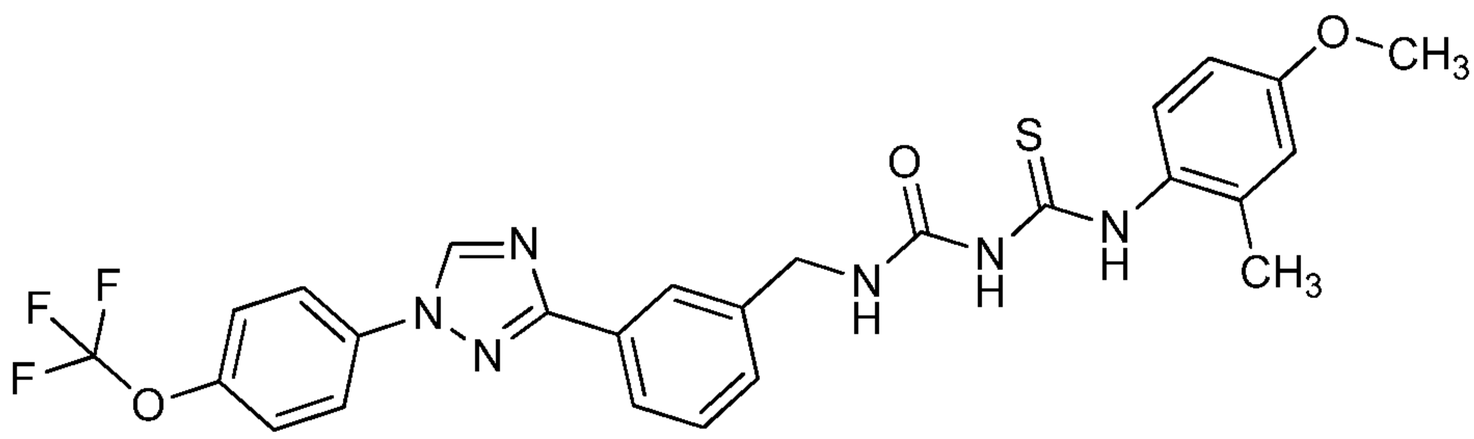
The title compound was prepared as described in Example 75 using 3-(3-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CA44**) and 1-(5-methyl-2-propylphenyl)thiourea (**CA38**) isolated as a white solid (0.107 g, 34%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.99 (s, 1H), 10.09 (s, 1H), 9.42 (s, 1H), 8.14 - 8.05 (m, 2H), 8.05 - 7.95 (m, 2H), 7.61 (dd, *J* = 8.6, 1.3 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.44 - 7.34 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.07 - 6.97 (m, 2H), 3.46 (q, *J* = 6.5 Hz, 2H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.48 - 2.39 (m, 2H), 2.26 (s, 3H), 1.54 - 1.42 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.96; ESIMS *m/z* 583 ($[M+H]^+$), 581 ($[M-H]^-$).

Preparation of 1-(*o*-tolylcarbamothioyl)-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB18)



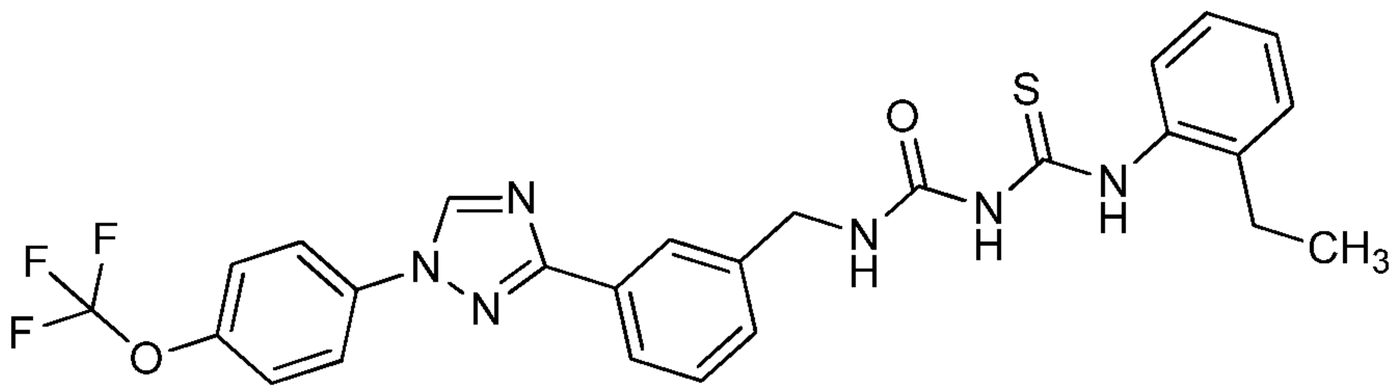
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(*o*-tolyl)thiourea and isolated as an off-white solid (0.148 g, 37%).

Preparation of 1-[(4-methoxy-2-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB19)



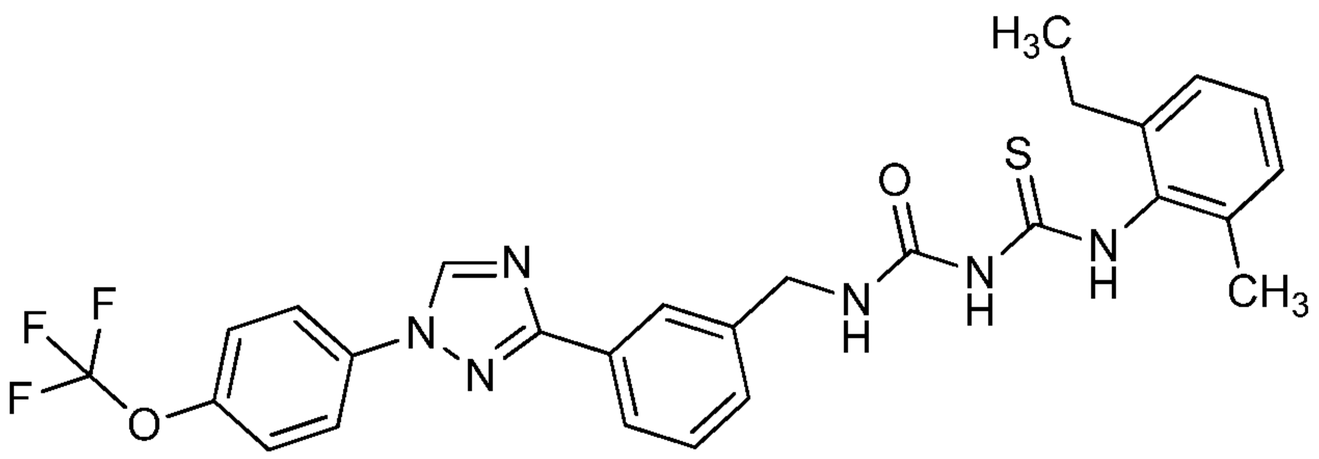
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as an off-white solid (0.212 g, 50%).

Preparation of 1-[(2-ethylphenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB20)



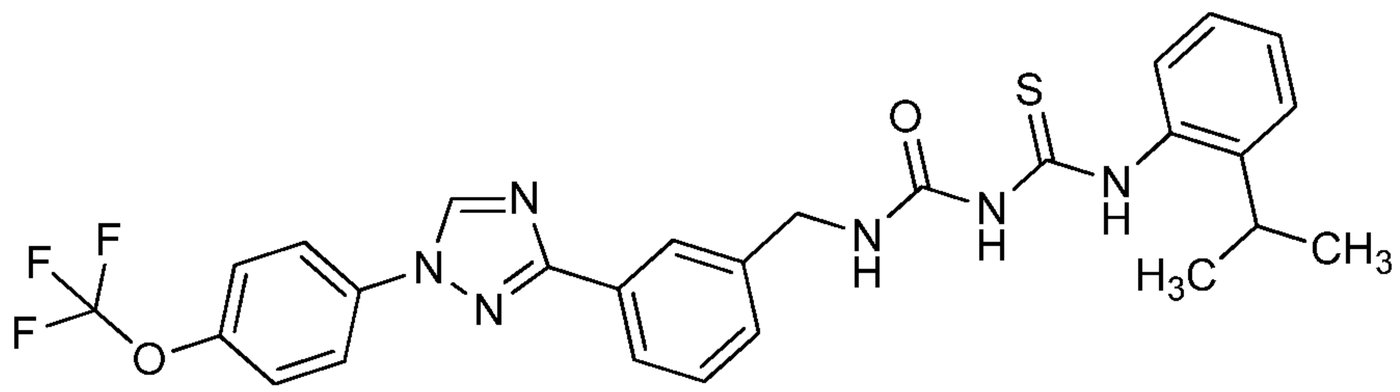
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(2-ethylphenyl)thiourea and isolated as an off-white solid (0.152 g, 37%).

Preparation of 1-[(2-ethyl-6-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB21)



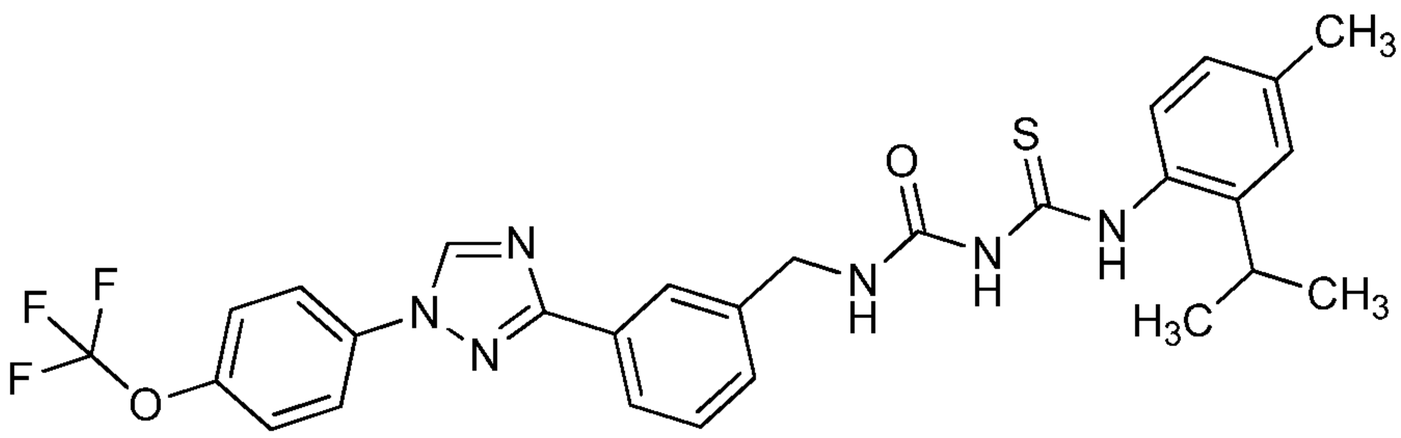
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(2-ethyl-6-methylphenyl)thiourea (**CA39**) and isolated as an off-white solid (0.212 g, 50%).

Preparation of 1-[(2-isopropylphenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB22)



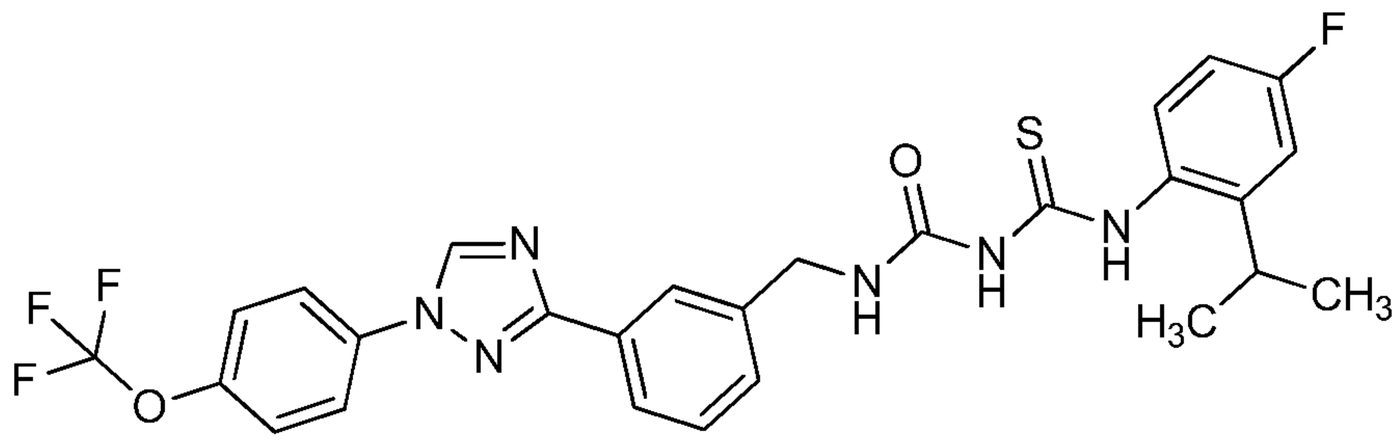
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(2-isopropylphenyl)thiourea and isolated as an off-white solid (0.213 g, 47%).

Preparation of 1-[(2-isopropyl-4-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB23)



The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as an off-white solid (0.216 g, 50%).

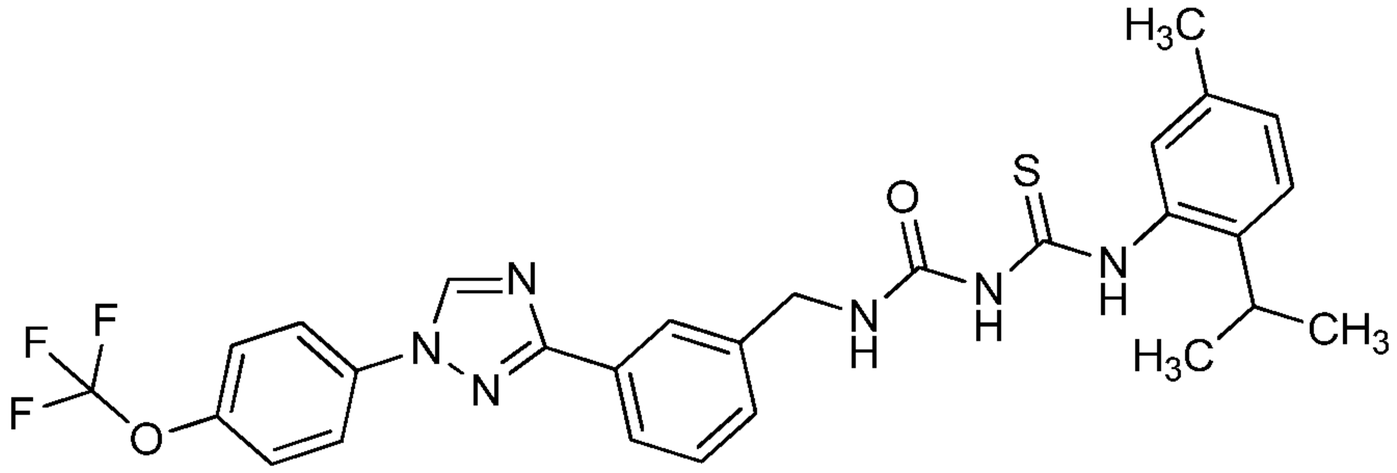
Preparation of 1-[(4-fluoro-2-isopropyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB24)



The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**)

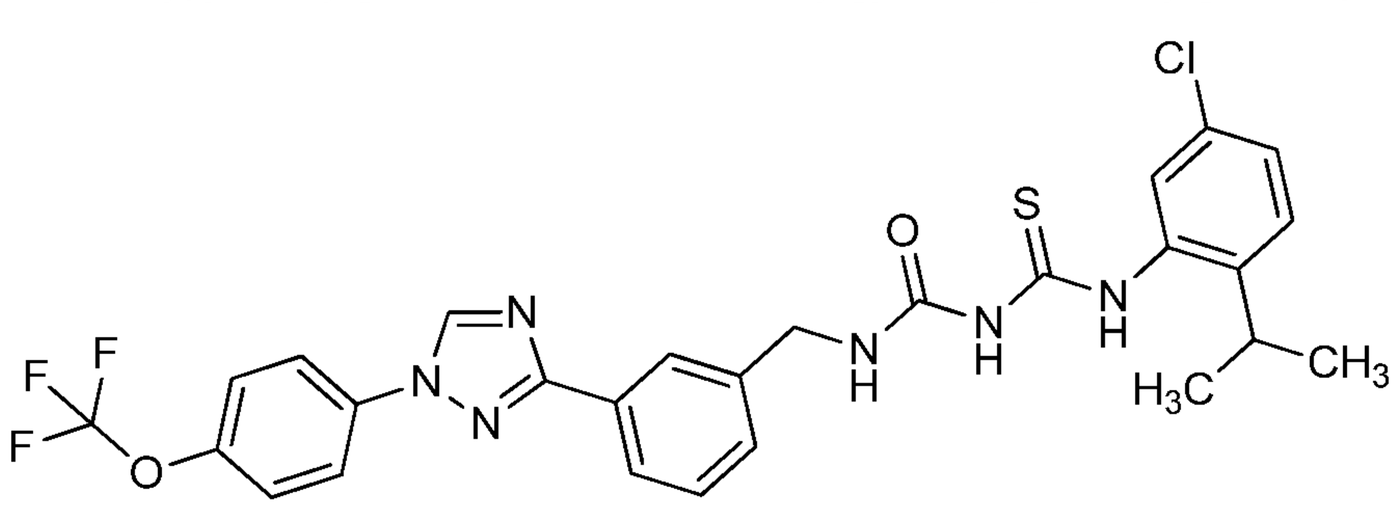
and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as an off-white solid (0.242 g, 56%).

Preparation of 1-[(2-isopropyl-5-methyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB25)



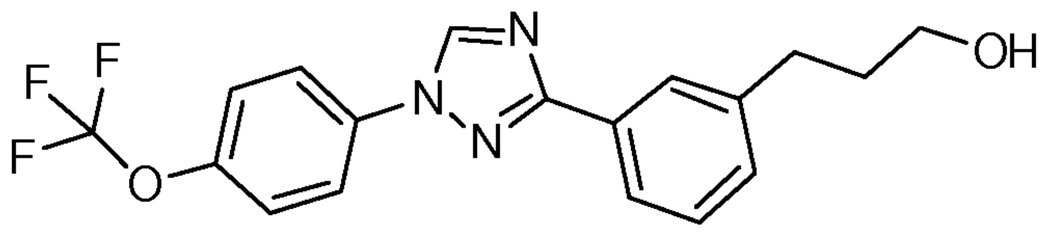
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as an off-white solid (0.181 g, 42%).

Preparation of 1-[(5-chloro-2-isopropyl-phenyl)carbamothioyl]-3-[[3-[1-[4-(trifluoromethoxy)phenyl] -1*H*-1,2,4-triazol-3-yl]phenyl]methyl]urea (FB26)



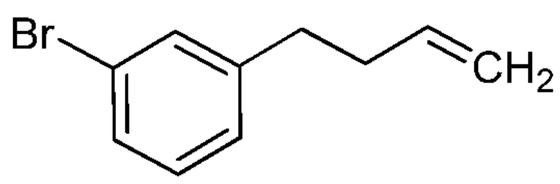
The title compound was prepared as described in Example 75 using 3-(3-(isocyanatomethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB34**) and 1-(5-chloro-2-isopropylphenyl)thiourea (**CB32**) and isolated as an off-white solid (0.170 g, 38%).

Example 76: Preparation of 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-ol (CA45)



In a 500 mL round bottomed flask 3-(3-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoic acid (**CA13**) (5.68 g, 15.1 mmol) was dissolved in tetrahydrofuran (151 mL). The reaction was cooled in an ice water bath and placed under inert atmosphere. Aluminum(III) lithium hydride (2.0 M in tetrahydrofuran, 15.8 mL, 31.6 mmol) was added dropwise. The reaction was allowed to gradually warm to room temperature and stir overnight. The reaction was cooled in an ice bath and water (1.2 mL) was added dropwise to quench excess aluminum(III) lithium hydride, the reaction mixture was allowed to stir for 1 hour. Then sodium hydroxide (15 wt %, 1.2 mL) was added dropwise. The reaction was allowed to stir for 1 hour. Then water (3.6 mL) was added. The resulting precipitate was removed *via* filtration. The filtrate was concentrated to give a yellow solid (5.20 g). The solid was purified by flash column chromatography using 0-60% ethyl acetate/hexanes as eluent providing the title compound as a white solid (4.01 g, 72%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.18 - 8.04 (m, 2H), 7.99 - 7.89 (m, 2H), 7.68 - 7.57 (m, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.32 (dt, J = 7.7, 1.5 Hz, 1H), 4.51 (t, J = 5.2 Hz, 1H), 3.45 (td, J = 6.4, 5.1 Hz, 2H), 2.71 (dd, J = 8.8, 6.7 Hz, 2H), 1.87 - 1.70 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -56.97; ESIMS *m/z* 364 ([M+H]$^+$).

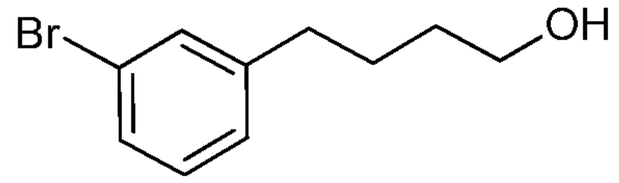
Example 77: Preparation of 1-bromo-3-(but-3-en-1-yl)benzene (CA46)



To a solution of 1-bromo-3-(bromomethyl)benzene (10.0 g, 40.0 mmol) in tetrahydrofuran (50 mL), under an inert atmosphere was added allylmagnesium bromide (1.0 M in diethyl ether, 40.0 mL, 40.0 mmol). The reaction was allowed to reflux overnight. The reaction was quenched with sulfuric acid (2 M, 45 mL). The resulting biphasic solution was solution was partitioned. The aqueous layer was extracted with diethyl ether (2 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The resulting residue was purified by flash column chromatography using 100% hexanes as eluent providing the title compound as a clear liquid (7.51 g, 71%, ~80% pure): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.42 (ddd, J = 2.1, 1.4, 0.7 Hz, 1H), 7.37 (dt, J = 7.1, 2.1 Hz, 1H), 7.28 - 7.18 (m, 2H), 5.81 (ddt, J = 16.9, 10.2, 6.5 Hz, 1H), 5.09 - 4.90 (m, 2H), 2.67 (dd, J =

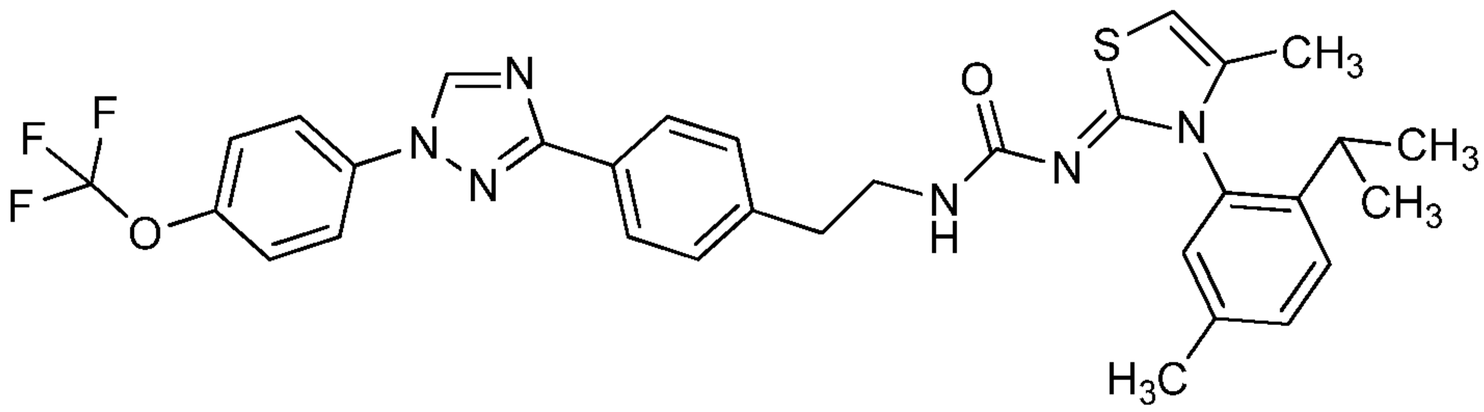
8.6, 6.8 Hz, 2H), 2.32 (tdt, *J* = 7.7, 6.5, 1.5 Hz, 2H); 13C NMR (101 MHz, DMSO-d_6) δ 144.35, 137.61, 131.05, 130.28, 128.62, 127.44, 121.53, 115.37, 34.59, 33.91; EIMS *m/z* 210 ($[M]^+$).

Example 78: Preparation of 4-(3-bromophenyl)butan-1-ol (CA47)



To a solution of 1-bromo-3-(but-3-en-1-yl)benzene (**CA46**) (7.51 g, 35.6 mmol) in hexanes (80 mL) was added (1*S*,5*S*)-9-borabicyclo[3.3.1]nonane (0.5 M in tetrahydrofuran, 74.7 mL, 37.4 mmol). The reaction was allowed to stir at room temperature overnight. To the resulting clear solution sodium hydroxide (6.0 M, 5.93 mL, 35.6 mmol) was added dropwise. The reaction was placed in an ice water bath and hydrogen peroxide (13.8 mL, 135 mmol) was added. The resulting mixture was then heated to an internal temperature of 50 °C for overnight. The reaction mixture was cooled to room temperature. The biphasic solution was partitioned, and the organic layer was washed with sodium bisulfite, and brine solution. The combined aqueous layers were made basic with saturated sodium carbonate, and extracted with diethyl ether (2 x 100 mL). The combined organics were dried over magnesium sulfate, filtered, and concentrated. The liquid was loaded on to silica and purified by flash column chromatography using 0-40% ethyl acetate/hexanes as eluent providing the title compound as a clear liquid (7.50 g, 90%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40 (t, *J* = 1.9 Hz, 1H), 7.37 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.28 - 7.17 (m, 2H), 4.39 (t, *J* = 5.2 Hz, 1H), 3.40 (td, *J* = 6.5, 5.2 Hz, 2H), 2.57 (t, *J* = 7.6 Hz, 2H), 1.65 - 1.51 (m, 2H), 1.49 - 1.35 (m, 2H); EIMS *m/z* 228 ($[M]^+$).

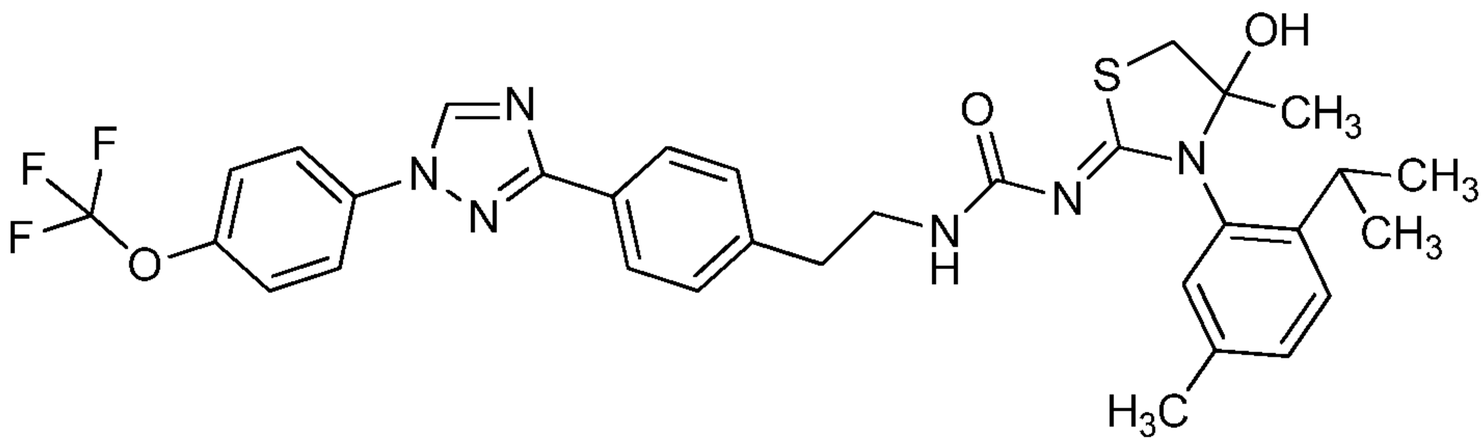
Example 79: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-methylthiazol-2(3*H*)-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P65)



To *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) (0.23 g, 0.40 mmol) in butanone (4 mL) was added triethylamine (0.060 mL, 0.43 mmol) and chloroacetone (0.035 mL,0.44 mmol) and heated at 80 ℃ overnight. The reaction was cooled, diluted with water, extracted dichloromethane (2x), and filtered through a phase separator. The organic layer was concentrated and loaded onto Celite® cartridge with dichloromethane. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes as eluent, followed by drying in a vacuum oven provided the title compound as an orange solid (0.085 g, 34%).

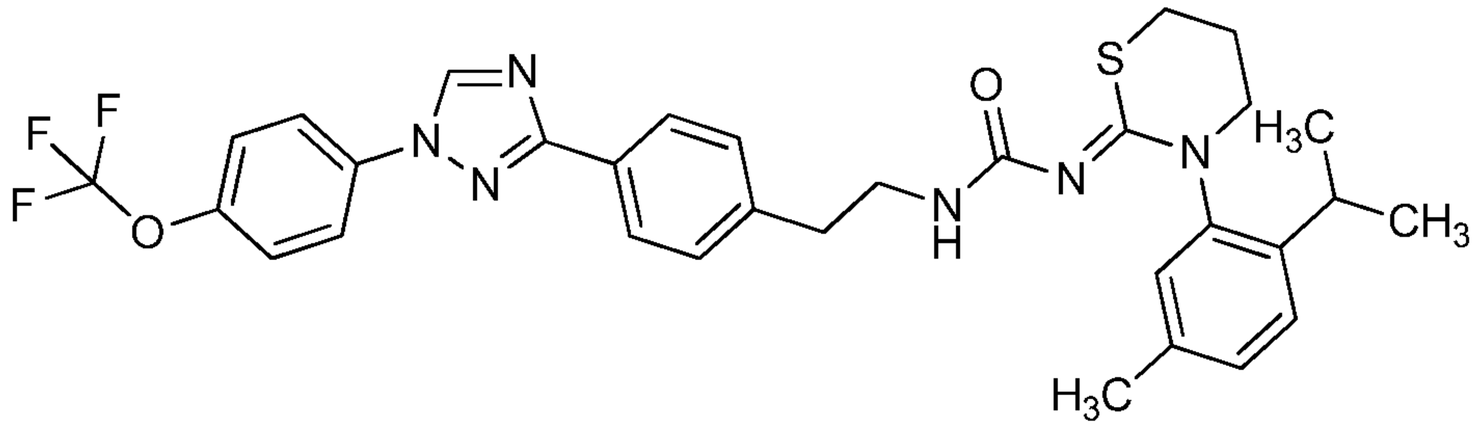
The following compounds were prepared in accordance to the procedure in Example 79.

Preparation of (*Z*)-1-(4-hydroxy-3-(2-isopropyl-5-methylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB67)



The title compound was prepared as described in Example 79 using *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) and sodium acetate as base at room temperature; purified by reverse-phase flash column chromatography using 0-100 % acetonitrile/water as eluent and isolated as a clear oil (0.036 g, 33%).

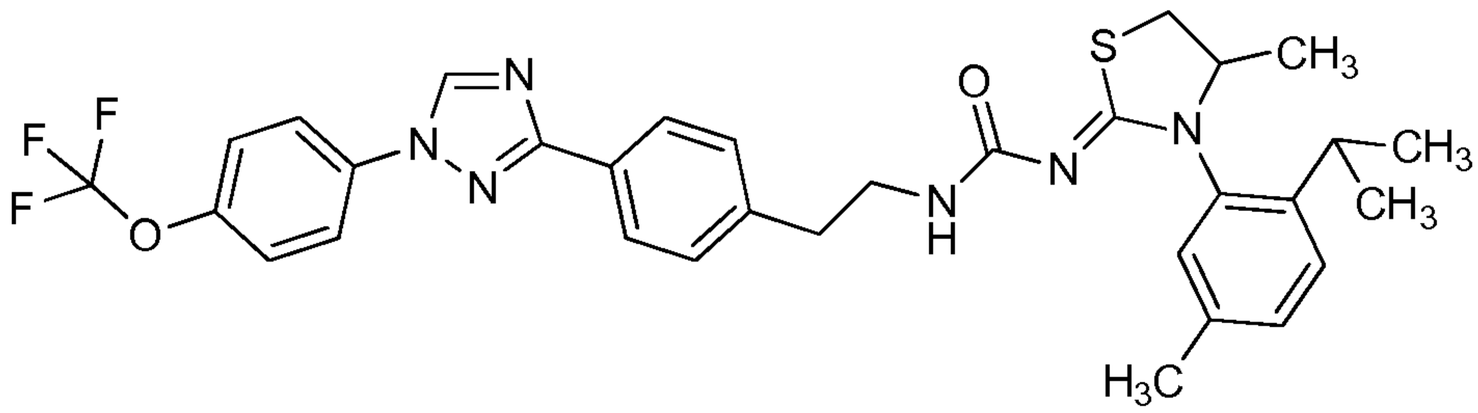
Example 80: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-1,3-thiazinan-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P59)



To *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) (181 mg, 0.31 mmol) and potassium carbonate (0.064 g, 0.47 mmol) in butanone (3.1 mL) was added 1-bromo-3-chloropropane (0.050 mL, 0.47 mmol). The reaction was heated at 60 °C overnight. The reaction mixture was cooled, diluted with water, extracted with dichloromethane (2x), and filtered through a phase separator. The organic layer was concentrated and loaded onto a Celite® cartridge with dichloromethane. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes as eluent, followed by reverse-phase flash column chromatography using 0-100% acetonitrile/water as eluent and drying in a vacuum oven provided the title compound as a white solid (0.032 g, 16%).

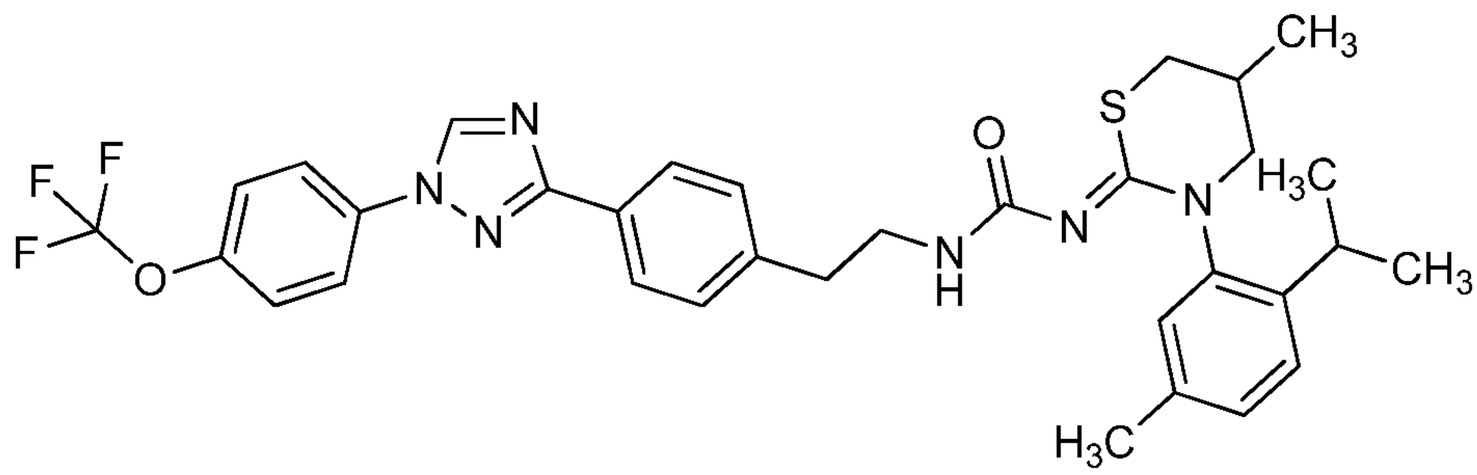
The following compounds were prepared in accordance to the procedure in Example 80.

Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P58)



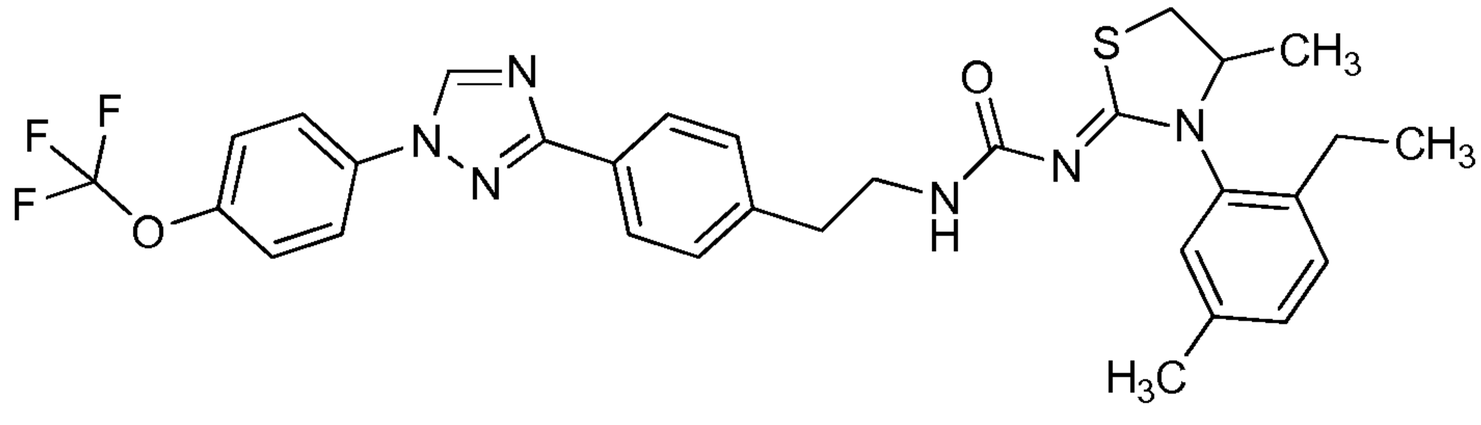
The title compound was prepared as described in Example 80 using *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) and 1,2-dibromopropane at 80 ºC and isolated as a yellow oil (0.050 g, 26%).

Preparation of (Z)-1-(3-(2-isopropyl-5-methylphenyl)-5-methyl-1,3-thiazinan-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (P64)



The title compound was prepared as described in Example 80 using *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) and 1-bromo-3-chloro-2-methylpropane and isolated as a white solid (0.061 g, 14%).

Example 80a: Preparation of (*Z*)-1-(3-(2-ethyl-5-methylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB55)

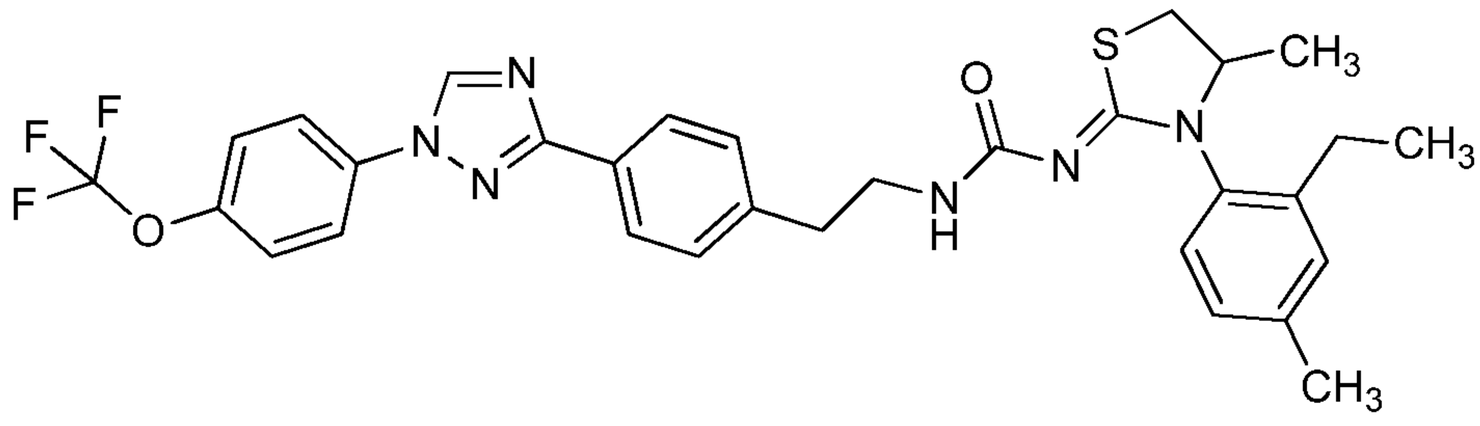


3-(4-(2-Isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**)(0.16 g, 0.42 mmol), 1-(2-ethyl-5-methylphenyl)thiourea (**CA41**) (0.081 g, 0.42 mmol), and cesium carbonate (0.13 g, 0.39 mmol) in acetonitrile (1.9 mL) was stirred at room temperature for 3 hours. The reaction was diluted with butanone (2 mL) and potassium carbonate (0.12 g, 0.83 mmol) and 1,2-dibromopropane (0.090 mL, 0.83 mmol) were added. The reaction was heated to 60

℃ for 6 hours. The reaction was diluted with water and extracted with dichloromethane (2x) and the organic layers were filtered through a phase separator and concentrated. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided the title compound as a yellow oil (0.034 g, 13%).

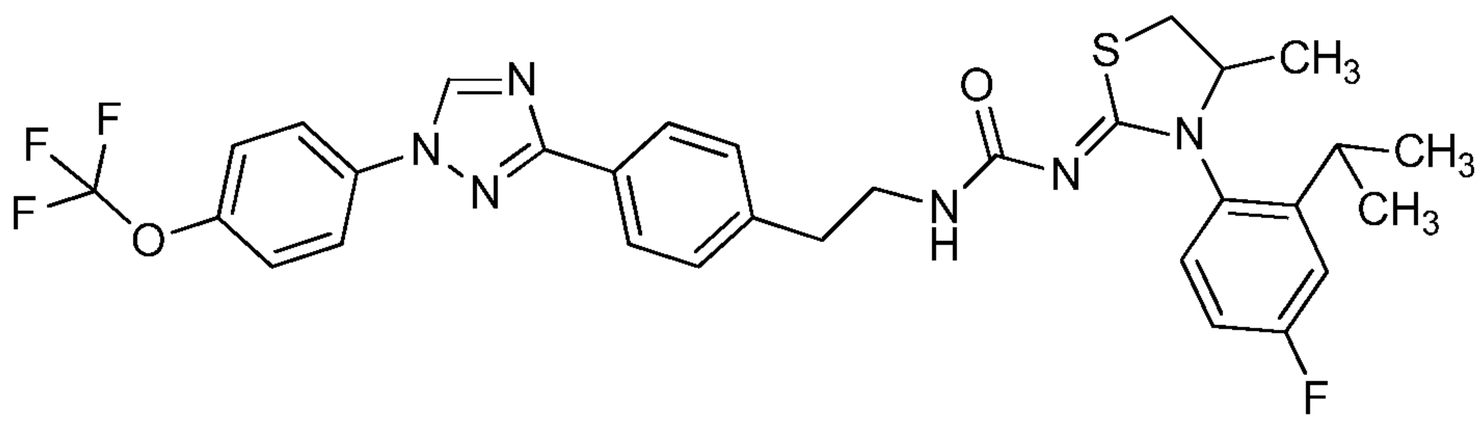
The following compounds were prepared in accordance to the procedure in Example 80a.

Preparation of (*Z*)-1-(3-(2-ethyl-4-methylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB56)



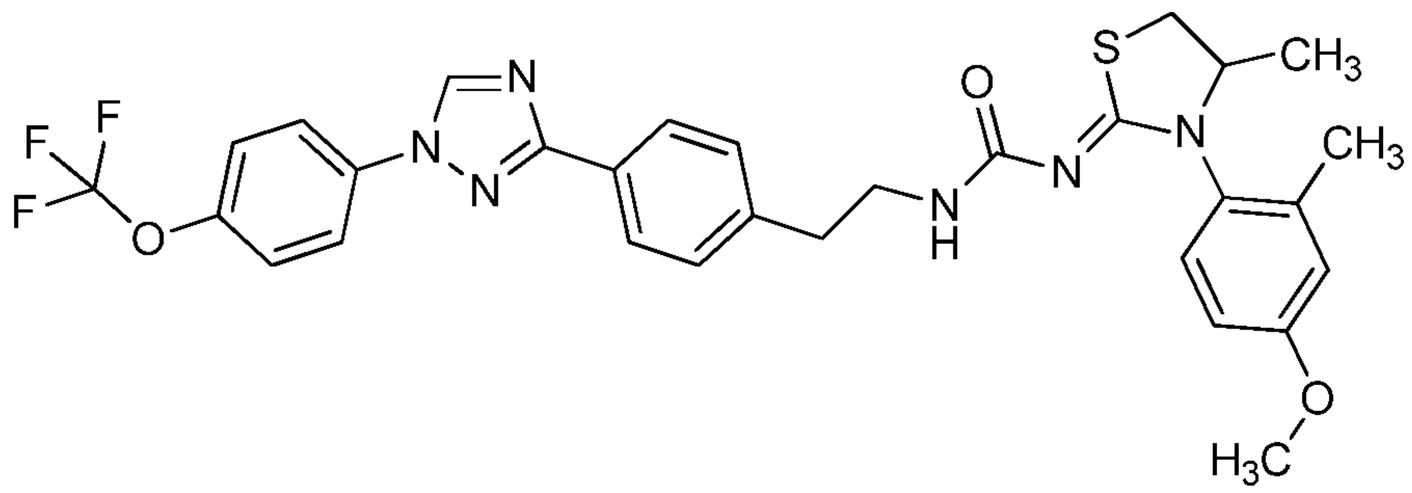
The title compound was prepared as described in Example 80a using 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and 1-(2-ethyl-4-methylphenyl)thiourea (**CA42**) isolated as a yellow oil (0.040 g, 16%).

Preparation of (*Z*)-1-(3-(4-fluoro-2-isopropylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB57)



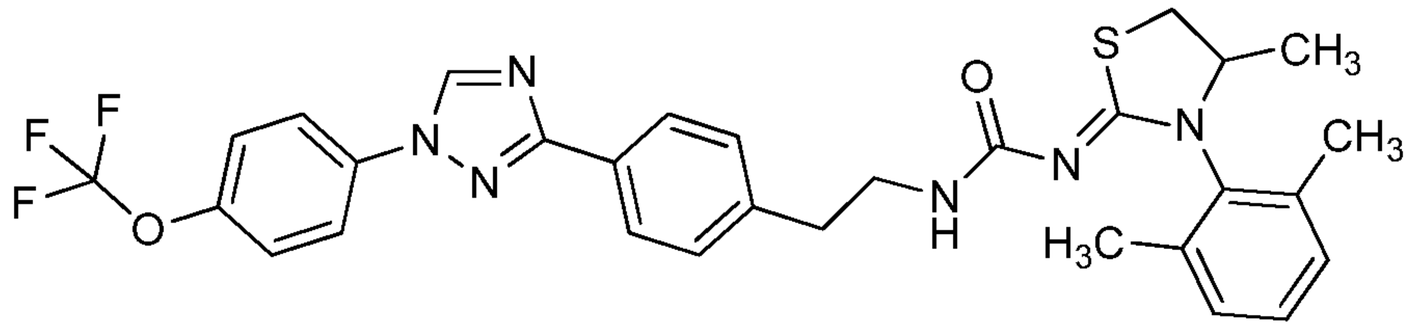
The title compound was prepared as described in Example 80a using 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and 1-(4-fluoro-2-isopropylphenyl)thiourea and isolated as a yellow oil (0.056 g, 22%).

Preparation of (*Z*)-1-(3-(4-methoxy-2-methylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB58)



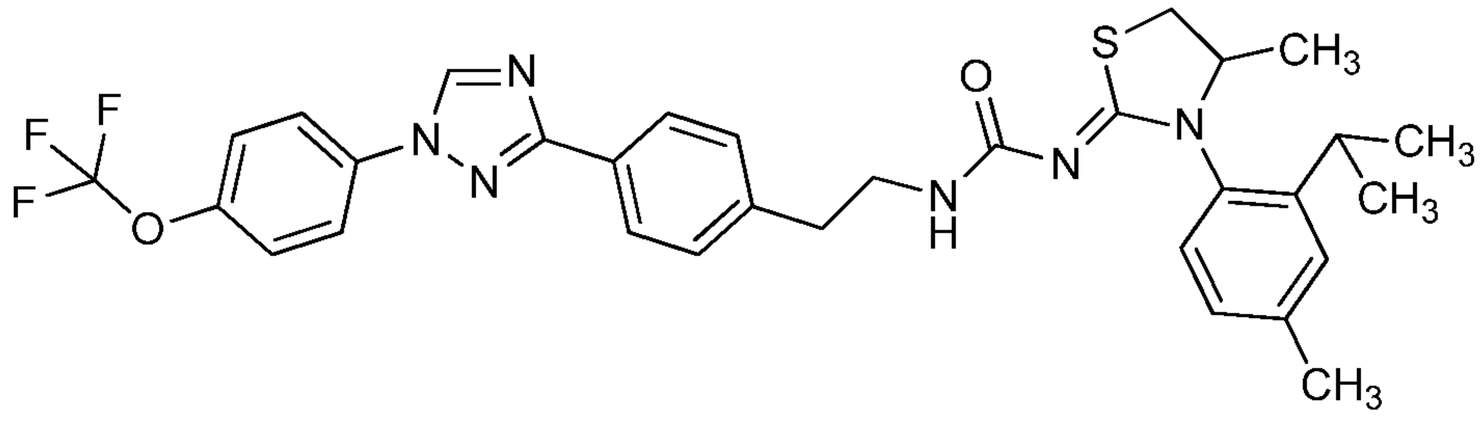
The title compound was prepared as described in Example 80a using 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and 1-(4-methoxy-2-methylphenyl)thiourea and isolated as a yellow oil (0.054 g, 21%).

Preparation of (Z)-1-(3-(2,6-dimethylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB59)



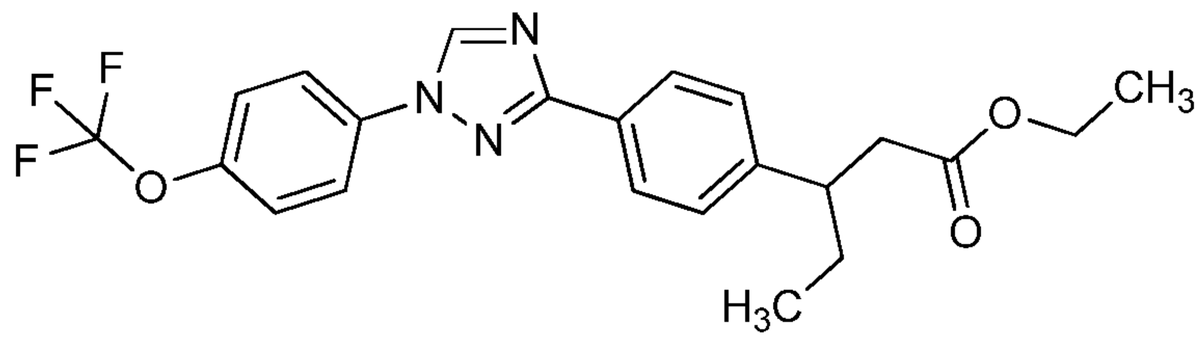
The title compound was prepared as described in Example 80a using 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and 1-(2,6-dimethylphenyl)thiourea and isolated as a clear oil (0.044 g, 18%).

Preparation of (*Z*)-1-(3-(2-isopropyl-4-methylphenyl)-4-methylthiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB60)



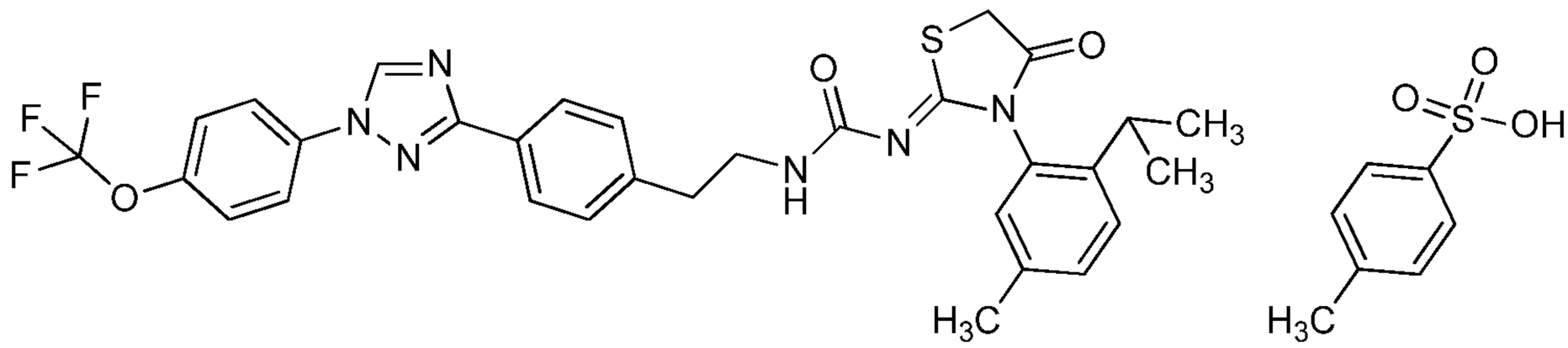
The title compound was prepared as described in Example 80a using 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) and 1-(2-isopropyl-4-methylphenyl)thiourea and isolated as a yellow foam (0.047 g, 17%).

Example 81: Preparation of ethyl 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)pentanoate (CA48)



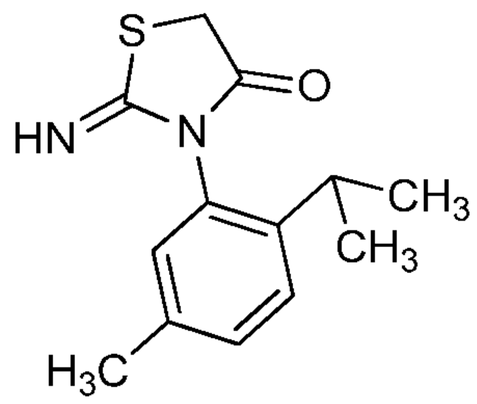
Sodium hydride (60% immersion in oil, 0.32 g, 7.9 mmol) was weighed into an oven-dried three neck round bottomed flask. The flask was placed under nitrogen and tetrahydrofuran (44 mL) was added. The stirring mixture was placed in an ice bath. Triethylphosphonoacetate (1.4 mL, 6.9 mmol) was added and the mixture was stirred for 2 hours. Added 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-one (**CA7**) (2.4 g, 6.5 mmol) as a solid and warmed to room temperature overnight. The reaction was diluted with water and extracted with ethyl acetate/hexanes (1:1, 2x). The organic layers were dried over sodium sulfate, filtered, and concentrated. To the crude residue was added palladium on carbon (10 wt%, 0.70 g, 0.66 mmol) and dissolved in ethyl acetate (20 mL). The reaction was stirred under hydrogen by balloon overnight. The reaction mixture was filtered through Celite® and concentrated to give the title compound as a brown liquid (2.7 g, 90%):^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 0.6 Hz, 1H), 8.11 (dd, *J* = 8.1, 6.0 Hz, 2H), 7.83 - 7.76 (m, 2H), 7.38 (dq, *J* = 7.9, 1.0 Hz, 2H), 7.35 - 7.27 (m, 2H), 4.24 - 4.14 (m, 1H), 4.04 (qd, *J* = 7.1, 1.6 Hz, 1H), 3.13 - 2.99 (m, 1H), 2.74 - 2.55 (m, 2H), 1.79 - 1.61 (m, 2H), 1.38 - 1.24 (m, 3H), 1.06 (dt, *J* = 72.0, 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 434 ($[M+H]^+$).

Example 82: Preparation of *para*-toluenesulfonic acid salt of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F5A)



To (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (**F5**) (4.82 g, 7.46 mmol) in a 250 mL round bottomed flask was added isopropanol (50 mL). The suspension was warmed to 50 °C and stirred for 20 minutes. Acetone (50 mL) was added. 4-Methylbenzenesulfonic acid hydrate (1.42 g, 7.46 mmol) dissolved in acetone (20 mL) and added to the above solution in a dropwise manner. The resulting clear light brown solution was concentrated at 50 °C. The resultant residue was dried in a vacuum oven at 50 °C overnight. The brown foam was transferred to a 500 mL round bottomed flask and dissolved in acetone (200 mL). The mixture was heated to reflux for 15 hours. The solution was concentrated providing the title compound as a dark gray foam (5.90 g, 95%).

Example 83: Preparation of 2-imino-3-(2-isopropyl-5-methylphenyl)thiazolidin-4-one (CA49)



Method A. To (1-(2-isopropyl-5-methylphenyl)thiourea (0.20 g, 0.96 mmol) in ethanol (8.0 mL) was added methyl bromoacetate (0.17 mL, 1.9 mmol) and sodium acetate (0.23 g, 2.8 mmol). The reaction was stirred overnight at room temperature. The solution was poured onto water and extracted with ethyl acetate (3x) and the organics were dried and concentrated to give the title compound as a red solid (0.24 g, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 7.9 Hz, 1H), 7.07 (dd, J = 8.3, 1.8

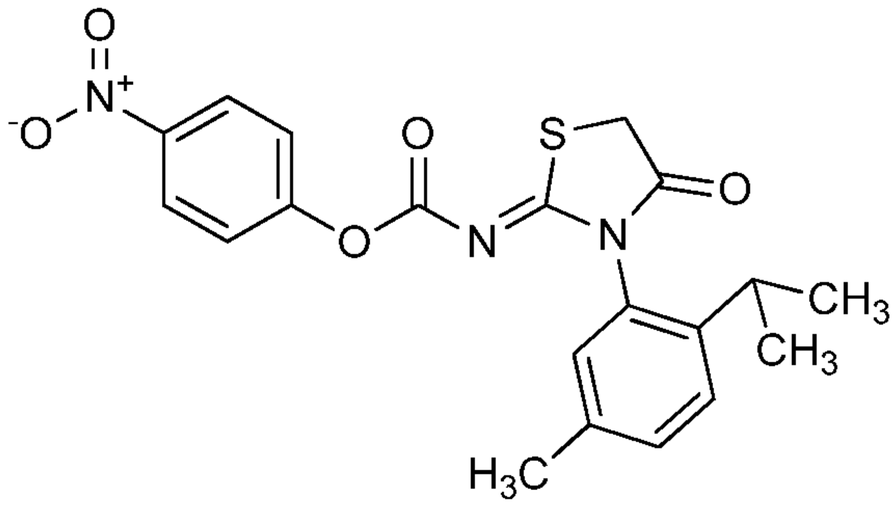
Hz, 1H), 6.85 (d, *J* = 1.6 Hz, 1H), 3.85 (d, *J* = 0.9 Hz, 2H), 3.03 (p, *J* = 6.9 Hz, 1H), 2.31 (t, *J* = 0.7 Hz, 4H), 1.15 (d, *J* = 6.9 Hz, 6H); ESIMS *m/z* 248 ($[M]^+$).

Method B, Step 1. 2-Isopropyl-5-methylaniline (286 g, 1.91 mol) and sodium bicarbonate (270 g, 3.22 mol) were charged in to a round bottomed flask with stirring under nitrogen atmosphere and cooled to 0 – 5 ºC. 2-Chloroacetyl chloride (218 g,1.93 mol) was added drop wise at 0 - 5 ºC over a period of 1 hour. The reaction was stirred at 0 – 5 ºC for 1 hour. After completion of the reaction, purified water (2.86 L) was added and stirred at 25 – 30 ºC for 15 minutes. The layers were then separated. The organic layer was washed with water (2 x 2.86 L) and with brine (1.43 L). The aqueous layers were combined and extracted with ethyl acetate (1.43 L). The organic layers were dried with sodium sulphate, filtered, and concentrated at 50 – 55 ºC under vacuum (500 – 600 mm Hg) to 2/5^{ths} volume. Hexanes (2.86 L) were added and the mixture was stirred at 25 – 30 ºC for 1 hour. The solid was filtered, washed with hexanes (1.43 L), and dried at 45 – 50 ºC under vacuum (500 – 600 mm Hg) to give 2-chloro-*N*-(2-isopropyl-5-methylphenyl)acetamide as an off-white solid (270 g, 66%): mp 97-99 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.60 (s, 1H), 7.20 (d, *J* = 7.95 Hz, 1H), 7.04 (d, *J* = 7.89 Hz, 1H), 4.25 (s, 2H), 2.99 (q, *J* = 6.78 Hz, 1H), 2.34 (s, 3H), 1.26 (d, *J* = 6.84 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.07, 137.28, 136.33, 132.95, 127.35, 125.62, 124.46, 43.21, 27.86, 22.98, 21.00; ESIMS *m/z* 226 ($[M+H]^+$).

Step 2. 2-Chloro-*N*-(2-isopropyl-5-methylphenyl)acetamide (290 g, 1.28 mol) and acetone (1.60 L) were charged in to a round bottomed flask with stirring under a nitrogen atmosphere. Potassium thiocyanate (250 g, 2.57 mol) was added in portions over a period of 30 minutes maintaining the temperature at 15 - 20 ºC. The reaction was stirred at 15 – 20 ºC for 10 minutes after which time the temperature was slowly raised 53 - 55 ºC and maintained at 53 - 55 ºC for 3 hours. The reaction was then cooled to 20 – 25 ºC, cesium carbonate (20.9 g, 0.0641 mol) was added, and the reaction mixture was stirred at 20 – 25 ºC for 30 minutes. After completion, the reaction mixture was filtered through Celite®, washed with acetone (1.45 L), and the filtrate collected. The filtrate was concentrated at 40 – 45 ºC under vacuum (500 – 600 mm Hg) providing a syrup. The syrup was dissolved in ethyl acetate (2.90 L),

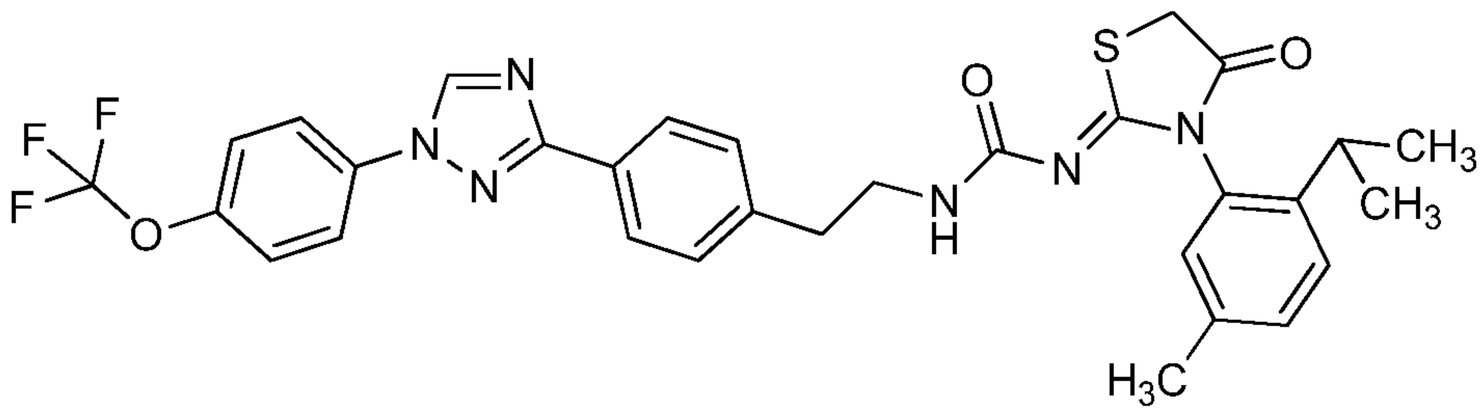
washed with water (2 x 2.90 L) and with brine (1.45 L). The organic layers were dried with sodium sulphate, filtered, and concentrated at 50 – 55 °C under vacuum (500 – 600 mm Hg) to provide the title compound as a dark brown syrup (345 g, 99%).

Example 84: Preparation of (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (CA50)



A round-bottomed flask was charged with 2-imino-3-(2-isopropyl-5-methylphenyl)thiazolidin-4-one (**CA49**) (1.30 g, 5.23 mmol), 4-Nitrophenyl chloroformate (1.06 g, 5.23 mmol) and cesium carbonate (1.71 g, 5.23 mmol) were dissolved in acetonitrile (13 mL). The reaction mixture was stirred at room temperature for 1.5 hours. The reaction was diluted with dichloromethane and adsorbed onto silica gel. Purification by flash column chromatography using 0–100% ethyl acetate/hexanes as eluent provided the title compound as a dark red solid (1.88 g, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 - 8.18 (m, 2H), 7.39 - 7.27 (m, 4H), 6.92 - 6.83 (m, 1H), 4.14 - 4.00 (m, 2H), 2.61 (p, *J* = 6.9 Hz, 1H), 2.36 (d, *J* = 0.7 Hz, 3H), 1.30 - 1.10 (m, 6H); ESIMS *m/z* 414 ([M+H]$^+$).

Example 85: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (F5)

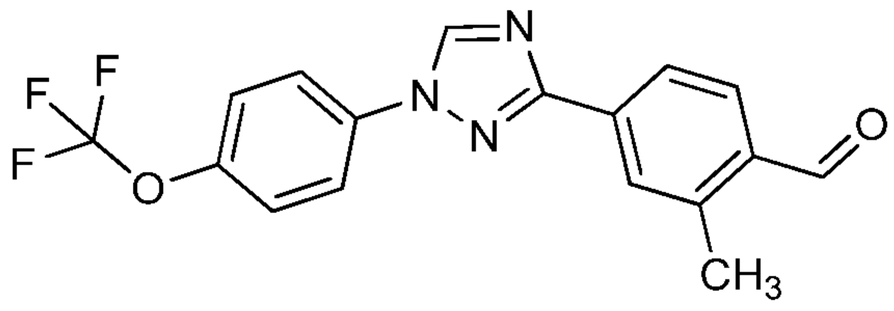


Method A. To 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (**CA51**) (0.030 g, 0.086 mmol) and cesium carbonate (0.028 g, 0.086 mmol) in anhydrous acetonitrile under nitrogen was added (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**) (0.039 g, 0.095 mmol) dropwise. The reaction mixture was stirred room temperature for 3 hours. The crude mixture was concentrated *in vacuo*. Purification by flash column chromatography using 10-60% ethyl acetate/hexanes as eluent provided the title compound as an orange foam (0.036 g, 67%).

Method B. To a solution of 3-(4-(2-isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) (3.00 g, 8.01 mmol) in toluene (20.0 mL) was added cesium carbonate (0.261 g, 0.801 mmol). To this was added 2-imino-3-(2-isopropyl-5-methylphenyl)thiazolidin-4-one (**CA49**) (1.99 g, 8.01 mmol) in acetonitrile (20.0 mL). The reaction was stirred at room temperature for 3.5 hours after which time the reaction mixture was concentrated. Acetone (200 mL) was added and the solid was filtered. The filtrate was concentrated providing a red solid. The red solid was dissolved in acetone, hexanes was added until precipitate was formed. The solid was filtered and the filtrate was concentrated. Purification by flash column chromatography using 0-20% acetone/dichloromethane as eluent provide the title compound as an off-white solid (3.10 g, 62%).

Method C. 3-(4-(2-Isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) (432 g, 1.15 mol) and acetonitrile (1.51 L) were charged in to a round bottomed flask with stirring under nitrogen atmosphere. A solution of 2-imino-3-(2-isopropyl-5-methylphenyl)thiazolidin-4-one (**CA49**) (320 g, 1.29 mol) in acetonitrile (1.43 L) was added at 25 - 30 °C. The reaction was stirred at 25 – 30 °C for 20 hours. After completion of the reaction, the reaction mixture was filtered, washed with acetonitrile (2.16 L), heptane (464 mL), and dried at 50 – 55 °C under vacuum (500 – 600 mm Hg) to give the title compound as an off-white solid (540 g, 75%).

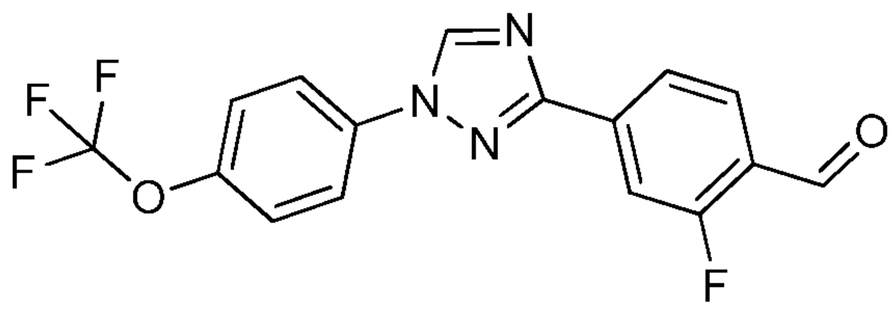
Example 86: Preparation of 2-methyl-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (CB35)



3-Bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) (0.30 g, 1.0 mmol), 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (**CB4**) (0.25 g, 1.0 mmol), sodium bicarbonate (0.25 g, 2.9 mmol), tetrakis(triphenylphosphine) palladium(0) (0.17 g, 0.15 mmol), dioxane (3.9 mL), and water (0.97 mL). in a 0.5 - 2.0 mL vial was capped and heated at 140 ºC for 30 minutes in a Biotage Initiator® microwave reactor with external IR-sensor temperature monitoring from the side of the vessel. The reaction mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate. The organic layers were poured through a phase separator and concentrated. Purification by flash column chromatography using 0-20% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided the title compound as a white solid (0.19 g, 57 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.61 (s, 1H), 8.19 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.13 (t, *J* = 1.1 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.86 - 7.78 (m, 2H), 7.45 - 7.37 (m, 2H), 2.77 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.01; ESIMS *m/z* 348 ($[M+H]^+$)

The following compounds were prepared in accordance to the procedure in Example 86.

Preparation of 2-fluoro-4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzaldehyde (CB36)



The title compound was prepared as described in Example 86 using 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) and 2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (**CB5**) and isolated as a white solid (0.569 g, 47%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (d, *J* = 0.7 Hz, 1H), 8.61 (s,

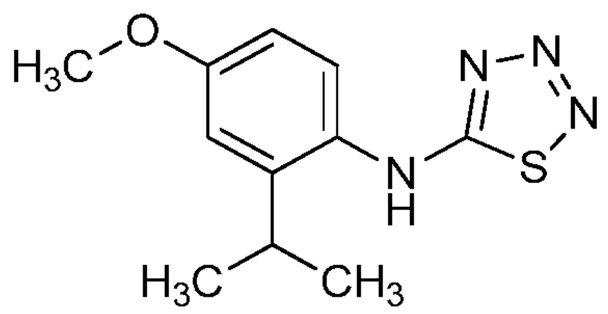
1H), 8.12 (ddd, *J* = 8.1, 1.5, 0.8 Hz, 1H), 8.05 - 7.95 (m, 1H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.45 - 7.39 (m, 2H); ESIMS *m/z* 352 ($[M+H]^+$).

Example 87: Preparation of *N*-(2-ethylphenyl)-1,2,3,4-thiatriazol-5-amine (CB37)

To a stirred and cooled mixture of *N*-(2-ethylphenyl)hydrazinecarbothioamide (0.500 g, 2.56 mmol) and acetic acid (2.00 mL, 17.5 mmol) was added sodium nitrite (0.177 g, 2.56 mmol) in water (1 mL). The mixture turned yellow upon addition and the reaction was stirred for 1 hour. The solid was filtered and the title compound was obtained as an orange solid (0.389 g, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.42 - 7.28 (m, 4H), 2.76 (q, *J* = 7.5 Hz, 2H), 1.25 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.69, 137.90, 130.38, 128.28, 128.14, 121.60, 24.73, 14.79; ESIMS *m/z* 179 ($[M+H]-N_2^+$).

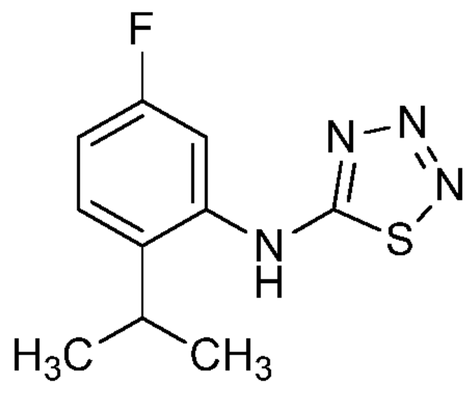
The following compounds were prepared in accordance to the procedure in Example 87.

Preparation of *N*-(2-isopropyl-4-methoxyphenyl)-1,2,3,4-thiatriazol-5-amine (CB38)



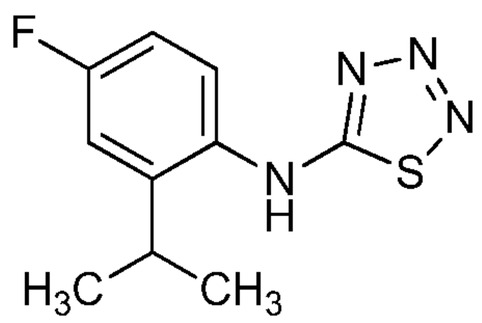
The title compound was prepared as described in Example 87 using *N*-(2-isopropyl-4-methoxyphenyl)hydrazinecarbothioamide (**CB53**) and isolated as an orange solid (0.531 g, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.28 (d, *J* = 8.7 Hz, 1H), 6.91 (d, *J* = 2.9 Hz, 1H), 6.80 (dd, *J* = 8.7, 2.9 Hz, 1H), 3.85 (s, 3H), 3.17 (dq, *J* = 13.7, 6.9 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.18, 146.49, 131.57, 128.24, 126.34, 113.46, 112.61, 55.95, 28.88, 23.81.

Preparation of *N*-(5-fluoro-2-isopropylphenyl)-1,2,3,4-thiatriazol-5-amine (CB39)



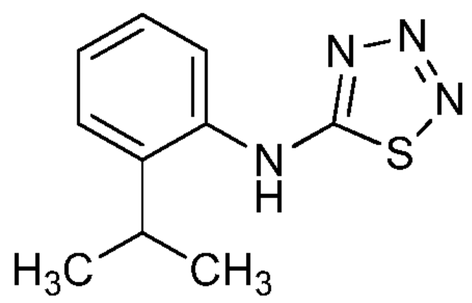
The title compound was prepared as described in Example 87 using *N*-(5-fluoro-2-isopropylphenyl)hydrazinecarbothioamide and isolated as a red solid (0.520 g, 64%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.7, 6.2 Hz, 1H), 7.13 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.04 (ddd, *J* = 8.7, 7.9, 2.7 Hz, 1H), 3.19 (dt, *J* = 13.7, 6.9 Hz, 2H), 1.24 (d, *J* = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.32; ESIMS *m/z* 237 ($[M-H]^-$).

Preparation of *N*-(4-fluoro-2-isopropylphenyl)-1,2,3,4-thiatriazol-5-amine (CB40)



The title compound was prepared as described in Example 87 using *N*-(4-fluoro-2-isopropylphenyl)hydrazinecarbothioamide and isolated as a red solid (0.520 g, 64%): ^{1}H NMR (400 MHz, $CDCl_3$) δ (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.35 (dd, *J* = 8.7, 5.2 Hz, 1H), 7.11 (dd, *J* = 9.8, 3.0 Hz, 1H), 7.00 (ddd, *J* = 8.7, 7.5, 2.9 Hz, 1H), 3.20 (pd, *J* = 6.8, 1.7 Hz, 1H), 1.23 (d, *J* = 6.8 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.20; ESIMS *m/z* 238 ($[M]^+$).

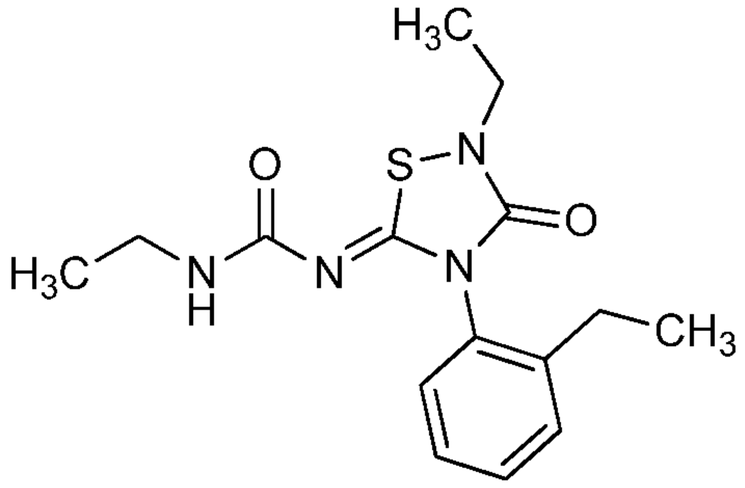
Preparation of *N*-(2-isopropylphenyl)-1,2,3,4-thiatriazol-5-amine (CB41)



The title compound was prepared as described in Example 87 using *N*-(2-isopropylphenyl)hydrazinecarbothioamide and isolated as a mustard yellow solid (0.574 g, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.44 - 7.39 (m, 1H), 7.39 - 7.34 (m, 2H), 7.34 - 7.29 (m, 1H), 3.21 (p, *J* = 6.7 Hz, 1H), 1.26 (d, *J* = 6.9 Hz, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.95, 143.24, 138.10, 128.78, 128.17, 127.56, 122.85, 28.54, 23.73.

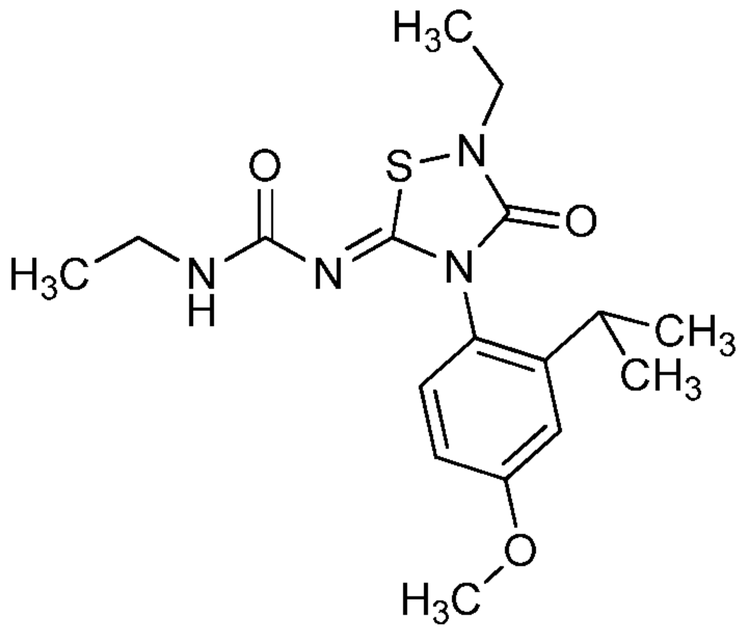
Example 88: Preparation of (*Z*)-1-ethyl-3-(2-ethyl-4-(2-ethylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (CB42)



N-(2-Ethylphenyl)-1,2,3,4-thiatriazol-5-amine (**CB37**) (0.350 g, 1.70 mmol) was dissolved in tetrahydrofuran (5 mL). Ethyl isocyanate (0.121 mL, 1.53 mmol) and triethylamine (5 drops) were added. The reaction was stirred at room temperature overnight. The solution was concentrated to give the title compound as an orange oil (0.484 g, 89%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.36 (m, 2H), 7.36 - 7.29 (m, 1H), 7.19 (dd, *J* = 7.8, 1.4 Hz, 1H), 5.54 - 5.43 (m, 1H), 3.68 (q, *J* = 7.2 Hz, 2H), 3.26 (qdd, *J* = 7.3, 5.9, 4.8 Hz, 2H), 2.51 (qd, *J* = 7.6, 2.9 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.6 Hz, 3H), 1.12 (t, *J* = 7.3 Hz, 3H); ESIMS *m/z* 320 ($[M]^+$).

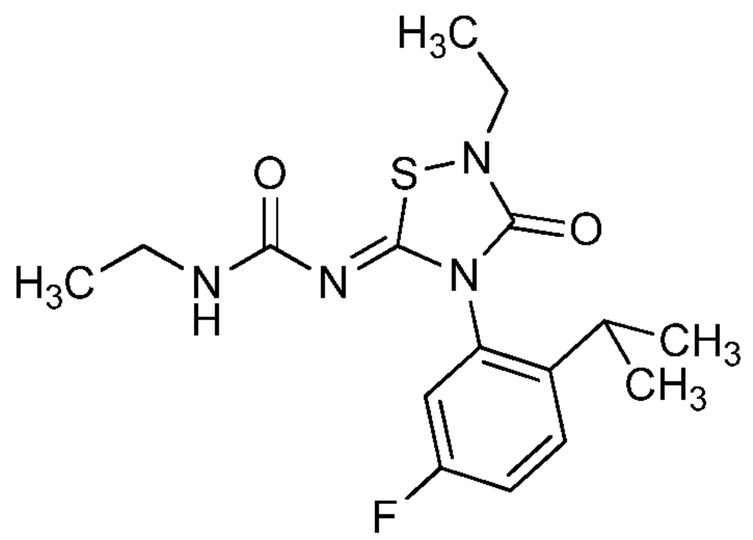
The following compounds were prepared in accordance to the procedure in Example 88.

Preparation of (*Z*)-1-ethyl-3-(2-ethyl-4-(2-isopropyl-4-methoxyphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (CB43)



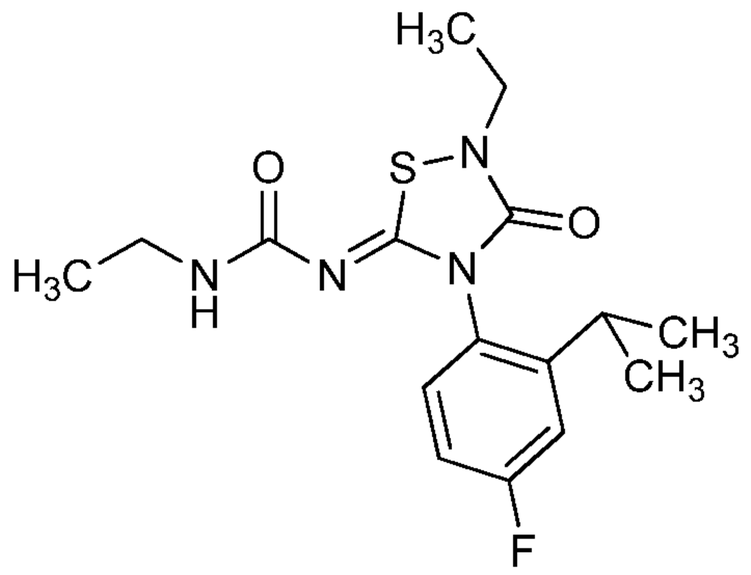
The title compound was prepared as described in Example 88 using *N*-(2-isopropyl-4-methoxyphenyl)-1,2,3,4-thiatriazol-5-amine (**CB38**) and isolated as a dark brown oil (0.693 g, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.7 Hz, 1H), 6.94 (d, *J* = 2.8 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.8 Hz, 1H), 5.48 (t, *J* = 5.8 Hz, 1H), 3.84 (s, 3H), 3.67 (q, *J* = 7.3 Hz, 2H), 3.08 (q, *J* = 7.3 Hz, 2H), 2.70 (p, *J* = 6.9 Hz, 1H), 1.34 (dt, *J* = 10.0, 7.3 Hz, 3H), 1.18 (t, *J* = 6.9 Hz, 6H), 1.12 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.43, 165.14, 161.07, 148.57, 144.62, 129.93, 126.14, 113.06, 112.28, 55.82, 46.36, 39.68, 36.02, 29.31, 24.01, 15.31, 14.56; ESIMS *m/z* 364 ($[M]^+$).

Preparation of (*Z*)-1-ethyl-3-(2-ethyl-4-(5-fluoro-2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (CB44)



The title compound was prepared as described in Example 88 using *N*-(5-fluoro-2-isopropylphenyl)-1,2,3,4-thiatriazol-5-amine (**CB39**) and isolated as a dark brown oil (0.316 g, 37%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.21 - 7.13 (m, 1H), 6.92 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.46 (d, *J* = 6.8 Hz, 1H), 3.75 - 3.56 (m, 2H), 3.36 - 3.15 (m, 2H), 2.72 (p, *J* = 6.8 Hz, 1H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.18 (dd, *J* = 10.9, 6.9 Hz, 6H), 1.13 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.44; ESIMS *m/z* 352 ($[M]^+$).

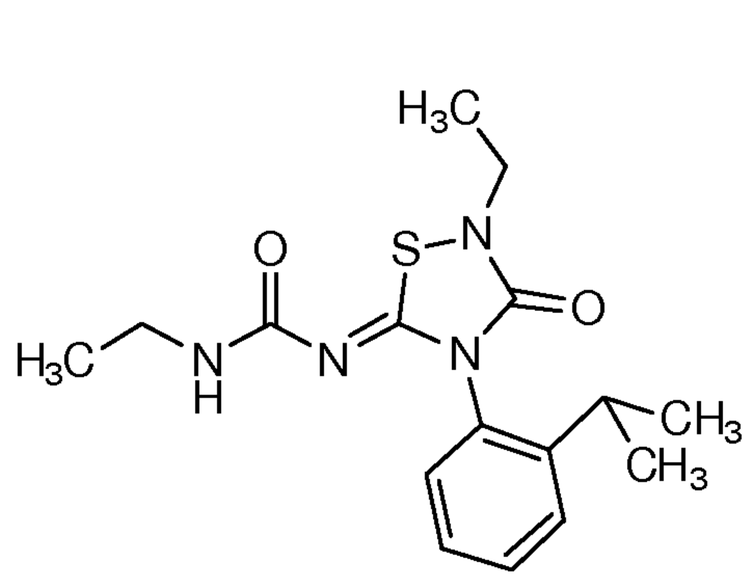
Preparation of (*Z*)-1-ethyl-3-(2-ethyl-4-(4-fluoro-2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (CB45)



F

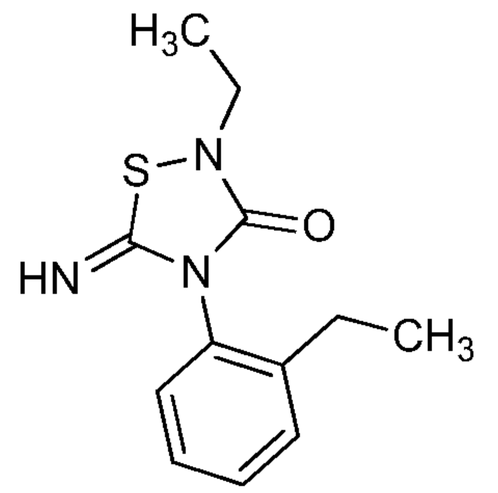
The title compound was prepared as described in Example 88 using *N*-(4-fluoro-2-isopropylphenyl)-1,2,3,4-thiatriazol-5-amine (**CB40**) and isolated as a red oil (0.340 g, 44%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 - 7.08 (m, 2H), 7.00 (ddd, *J* = 8.7, 7.6, 2.9 Hz, 1H), 5.46 (t, *J* = 5.8 Hz, 1H), 3.67 (q, *J* = 7.2 Hz, 2H), 3.36 - 3.17 (m, 2H), 2.72 (td, *J* = 6.8, 1.8 Hz, 1H), 1.33 (t, *J* = 7.3 Hz, 3H), 1.22 - 1.07 (m, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.31; ESIMS *m/z* 352 ($[M]^+$).

Preparation of (*Z*)-1-ethyl-3-(2-ethyl-4-(2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (CB46)



The title compound was prepared as described in Example 88 using *N*-(2-isopropylphenyl)-1,2,3,4-thiatriazol-5-amine (**CB41**) and isolated as a red oil (0.788 g, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.44 (m, 2H), 7.34 - 7.28 (m, 1H), 7.19 - 7.15 (m, 1H), 3.68 (q, *J* = 7.2 Hz, 2H), 3.34 - 3.19 (m, 3H), 2.75 (p, *J* = 6.9 Hz, 1H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.20 (dd, *J* = 7.8, 6.8 Hz, 6H), 1.12 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.07, 165.09, 152.63, 147.13, 133.37, 130.65, 128.95, 127.37, 127.30, 46.36, 39.67, 36.01, 29.08, 24.07, 15.32, 14.56; ESIMS *m/z* 334 ($[M]^+$).

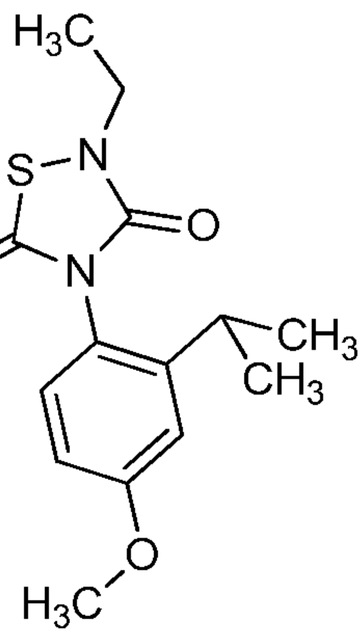
Example 89: Preparation of 2-ethyl-4-(2-ethylphenyl)-5-imino-1,2,4-thiadiazolidin-3-one (CB47)



(*Z*)-1-Ethyl-3-(2-ethyl-4-(2-ethylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (**CB42**) (0.484 g, 1.51 mmol) was dissolved in methanol (150 mL). Sodium hydroxide (3.36 g, 84.0 mmol) was slowly added and the reaction was stirred at room temperature. After 4 hours the solution was concentrated to 1/2 volume, poured onto water, and extracted with ethyl acetate. The organics were dried and concentrated to give the title compound as an orange solid (0.249 g, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.32 (m, 2H), 7.30 (dd, *J* = 5.4, 1.5 Hz, 1H), 7.25 - 7.20 (m, 1H), 3.65 (q, *J* = 7.2 Hz, 2H), 3.39 - 3.19 (m, 1H), 2.73 (q, *J* = 7.6 Hz, 2H), 1.26 - 1.13 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.32, 165.49, 141.20, 135.74, 130.42, 129.31, 127.67, 126.01, 39.50, 24.79, 15.22, 14.93; ESIMS *m/z* 250 ($[M]^+$).

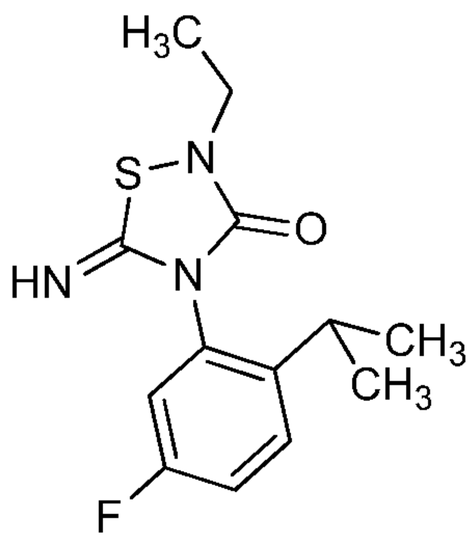
The following compounds were prepared in accordance to the procedure in Example 89.

Preparation of 2-ethyl-5-imino-4-(2-isopropyl-4-methoxyphenyl)-1,2,4-thiadiazolidin-3-one (CB48)



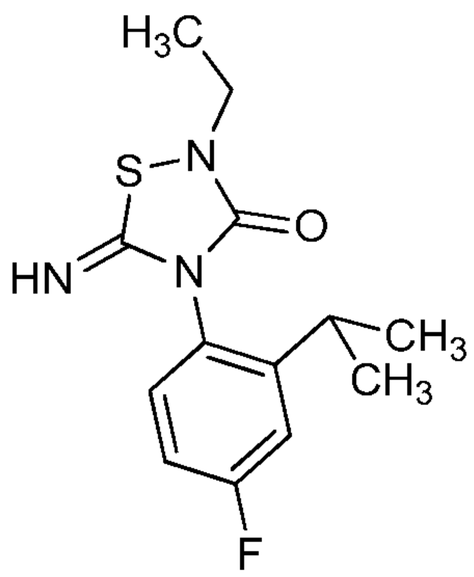
The title compound was prepared as described in Example 89 using (*Z*)-1-ethyl-3-(2-ethyl-4-(2-isopropyl-4-methoxyphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (**CB43**) and isolated as a red oil (0.442 g, 63%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 1H), 6.90 (d, *J* = 2.9 Hz, 1H), 6.74 (dd, *J* = 8.7, 2.9 Hz, 1H), 3.83 (s, 3H), 3.68 - 3.57 (m, 2H), 3.24 - 3.13 (m, 2H), 1.20 (dd, *J* = 8.5, 7.1 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.84, 160.88, 148.76, 129.20, 126.94, 126.13, 113.50, 112.05, 55.90, 39.44, 28.90, 23.87, 15.23; ESIMS *m/z* 293 ($[M]^+$).

Preparation of 2-ethyl-4-(5-fluoro-2-isopropylphenyl)-5-imino-1,2,4-thiadiazolidin-3-one (CB49)



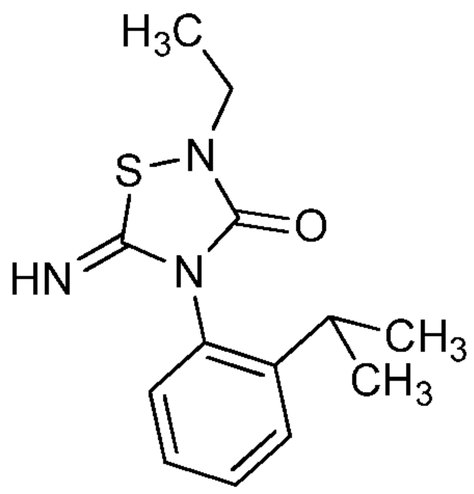
The title compound was prepared as described in Example 89 using (*Z*)-1-ethyl-3-(2-ethyl-4-(5-fluoro-2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (**CB44**) and isolated as a red solid (0.145 g, 56%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.28 (m, 1H), 7.06 - 6.94 (m, 2H), 3.64 (q, *J* = 7.1 Hz, H), 3.18 (p, *J* = 6.8 Hz, 1H), 1.30 - 1.05 (m, 10H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.44; ESIMS *m/z* 281 ($[M]^+$).

Preparation of 2-ethyl-4-(4-fluoro-2-isopropylphenyl)-5-imino-1,2,4-thiadiazolidin-3-one (CB50)



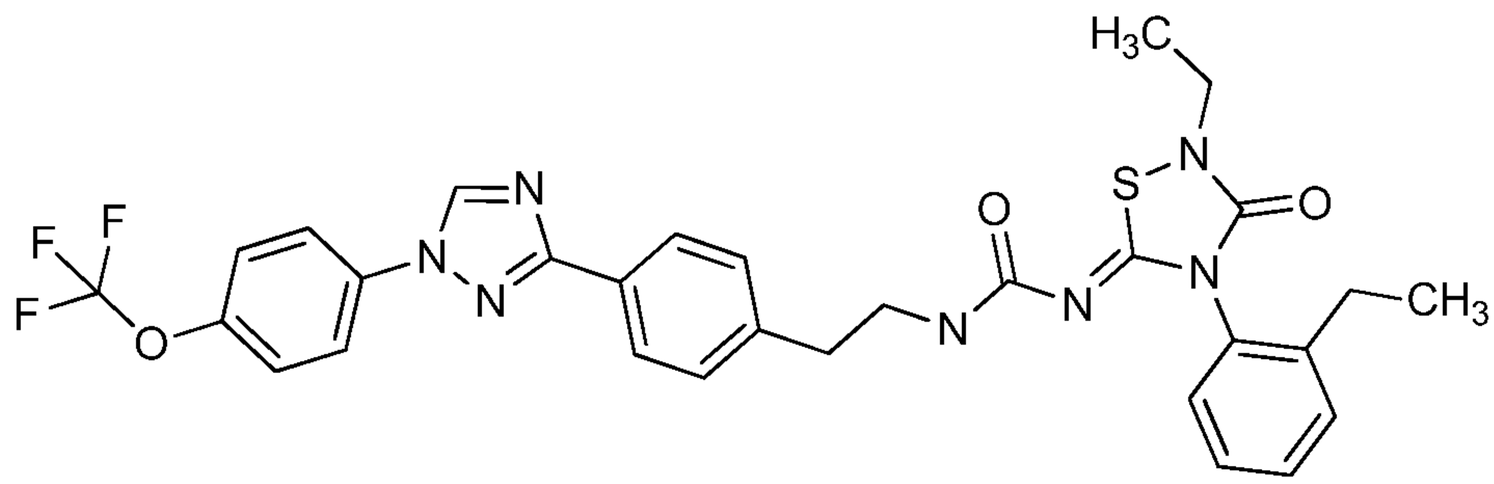
The title compound was prepared as described in Example 89 using (*Z*)-1-ethyl-3-(2-ethyl-4-(4-fluoro-2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (**CB45**) and isolated as a yellow oil (0.110 g, 38%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 - 7.25 (m, 1H), 7.08 (dd, *J* = 9.9, 2.9 Hz, 1H), 6.92 (ddd, *J* = 8.7, 7.6, 2.9 Hz, 1H), 3.75 - 3.57 (m, 3H), 3.32 - 3.13 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 6H), 1.19 (t, *J* = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.83; ESIMS *m/z* 281 ($[M]^+$).

Preparation of 2-ethyl-5-imino-4-(2-isopropylphenyl)-1,2,4-thiadiazolidin-3-one (CB51)



The title compound was prepared as described in Example 89 using (*Z*)-1-ethyl-3-(2-ethyl-4-(2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)urea (**CB46**) and isolated as a red oil (0.421 g, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.34 (m, 2H), 7.31 - 7.27 (m, 1H), 7.22 (dd, *J* = 9.2, 6.5 Hz, 1H), 4.06 (s, 1H), 3.65 (d, *J* = 8.5 Hz, 2H), 3.34 - 3.13 (m, 1H), 1.21 (m, 9H); ESIMS *m/z* 263 ($[M]^+$).

Example 90: Preparation of (*Z*)-1-(2-ethyl-4-(2-ethylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB10)

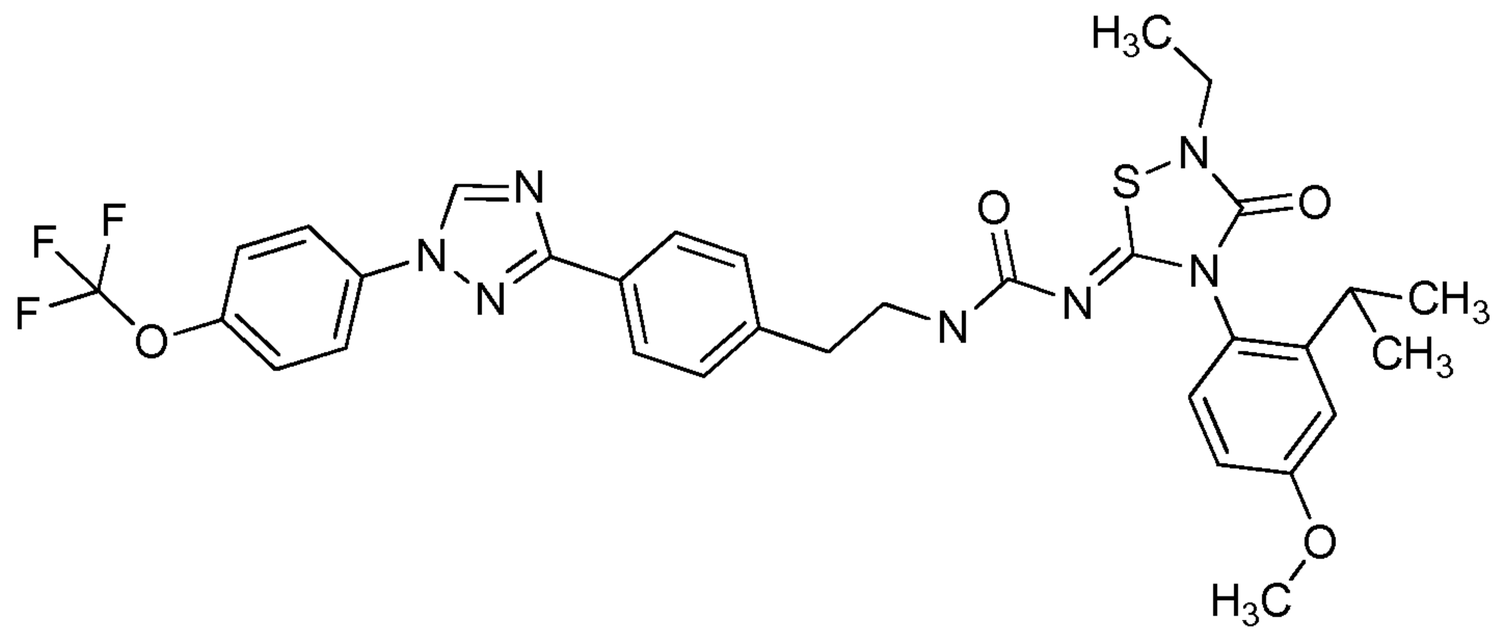


A solution of 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) (0.100 g, 0.249 mmol) in acetonitrile (4 mL) was heated at 70 °C for 2 hours. The reaction was cooled to room temperature, and then

2-ethyl-4-(2-ethylphenyl)-5-imino-1,2,4-thiadiazolidin-3-one (**CB47**) (0.0660 g, 0.265 mmol) in tetrahydrofuran and triethylamine (3 drops) were added. The reaction was stirred overnight. The solution was diluted in ethyl acetate and washed with water. The organics were extracted, dried, and concentrated. Purification by reverse-phase preparative HPLC using 0-90% acetonitrile/water (0.1% acetic acid) as eluent provided the title compound as a white solid (0.045 g, 26%).

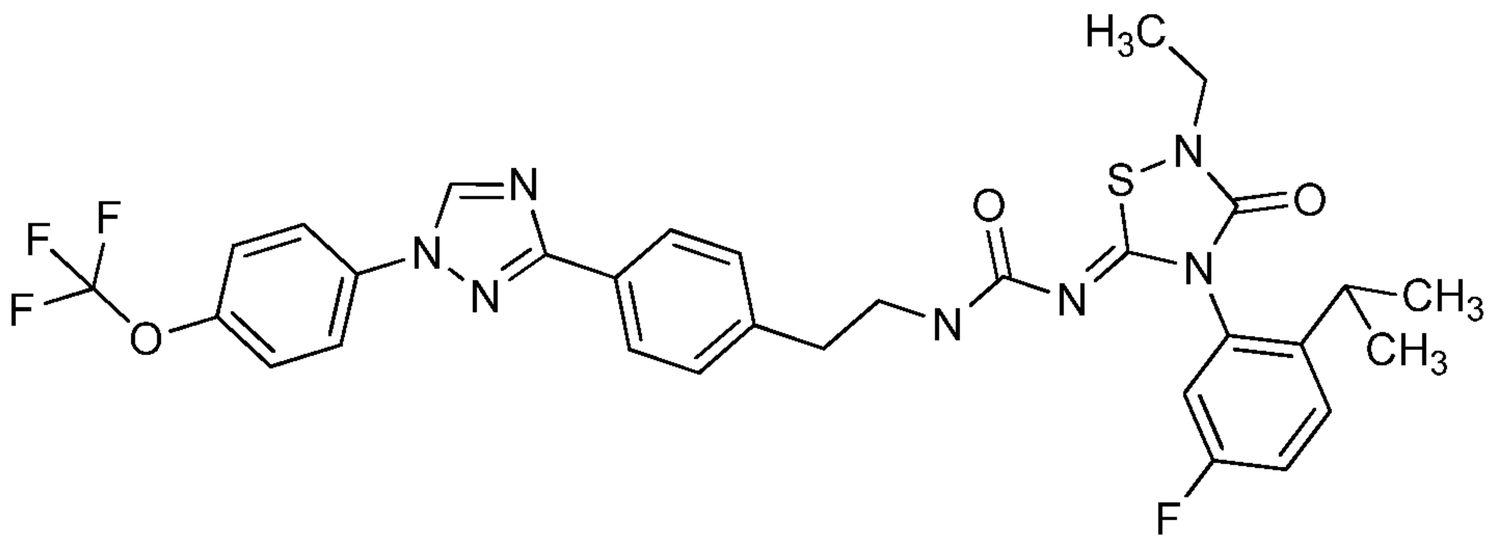
The following compounds were prepared in accordance to the procedure in Example 90.

Preparation of (*Z*)-1-(2-ethyl-4-(2-isopropyl-4-methoxyphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB11)



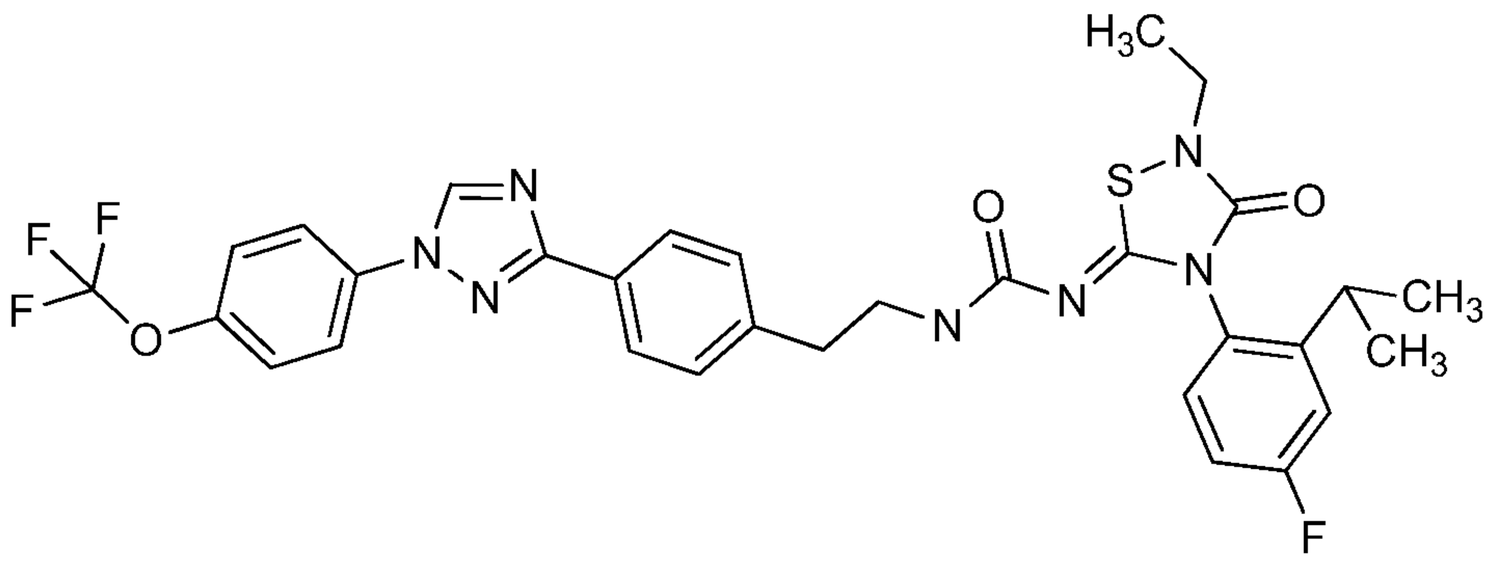
The title compound was prepared as described in Example 90 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) and 2-ethyl-5-imino-4-(2-isopropyl-4-methoxyphenyl)-1,2,4-thiadiazolidin-3-one (**CB48**) and isolated as a yellow solid (0.016 g, 7%).

Preparation of (*Z*)-1-(2-ethyl-4-(5-fluoro-2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB12)



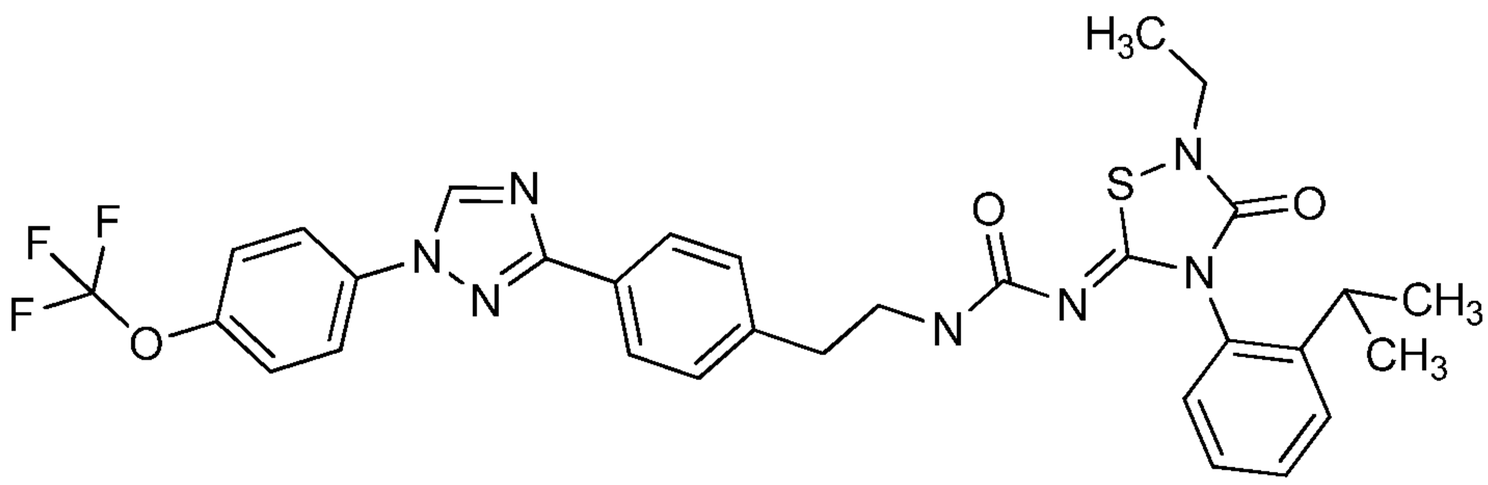
The title compound was prepared as described in Example 90 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) and 2-ethyl-4-(5-fluoro-2-isopropylphenyl)-5-imino-1,2,4-thiadiazolidin-3-one (**CB49**) and isolated as a yellow oil (0.068 g, 40%).

Preparation of (*Z*)-1-(2-ethyl-4-(4-fluoro-2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB13)



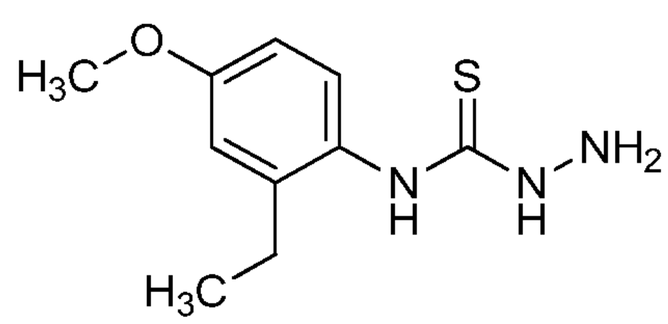
The title compound was prepared as described in Example 90 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) and 2-ethyl-4-(4-fluoro-2-isopropylphenyl)-5-imino-1,2,4-thiadiazolidin-3-one (**CB50**) and isolated as a yellow oil (0.018 g, 14%).

Preparation of (*Z*)-1-(2-ethyl-4-(2-isopropylphenyl)-3-oxo-1,2,4-thiadiazolidin-5-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1H-1,2,4-triazol-3-yl)phenethyl)urea (FB14)



The title compound was prepared as described in Example 90 using 3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propanoyl azide (**C34**) and 2-ethyl-5-imino-4-(2-isopropylphenyl)-1,2,4-thiadiazolidin-3-one (**CB51**) and isolated as a yellow solid (0.047 g, 23%).

Example 91: Preparation of *N*-(2-ethyl-4-methoxyphenyl)hydrazinecarbothioamide (CB52)



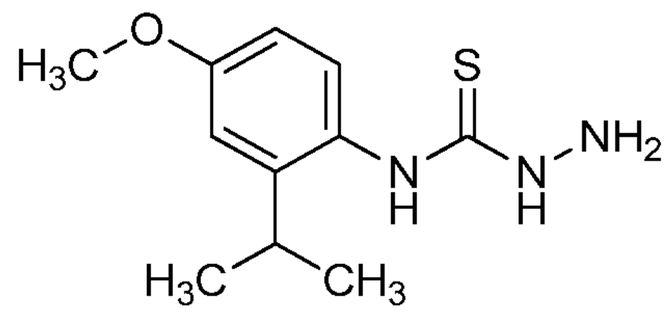
Step 1. To solution of 2-ethyl-4-methoxyaniline (4.5 g, 30 mmol) and triethylamine (6.0 g, 60 mmol) in dichloromethane (31 mL) was added thiophosgene (3.4 g, 30 mmol) was added drop wise at 0 ºC over the period of 1 hour. After completion, the reaction mixture was poured into ice-water (100 mL) and extracted with ethyl acetate (3 x 200 mL) and washed with ice water (2 x 100 mL), followed by brine (2 x 50 mL). The organic phase was dried over sodium sulfate, filtered, and evaporated under reduced pressure. Purification by flash column chromatography using 0-10% ethyl acetate/hexanes as eluent provided 2-ethyl-1-isothiocyanato-4-methoxybenzene as yellow oil (4.9 g, 25 mmol), which was taken onto the next step immediately.

Step 2. To a solution of 2-ethyl-1-isothiocyanato-4-methoxybenzene (4.9 g, 25 mmol) in ethanol (22 mL), was added slowly, hydrazine·hydrate (1.3 g, 28 mmol). The reaction mixture was stirred at room temperature for 18 hours. The reaction mixture was evaporated under reduced pressure and diluted with ethyl acetate (250 mL) and washed with water (2 x 50 mL), followed by brine (2 x 50 mL). The organic

phase was dried over sodium sulfate, filtered, and evaporated under reduced pressure. Purification by flash column chromatography using 0-40% ethyl acetate/hexanes as eluent provided the title compound as a white solid (4.9 g, 86%): mp 113-115 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (s, 1H), 8.89 (s, 1H), 7.20 - 7.19 (m, 1H), 6.77 – 6.71 (m, 2H), 4.71 (bs, 2H), 3.74 (s, 3H), 2.52 – 2.47 (m, 2H), 1.13 – 1.08 (m, 3H); ESIMS *m/z* 224 ([M-H]$^-$).

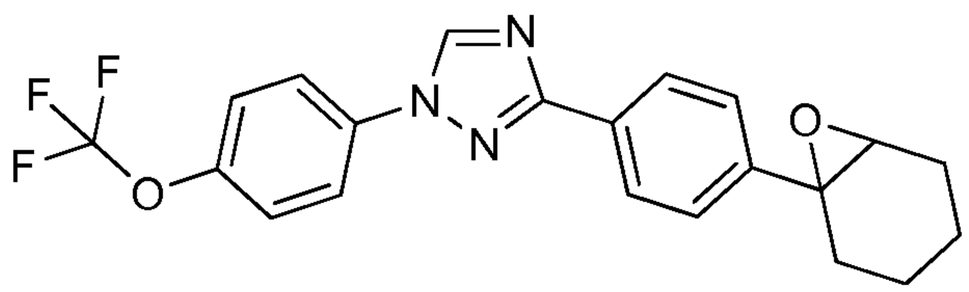
The following compounds were prepared in accordance to the procedure in Example 91.

Preparation of *N*-(2-isopropyl-4-methoxyphenyl)hydrazinecarbothioamide (CB53)



The title compound was prepared as described in Example 88 using 2-isopropyl-4-methoxyaniline and isolated as a white solid (9.5 g): mp 153-156 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.96 (s, 1H), 7.12 - 7.10 (m, 1H), 6.78 – 6.78 (m, 2H), 4.71 (bs, 2H), 3.17 (s, 3H), 3.05 – 3.00 (m, 1H), 1.14 (d, J = 6.6 Hz, 6H); ESIMS *m/z* 238 ([M-H]$^-$).

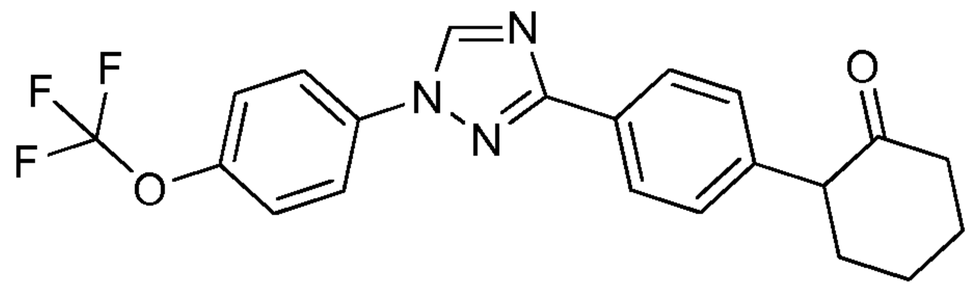
Example 92: Preparation of 3-(4-(7-oxabicyclo[4.1.0]heptan-1-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (CB54)



To a solution of 3-(2',3',4',5'-tetrahydro-[1,1'-biphenyl]-4-yl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB10**) (3.11 g, 8.07 mmol) in diethyl ether (60 mL) was added *meta*-chloroperoxybenzoic acid (70%; 2.79 g, 11.3 mmol) slowly at 0 ºC. The reaction was stirred and allowed to gradually warm to room temperature, then stirring was continued for 18 hours. The solution was diluted in diethyl ether, washed with sodium bicarbonate, extracted with diethyl ether, washed

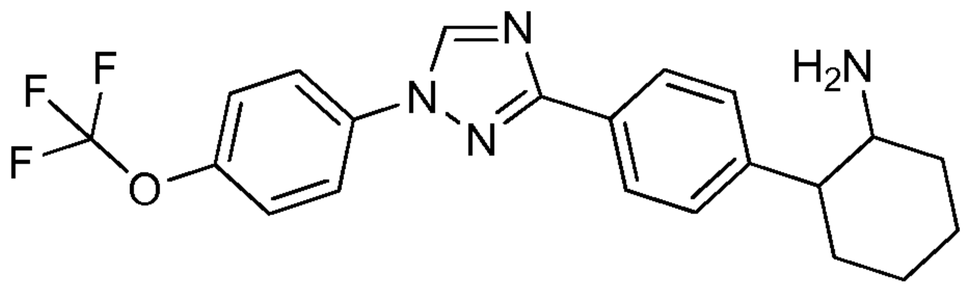
with water, and extracted again with diethyl ether. The organics were dried, filtered, and concentrated providing the title compound as a white solid (2.5 g, 77%) which was used without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.20 - 8.11 (m, 2H), 7.84 - 7.77 (m, 2H), 7.52 - 7.46 (m, 2H), 7.39 (dt, *J* = 8.0, 1.0 Hz, 2H), 3.12 (dd, *J* = 3.1, 1.7 Hz, 1H), 2.34 (ddd, *J* = 14.9, 8.5, 5.3 Hz, 1H), 2.09 - 1.95 (m, 2H), 1.74 - 1.45 (m, 4H), 1.42 - 1.28 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 402 ($[M+H]^+$).

Example 93: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclohexanone (CB55)



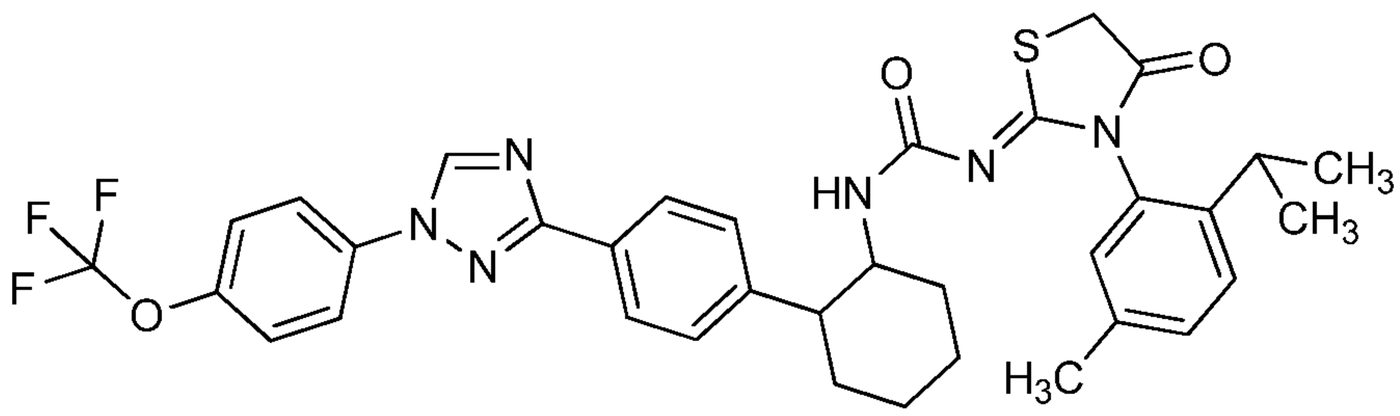
To a stirred solution of indium chloride (1.259 g, 5.69 mmol) in 15 mL of dry THF in a 100 mL flask was added a solution of 3-(4-(7-oxabicyclo[4.1.0]heptan-1-yl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**CB54**) (1.14 g, 2.85 mmol) in dry tetrahydrofuran (10 mL). Stirring was continued under nitrogen for 24 hours, then the solution was diluted with diethyl ether (50 mL) and washed with water, dried, and concentrated *in vacuo*. Purification by flash column chromatography using 0-60% ethyl acetate/hexanes as eluent provided the title compound as a white solid (0.566 g, 35%): ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.16 (dd, *J* = 8.6, 2.1 Hz, 2H), 7.83 - 7.72 (m, 2H),7.43 - 7.33 (m, 2H), 7.30 - 7.21 (m, 2H), 3.68 (dd, *J* = 12.2, 5.4 Hz, 1H), 2.61 - 2.41 (m, 2H), 2.37 - 2.24 (m, 1H), 2.23 - 1.92 (m, 3H), 1.85-1.60 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 402 ($[M+H]^+$).

Example 94: Preparation of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclohexanamine (CB56)



To a dry flask was added a solution of 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclohexanone (**CB55**) (0.98 g, 2.4 mmol) in dry methanol (30 mL). The flask was evacuated/backfilled with nitrogen and ammonium acetate (2.6 g, 34 mmol) was added, followed by sodium cyanoborohydride (0.18 g, 2.9 mmol). The reaction was stirred at room temperature overnight. The solution was quenched with water and extracted with ethyl acetate. The organics were dried, filtered, and concentrated to provide the title compound as a white solid (0.42 g, 34%): ^{1}H NMR indicated the presence of 2 isomers, which were not separated. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (*two s,* 1H), 8.14 – 8.03 (m, 4H), 7.66-7.60 (m, 2H), 7.53 – 7.40 (m, 2H), 3.47 – 3.16 (br s, 2H), 3.29 (td, J = 11.0, 3.8 Hz, 1H), 2.59 (td, *J* = 11.6, 11.1, 3.7 Hz, 1H), 2.17 – 2.04 (m, 1H), 1.86 – 1.68 (m, 3H), 1.68 – 1.30 (m, 4H); ESIMS *m/z* 402 ([M]$^+$).

Example 95: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclohexyl)urea (FB15)

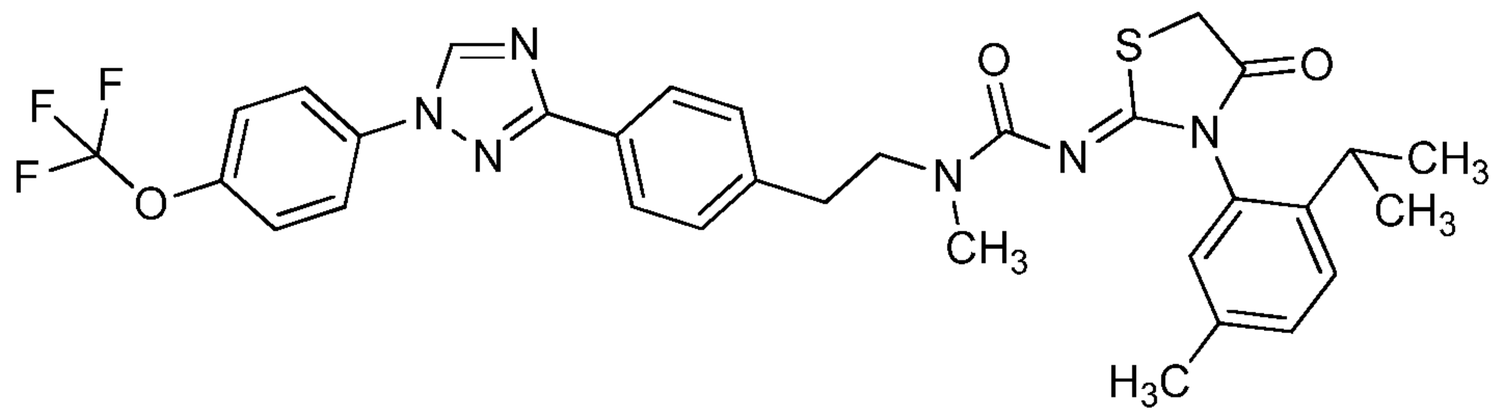


To 2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)cyclohexanamine (**CB56**) (0.200 g, 0.497 mmol) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**) (0.205 g, 0.497 mmol) were dissolved in acetonitrile (10 mL) in a vial. Cesium carbonate (0.162 g, 0.497 mmol) was added, and the reaction was stirred at room temperature for 25 hours. The solution was adsorbed onto silica. Purification by reverse-phase

flash column chromatography using 0-100% acetonitrile/water as eluent afforded the title compound as a red oil (0.020 g, 6%).

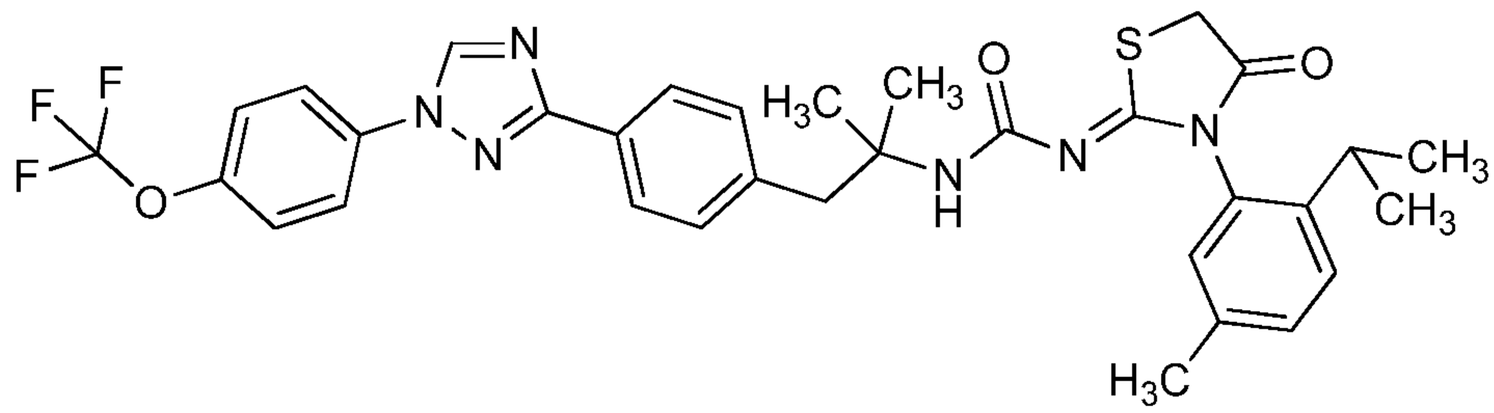
The following compounds were prepared in accordance to the procedure in Example 95.

Preparation of *(Z)*-3-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-1-methyl-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB51)



The title compound was prepared as described in Example 95 using *N*-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (**CB24**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as a pale orange foam (0.160 g, 63%).

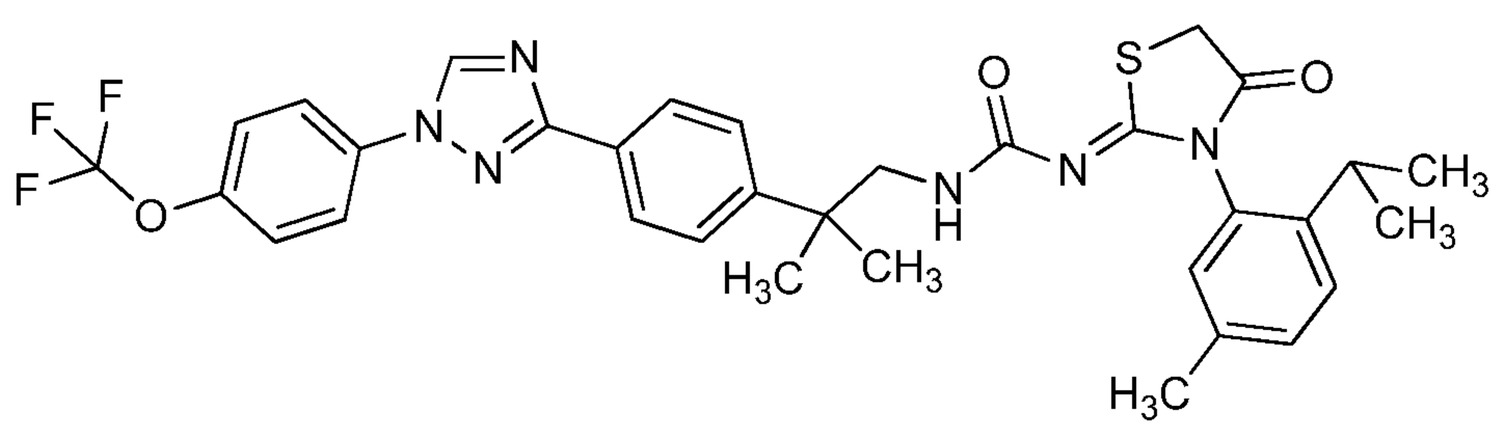
Preparation of *(Z)*-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-methyl-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (FB52)



The title compound was prepared as described in Example 95 using 2-methyl-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (**CB28**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100%

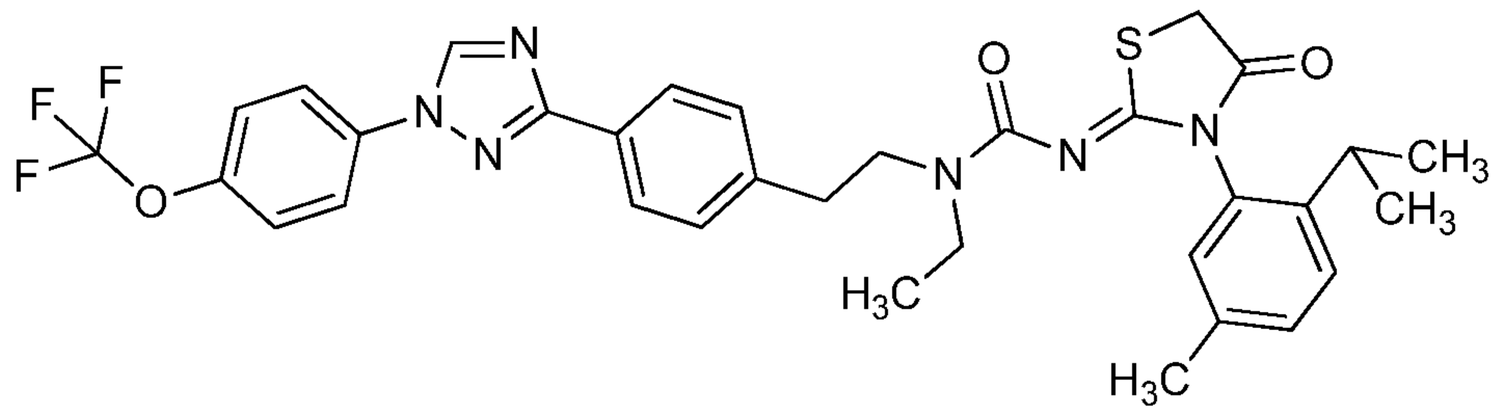
ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as a brown oil (0.018 g, 9%).

Preparation of *(Z)*-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(2-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)urea (FB53)



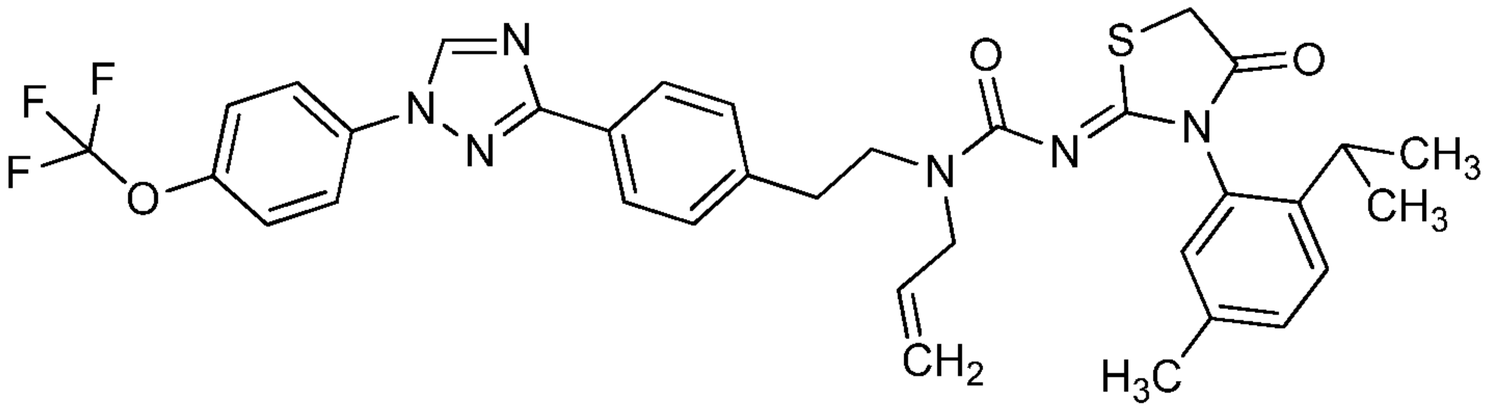
The title compound was prepared as described in Example 95 using 2-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-1-amine (**CB29**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as a brown glassy foam (0.084 g, 46%).

Preparation of *(Z)*-1-ethyl-3-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB54)



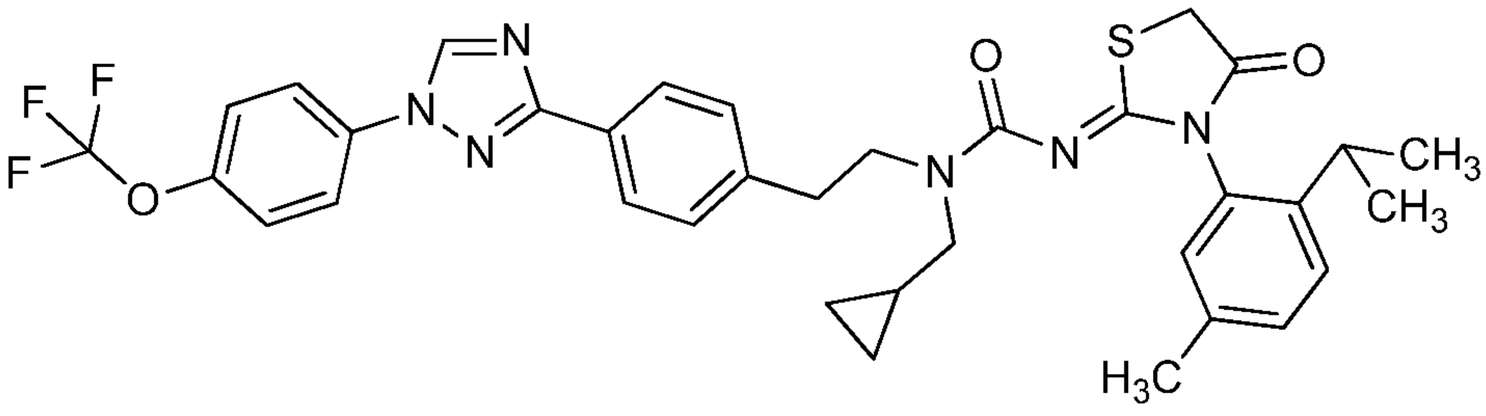
The title compound was prepared as described in Example 95 using *N*-ethyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (**CB25**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as a red solid (0.075 g, 56%).

Preparation of *(Z)*-1-allyl-3-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1H-1,2,4-triazol-3-yl)phenethyl)urea (FB61)



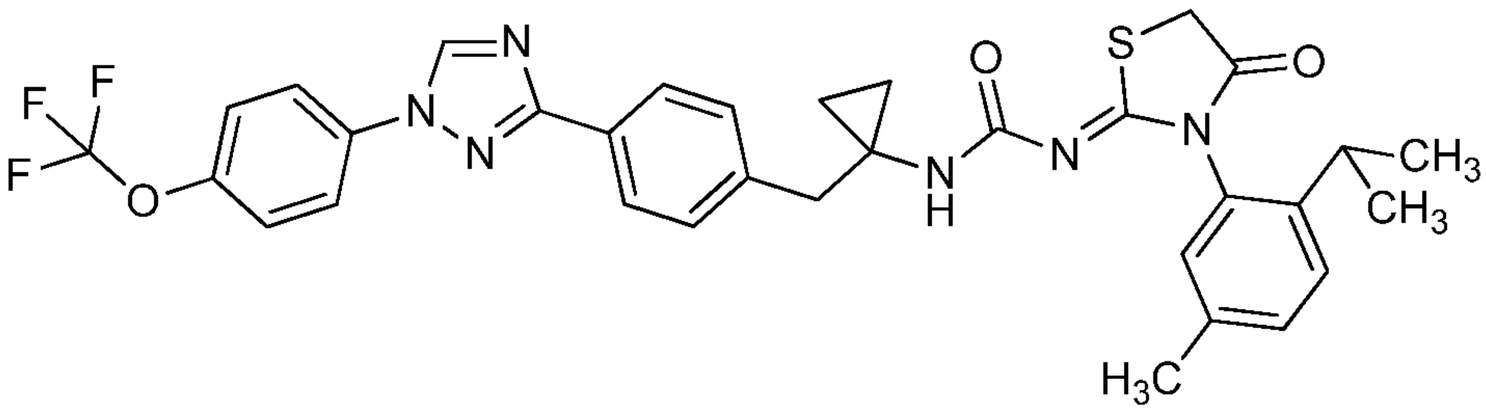
The title compound was prepared as described in Example 95 using *N*-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)prop-2-en-1-amine (**CB26**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as a brown oil (0.040 g, 43%).

Preparation of *(Z)*-1-(cyclopropylmethyl)-3-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB62)



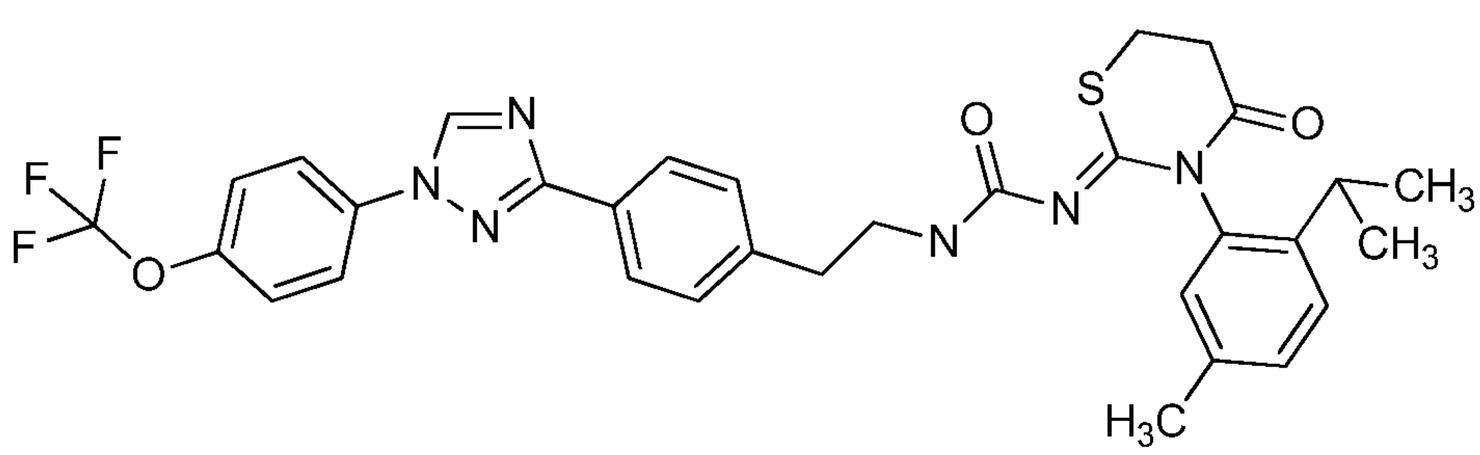
The title compound was prepared as described in Example 95 using *N*-(cyclopropylmethyl)-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethanamine (**CB27**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as red-orange oil (0.127 g, 60%).

Preparation of *(Z)*-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)cyclopropyl)urea (FB63)



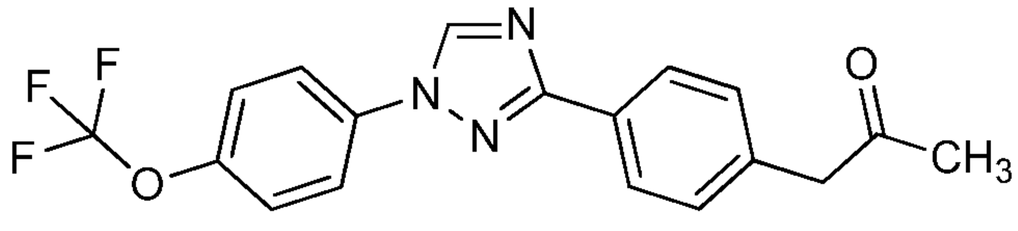
The title compound was prepared as described in Example 95 using 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)cyclopropanamine (**CB30**) and (*Z*)-4-nitrophenyl (3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)carbamate (**CA50**), purified by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent and isolated as red oil (0.104 g, 37%).

Example 96: Preparation of (Z)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxo-1,3-thiazinan-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB41)



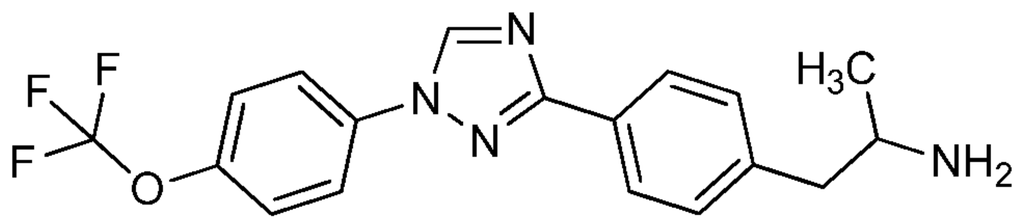
3-(4-(2-Isocyanatoethyl)phenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C34a**) (0.18 g, 0.47 mmol), 1-(2-isopropyl-5-methylphenyl)thiourea (0.10 g, 0.50 mmol), and cesium carbonate (0.21 g, 0.63 mmol) in acetonitrile (2.3 mL) were stirred at room temperature overnight. The reaction was diluted with ethyl acetate and washed with water. The organic layers were dried over sodium sulfate, filtered, and concentrated. The crude material was dissolved in butanone (2.3 mL) followed by addition of acryloyl chloride (0.045 mL, 0.55 mmol). The reaction was heated at 40 ℃ for 4 hours. The reaction was cooled and concentrated. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent followed by drying in a vacuum oven provided the title compound as a yellow oil (0.13 g, 44%).

Example 97: Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-one (CB57)



3-(4-Bromophenyl)-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C52**) (11 g, 29 mmol), copper(I) iodide (0.55 g, 2.9 mmol), potassium phosphate (18 g, 86 mmol), and pentane-2,4-dione (8.9 mL, 86 mmol) were dissolved in dimethylsulfoxide (120 mL) in a 500 mL round bottomed flask. The reaction was heated at 110 ℃ for 19 hours. The solution was cooled to room temperature and then quenched with hydrogen chloride (2 N). The excess base was removed by gravity filtration and the filtrate was extracted with ethyl acetate. The organics were washed with water, extracted, dried, and concentrated. Purification by flash column chromatography using 0-30% ethyl acetate/hexanes afforded the title compound as a pure orange solid (3.7 g, 35%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.17 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 9.0 Hz, 2H), 7.39 (dt, *J* = 8.1, 1.0 Hz, 2H), 7.33 (dd, *J* = 8.1, 0.6 Hz, 2H), 3.76 (s, 2H), 2.19 (s, 3H); ESIMS *m/z* 361 ($[M]^+$).

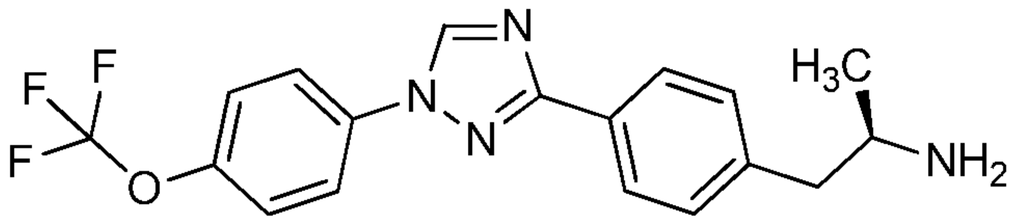
Example 98: Preparation of 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (CB58)

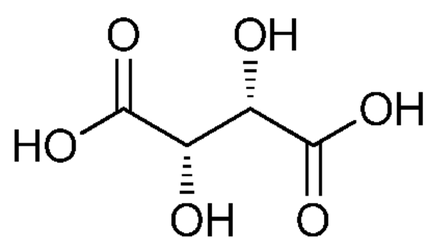


1-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-one (**CB57**) (1.0 g, 2.8 mmol) and ammonium acetate (1.7 g, 22 mmol) were combined in dry methanol (22 mL)_and stirred at room temperature while sodium cyanoborohydride (0.17 g, 2.7 mmol) was added in 3 equal portions over 30 minutes. The reaction was stirred overnight. The reaction was concentrated and partitioned between aqueous potassium carbonate and diethyl ether. The layers were separated, dried, filtered, and concentrated. Purification by reverse-phase flash column (C18) chromatography using 0-100% acetonitrile/water as eluent provided the title compound as a tan solid (1.0 g, 38%): mp 140-160 ºC; ^{1}H NMR (400 MHz,

$CDOD_3$) d 9.13 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 9.0 Hz, 2H), 7.52 7.43 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 3.40 - 3.33 (m, 1H), 2.86 (t, *J* = 6.7 Hz, 1H), 2.77 (dd, *J* = 13.3, 7.3 Hz, 1H), 1.18 (d, *J* = 6.2 Hz, 3H) ($N\underline{H}_2$ not observed); ESIMS *m/z* 363 ($[M+H]^+$).

Example 99: Preparation of (*R*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (2*S*,3*S*)-2,3-dihydroxysuccinate (CB59)

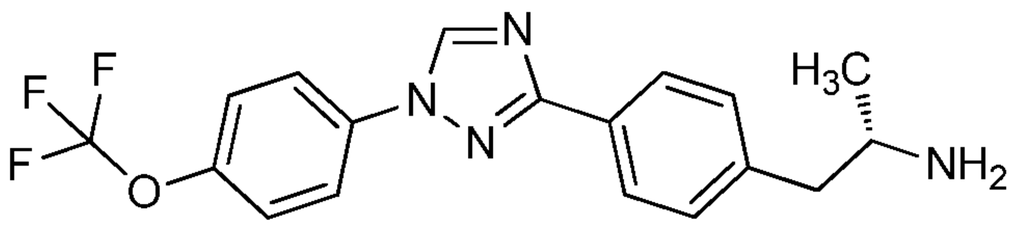


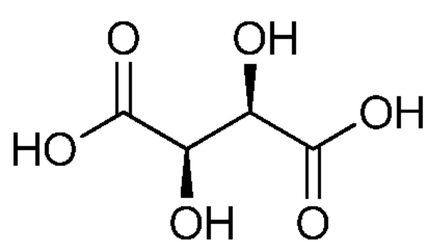


To 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (**CB58**) (0.60 g, 1.7 mmol) in methanol (10 mL) was added (2*S*,3*S*)-2,3-dihydroxysuccinic acid (0.25 g, 1.7 mmol). The resultant solid was filtered and air dried overnight: mp 182-185 ºC. The solid was redissolved in methanol (10 mL) and heated to reflux (~65 ºC). The solution was cooled to room temperature and let stand overnight. The white solid that formed was filtered and air-dried to give the title compound as a white solid (0.40 g, 46%): mp 191-194 ºC; ^{1}H NMR (400 MHz, $CDOD_3$) d 9.16 (s, 1H), 8.15 (d, *J* = 8.2 Hz, 2H), 8.02 (d, *J* = 9.1 Hz, 2H), 7.50 (dd, *J* = 9.2, 1.0 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 4.40 (s, 2H), 3.59 (dt, *J* = 8.1, 6.2 Hz, 1H), 3.07 (dd, *J* = 13.6, 6.1 Hz, 1H), 2.88 (dd, *J* = 13.6, 8.3 Hz, 1H), 1.29 (d, *J* = 6.5 Hz, 3H) (O<u>H</u> and $N\underline{H}_2$ not observed).

The following compounds were prepared in accordance to the procedure in Example 99.

Preparation of (*S*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (2*R*,3*R*)-2,3-dihydroxysuccinate (CB60)

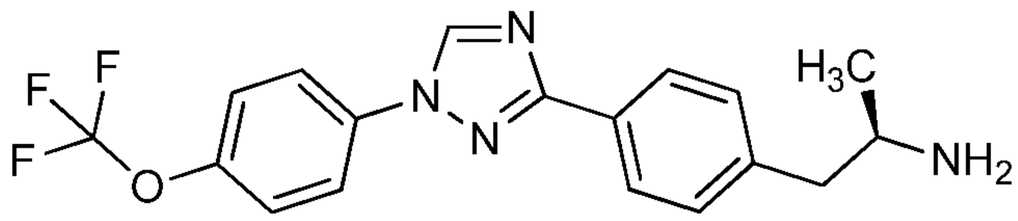




The title compound was prepared as described in Example 99 using 1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (**CB58**) and (2*R*,3*R*)-2,3-dihydroxysuccinic acid and isolated as a white solid (0.70 g, 49%): mp

187-191 ºC; ^{1}H NMR ^{1}H NMR (400 MHz, DMSO-d_6) d 9.40 (s, 1H), 8.08 (dd, J = 8.6, 3.6 Hz, 4H), 7.63 (dt, J = 8.1, 1.0 Hz, 2H), 7.49 7.32 (m, 2H), 3.81 (s, 2H), 3.47 (dt, J = 8.5, 6.2 Hz, 1H), 3.01 (dd, J = 13.4, 5.5 Hz, 1H), 2.74 (dd, J = 13.4, 8.7 Hz, 1H), 1.13 (d, J = 6.4 Hz, 3H) (OH and NH_2 not observed).

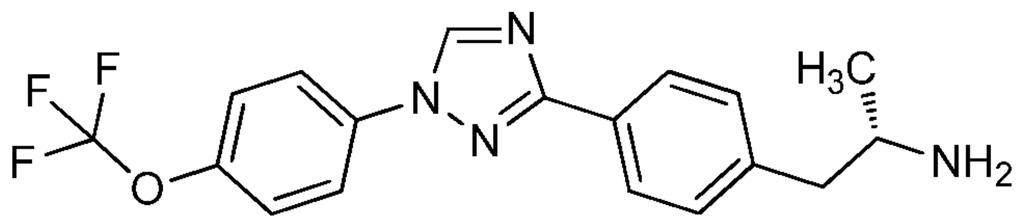
Example 100: Preparation of (*R*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (CB61)



(*R*)-1-(4-(1-(4-(Trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (2*S*,3*S*)-2,3-dihydroxysuccinate (**CB59**) (0.35 g, 0.68 mmol) was slurried in methanol (20 mL) and SCX silica gel (2 g). The solution was stirred for 3 hours, filtered, and washed with methanol (20 mL). The compound was eluted from the SCX silica gel using ammonium hydroxide (5% in MeOH, 25 mL). The filtrate was concentrated providing the title compound as a white solid (0.22 g, 87%): mp 84-88 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) d 8.56 (s, 1H), 8.13 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 9.0 Hz, 2H), 7.44 7.35 (m, 2H), 7.31 (d, J = 8.1 Hz, 2H), 3.29 3.15 (m, 1H), 2.78 (dd, J = 13.2, 5.4 Hz, 1H), 2.60 (dd, J = 13.2, 8.0 Hz, 1H), 1.49 (s, 2H), 1.15 (d, J = 6.3 Hz, 3H).

The following compounds were prepared in accordance to the procedure in Example 100.

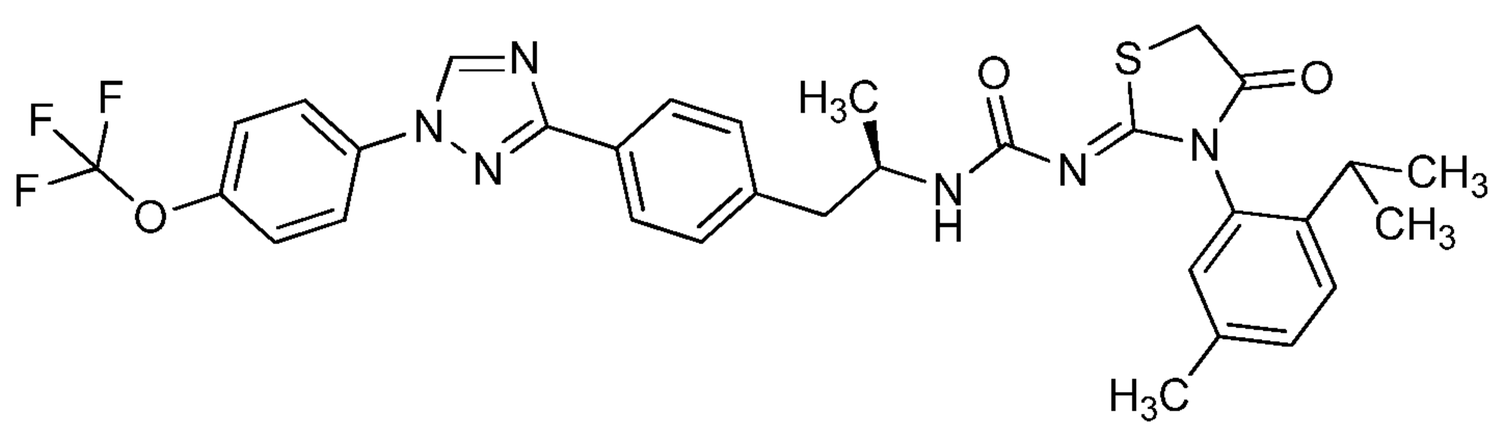
Preparation of (*S*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (CB62)



The title compound was prepared as described in Example 100 using (*S*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (2*R*,3*R*)-2,3-dihydroxysuccinate (**CB60**) and isolated as a white solid (0.40 g, 94%): mp 84-86 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) d 8.56 (s, 1H), 8.13 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 9.0 Hz, 2H), 7.44 7.35 (m, 2H), 7.35 7.28 (m, 2H), 3.29 3.16 (m, 1H),

2.78 (dd, *J* = 13.2, 5.3 Hz, 1H), 2.60 (dd, *J* = 13.2, 8.0 Hz, 1H), 1.15 (d, *J* = 6.3 Hz, 3H) ($N\underline{H}_2$ not observed).

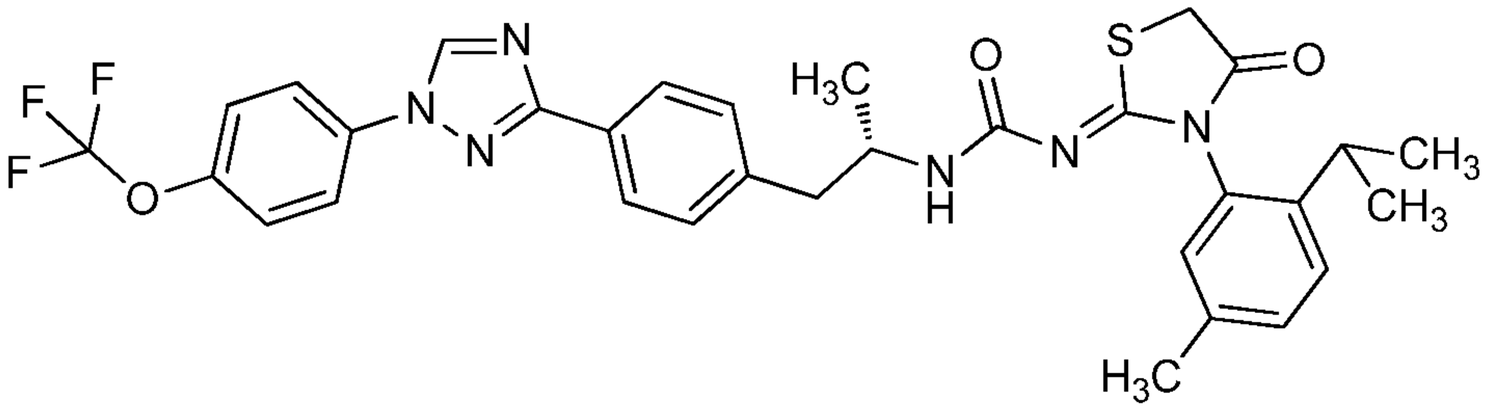
Example 101: Preparation of (*R,Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (FB45)



To (*R*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1H-1,2,4-triazol-3-yl)phenyl)propan-2-amine (**CB61**) (0.12 g, 0.32 mmol) and sodium bicarbonate (0.10 g, 1.2 mmol) in dichloromethane/water (2:1, 3.1 mL) in an ice bath was added triphosgene (0.052 g, 0.18 mmol). The reaction was quenched with few drops of water and diluted with dichloromethane. The reaction mixture was filtered through phase separator and concentrated. The residue was dissolved in acetonitrile (2 mL) and 1-(2-isopropyl-5-methylphenyl)thiourea (0.069 g, 0.33 mmol) and cesium carbonate (0.14 g, 0.42 mmol) were added in single portions. The reaction was stirred overnight at room temperature. Additional portions of 1-(2-isopropyl-5-methylphenyl)thiourea (0.070 g, 0.33 mmol) and cesium carbonate (0.070 g, 0.21 mmol) were added and the reaction was stirred overnight. Ethanol (4 mL), methyl 2-bromoacetate (0.10 mL, 0.96 mmol), and sodium acetate (0.079 g, 0.96 mmol) were added and the reaction was heated at 60 ℃ for 6 hours. The reaction was cooled and stirred at room temperature over the weekend. The reaction was diluted with water and extracted with ethyl acetate (2x). The organic layers were dried with sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided the title compound as a yellow oil (0.039 g, 19%).

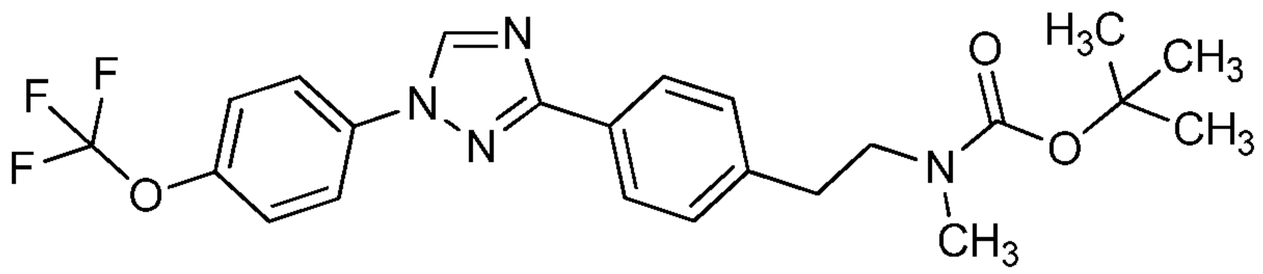
The following compounds were prepared in accordance to the procedure in Example 101.

Preparation of (*S*,*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)urea (FB46)



The title compound was prepared as described in Example 101 using (*S*)-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-amine (**CB62**) and 1-(2-isopropyl-5-methylphenyl)thiourea and isolated as an off-white foam (0.045 g, 24%).

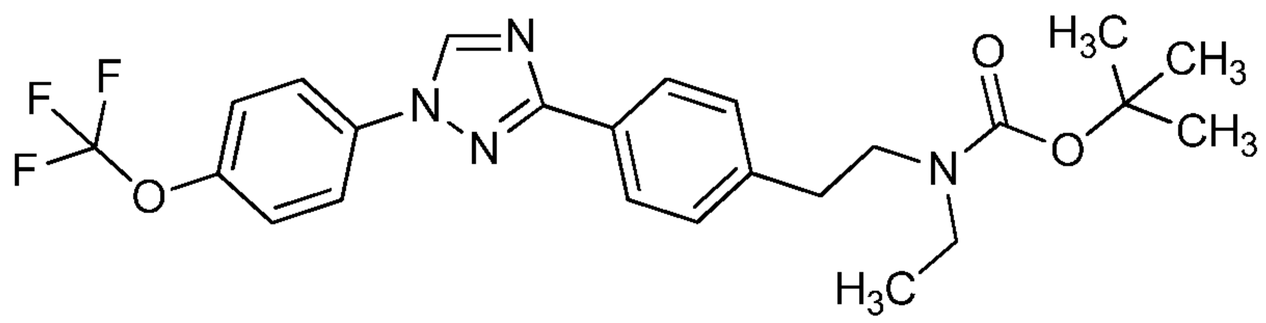
Example 102: Preparation of *tert*-butyl methyl(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (CB63)



To *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (**C50**) (0.021 g, 0.047 mmol) in anhydrous dimethylformamide (0.023 mL) at 0 ℃ was added sodium hydride (60% oil dispersion, 0.012 g, 0.30 mmol) and stirred in ice bath for 5 minutes. Iodomethane (0.013 g, 0.094 mmol) was added and the yellow solution immediately turned white. After 10 minutes, the reaction was quenched with water and extracted with dichloromethane. The organic layer was concentrated providing the title compound as a yellow oil(0.022 g, 97%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.12 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 9.0 Hz, 2H), 7.39 (dt, *J* = 8.0, 1.0 Hz, 2H), 7.37 – 7.20 (m, 2H), 3.47 (s, 2H), 2.86 (s, 2H), 1.57 (s, 3H), 1.44 (d, *J* = 13.7 Hz, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 463 ($[M+H]^+$).

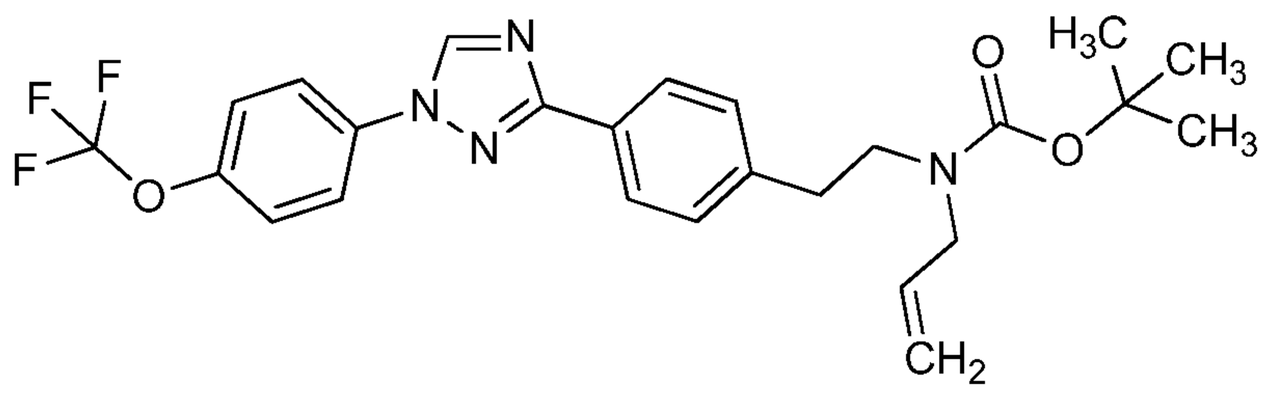
The following compounds were prepared in accordance to the procedure in Example 102.

Preparation of *tert*-butyl ethyl(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (CB64)



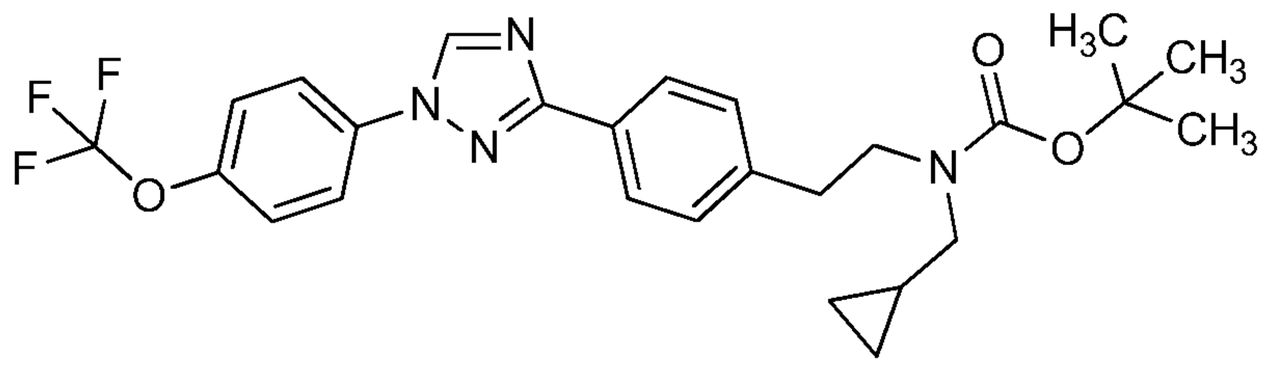
The title compound was prepared as described in Example 102 using *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (**C50**) and iodoethane and isolated as a yellow oil (0.175 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.16 - 8.06 (m, 2H), 7.89 - 7.73 (m, 2H), 7.45 - 7.36 (m, 2H), 7.31 (s, 2H), 3.42 (s, 2H), 3.23 (t, *J* = 35.4 Hz, 2H), 2.96 - 2.84 (m, 2H), 1.47 (s, 9H), 1.08 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 477 ($[M+H]^+$).

Preparation of *tert*-butyl allyl(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (CB65)



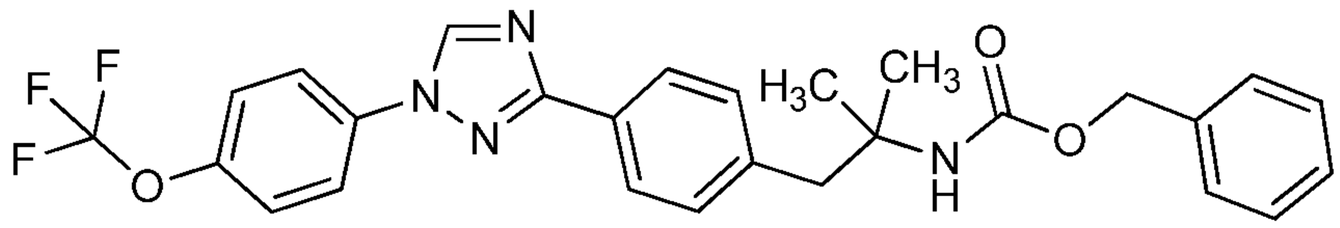
The title compound was prepared as described in Example 102 using *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (**C50**) and allyl bromide and isolated as a yellow oil (0.144 g, 99%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.15 - 8.08 (m, 2H), 7.85 - 7.76 (m, 2H), 7.39 (dq, *J* = 7.8, 1.0 Hz, 2H), 7.30 (s, 2H), 5.76 (s, 1H), 5.12 (s, 2H), 3.76 (d, *J* = 45.8 Hz, 2H), 3.42 (s, 2H), 2.89 (d, *J* = 0.7 Hz, 2H), 1.47 (s, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 489 ($[M+H]^+$).

Preparation of *tert*-butyl (cyclopropylmethyl)(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamate (CB66)



The title compound was prepared as described in Example 102 using *tert*-butyl 4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethylcarbamate (**C50**) and cyclopropylmethyl bromide and isolated as a clear oil (0.155 g, 96%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.16 - 8.07 (m, 2H), 7.84 - 7.77 (m, 2H), 7.39 (dq, *J* = 8.0, 0.9 Hz, 2H), 7.31 (s, 2H), 3.50 (t, *J* = 7.6 Hz, 2H), 3.17 - 2.86 (m, 4H), 1.48 (s, 9H), 0.87 (ddd, *J* = 11.2, 9.0, 6.7 Hz, 1H), 0.49 (d, *J* = 8.0 Hz, 2H), 0.21 (s, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 503 ($[M+H]^+$).

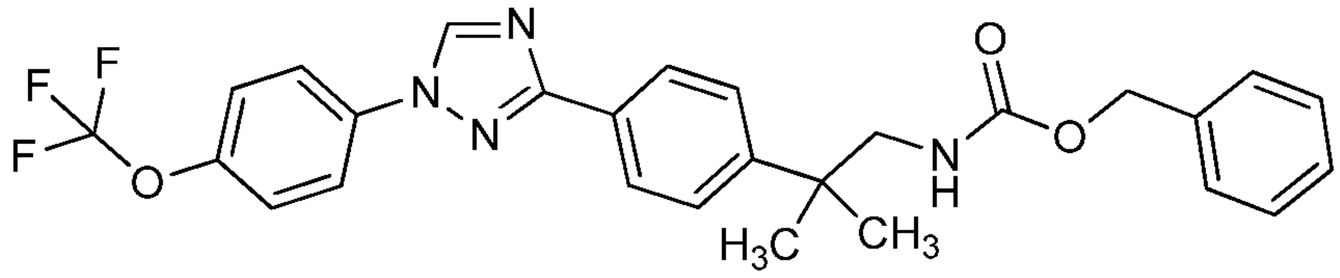
Example 103: Preparation of benzyl (2-methyl-1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propan-2-yl)carbamate (CB67)



A mixture of 3-bromo-1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazole (**C1**) (4.28 g, 13.9 mmol), benzyl (2-methyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-yl)carbamate (**CB7**) (6.12 g, 15.0 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (0.390 g, 1.40 mmol), palladium(II) acetate (0.150 g, 0.680 mmol), and cesium fluoride (4.34 g, 28.6 mmol) in dioxane/water (4:1, 90 mL) was heated at 70 °C overnight. The reaction was cooled and diluted with brine and extracted with ethyl acetate (2x). The organic layer was dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent provided the title compound as a clear oil (1.16 g, 15%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.06 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.44 - 7.32 (m, 7H), 7.19 (d, *J* = 8.2 Hz, 2H), 5.12 (s, 2H), 4.56 (s, 1H), 3.05 (s, 2H), 1.33 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.02; ESIMS *m/z* 511 ($[M+H]^+$).

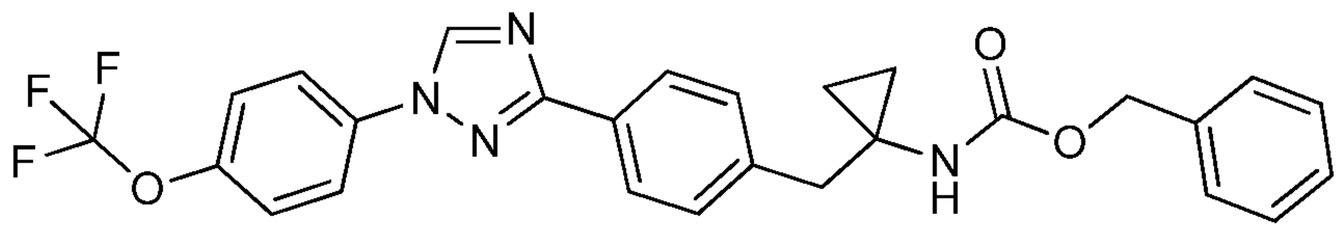
The following compounds were prepared in accordance to the procedure in Example 103.

Preparation of benzyl (2-methyl-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)propyl)carbamate (CB68)



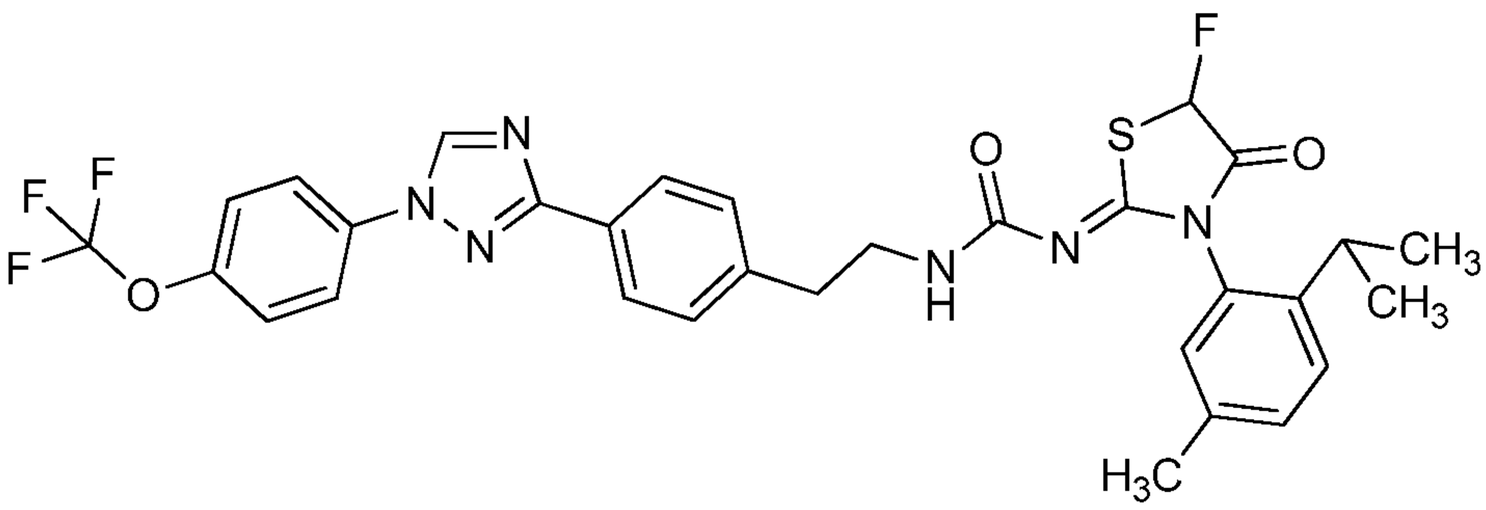
The title compound was prepared as described in Example 103 using benzyl (2-methyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propyl)carbamate (**CB8**) and isolated as a clear oil (0.045 g, 24%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.18 - 8.10 (m, 2H), 7.84 - 7.75 (m, 2H), 7.49 - 7.42 (m, 2H), 7.39 (dq, *J* = 9.0, 0.9 Hz, 2H), 7.31 (q, *J* = 6.8, 6.4 Hz, 5H), 5.06 (s, 2H), 4.52 (s, 1H), 3.45 (d, *J* = 6.3 Hz, 2H), 1.38 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 511 ($[M+H]^+$).

Preparation of benzyl (1-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)benzyl)cyclopropyl)carbamate (CB69)



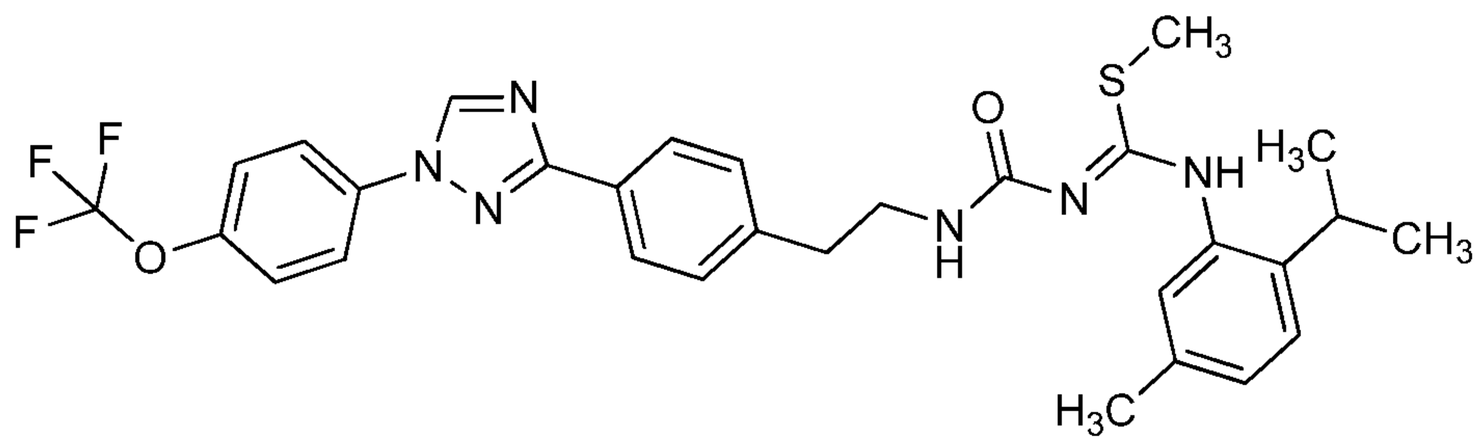
The title compound was prepared as described in Example 103 using benzyl (1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)cyclopropyl)carbamate (**CB9**) and isolated as a tan solid (2.19 g, 68%): mp 156-158 ºC; ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.56 (s, 1H), 8.10 (d, *J* = 8.1 Hz, 2H), 7.84 - 7.73 (m, 2H), 7.42 - 7.30 (m, 6H), 7.26 - 7.25 (m, 3H), 5.10 (s, 2H), 4.96 (s, 1H), 2.94 (s, 2H), 0.85 (s, 4H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.03; ESIMS *m/z* 509 ($[M+H]^+$).

Example 104: Preparation of (*Z*)-1-(5-fluoro-3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB64)



To (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (**F5**) (0.050 g, 0.080 mmol) and 2-fluorenone (0.0080 g, 0.044 mmol) in anhydrous acetonitrile (0.80 mL) was added Selectfluor® (0.062 g, 0.18 mmol). The reaction was stirred at room temperature overnight. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided the title compound as a yellow oil (0.033 g, 63%).

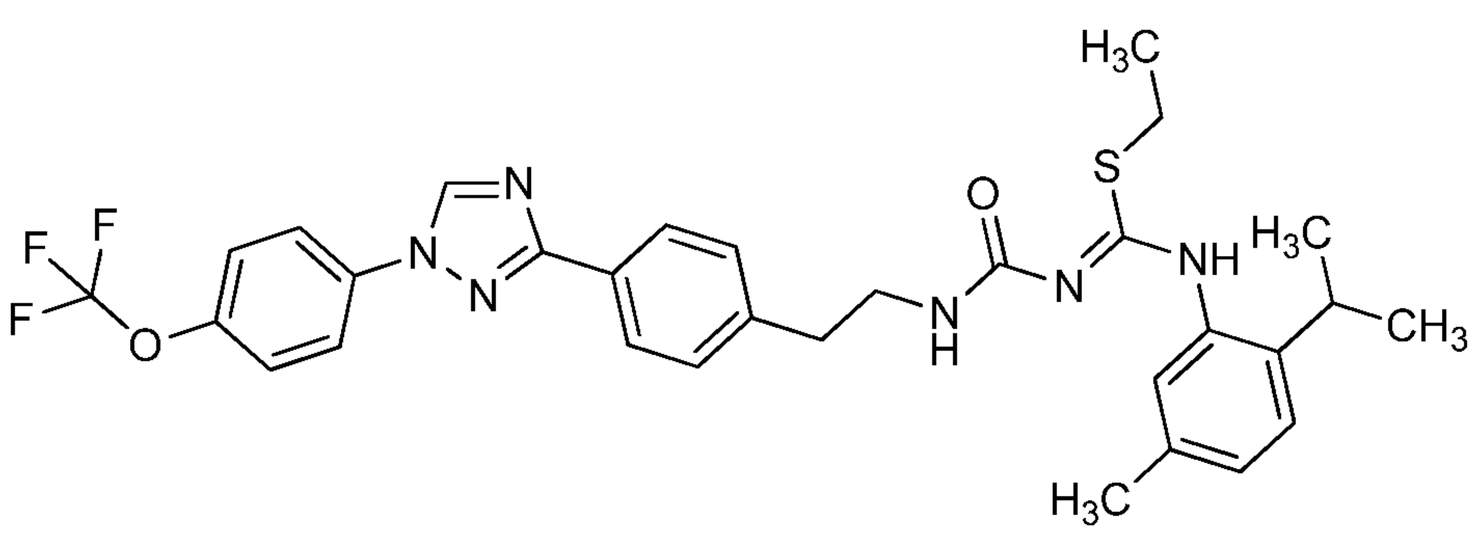
Example 105: Preparation of (*Z*)-methyl *N*-(2-isopropyl-5-methylphenyl)-*N'*-((4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamoyl)carbamimidothioate (FB65)



To *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) (0.15 g, 0.26 mmol) and sodium acetate (0.053 g, 0.65 mmol) in ethanol (1 mL) was added iodomethane (0.020 mL, 0.32 mmol). The reaction was stirred at room temperature overnight. The reaction mixture was diluted with water and the water was decanted off to leave white solid, which was dried under vacuum for 3 hours. Purification by flash column chromatography using 0-100% ethyl acetate/B, where B = 1:1 dichloromethane/hexanes, as eluent provided the title compound as a clear oil (0.081 g, 49%).

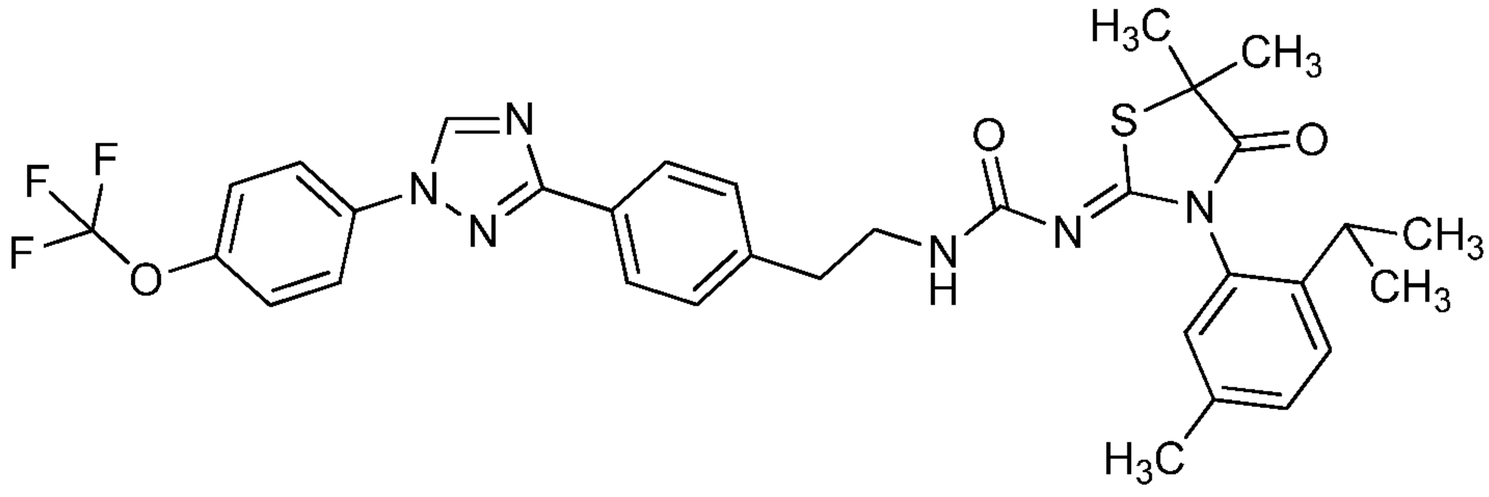
The following compounds were prepared in accordance to the procedure in Example 105.

Preparation of (*Z*)-ethyl *N*-(2-isopropyl-5-methylphenyl)-*N'*-((4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)carbamoyl)carbamimidothioate (FB66)



The title compound was prepared as described in Example 105 using *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) and iodoethane, purified by reverse-phase flash column chromatography using 0-100% acetonitrile/water as eluent, and isolated as a clear oil (0.050 g, 43%).

Example 106: Preparation of (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-5,5-dimethyl-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB68)

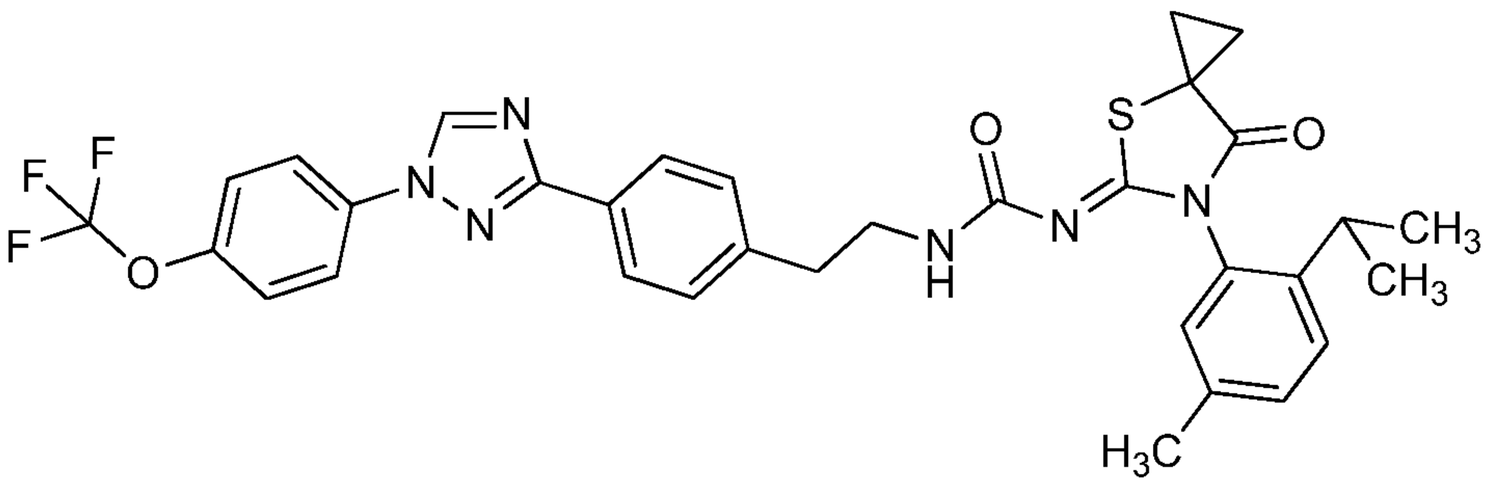


To a dry 2 dram vial equipped with magnetic stirrer was added (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (**F5**) (0.10 g, 0.16 mmol) and anhydrous dimethylformamide (0.5 mL). To this solution was added sodium hydride (60% oil dispersion, 0.0064 g, 0.16 mmol) followed by iodomethane

(0.022 g, 0.16 mmol). The reaction was stirred overnight at room temperature. Purification by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent provided the title compound as a pale yellow foam (0.054 g, 52%).

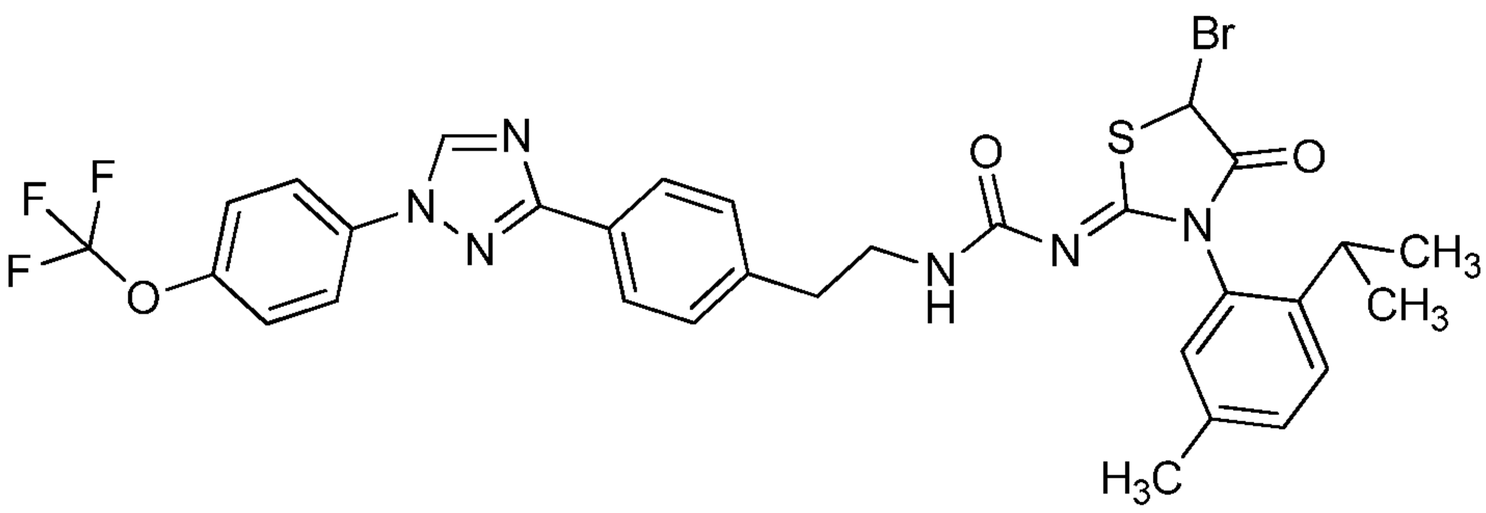
The following compounds were prepared in accordance to the procedure in Example 106.

Preparation of (*Z*)-1-(6-(2-isopropyl-5-methylphenyl)-7-oxo-4-thia-6-azaspiro[2.4]heptan-5-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB69)



The title compound was prepared as described in Example 106 using *N*-[5-methyl-2-isopropylphenyl]-*N'*-[2-(4-{1-[4-(trifluoromethoxy)-phenyl]-1*H*-1,2,4-triazol-3-yl}phenyl)ethyl]dicarbonimidothioic diamide (**F3**) and 1,2-dibromoethane and isolated as a white foam (0.023 g, 22%).

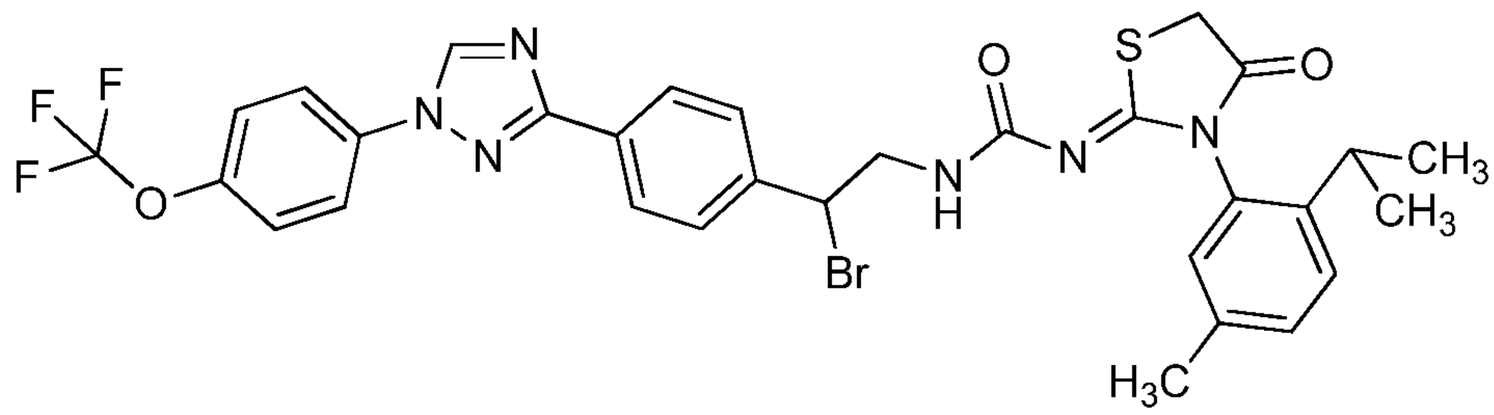
Example 107: Preparation of (*Z*)-1-(5-bromo-3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB70)



To a dry 2 dram vial equipped with magnetic stirrer was added (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (**F5**) (0.20 g, 0.32 mmol) and anhydrous dichloromethane (0.5 mL). To this solution was added

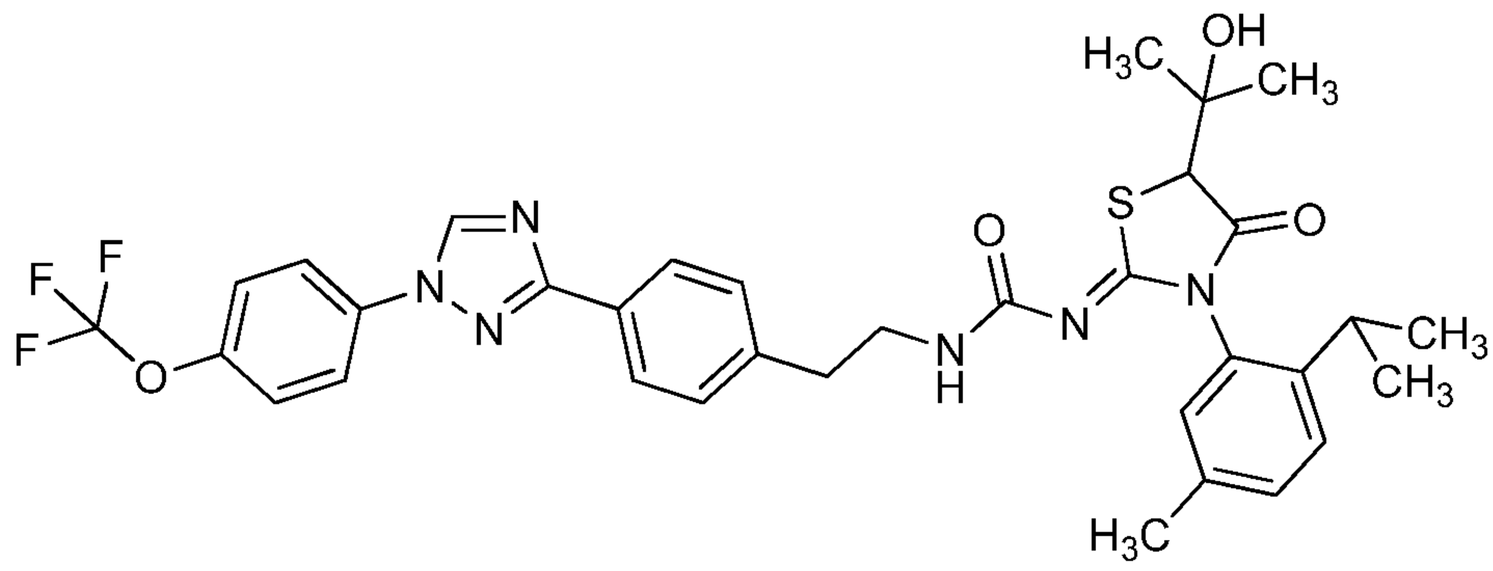
bromine (0.033 mL, 0.64 mmol). The reaction was stirred overnight at room temperature. Purification by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent provided the title compound as a clear colorless oil (0.041 g, 18%).

Example 108: Preparation of (*Z*)-1-(2-bromo-2-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenyl)ethyl)-3-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)urea (FB71)



To a dry round-bottomed flask (20 mL) equipped with a magnetic stirrer and a reflux condenser were added (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (**F5**) (0.20 g, 0.32 mmol), carbon tetrachloride (1 mL), *N*-bromosuccinimide (0.057 g, 0.32 mmol), and azobisisobutyronitrile (0.0053 g, 0.032 mmol). The reaction was heated to reflux for 2 hours. The reaction was cooled. Purification by flash column chromatography using 0-100% ethyl acetate/hexanes as eluent provided the title compound as a yellow oil (0.049 g, 21%).

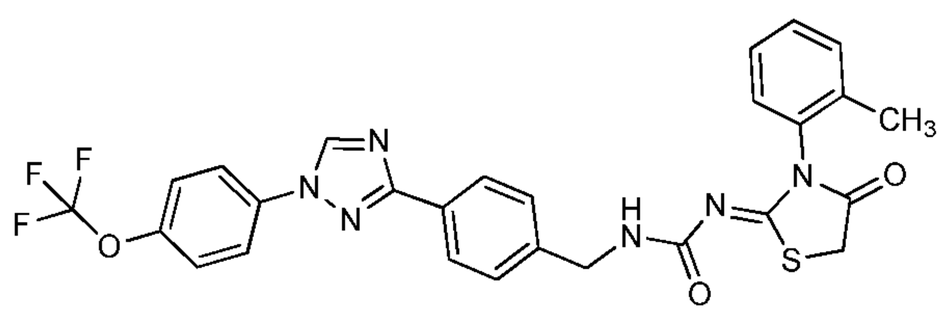
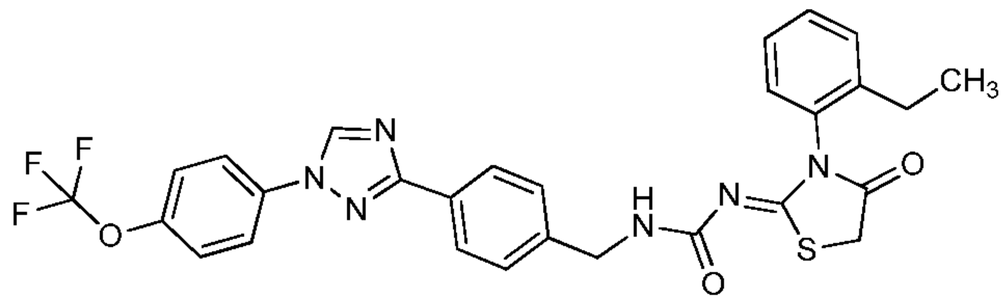
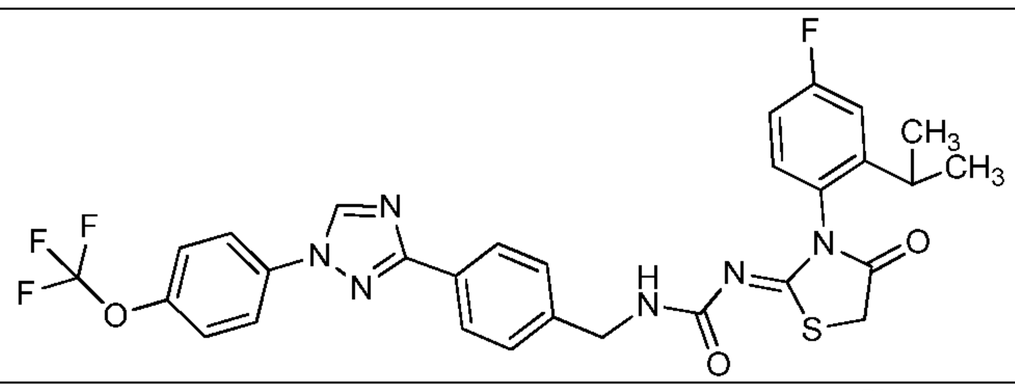
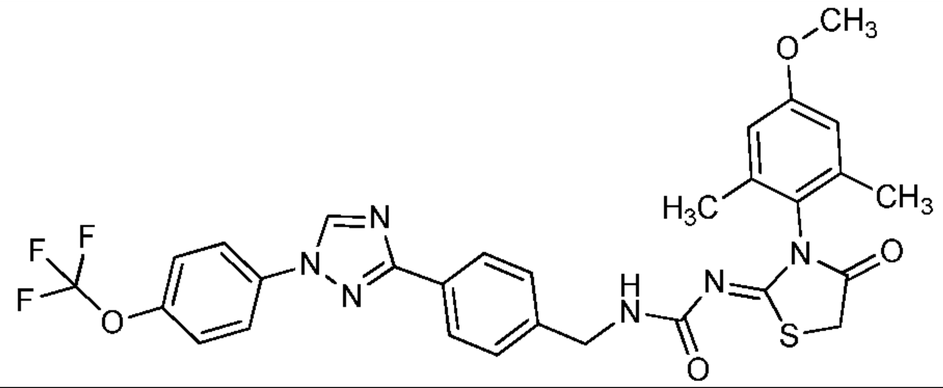
Example 109: Preparation of (*Z*)-1-(5-(2-hydroxypropan-2-yl)-3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (FB72)

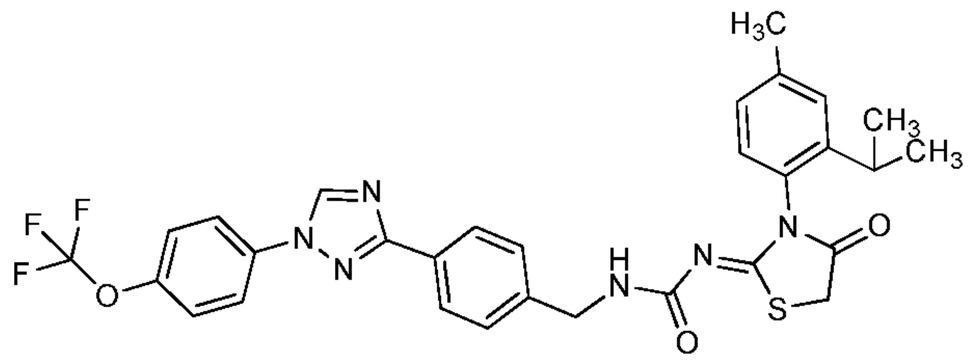
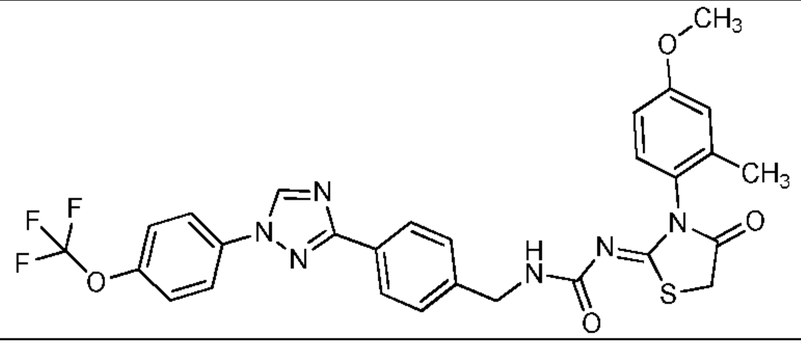
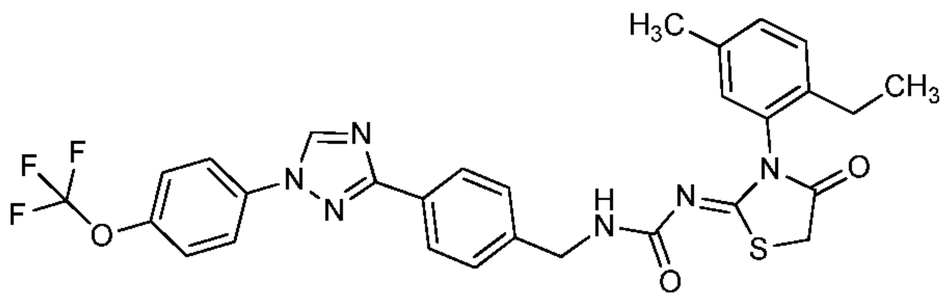
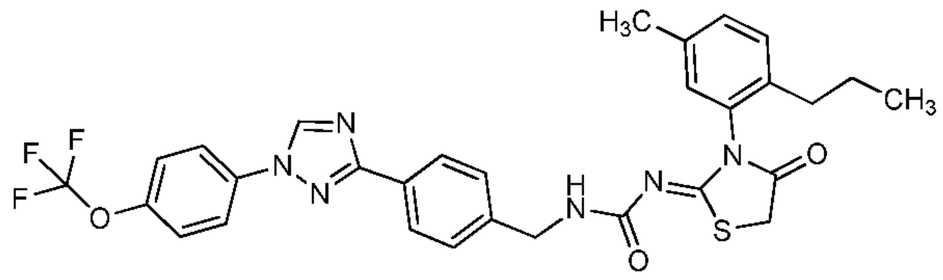
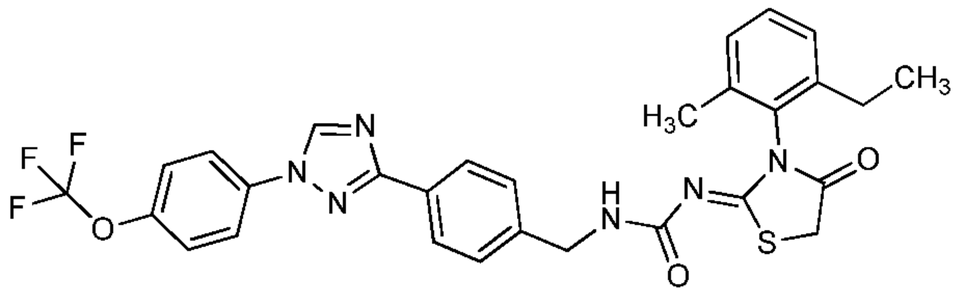
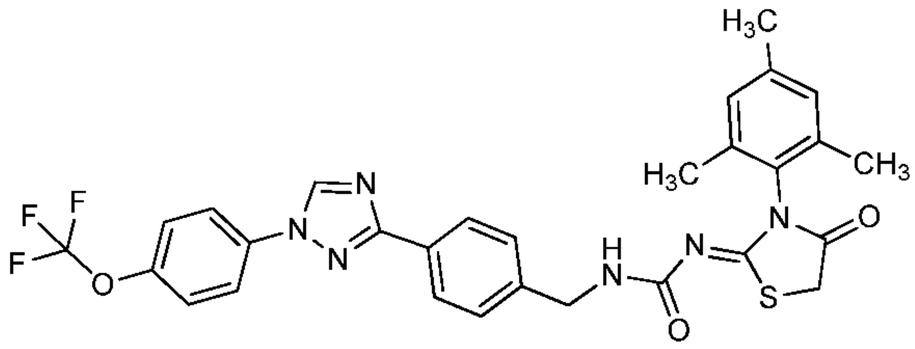
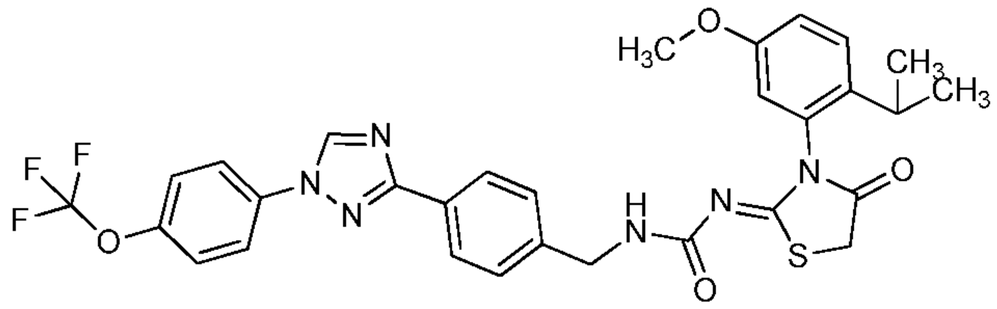


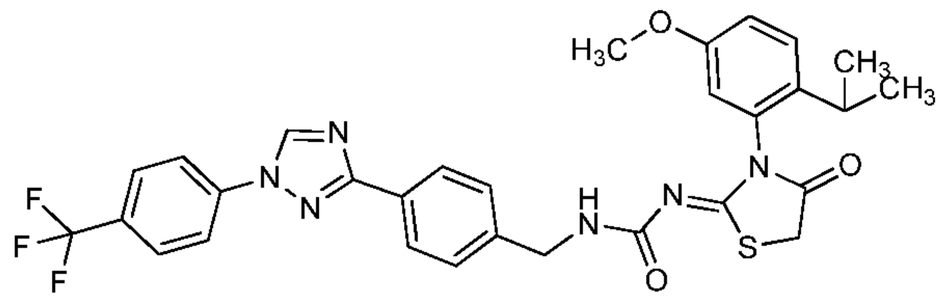
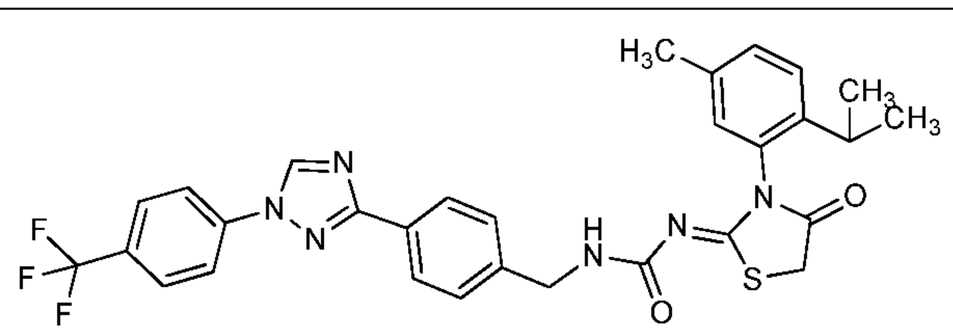
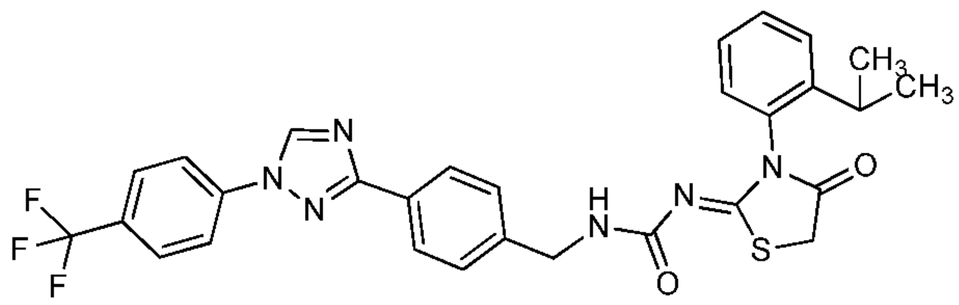
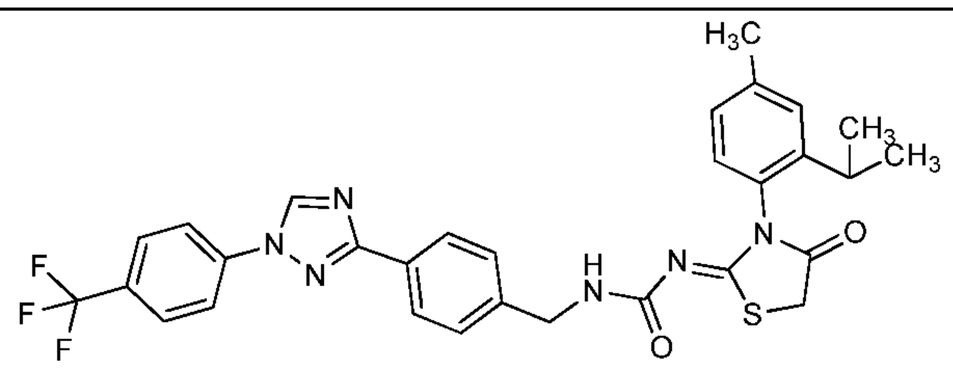
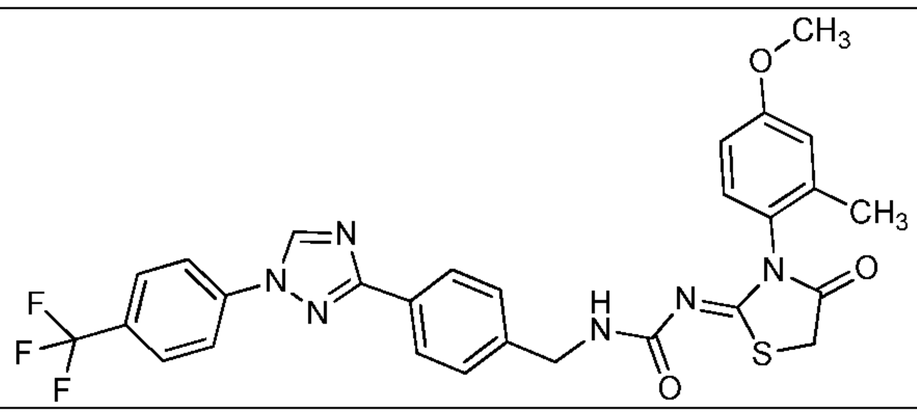
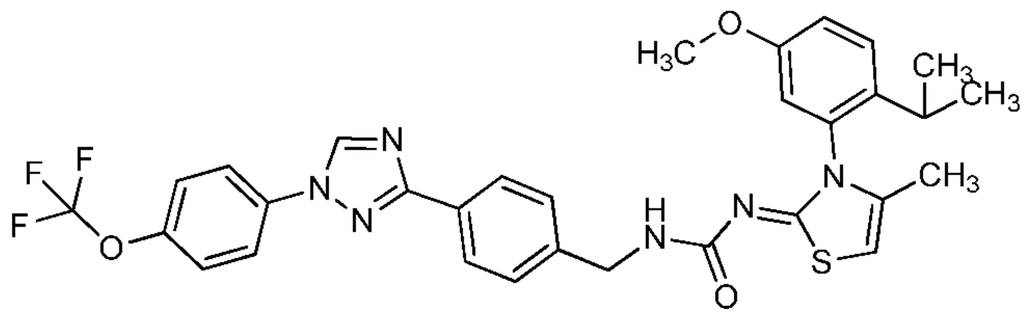
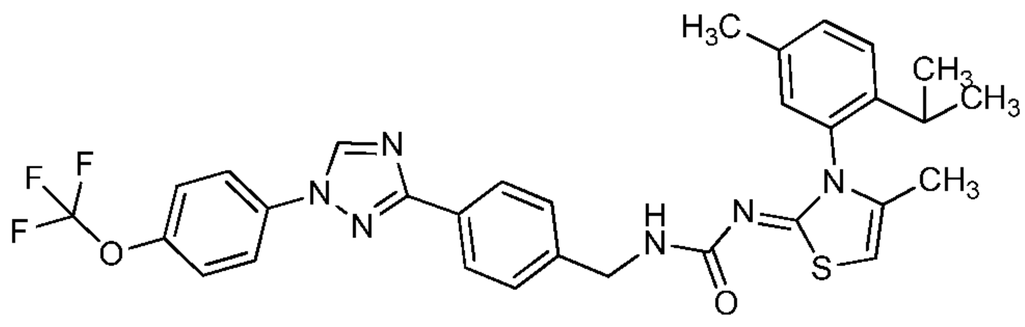
To (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea (**F5**) (0.40 g, 0.64 mmol) in acetone (30 mL) was added saturated aqueous sodium bicarbonate (3 mL). The reaction was heated to reflux for 12 hours, cooled, and concentrated. The reaction mixture was partitioned between ethyl acetate and water. The organic layer was dried and concentrated. Purification by flash column chromatography using 100-40% A/B, where A = 1:1 dichloromethane/hexanes and B = 3:1 ethyl acetate/acetone, as eluent provided the title compound as a white solid (0.095 g, 19%).

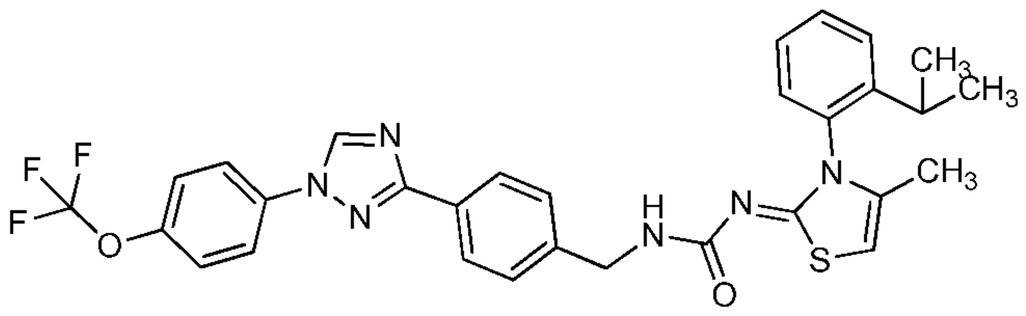
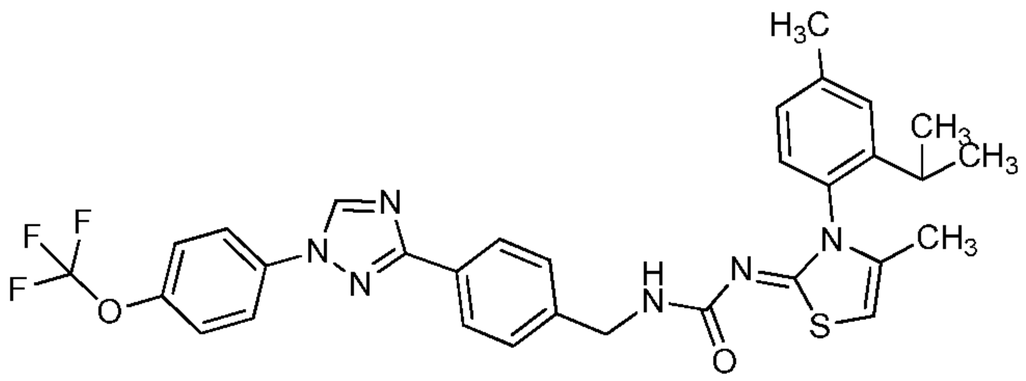
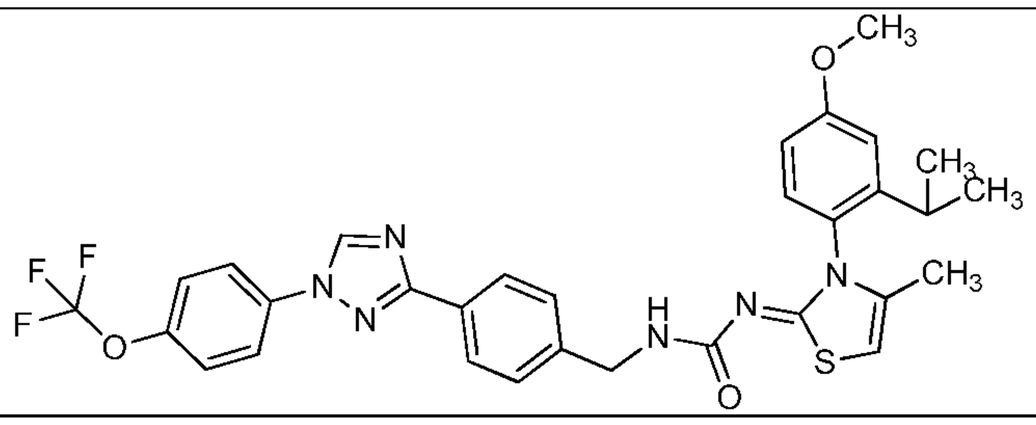
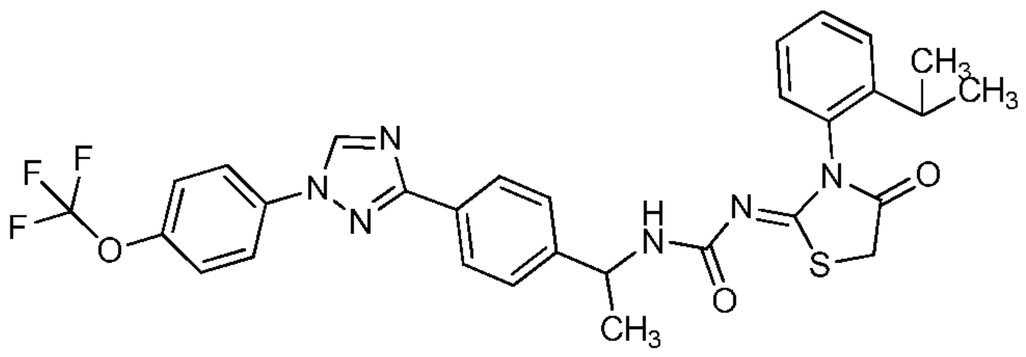
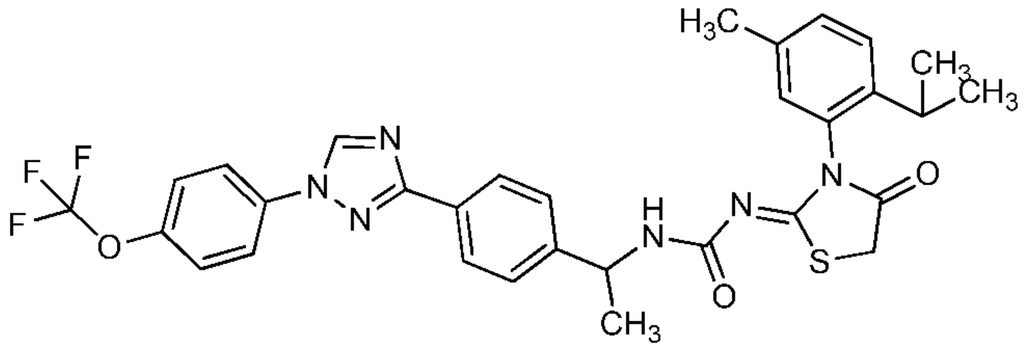
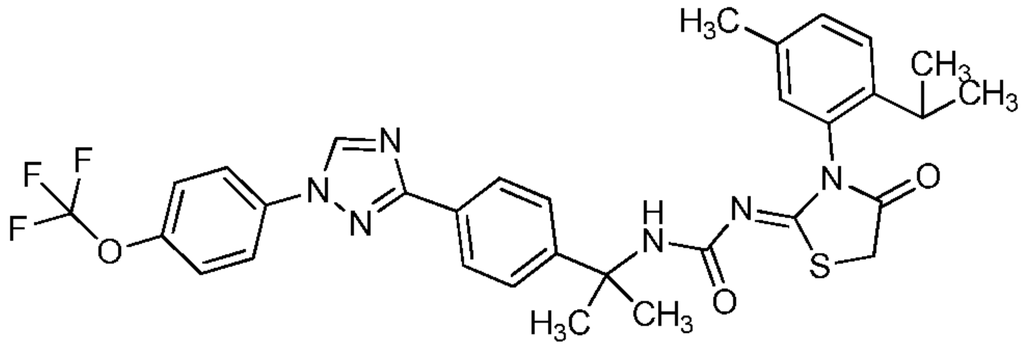
Using the procedures disclosed herein the following list of prophetic molecules having a structure according to Formula One may be made (Table P-One).

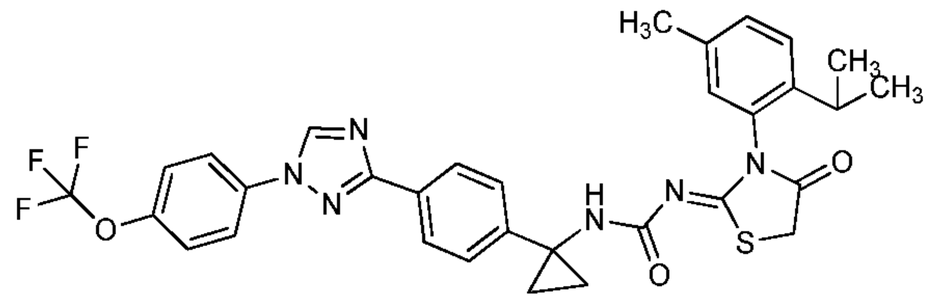
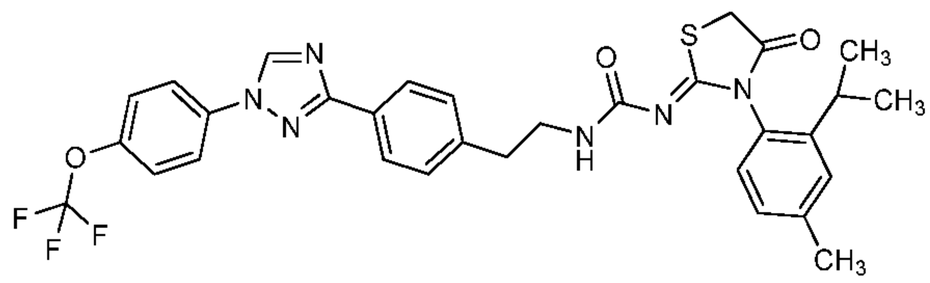
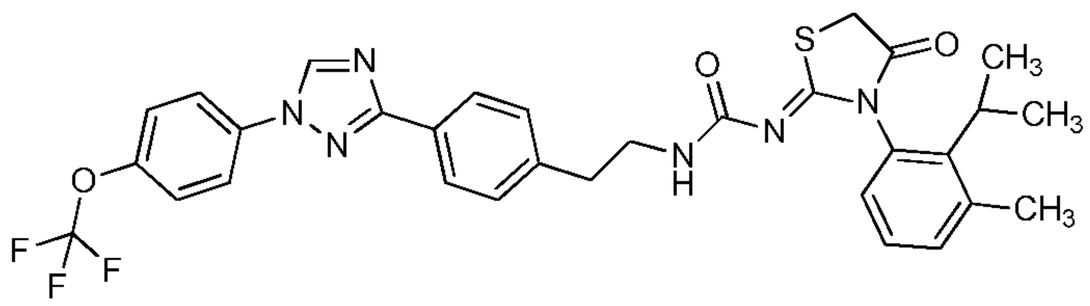
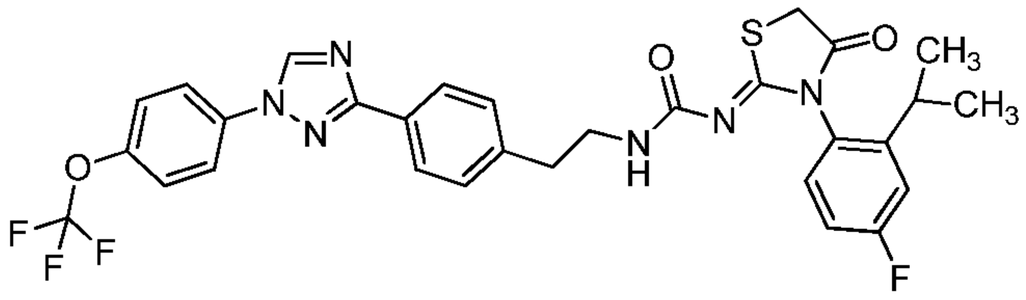
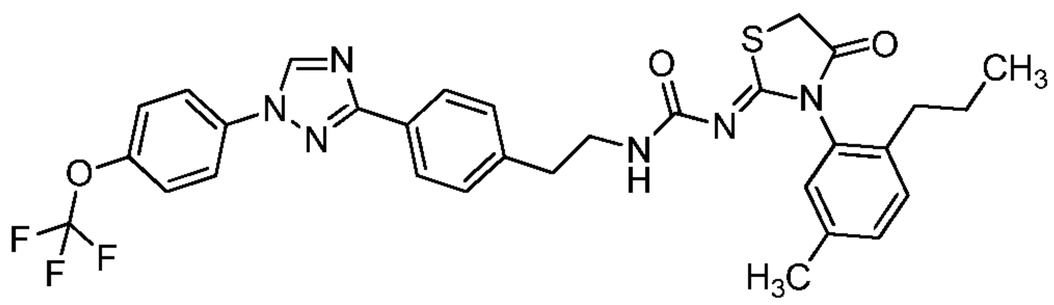
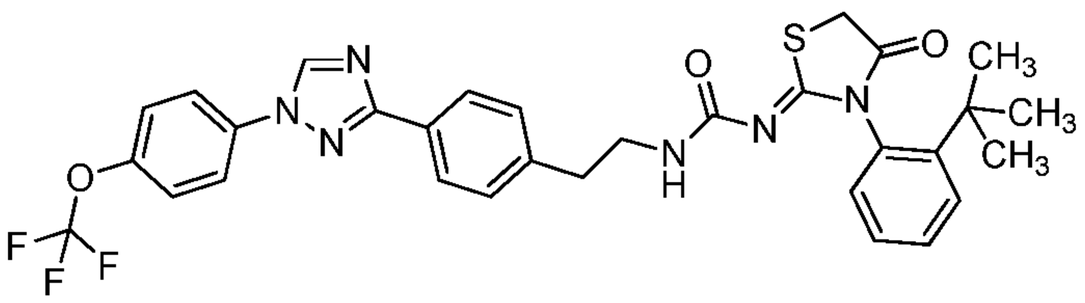
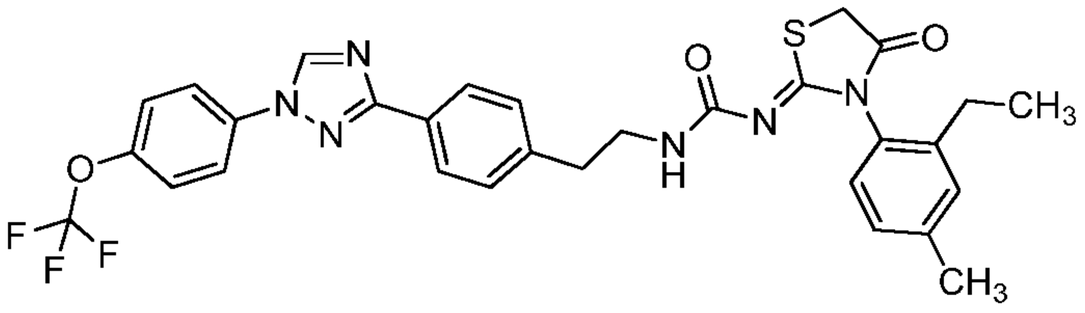
Table P-One

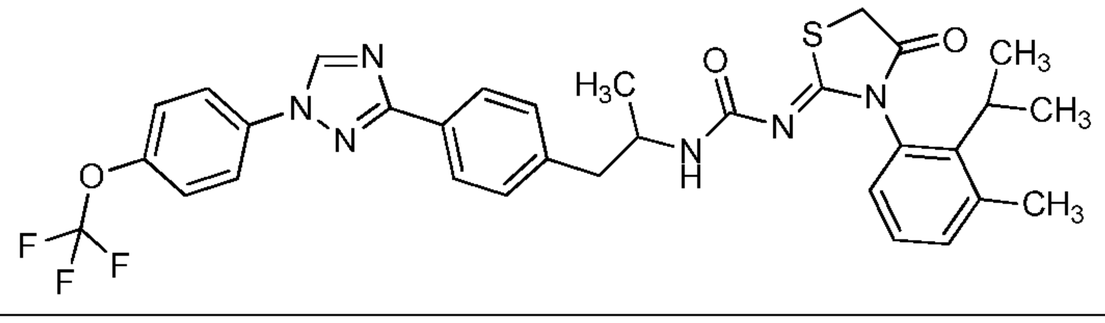
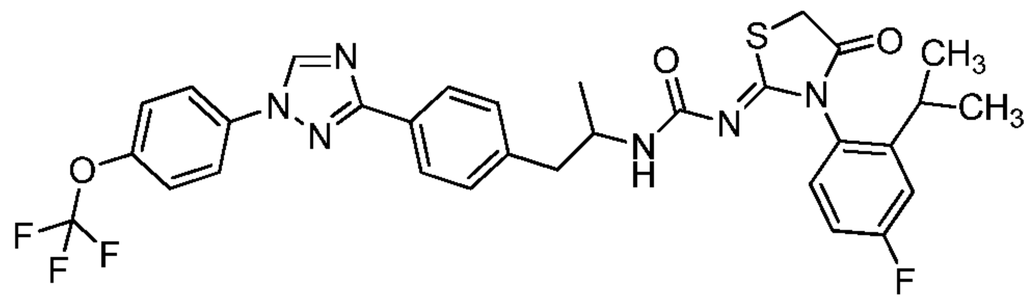
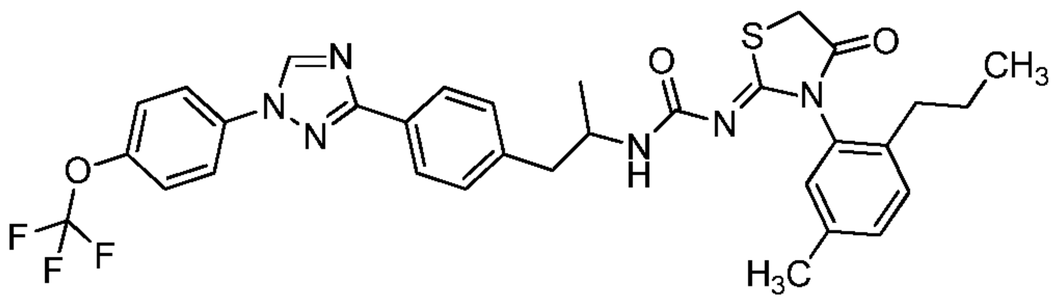
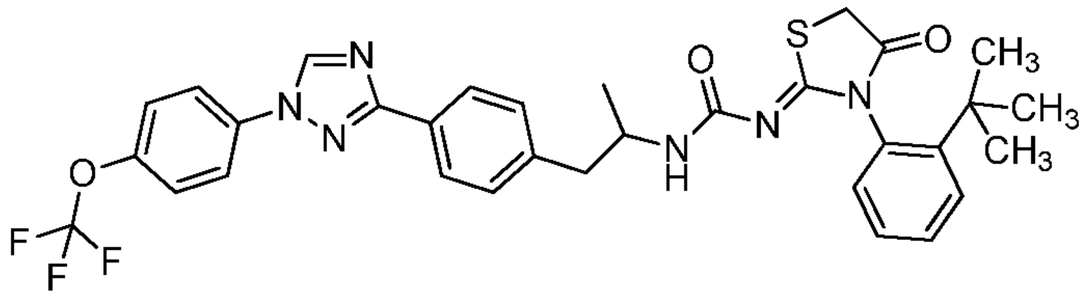
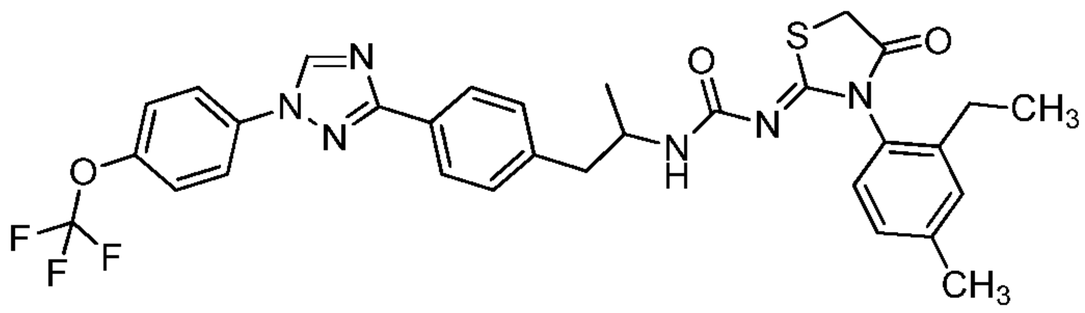
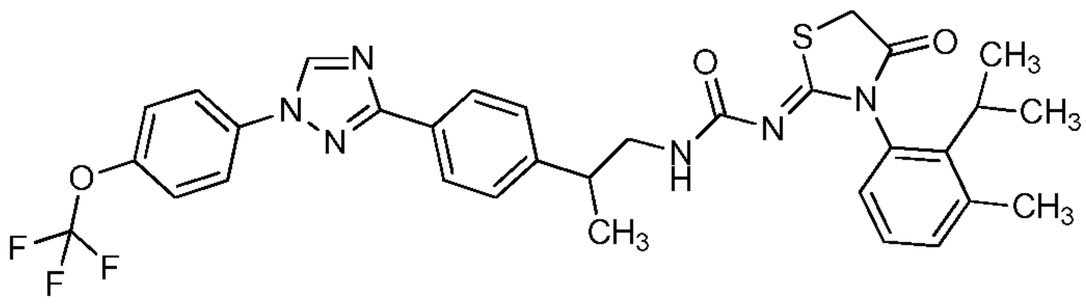
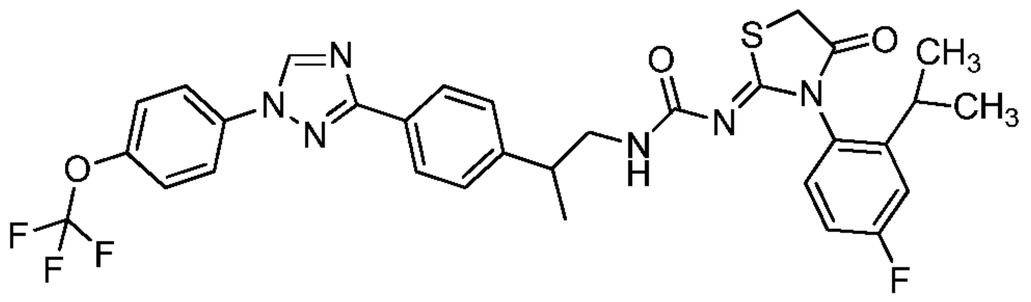
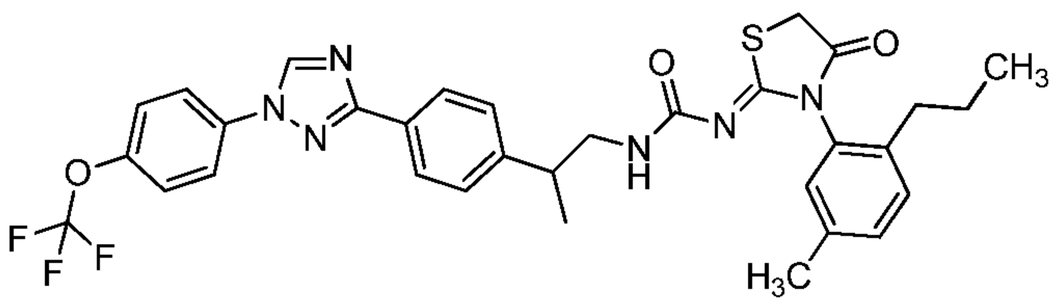
P1	
P2	
P3	
P4	

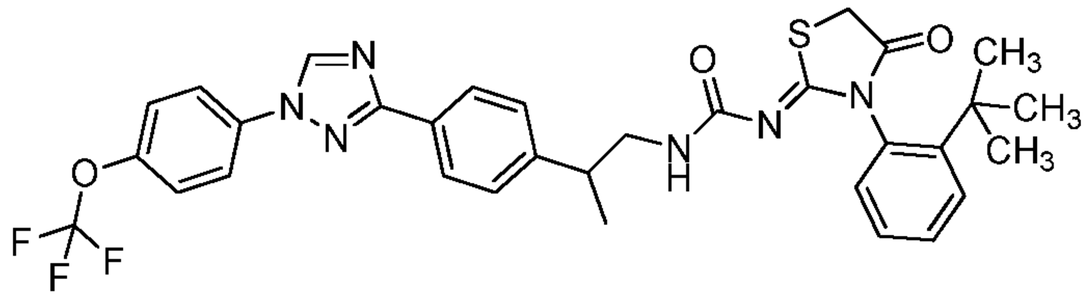
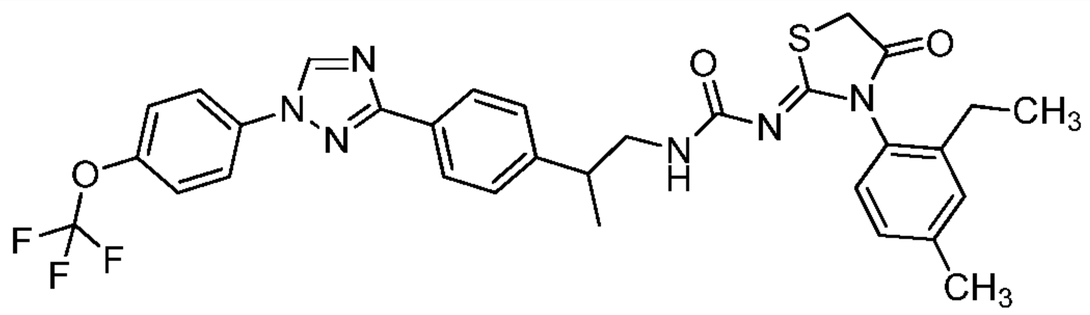
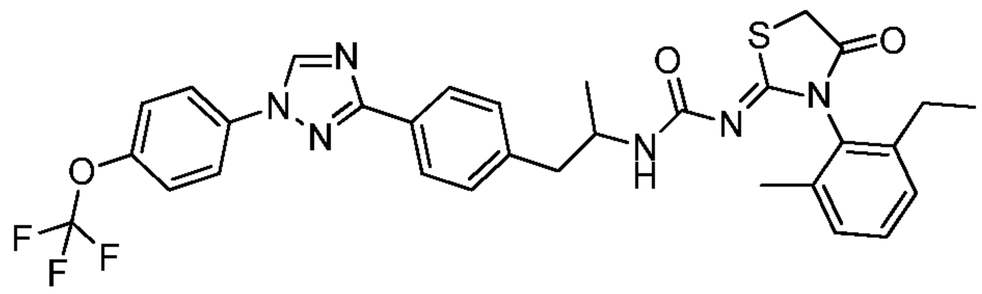
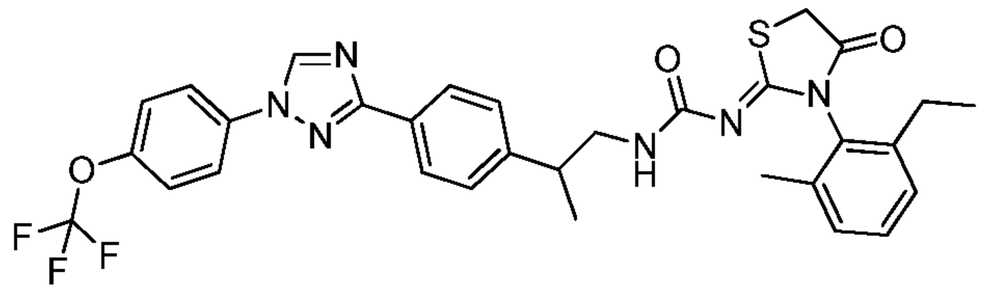
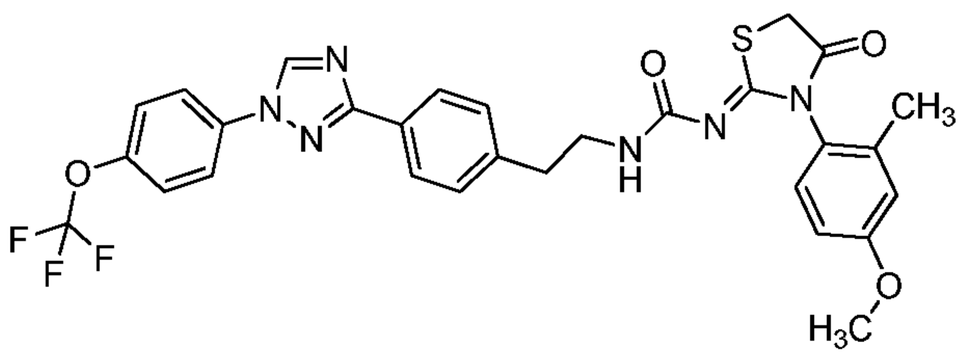
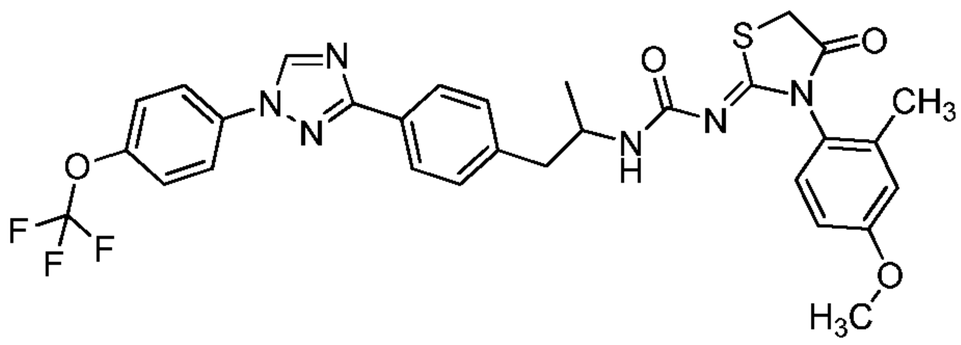
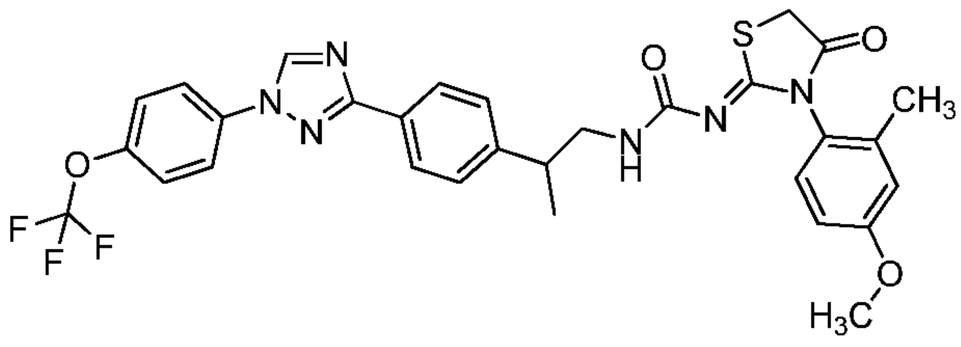
P5	
P6	
P7	
P8	
P9	
P10	
P11	

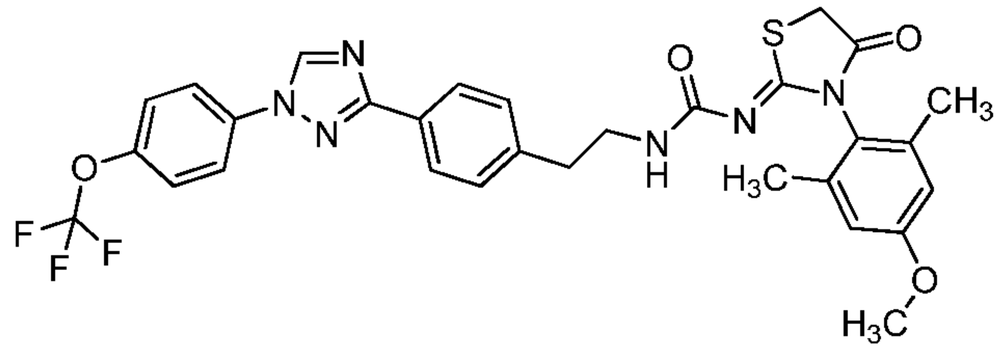
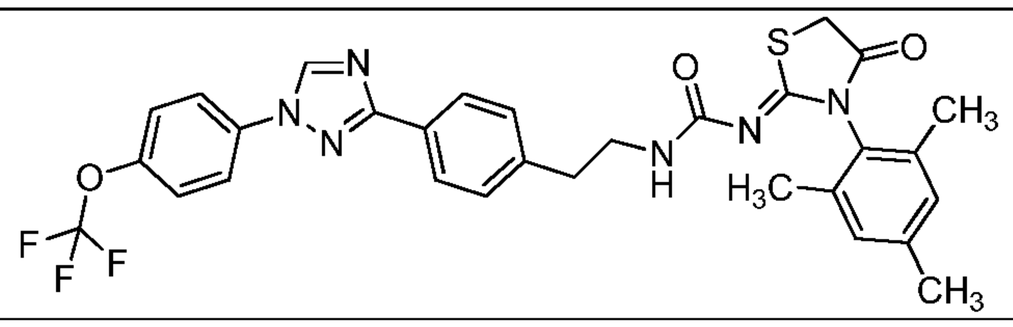
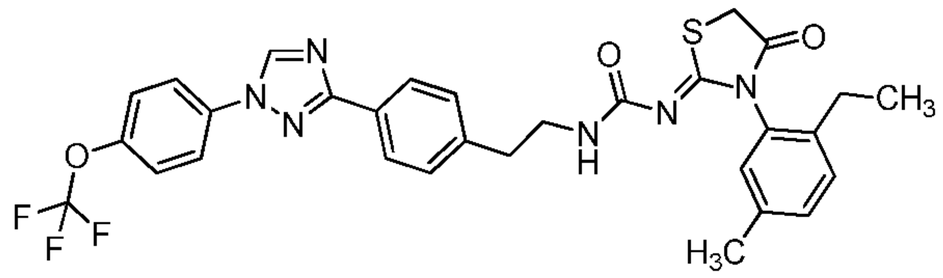
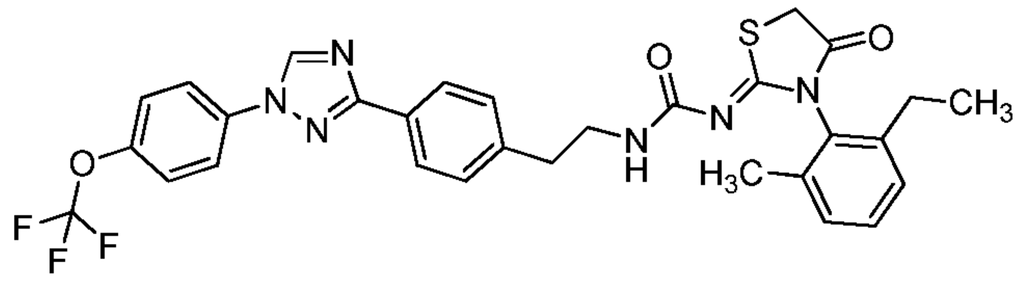
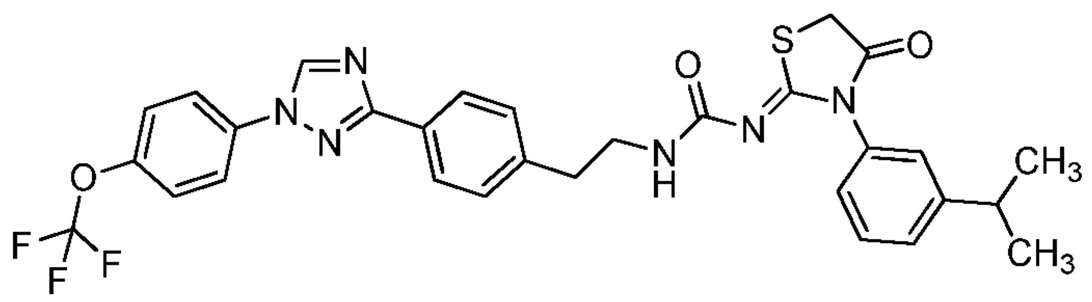
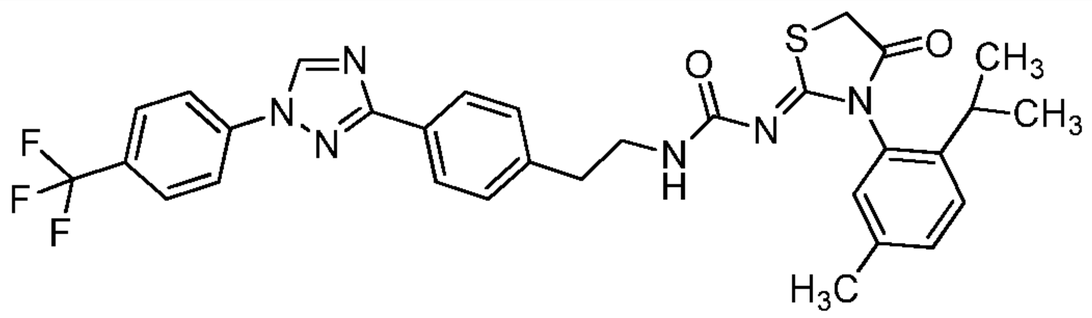
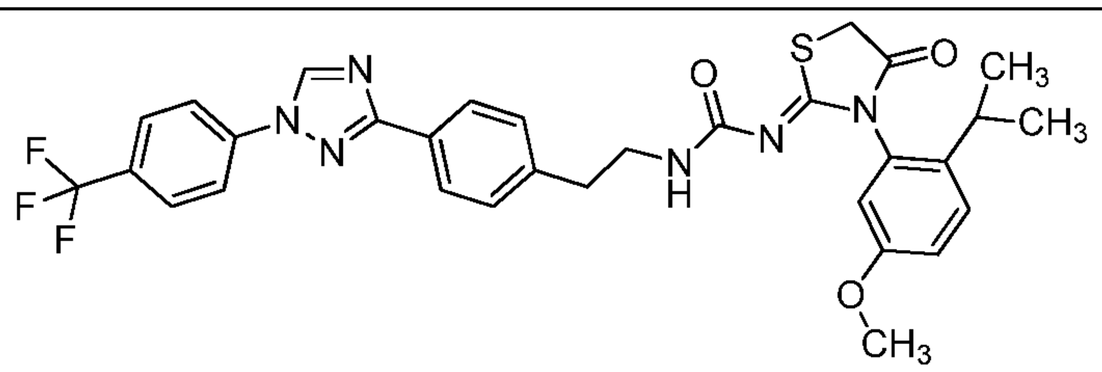
P12	
P13	
P14	
P15	
P16	
P17	
P18	

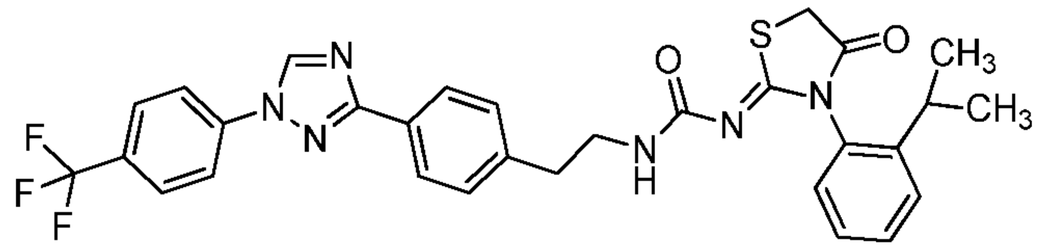
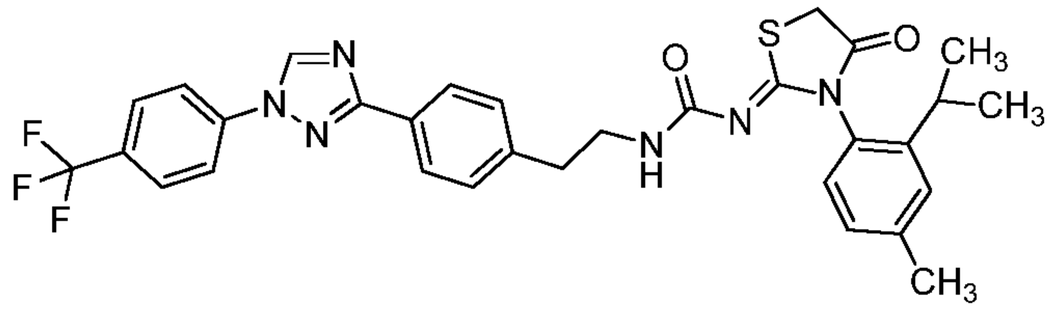
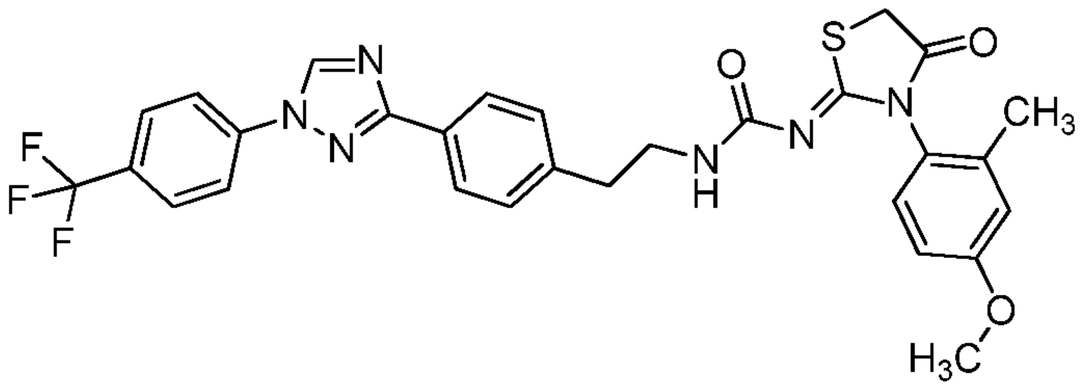
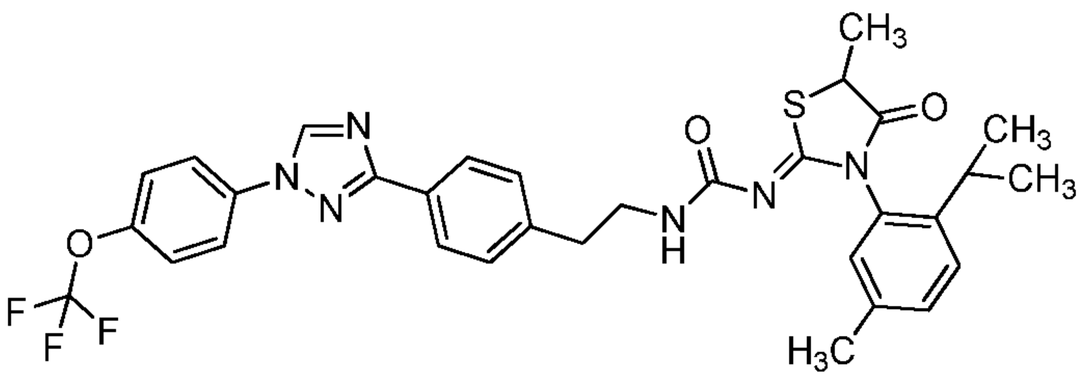
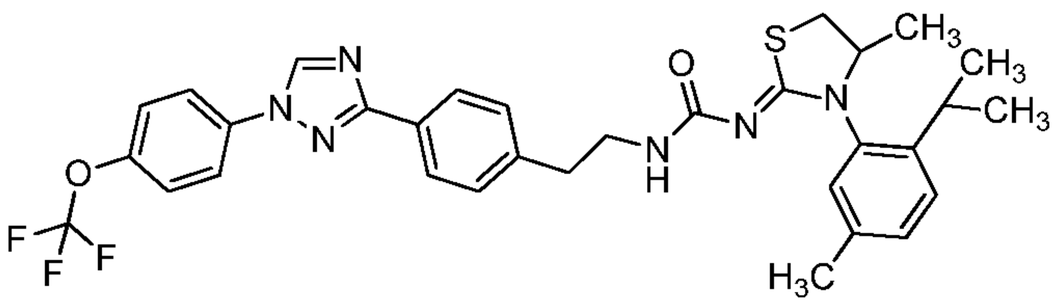
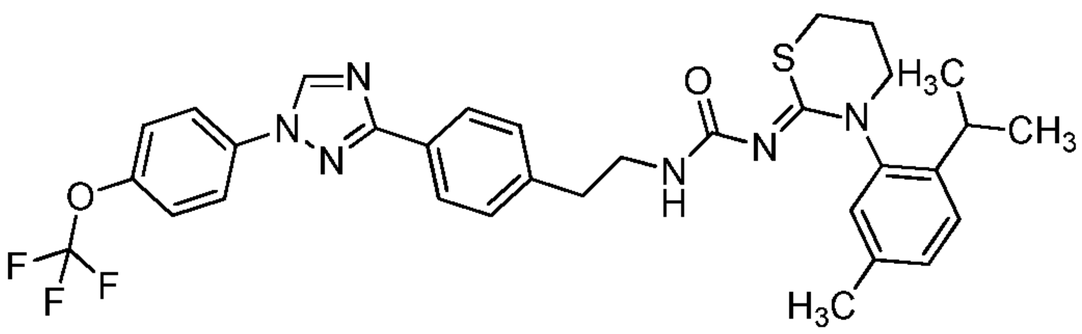
P19	
P20	
P21	
P22	
P23	
P24	

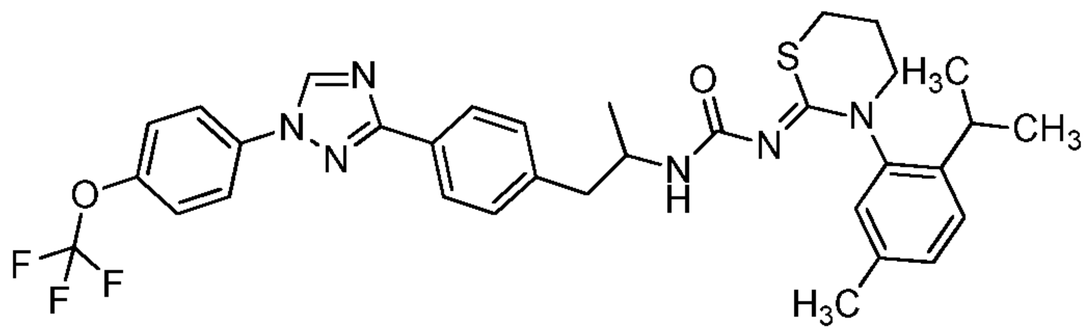
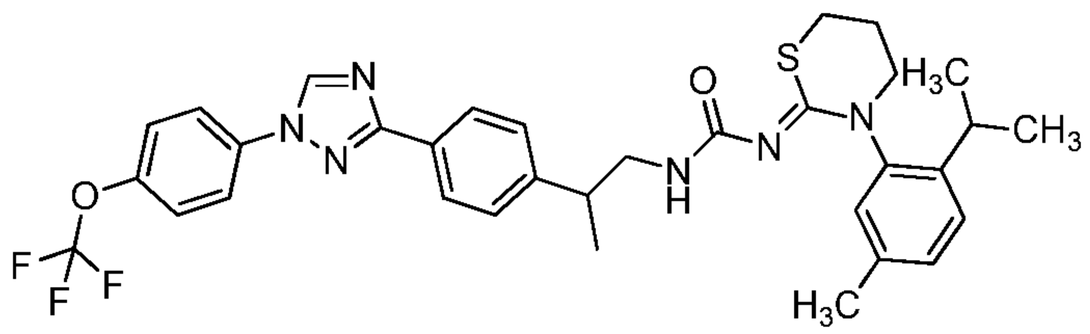
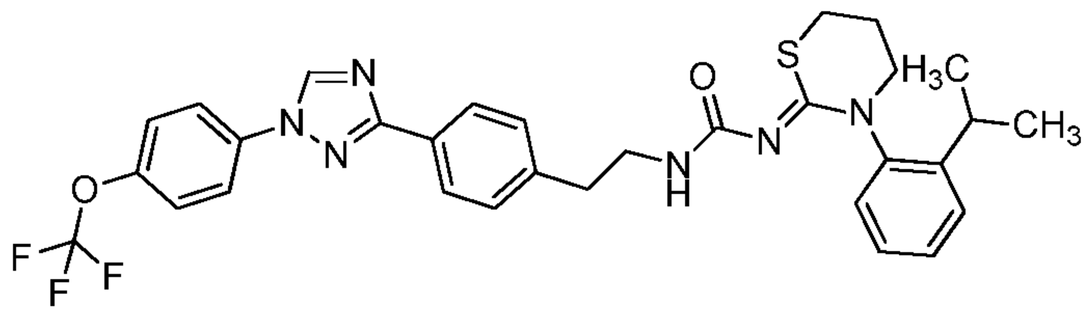
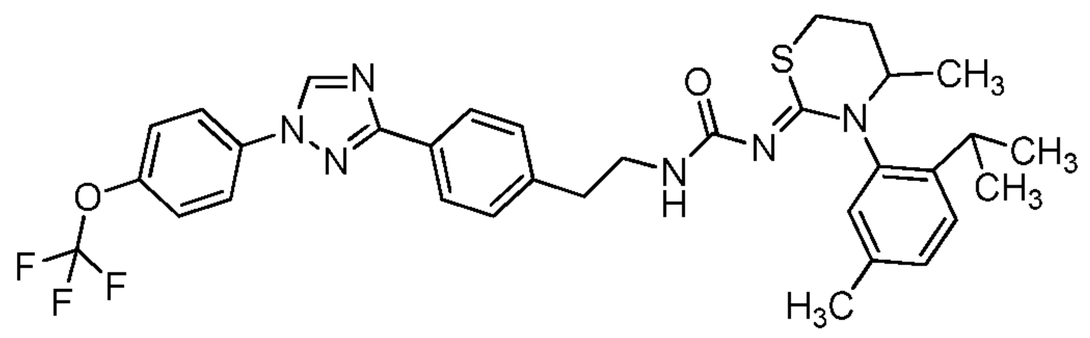
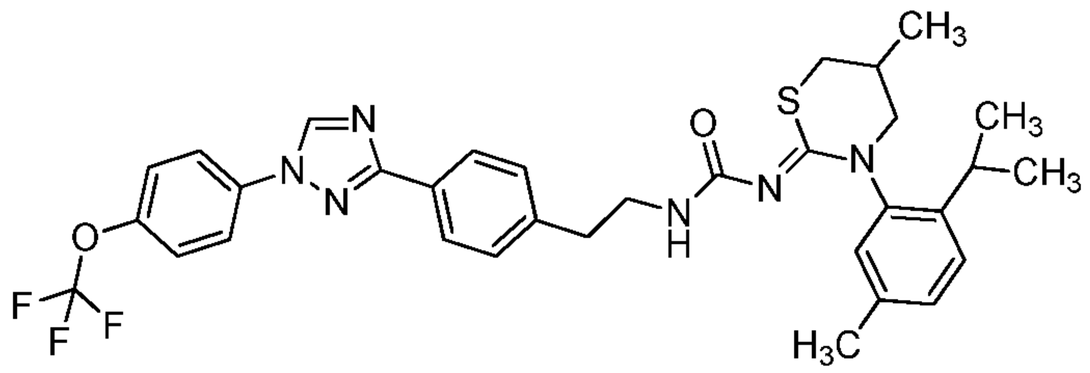
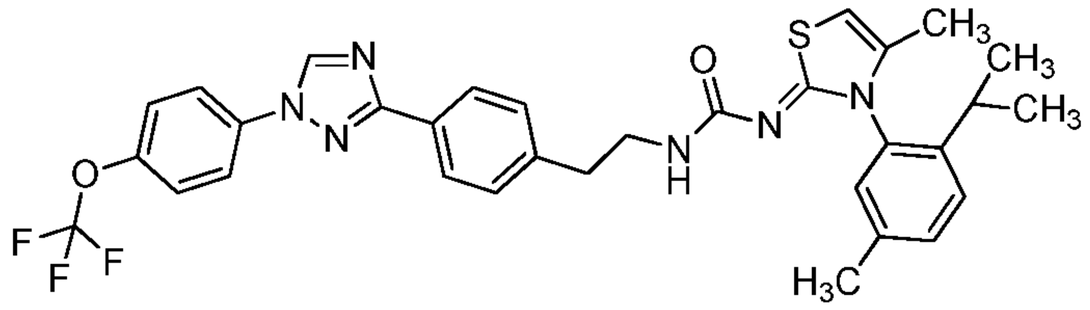
P25	
P26	
P27	
P28	
P29	
P30	
P31	

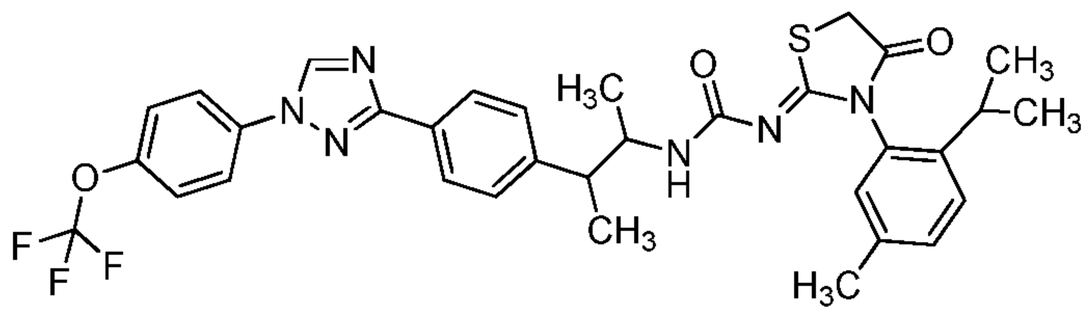
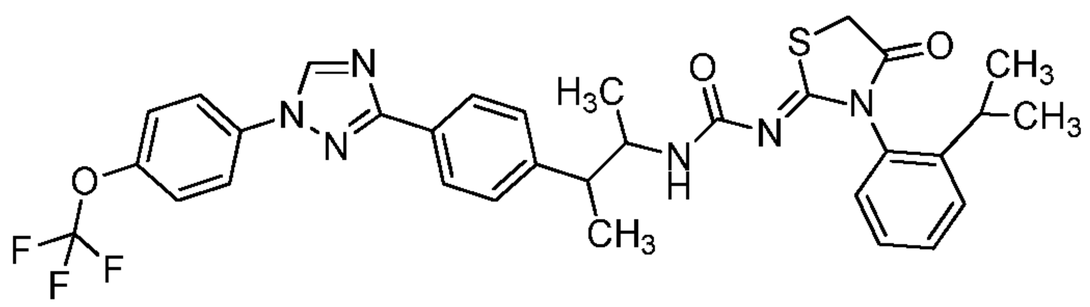
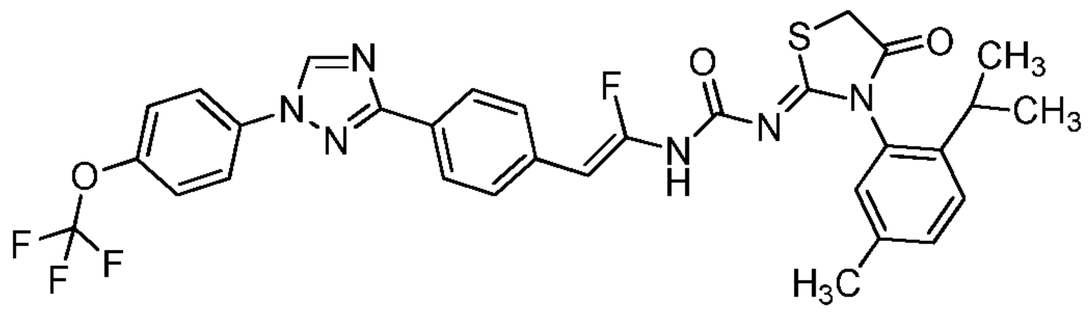
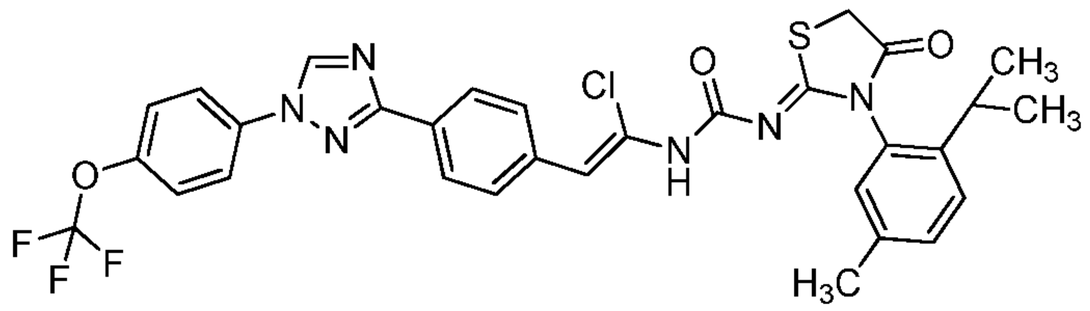
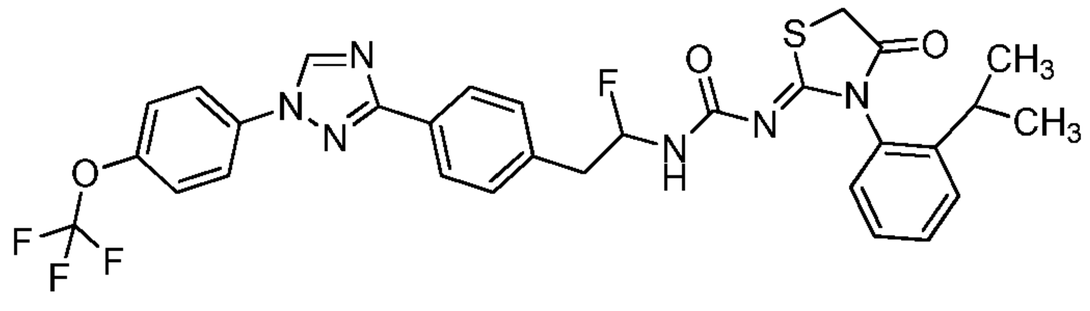
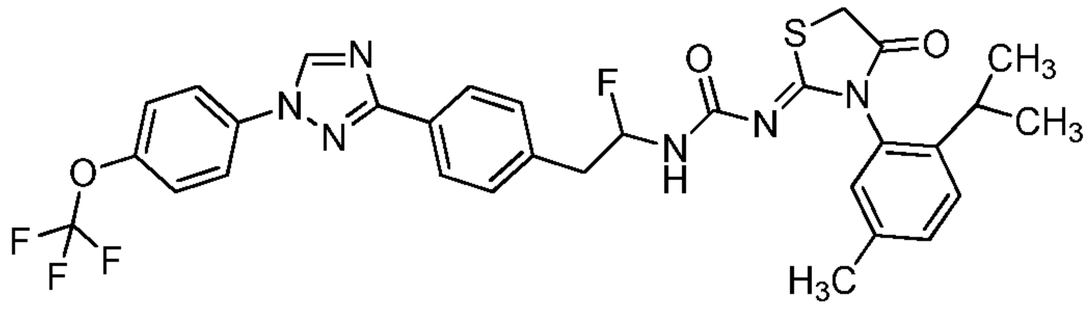
P32	
P33	
P34	
P35	
P36	
P37	
P38	
P39	

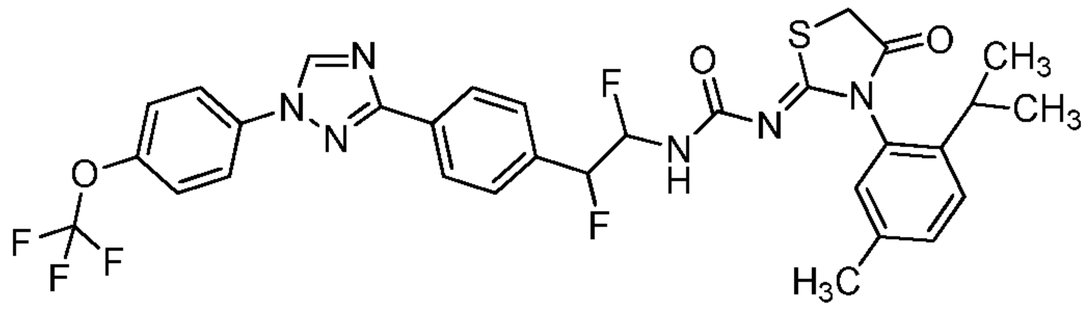
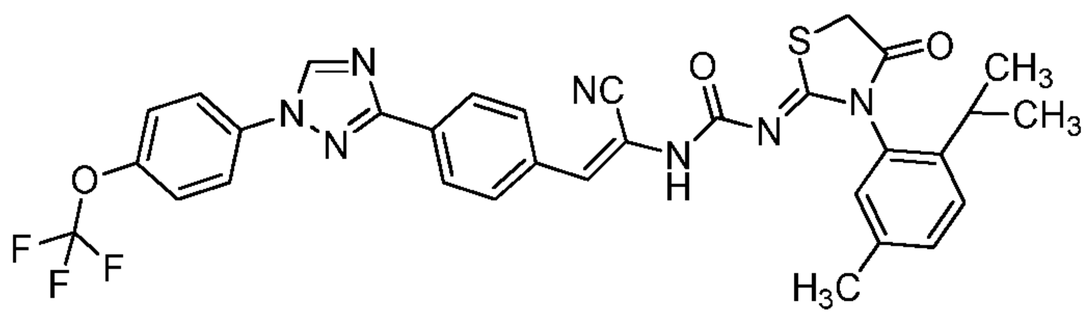
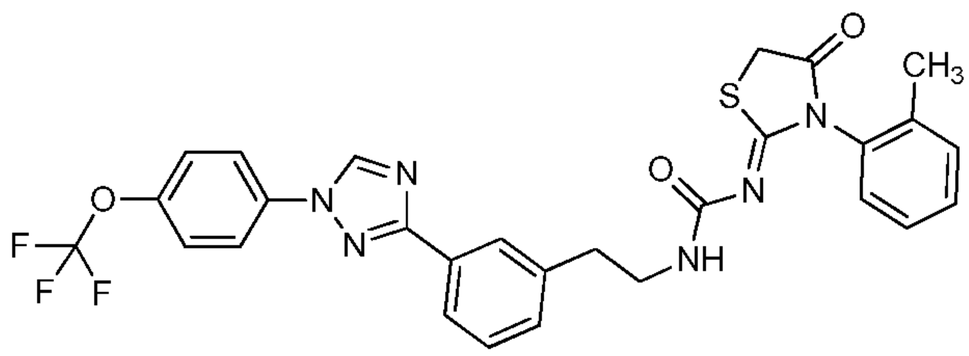
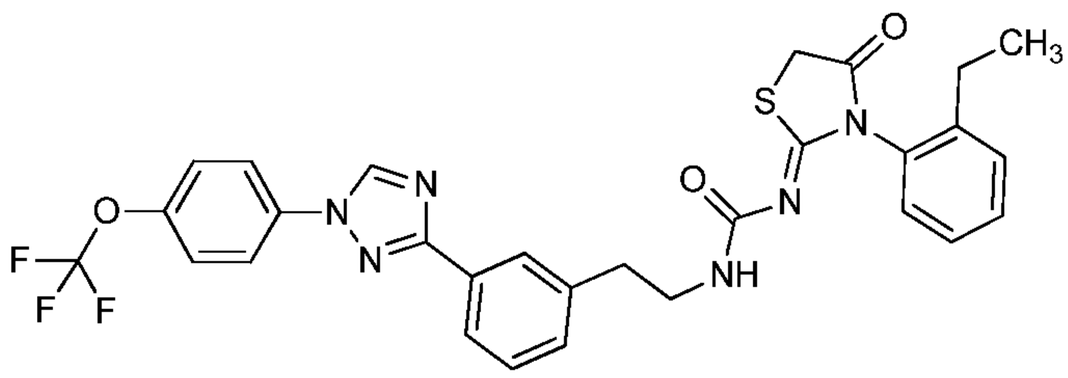
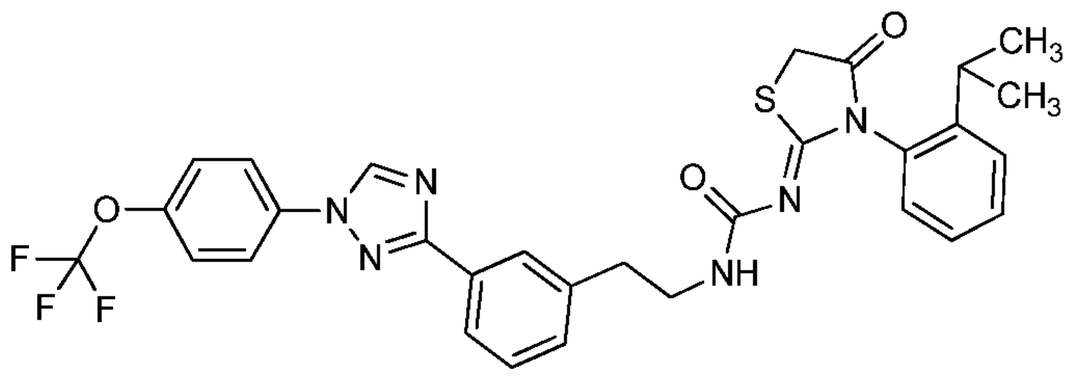
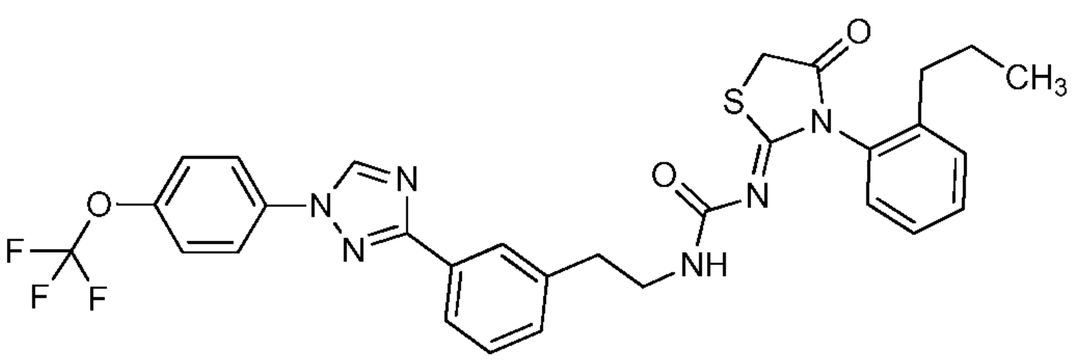
P40	
P41	
P42	
P43	
P44	
P45	
P46	

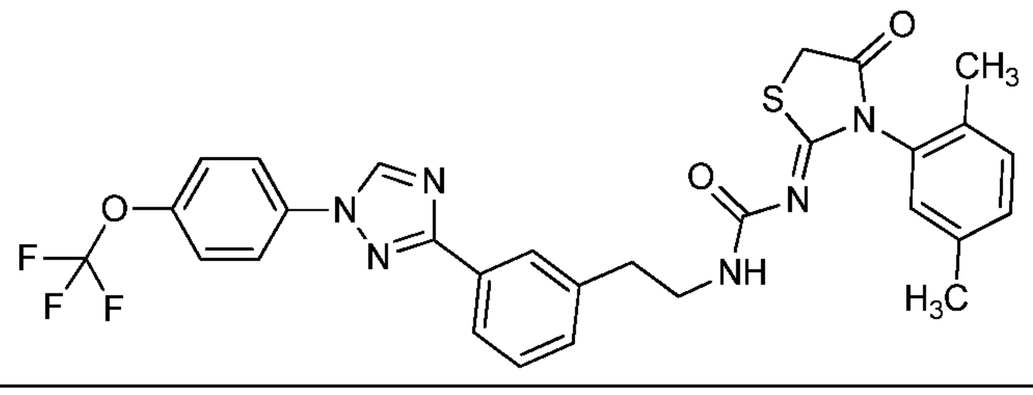
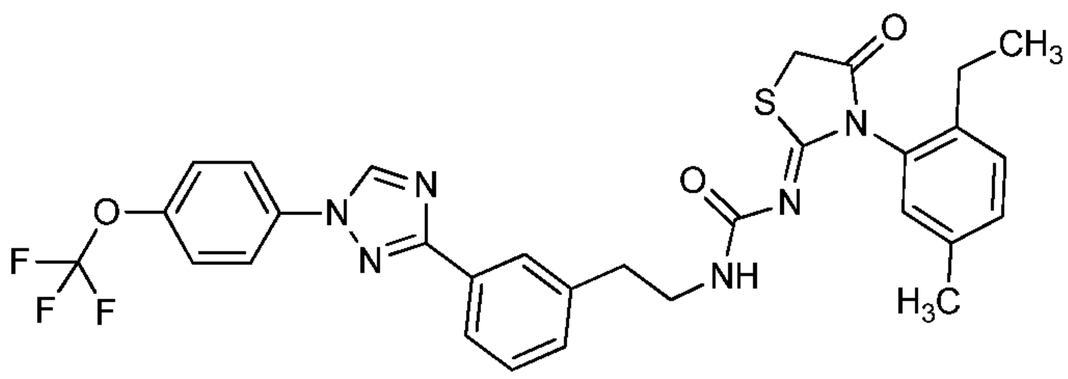
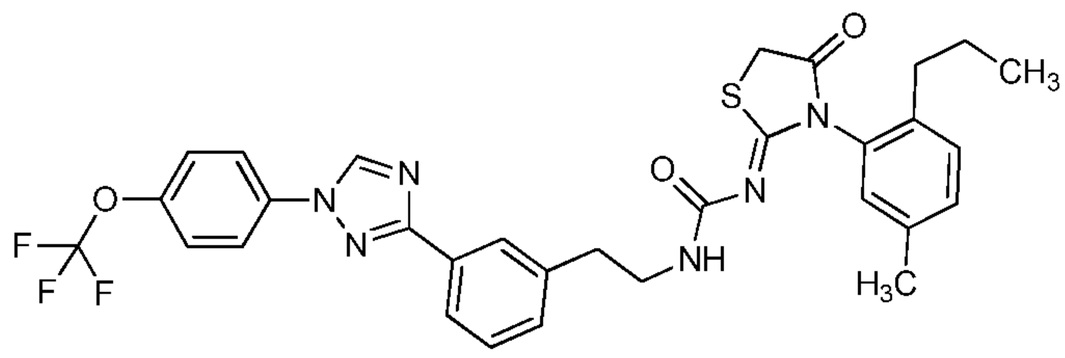
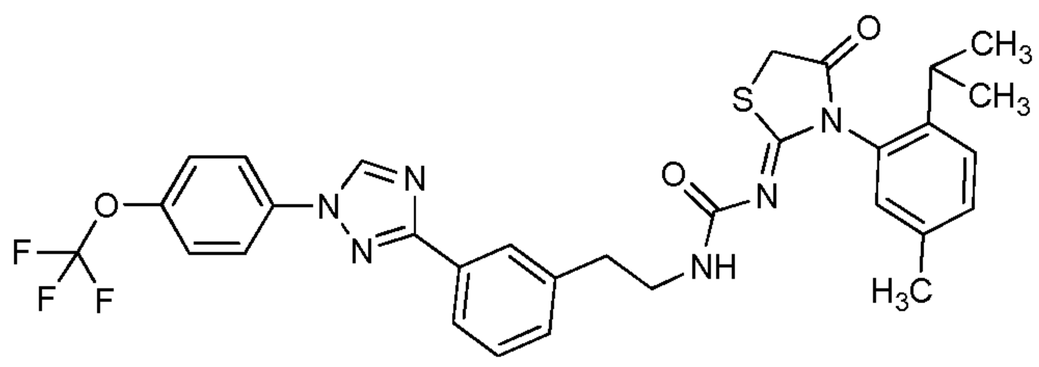
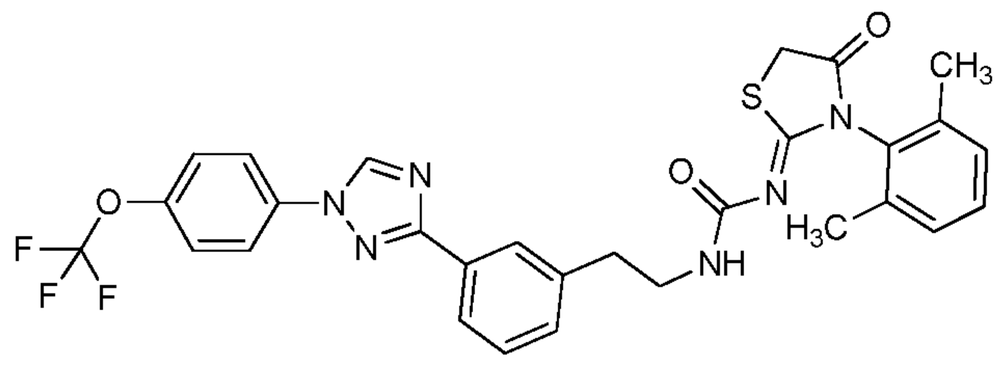
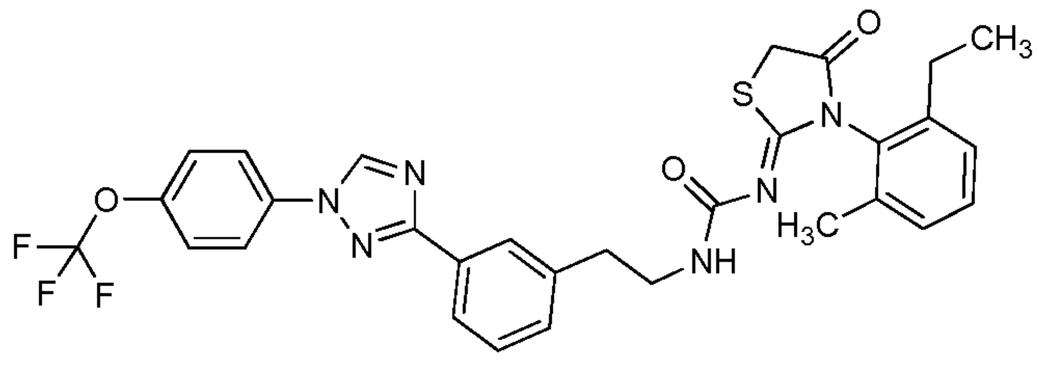
P47	
P48	
P49	
P50	
P51	
P52	
P53	

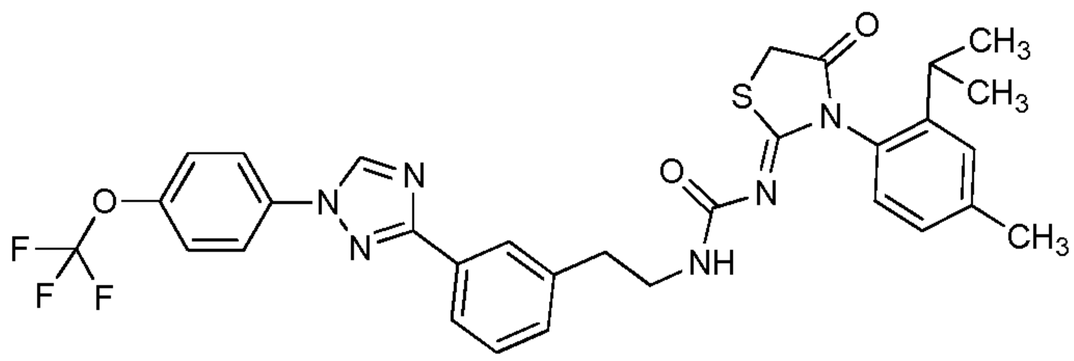
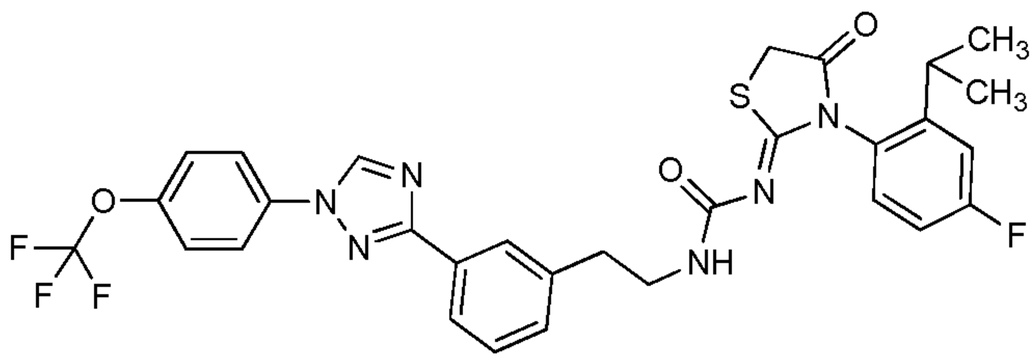
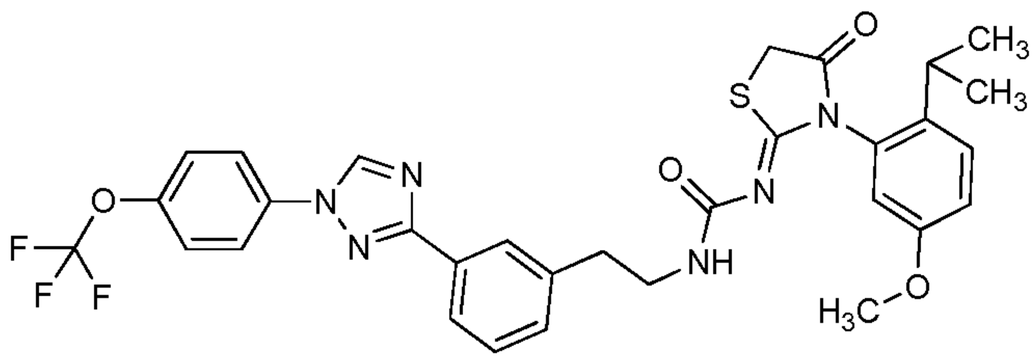
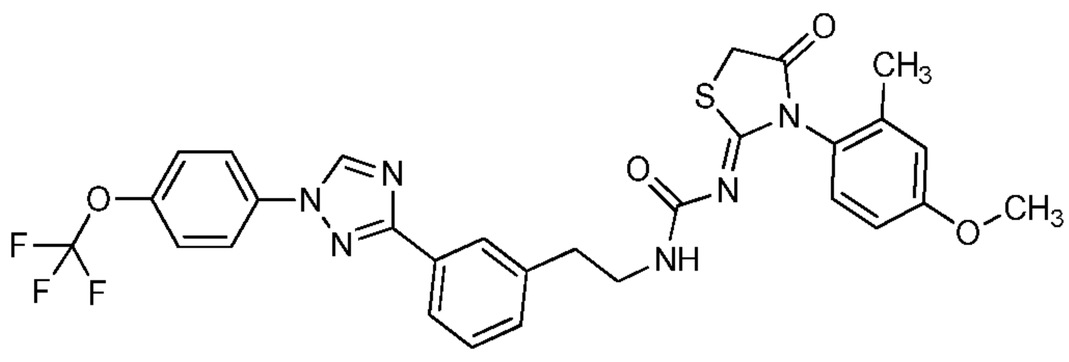
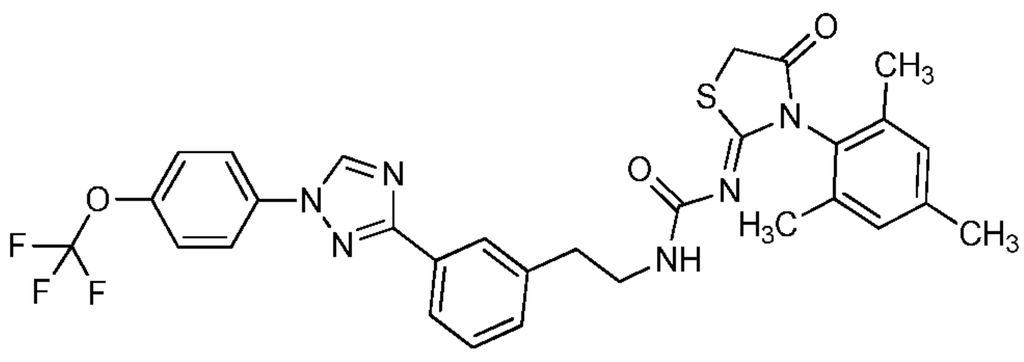
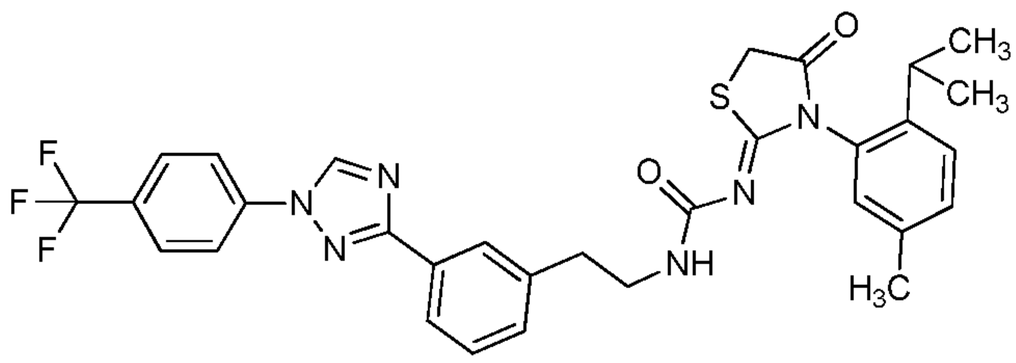
P54	
P55	
P56	
P57	
P58	
P59	

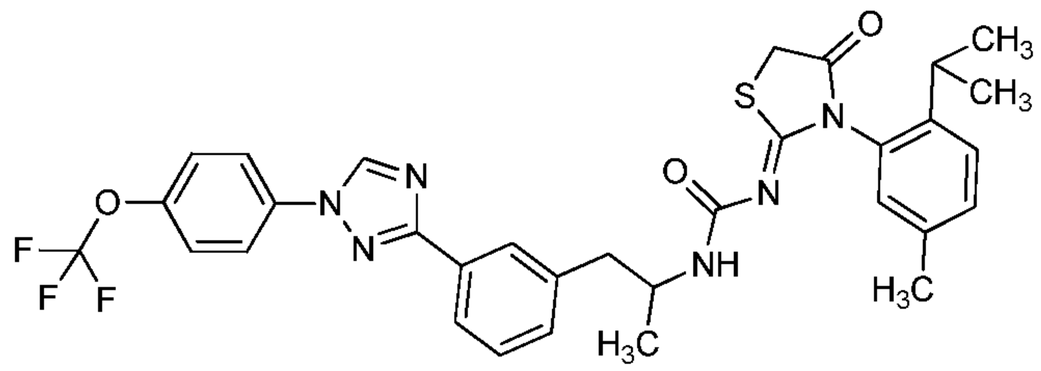
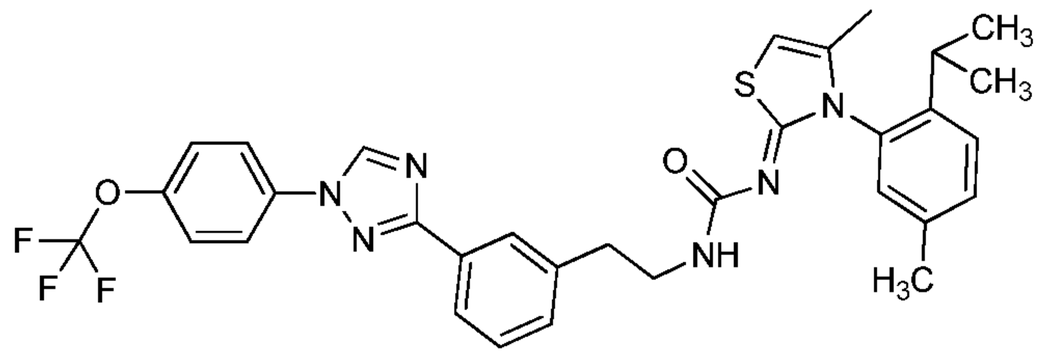
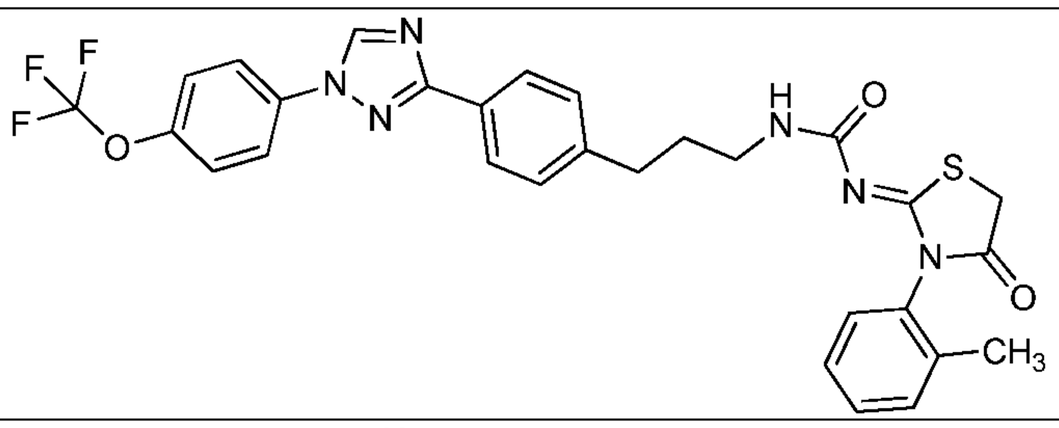
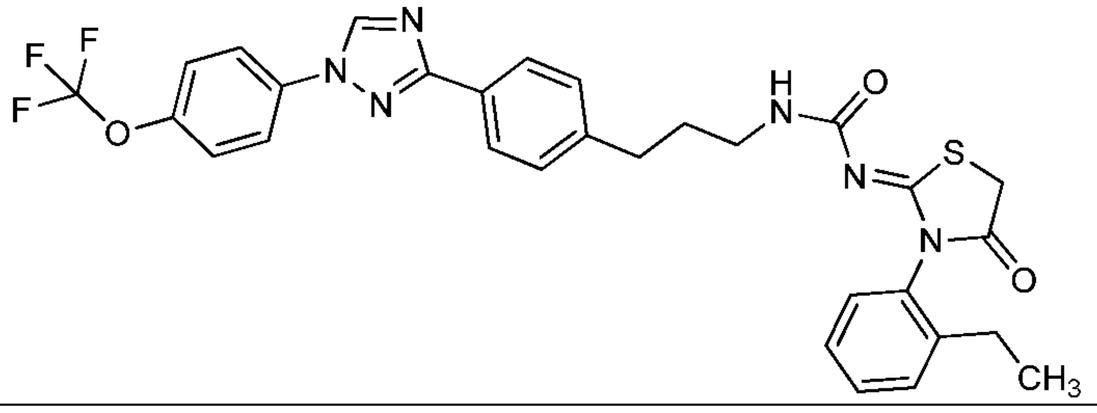
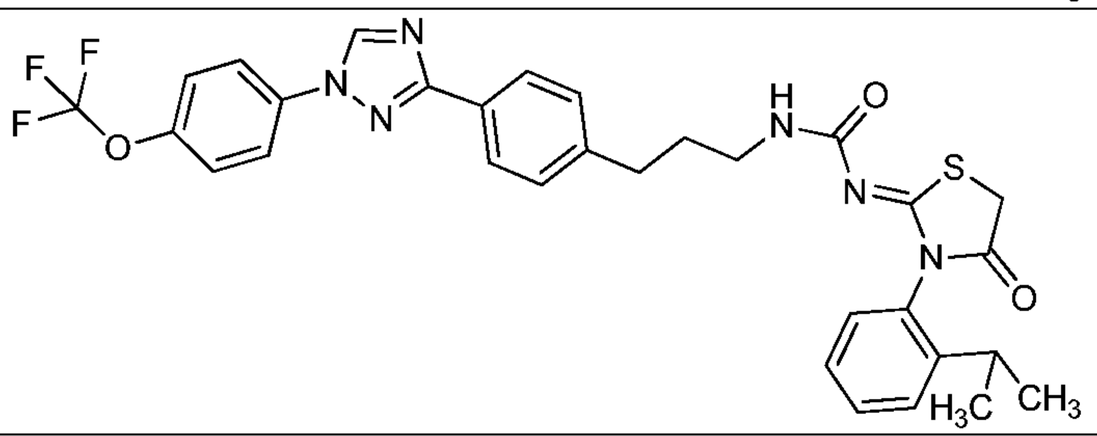
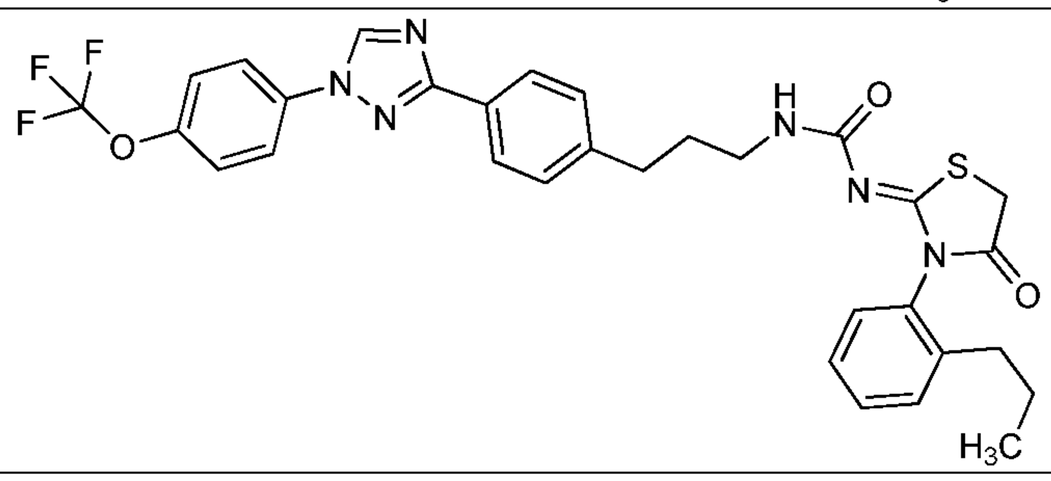
P60	
P61	
P62	
P63	
P64	
P65	

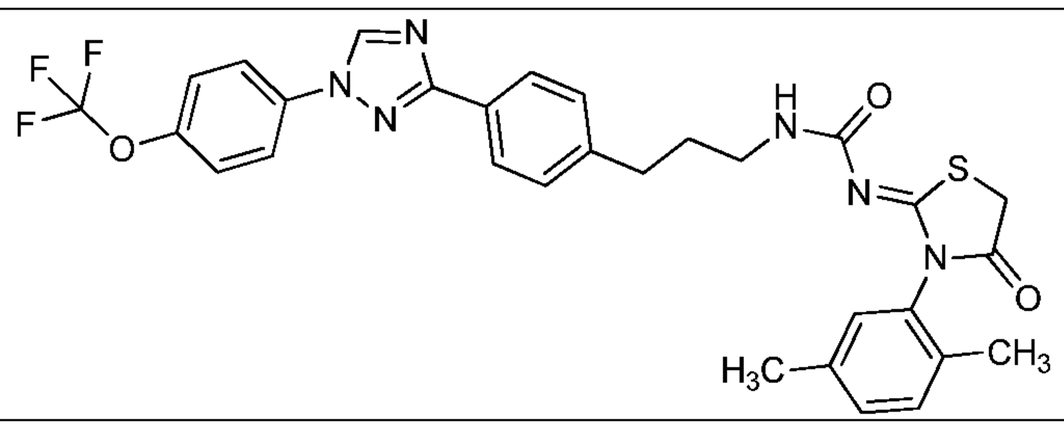
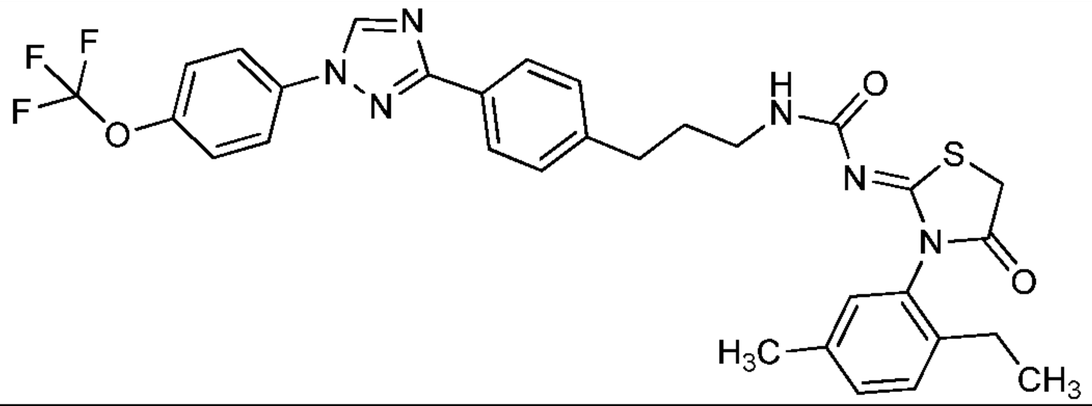
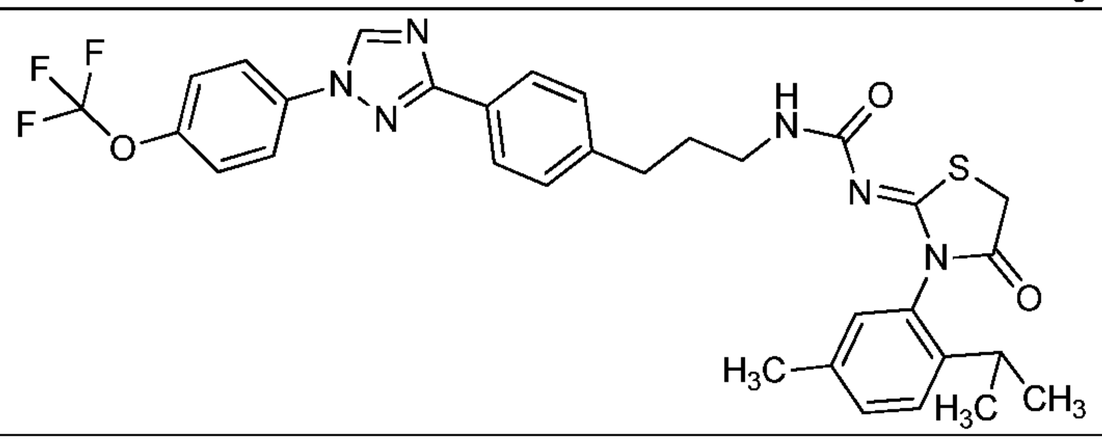
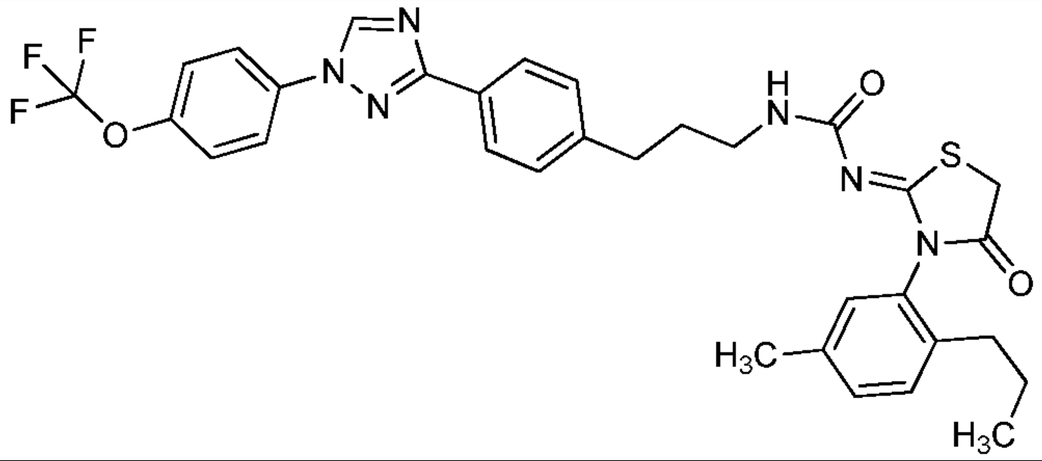
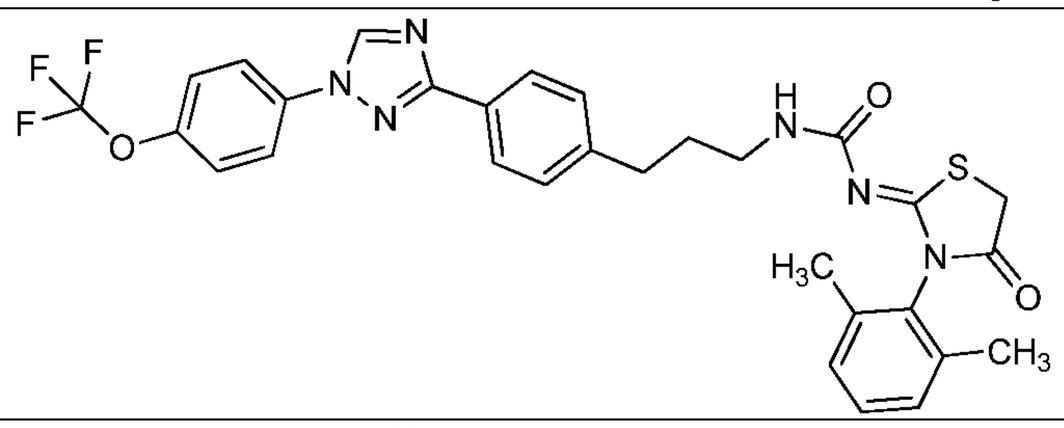
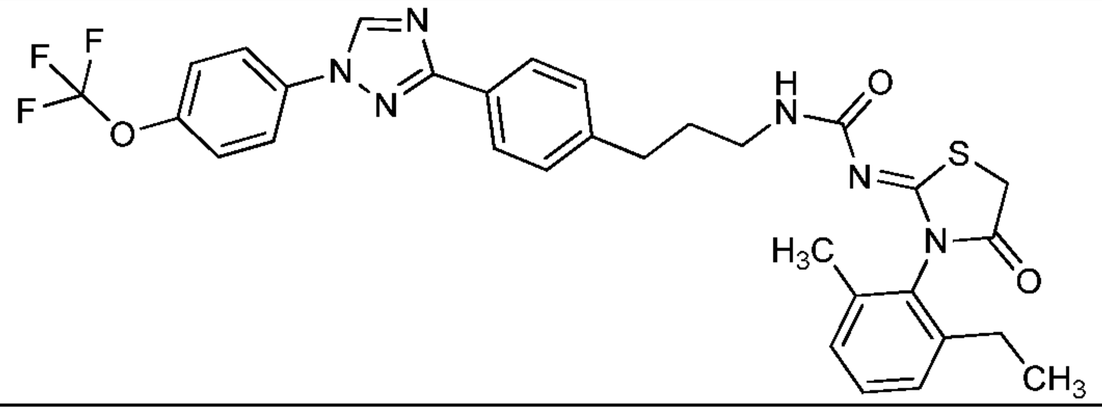
P66	
P67	
P68	
P69	
P70	
P71	

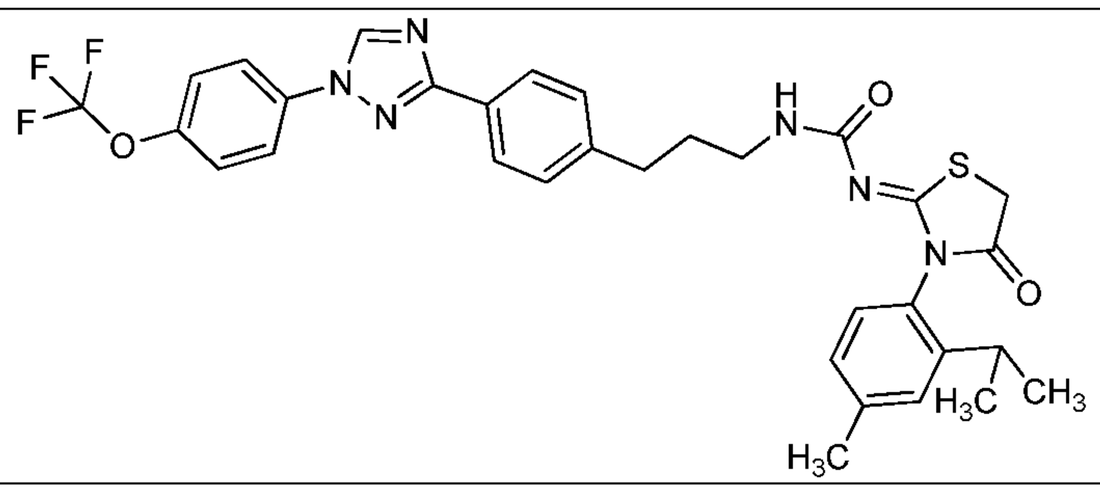
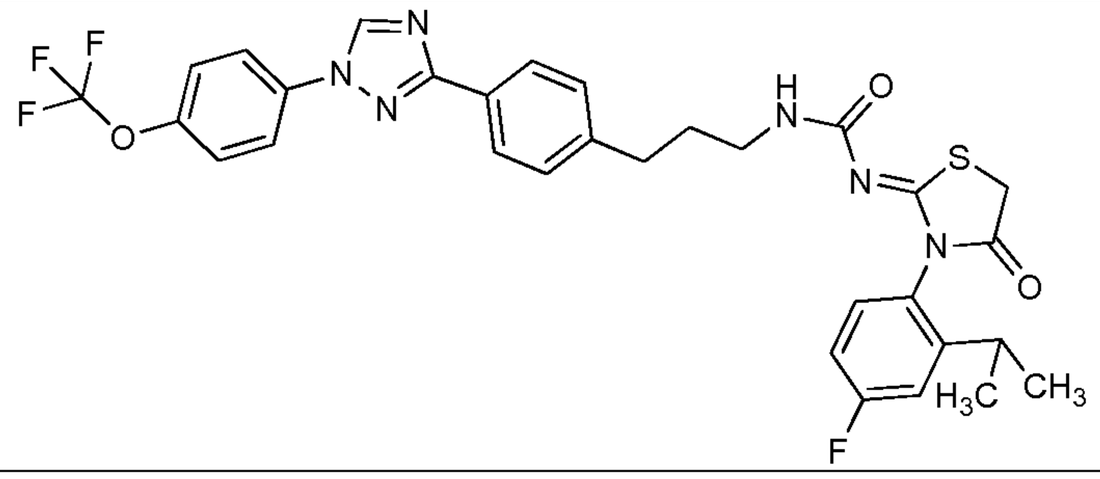
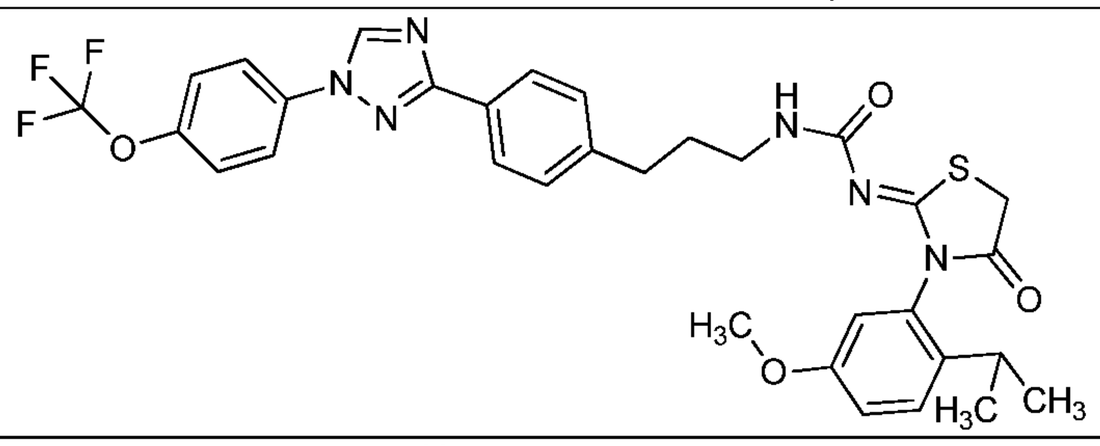
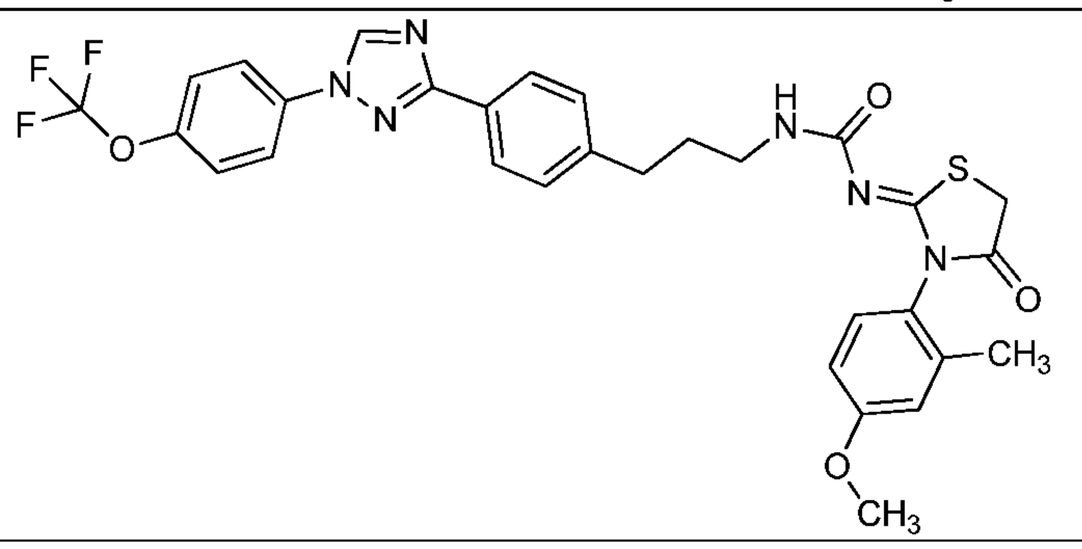
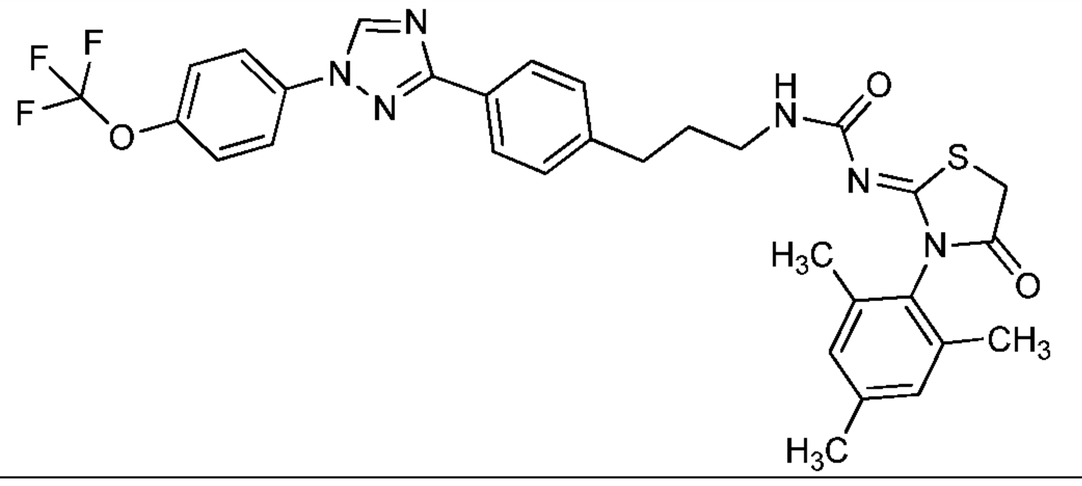
P72	
P73	
P74	
P75	
P76	
P77	

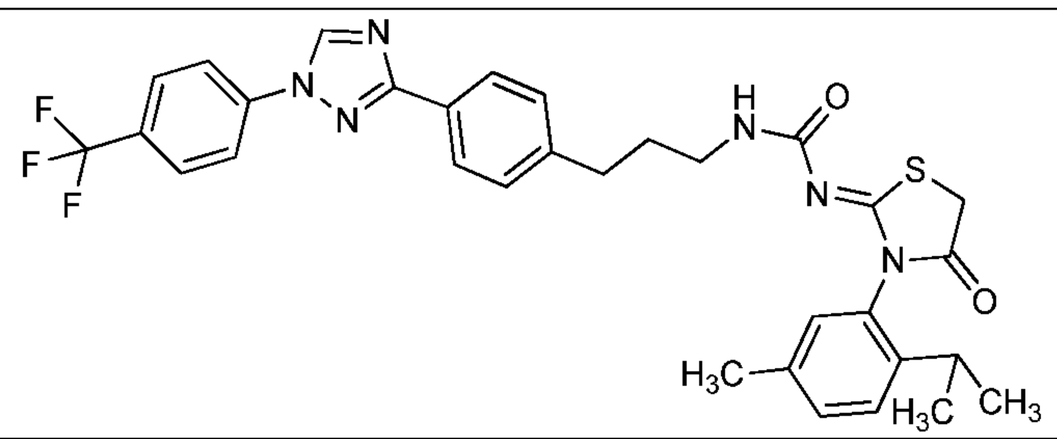
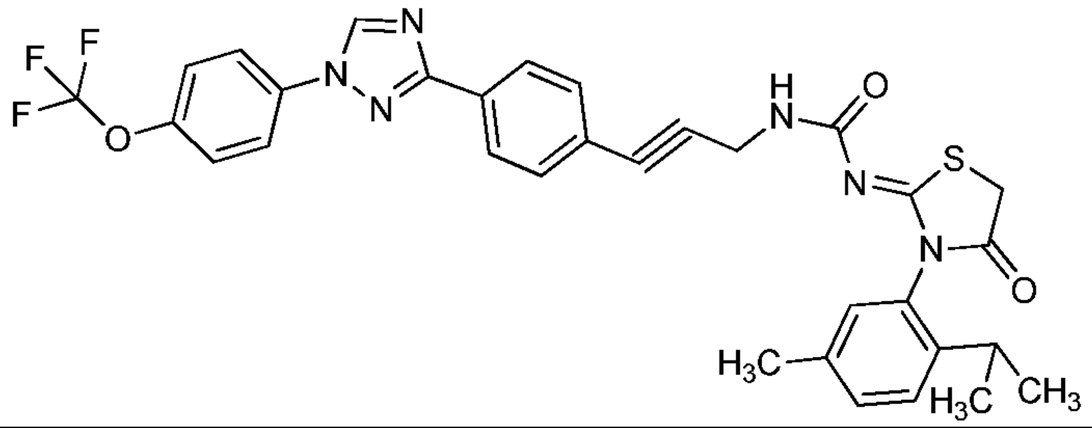
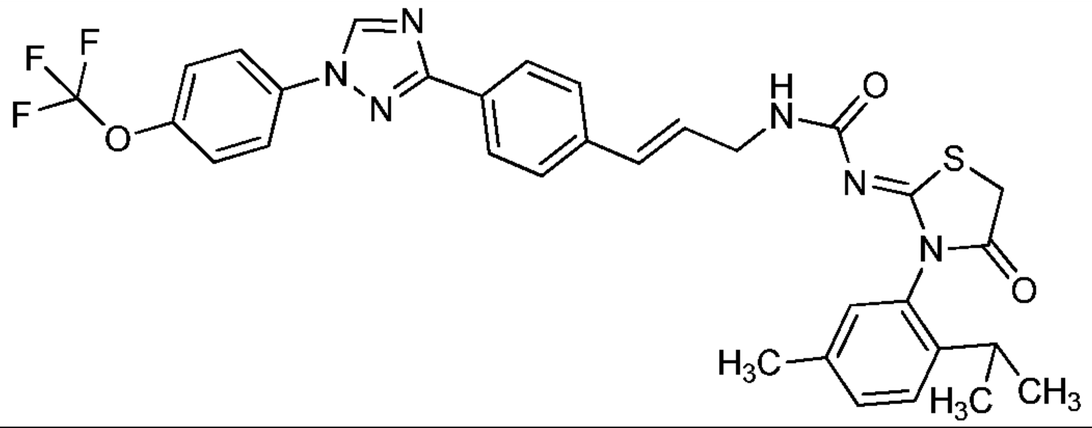
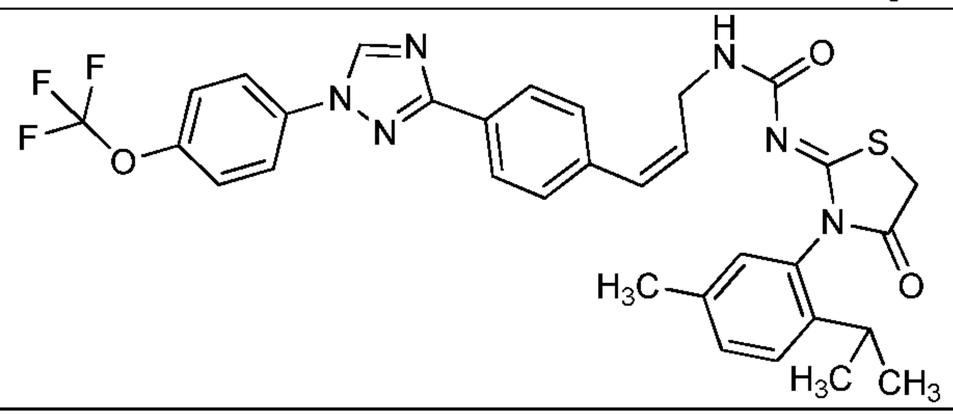
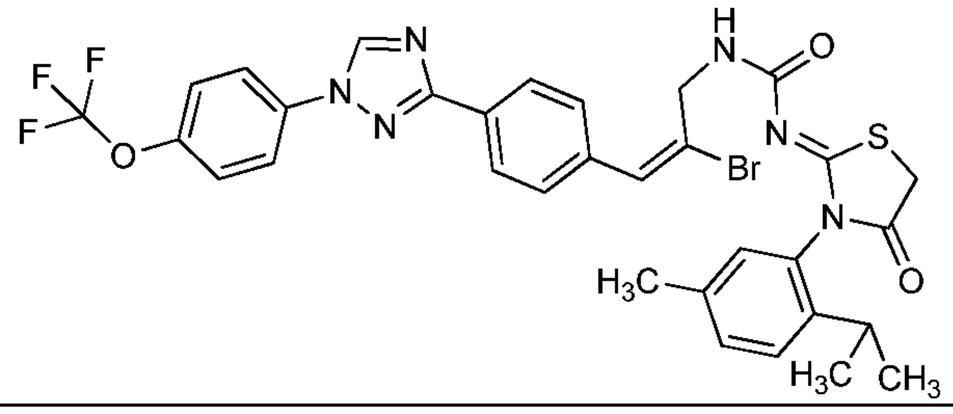
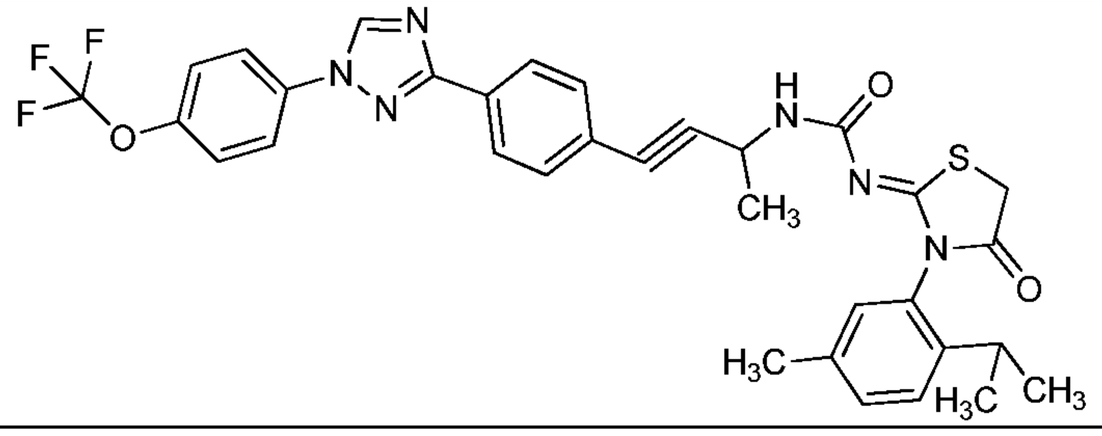
P78	
P79	
P80	
P81	
P82	
P83	

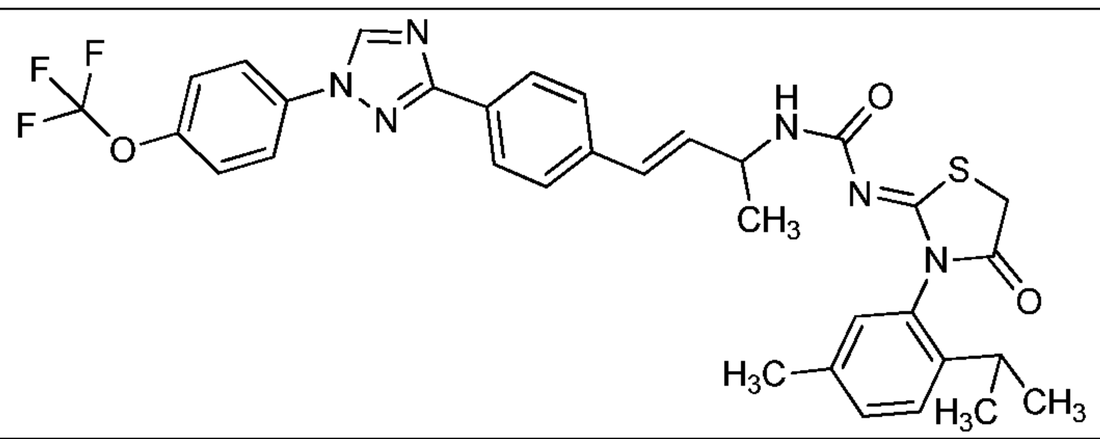
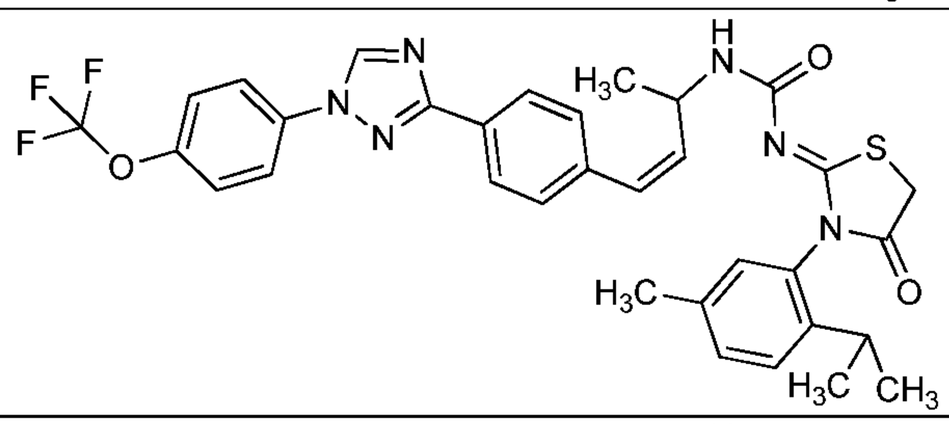
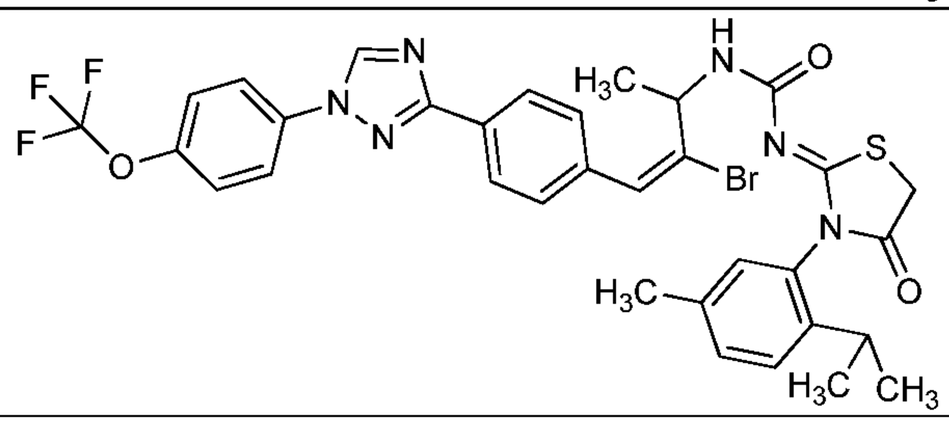
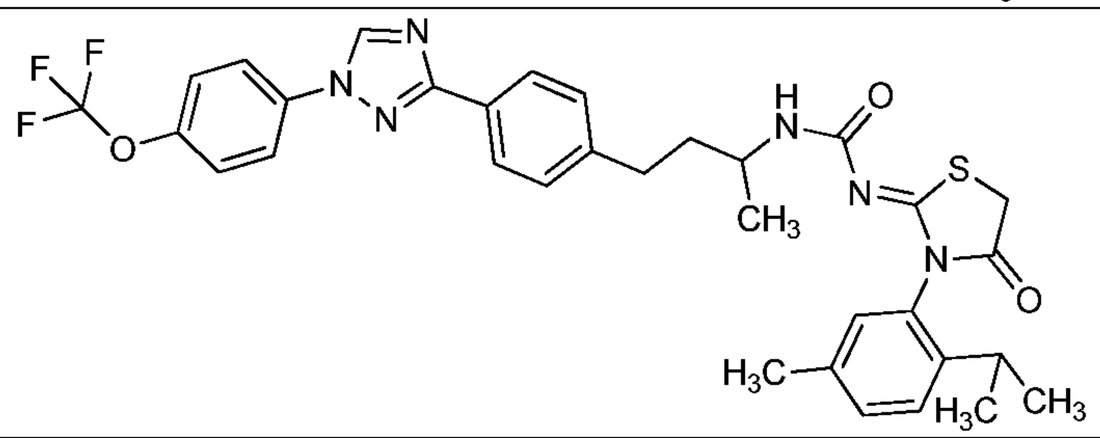
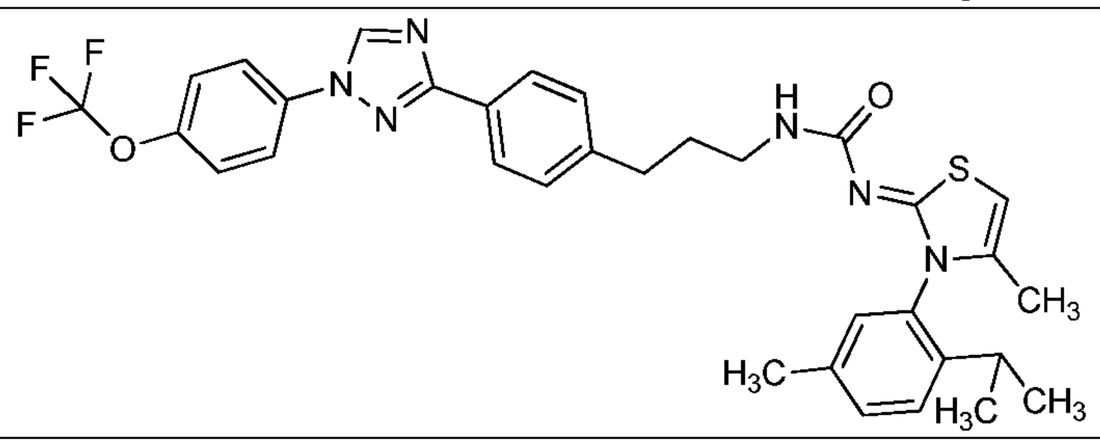
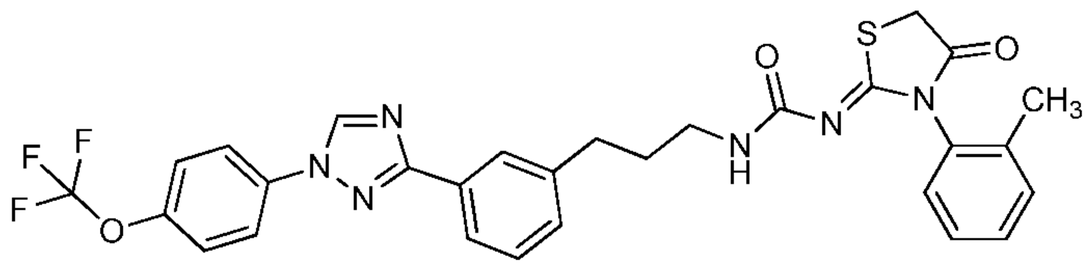
P84	
P85	
P86	
P87	
P88	
P89	

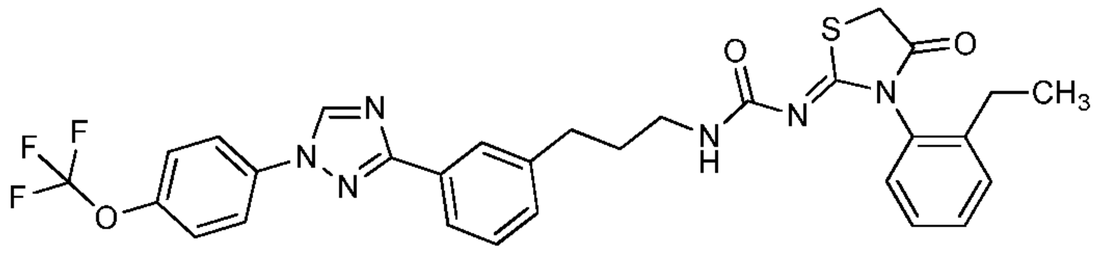
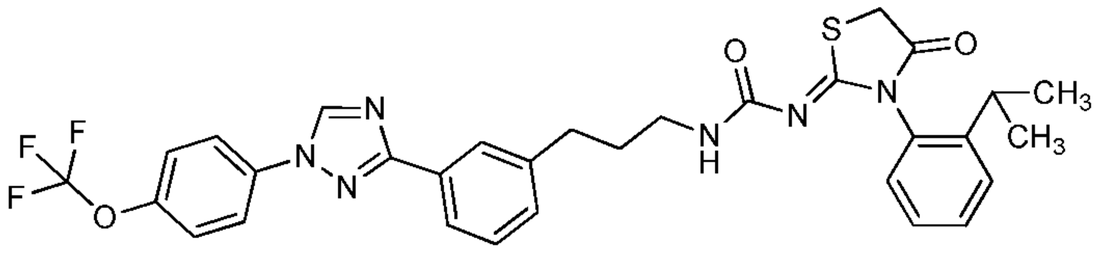
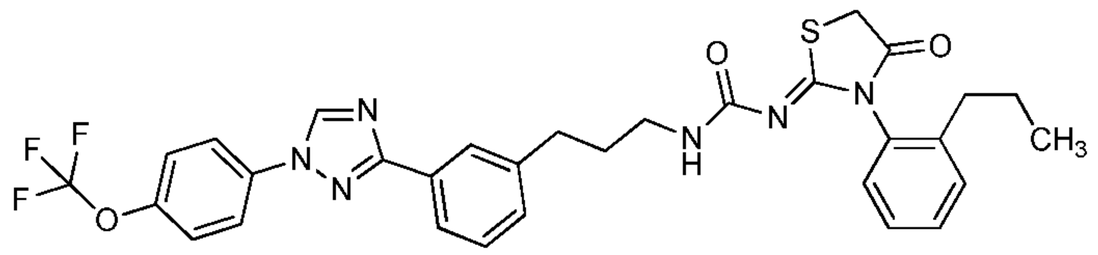
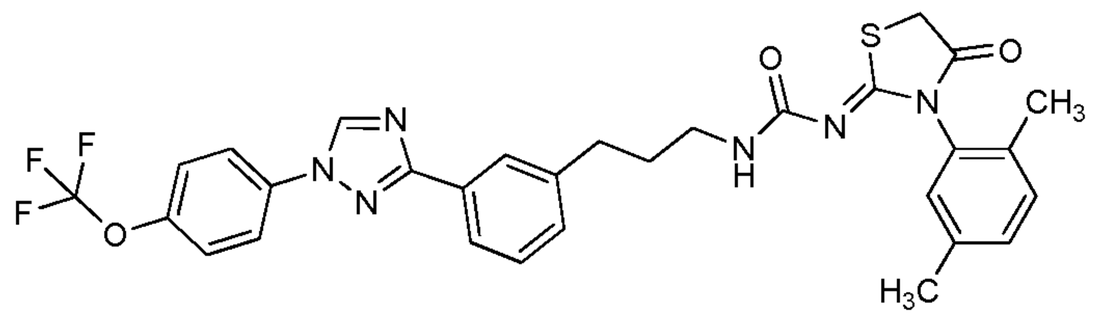
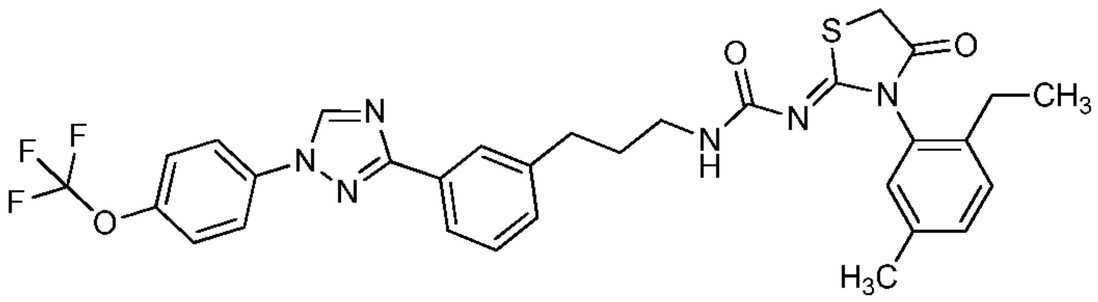
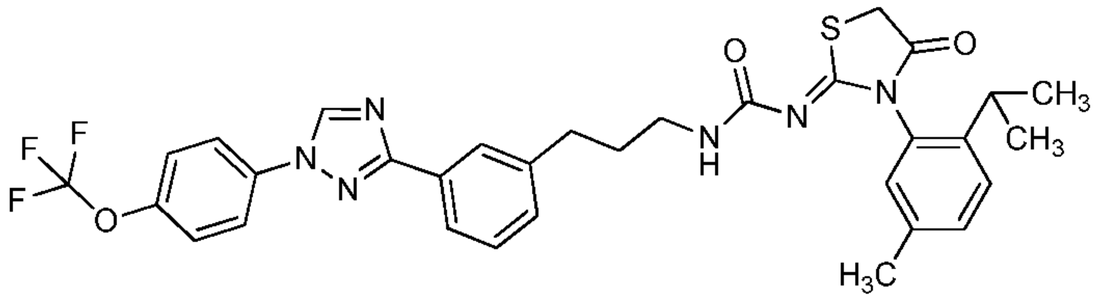
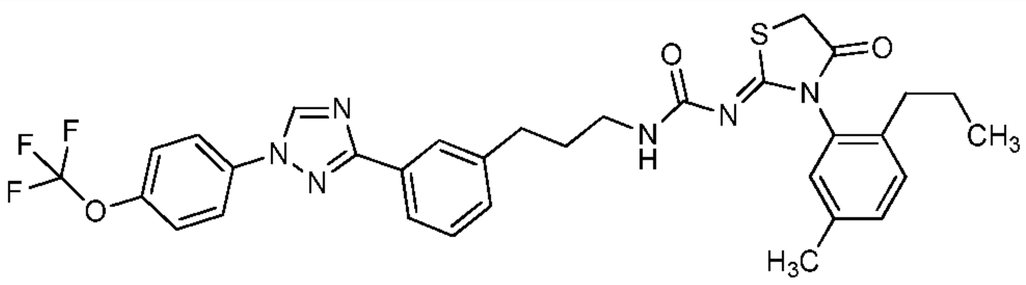
P90	
P91	
P92	
P93	
P94	
P95	

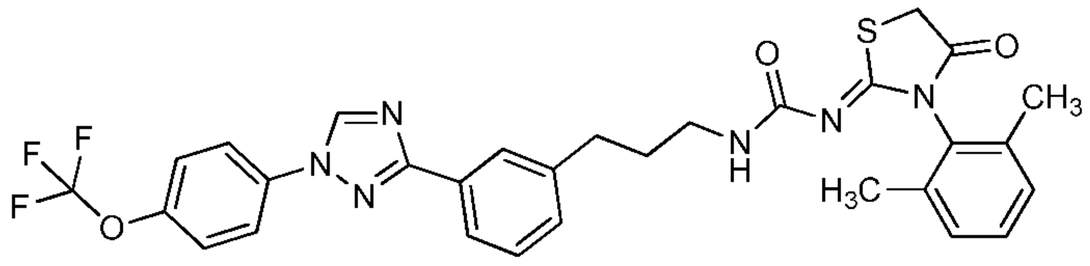
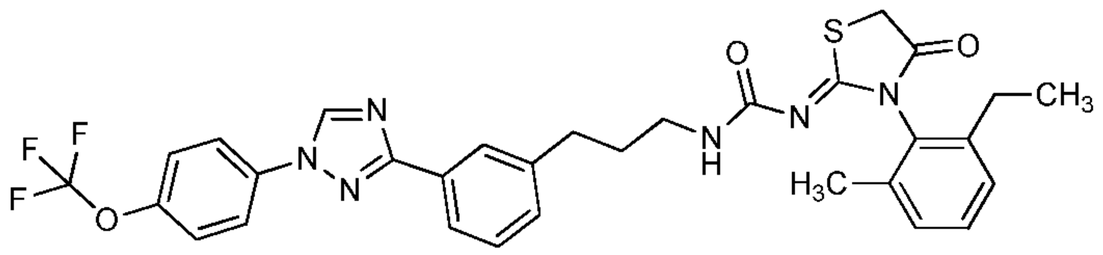
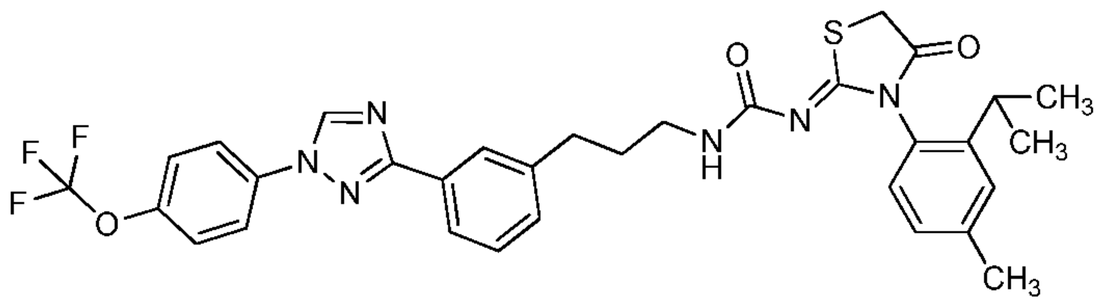
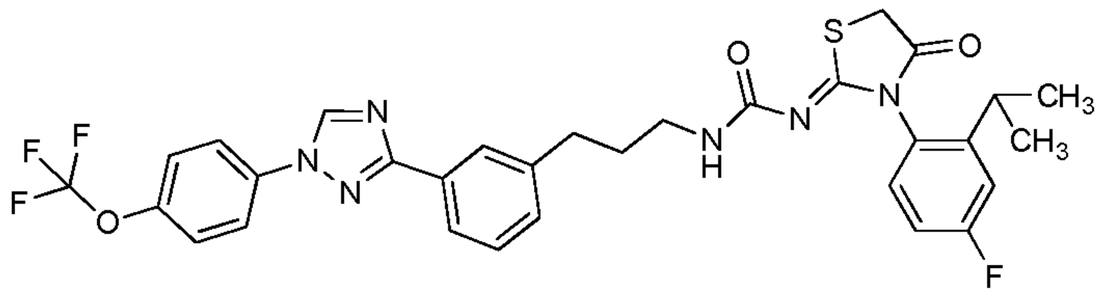
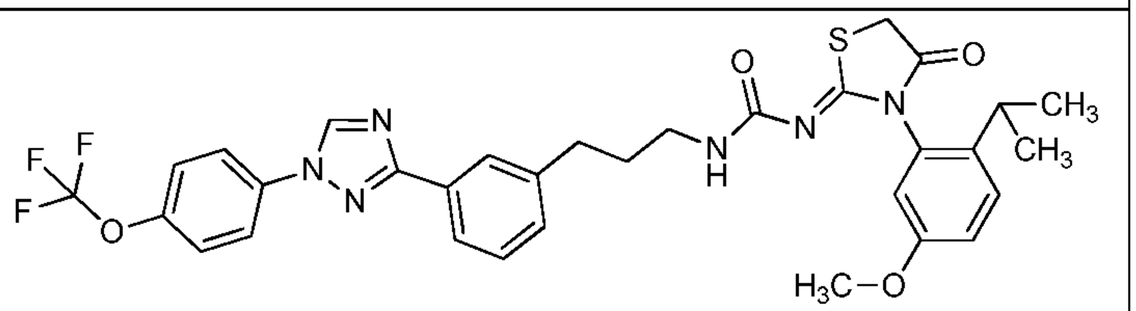
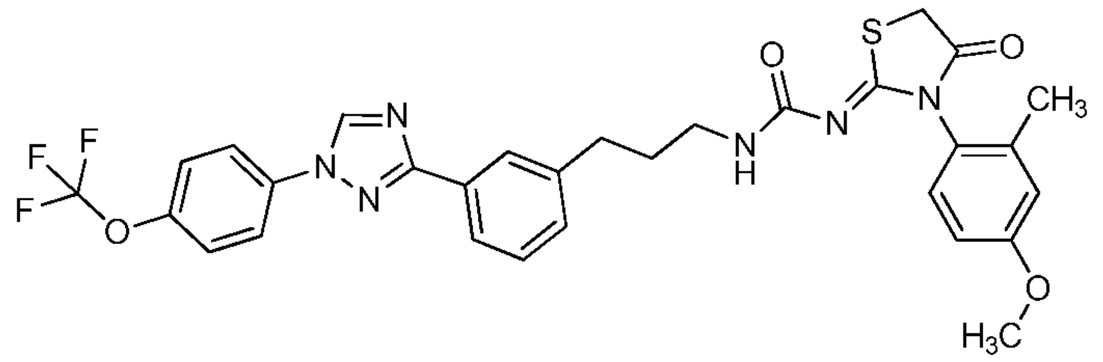
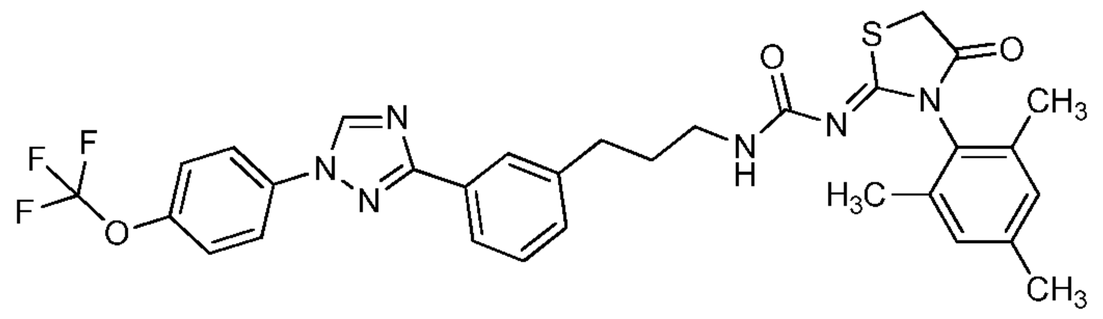
P96	
P97	
P98	
P99	
P100	
P101	

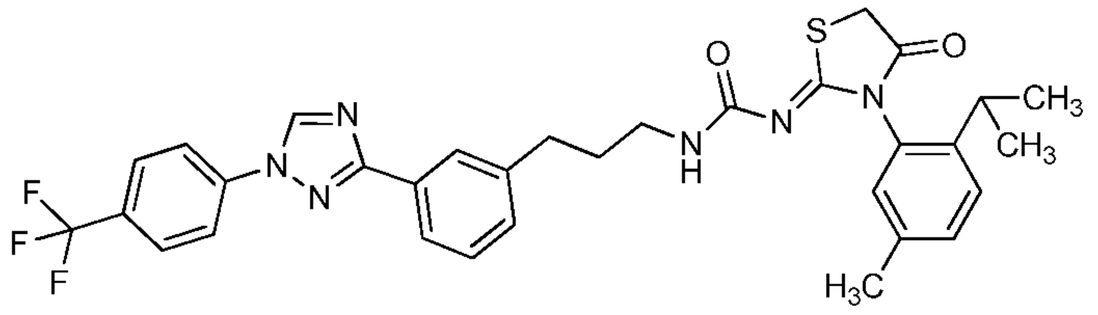
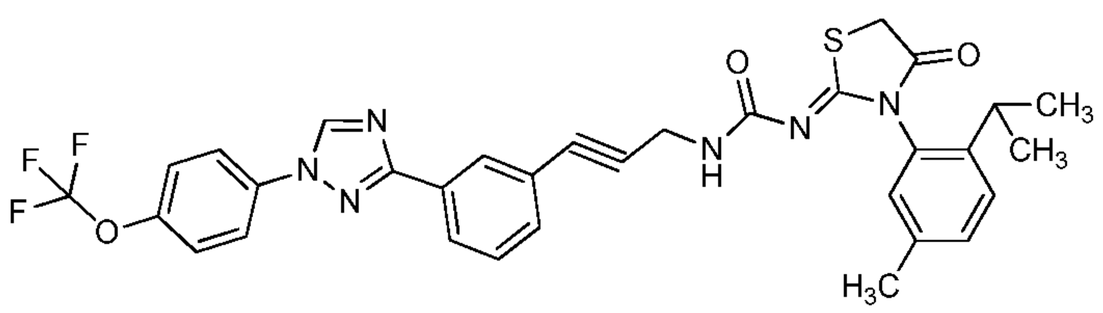
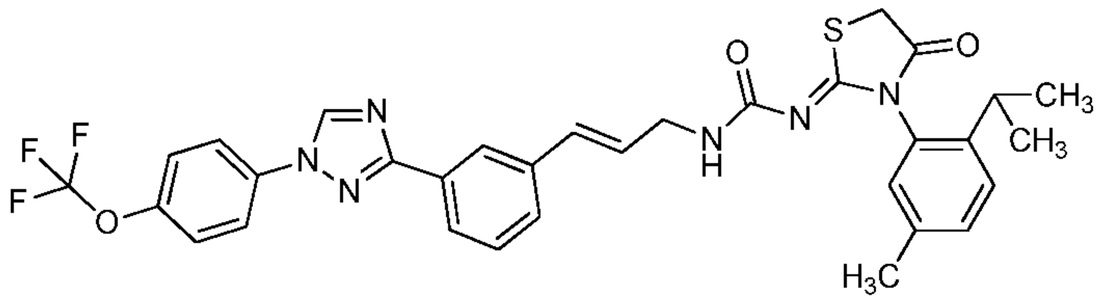
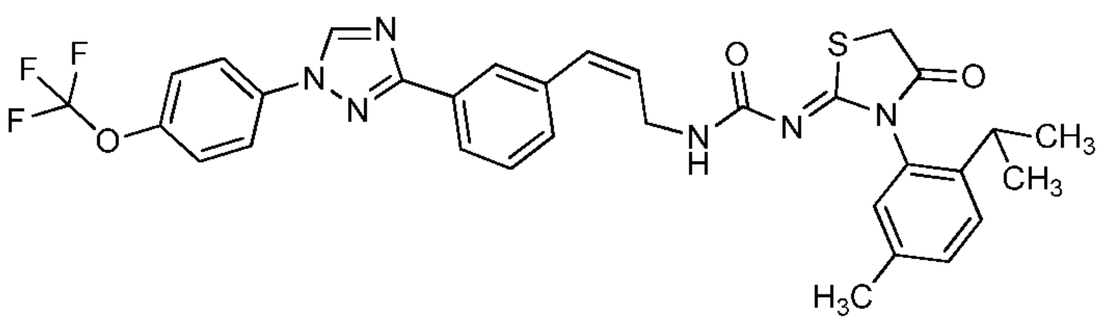
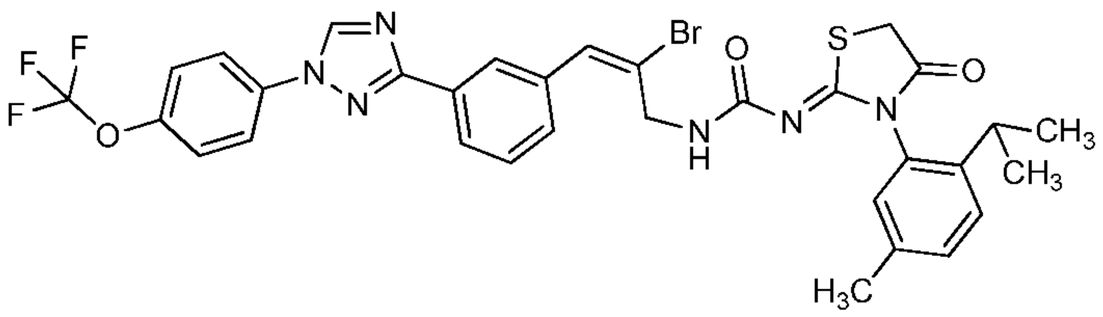
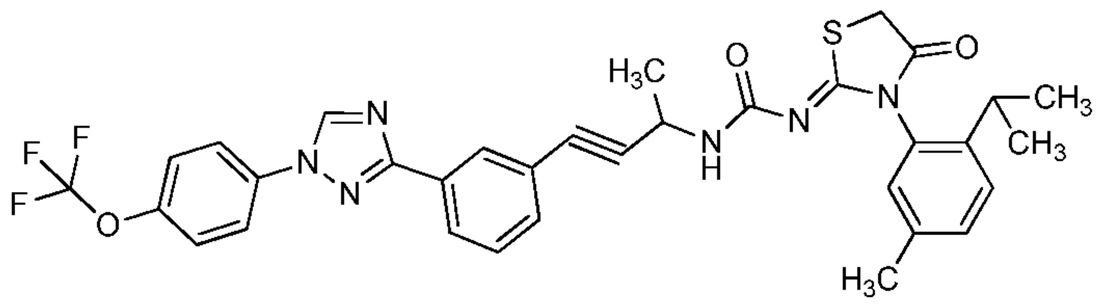
P102	
P103	
P104	
P105	
P106	

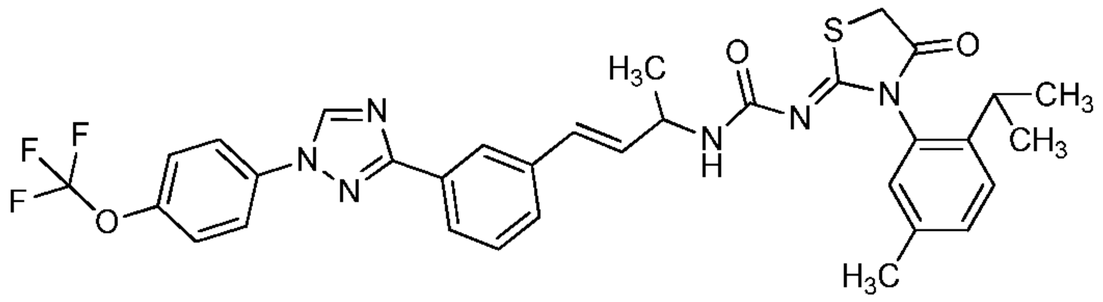
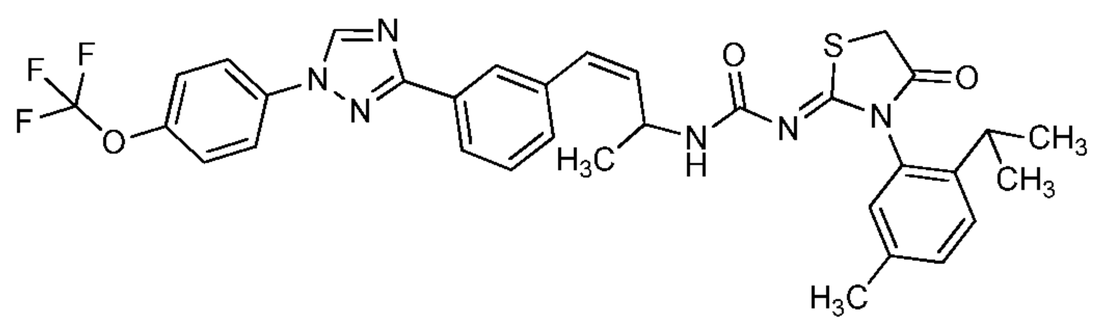
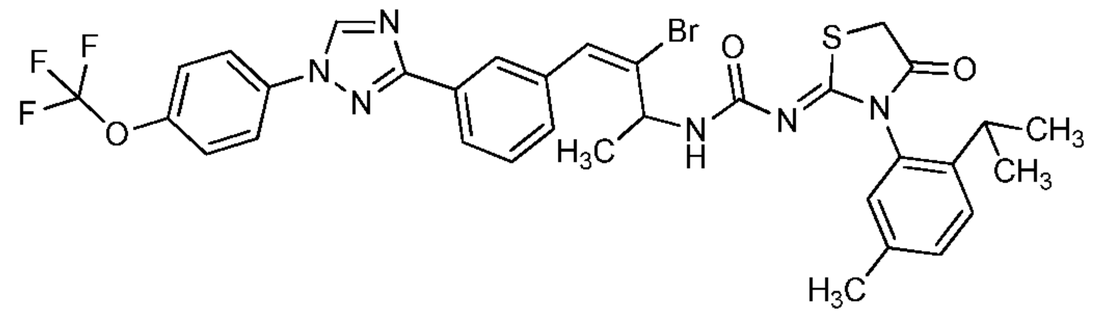
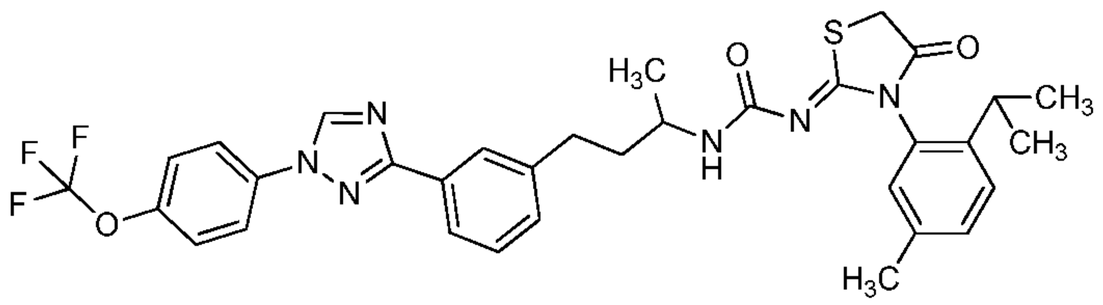
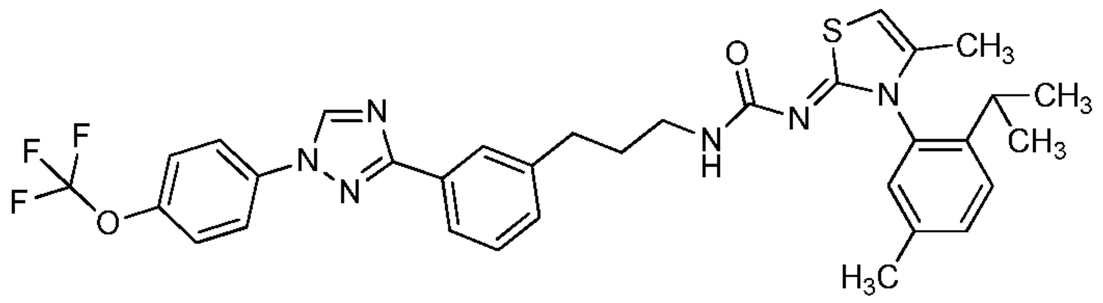
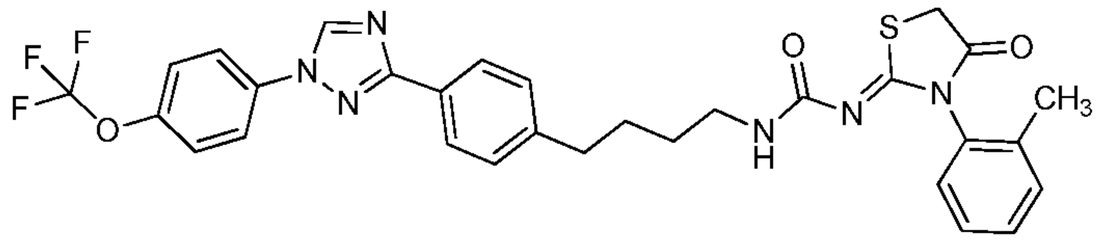
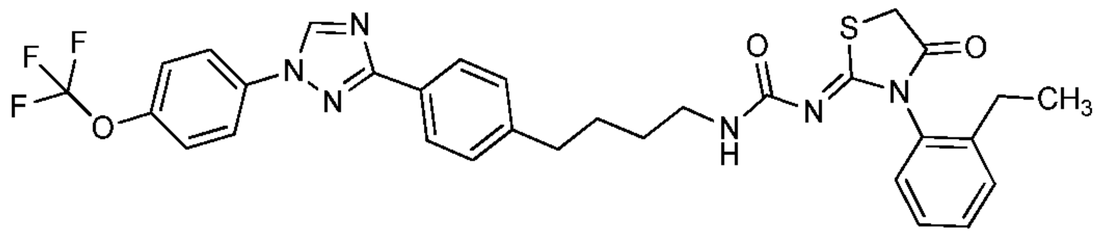
P107	
P108	
P109	
P110	
P111	
P112	

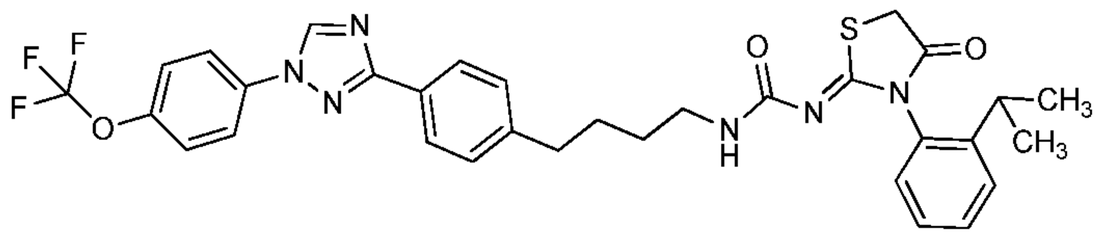
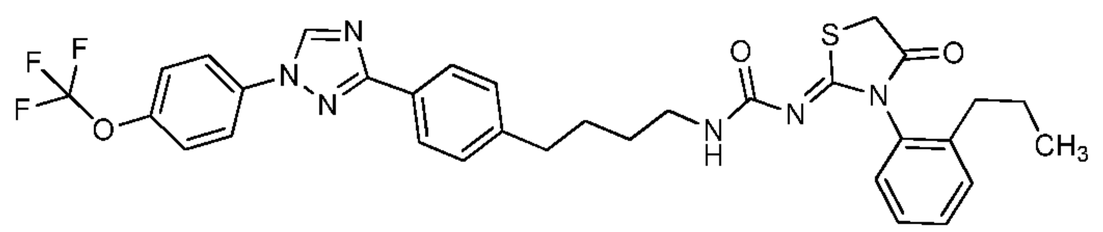
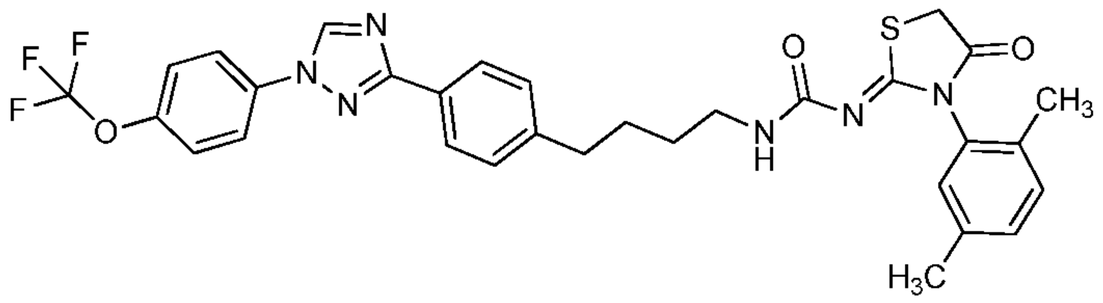
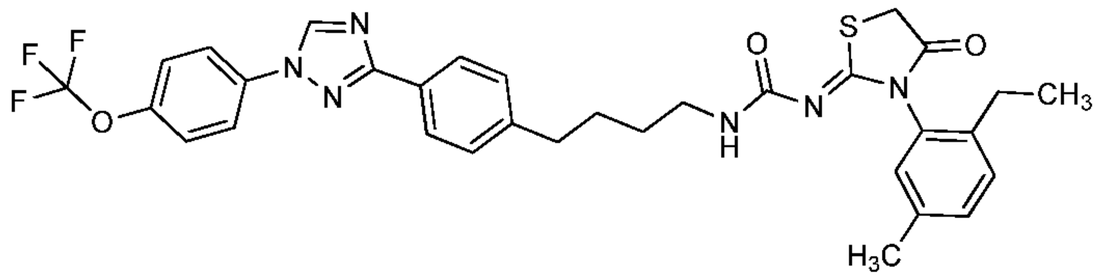
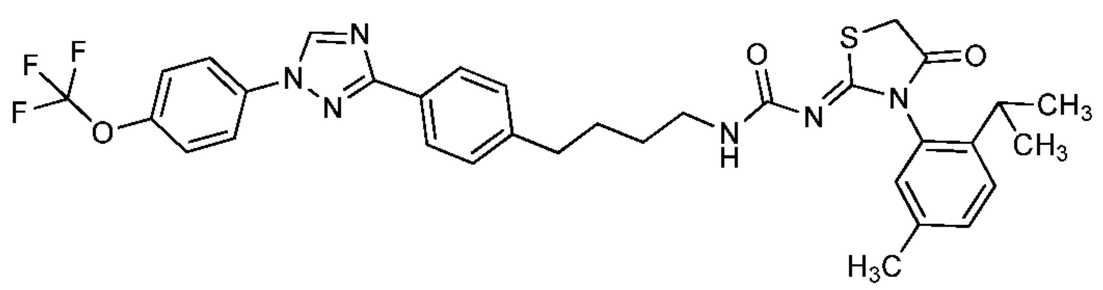
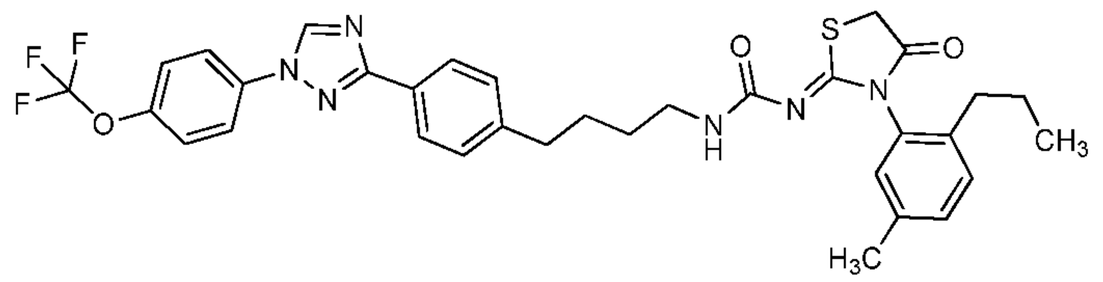
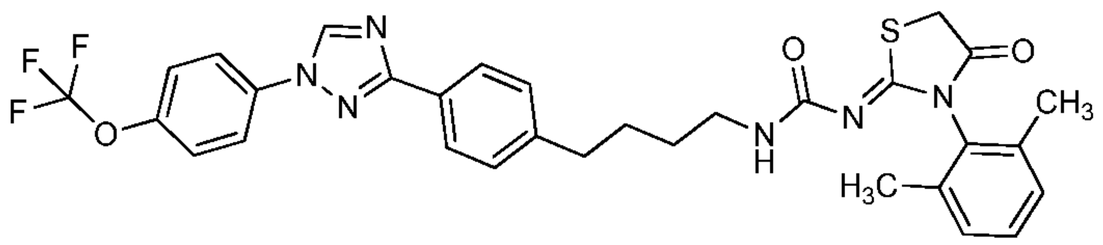
P113	
P114	
P115	
P116	
P117	
P118	

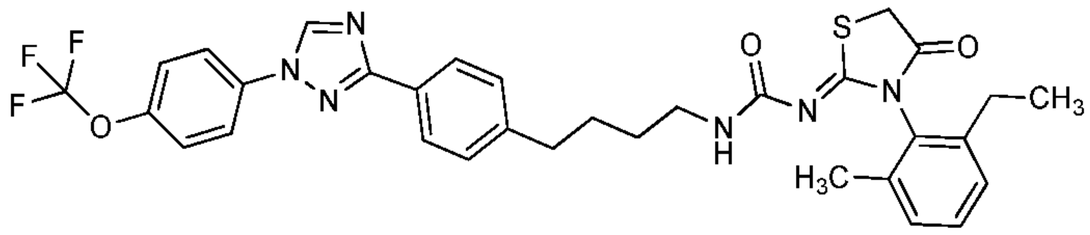
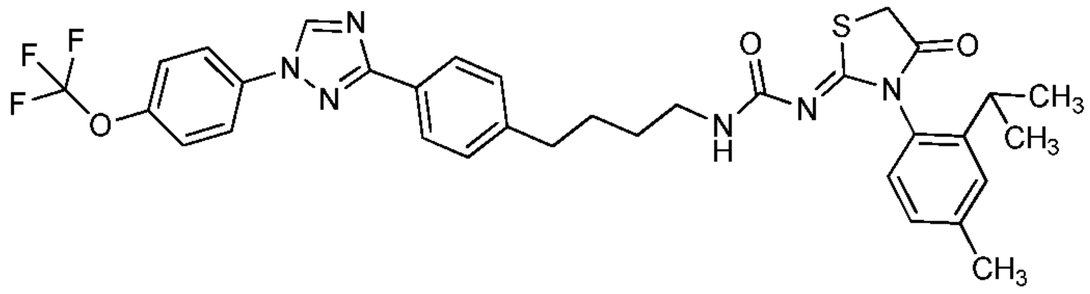
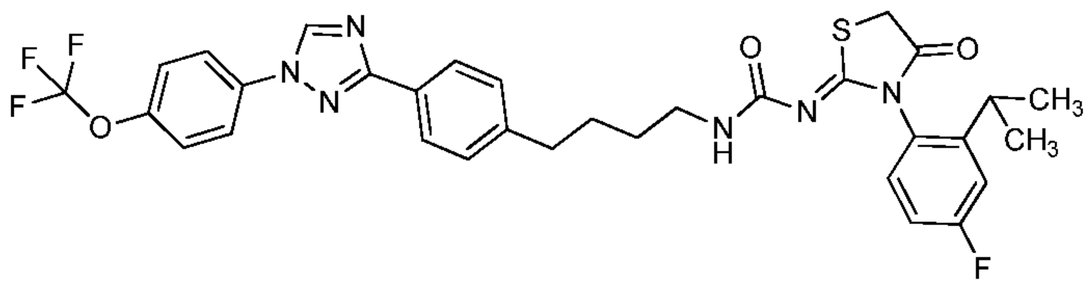
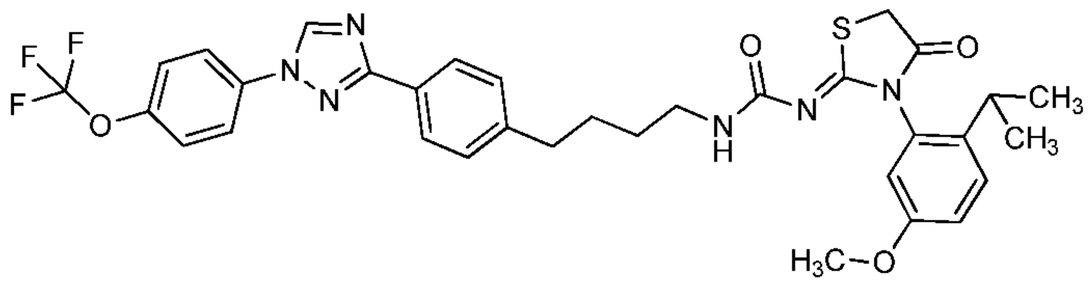
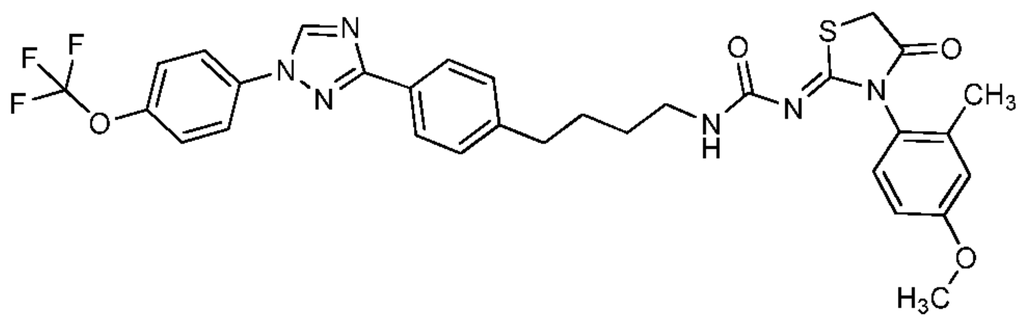
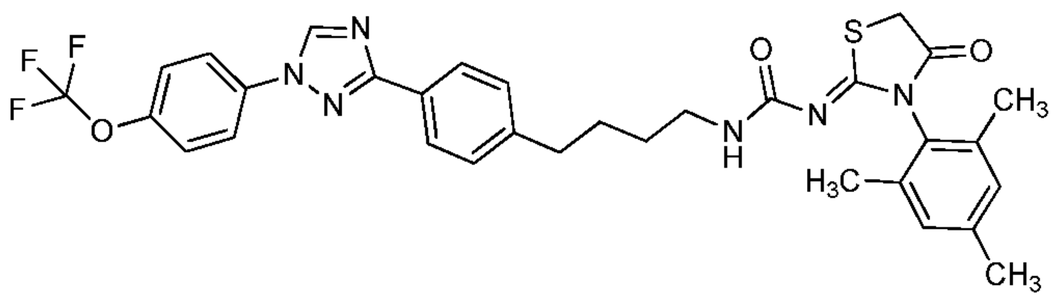
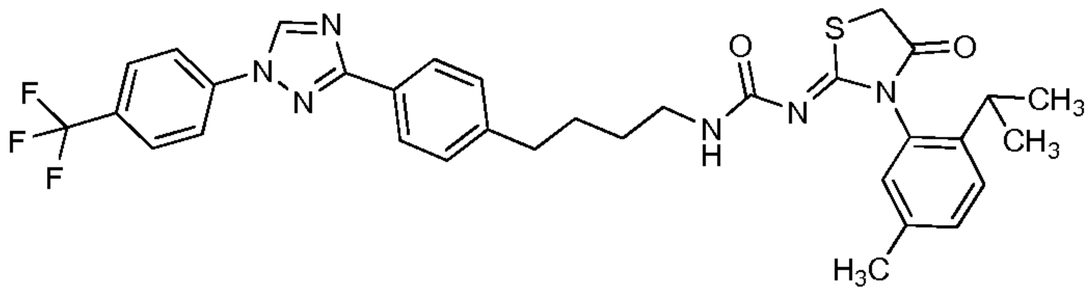
P119	
P120	
P121	
P122	
P123	
P124	
P125	

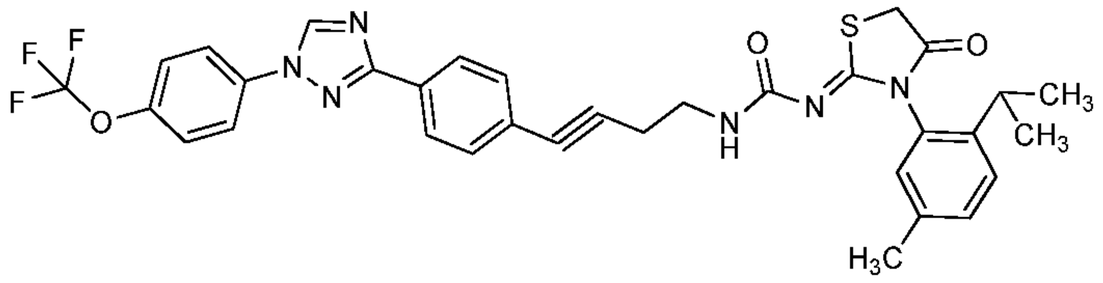
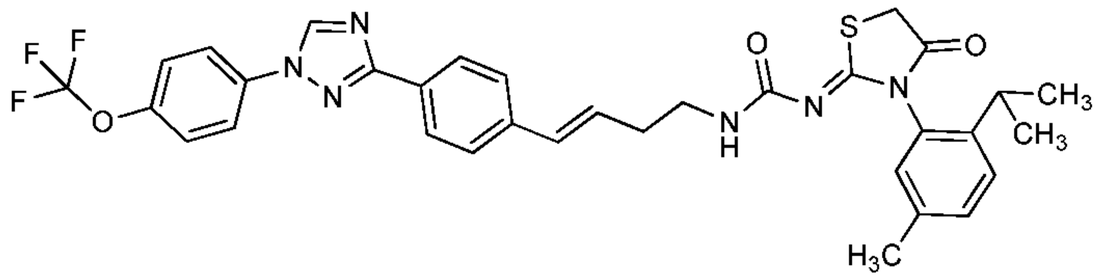
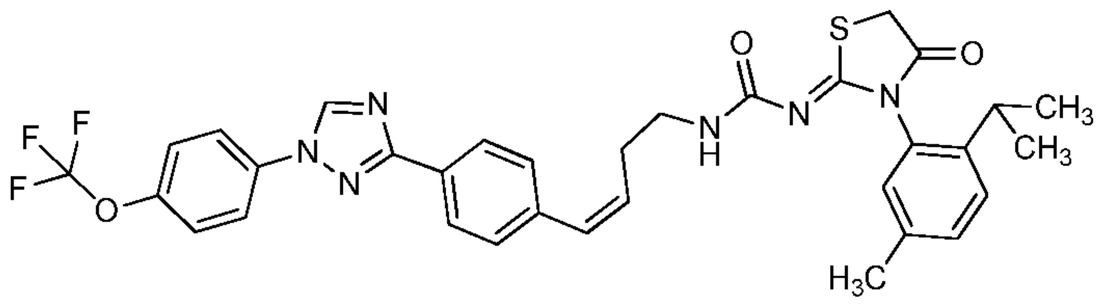
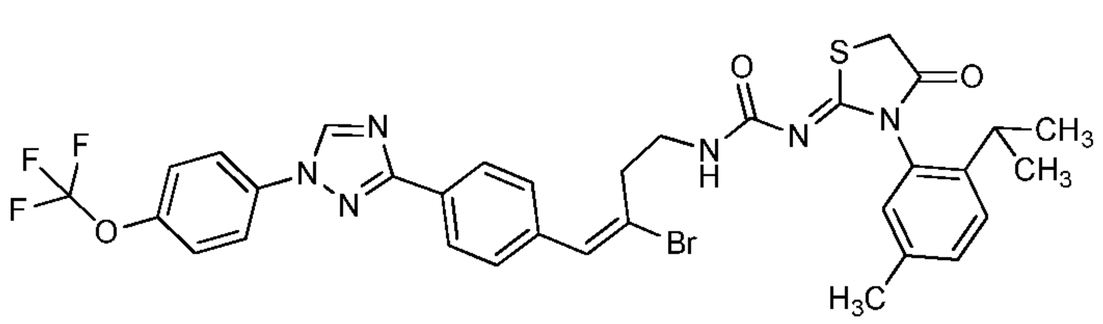
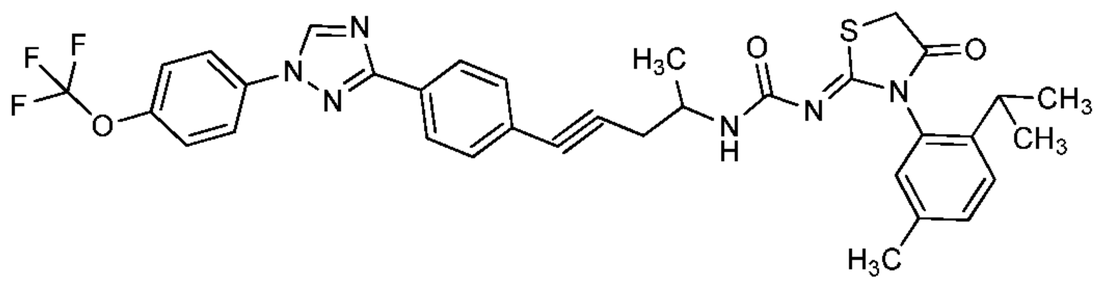
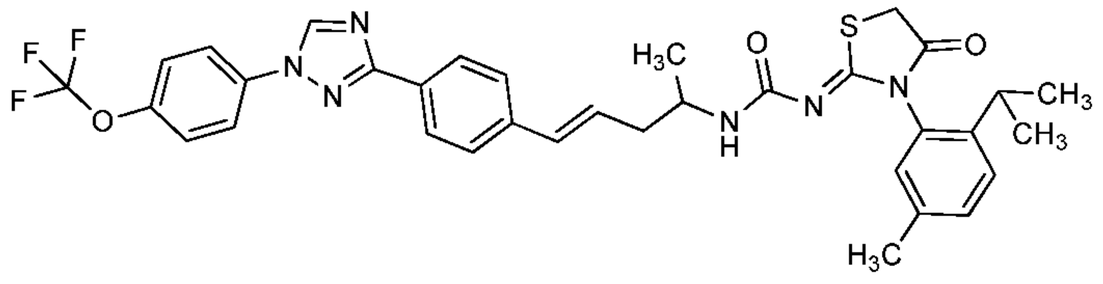
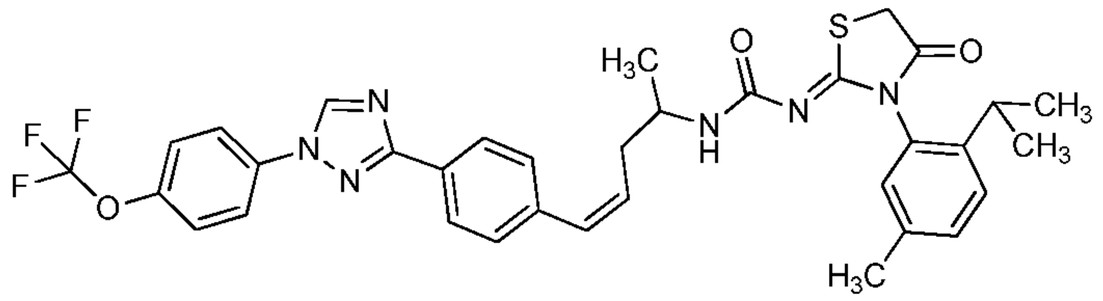
P126	
P127	
P128	
P129	
P130	
P131	
P132	

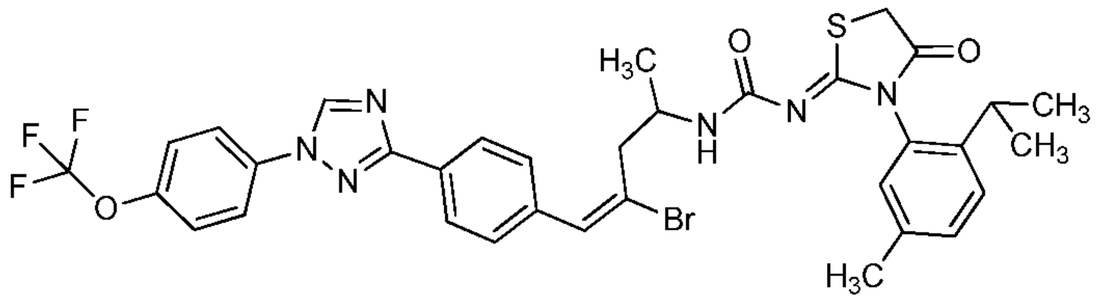
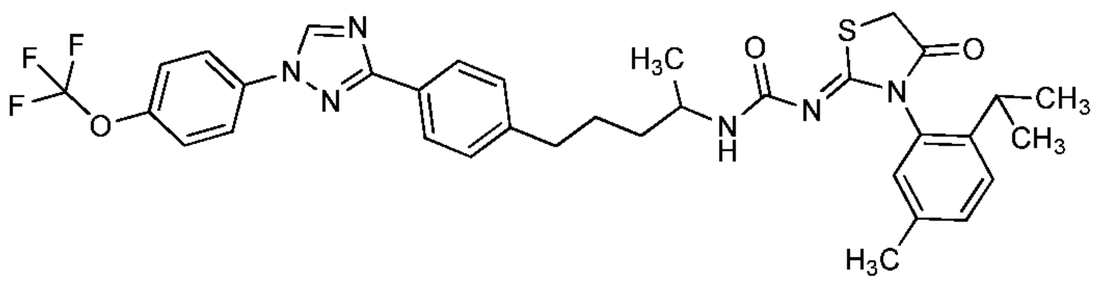
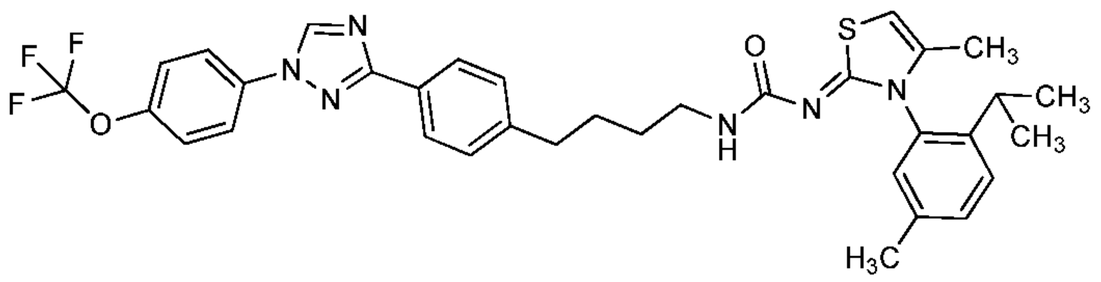
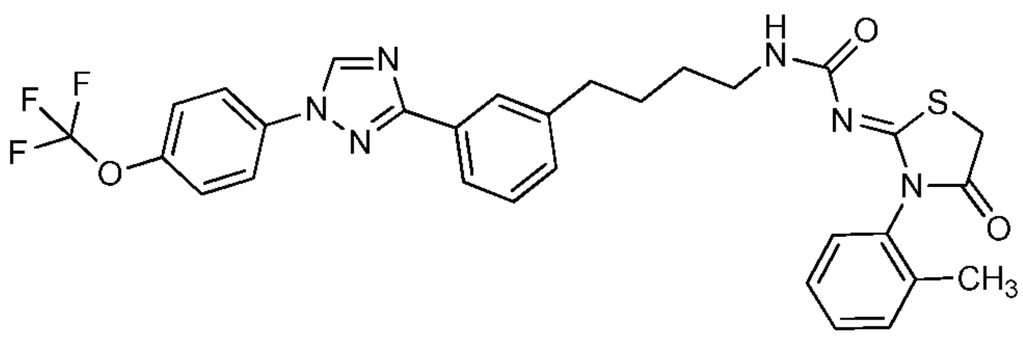
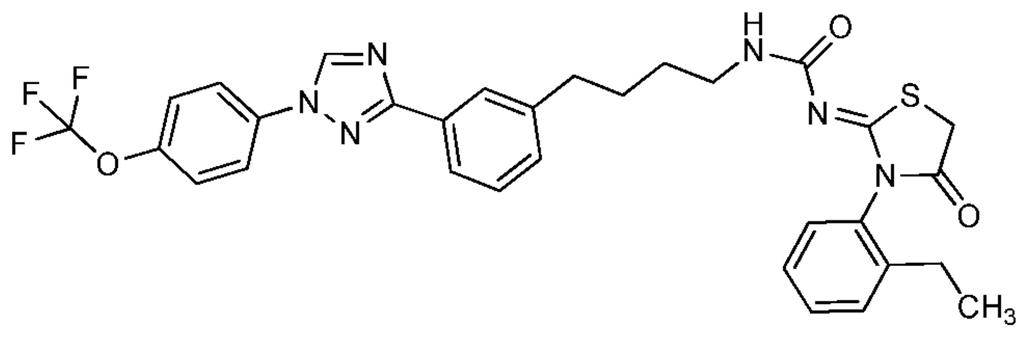
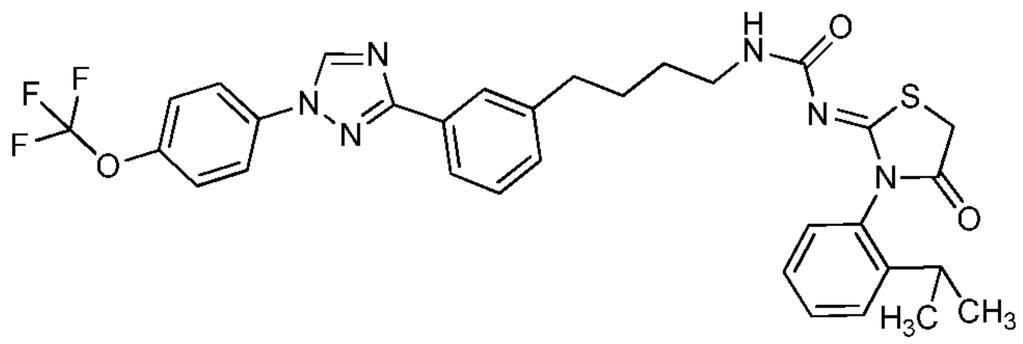
P133	
P134	
P135	
P136	
P137	
P138	

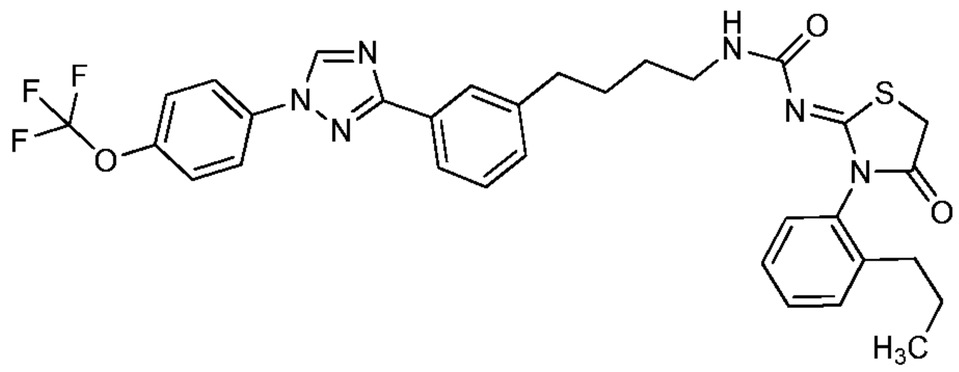
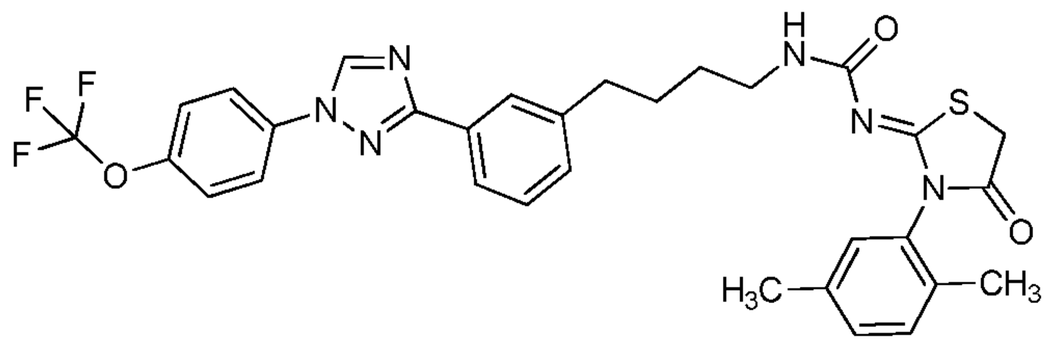
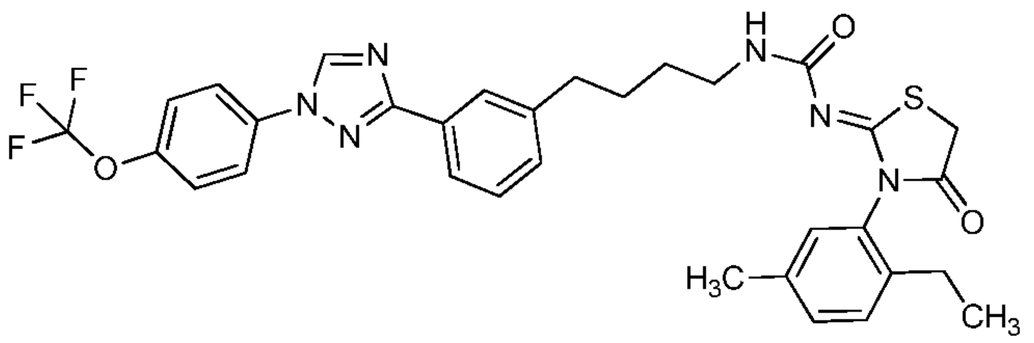
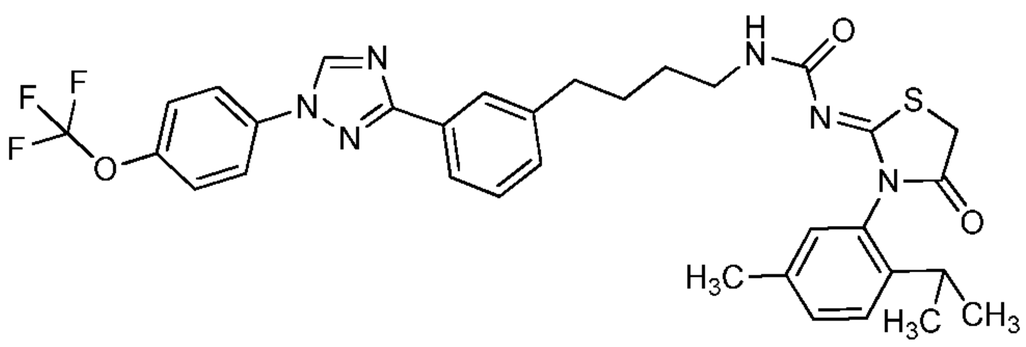
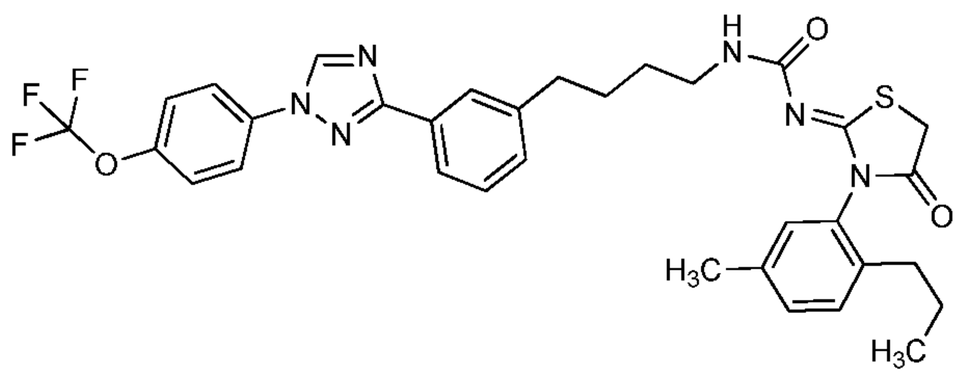
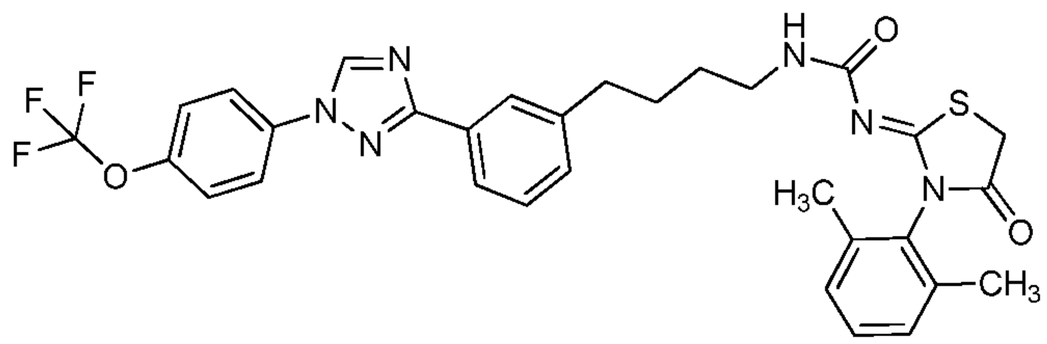
P139	
P140	
P141	
P142	
P143	
P144	
P145	

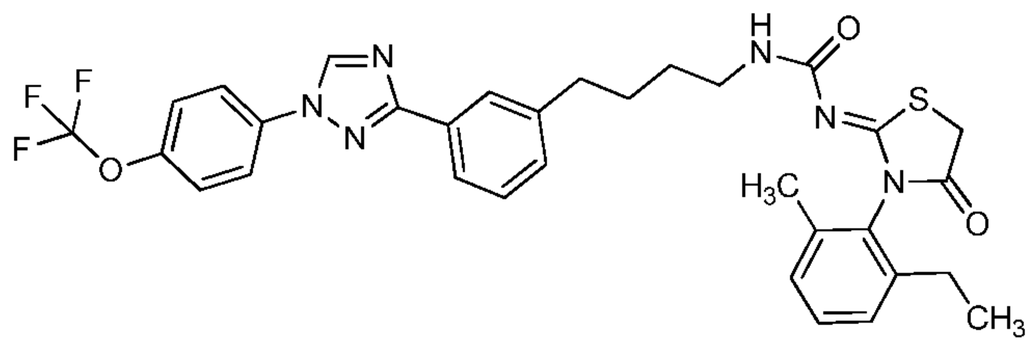
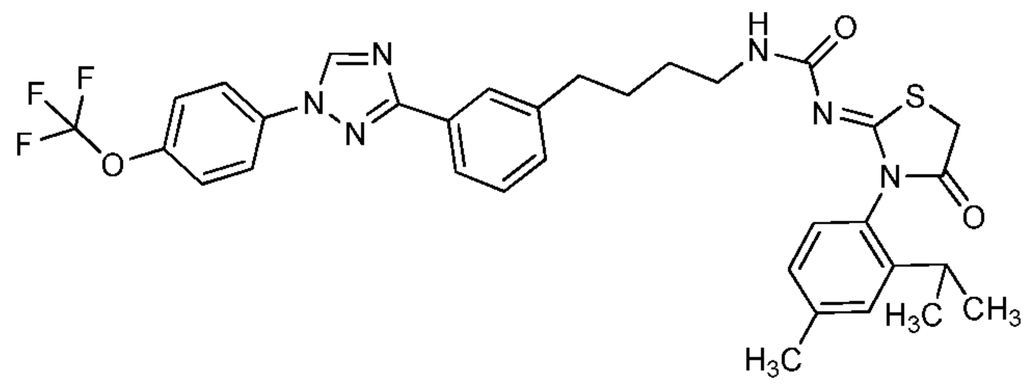
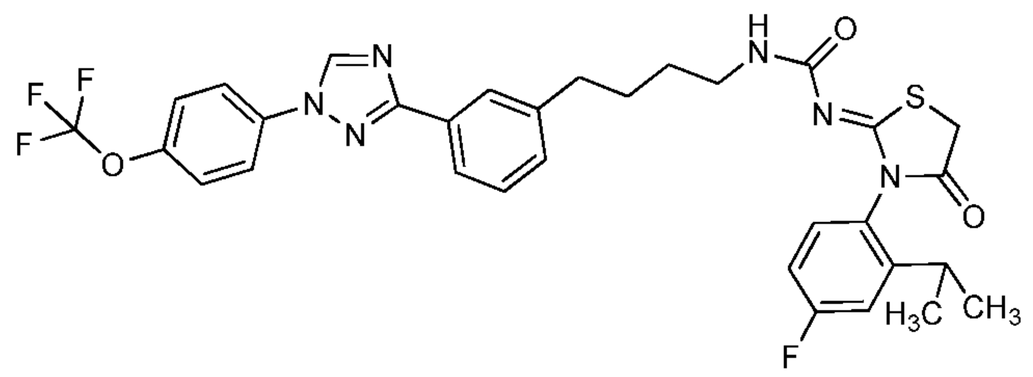
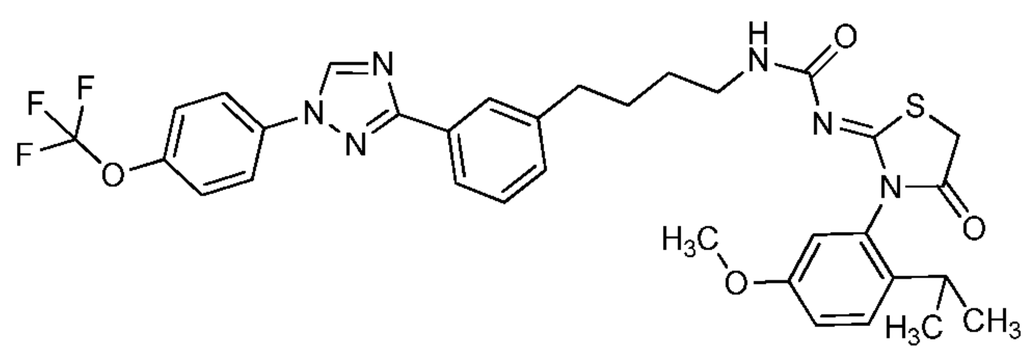
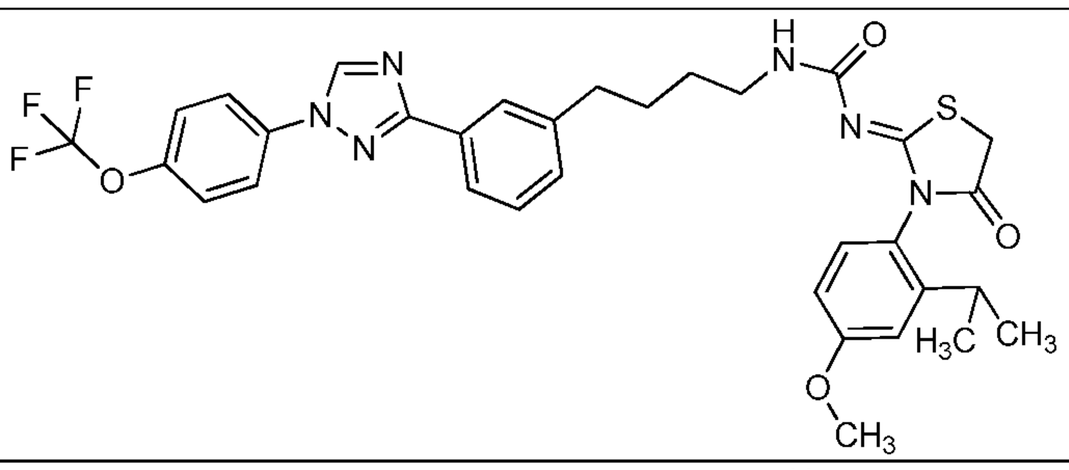
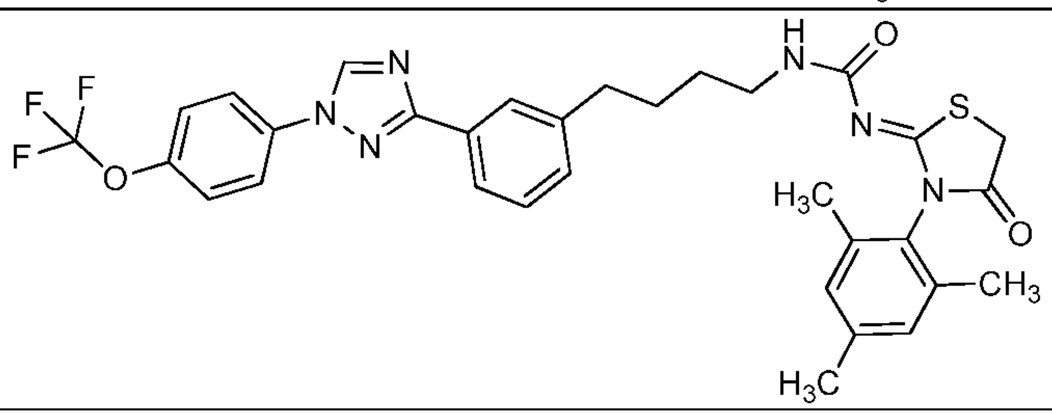
P146	
P147	
P148	
P149	
P150	
P151	
P152	

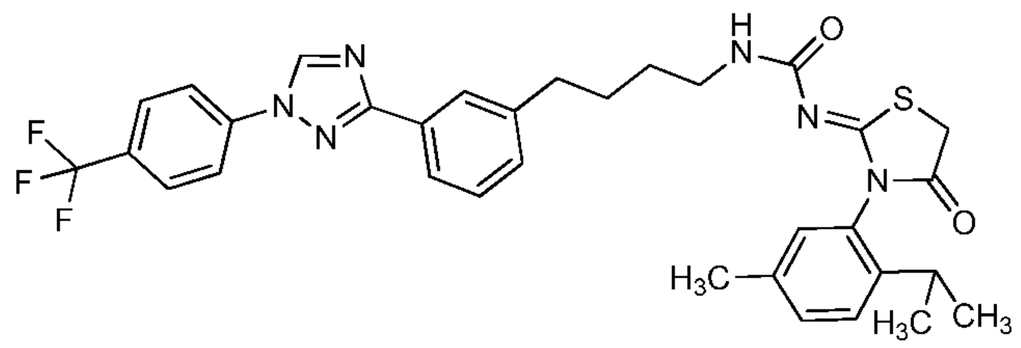
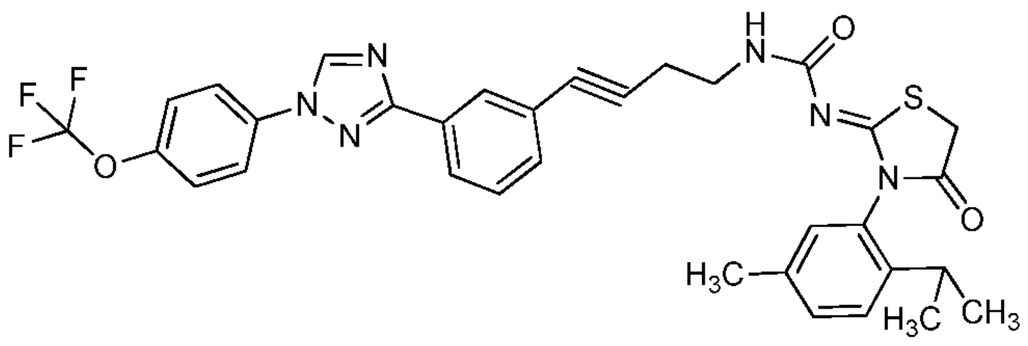
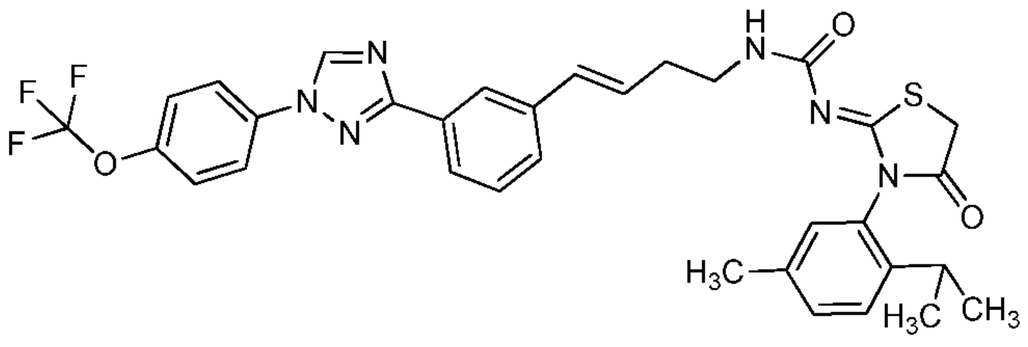
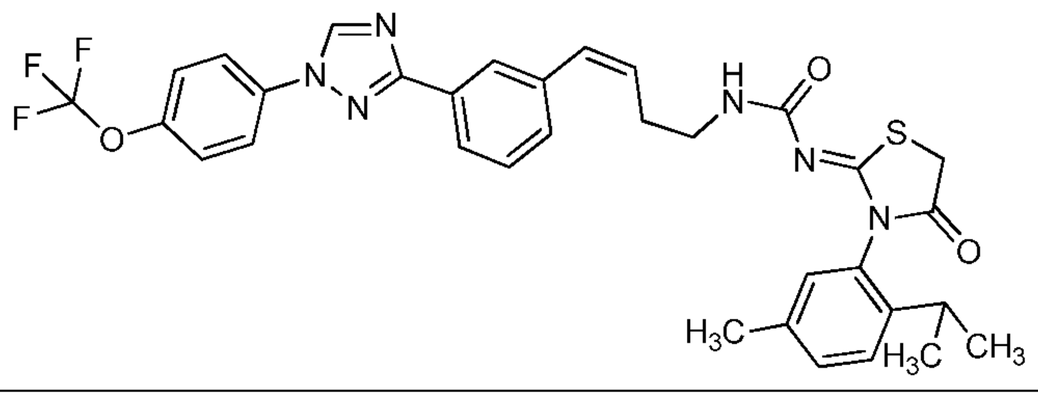
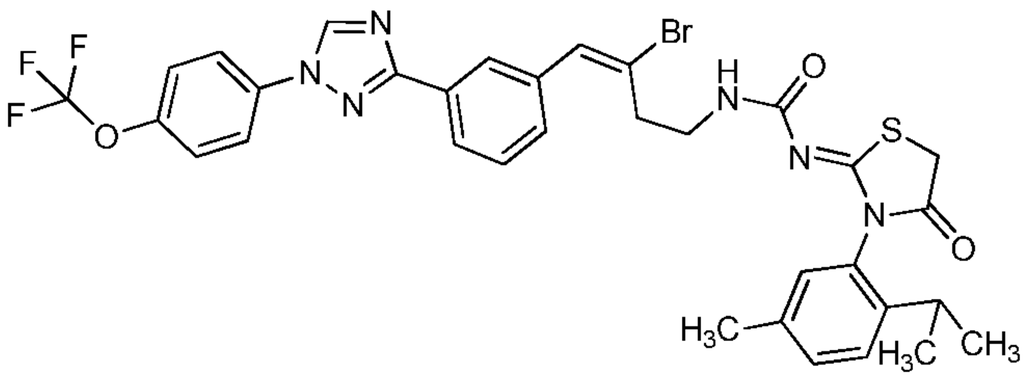
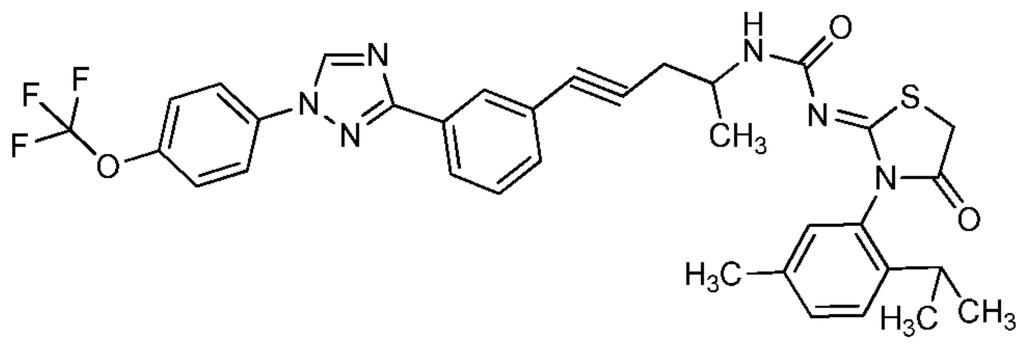
P153	
P154	
P155	
P156	
P157	
P158	
P159	

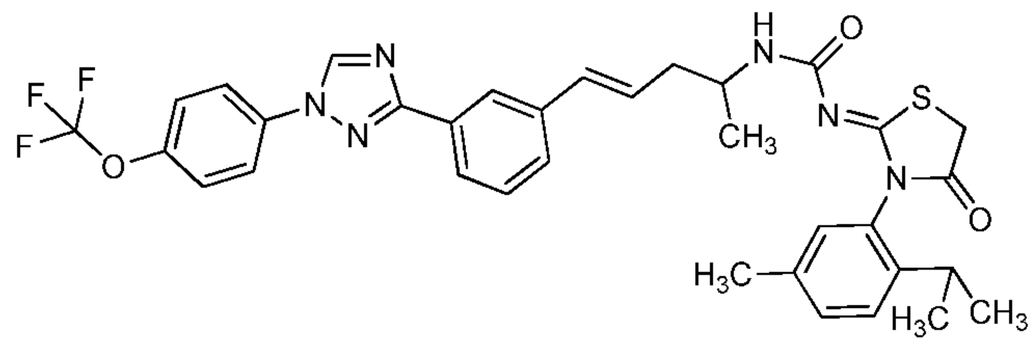
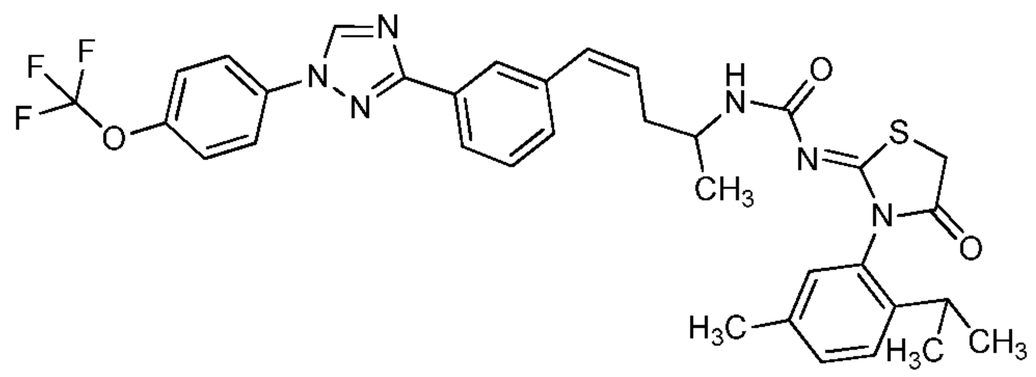
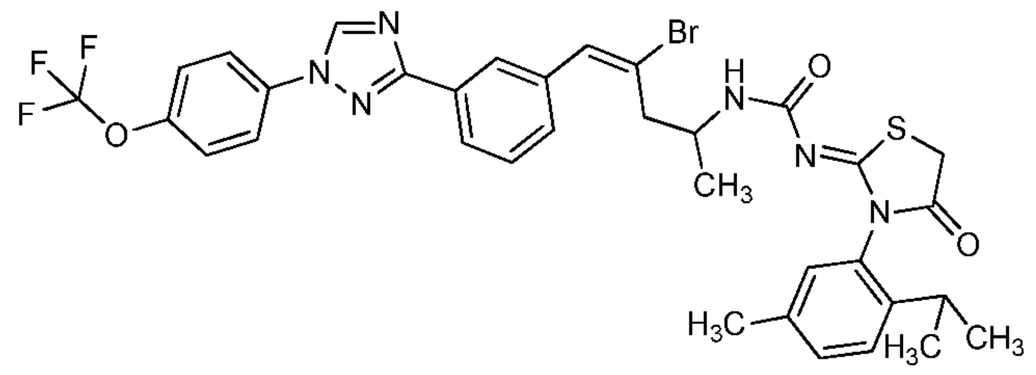
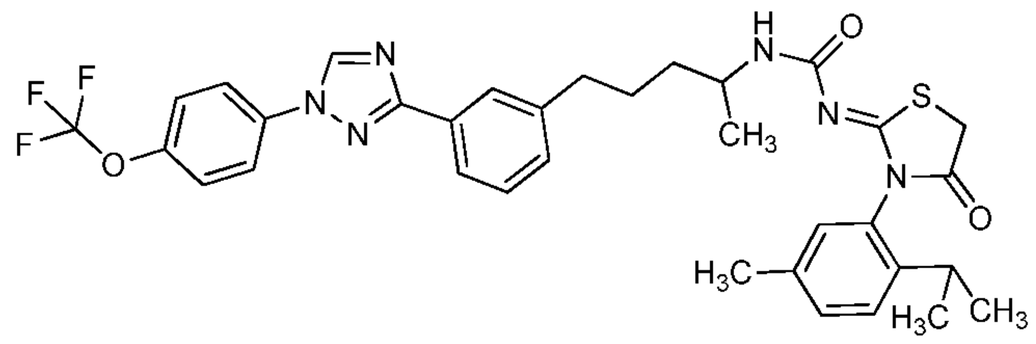
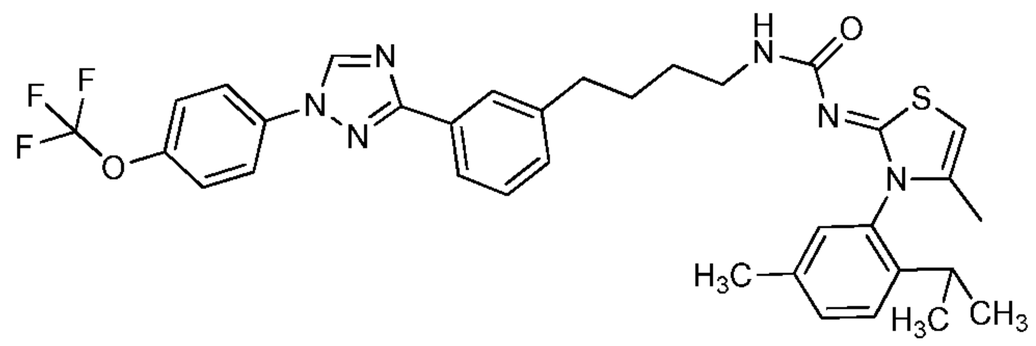
P160	
P161	
P162	
P163	
P164	
P165	
P166	

P167	
P168	
P169	
P170	
P171	
P172	

P173	
P174	
P175	
P176	
P177	
P178	

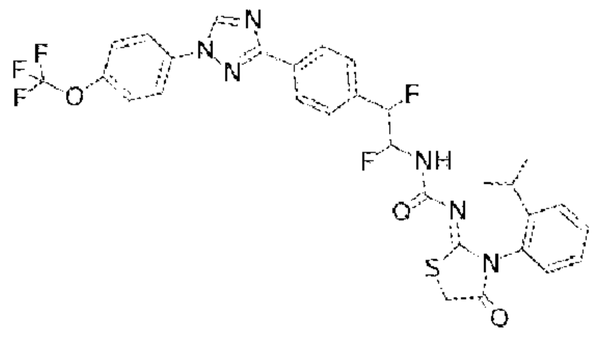
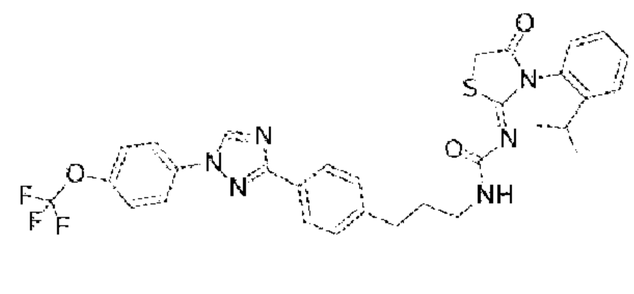
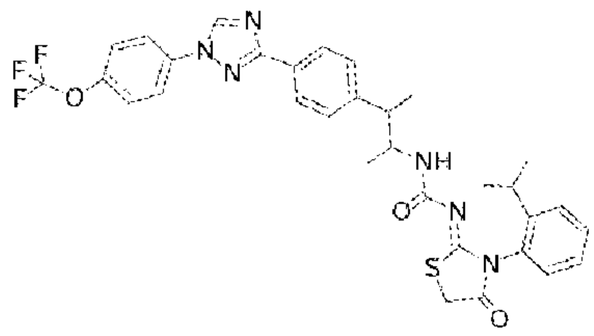
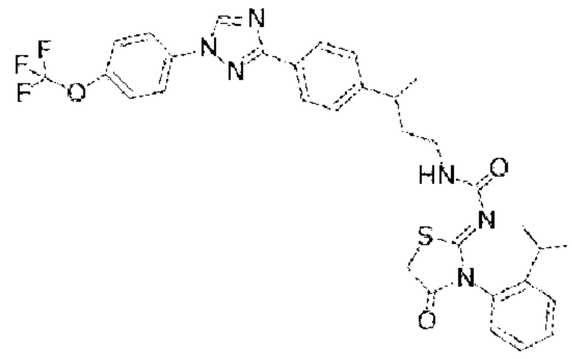
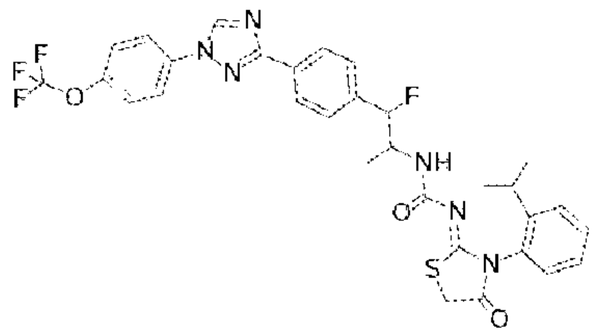
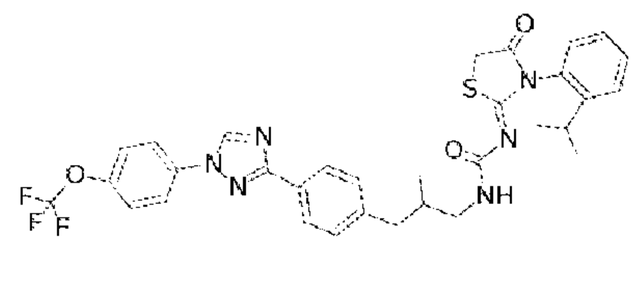
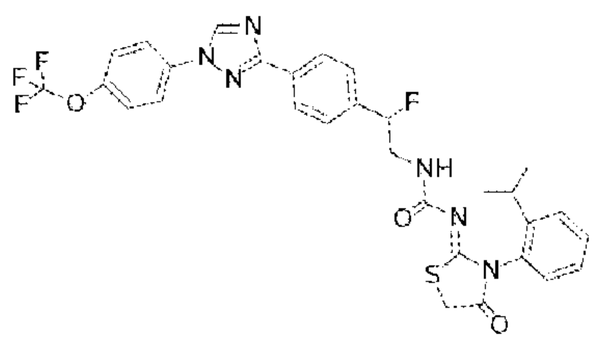
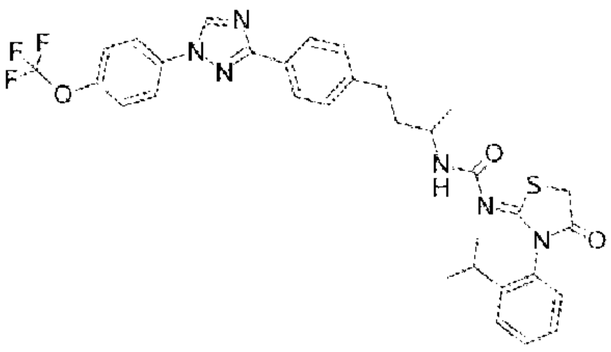
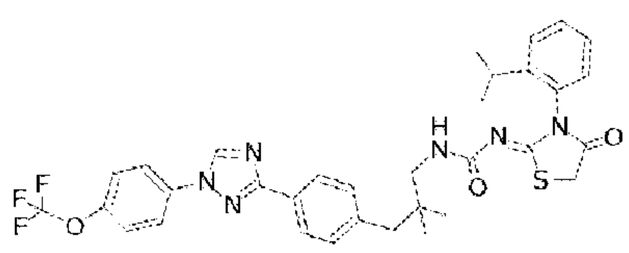
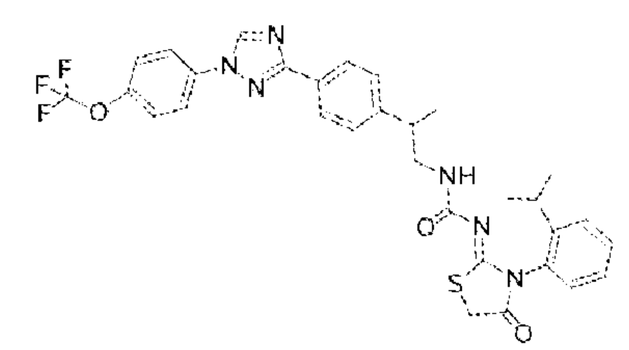
P179	
P180	
P181	
P182	
P183	
P184	

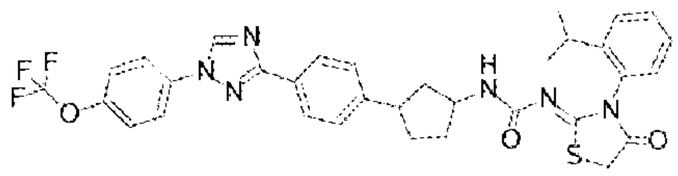
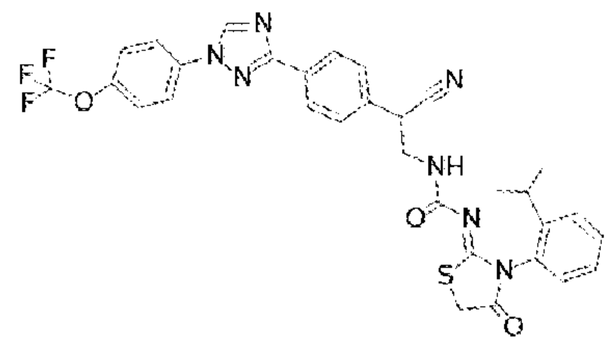
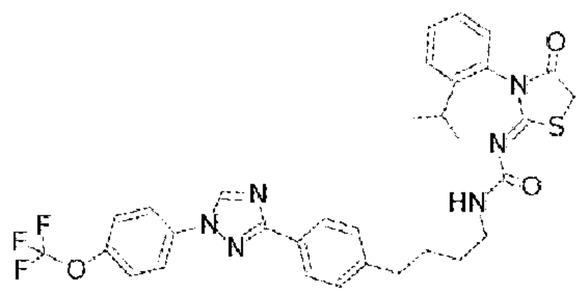
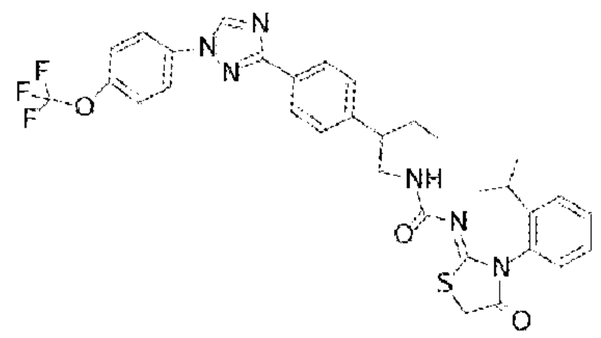
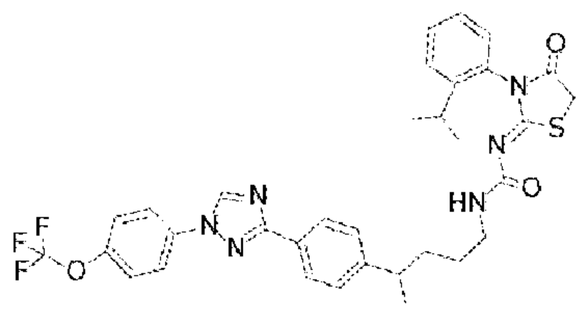
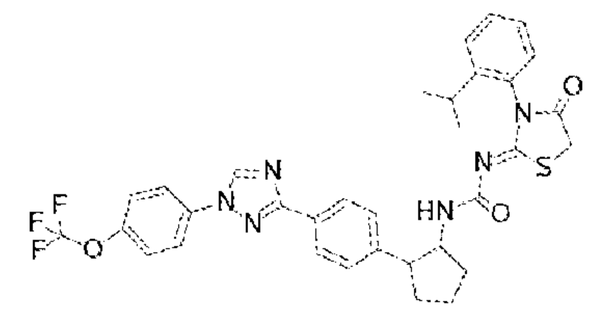
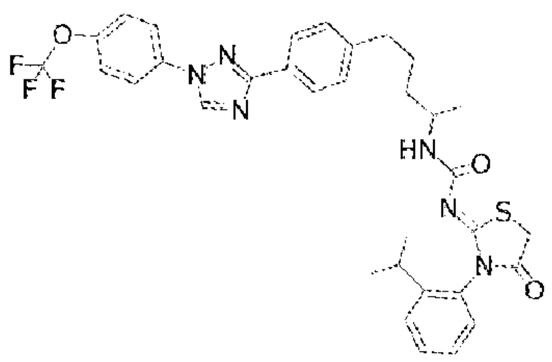
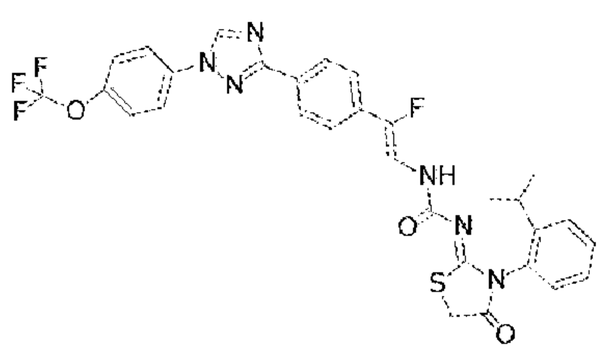
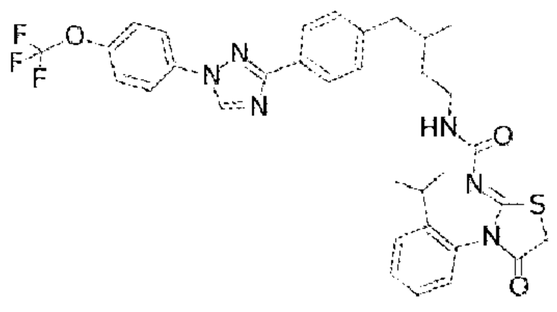
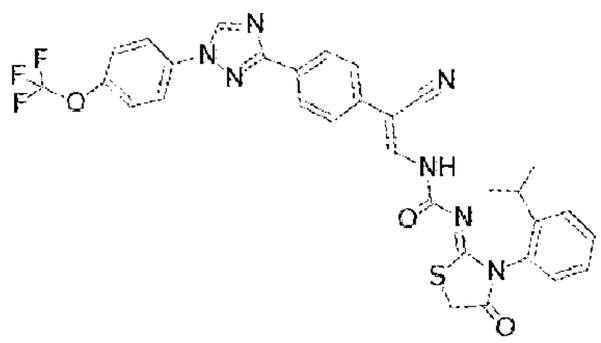
P185	
P186	
P187	
P188	
P189	
190	

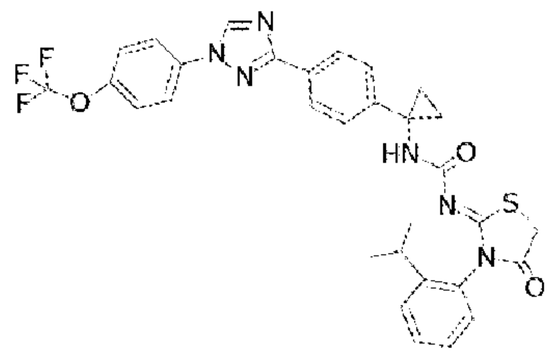
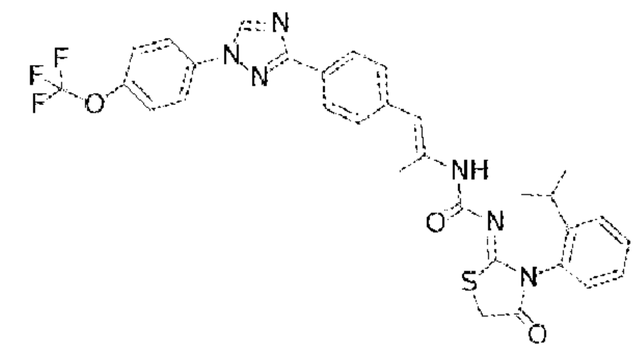
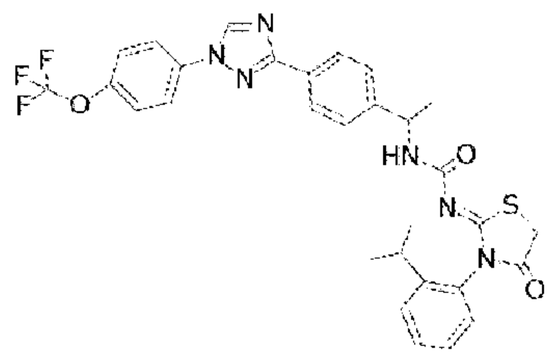
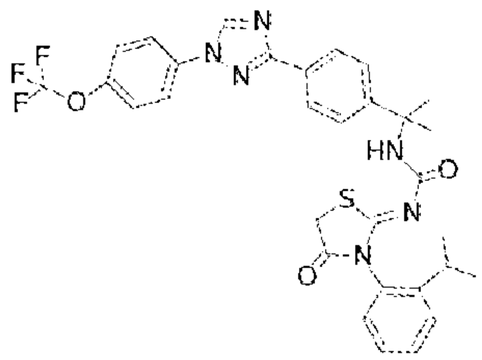
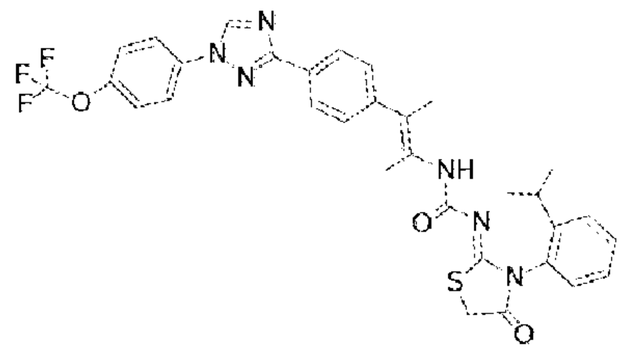
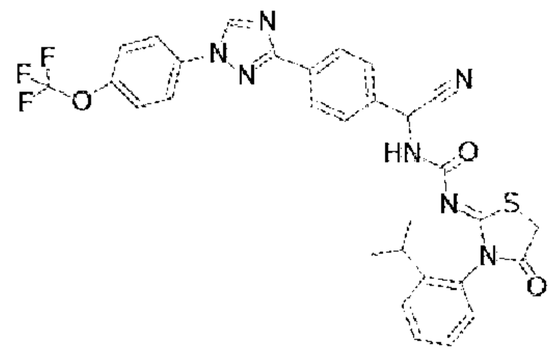
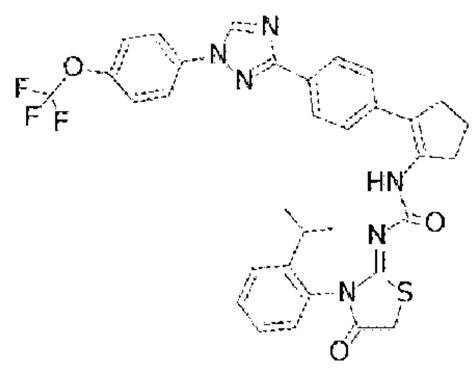
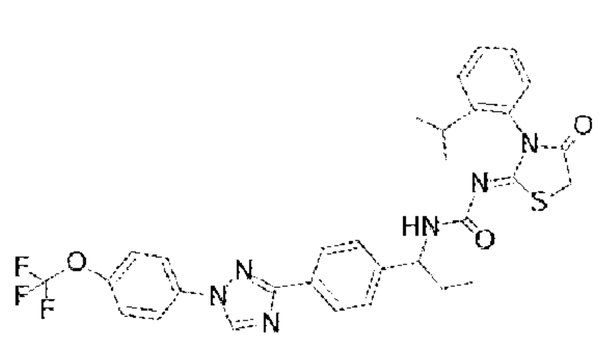
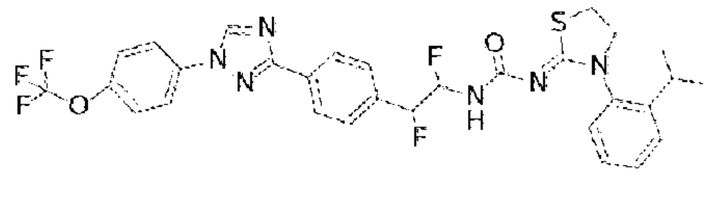
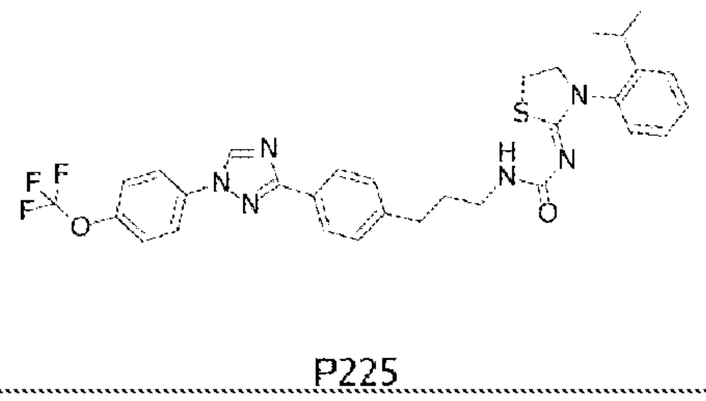
P191	
P192	
P193	
P194	
P195	

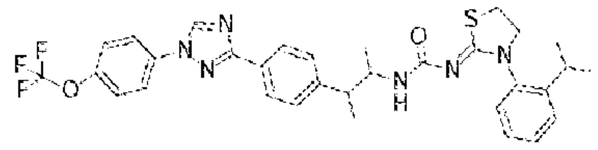
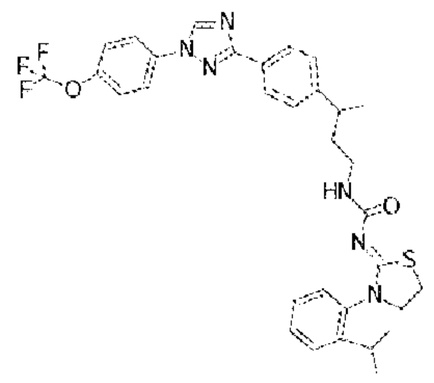
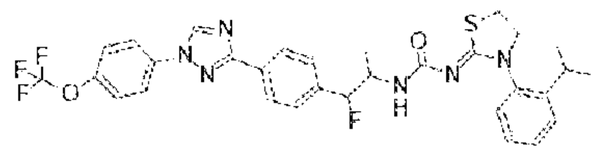
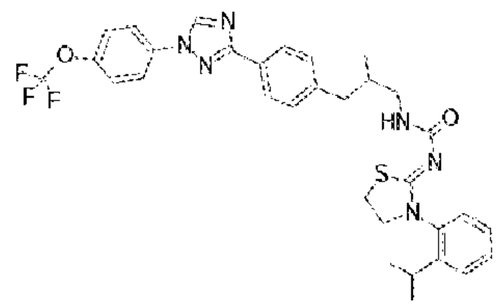
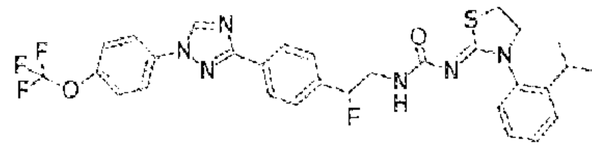
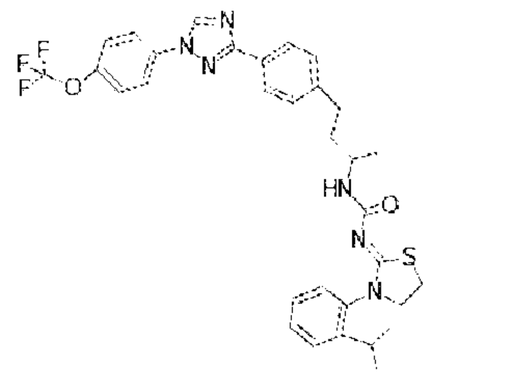
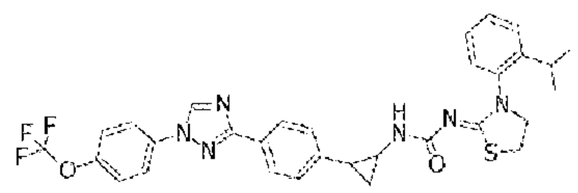
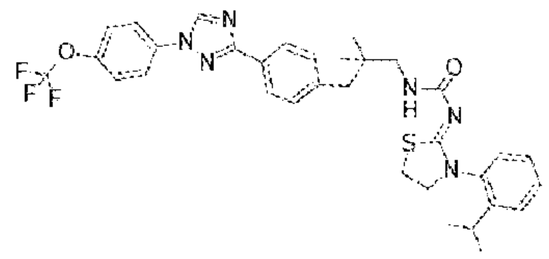
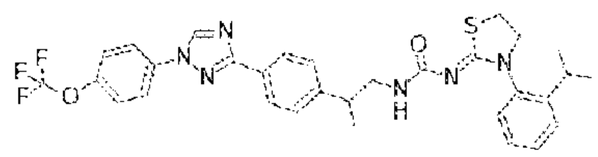
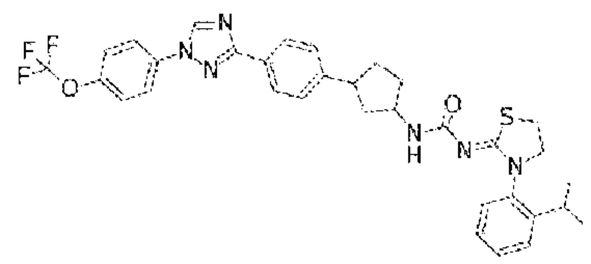
Additionally using the procedures disclosed herein the following list of prophetic molecules having a structure according to Formula One may be made (Table P-Two).

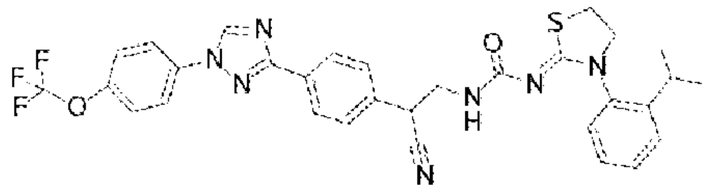
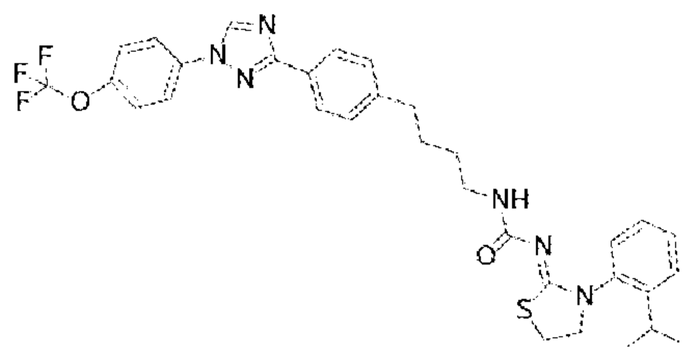
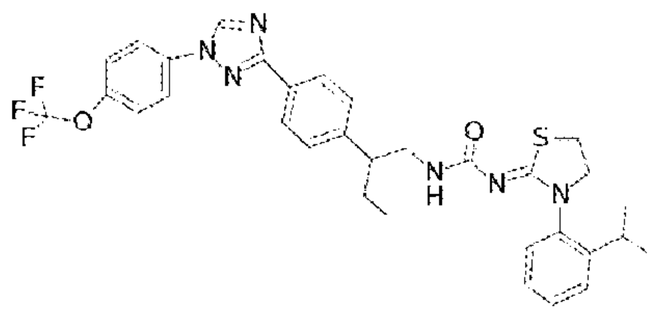
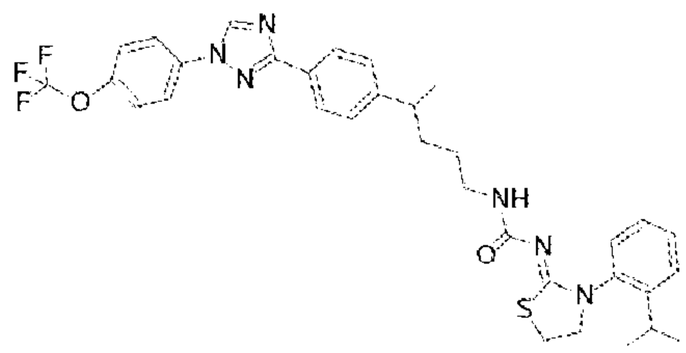
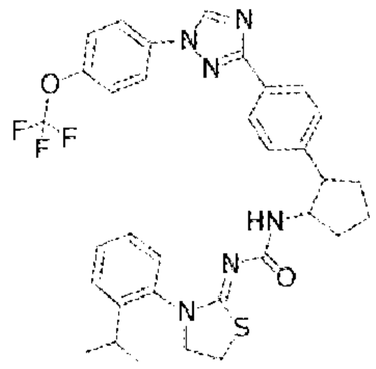
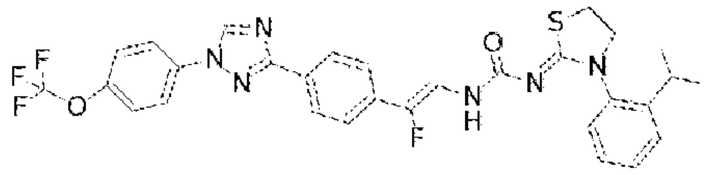
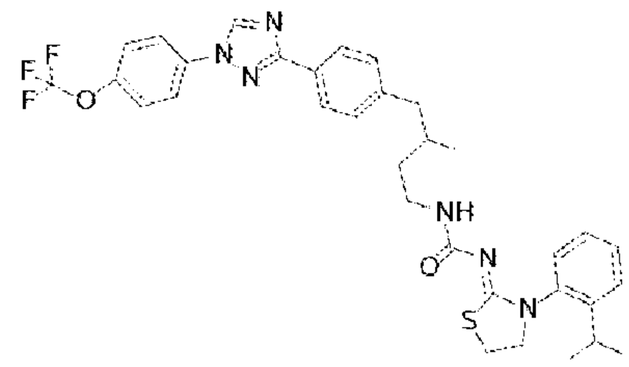
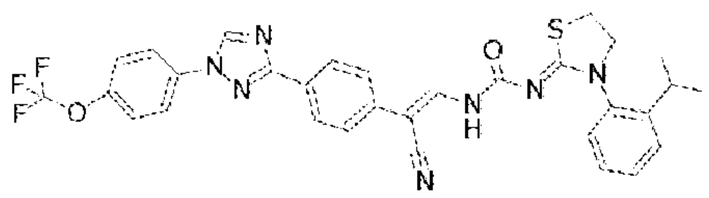
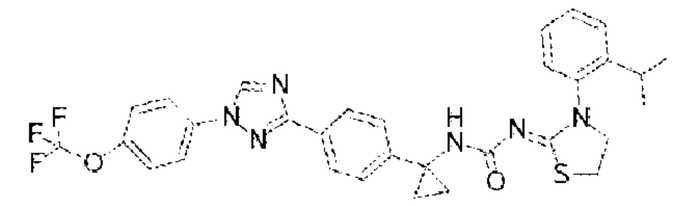
Table P-Two

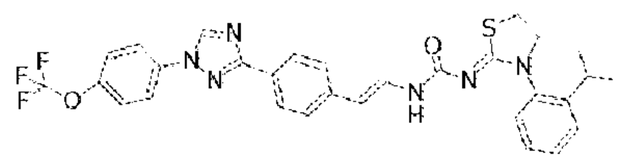
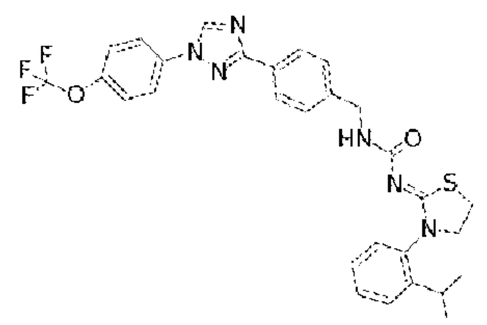
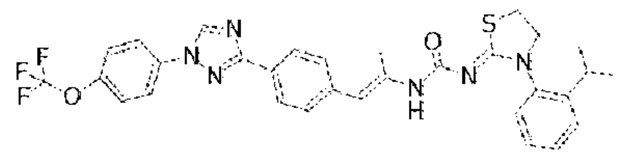
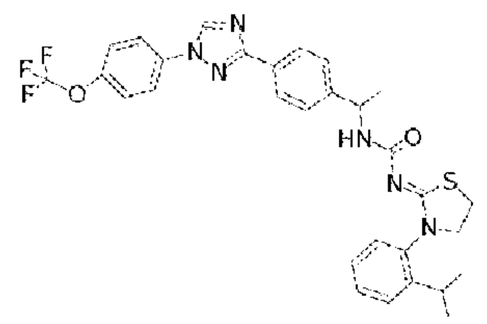
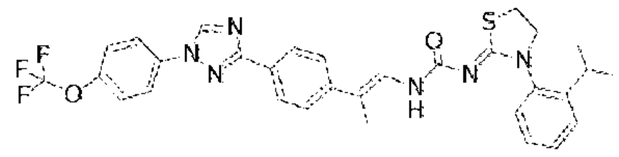
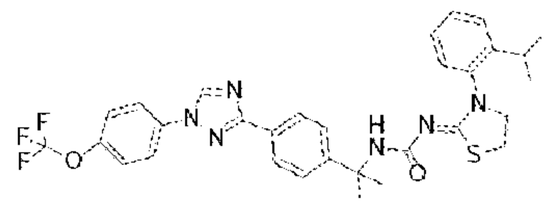
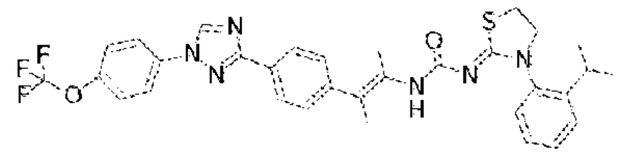
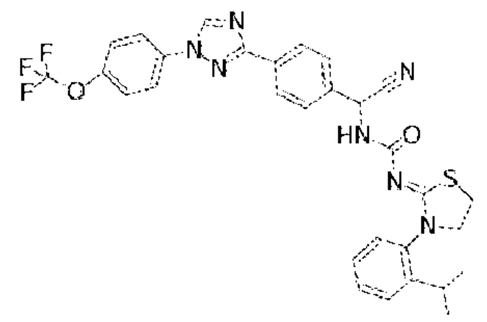
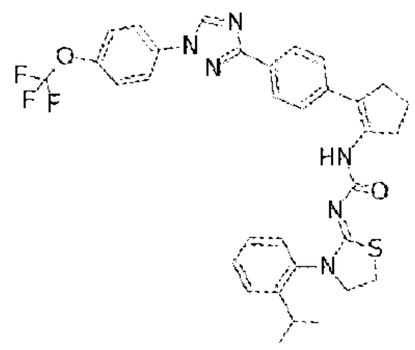
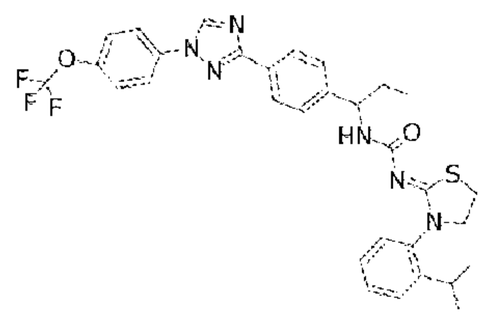
 P196	 P197
 P198	 P199
 P200	 P201
 P202	 P203
 P204	 P205

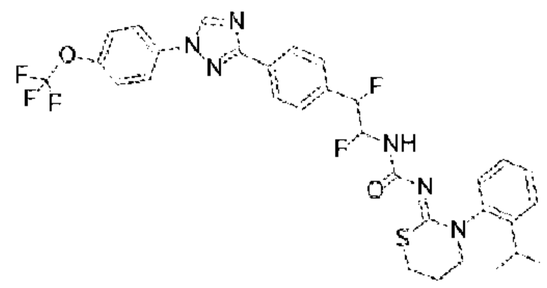
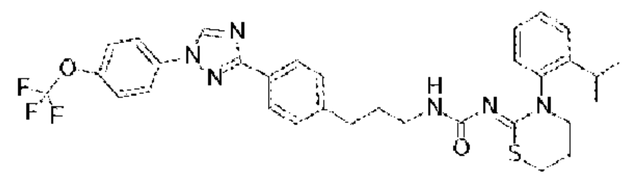
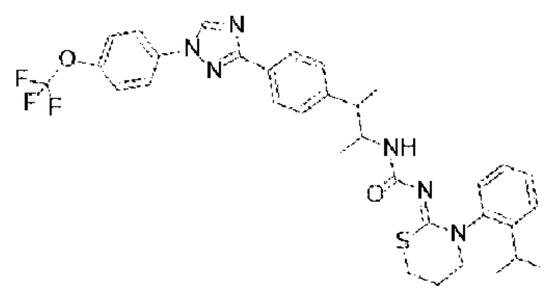
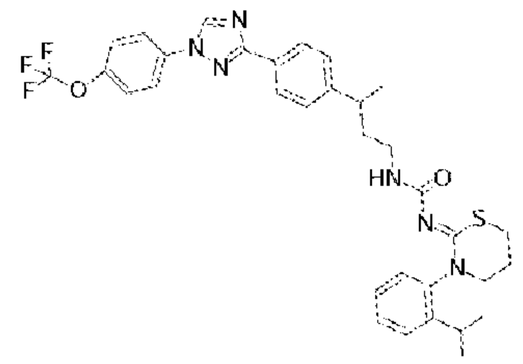
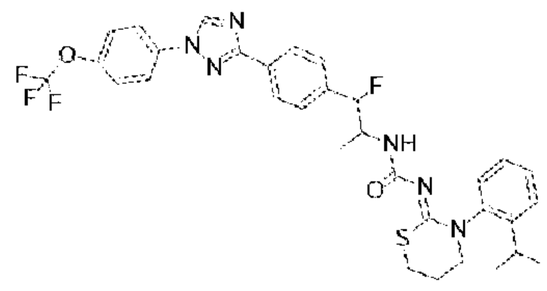
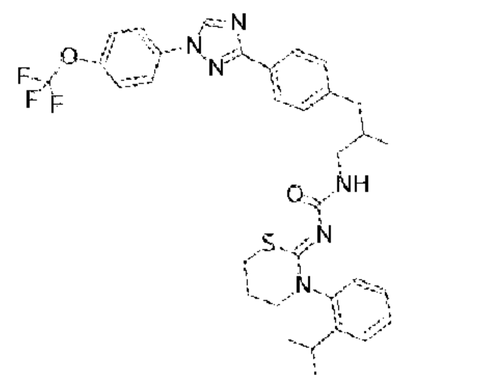
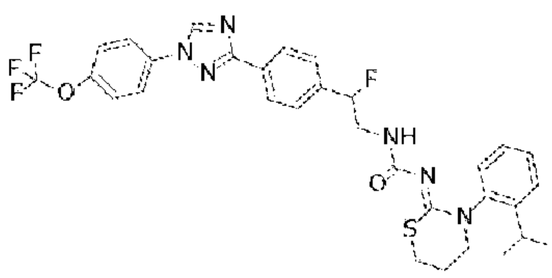
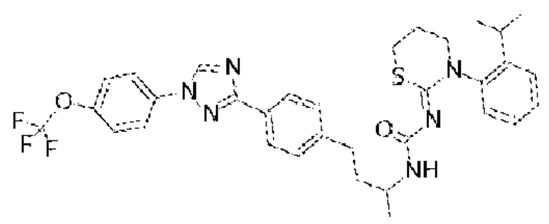
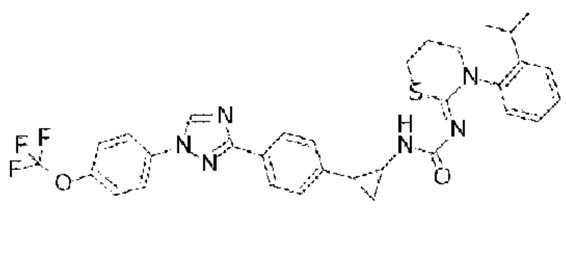
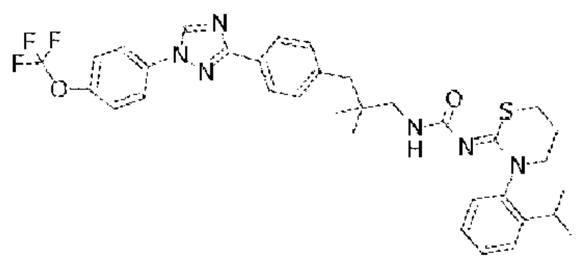
 P206	 P207
 P208	 P209
 P210	 P211
 P212	 P213
 P214	 P215

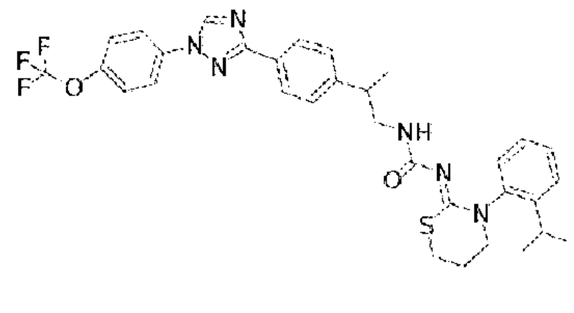
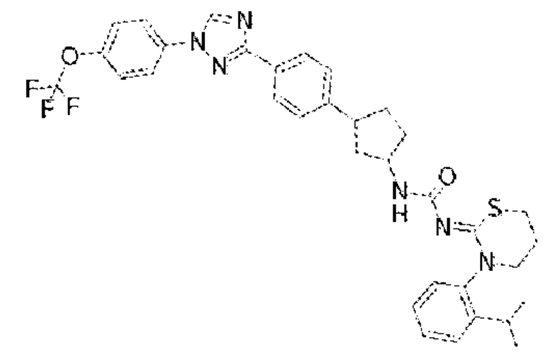
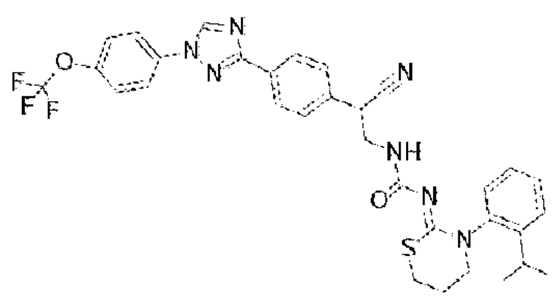
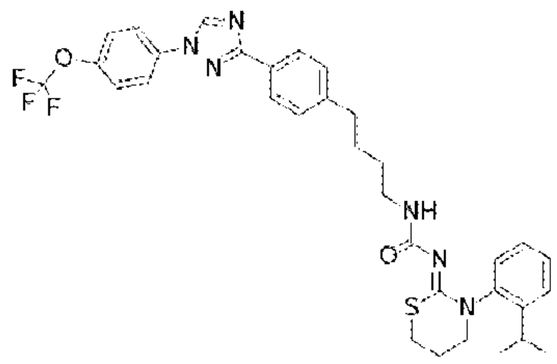
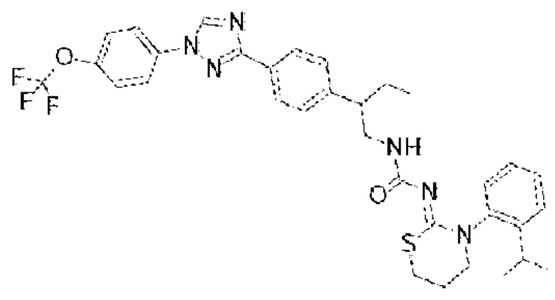
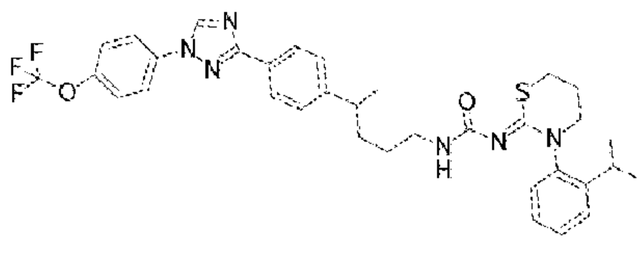
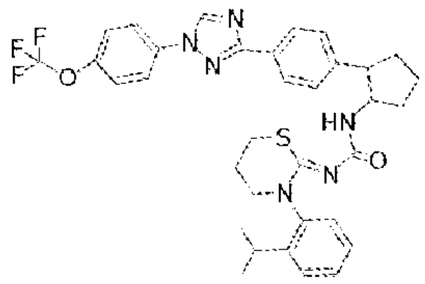
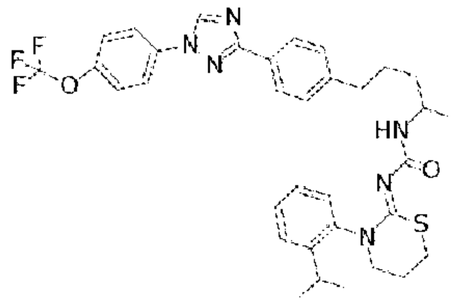
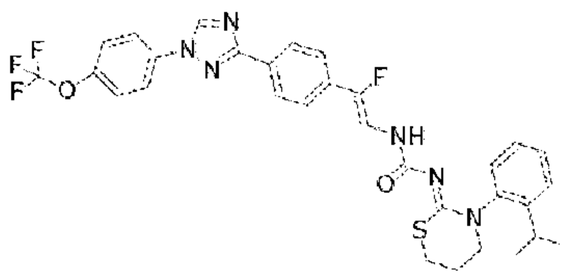
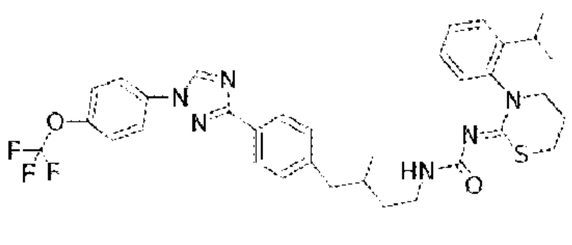
 P216	 P217
 P218	 P219
 P220	 P221
 P222	 P223
 P224	 P225

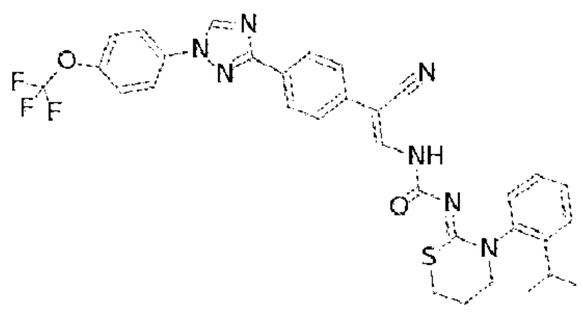
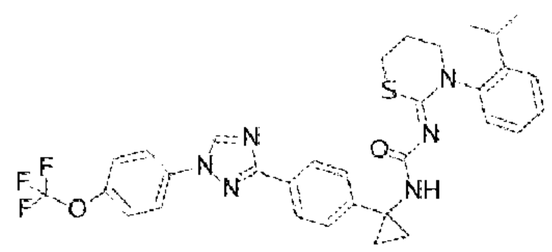
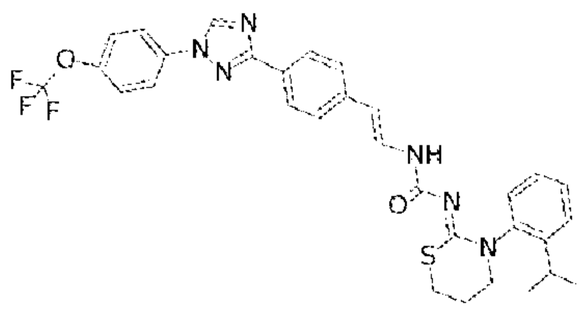
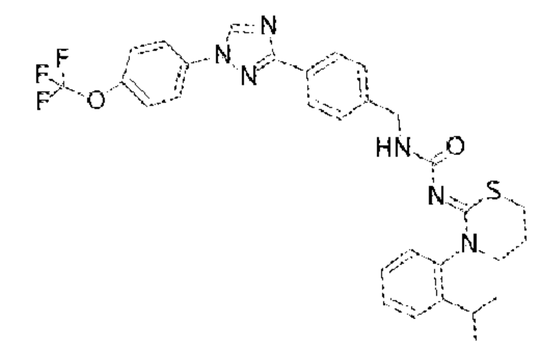
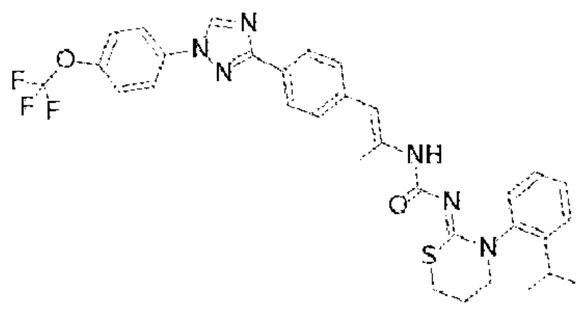
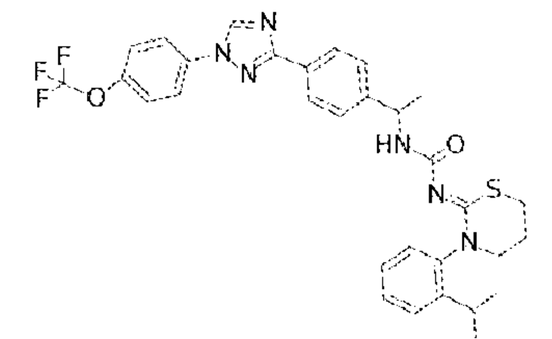
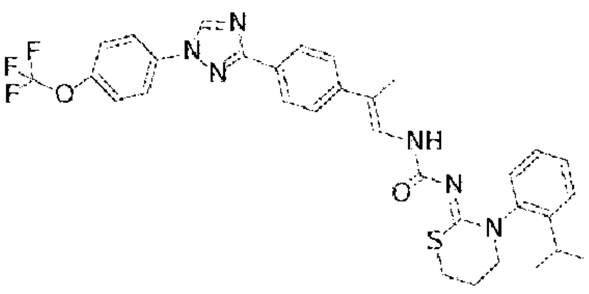
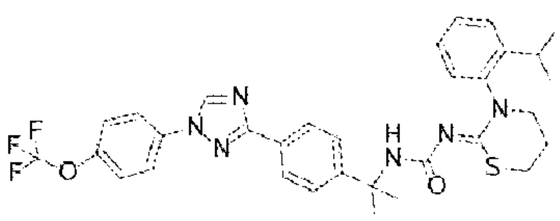
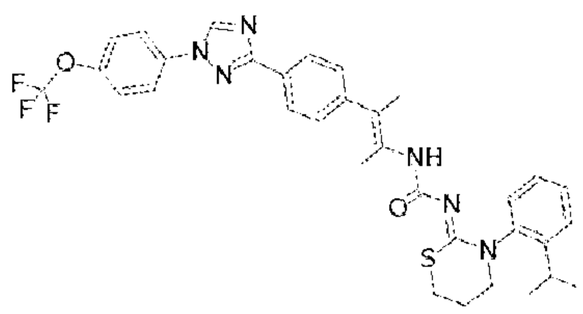
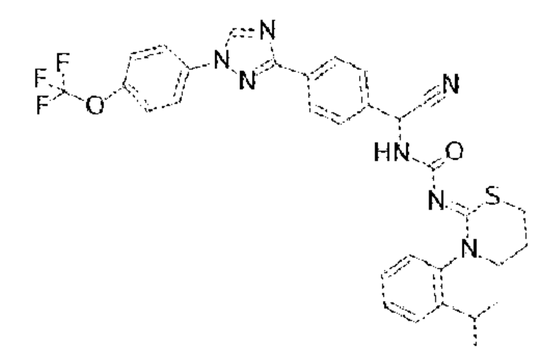
	
P226	P227
	
P228	P229
	
P230	P231
	
P232	P233
	
P234	P235

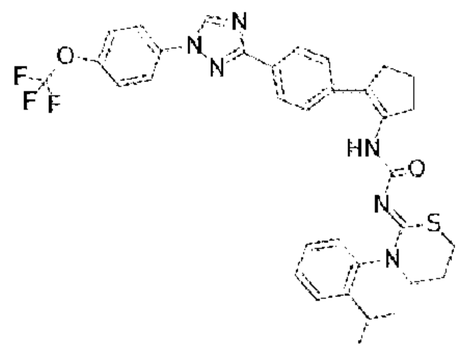
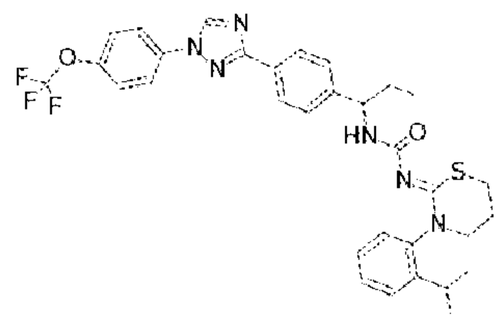
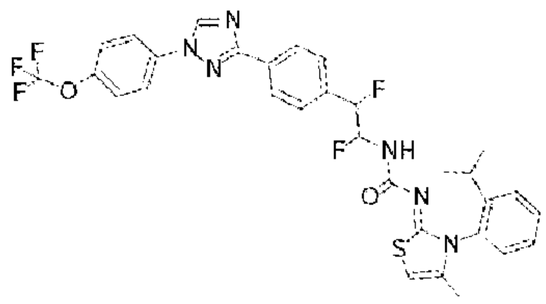
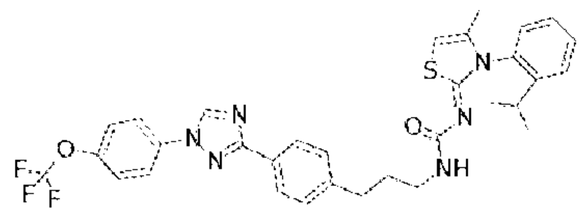
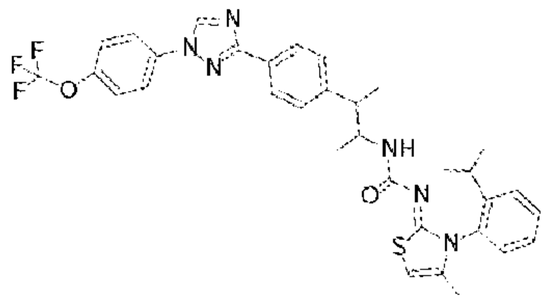
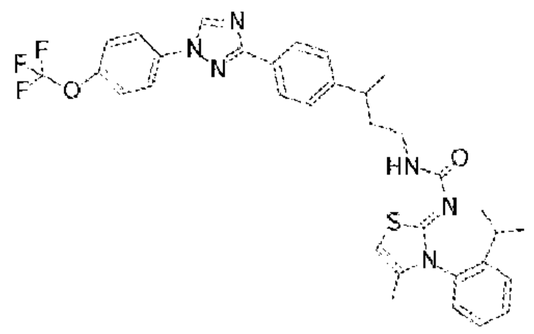
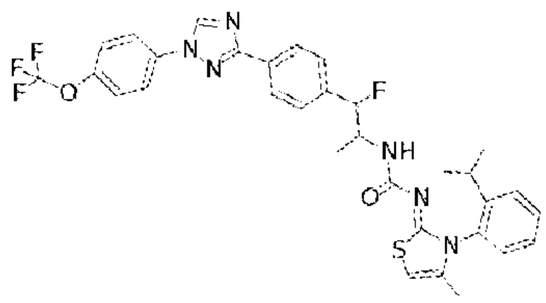
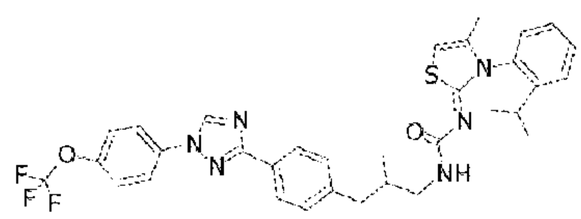
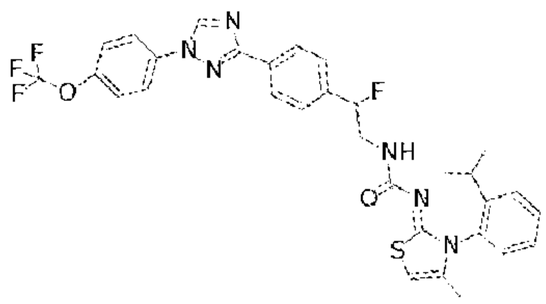
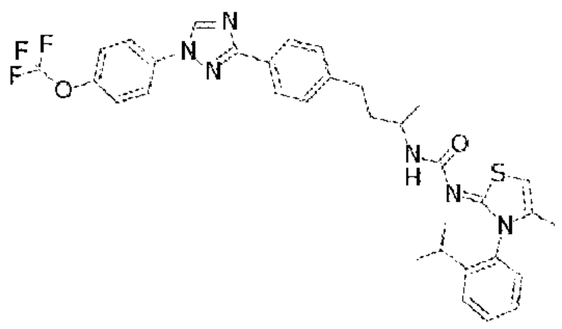
 P236	 P237
 P238	 P239
 P240	P241
 P242	 P243
 P244	 P245

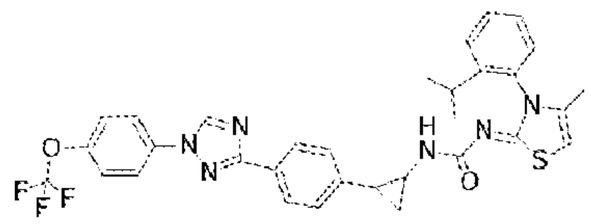
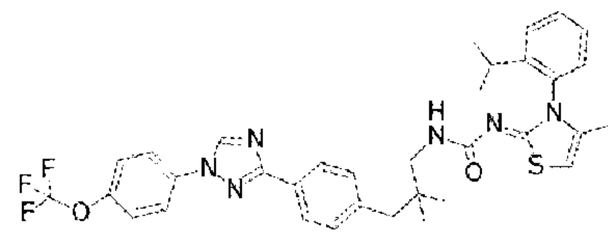
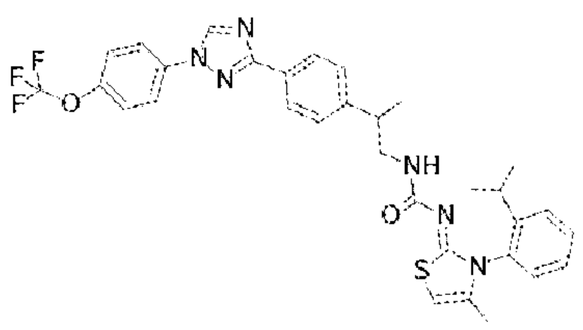
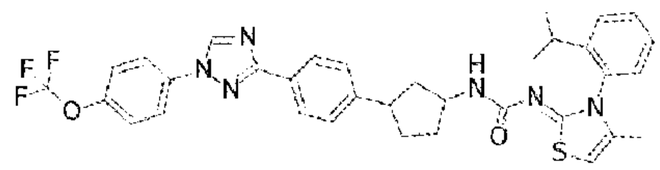
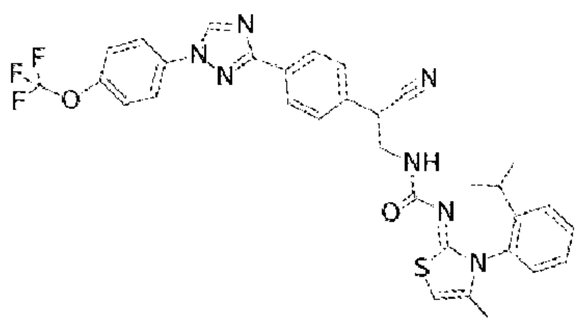
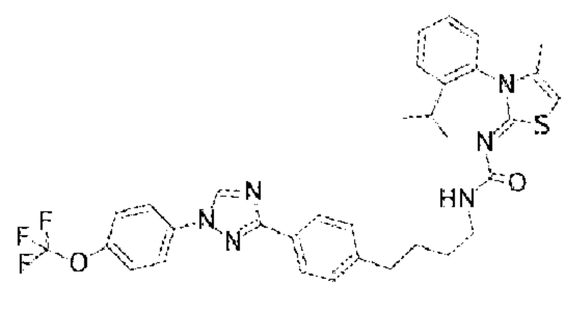
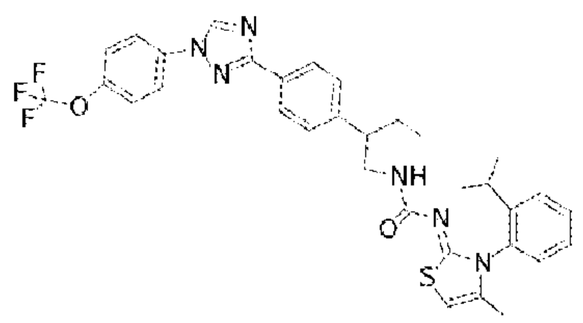
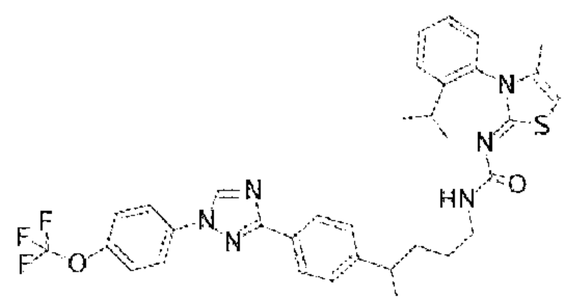
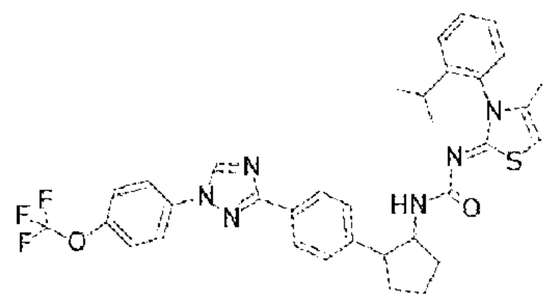
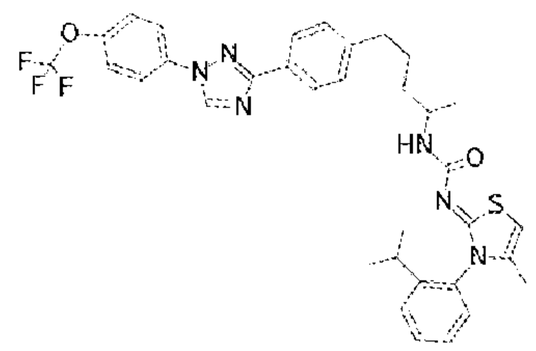
 P246	 P247
 P248	 P249
 P250	 P251
 P252	 P253
 P254	 P255

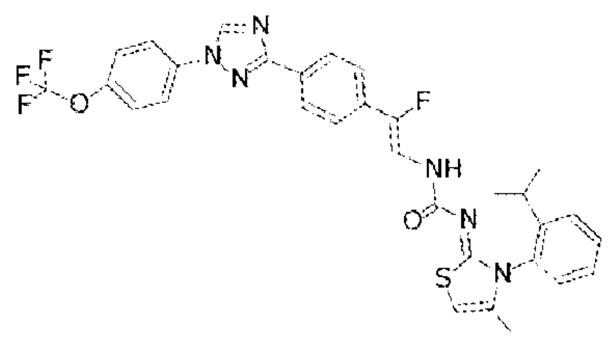
	
P256	P257
	
P258	P259
	
P260	P261
	
P262	P263
	
P264	P265

 P266	 P267
 P268	 P269
 P270	 P271
 P272	 P273
 P274	 P275

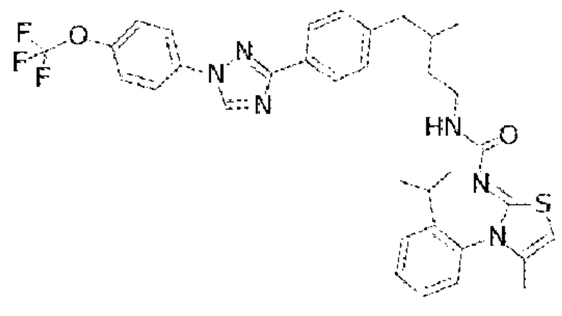
 P276	 P277
 P278	 P279
 P280	 P281
 P282	 P283
 P284	 P285

 P286	 P287
 P288	 P289
 P290	 P291
 P292	 P293
 P294	 P295

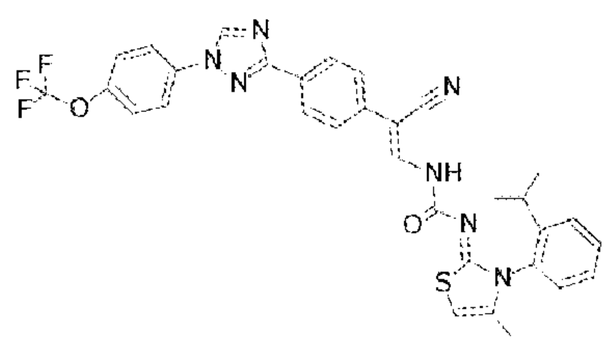
	
P296	P297
	
P298	P299
	
P300	P301
	
P302	P303
	
P304	P305



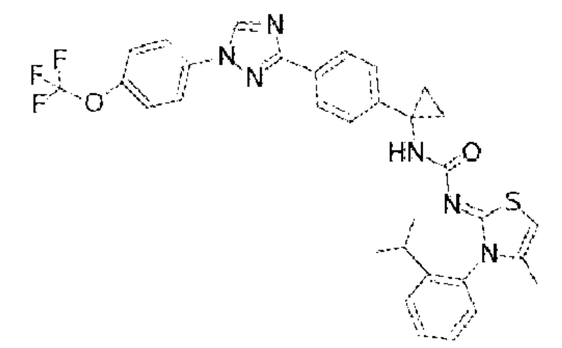
P306



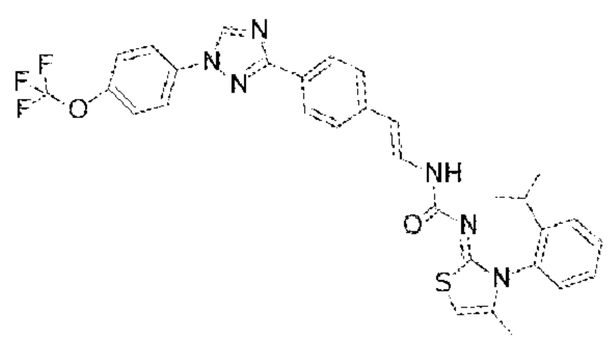
P307



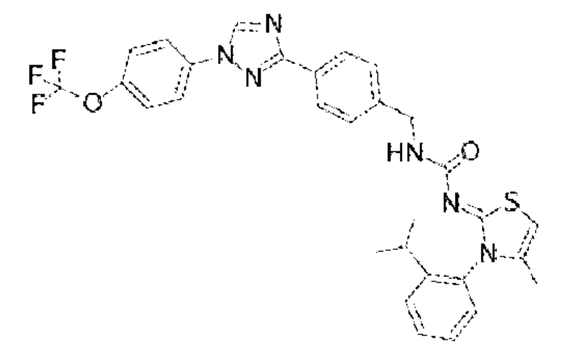
P308



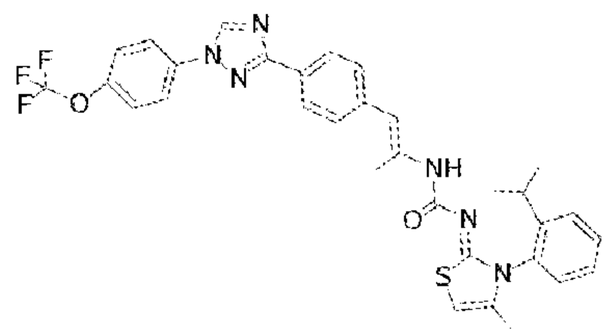
P309



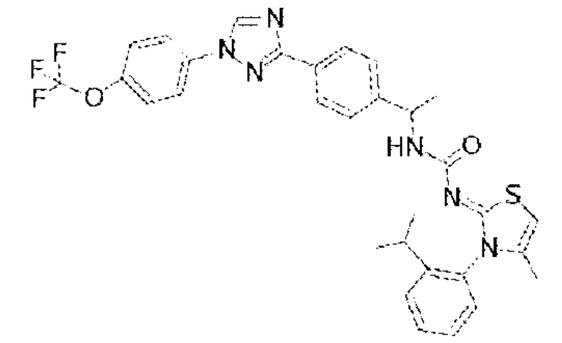
P310



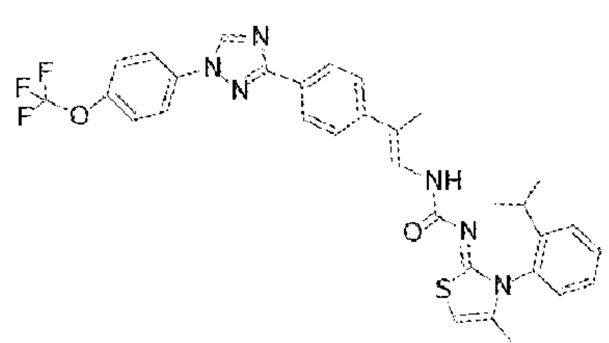
P311



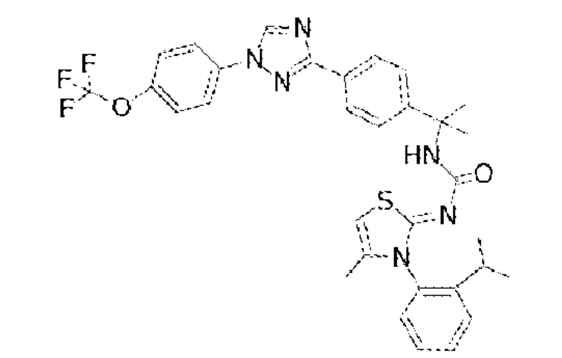
P312



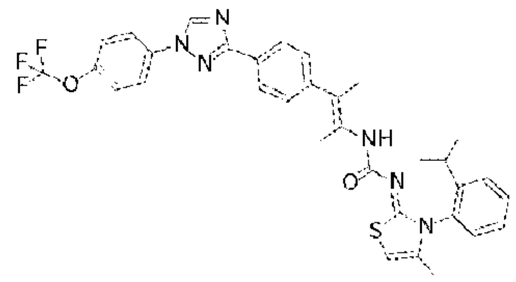
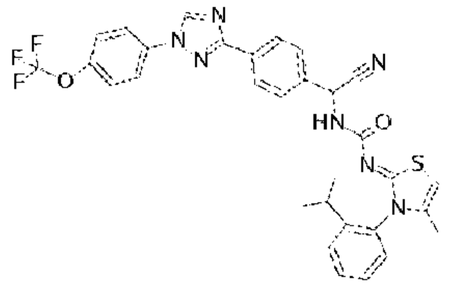
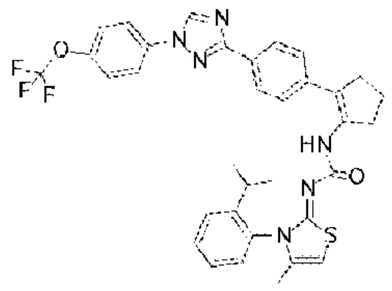
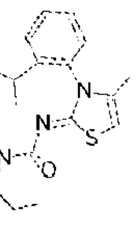
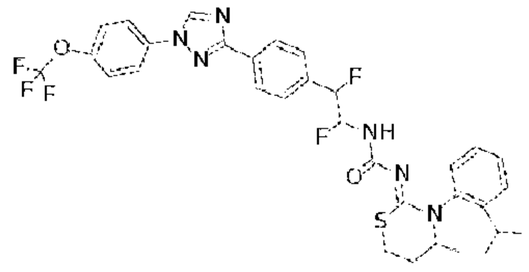
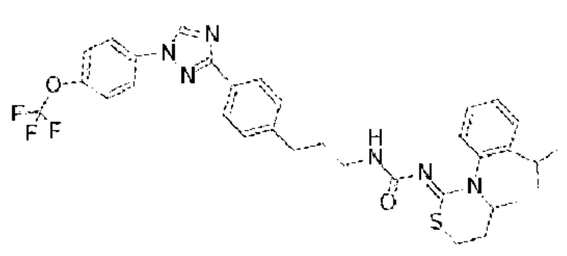
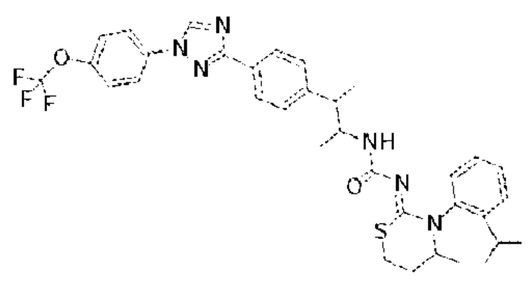
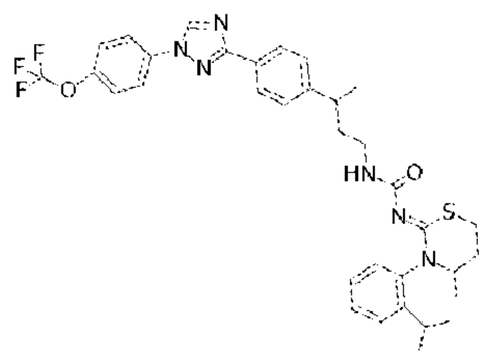
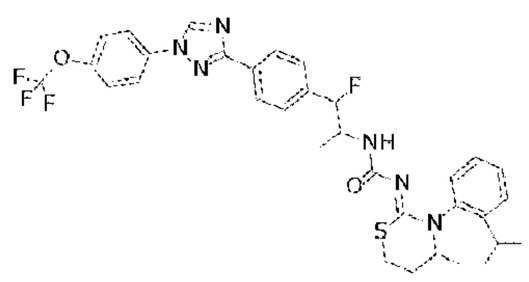
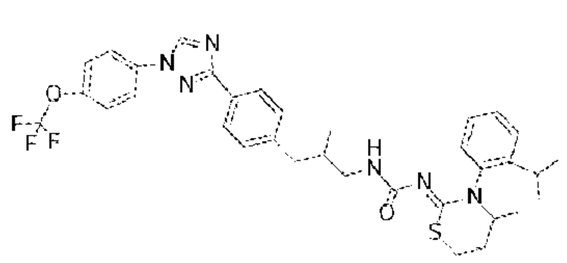
P313

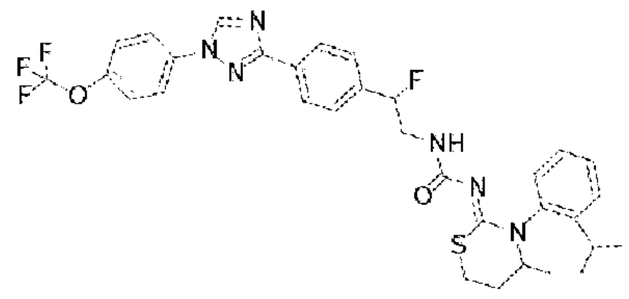
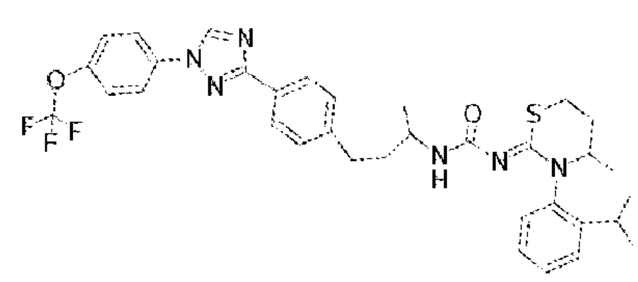
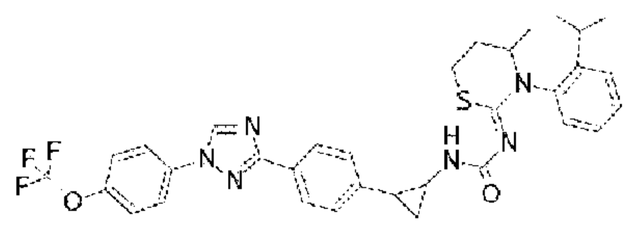
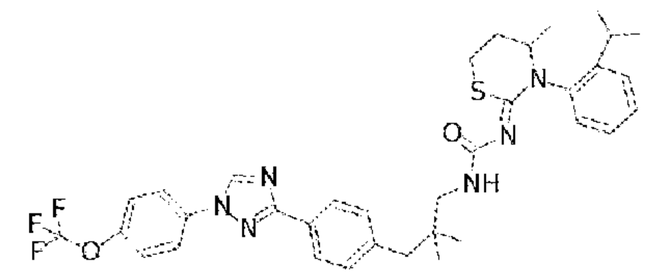
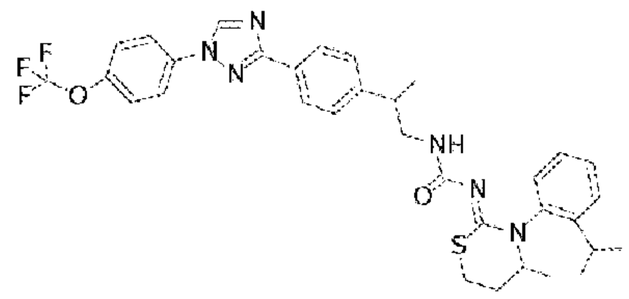
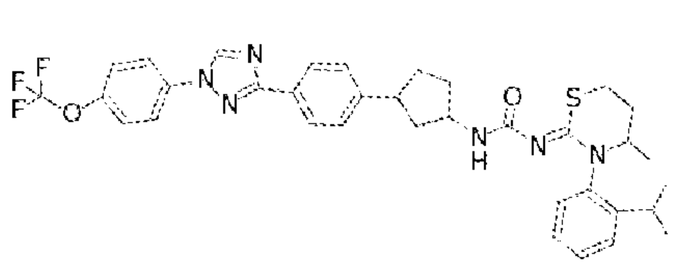
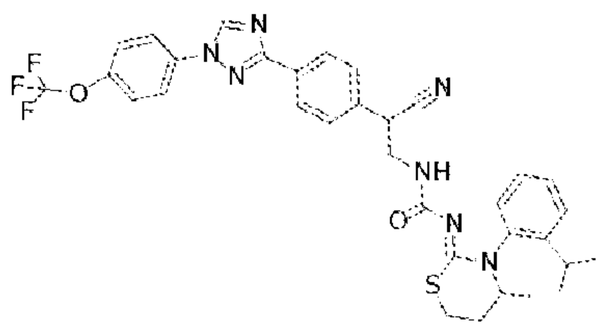
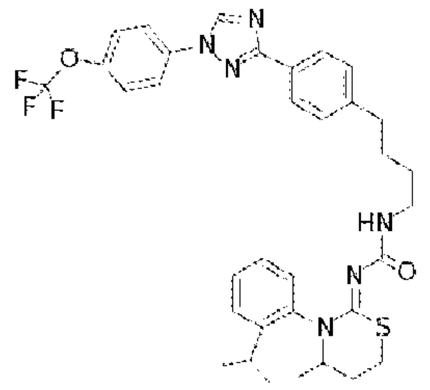
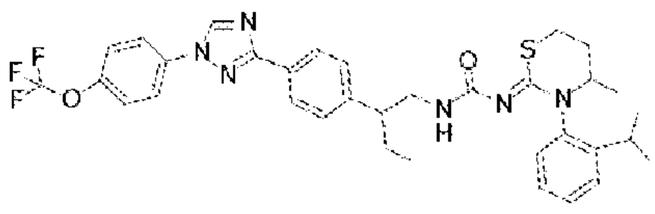
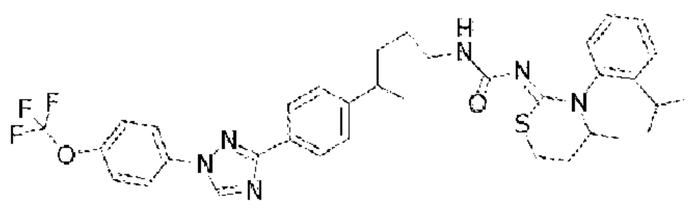


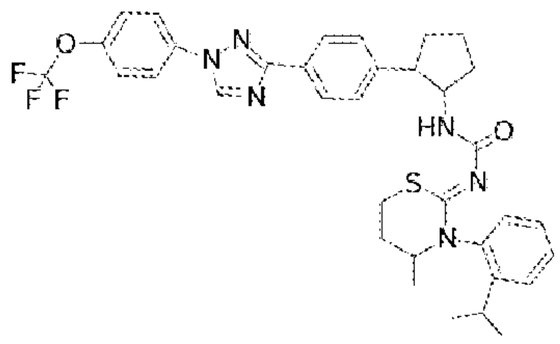
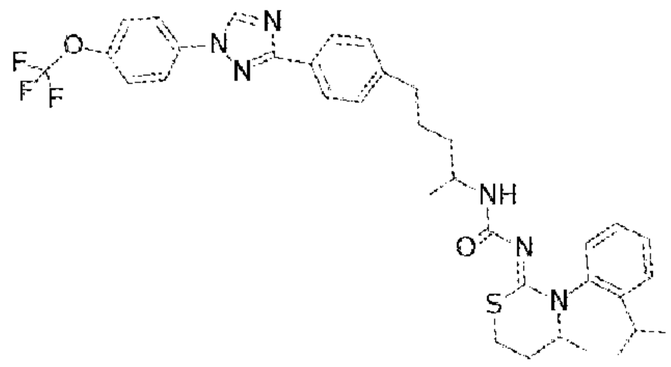
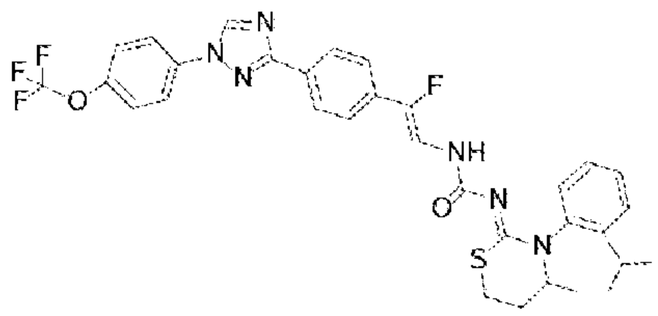
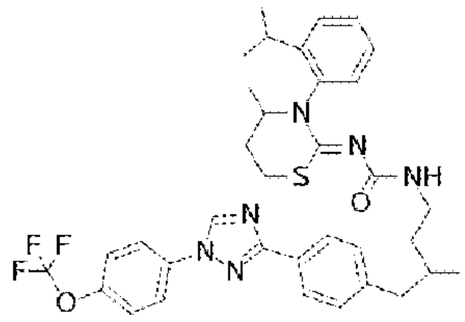
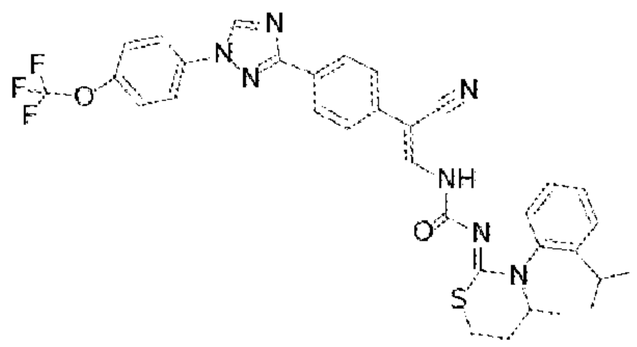
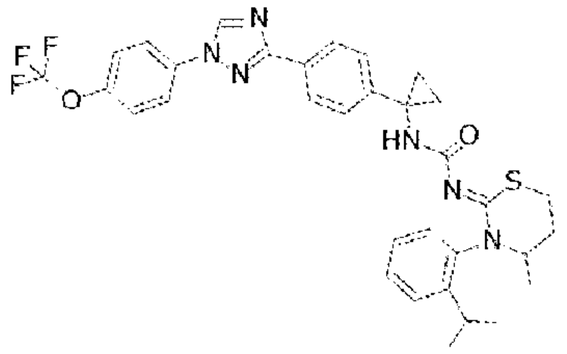
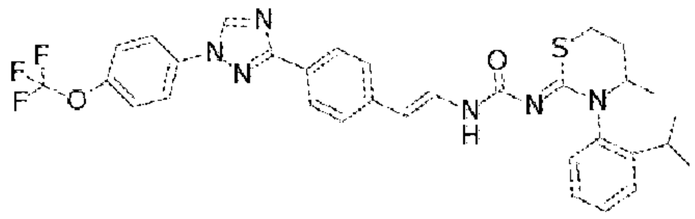
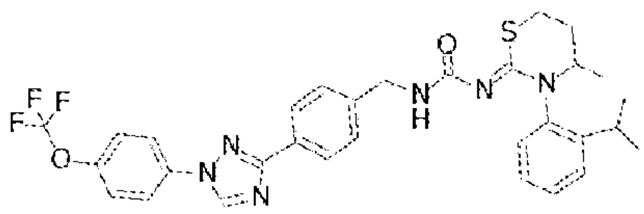
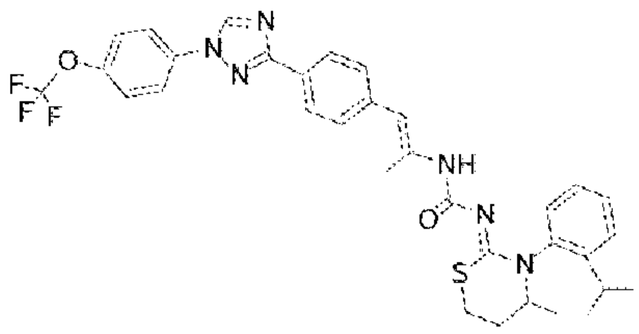
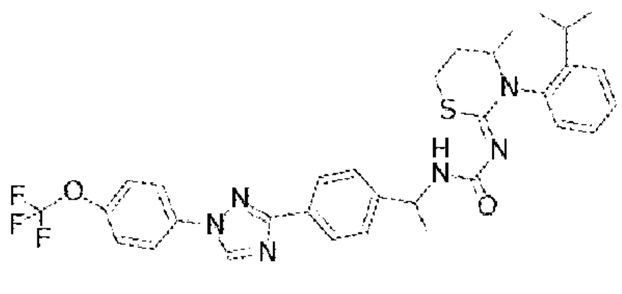
P314

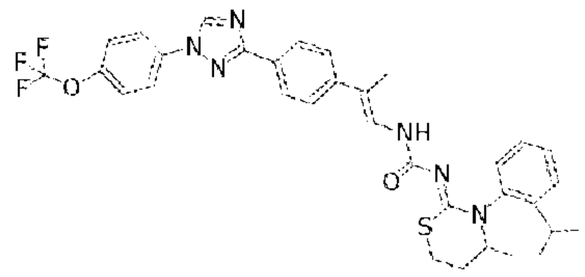


P315

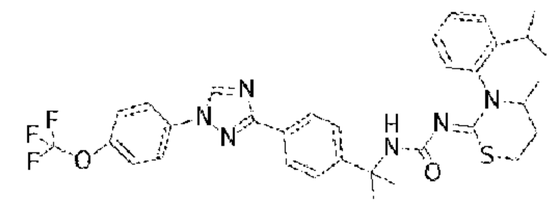
 P316	 P317
 P318	 P319
 P320	 P321
 P322	 P323
 P324	 P325

 P326	 P327
 P328	 P329
 P330	 P331
 P332	 P333
 P334	 P335

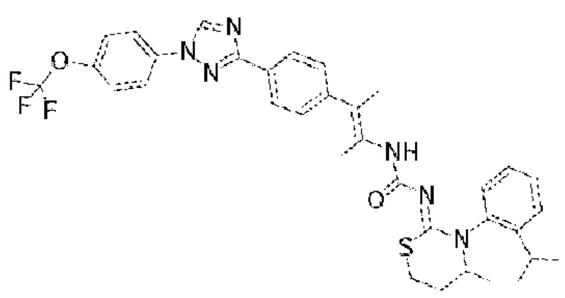
	
P336	P337
	
P338	P339
	
P340	P341
	
P342	P343
	
P344	P345



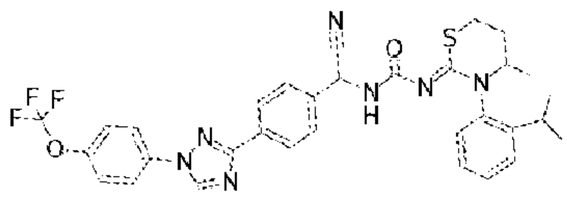
P346



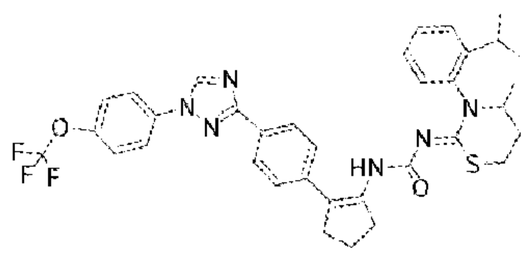
P347



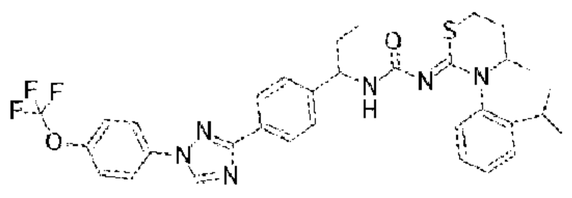
P348



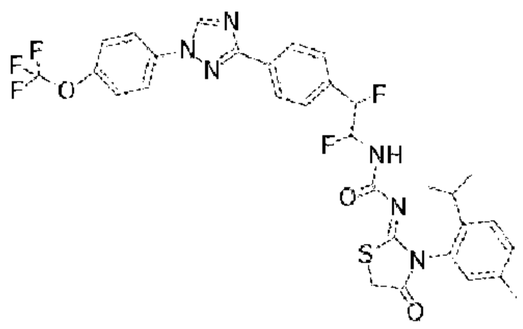
P349



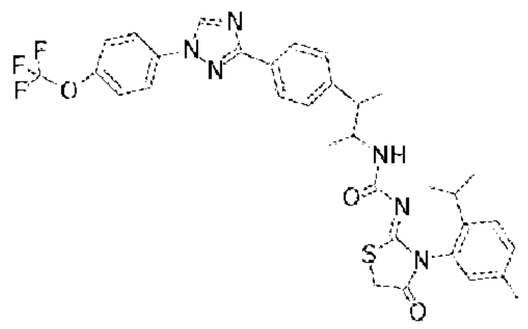
P350



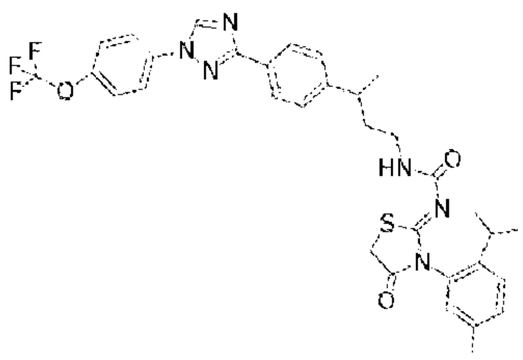
P351



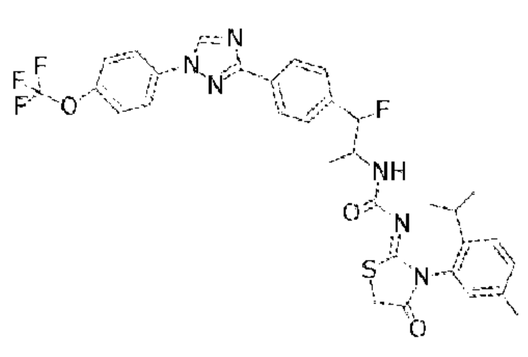
P352



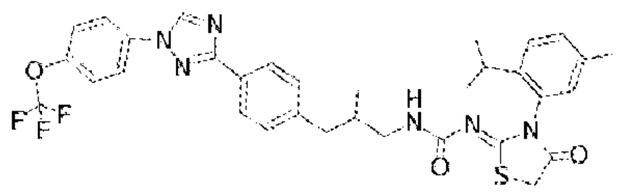
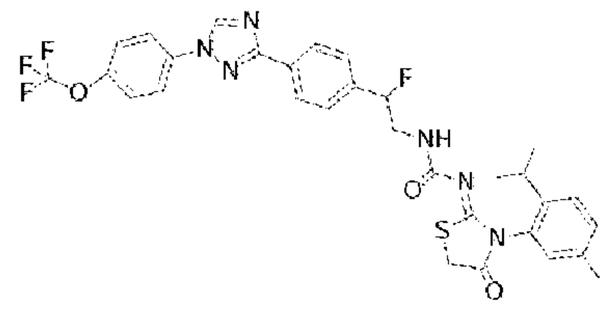
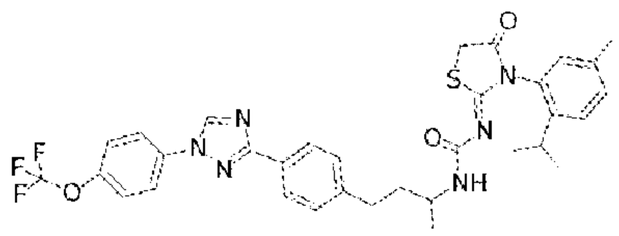
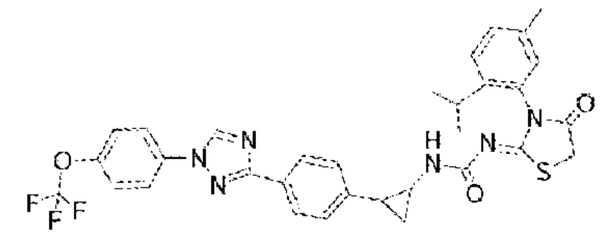
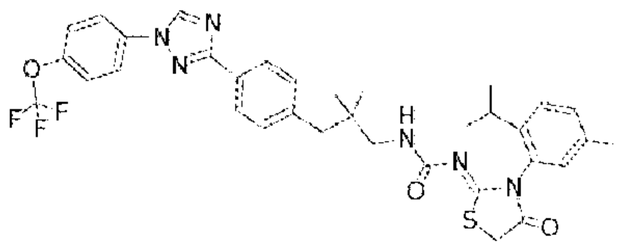
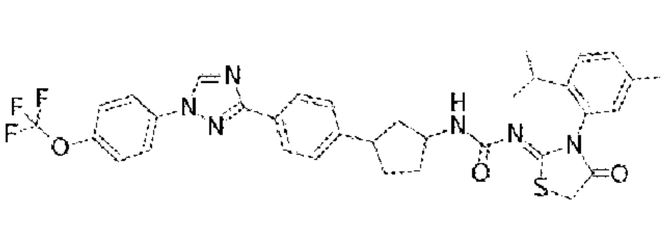
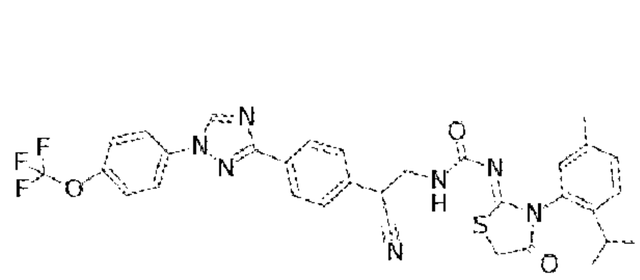
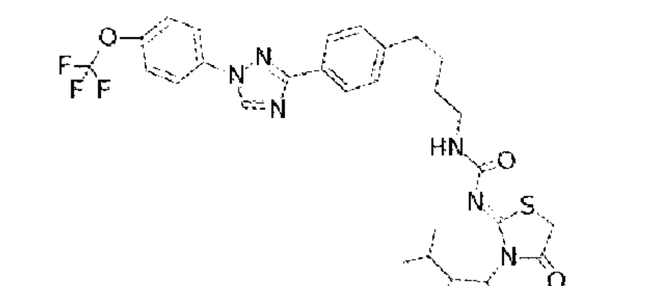
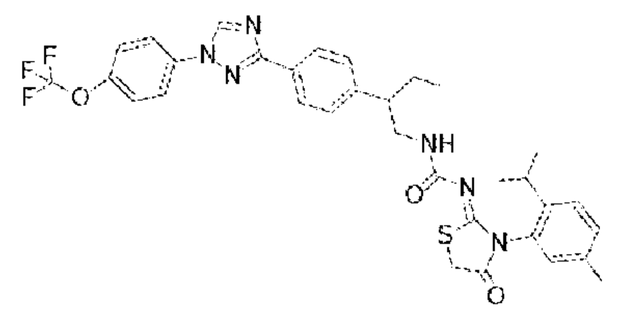
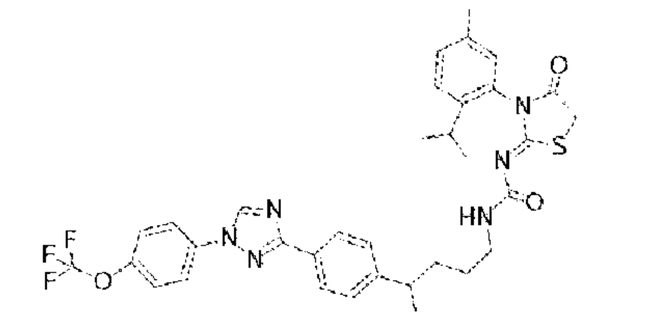
P353

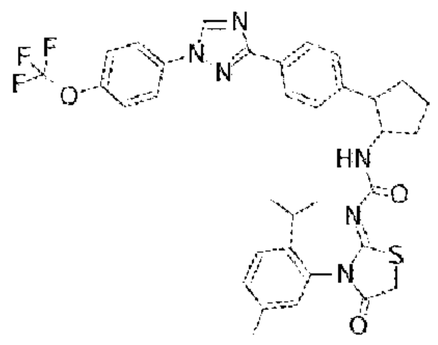
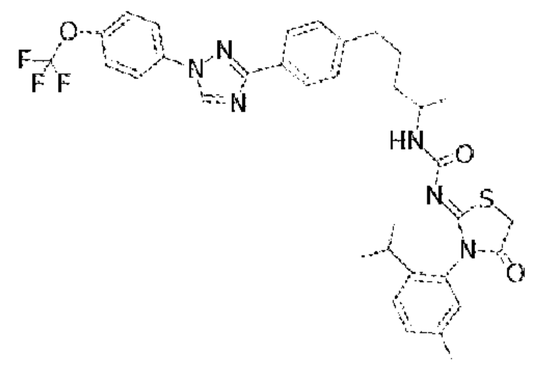
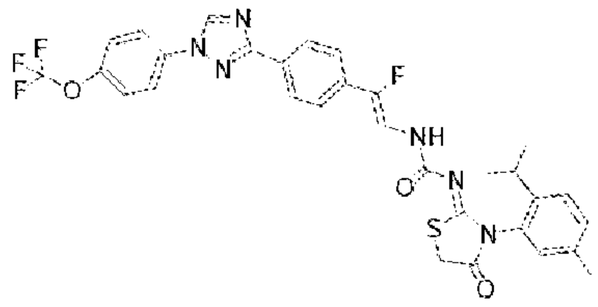
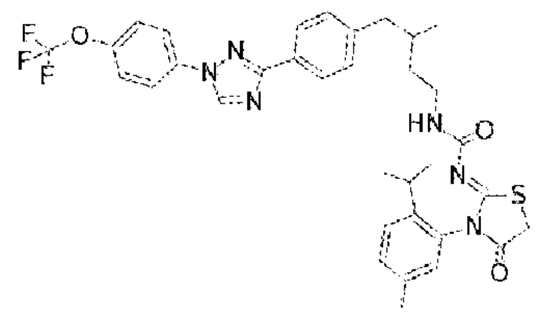
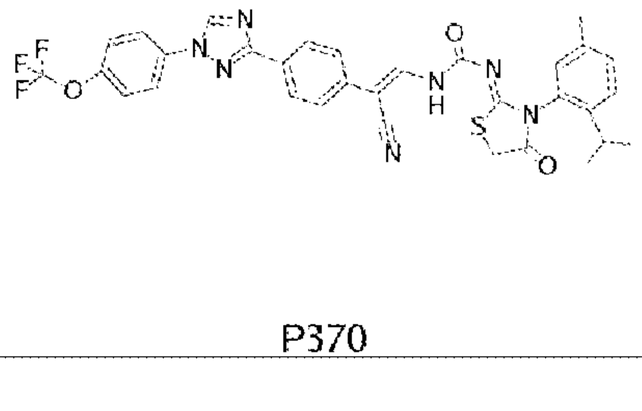
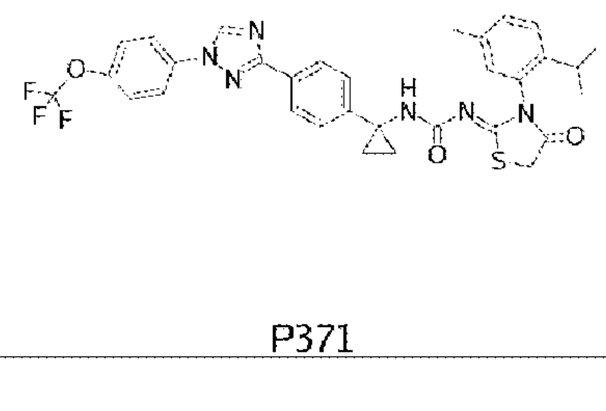
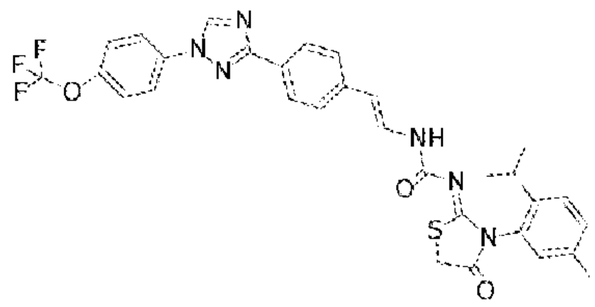
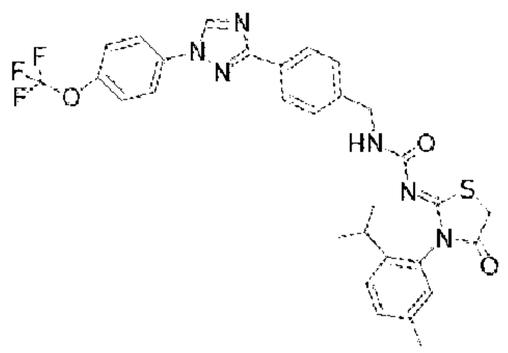
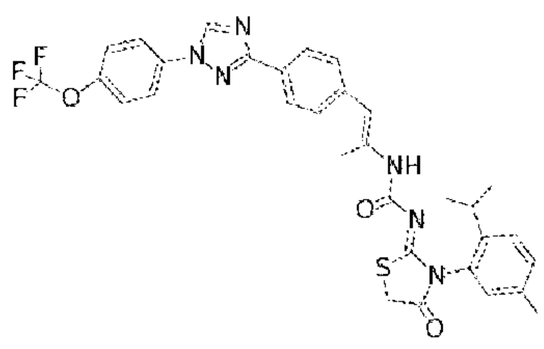
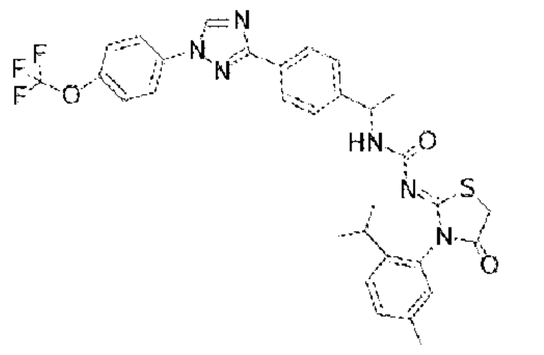


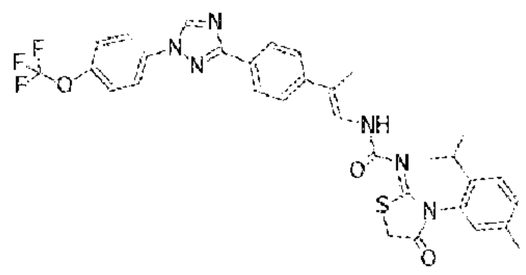
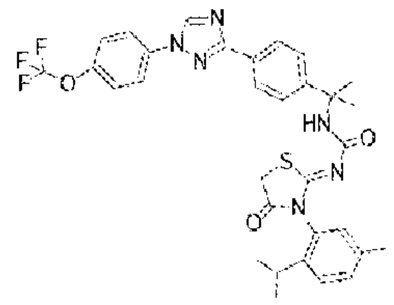
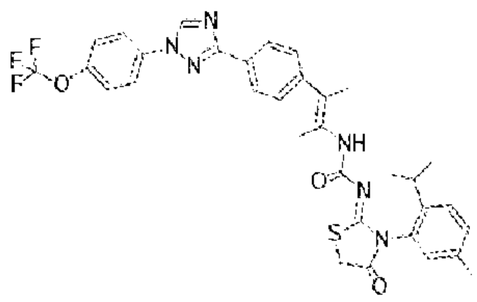
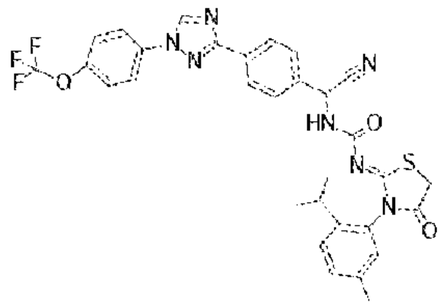
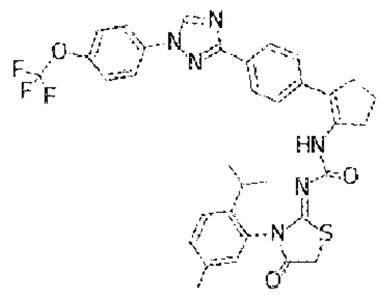
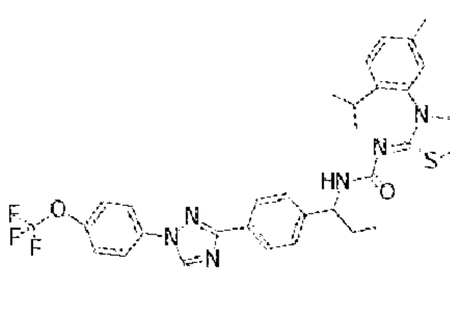
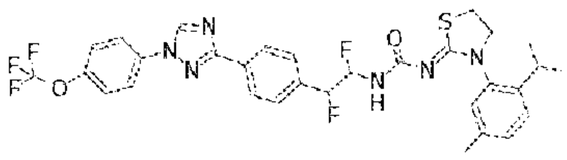
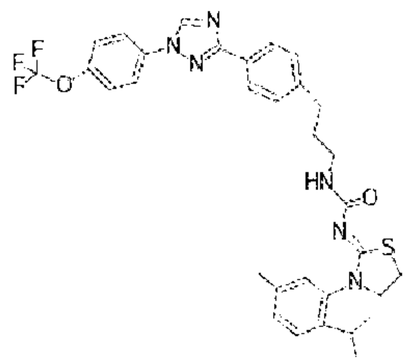
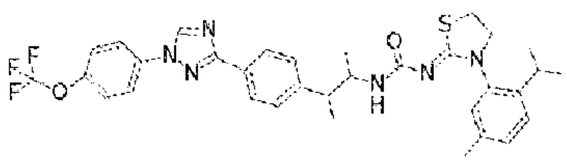
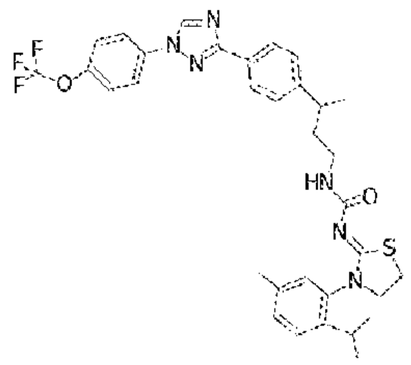
P354

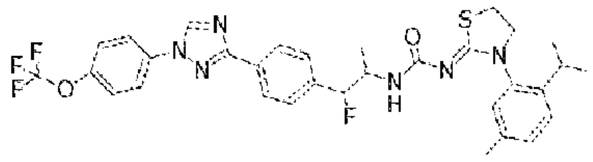
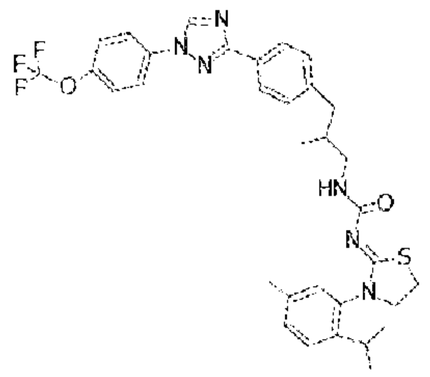
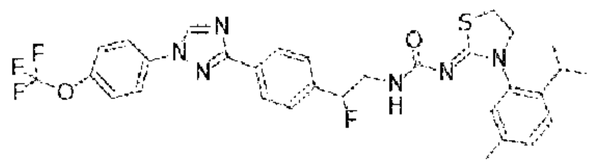
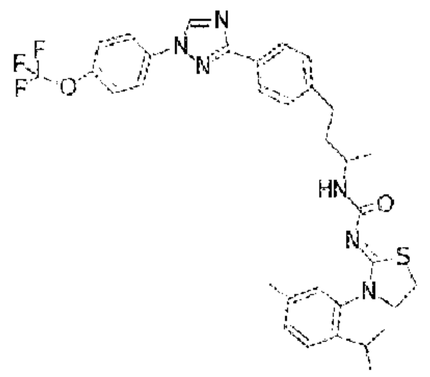
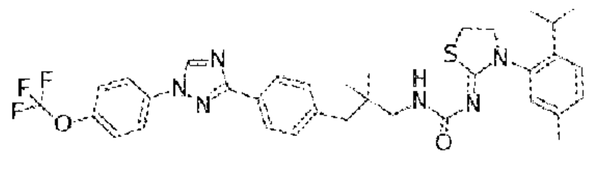
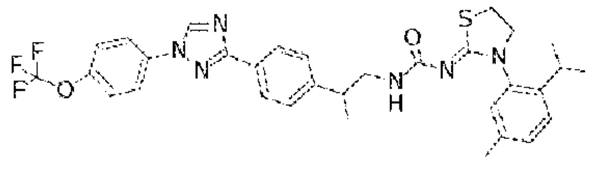
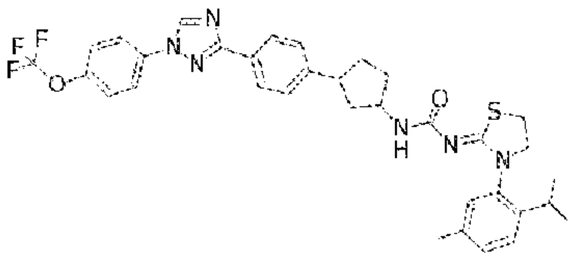
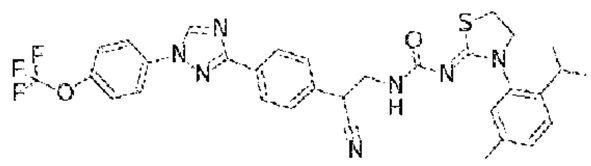
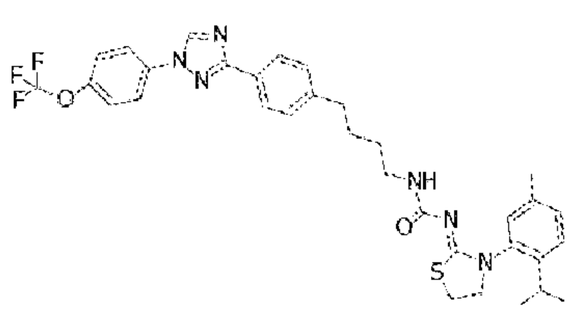
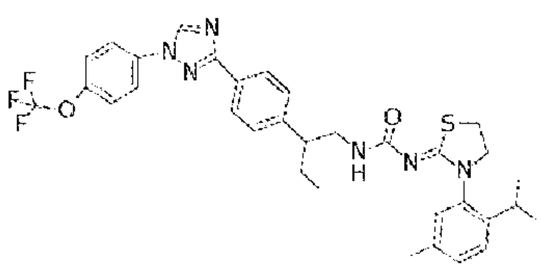


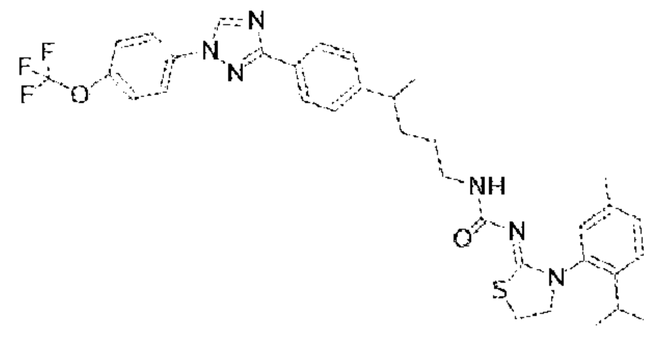
P355

 P356	 P357
 P358	 P359
 P360	 P361
 P362	 P363
 P364	 P365

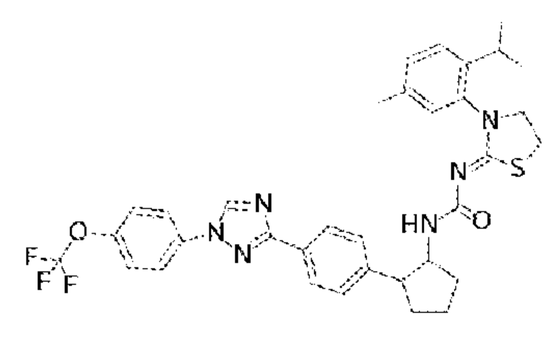
 P366	 P367
 P368	 P369
 P370	 P371
 P372	 P373
 P374	 P375

 P376	 P377
 P378	 P379
 P380	 P381
 P382	 P383
 P384	 P385

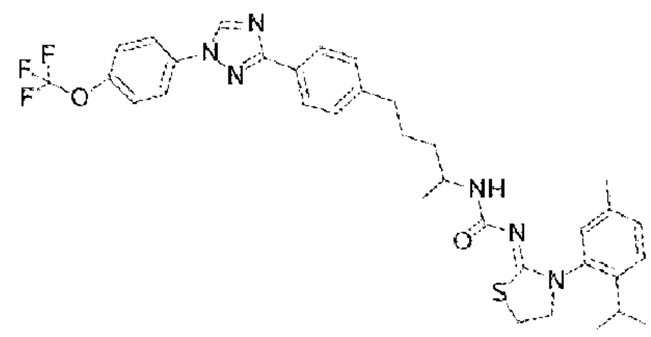
 P386	 P387
 P388	 P389
 P390	 P391
 P392	 P393
 P394	 P395



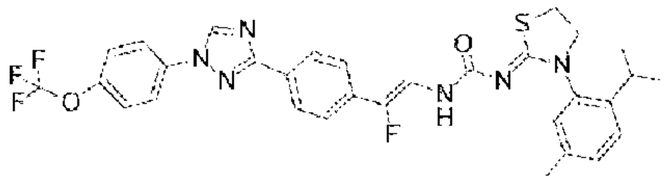
P396



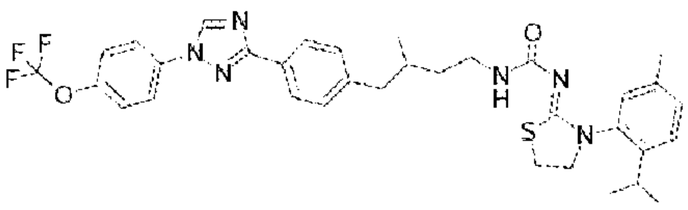
P397



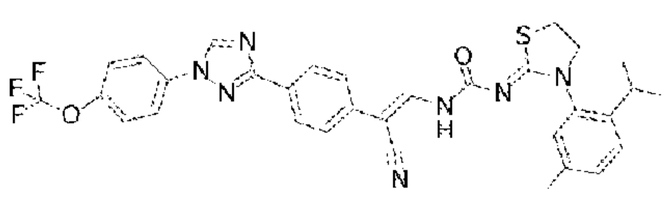
P398



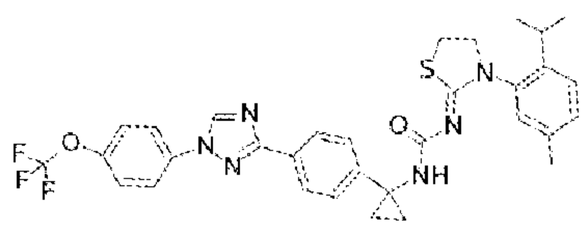
P399



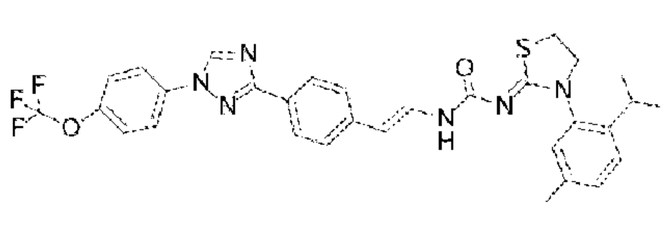
P400



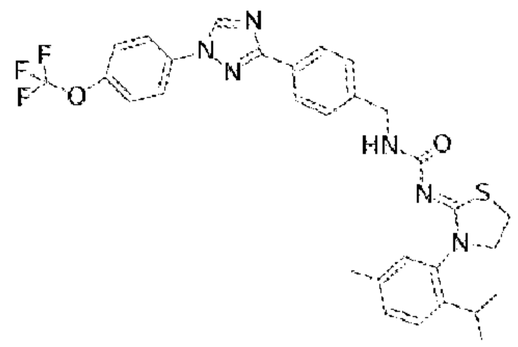
P401



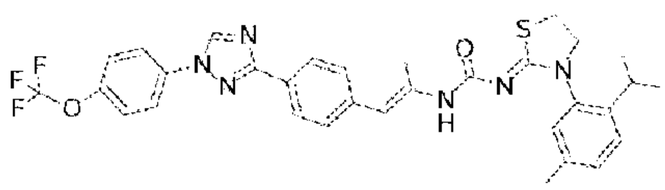
P402



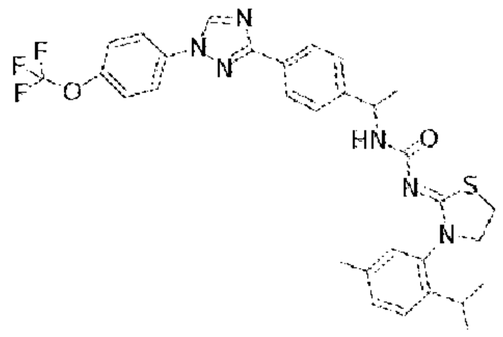
P403



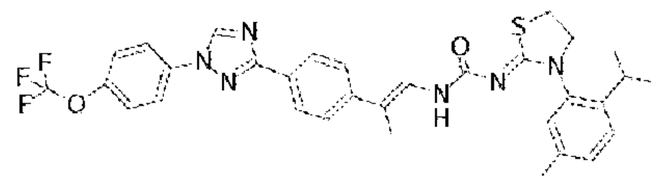
P404



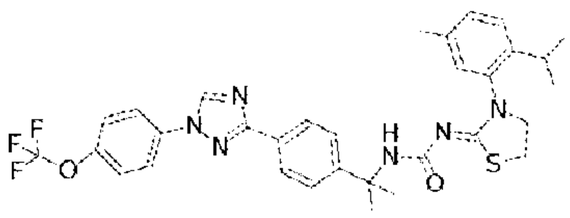
P405



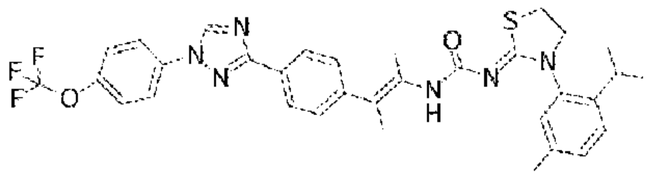
P406



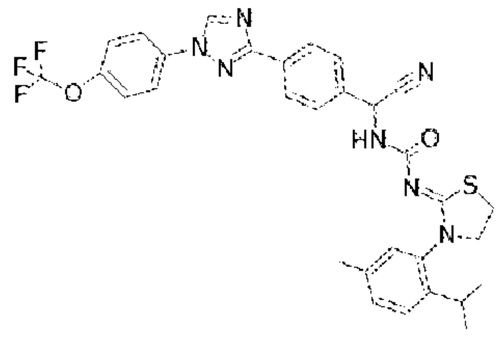
P407



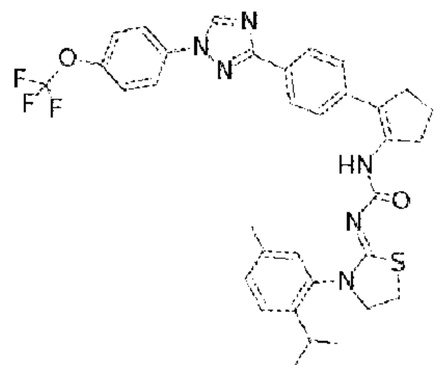
P408



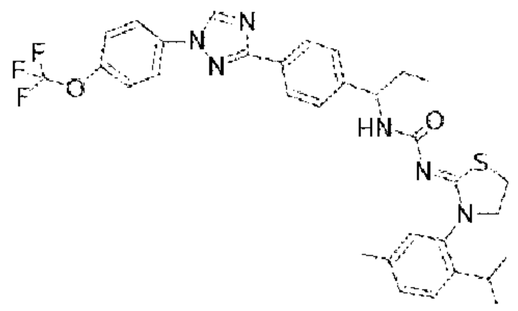
P409



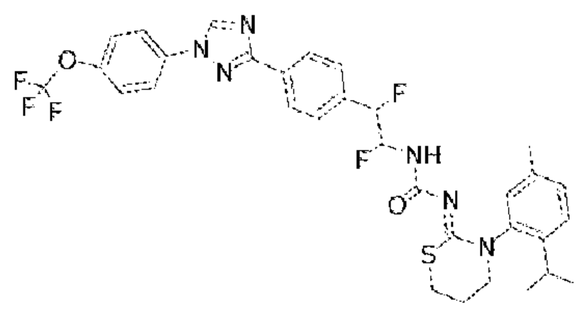
P410



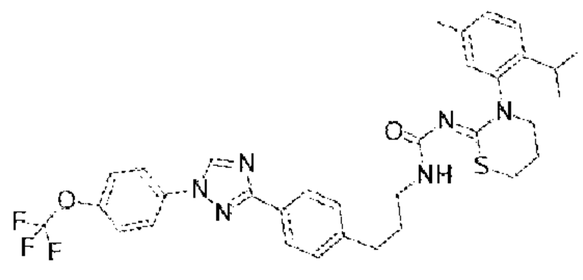
P411



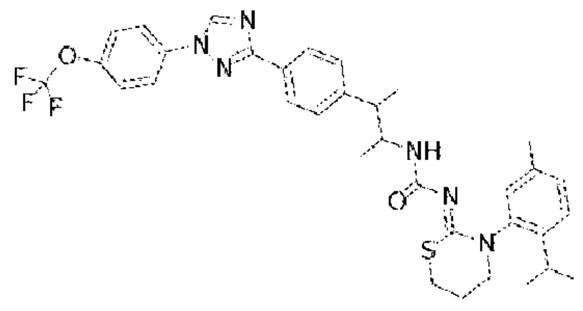
P412



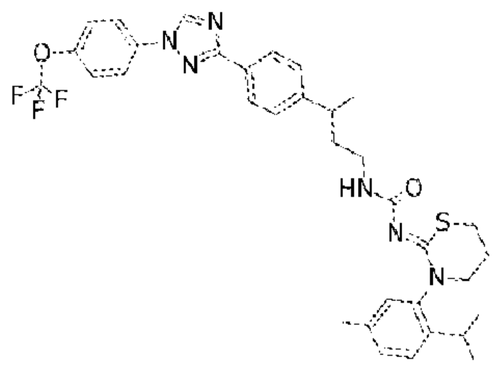
P413



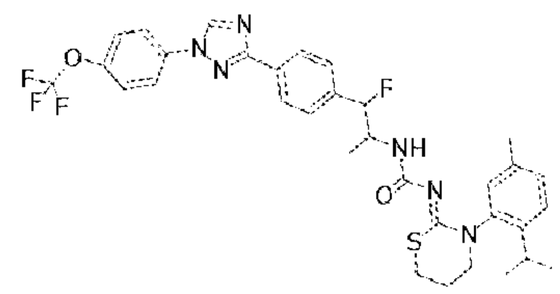
P414



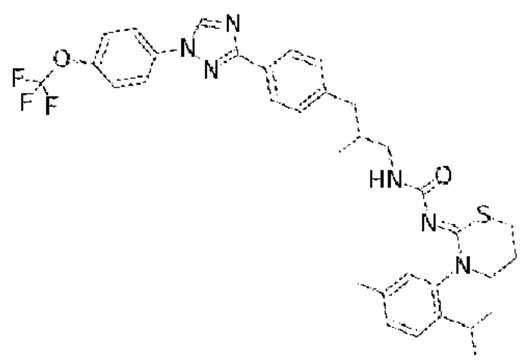
P415



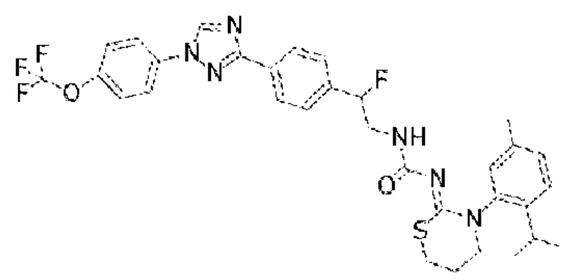
P416



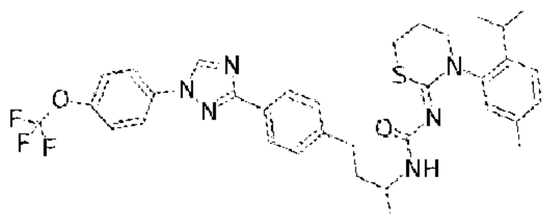
P417



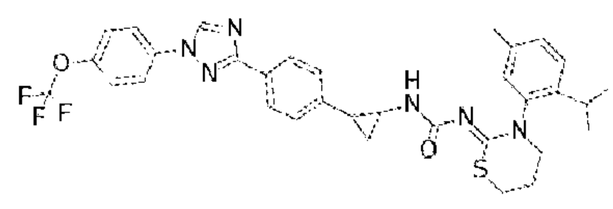
P418



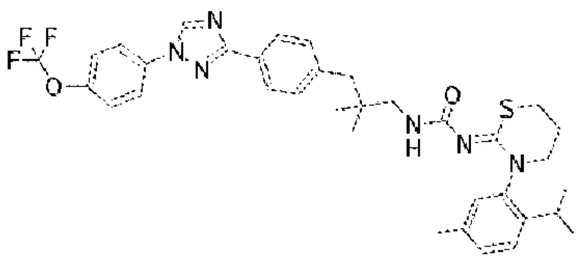
P419



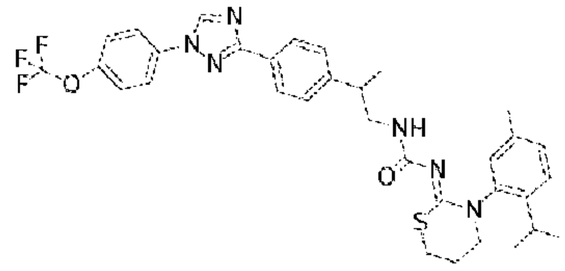
P420



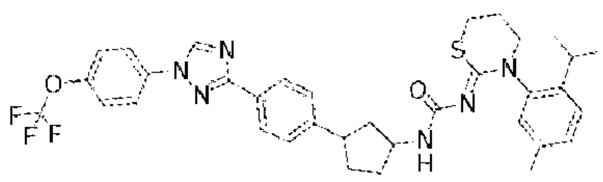
P421



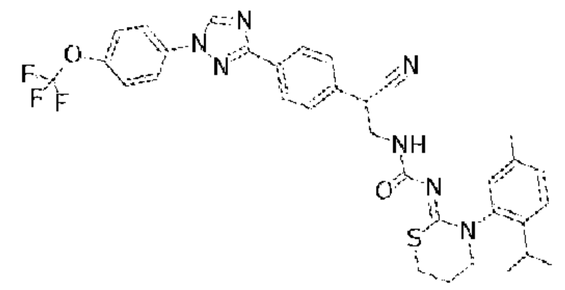
P422



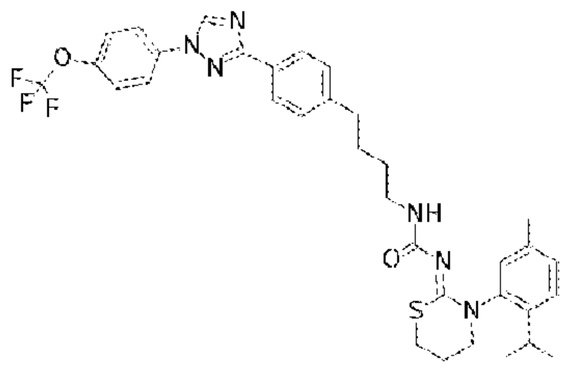
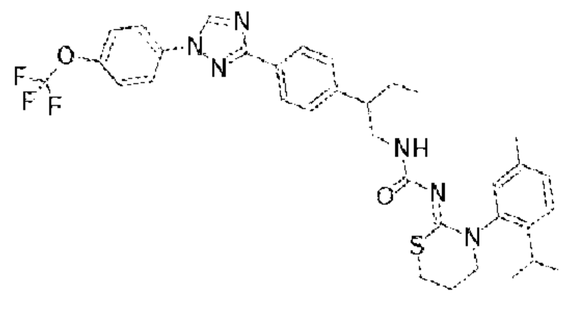
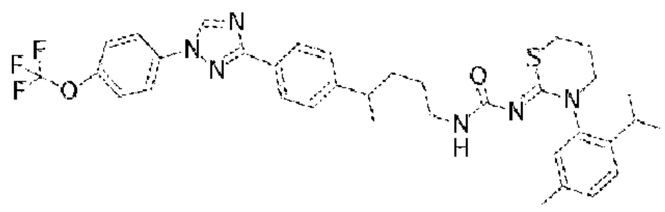
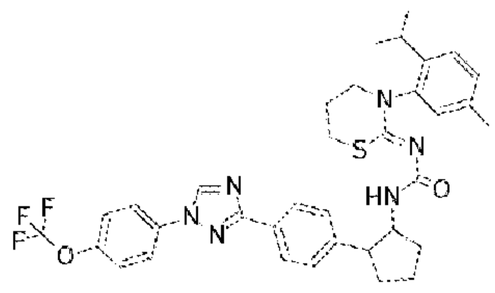
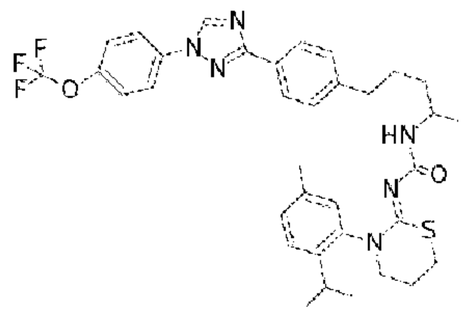
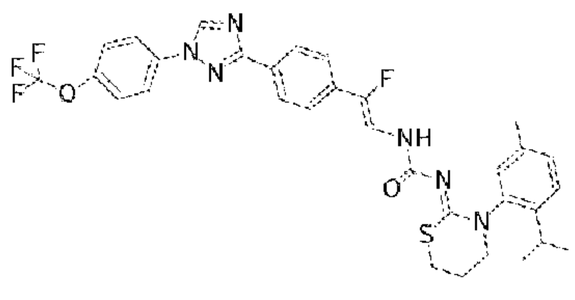
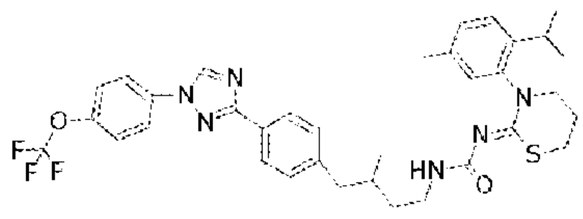
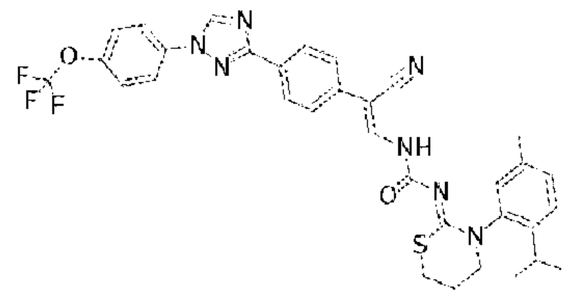
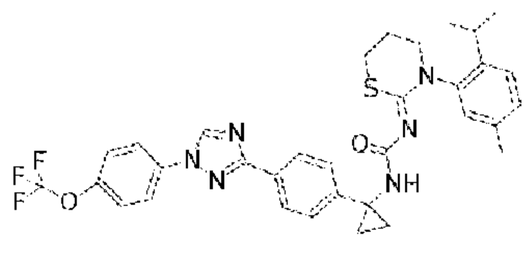
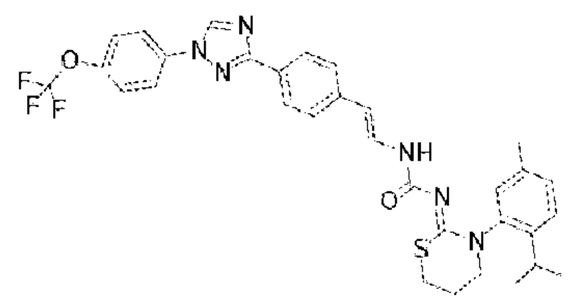
P423

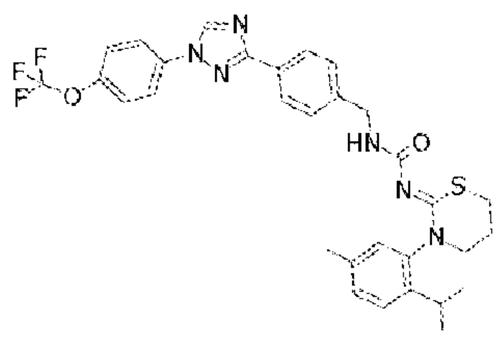


P424

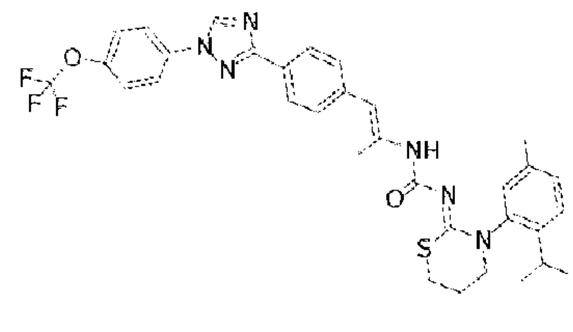


P425

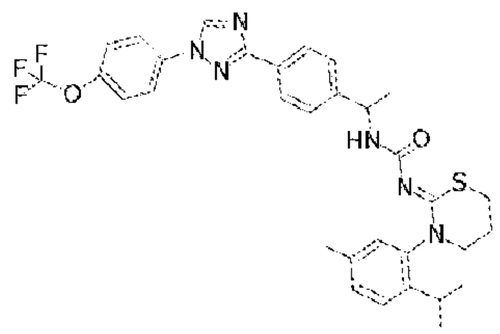
 P426	 P427
 P428	 P429
 P430	 P431
 P432	 P433
 P434	 P435



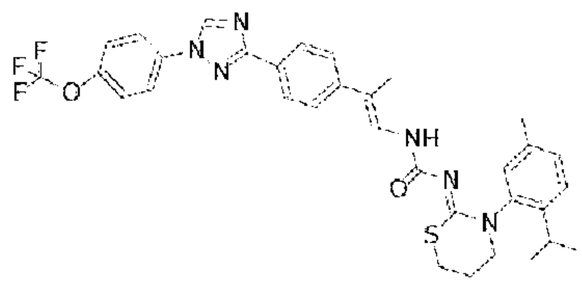
P436



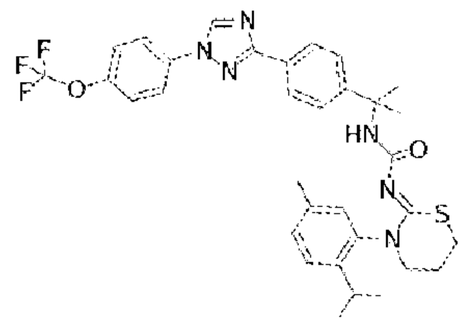
P437



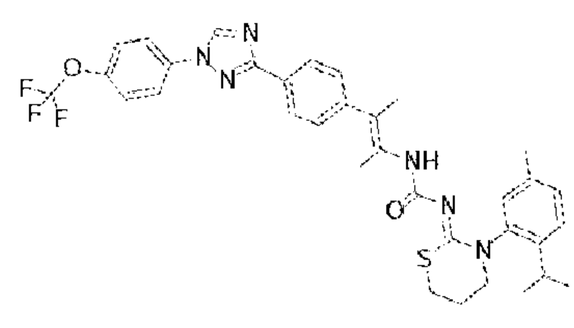
P438



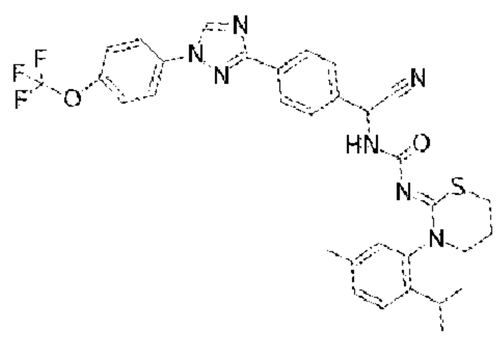
P439



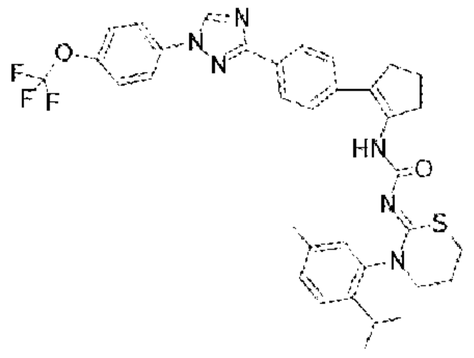
P440



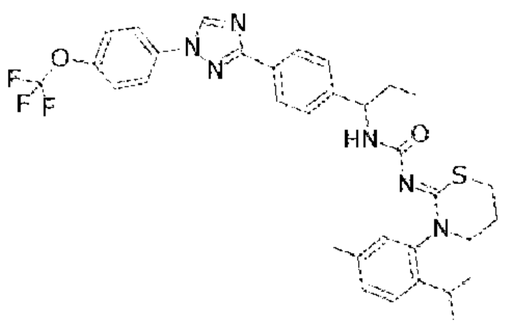
P441



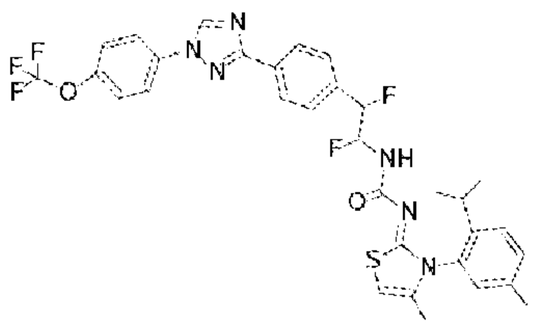
P442



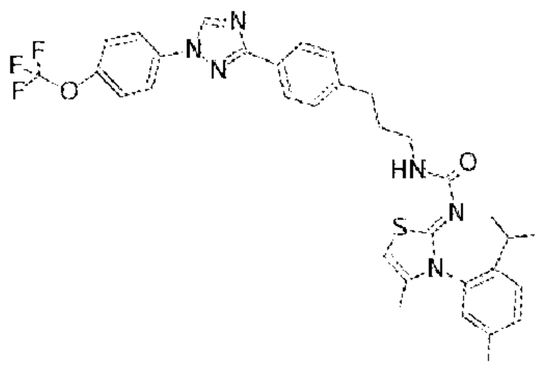
P443



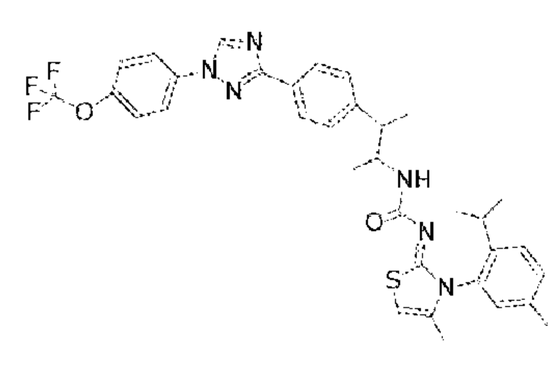
P444



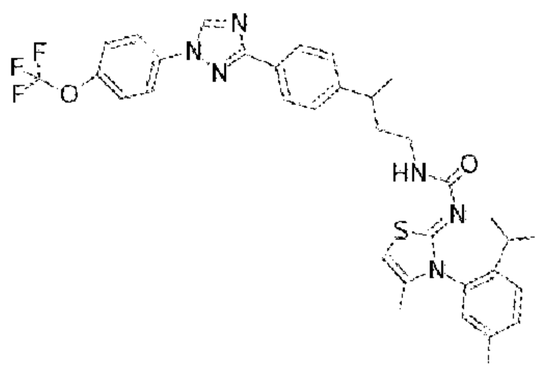
P445



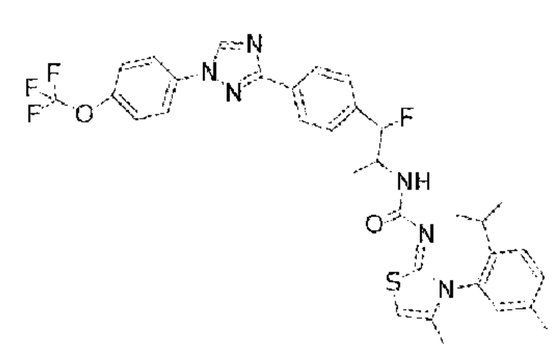
P446



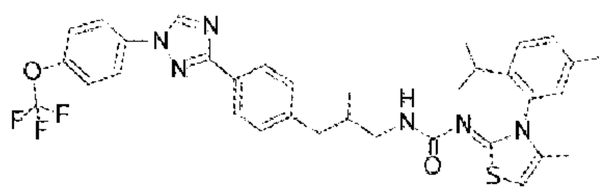
P447



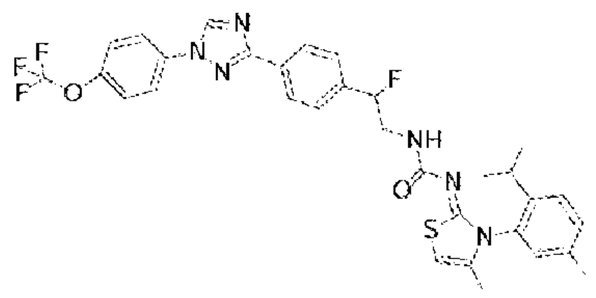
P448



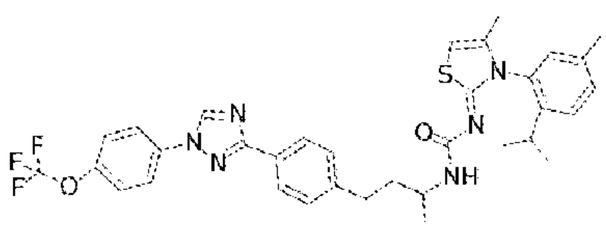
P449



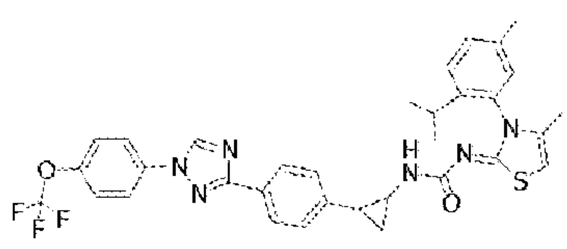
P450



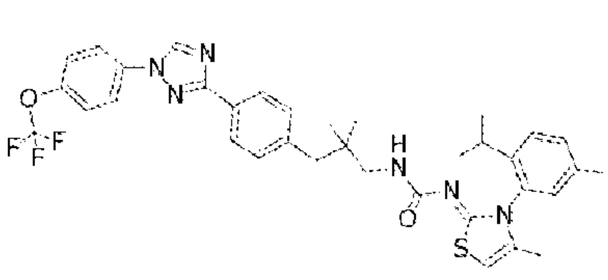
P451



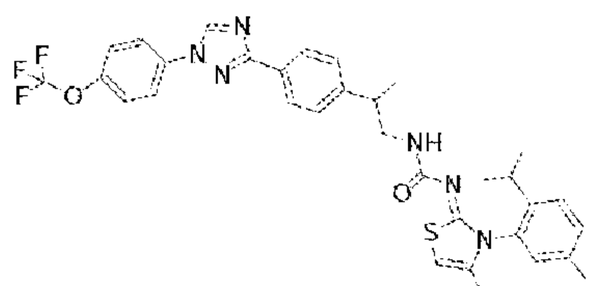
P452



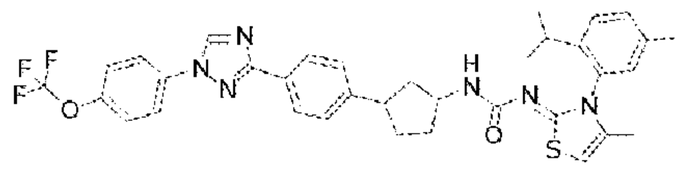
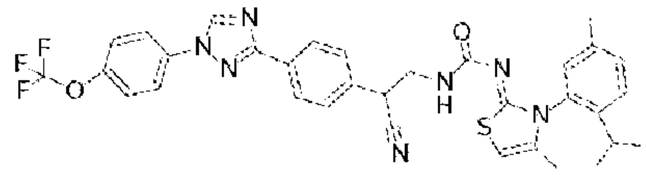
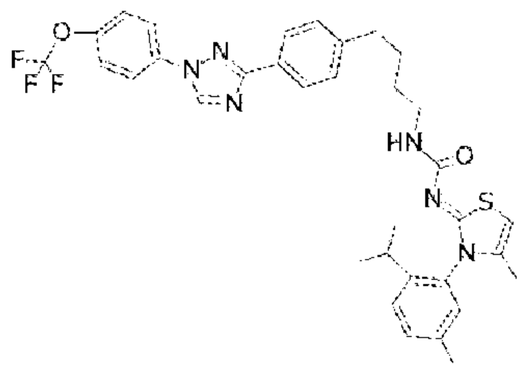
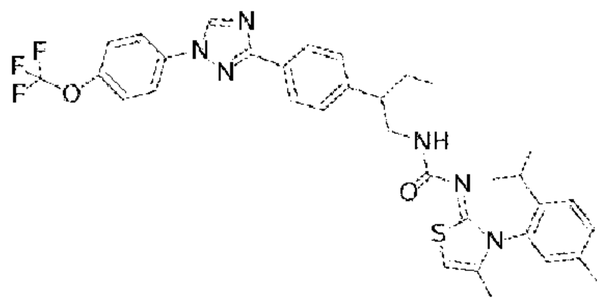
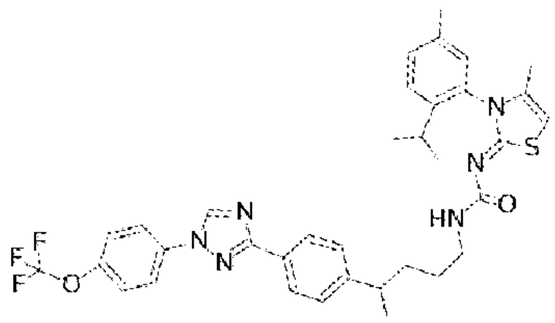
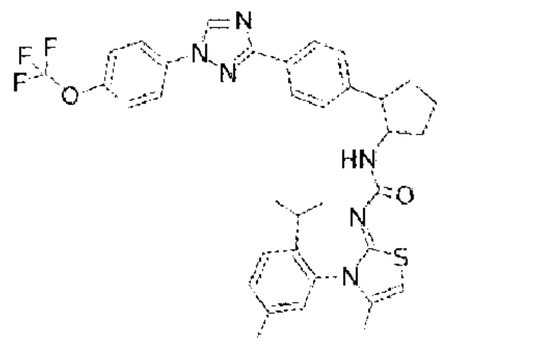
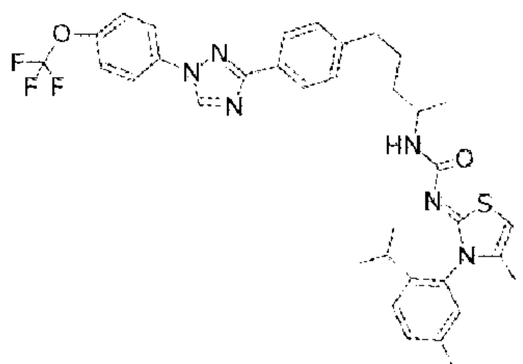
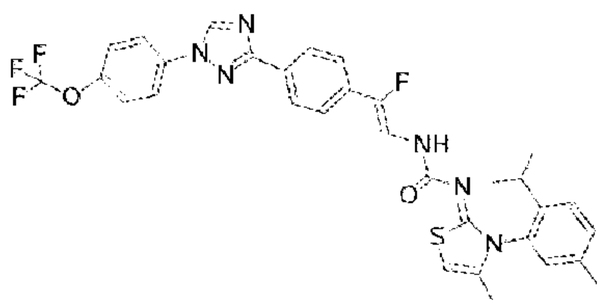
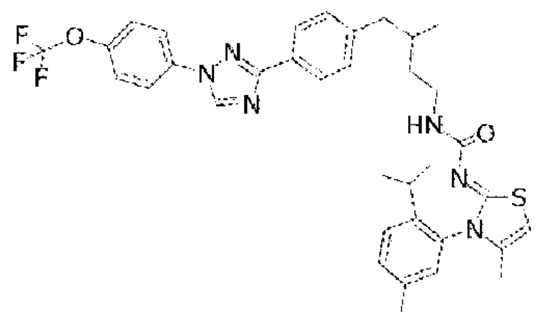
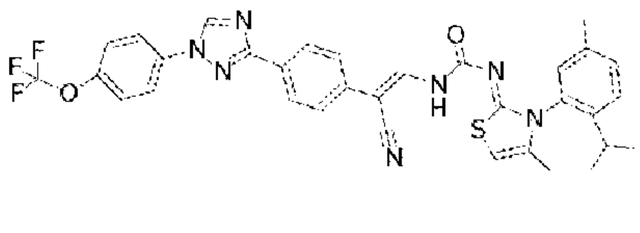
P453

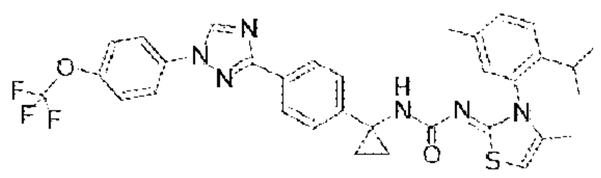
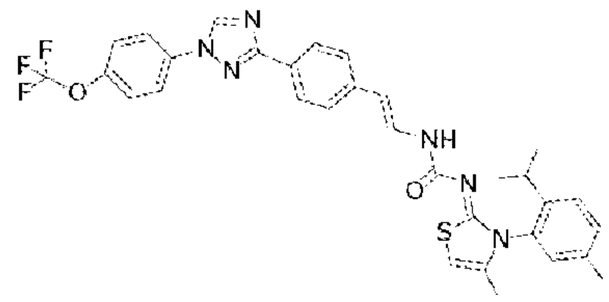
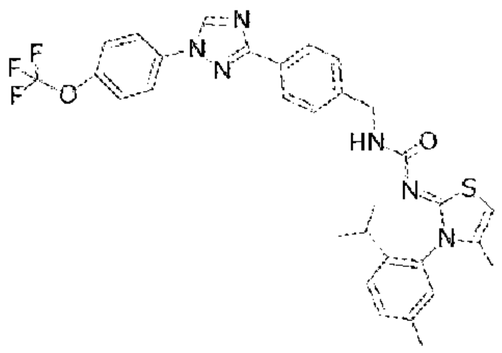
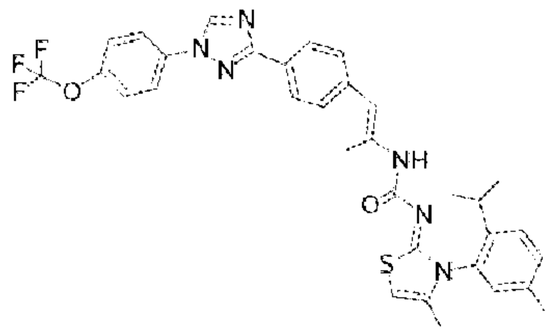
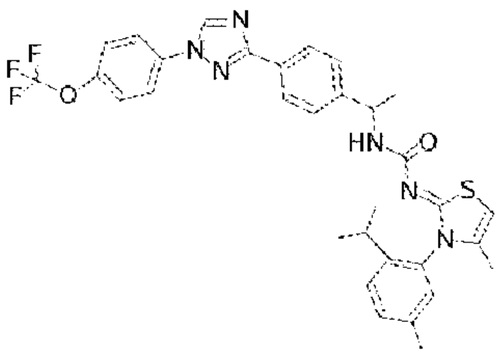
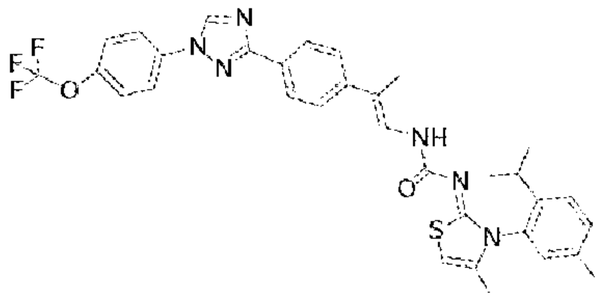
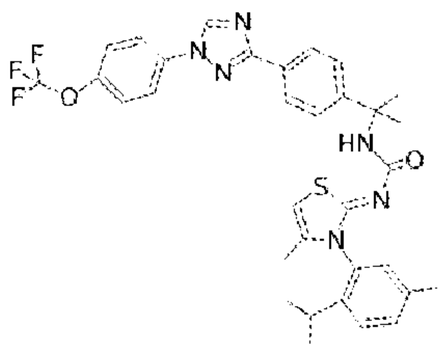
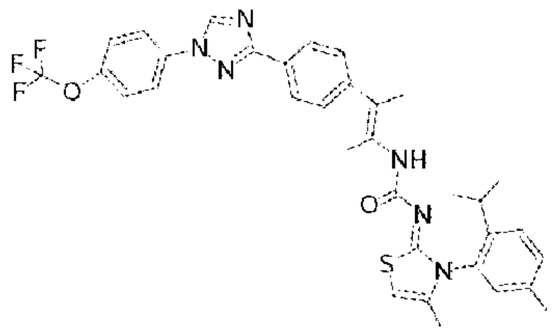
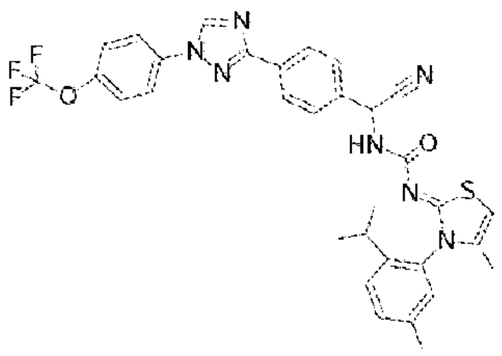
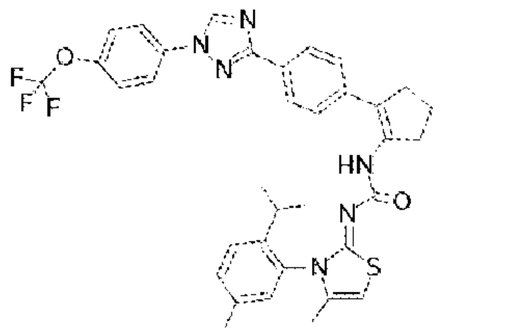


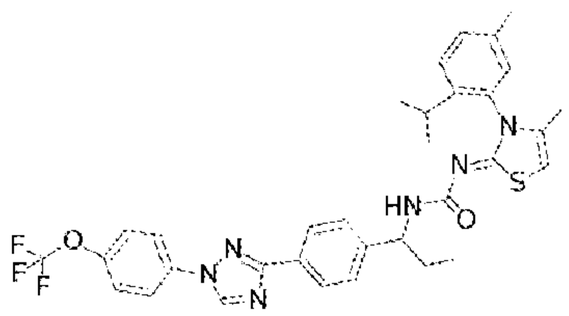
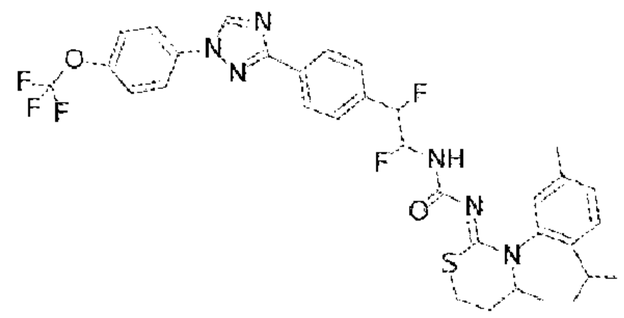
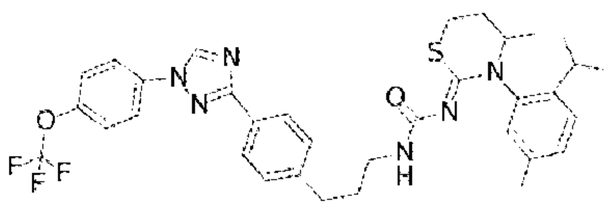
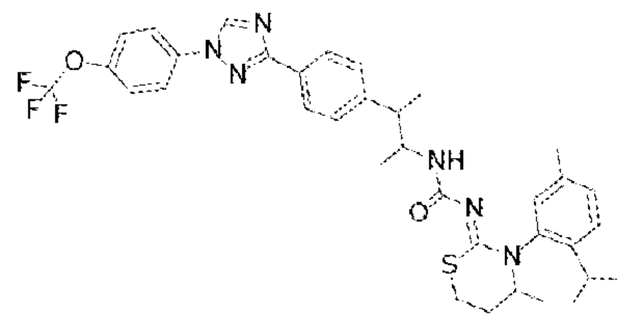
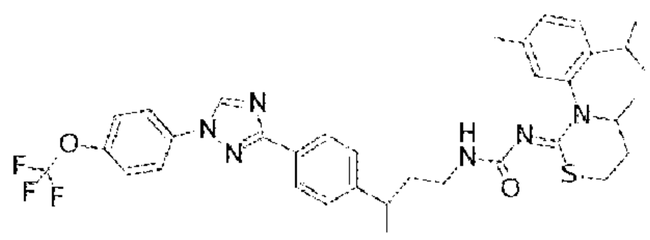
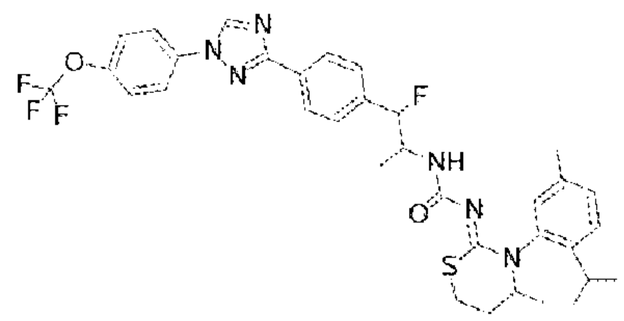
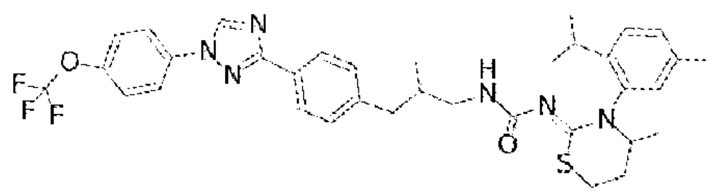
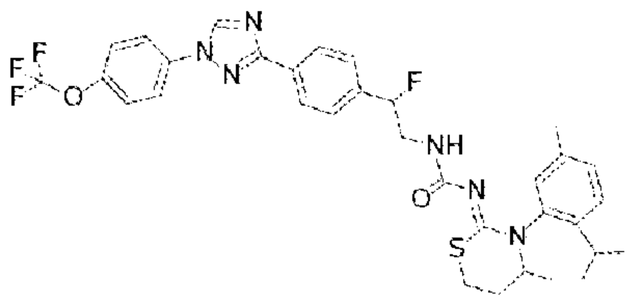
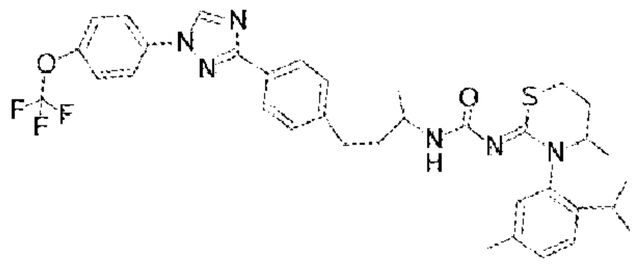
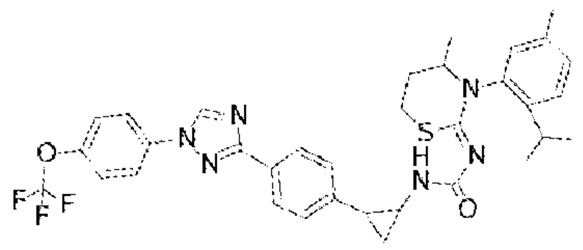
P454

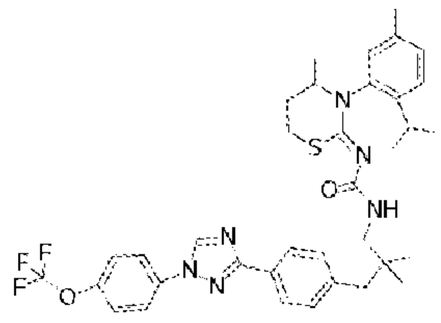
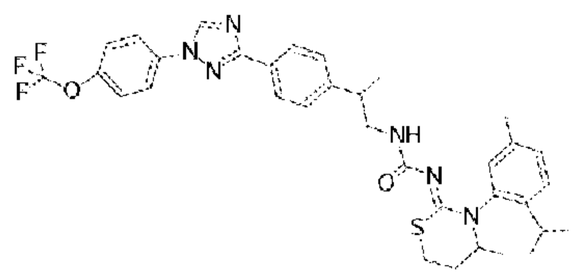
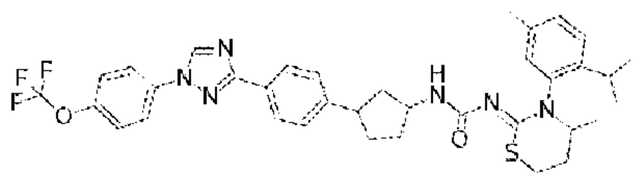
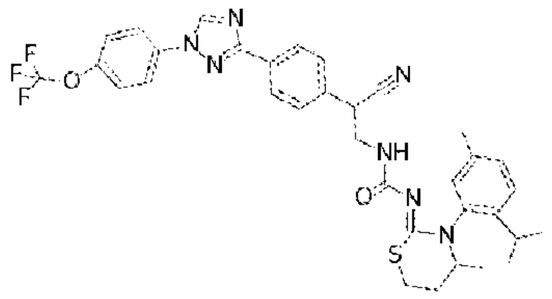
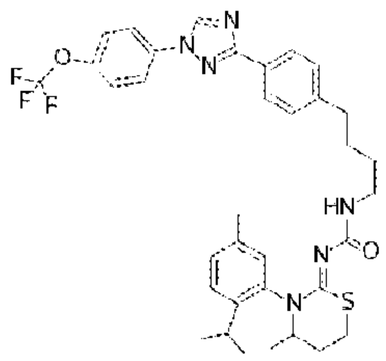
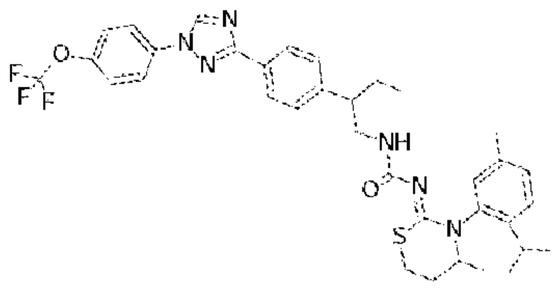
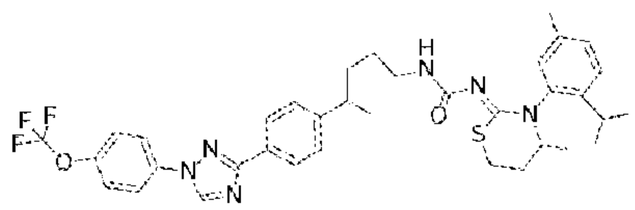
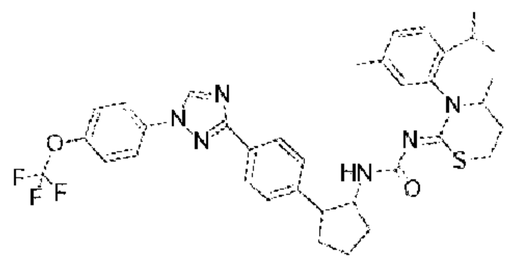
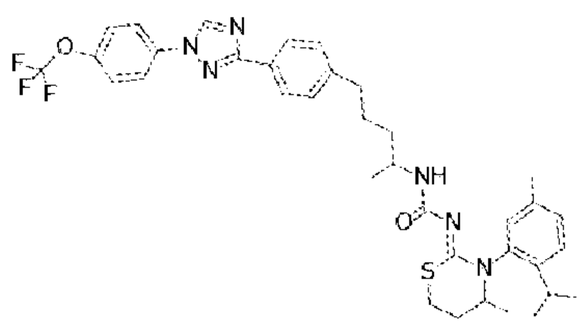
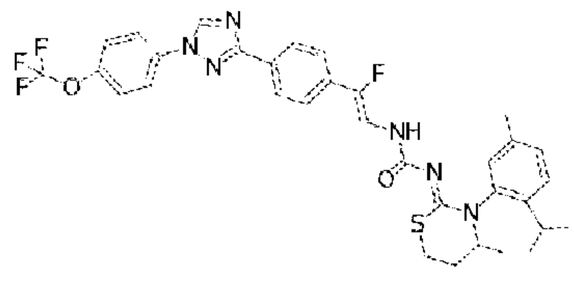


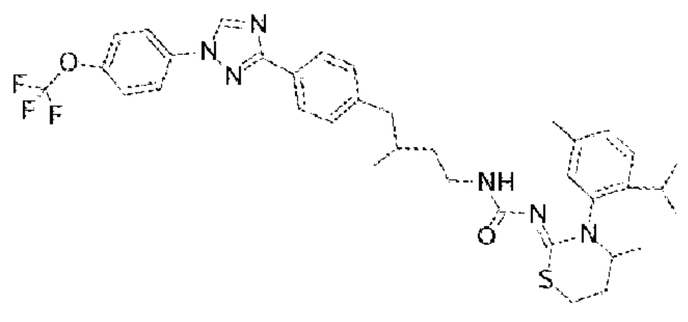
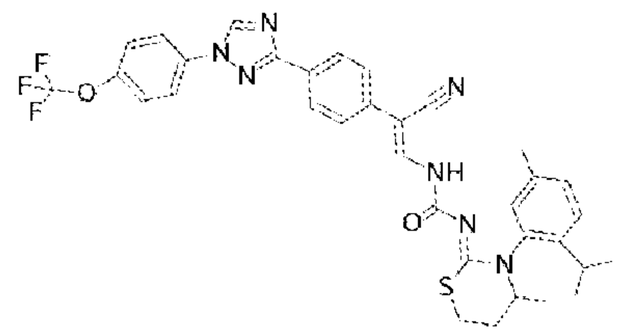
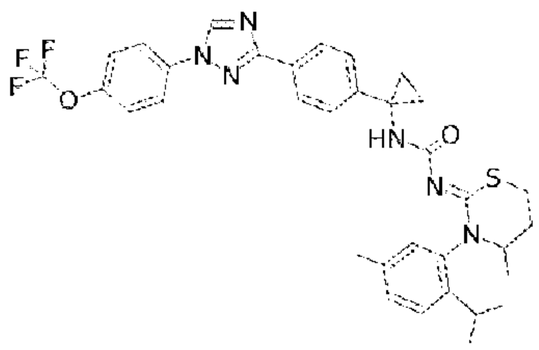
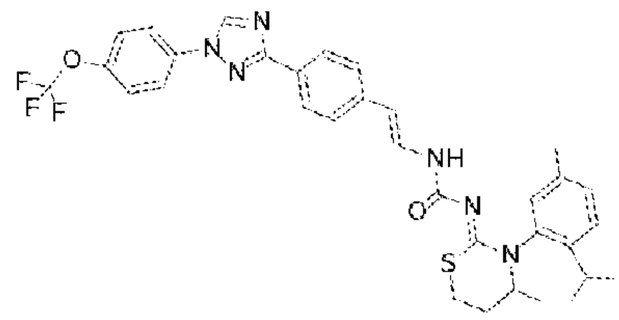
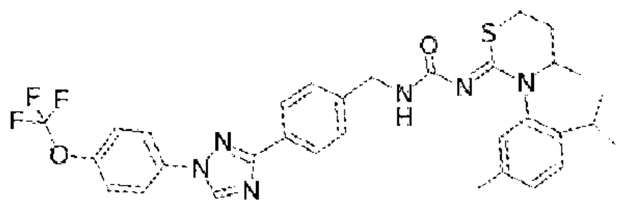
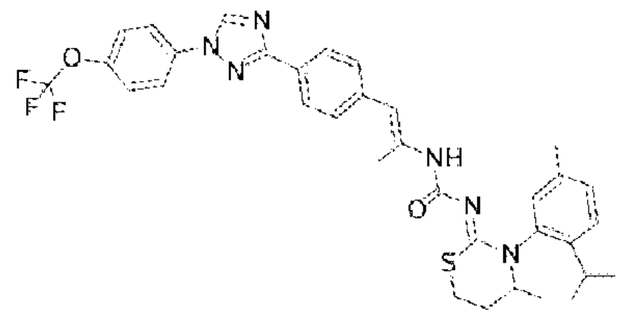
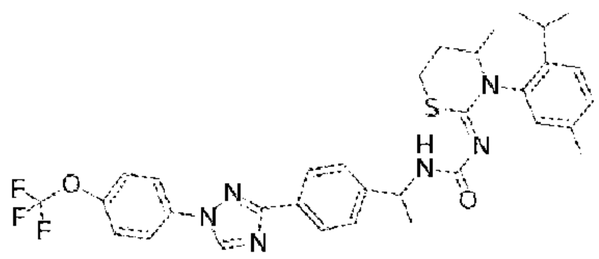
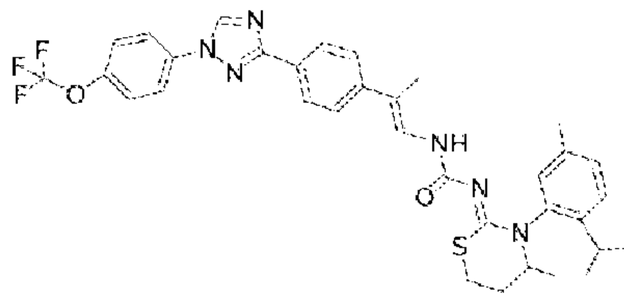
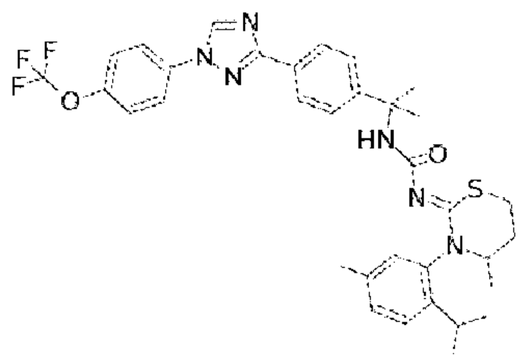
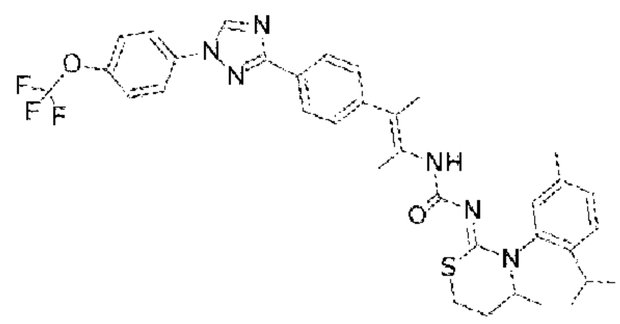
P455

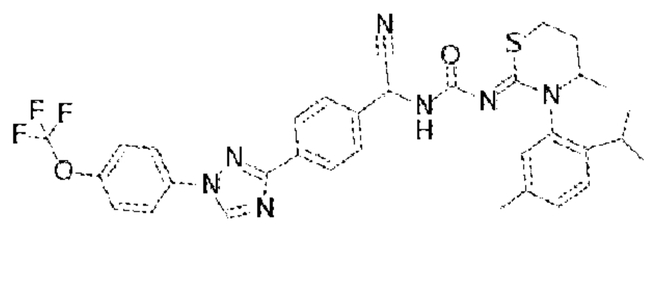
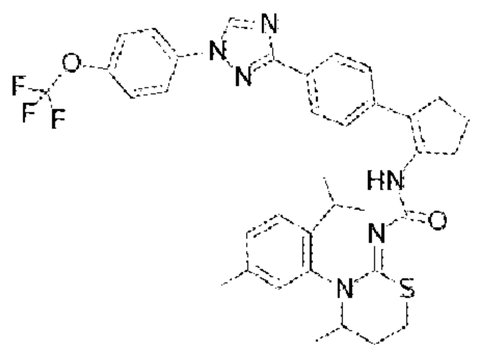
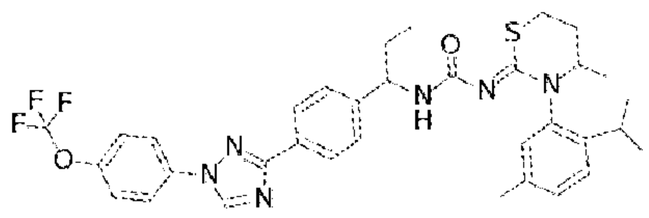
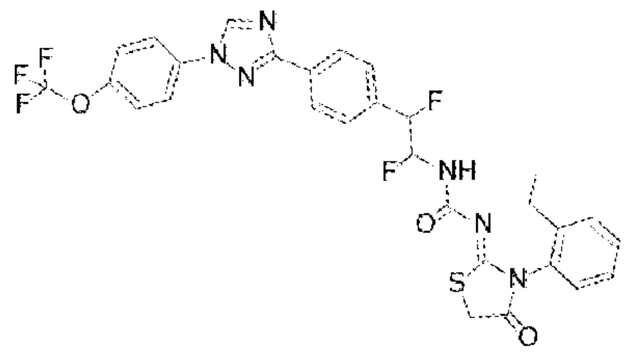
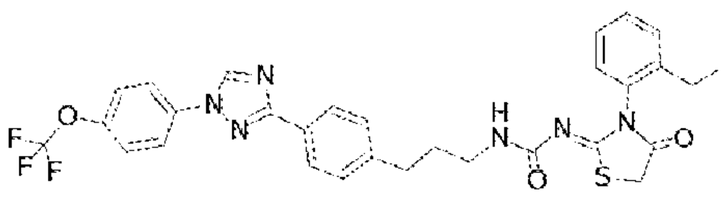
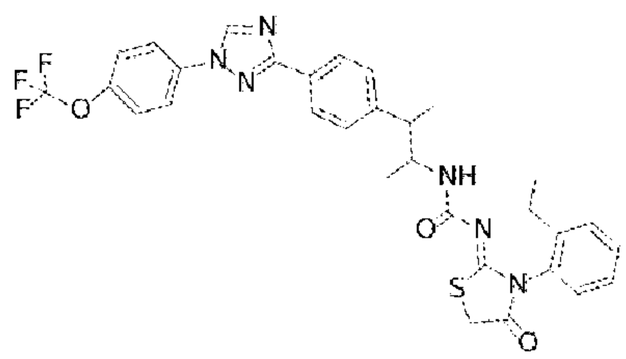
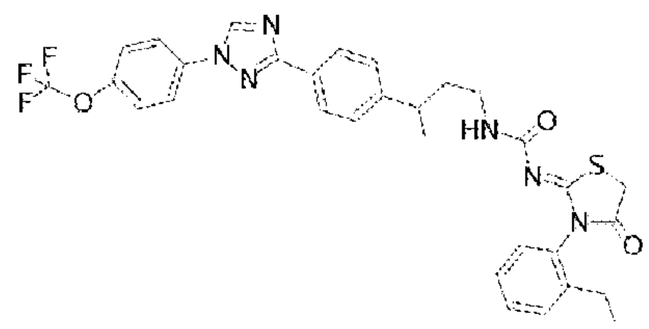
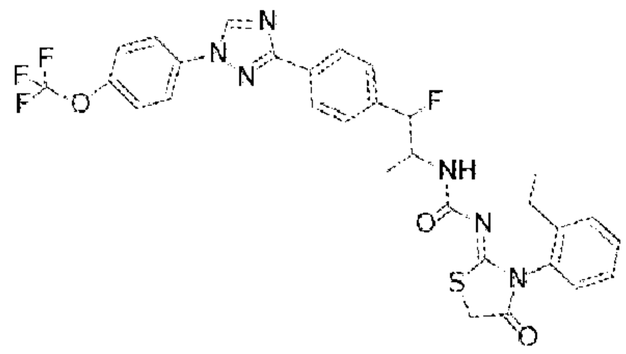
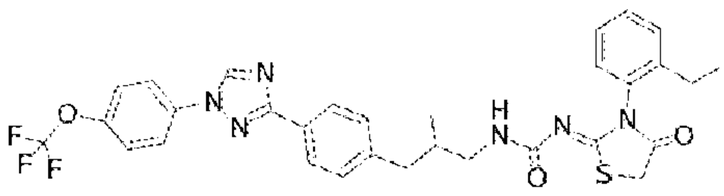
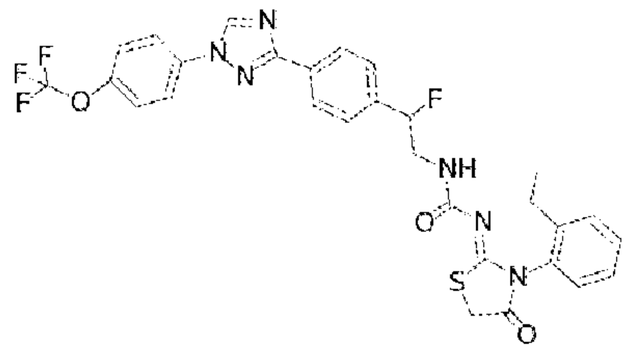
	
P456	P457
	
P458	P459
	
P460	P461
	
P462	P463
	
P464	P465

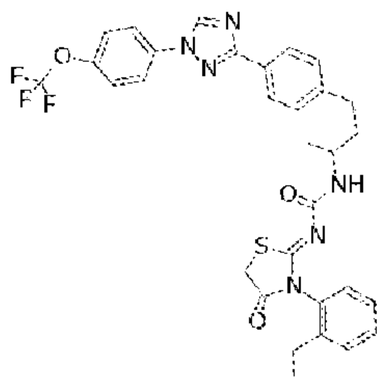
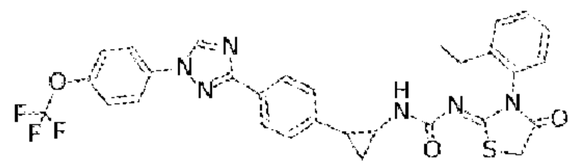
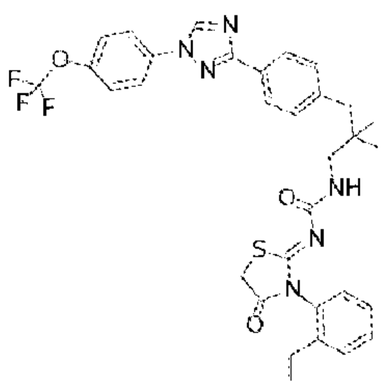
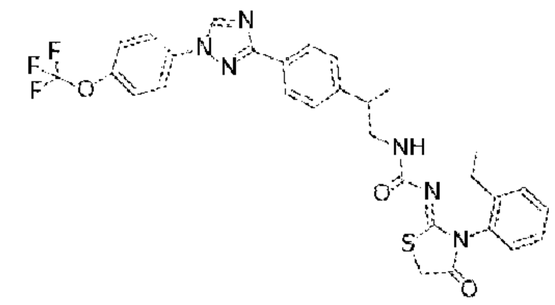
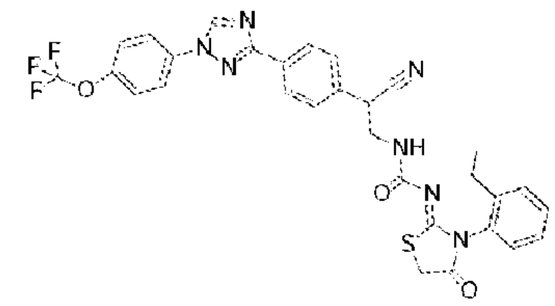
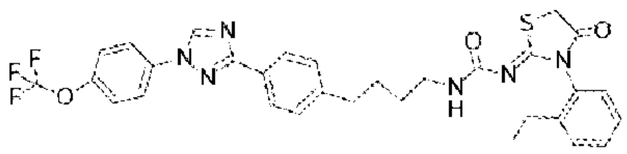
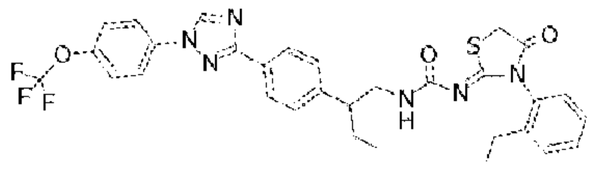
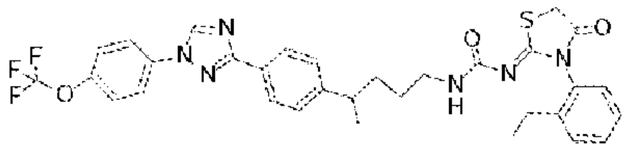
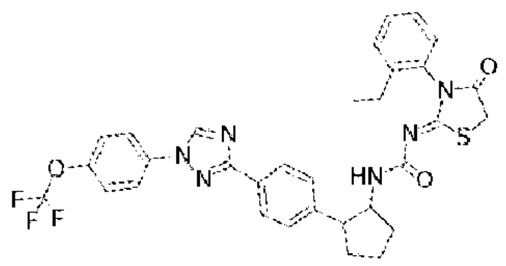
	
P466	P467
	
P468	P469
	
P470	P471
	
P472	P473
	
P474	P475

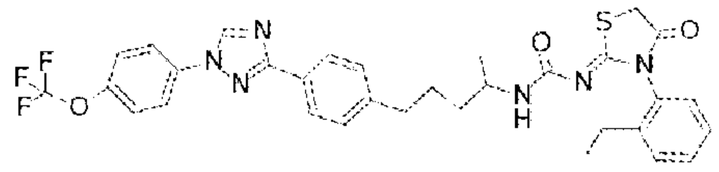
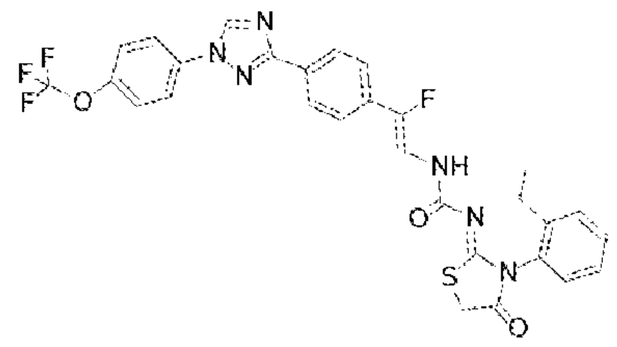
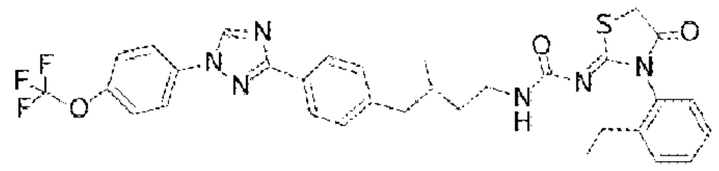
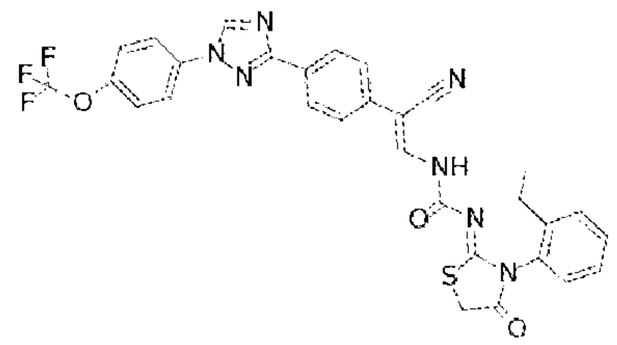
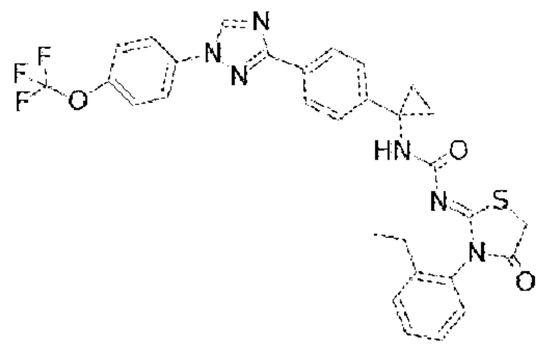
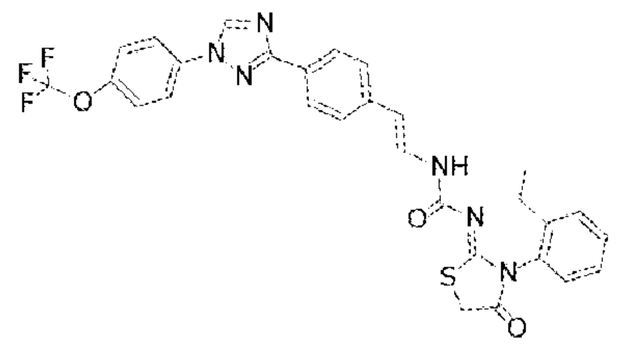
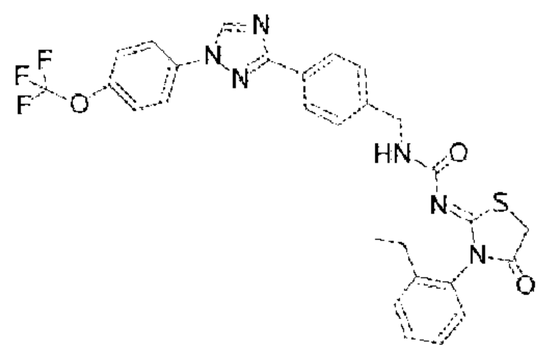
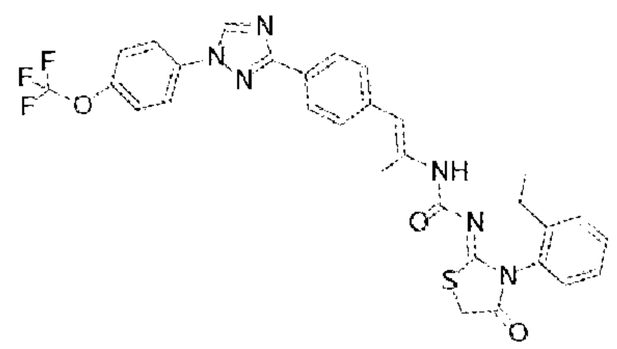
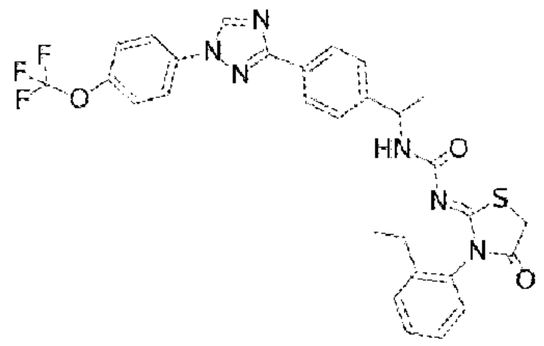
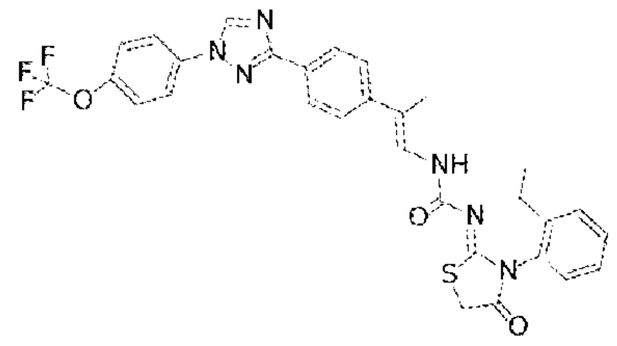
 P476	 P477
 P478	 P479
 P480	 P481
 P482	 P483
 P484	 P485

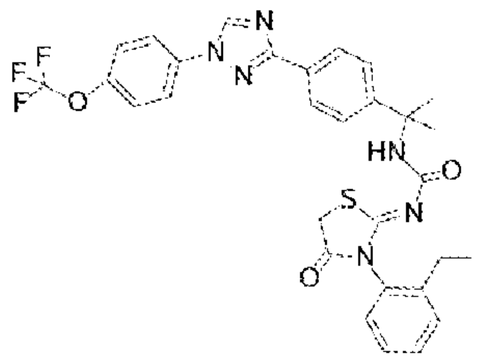
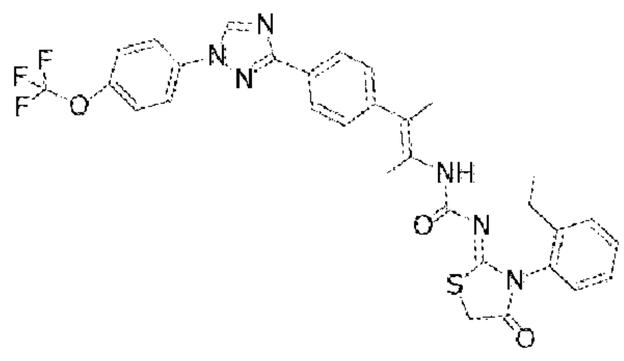
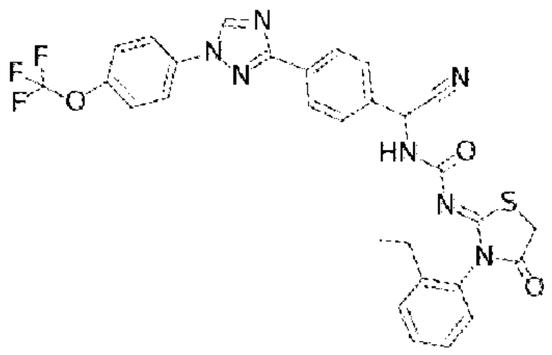
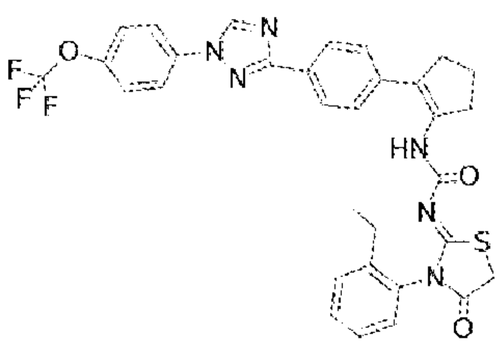
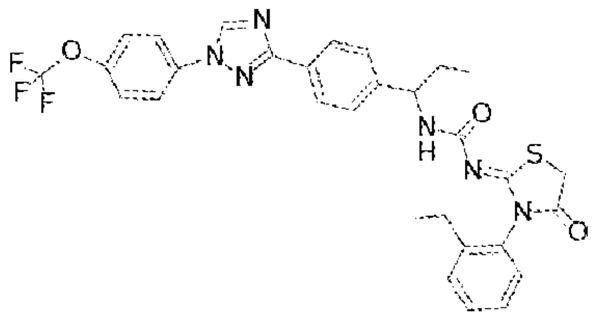
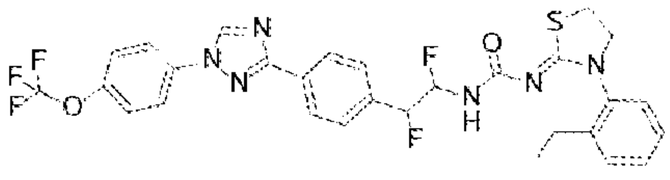
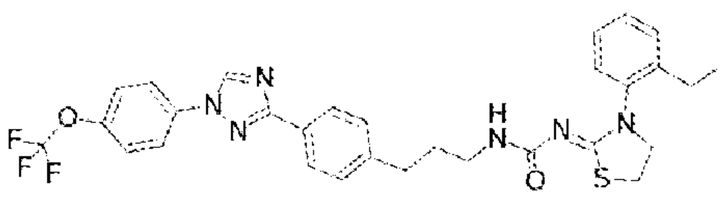
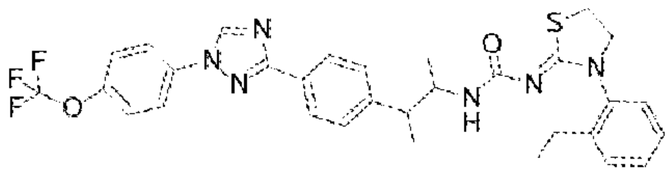
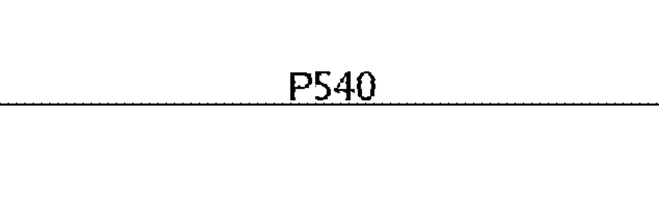
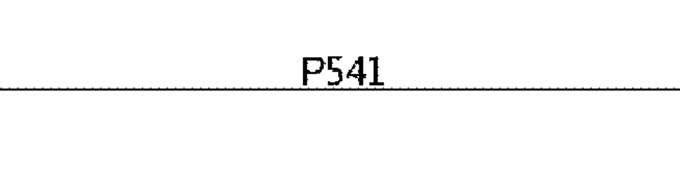
 P486	 P487
 P488	 P489
 P490	 P491
 P492	 P493
 P494	 P495

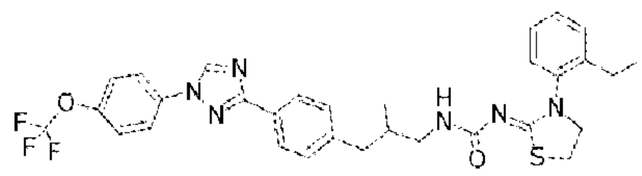
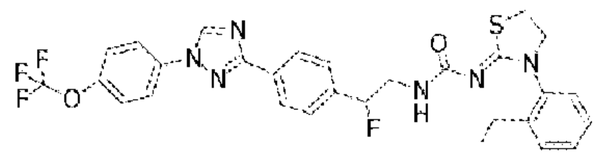
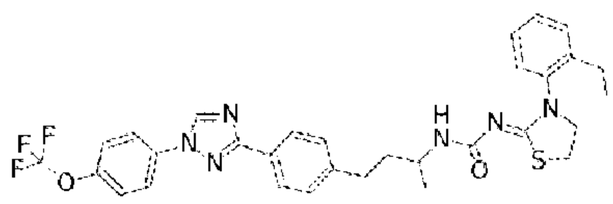
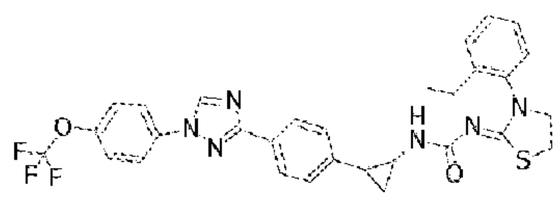
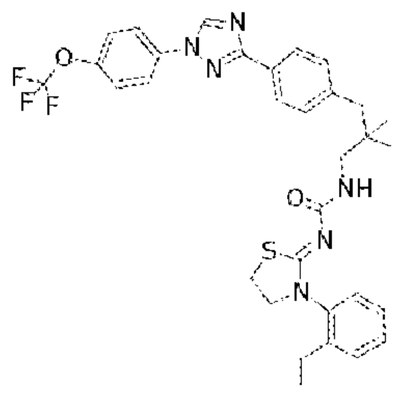
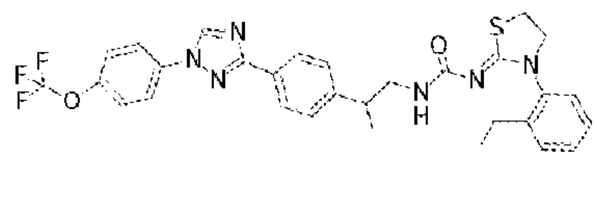
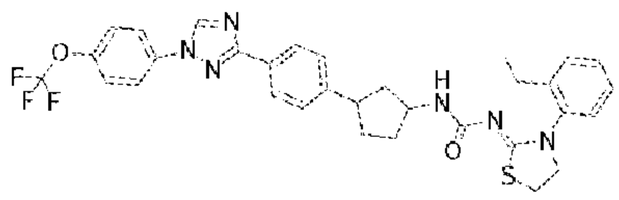
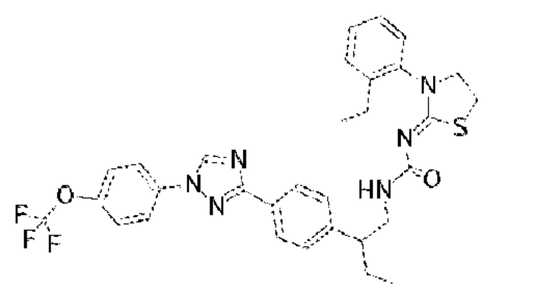
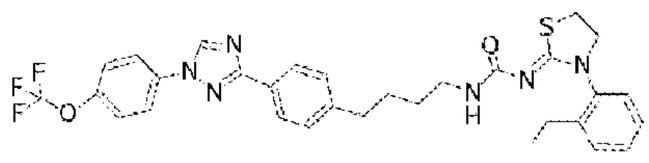
	
P496	P497
	
P498	P499
	
P500	P501
	
P502	P503
	
P504	P505

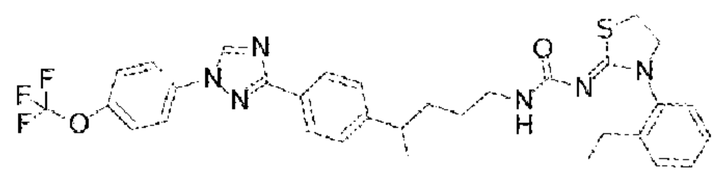
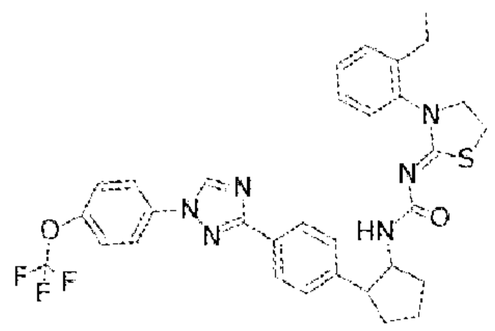
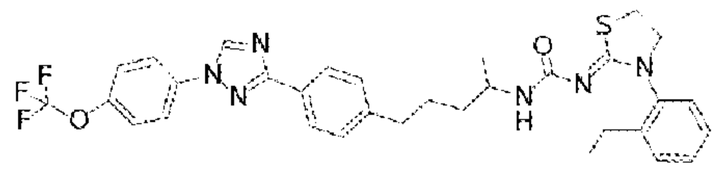
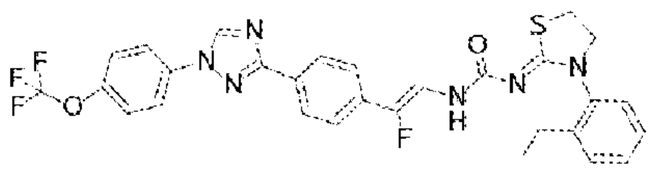
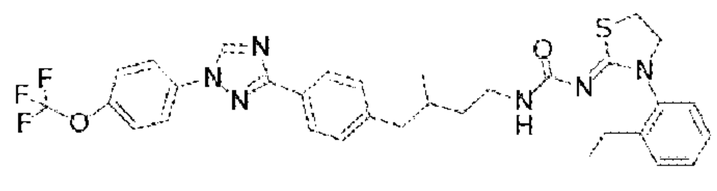
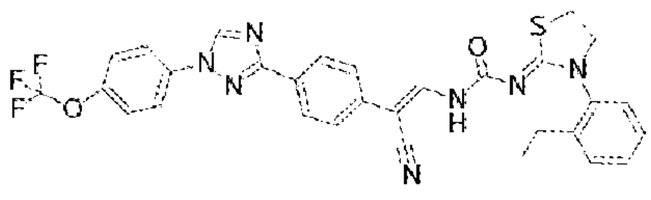
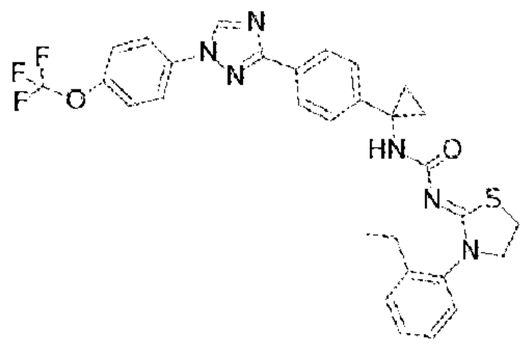
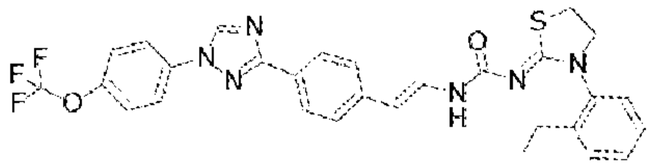
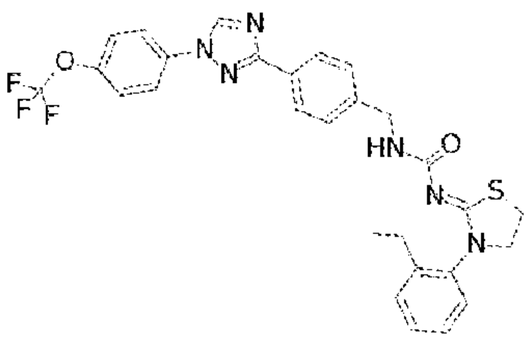
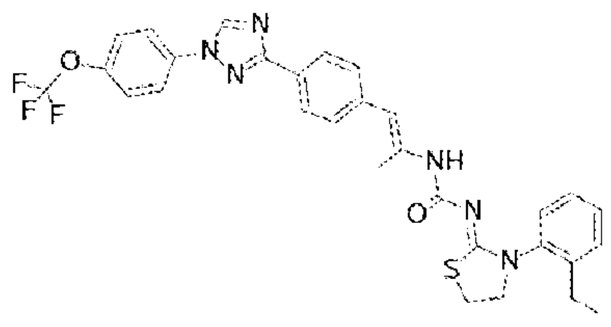
	
P506	P507
	
P508	P509
	
P510	P511
	
P512	P513
	
P514	P515

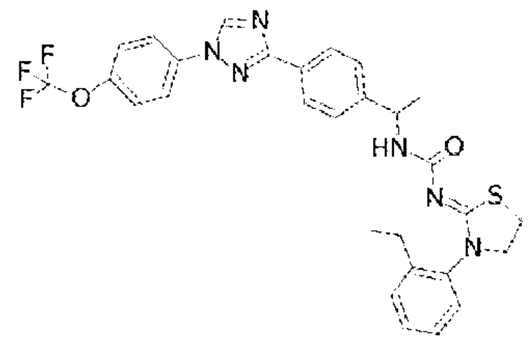
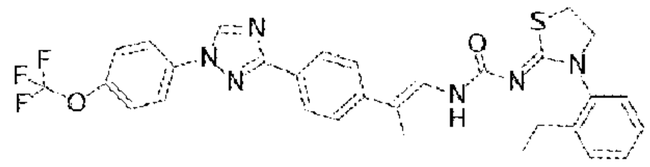
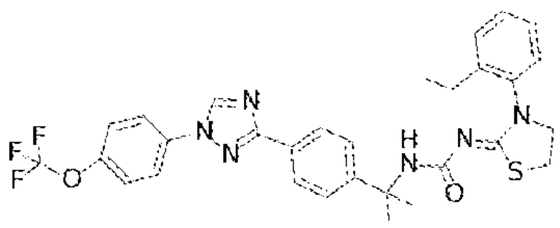
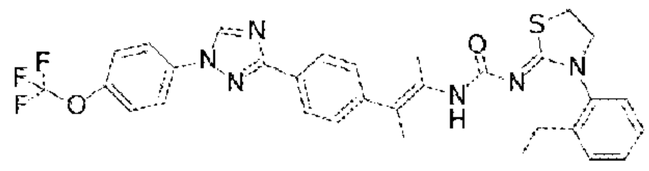
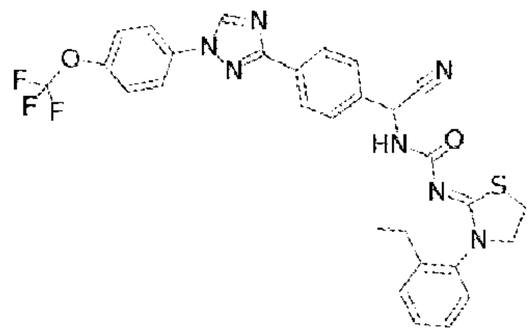
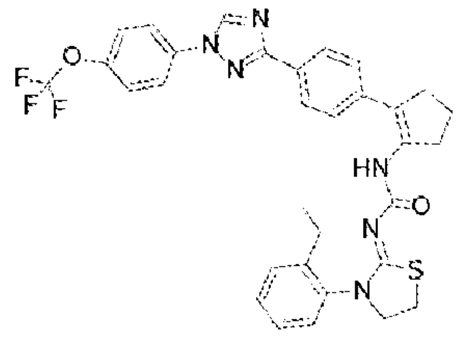
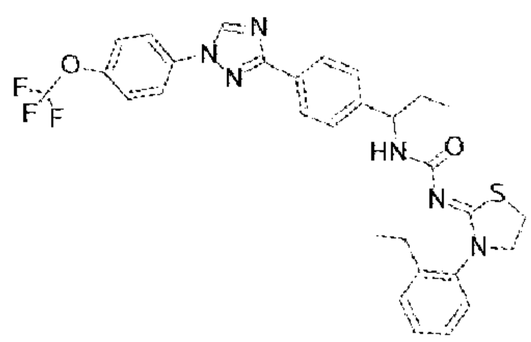
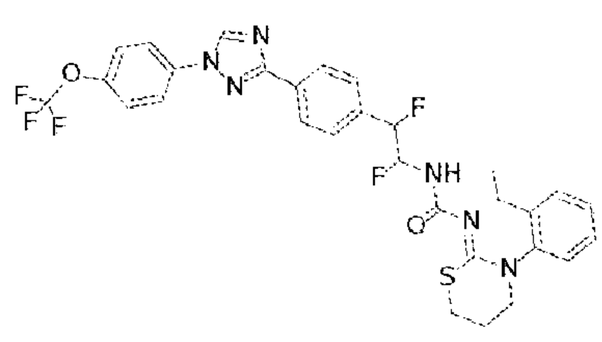
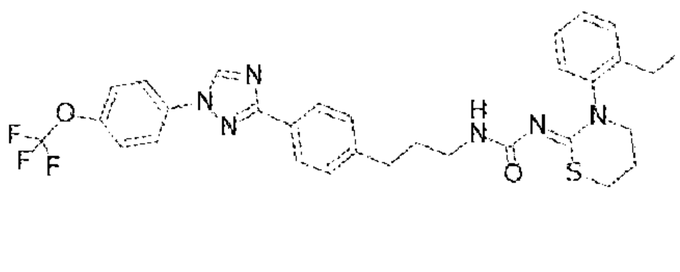
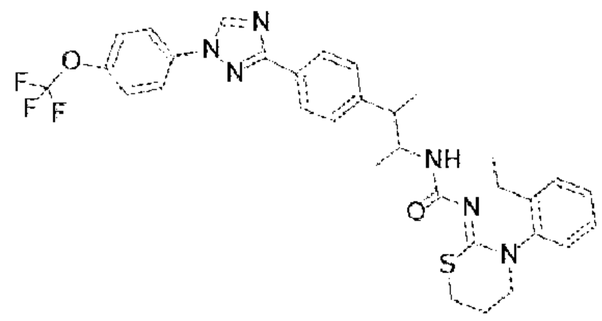
	
P516	P517
	
P518	P519
	
P520	P521
	
P522	P523
	
P524	P525

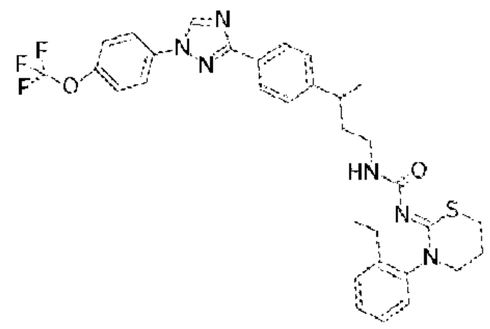
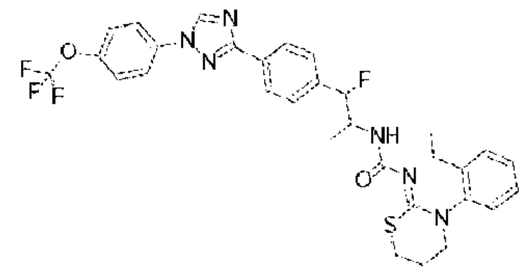
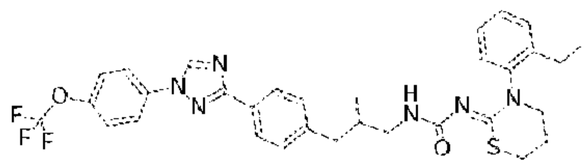
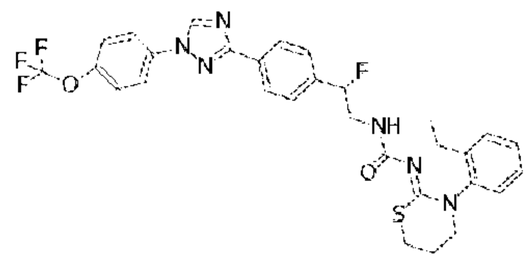
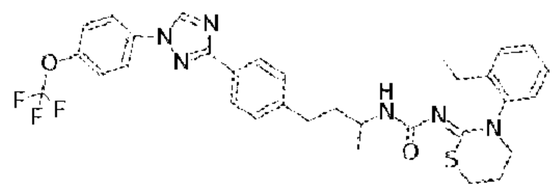
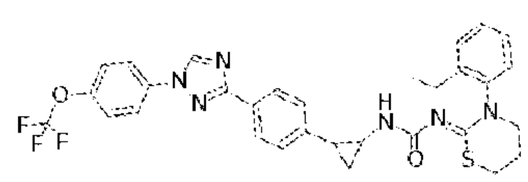
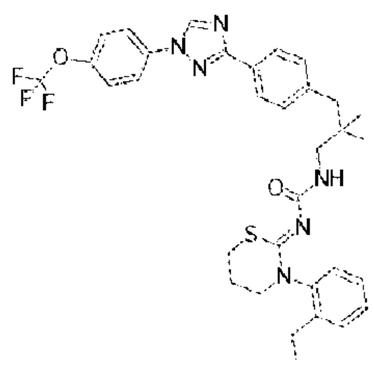
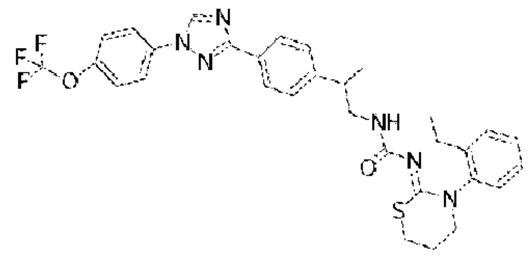
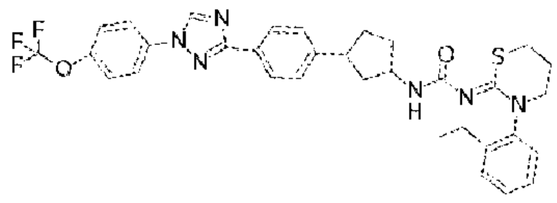
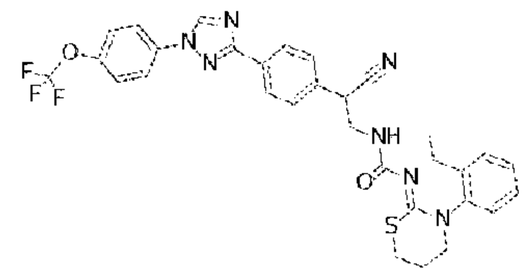
 P526	 P527
 P528	 P529
 P530	 P531
 P532	 P533
 P534	 P535

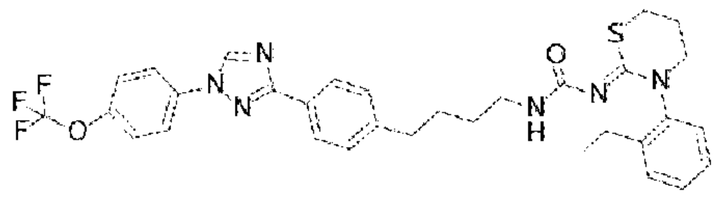
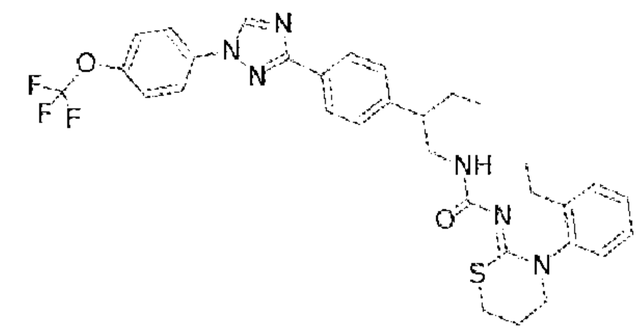
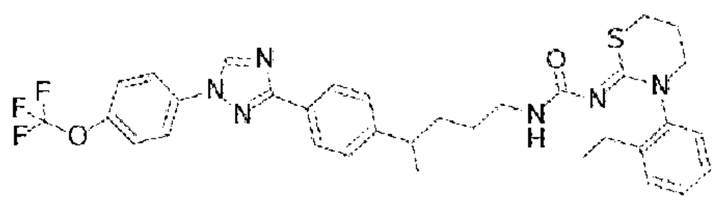
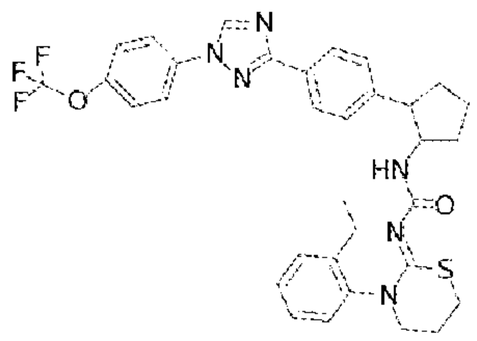
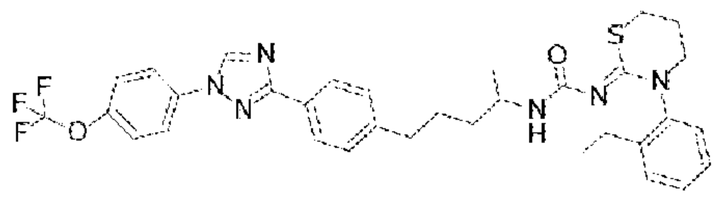
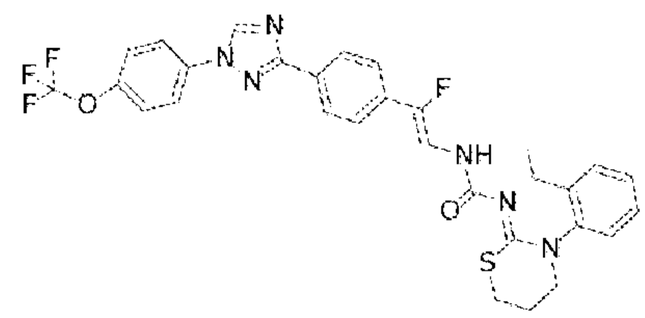
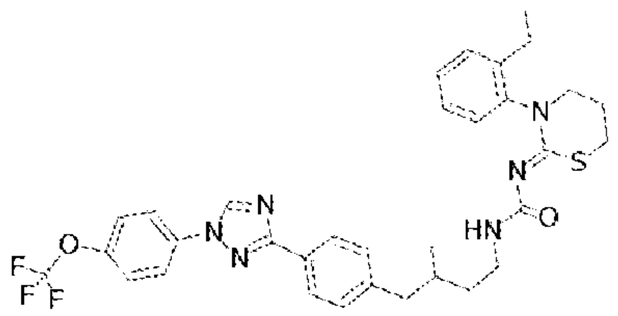
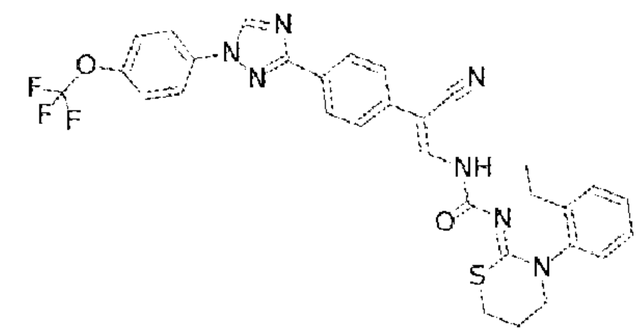
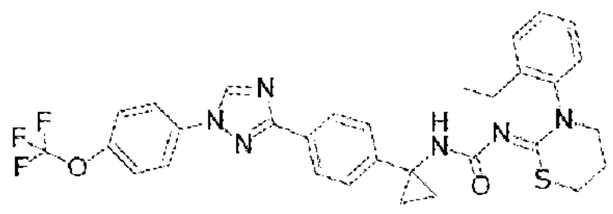
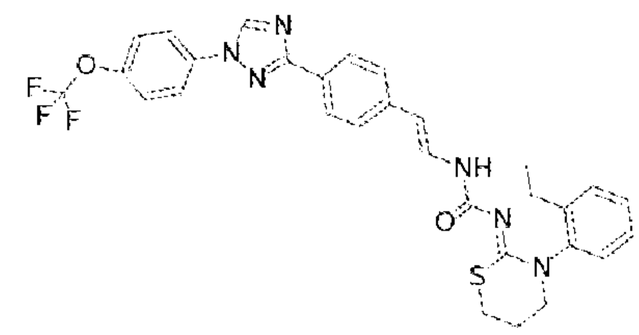
	
P536	P537
	
P538	P539
	
P540	P541
	
P542	P543
	
P544	P545

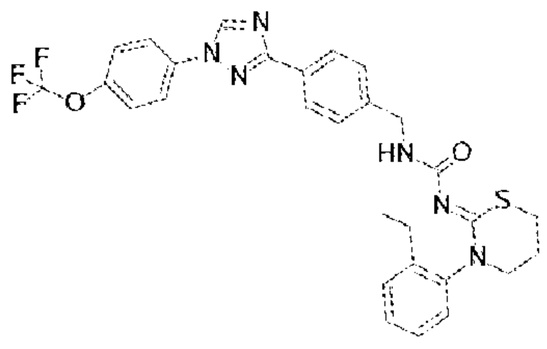
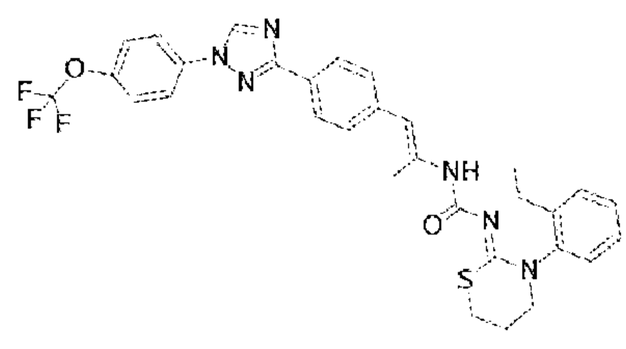
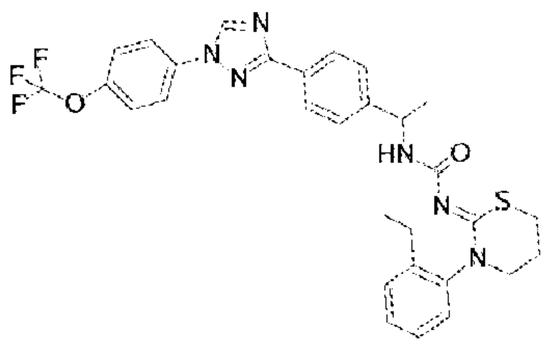
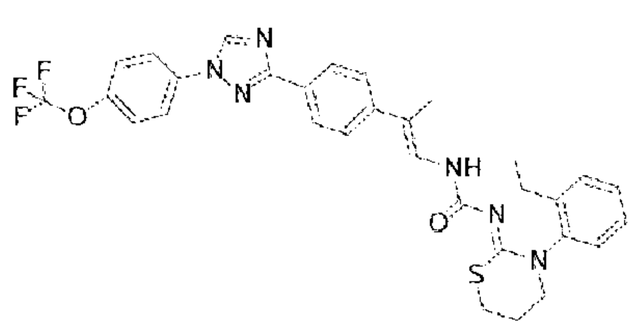
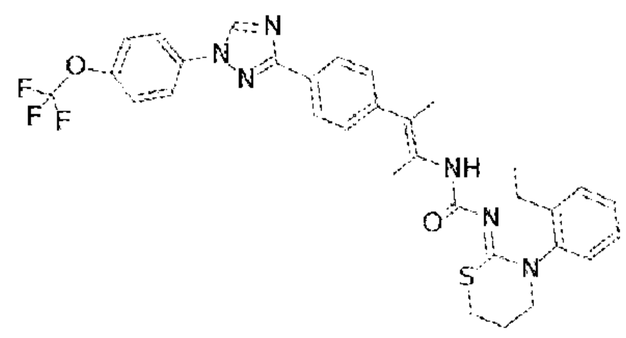
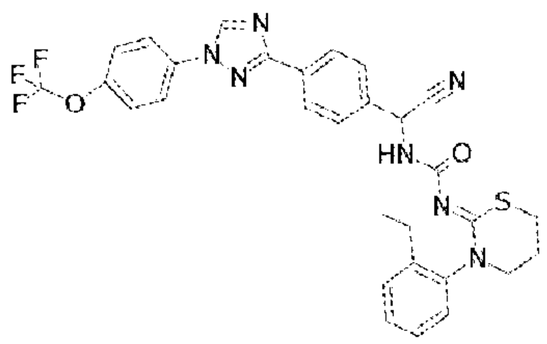
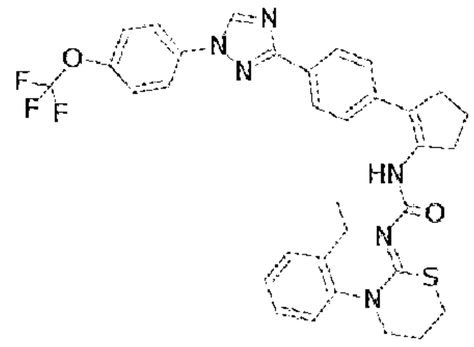
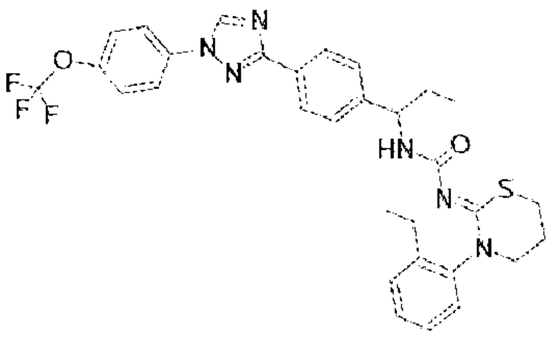
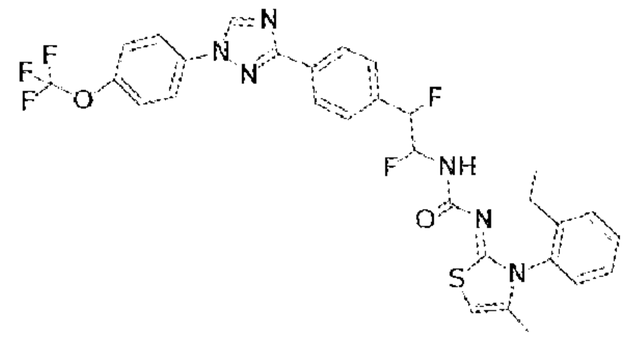
 P546	 P547
 P548	 P549
 P550	 P551
 P552	 P553
 P554	P555

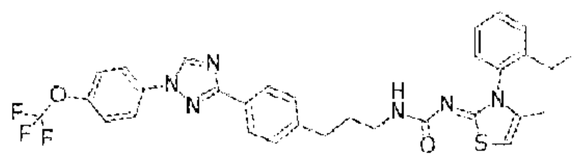
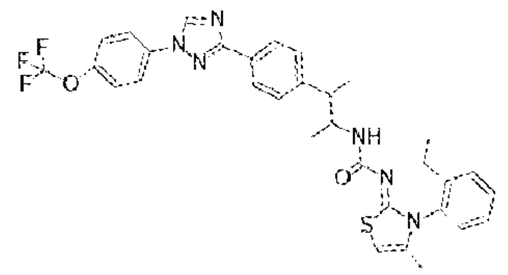
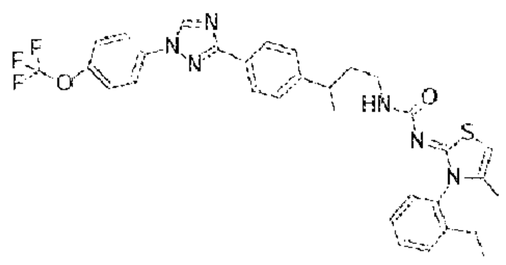
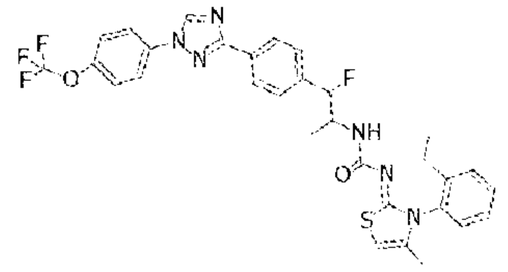
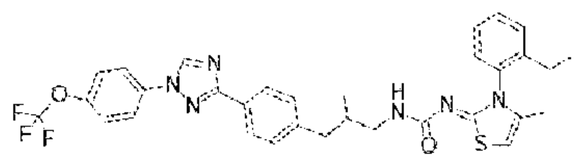
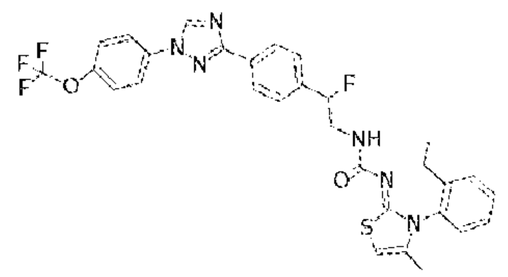
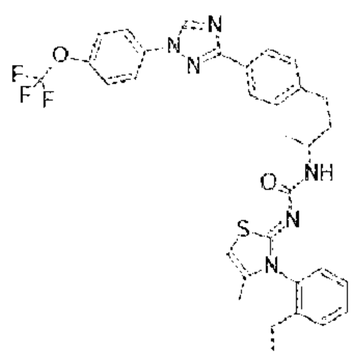
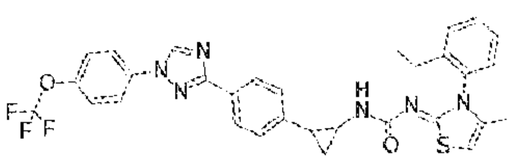
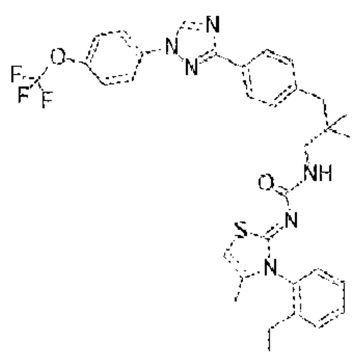
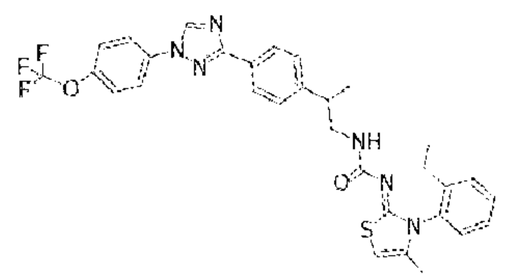
	
P556	P557
	
P558	P559
	
P560	P561
	
P562	P563
	
P564	P565

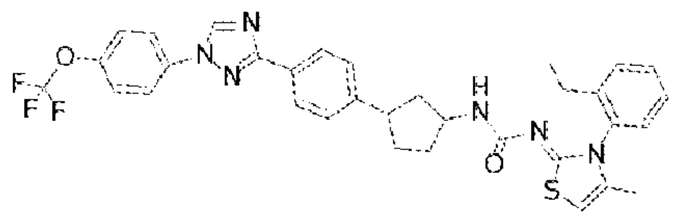
 P566	 P567
 P568	 P569
 P570	 P571
 P572	 P573
 P574	 P575

 P576	 P577
 P578	 P579
 P580	 P581
 P582	 P583
 P584	 P585

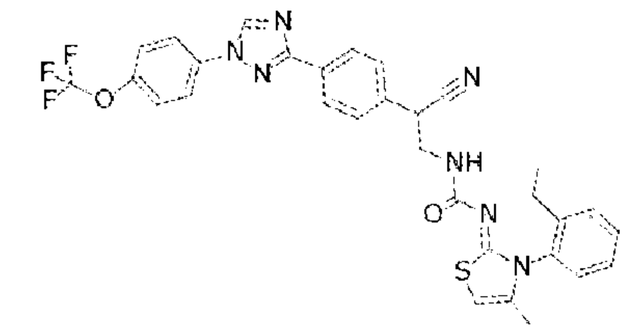
 P586	 P587
 P588	 P589
 P590	 P591
 P592	 P593
 P594	 P595

 P596	 P597
 P598	 P599
P600	 P601
 P602	 P603
 P604	 P605

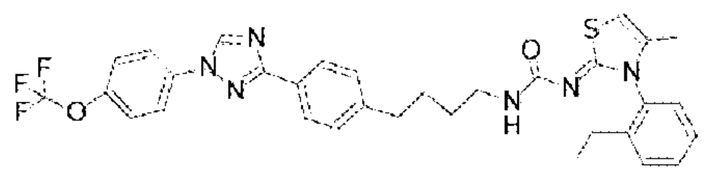
 P606	 P607
 P608	 P609
 P610	 P611
 P612	 P613
 P614	 P615



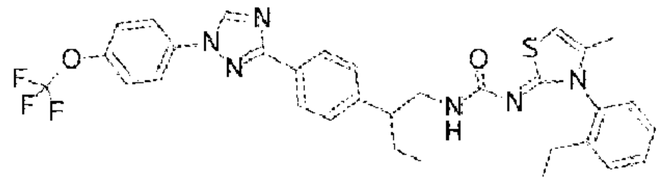
P616



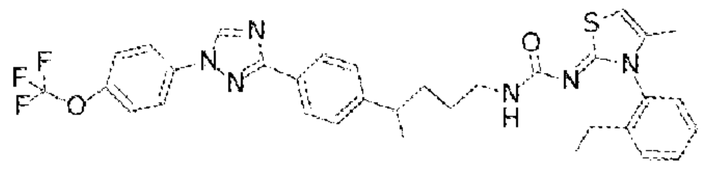
P617



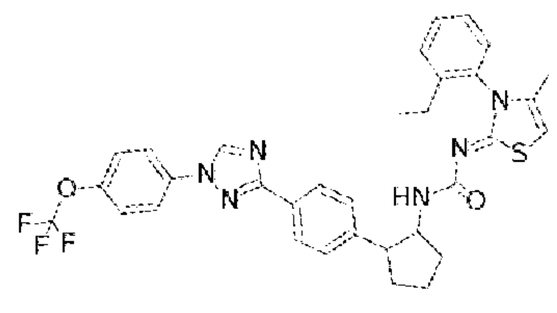
P618



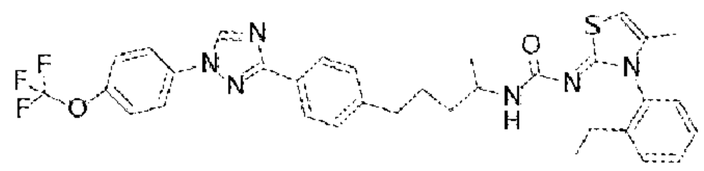
P619



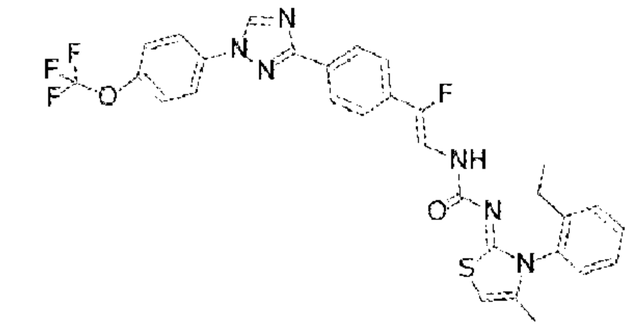
P620



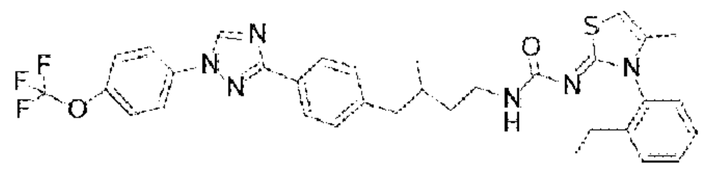
P621



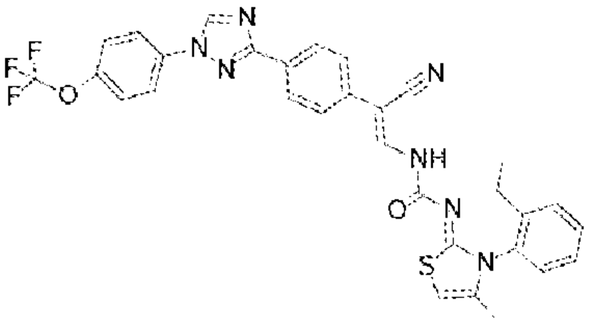
P622



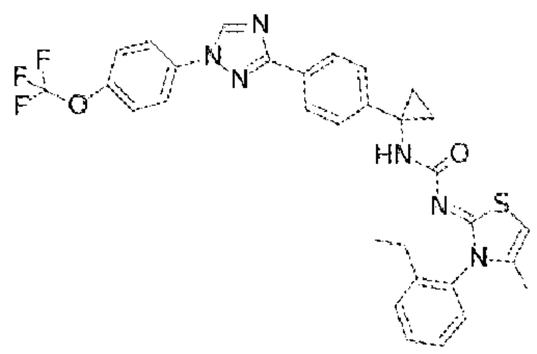
P623



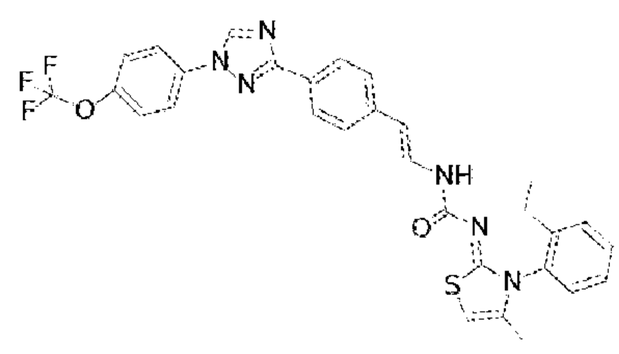
P624



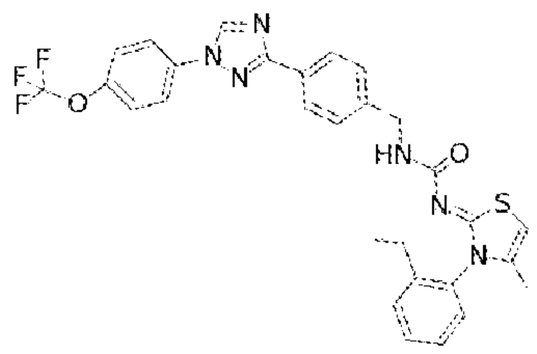
P625



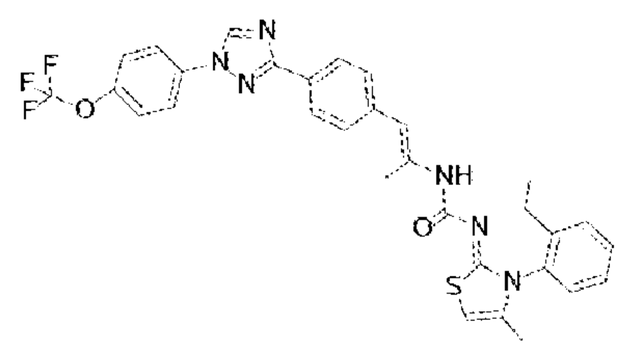
P626



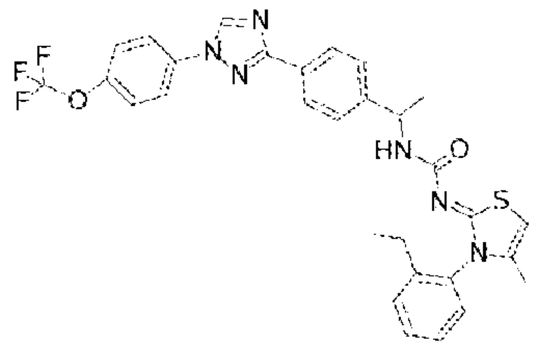
P627



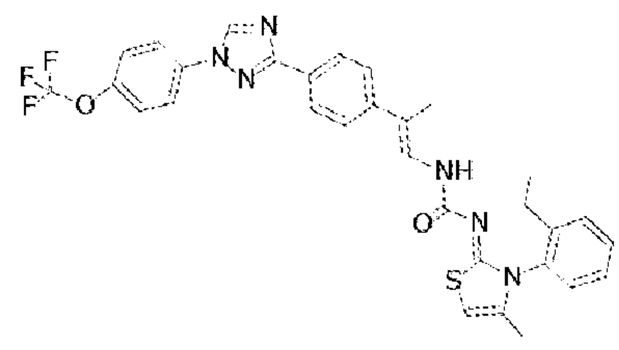
P628



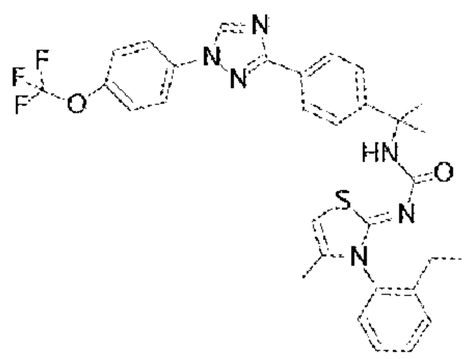
P629



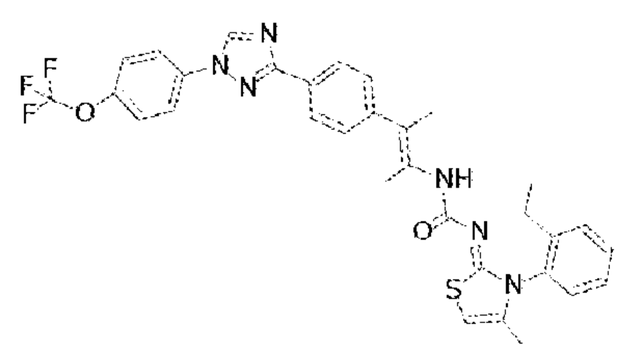
P630



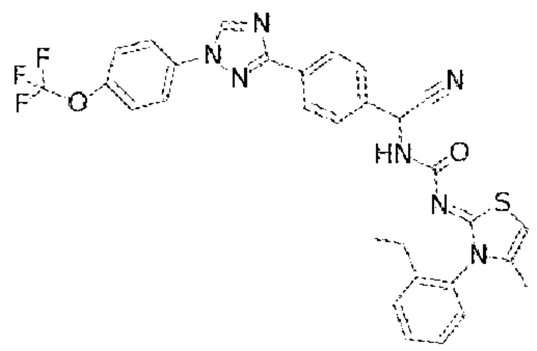
P631



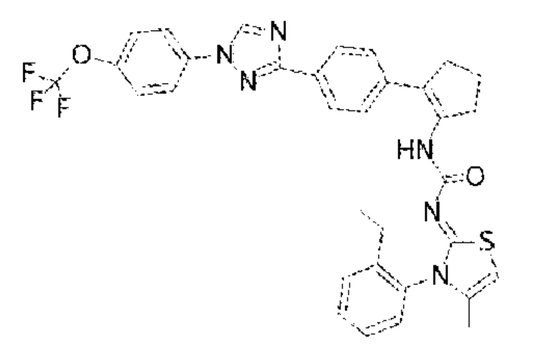
P632



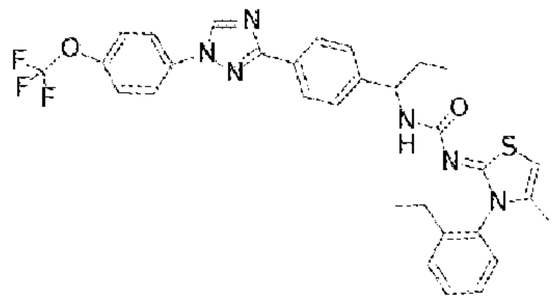
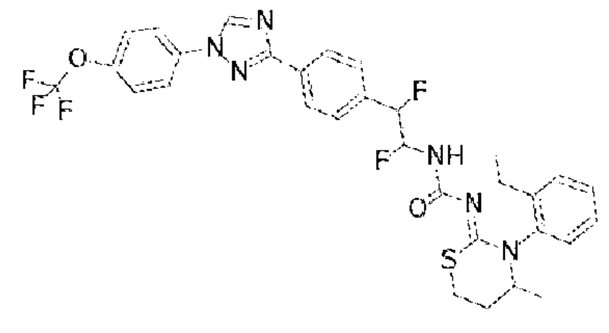
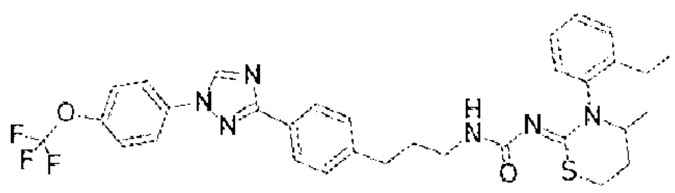
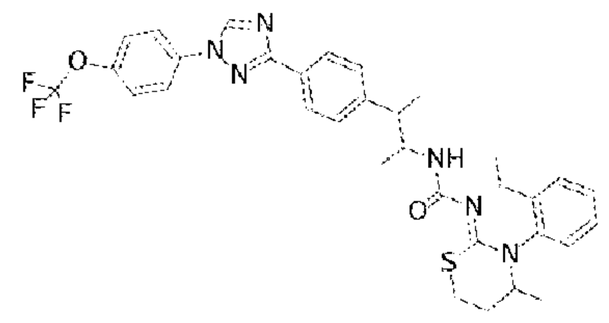
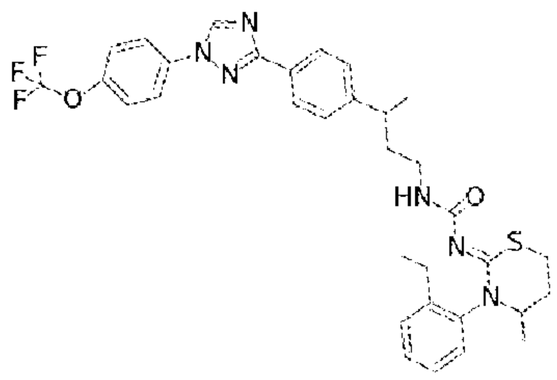
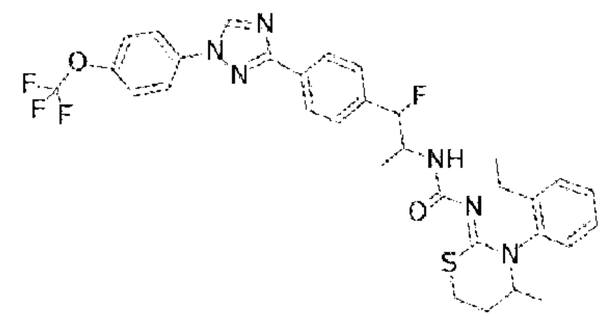
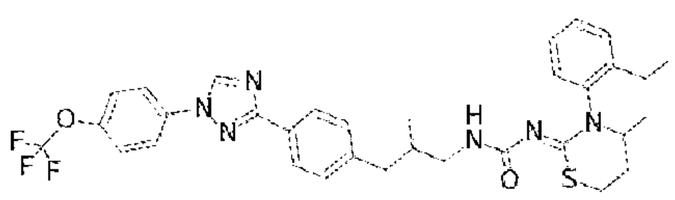
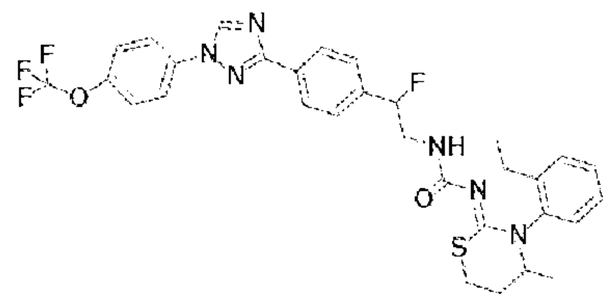
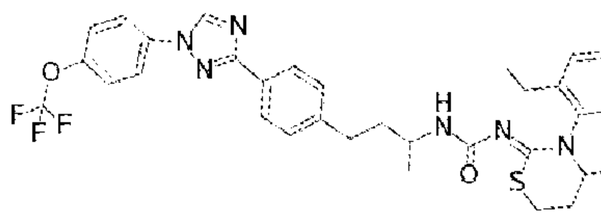
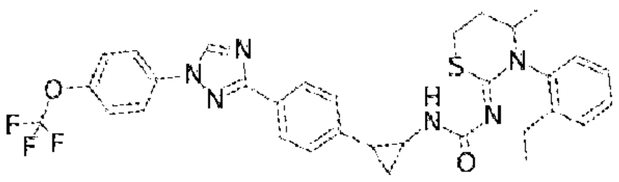
P633

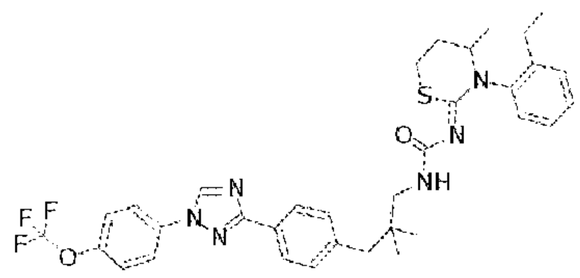
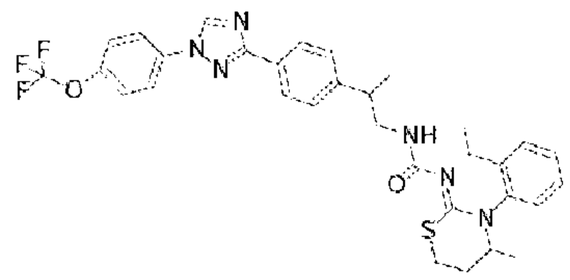
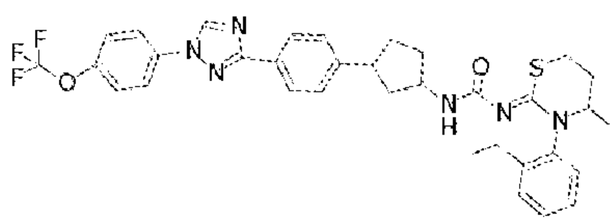
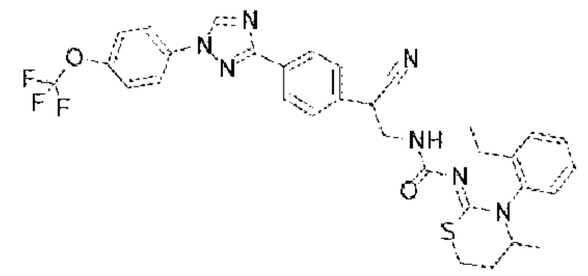
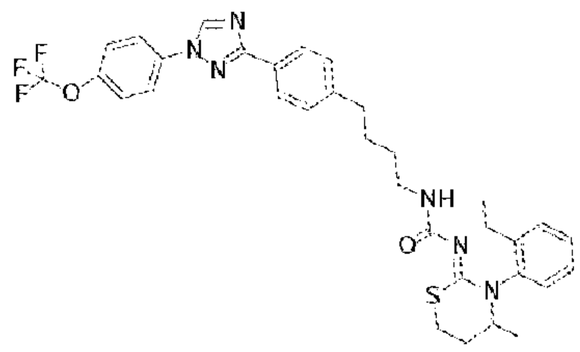
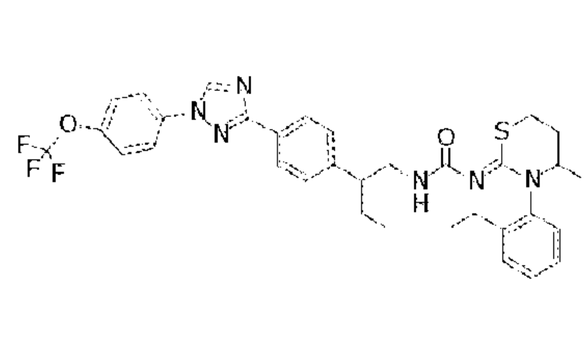
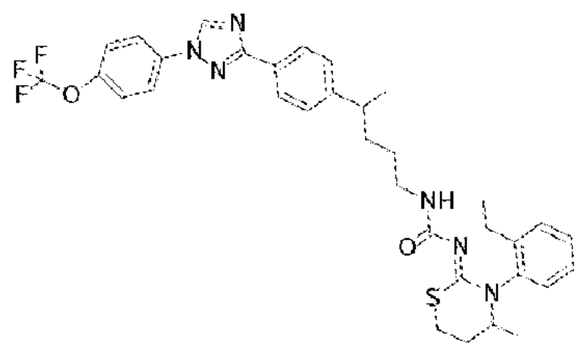
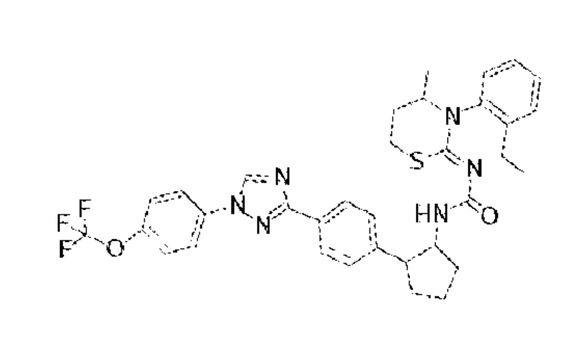
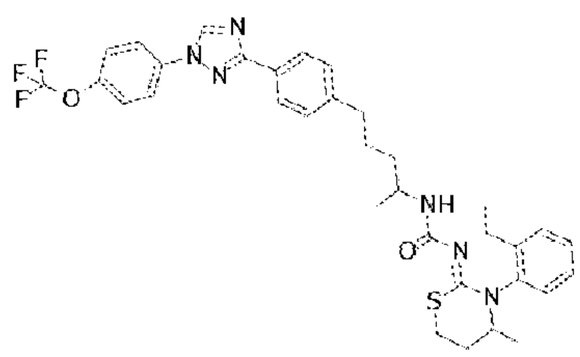
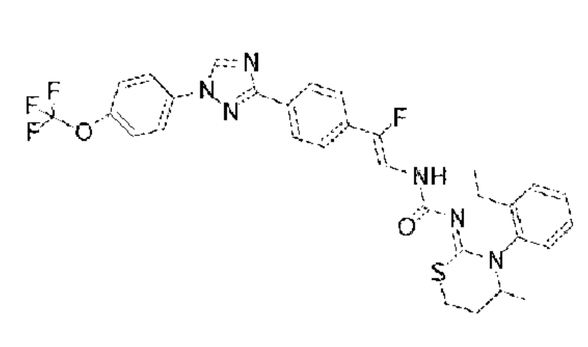


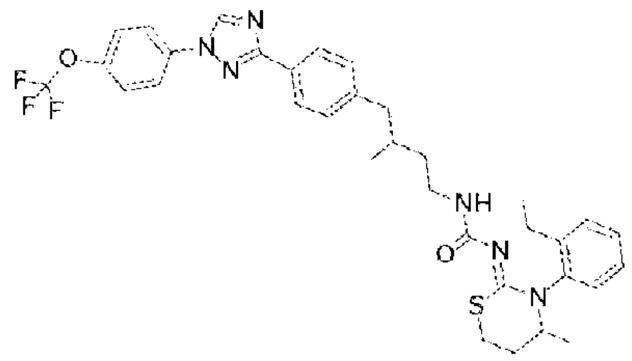
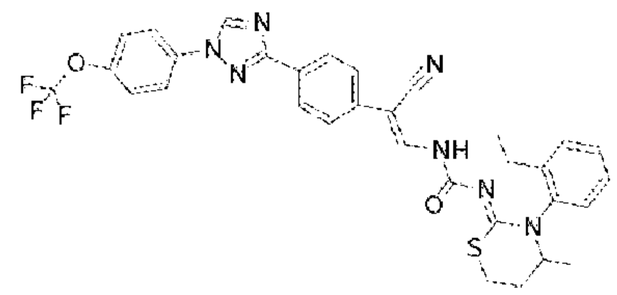
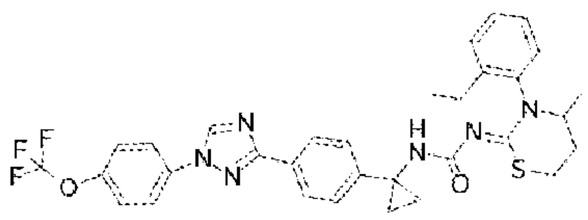
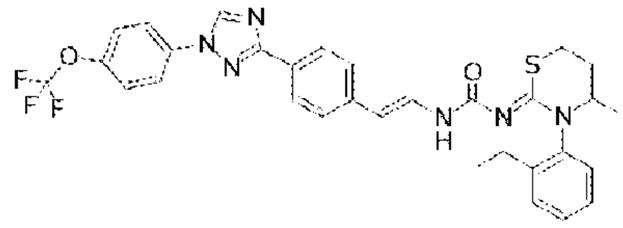
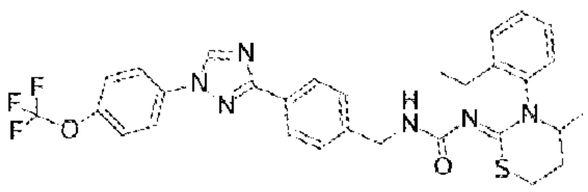
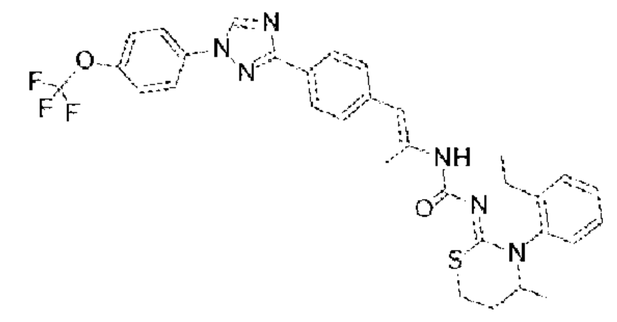
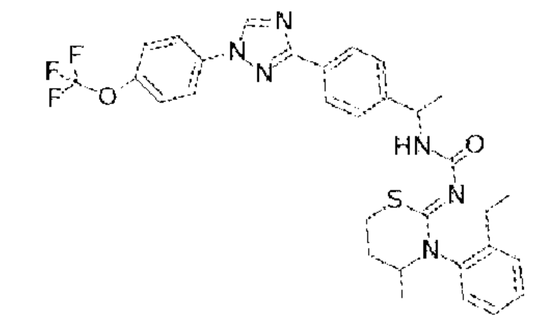
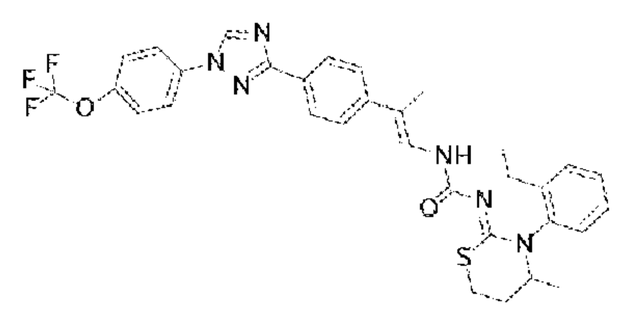
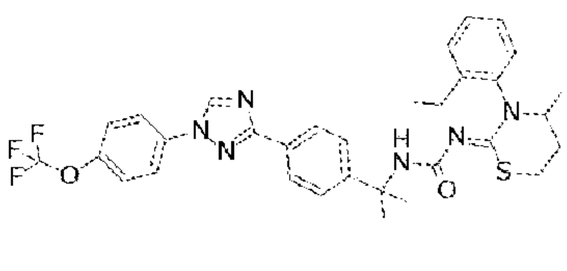
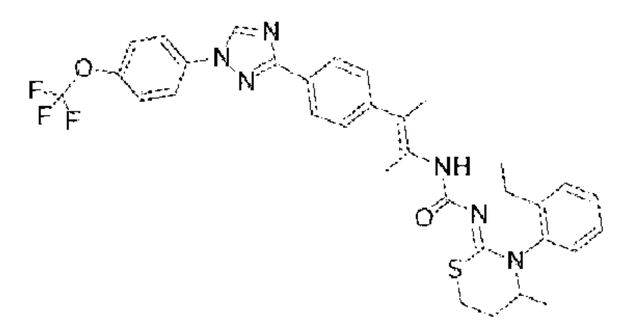
P634

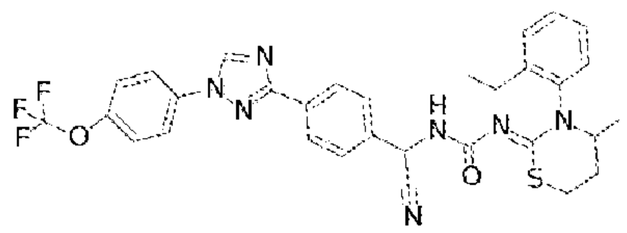
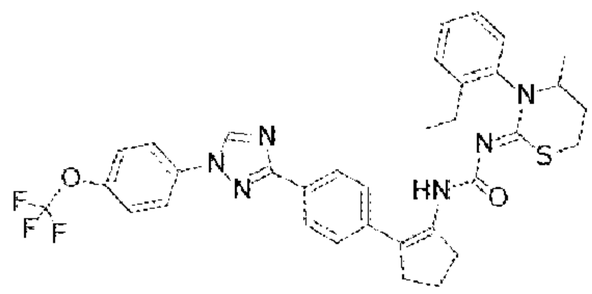
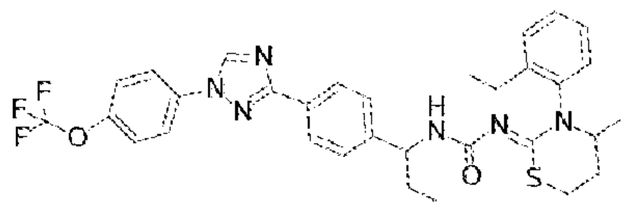
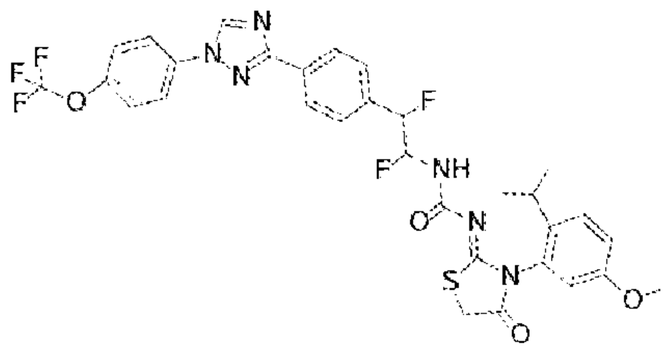
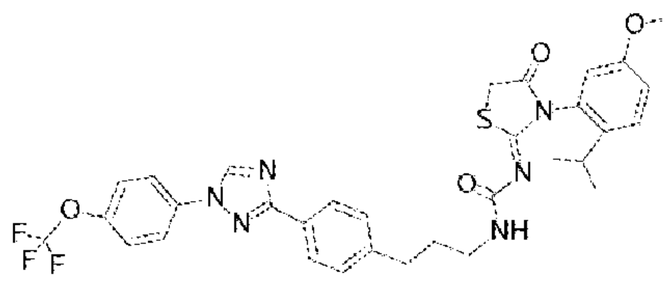
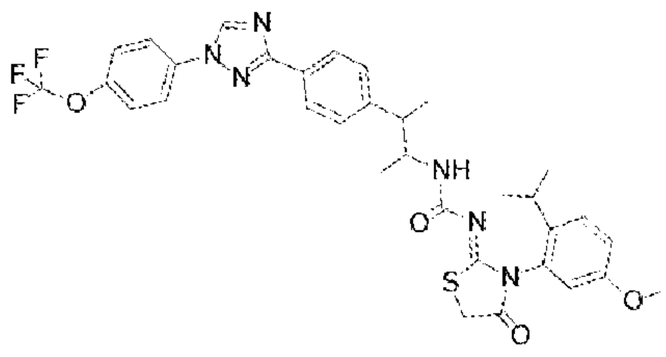
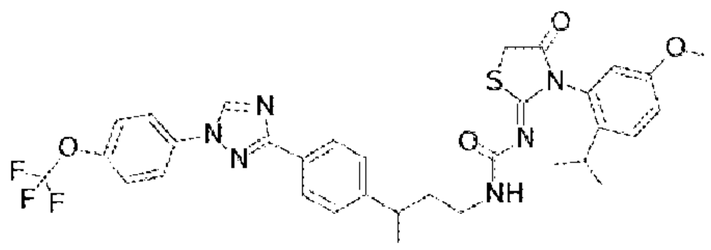
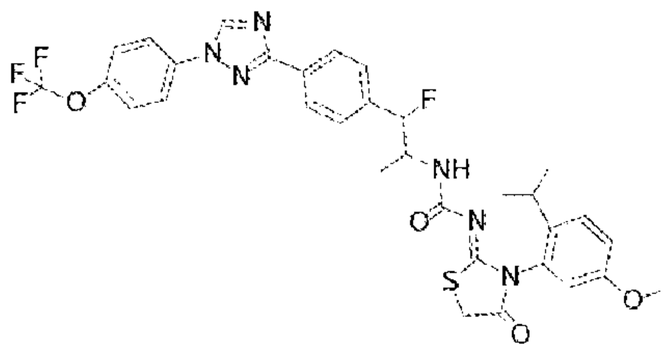
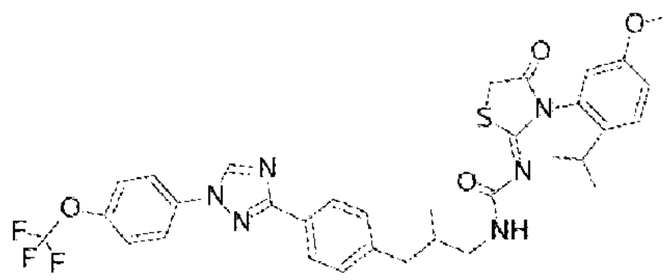
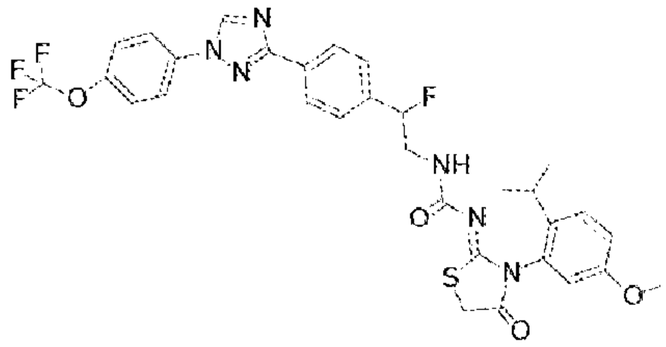


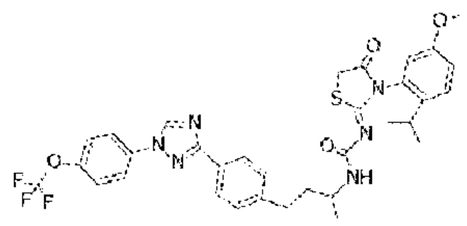
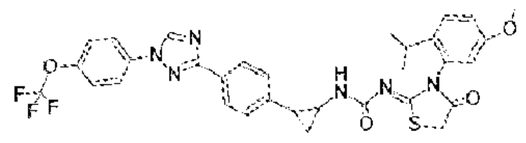
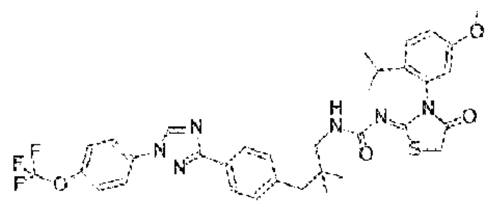
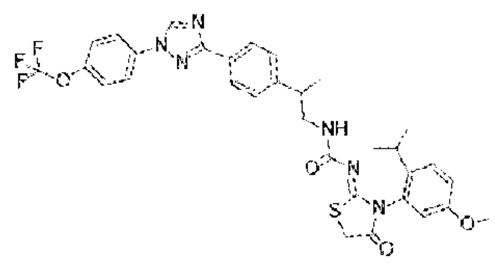
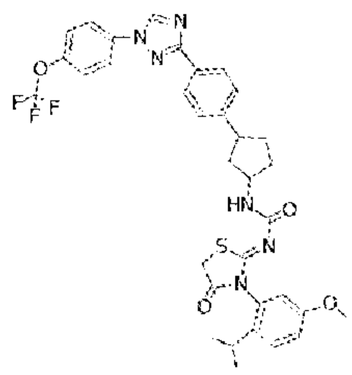
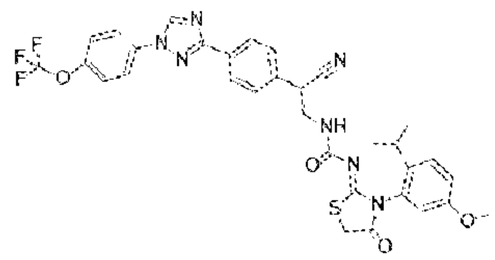
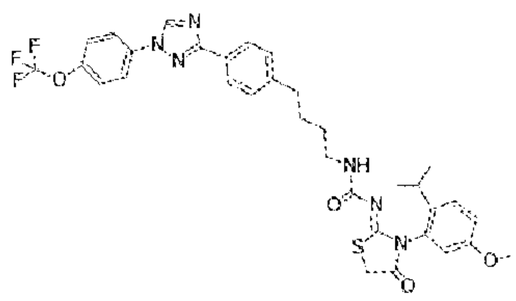
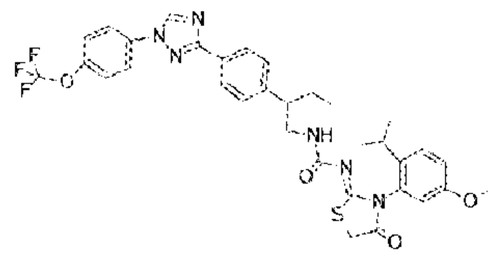
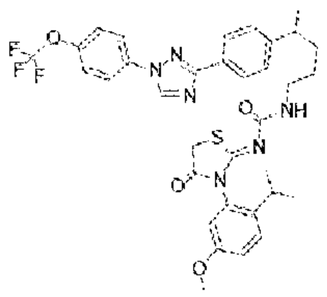
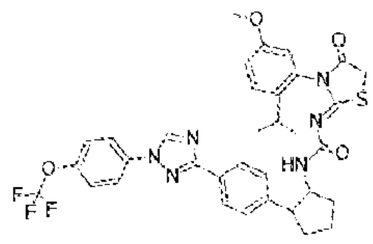
P635

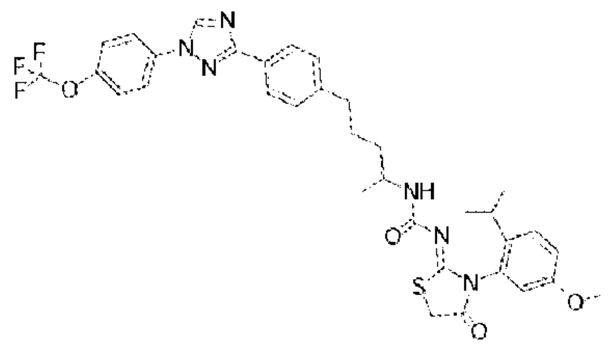
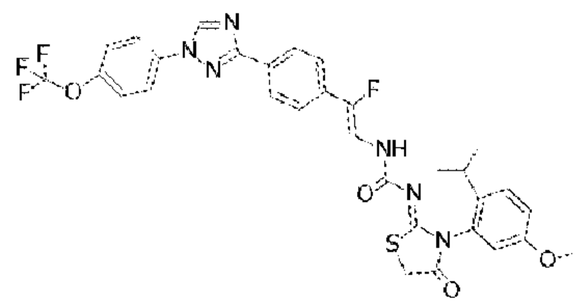
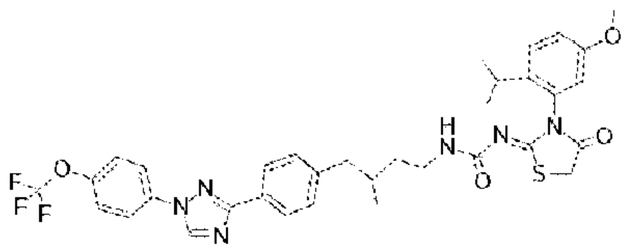
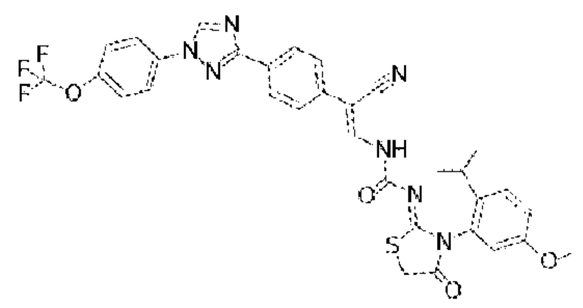
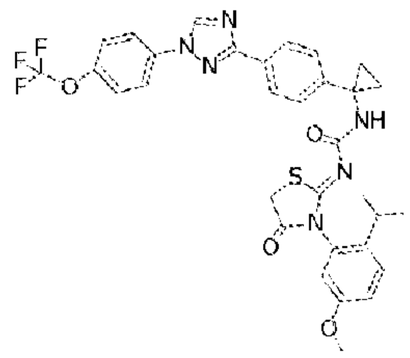
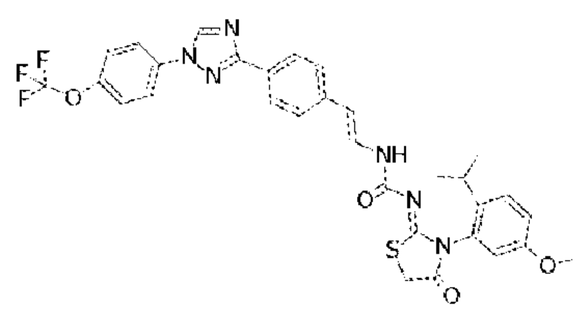
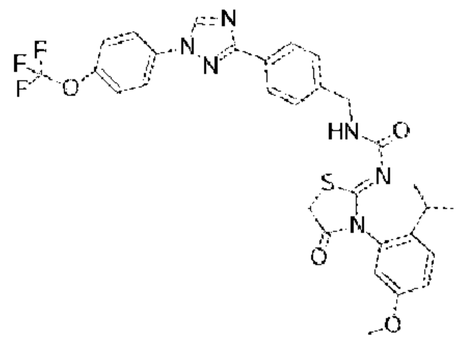
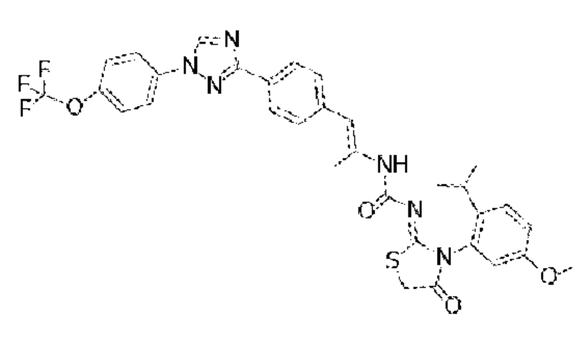
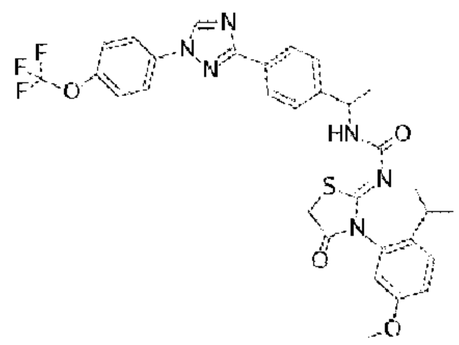
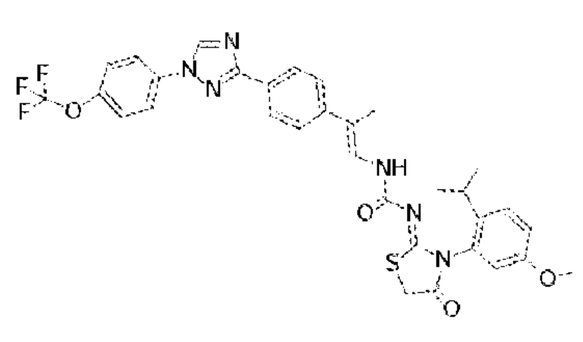
 P636	 P637
 P638	 P639
 P640	 P641
 P642	 P643
 P644	 P645

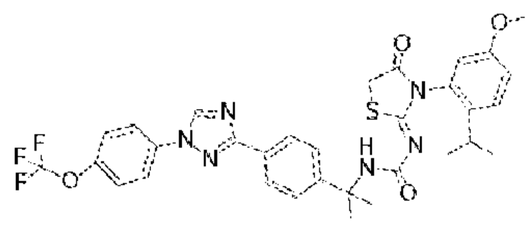
 P646	 P647
 P648	 P649
 P650	 P651
 P652	 P653
 P654	 P655

 P656	 P657
 P658	 P659
 P660	 P661
 P662	 P663
 P664	 P665

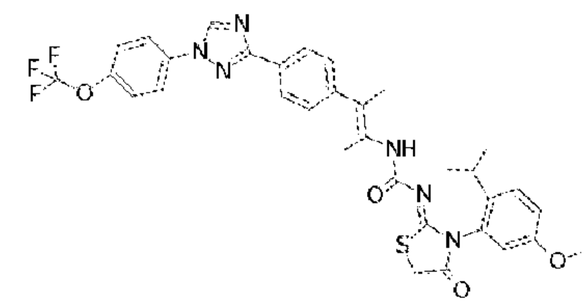
	
P666	P667
	
P668	P669
	
P670	P671
	
P672	P673
	
P674	P675

	
P676	P677
	
P678	P679
	
P680	P681
	
P682	P683
	
P684	P685

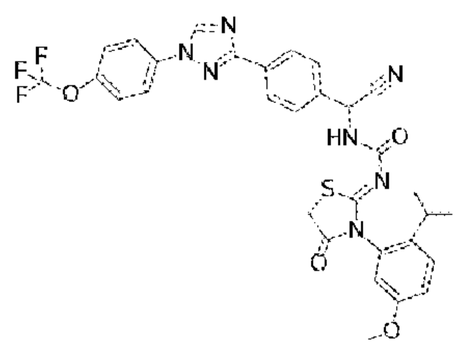
 P686	 P687
 P688	 P689
 P690	 P691
 P692	 P693
 P694	 P695



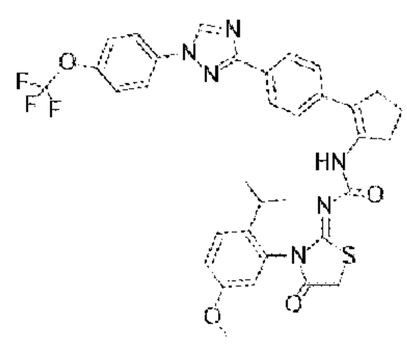
P696



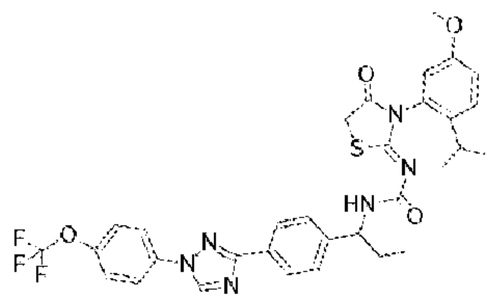
P697



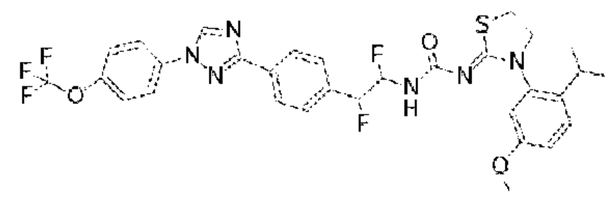
P698



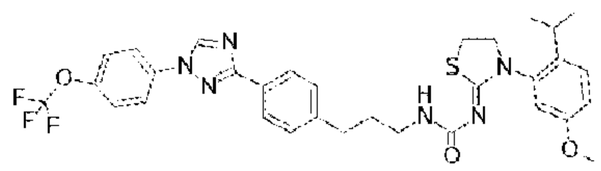
P699



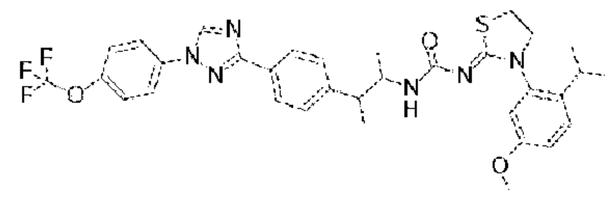
P700



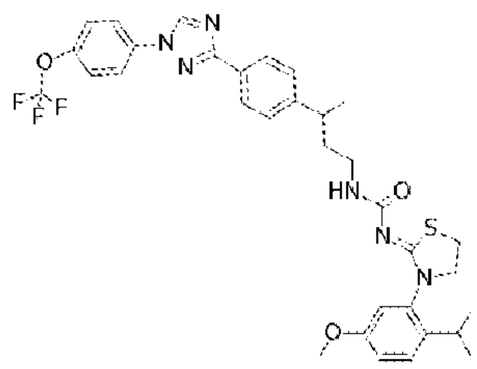
P701



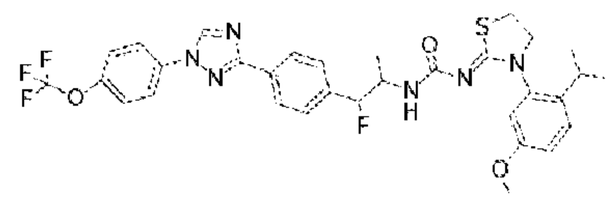
P702



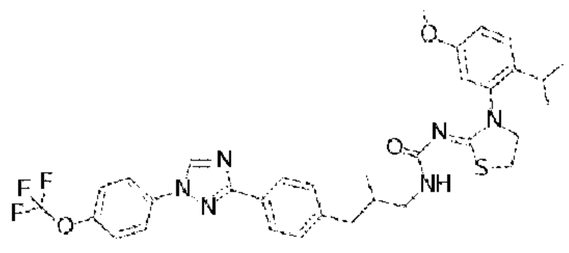
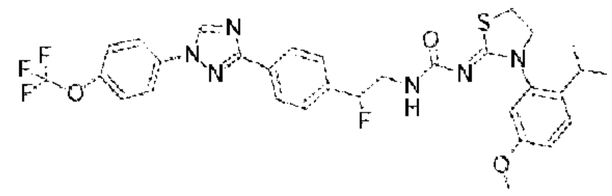
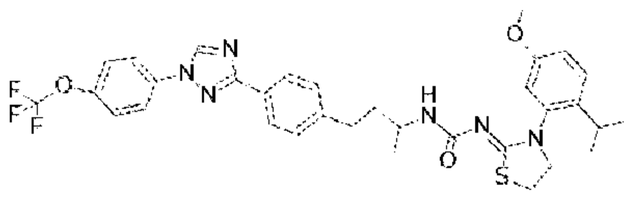
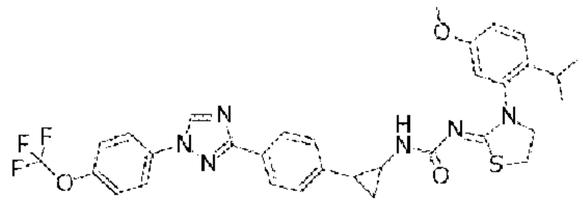
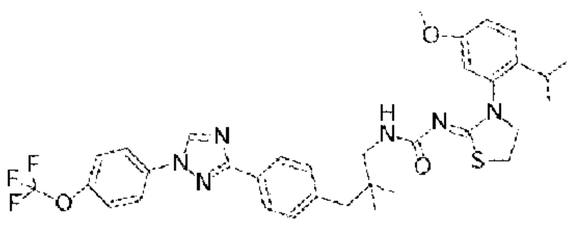
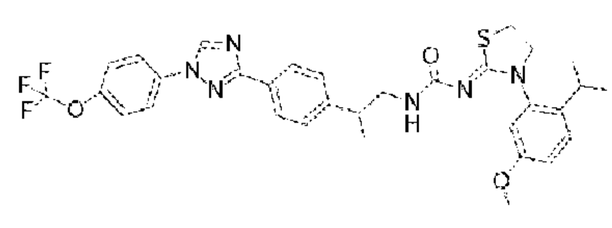
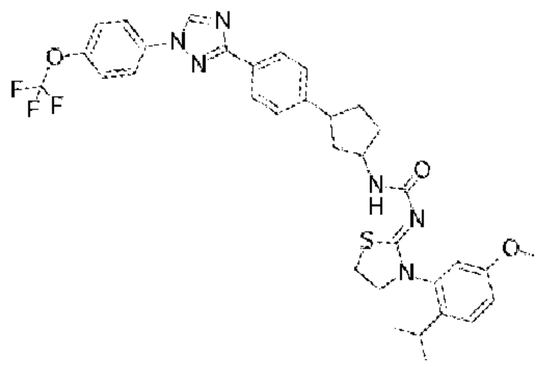
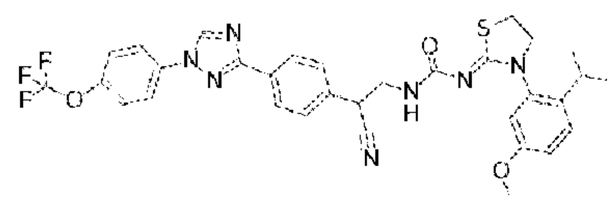
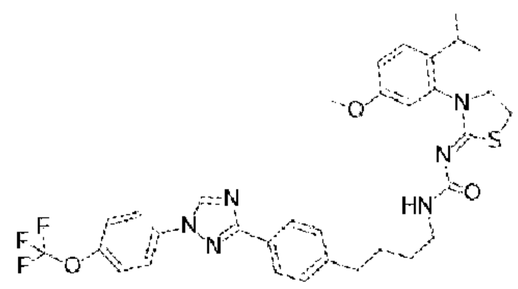
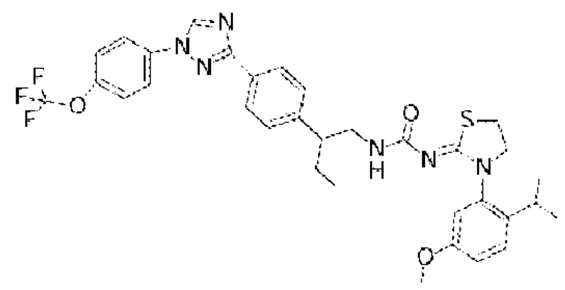
P703

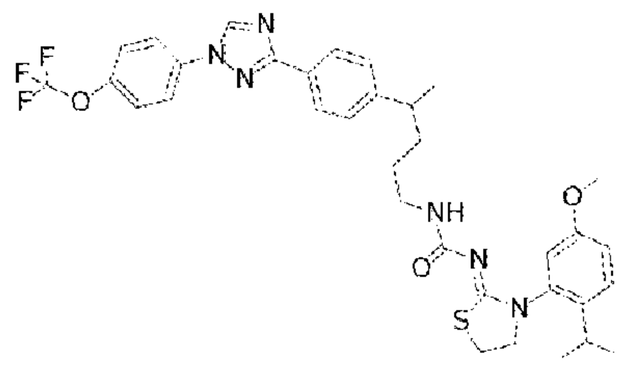
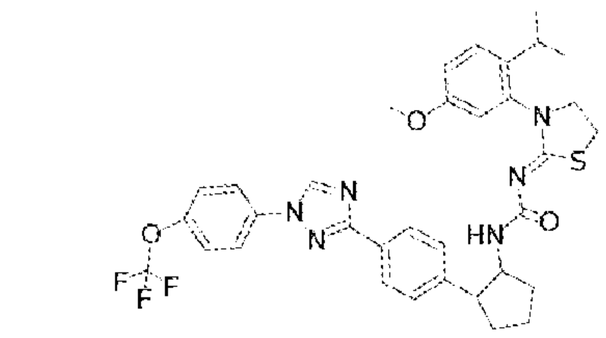
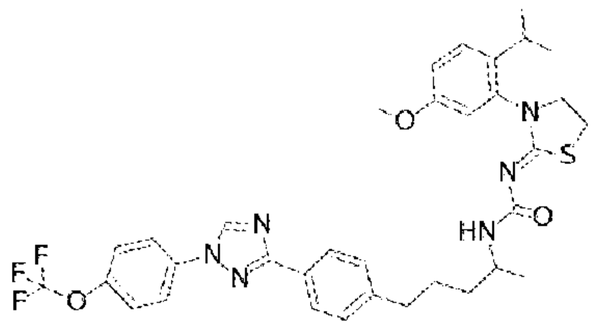
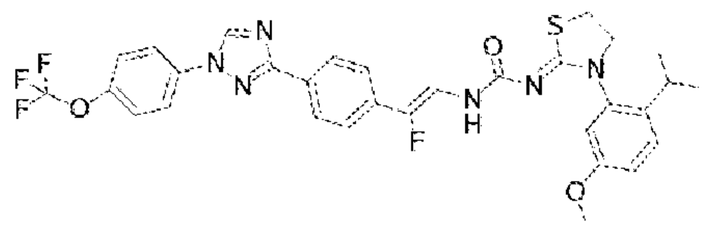
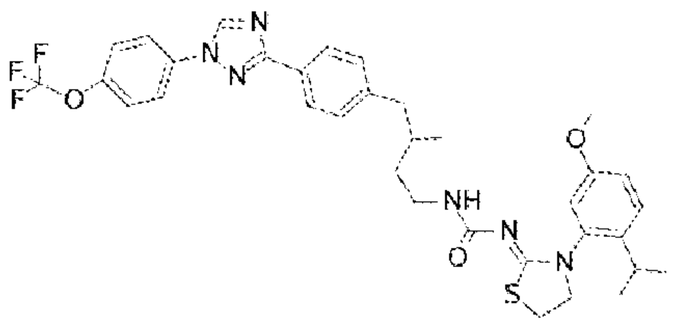
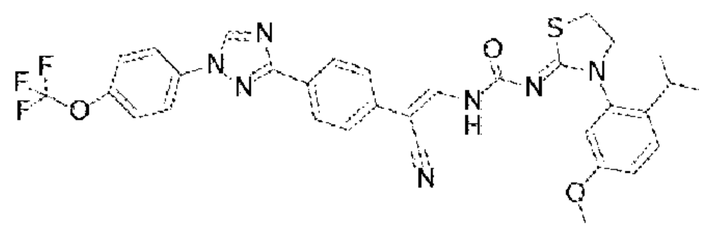
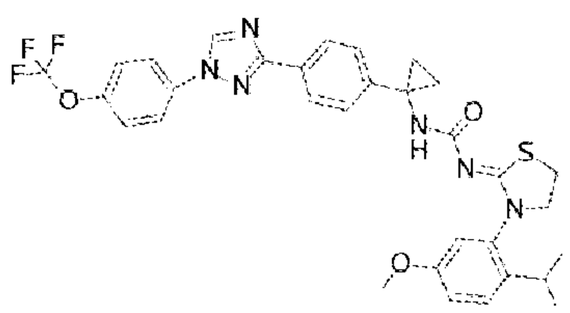
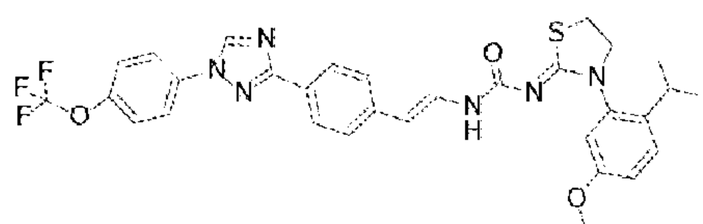
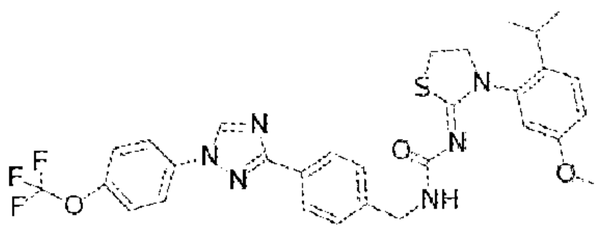
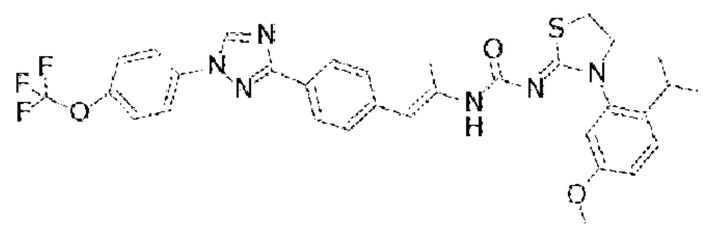


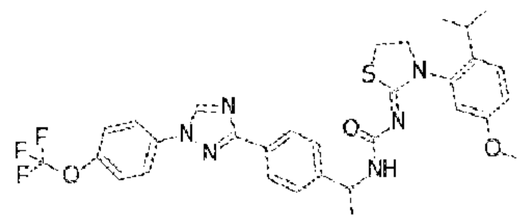
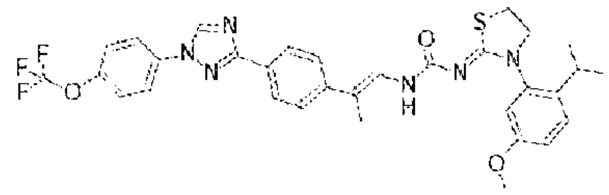
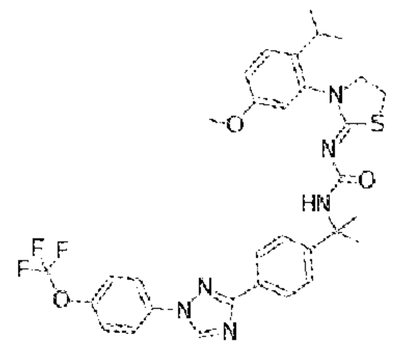
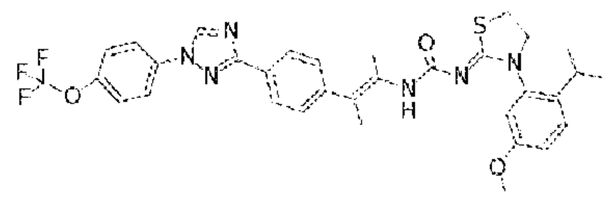
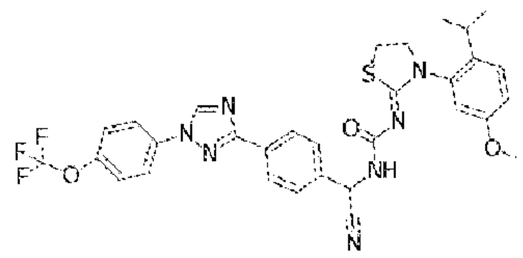
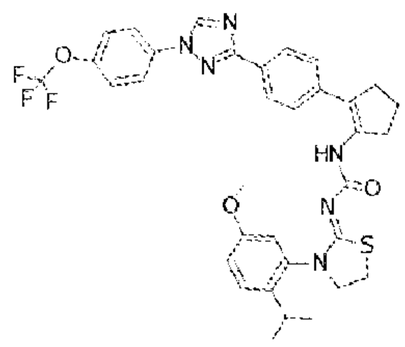
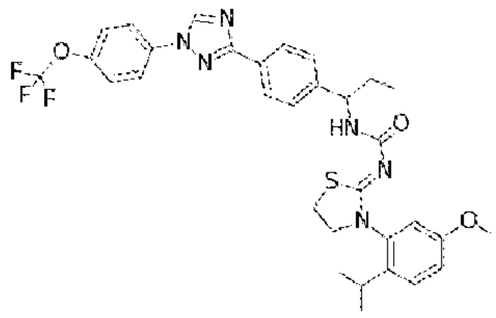
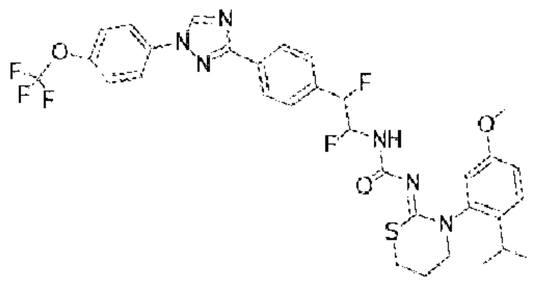
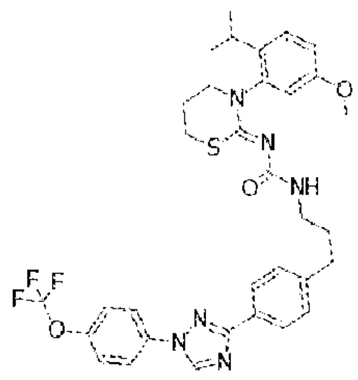
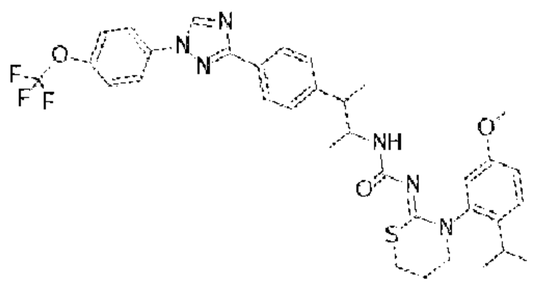
P704

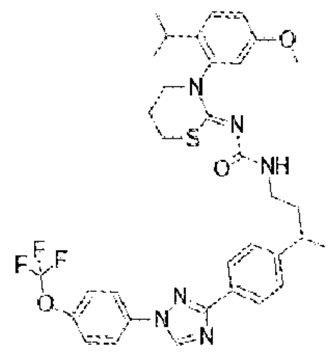
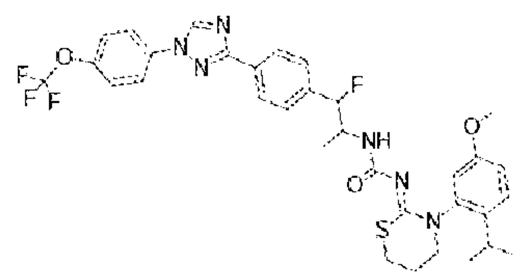
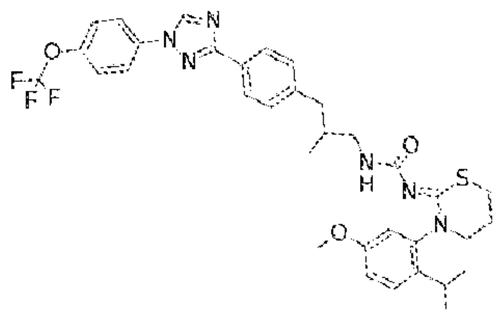
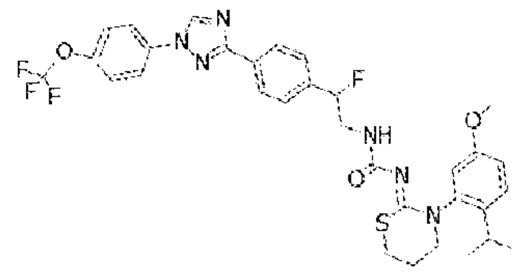
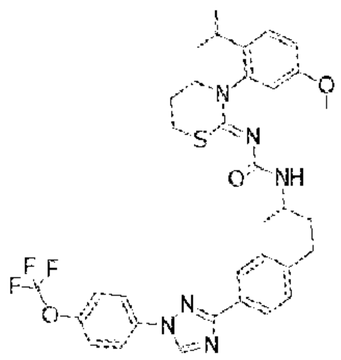
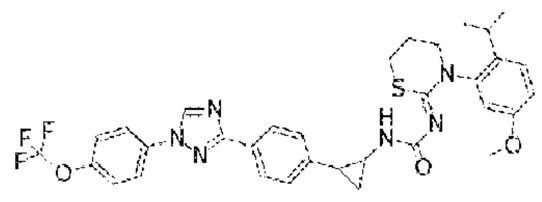
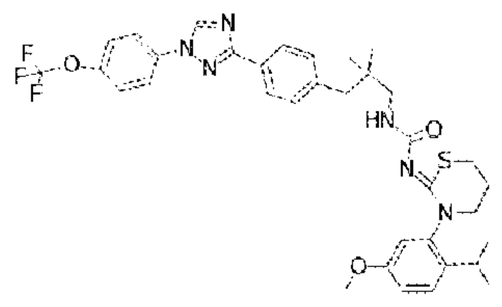
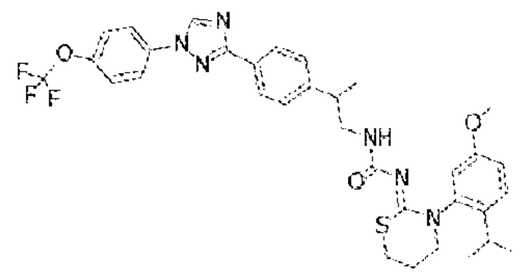
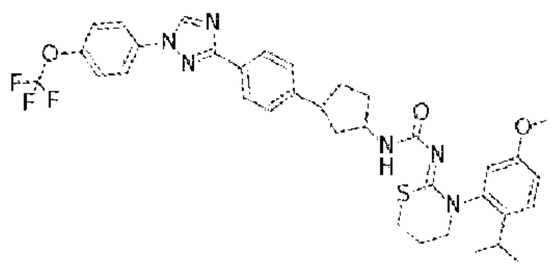
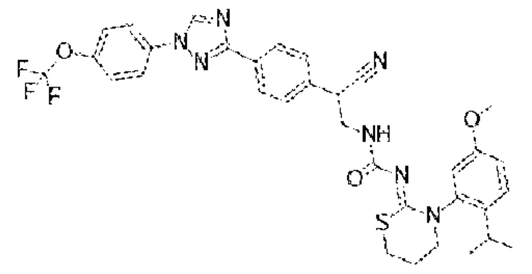


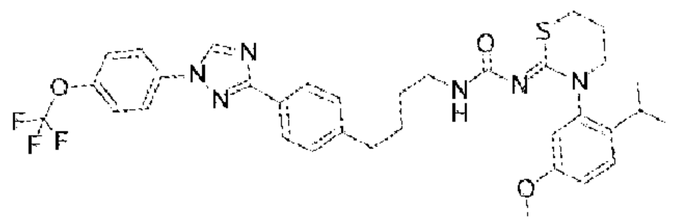
P705

 P706	 P707
 P708	 P709
 P710	 P711
 P712	 P713
 P714	 P715

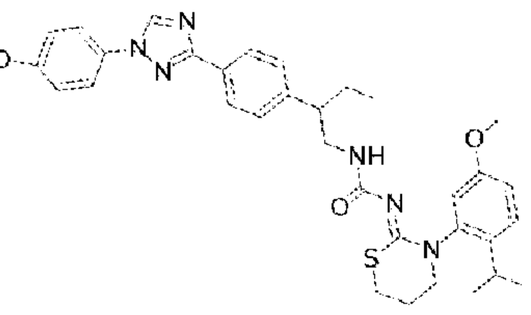
 P716	 P717
 P718	 P719
 P720	 P721
 P722	 P723
 P724	 P725

 P726	 P727
 P728	 P729
 P730	 P731
 P732	 P733
 P734	 P735

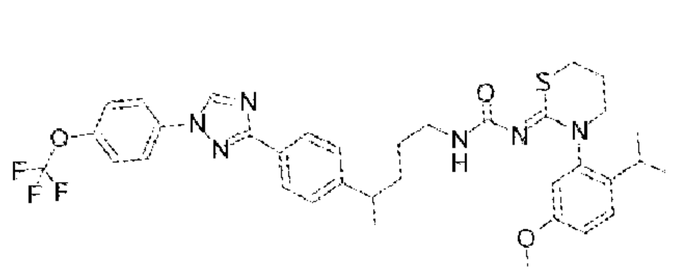
 P736	 P737
 P738	 P739
 P740	 P741
 P742	 P743
 P744	 P745



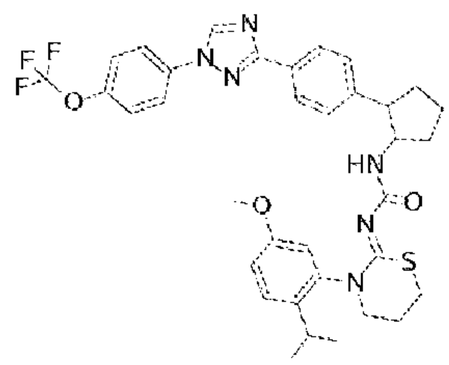
P746



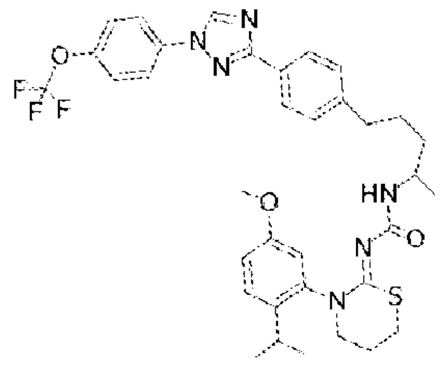
P747



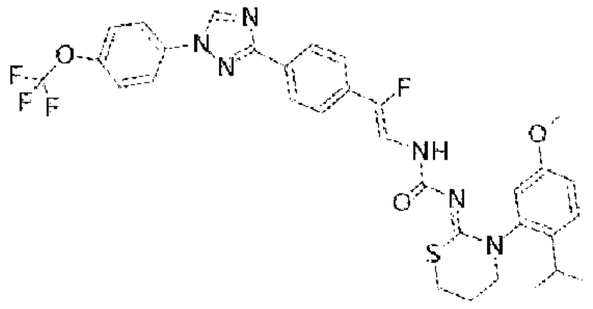
P748



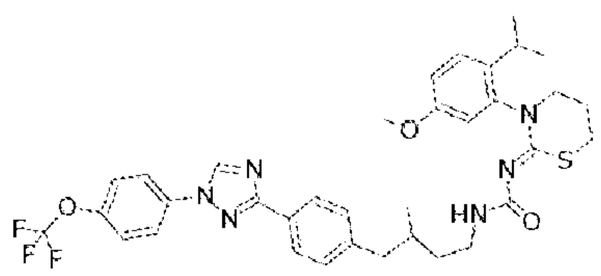
P749



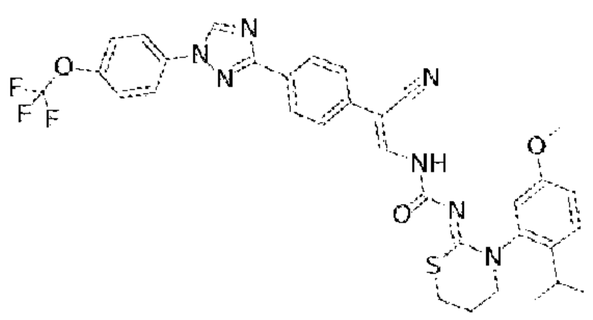
P750



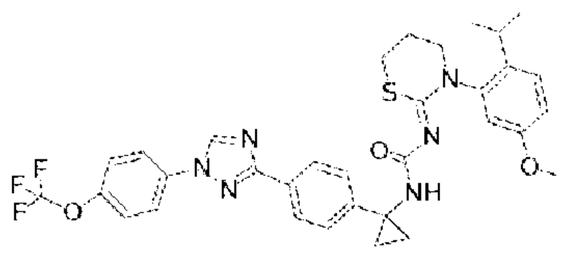
P751



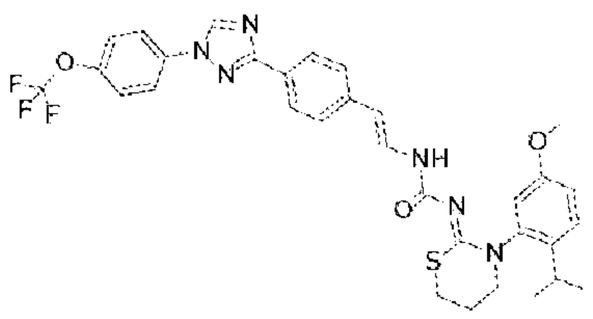
P752



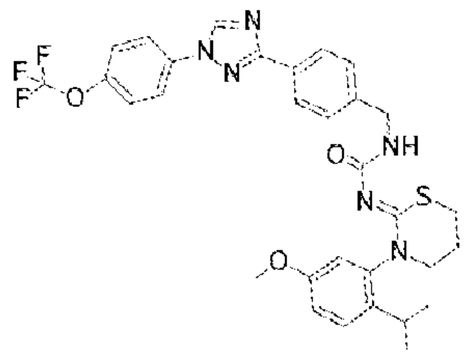
P753



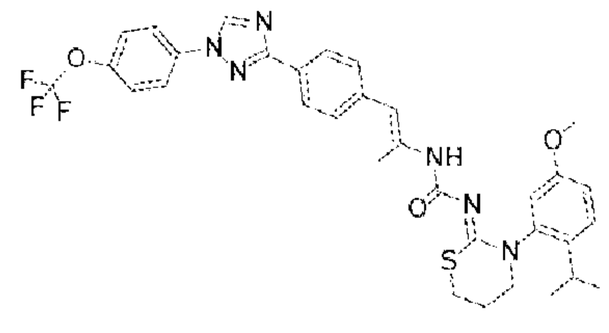
P754



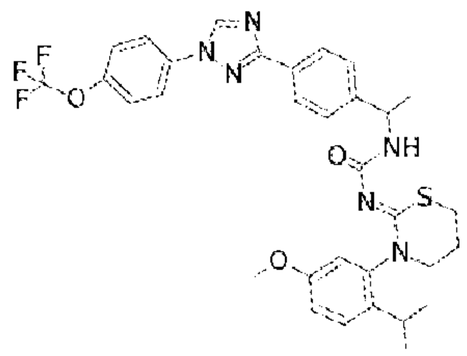
P755



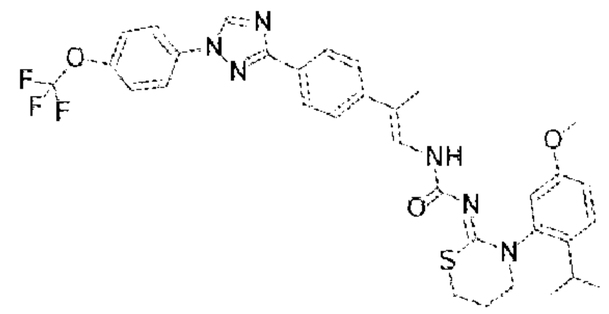
P756



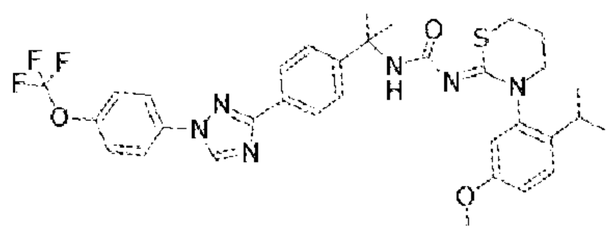
P757



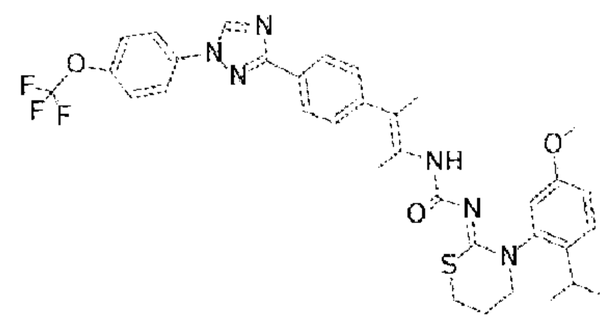
P758



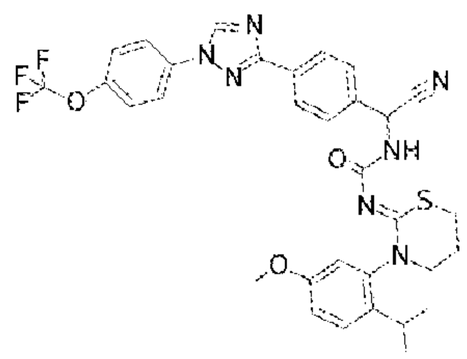
P759



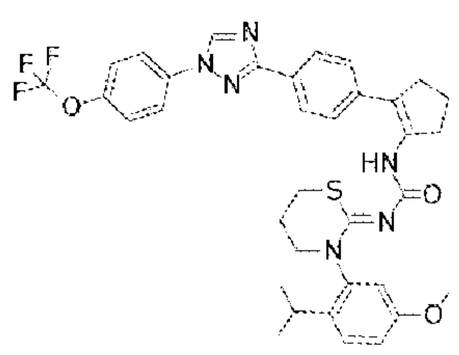
P760



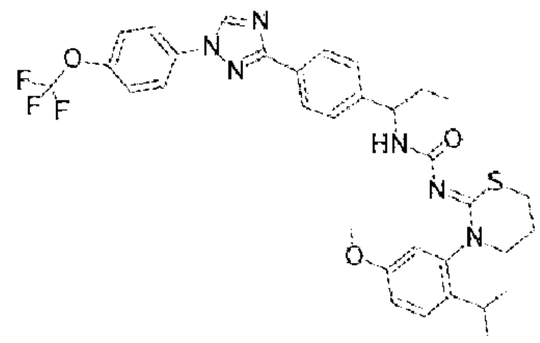
P761



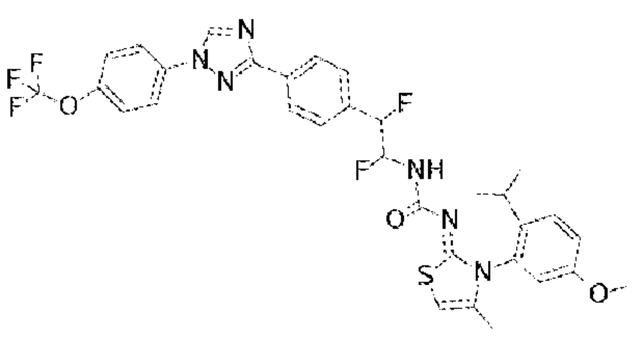
P762



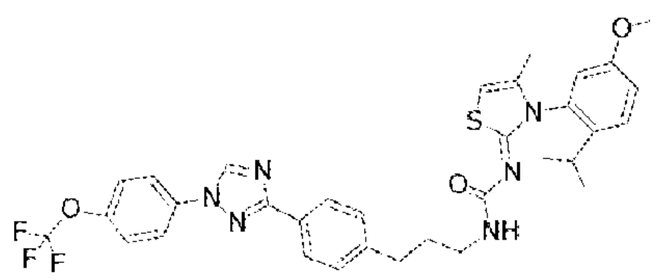
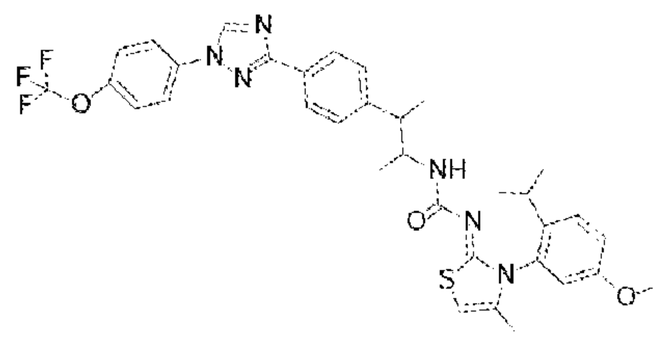
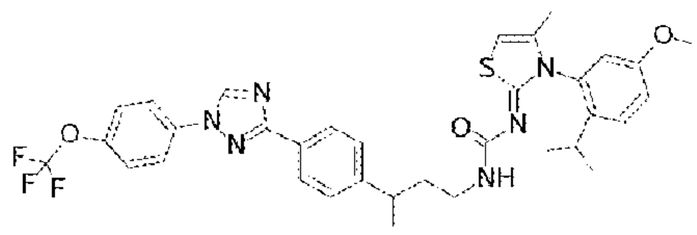
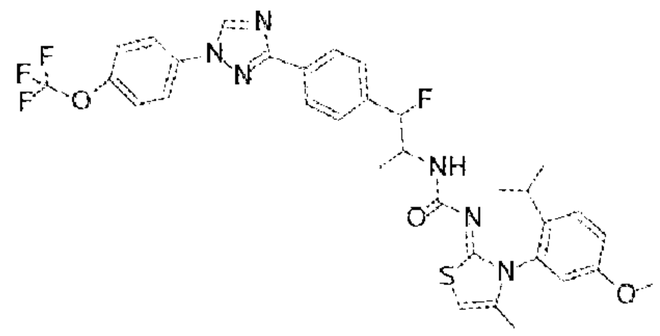
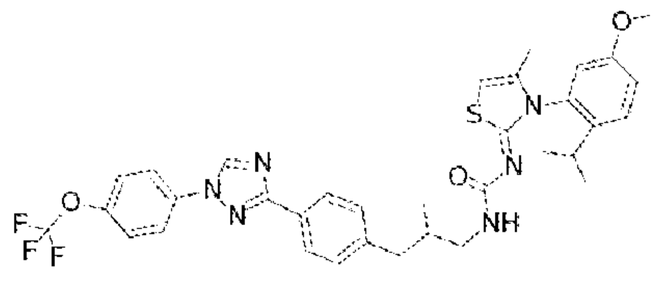
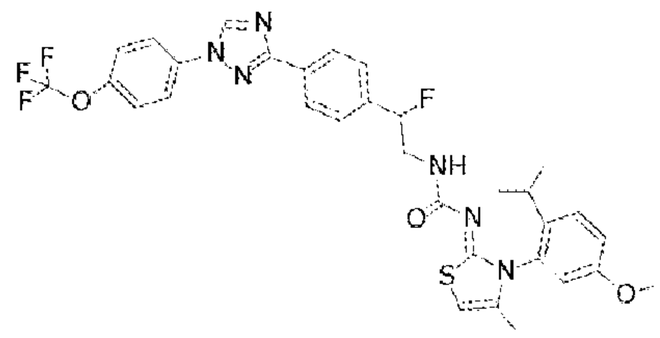
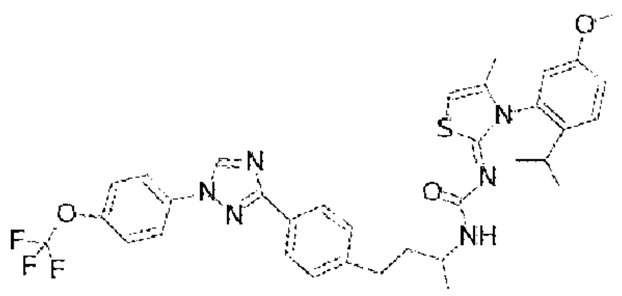
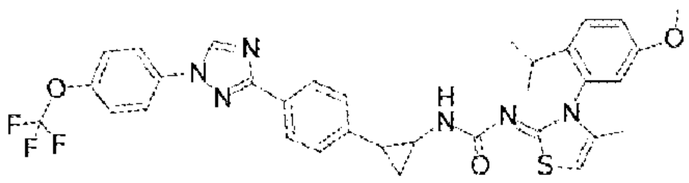
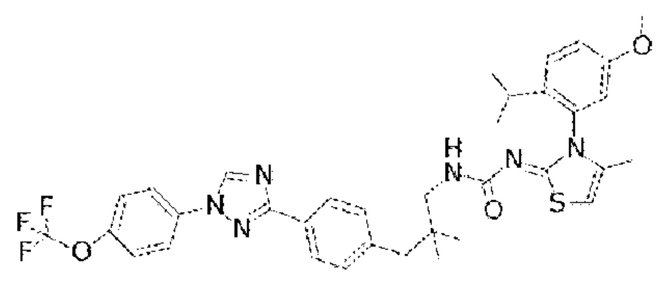
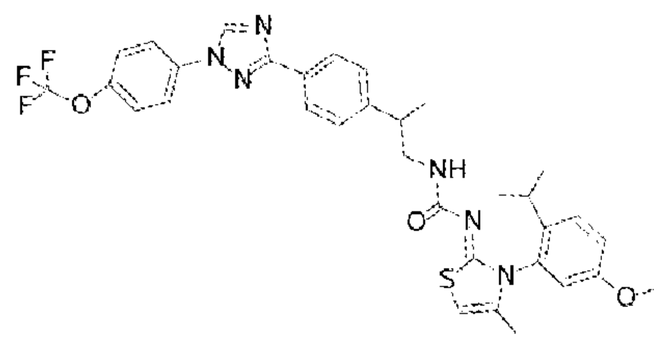
P763

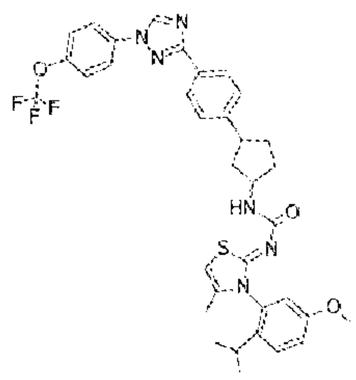
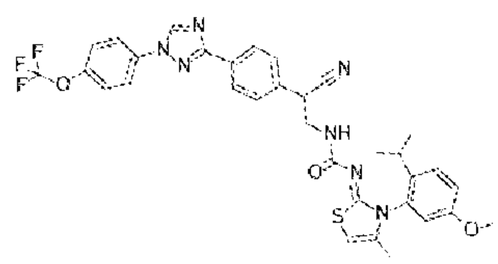
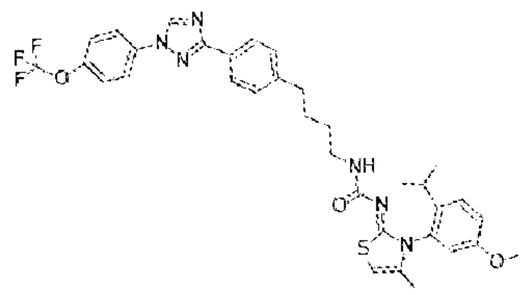
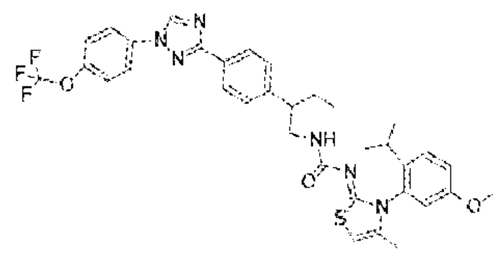
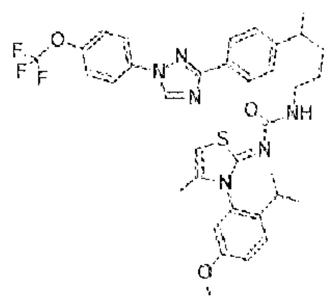
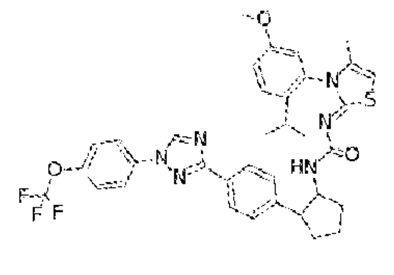
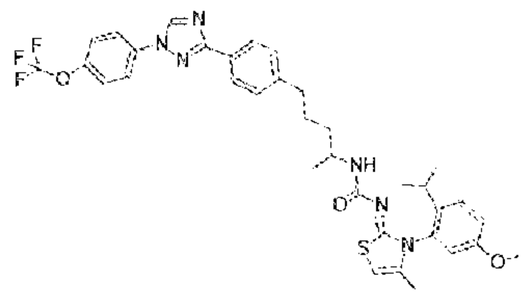
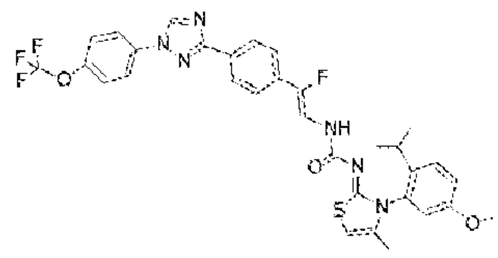
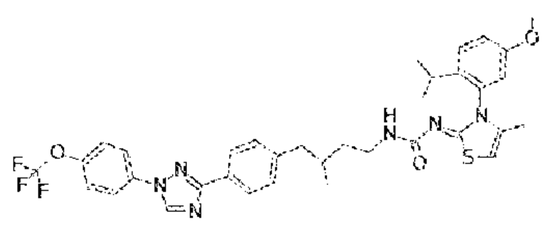
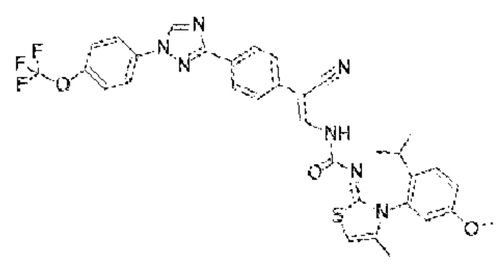


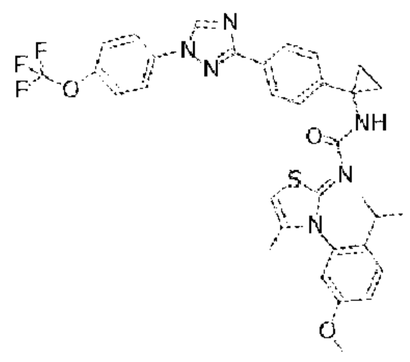
P764



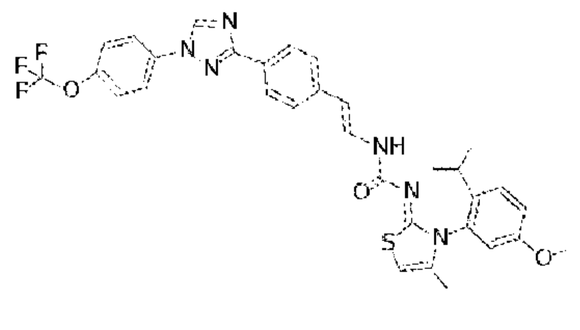
P765

 P766	 P767
 P768	 P769
 P770	 P771
 P772	 P773
 P774	 P775

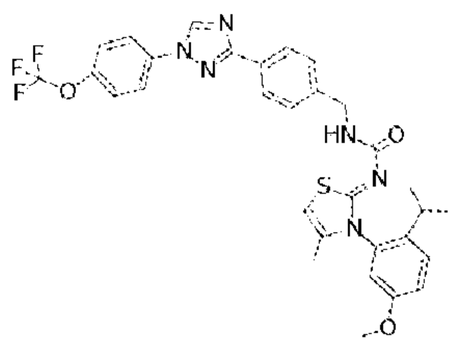
 P776	 P777
 P778	 P779
 P780	 P781
 P782	 P783
 P784	 P785



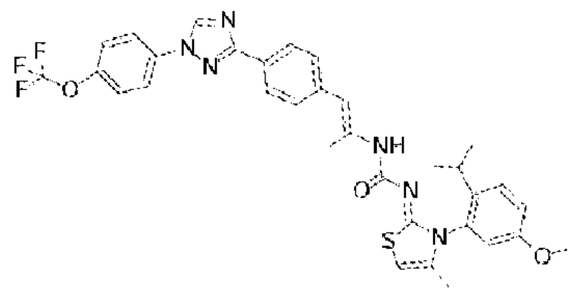
P786



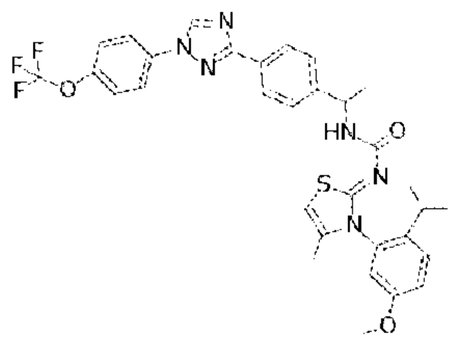
P787



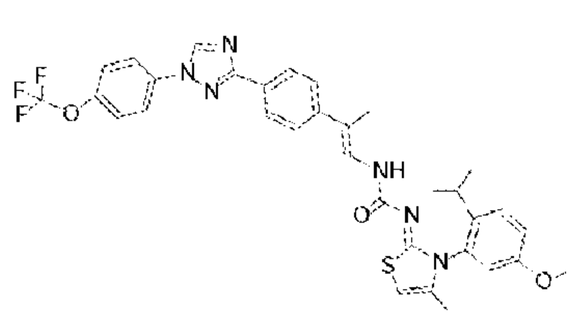
P788



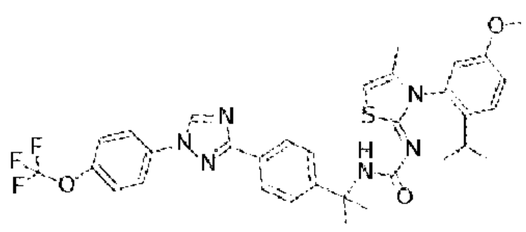
P789



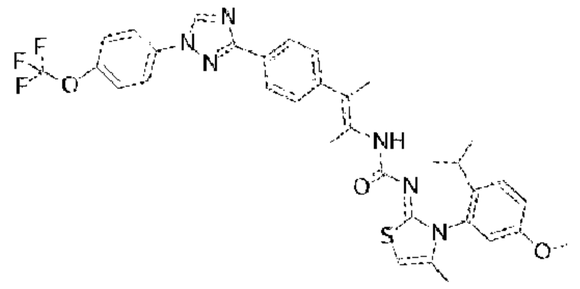
P790



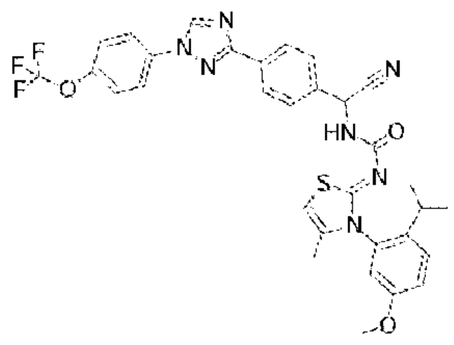
P791



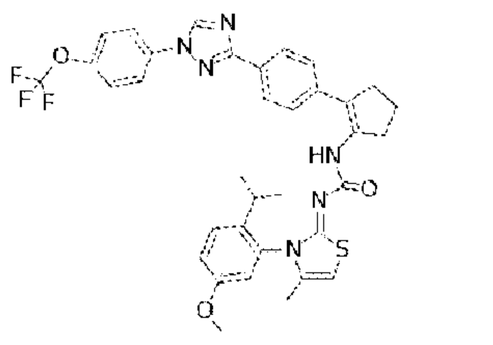
P792



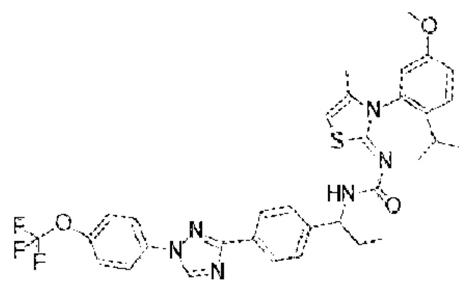
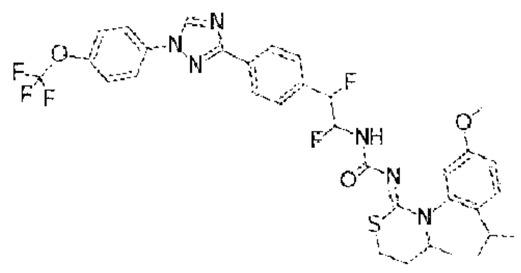
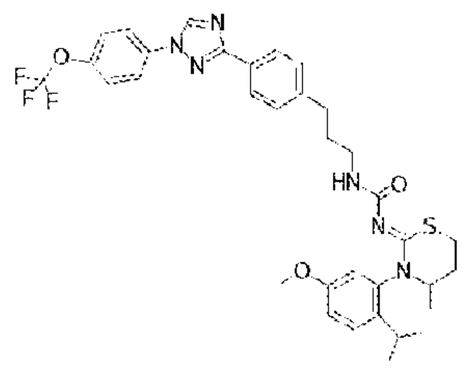
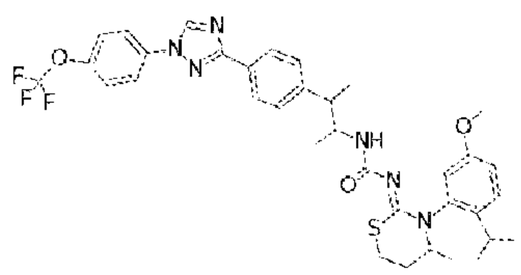
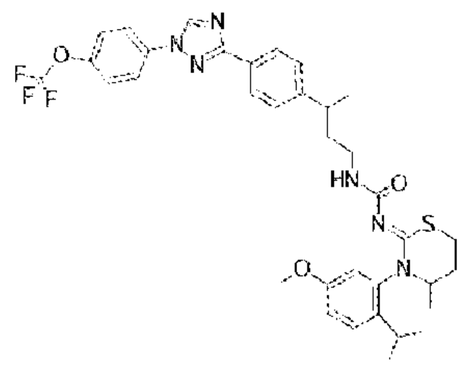
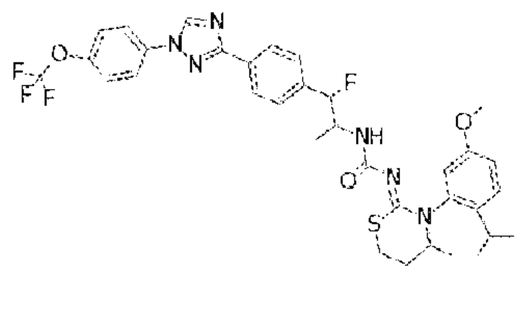
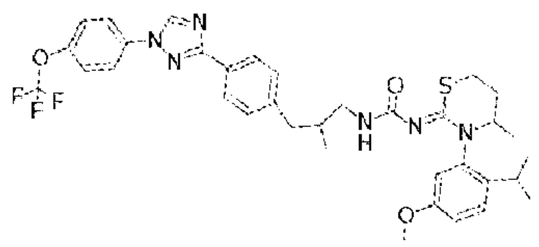
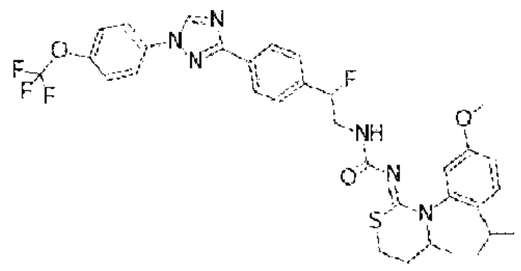
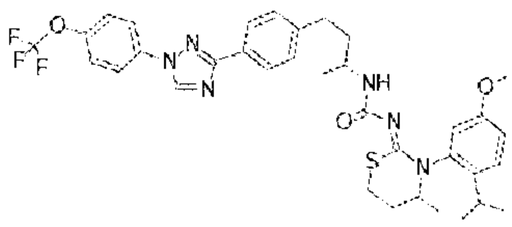
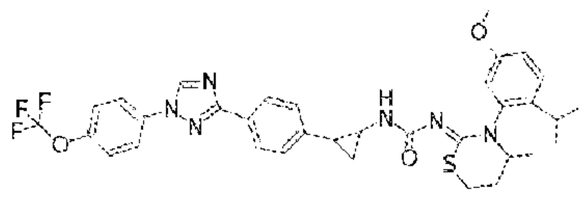
P793

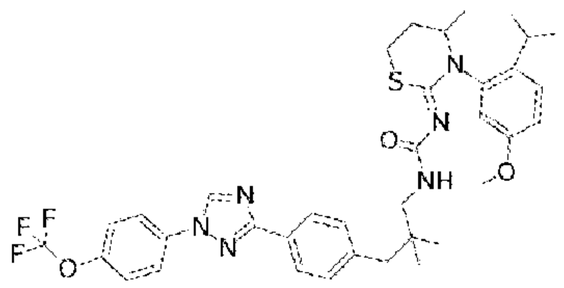
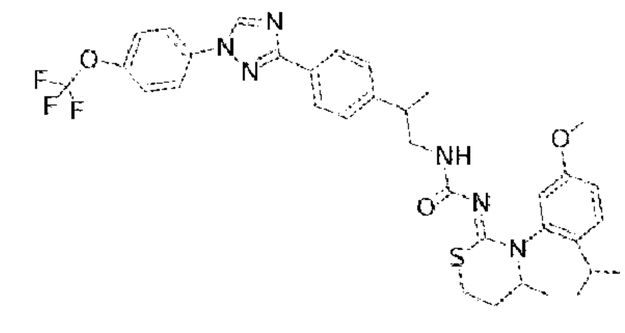
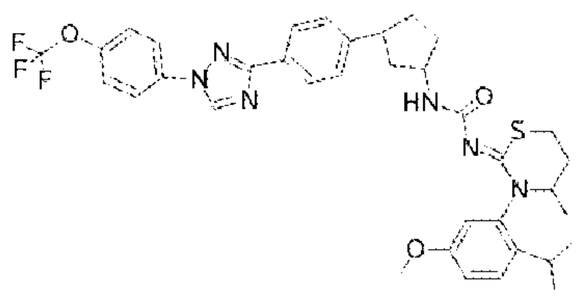
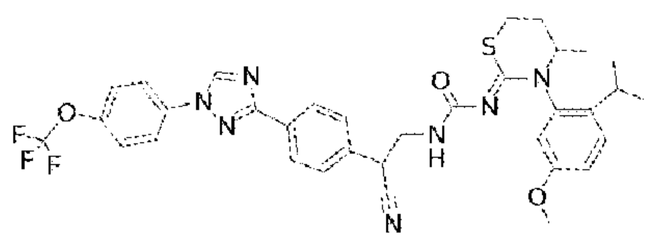
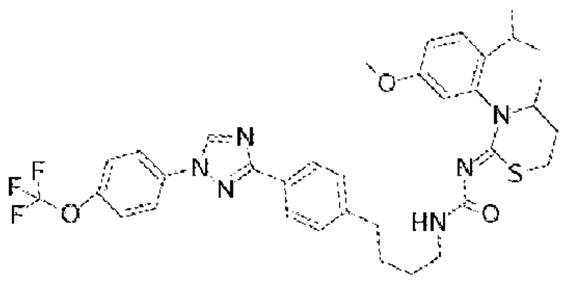
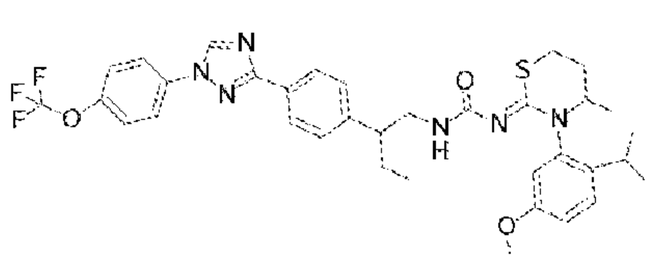
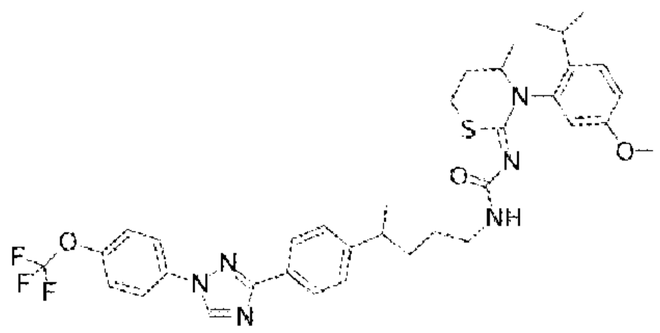
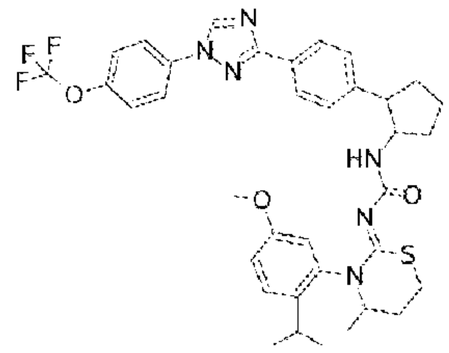
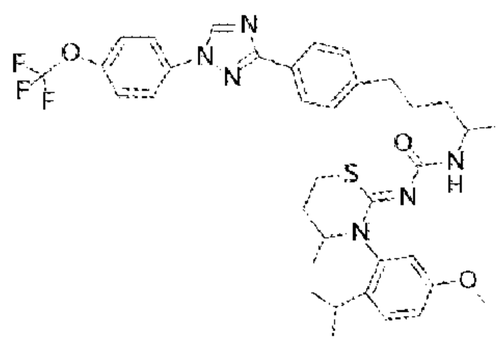
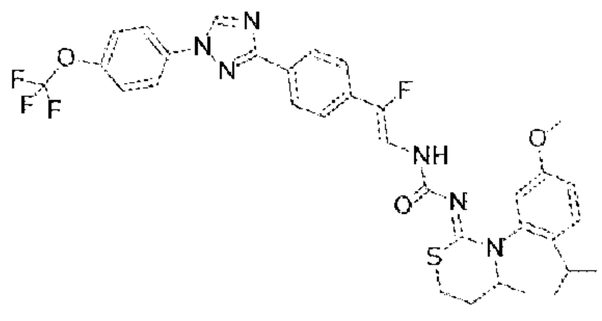


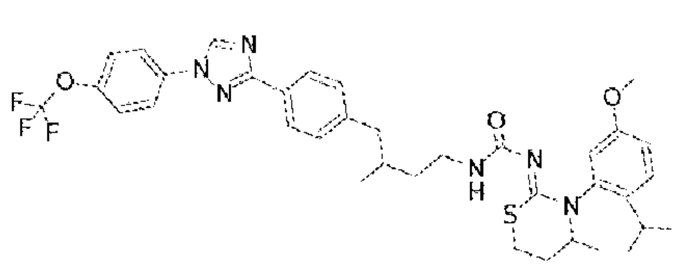
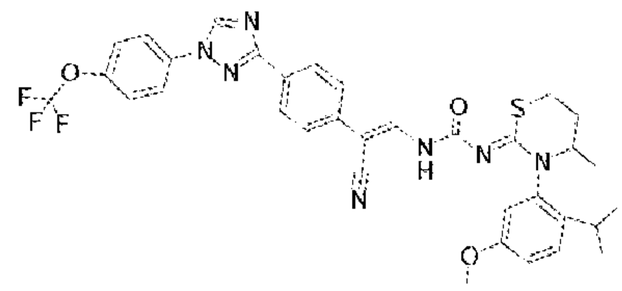
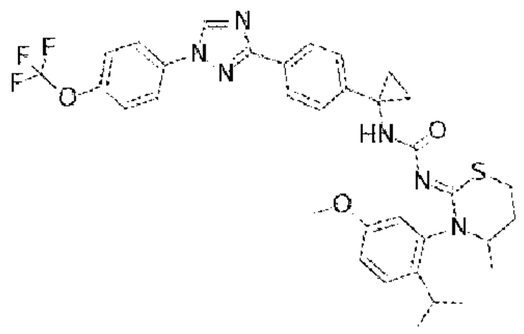
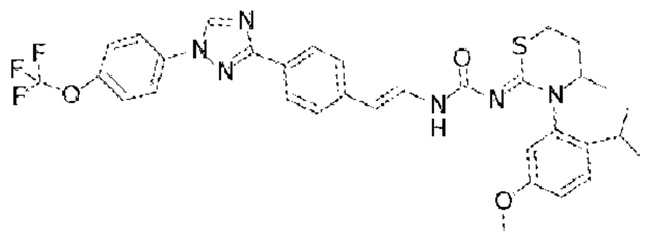
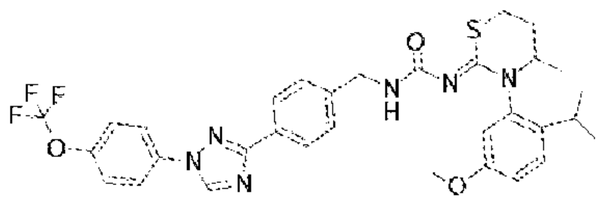
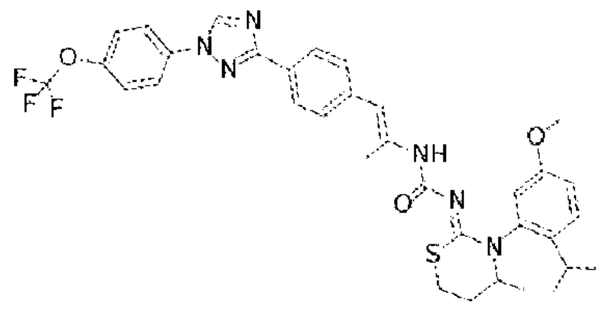
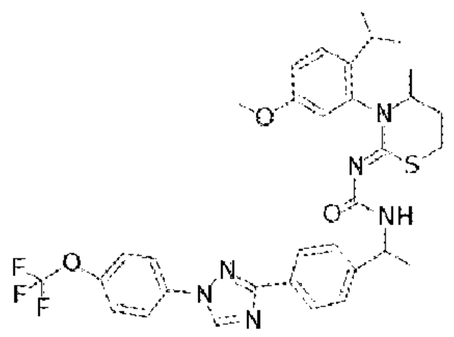
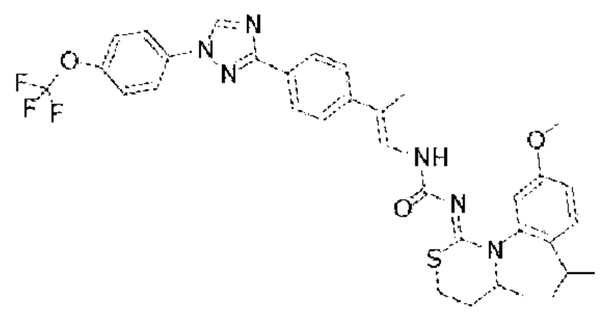
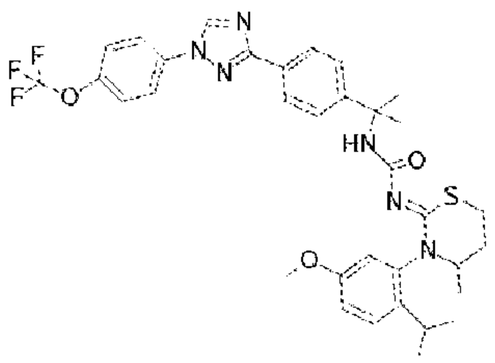
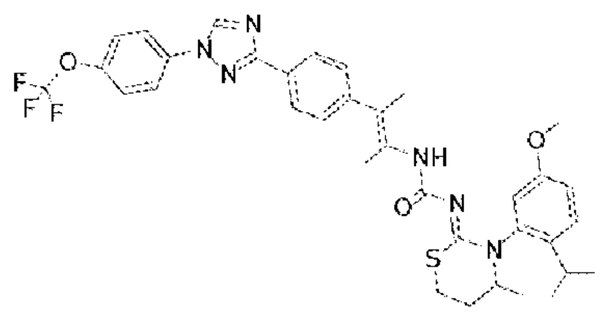
P794

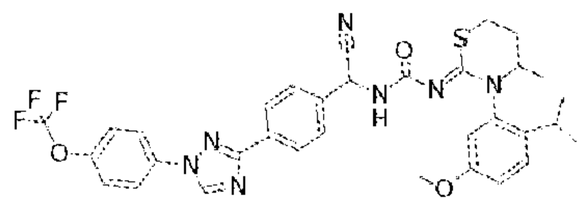


P795

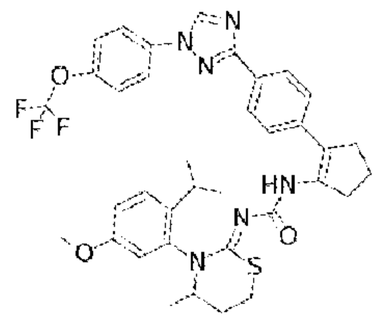
 P796	 P797
 P798	 P799
 P800	 P801
 P802	 P803
 P804	 P805

 P806	 P807
 P808	 P809
 P810	 P811
 P812	 P813
 P814	 P815

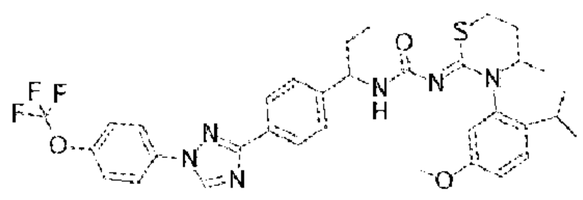
	
P816	P817
	
P818	P819
	
P820	P821
	
P822	P823
	
P824	P825



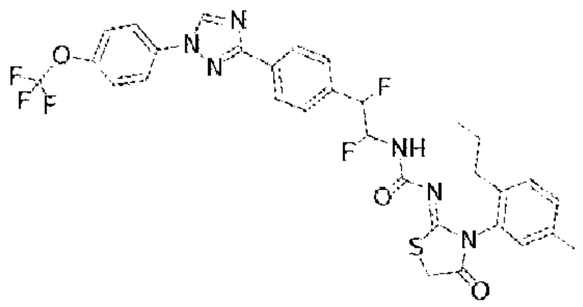
P826



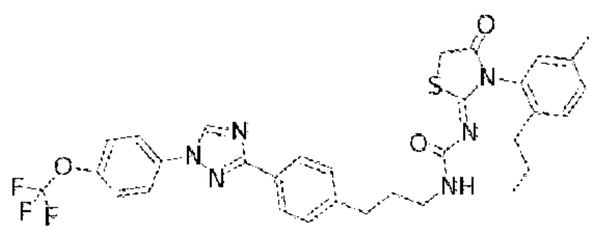
P827



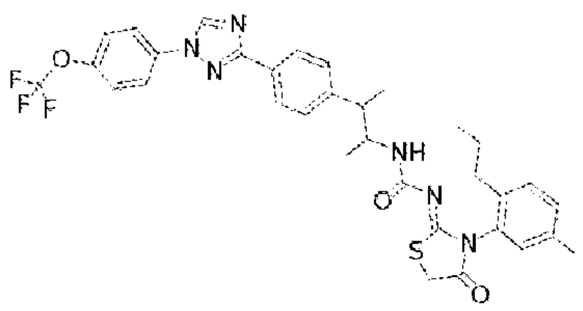
P828



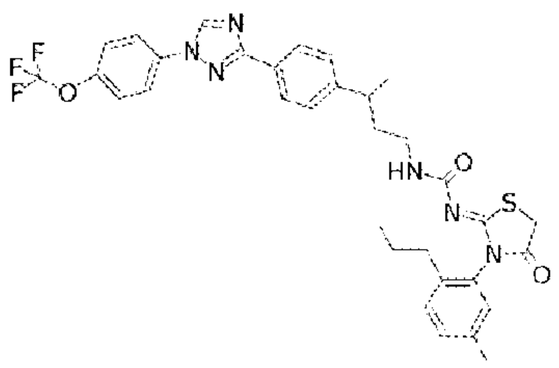
P829



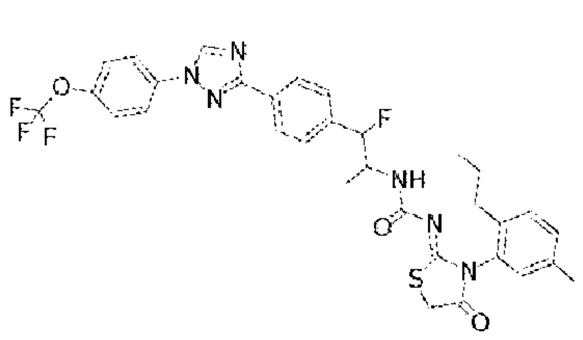
P830



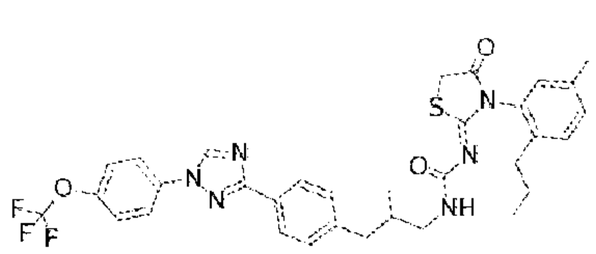
P831



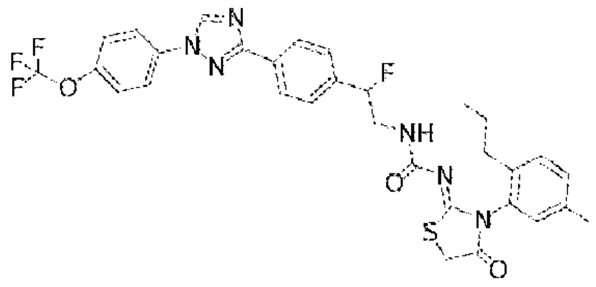
P832



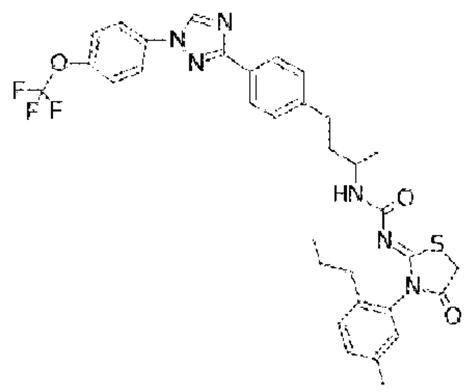
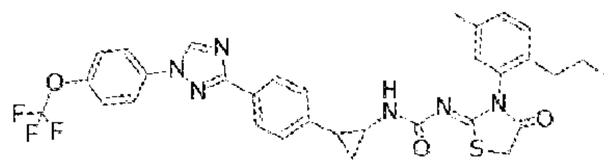
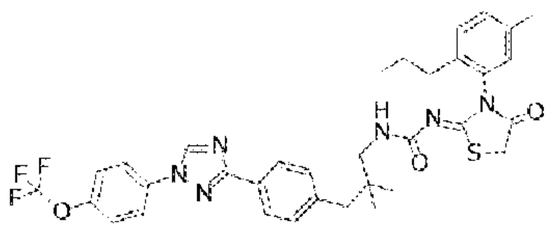
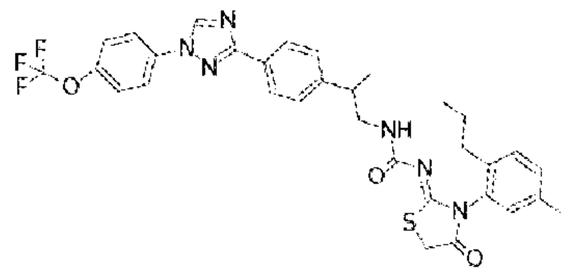
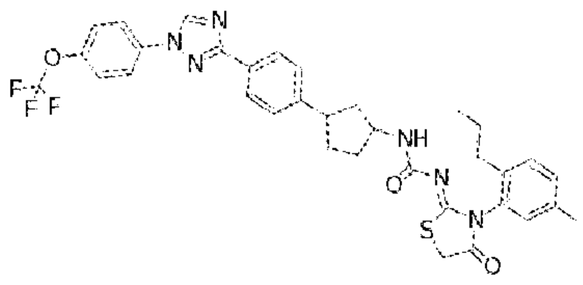
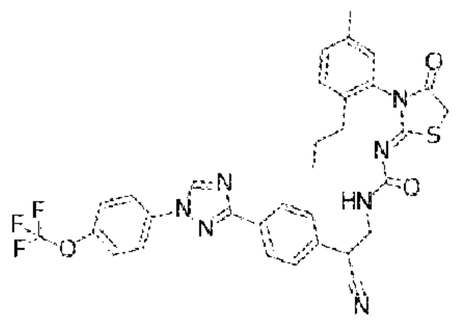
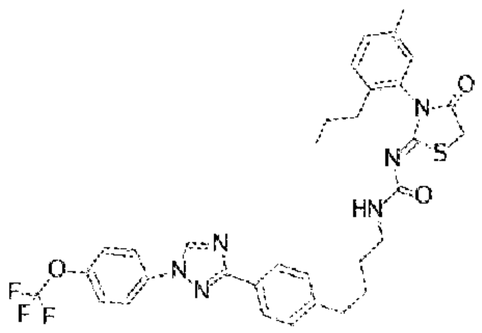
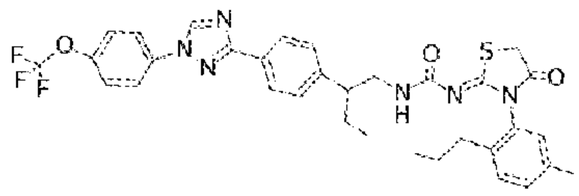
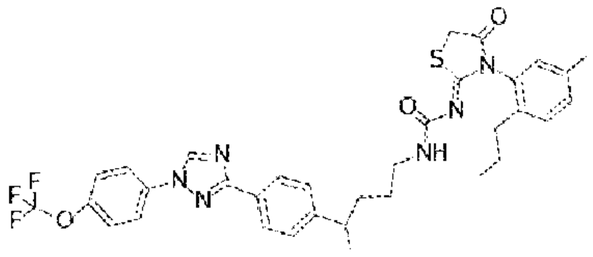
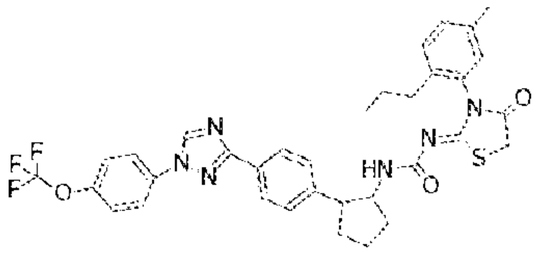
P833

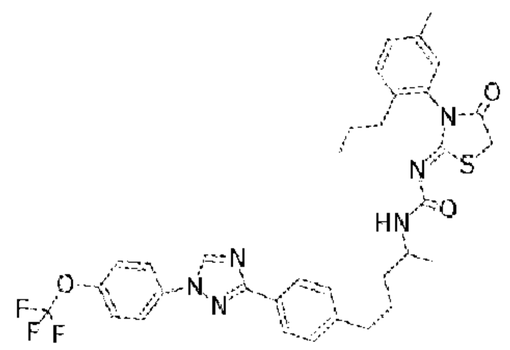
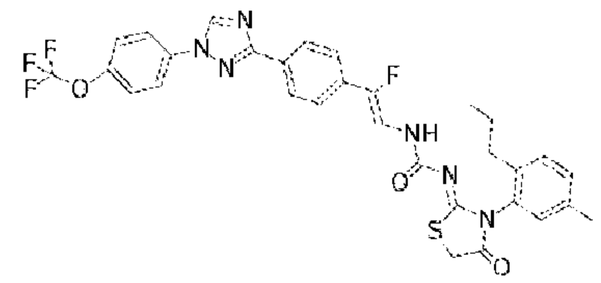
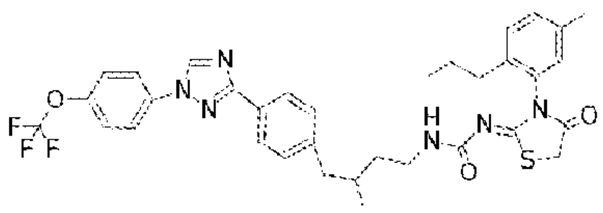
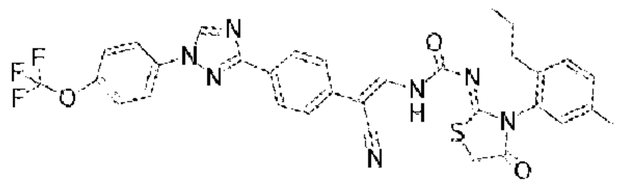
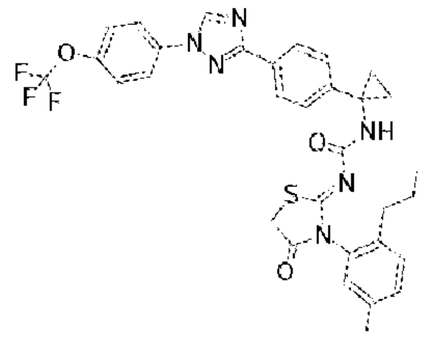
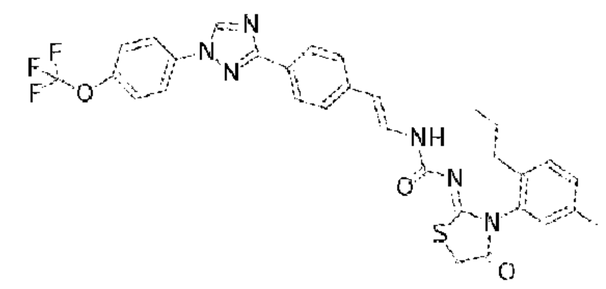
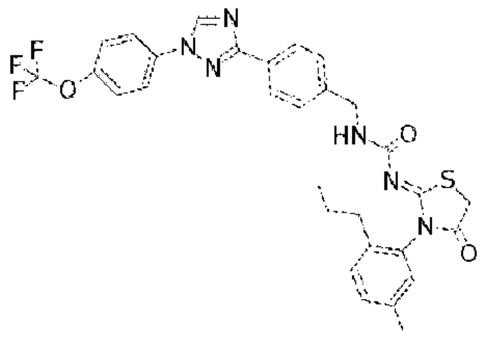
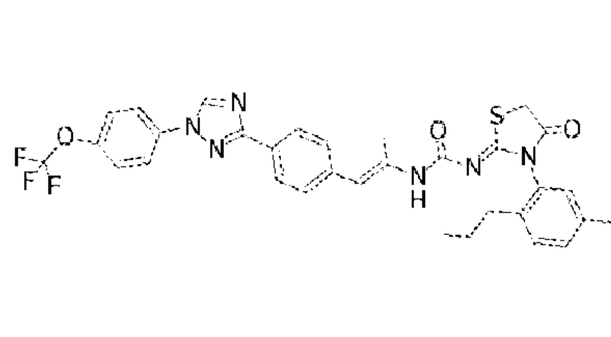
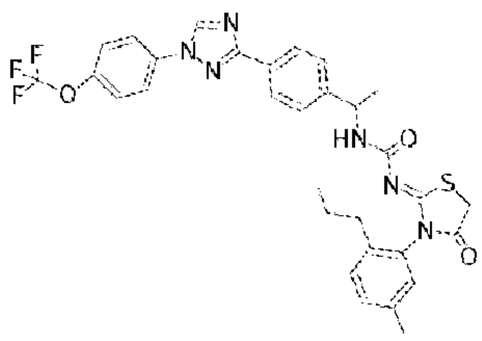
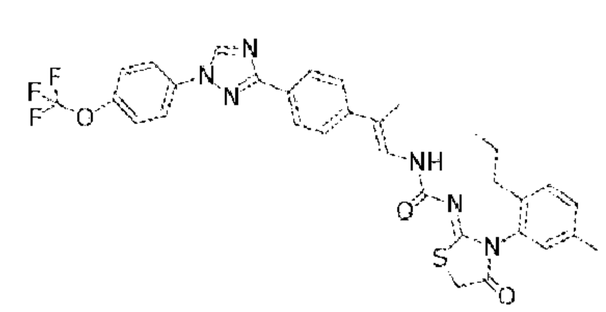


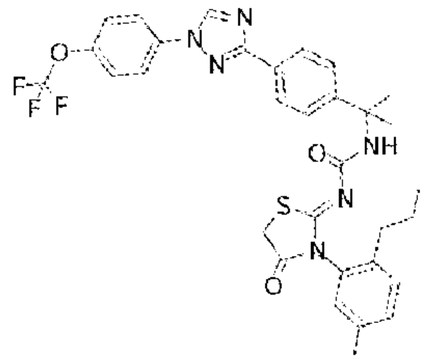
P834



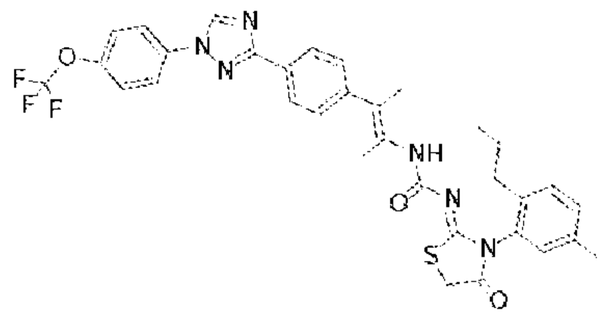
P835

	
P836	P837
	
P838	P839
	
P840	P841
	
P842	P843
	
P844	P845

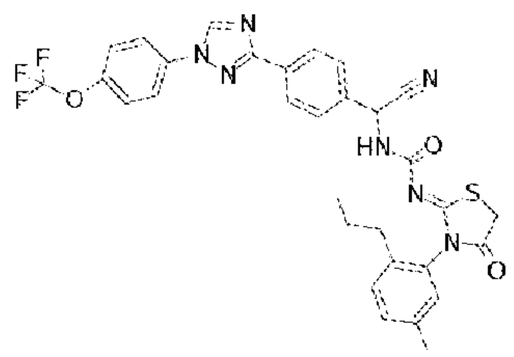
 P846	 P847
 P848	 P849
 P850	 P851
 P852	 P853
 P854	 P855



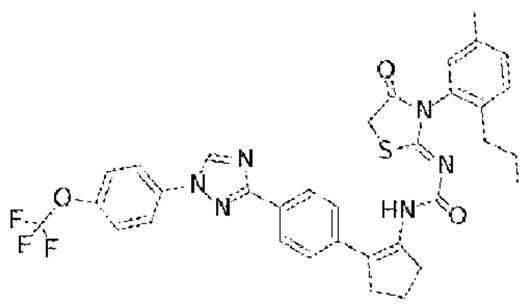
P856



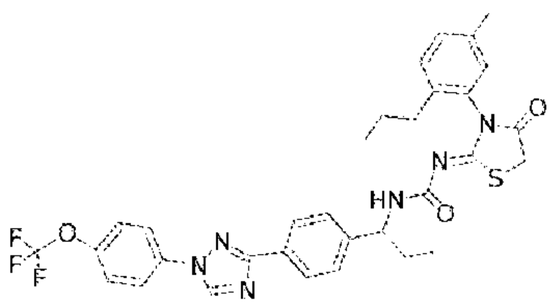
P857



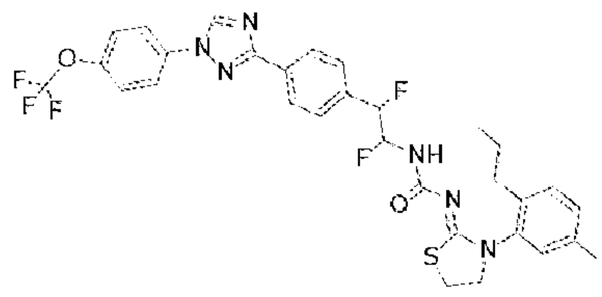
P858



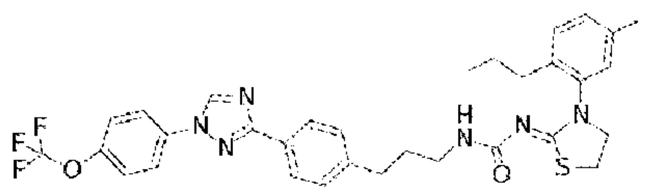
P859



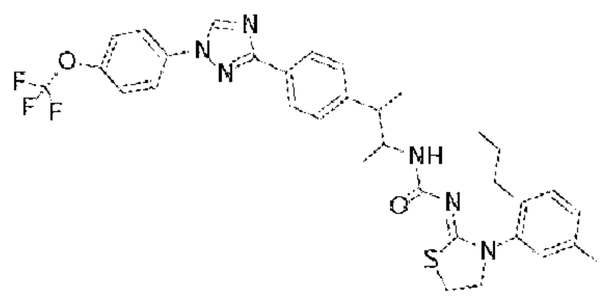
P860



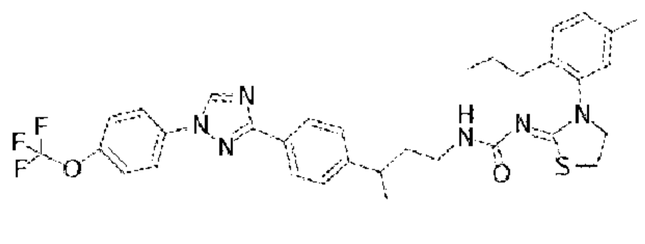
P861



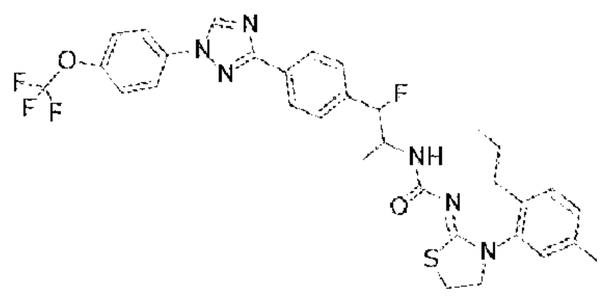
P862



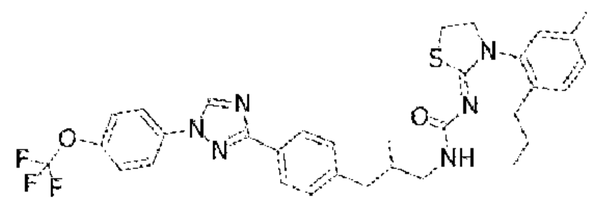
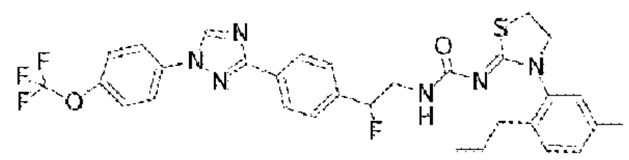
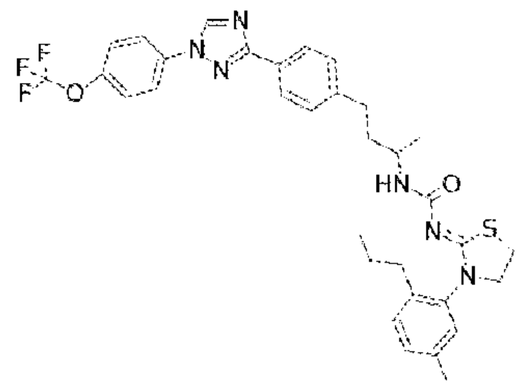
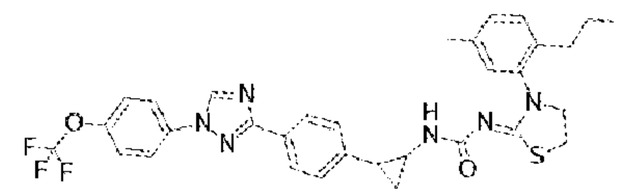
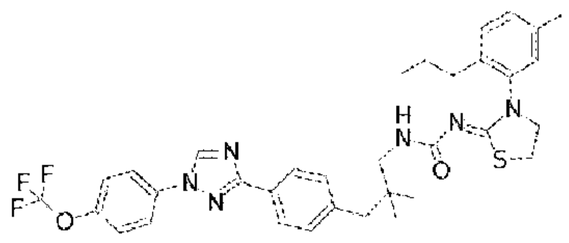
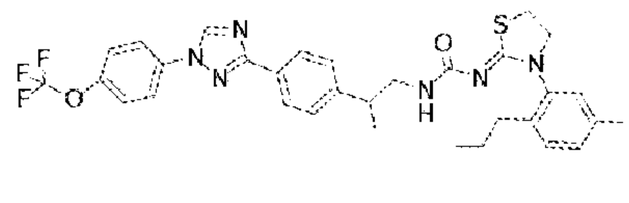
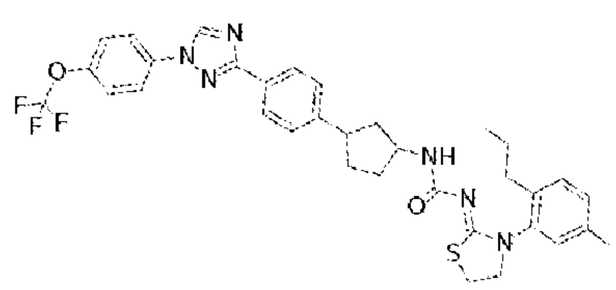
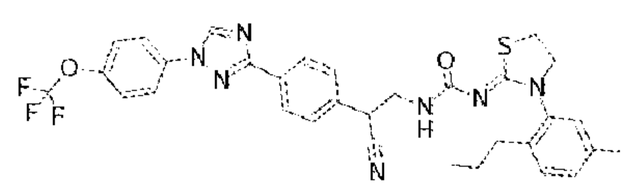
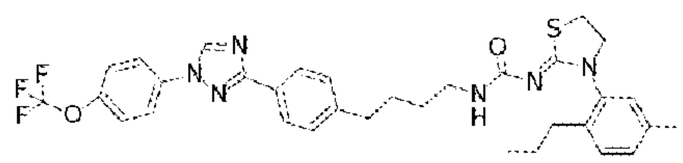
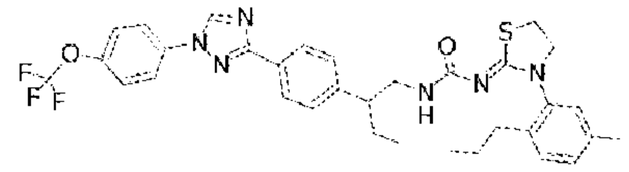
P863

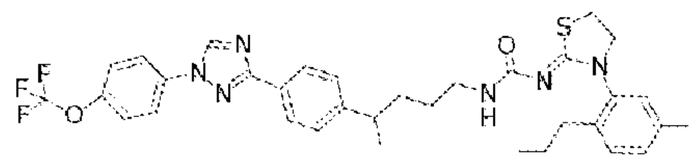
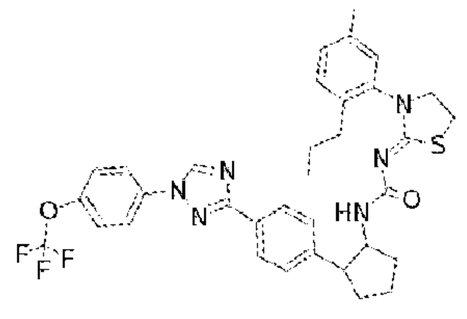
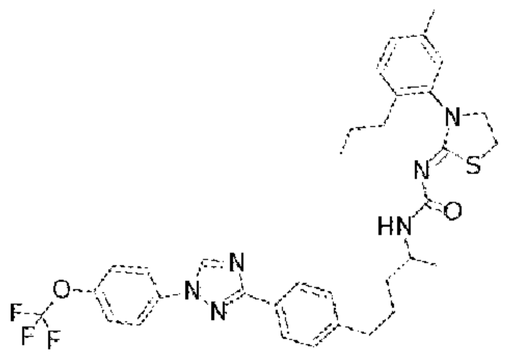
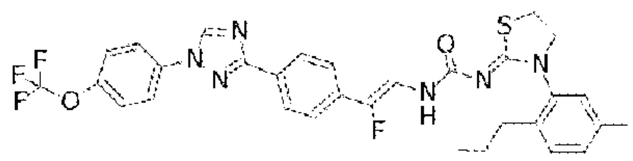
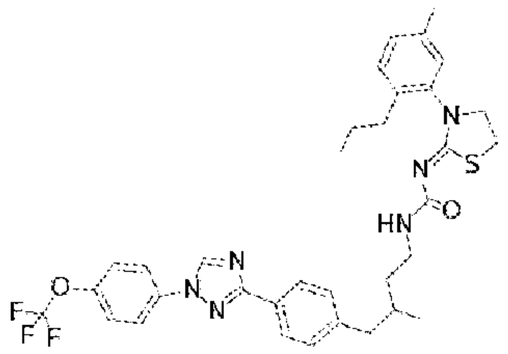
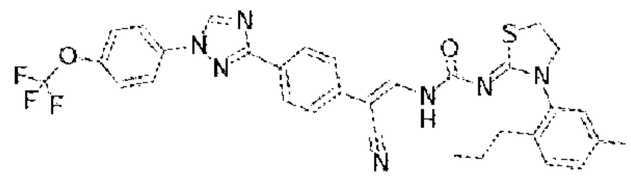
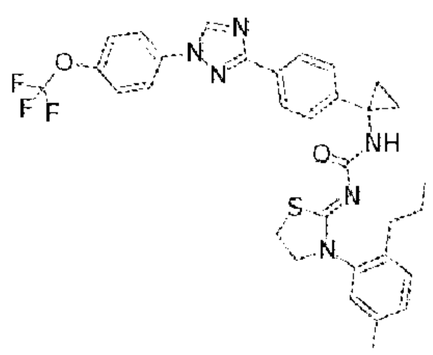
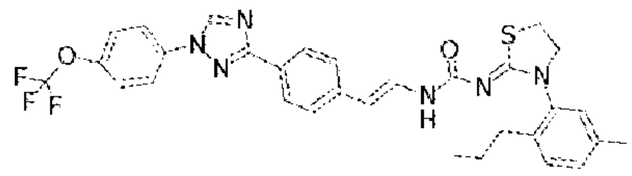
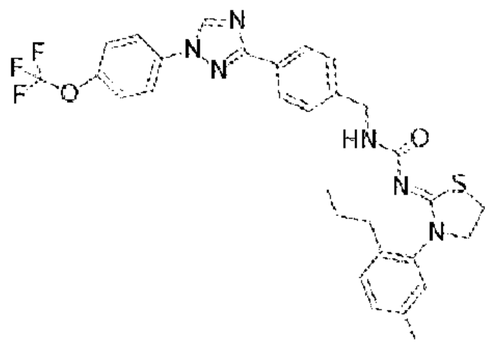
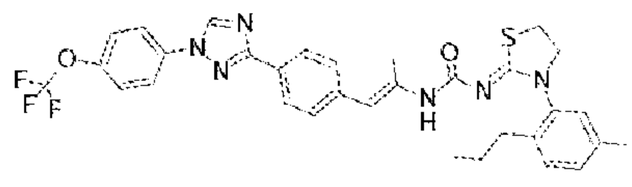


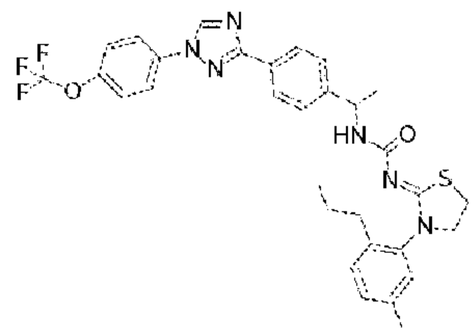
P864



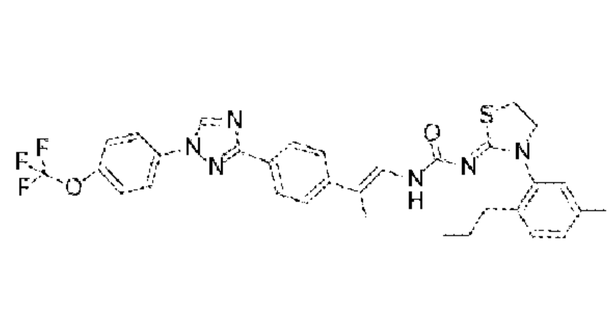
P865

 P866	 P867
 P868	 P869
 P870	 P871
 P872	 P873
 P874	 P875

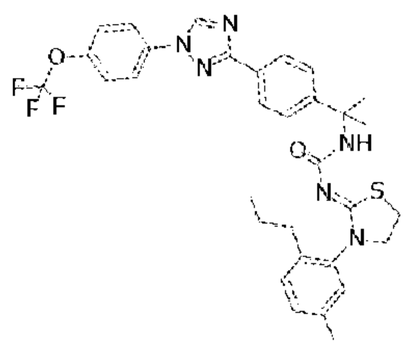
 P876	 P877
 P878	 P879
 P880	 P881
 P882	 P883
 P884	 P885



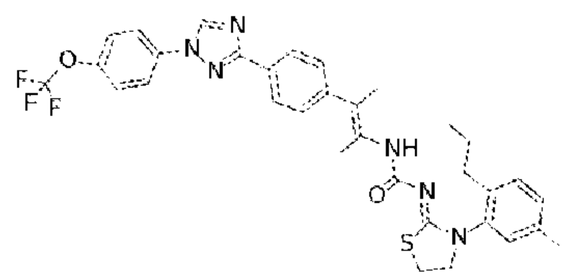
P886



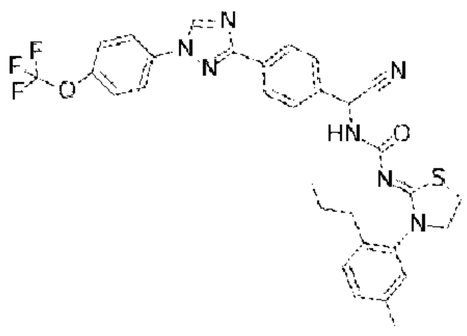
P887



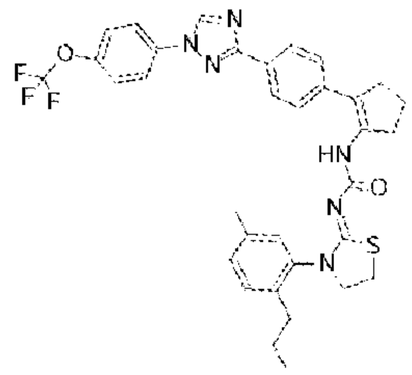
P888



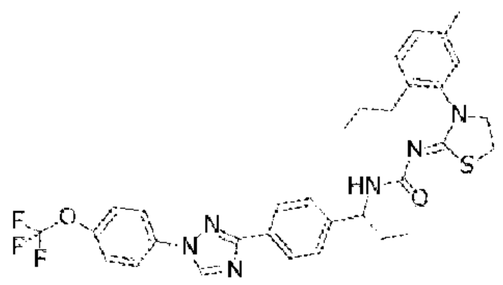
P889



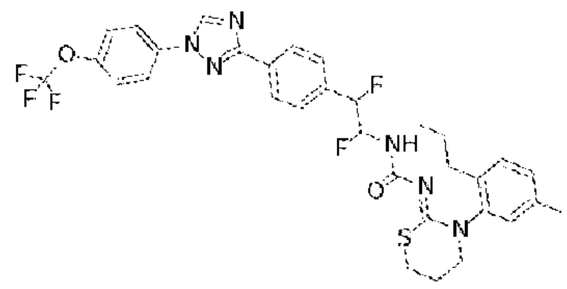
P890



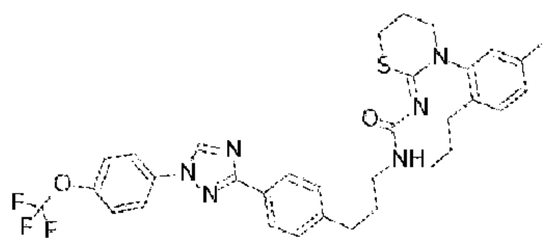
P891



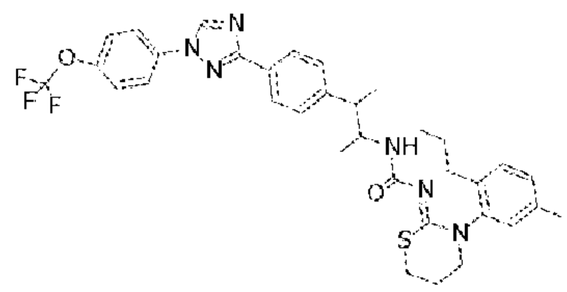
P892



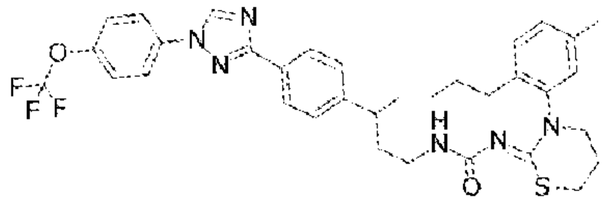
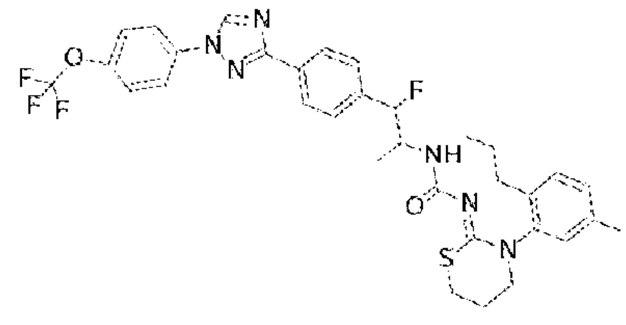
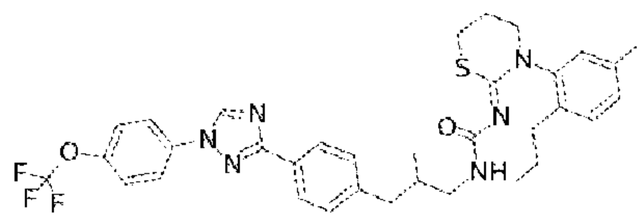
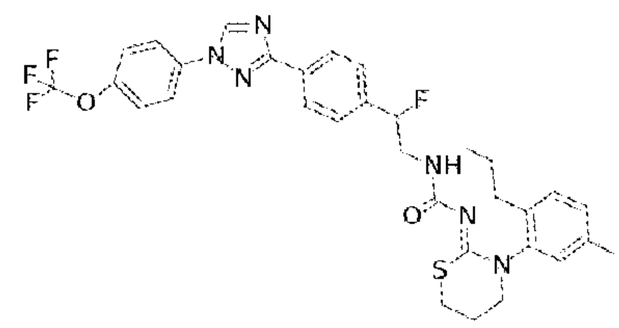
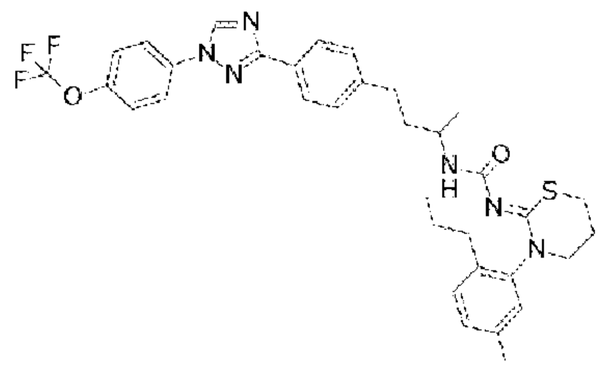
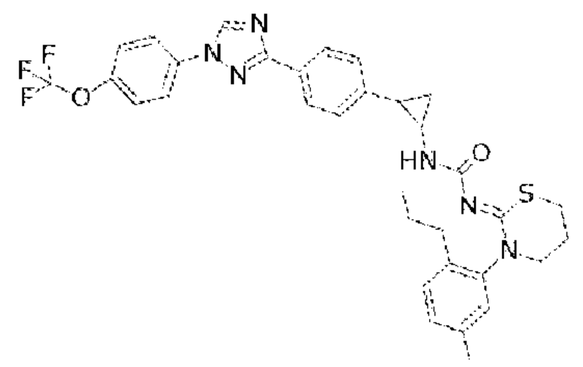
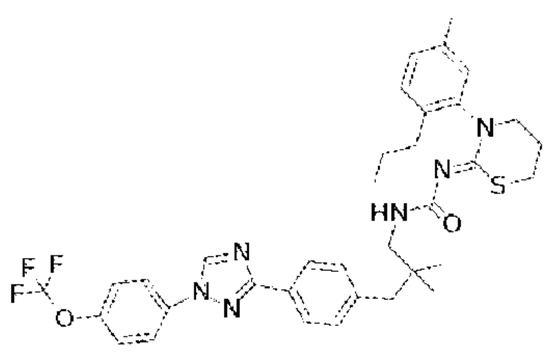
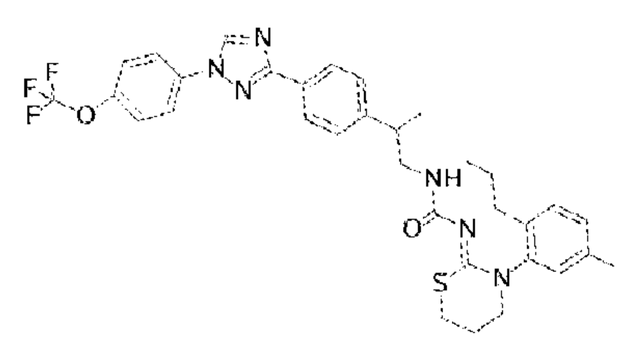
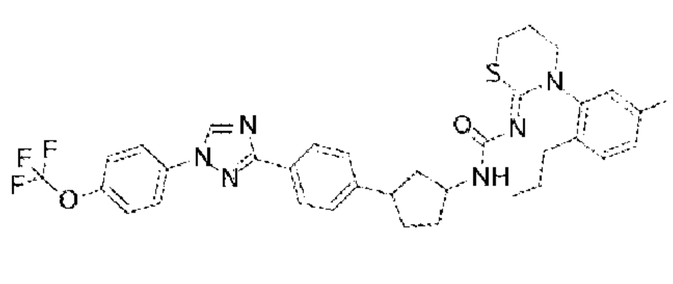
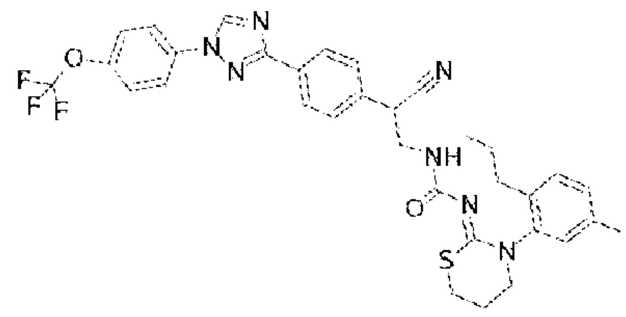
P893

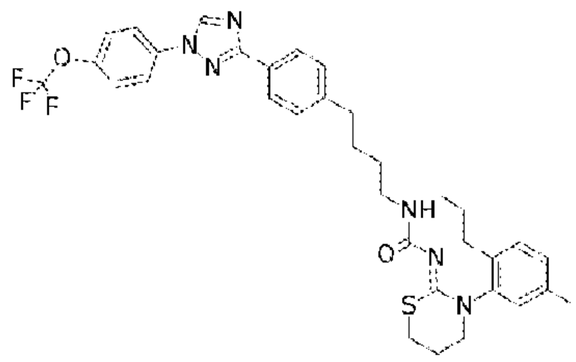
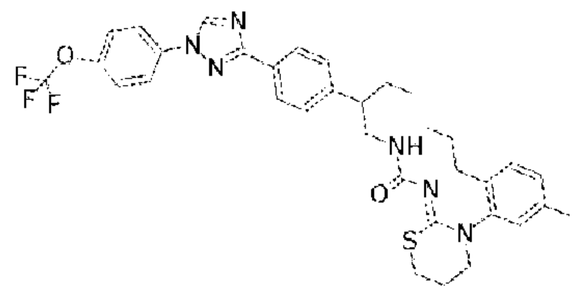
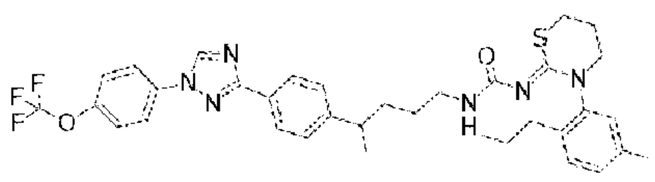
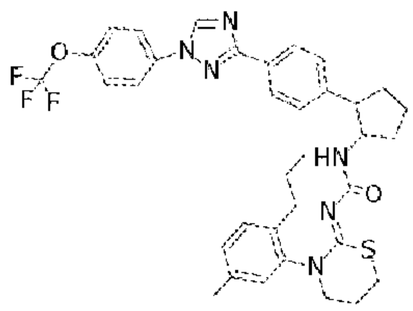
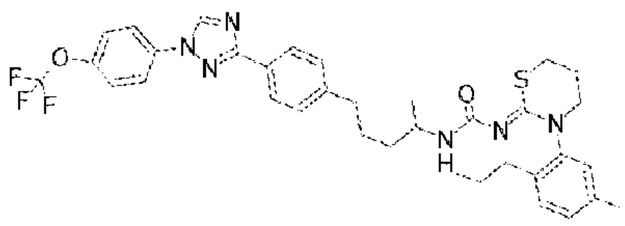
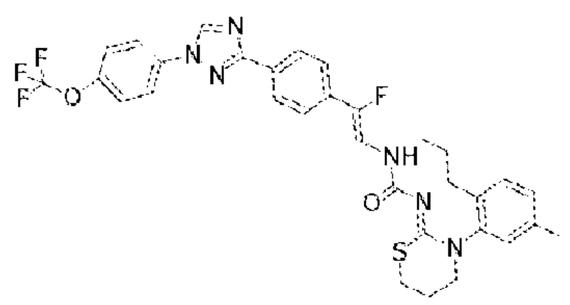
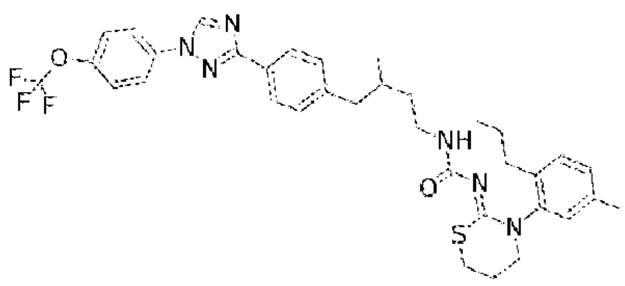
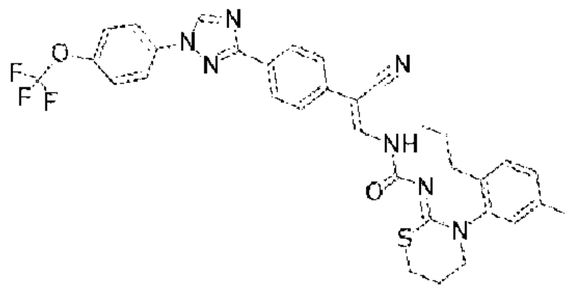
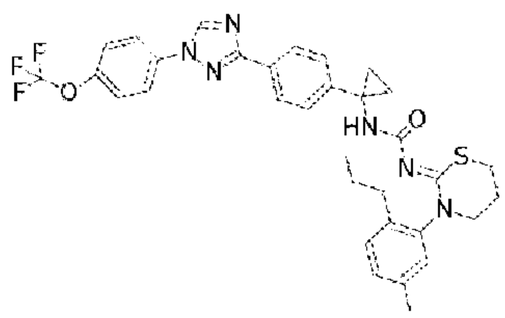
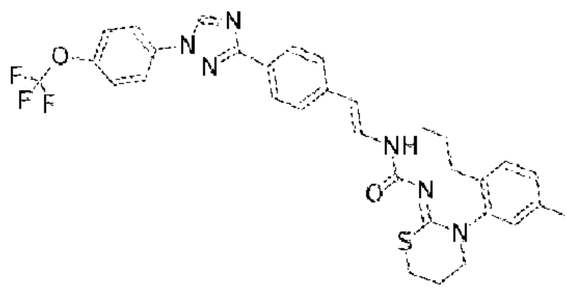


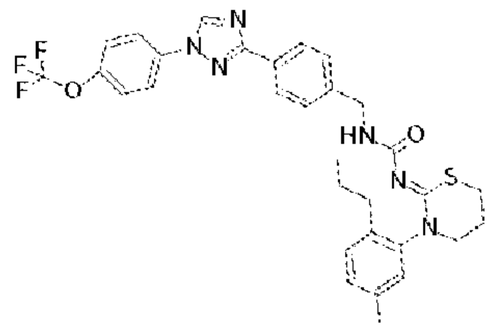
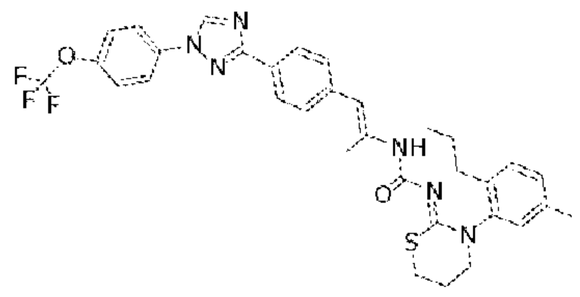
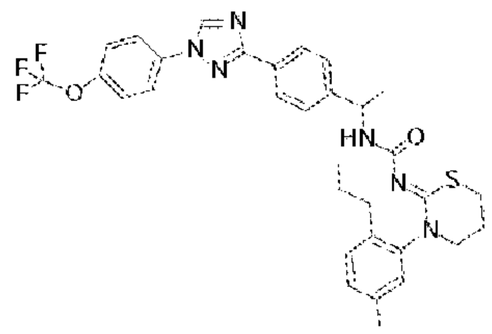
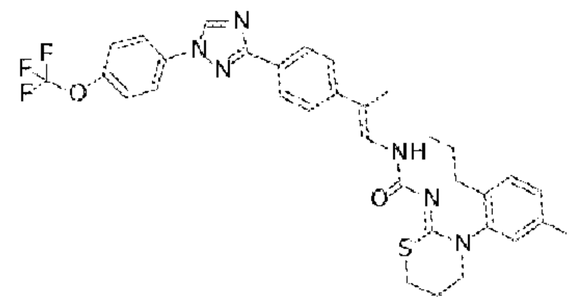
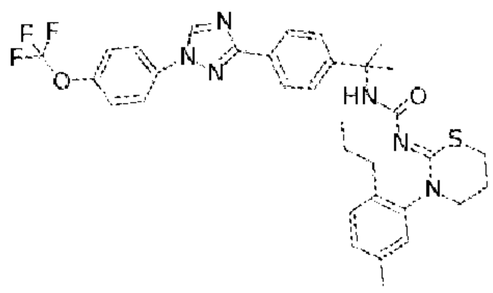
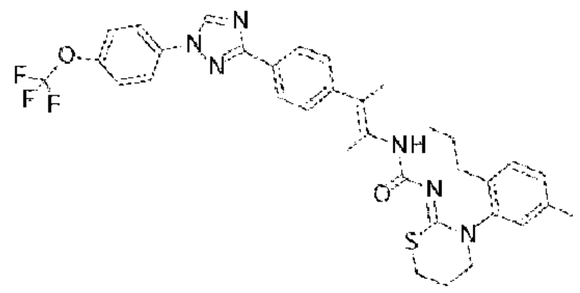
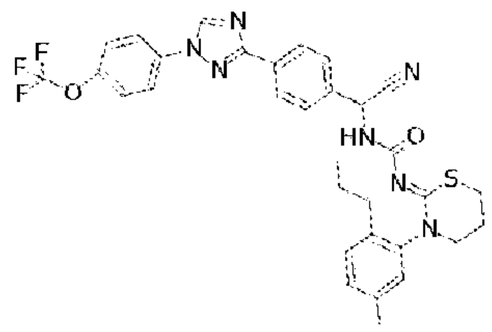
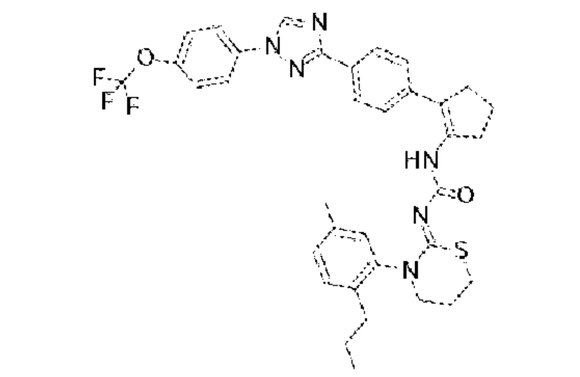
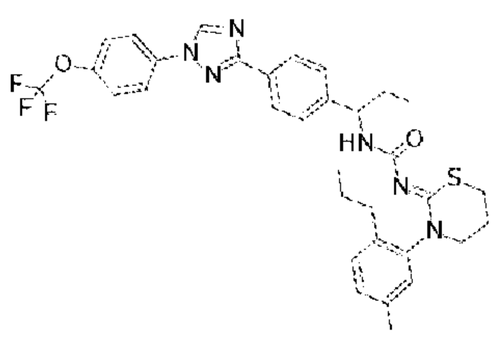
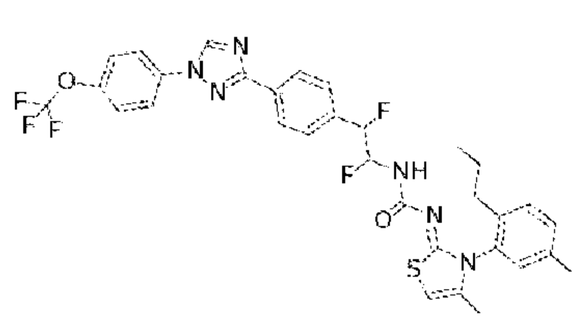
P894

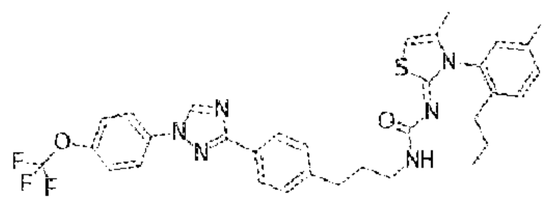
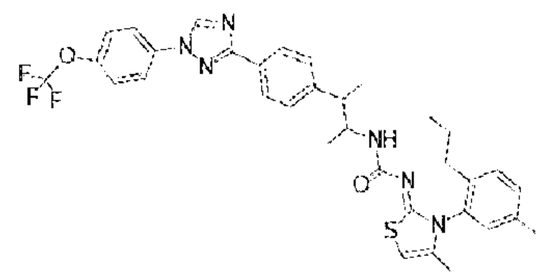
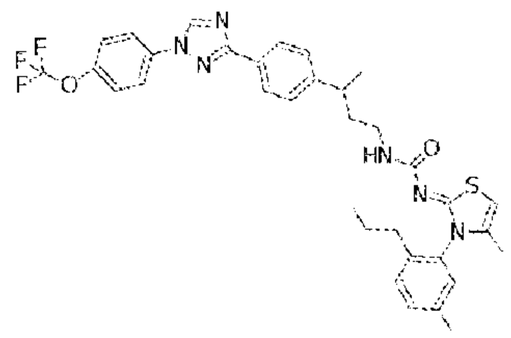
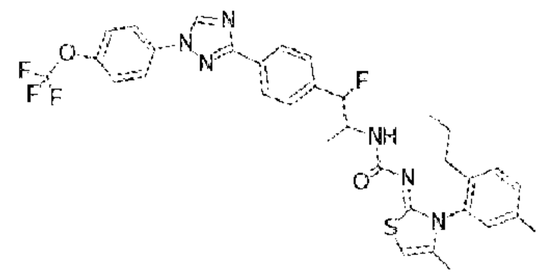
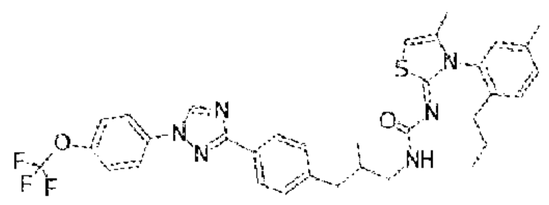
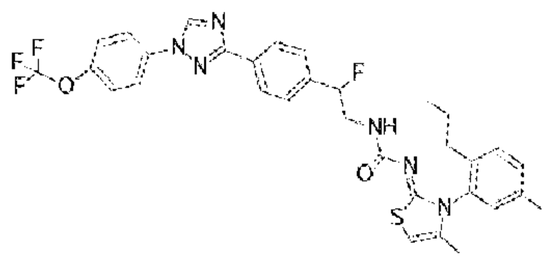
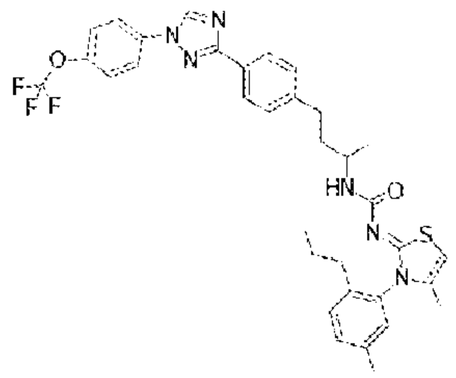
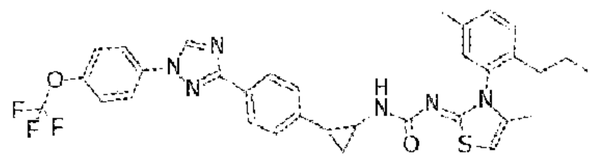
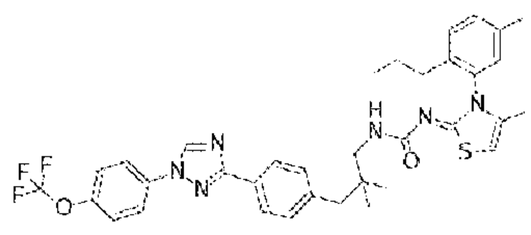
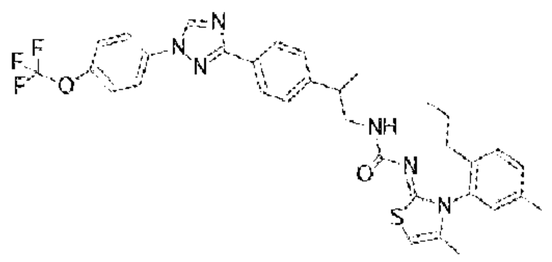


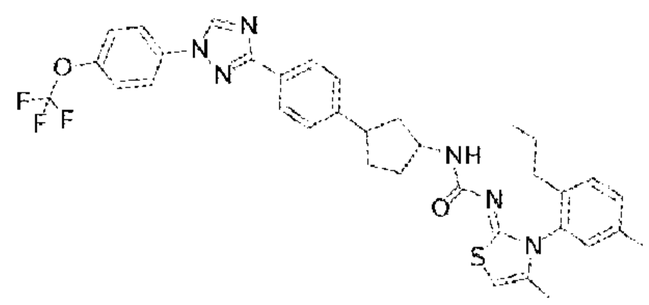
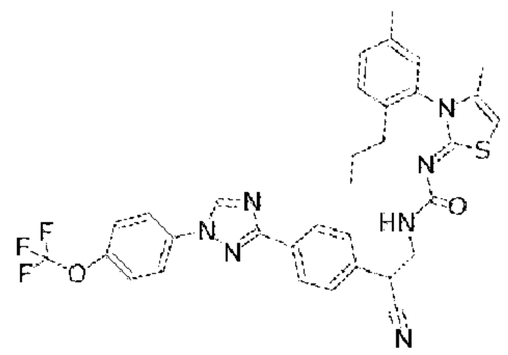
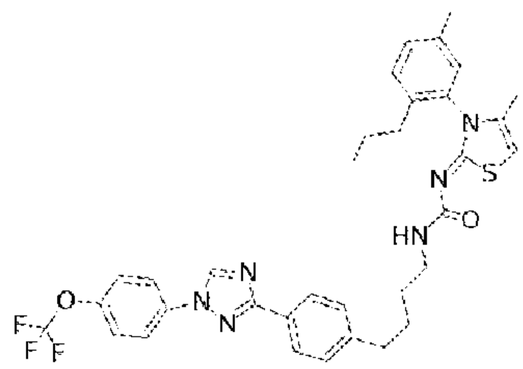
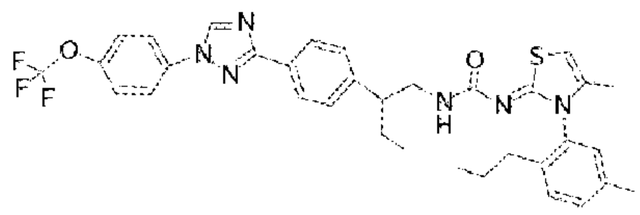
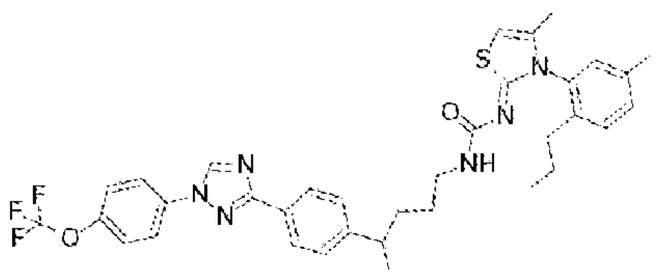
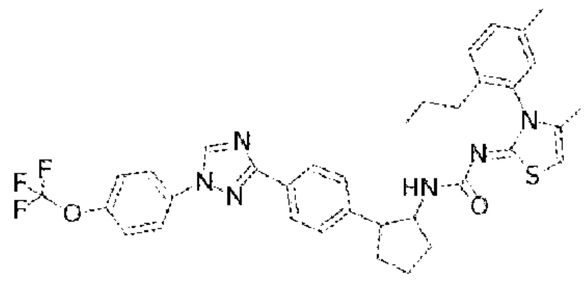
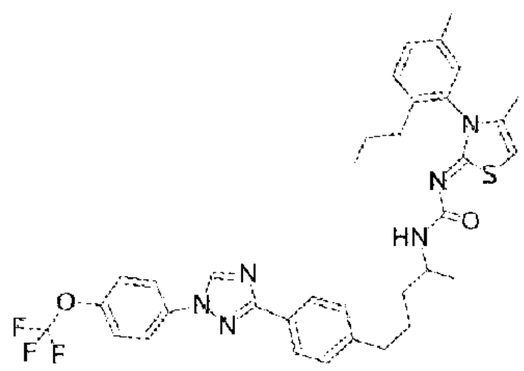
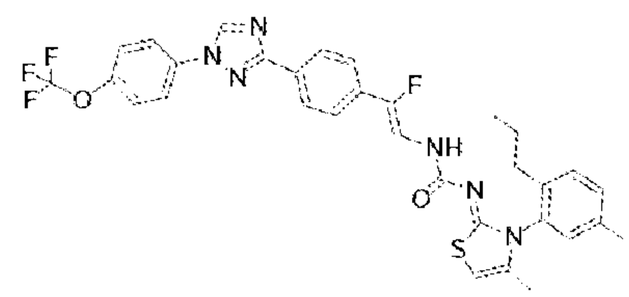
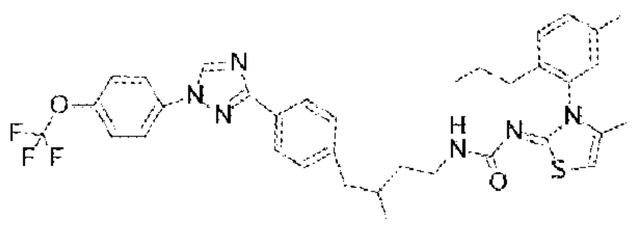
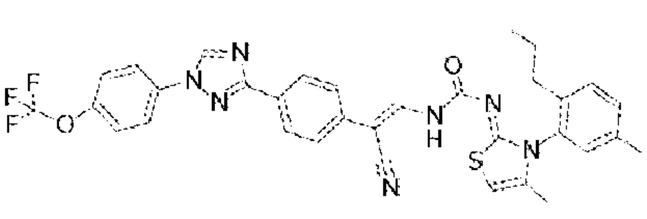
P895

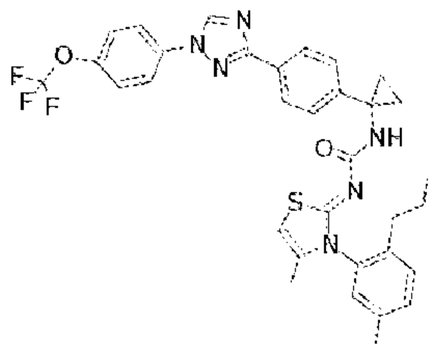
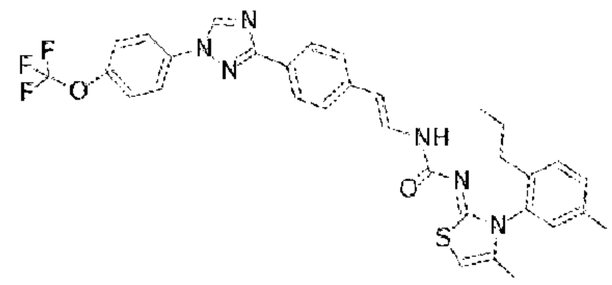
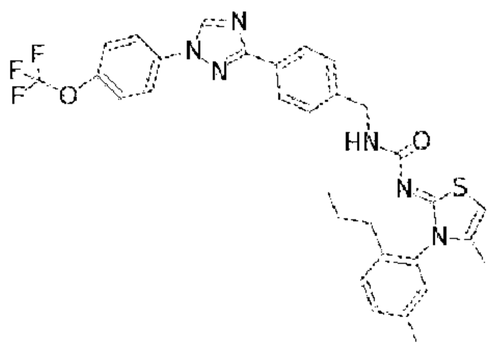
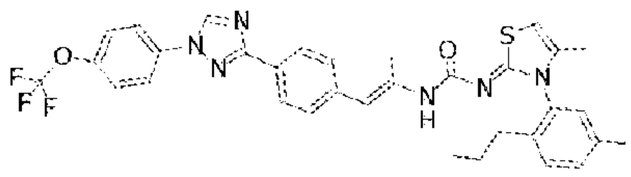
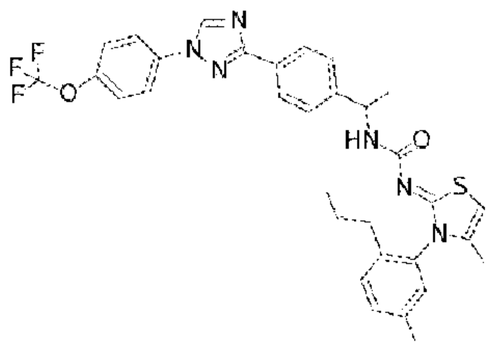
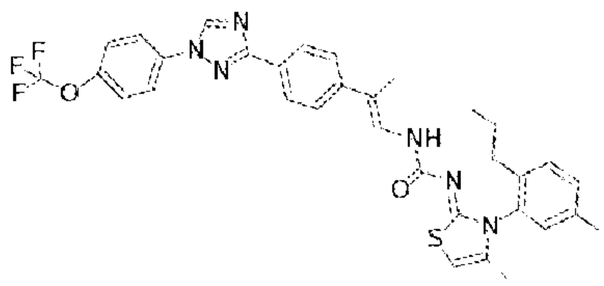
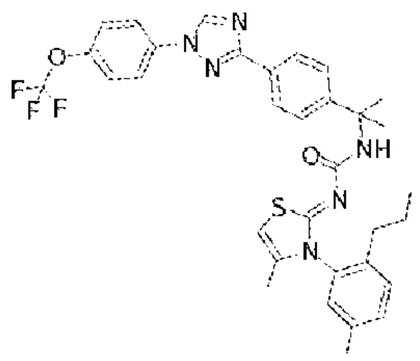
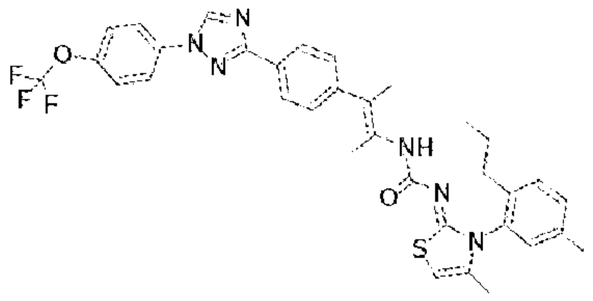
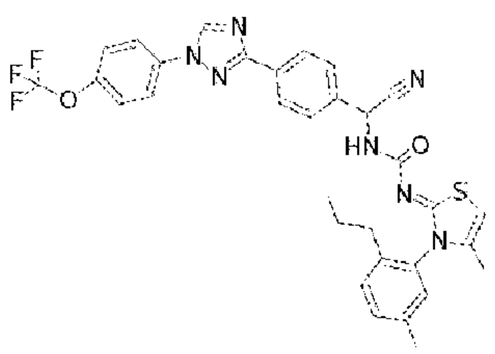
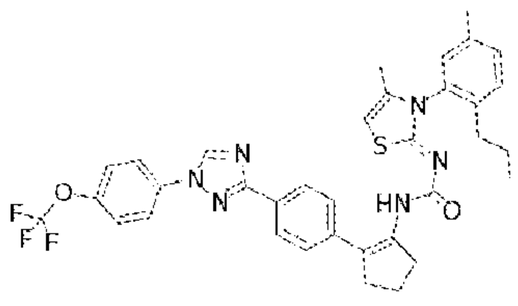
 P896	 P897
 P898	 P899
 P900	 P901
 P902	 P903
 P904	 P905

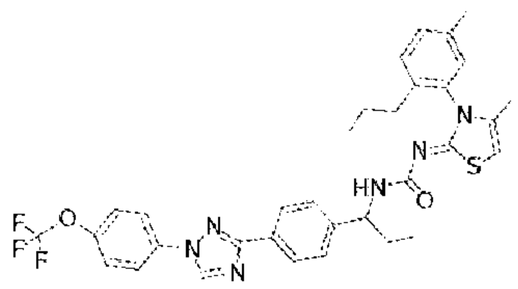
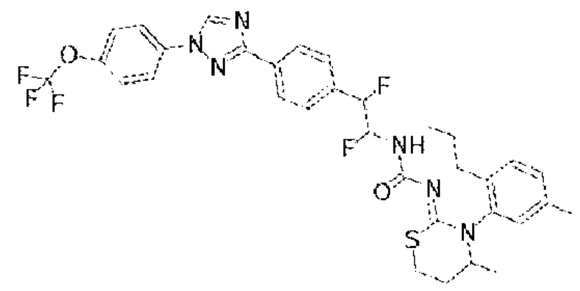
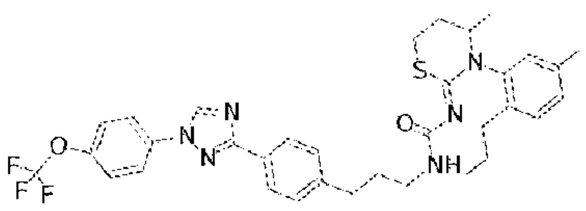
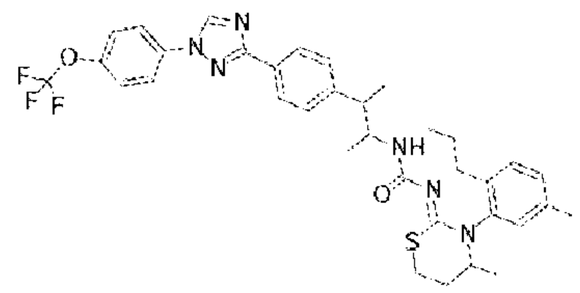
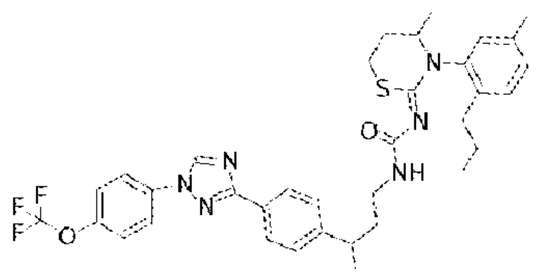
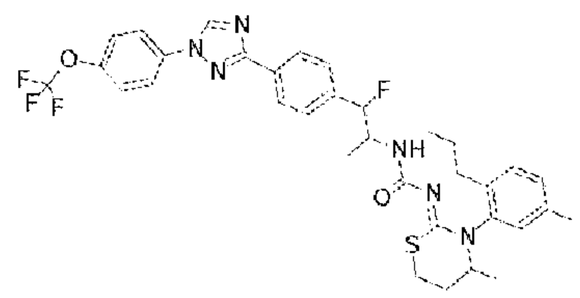
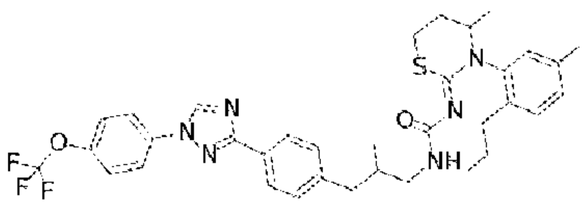
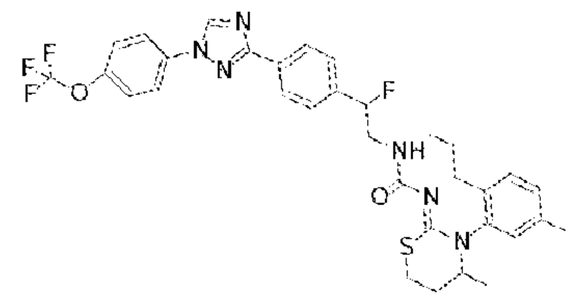
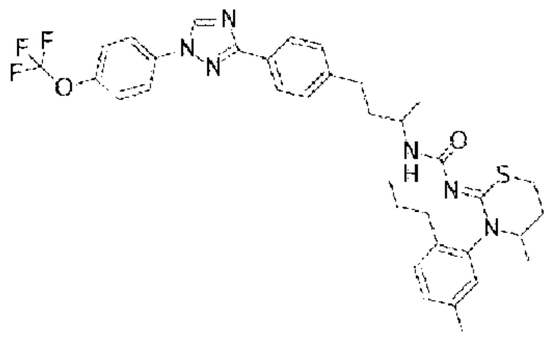
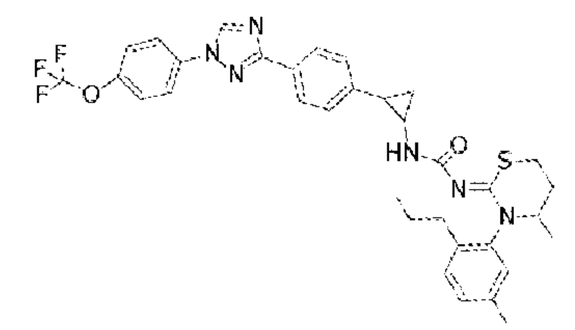
	
P906	P907
	
P908	P909
	
P910	P911
	
P912	P913
	
P914	P915

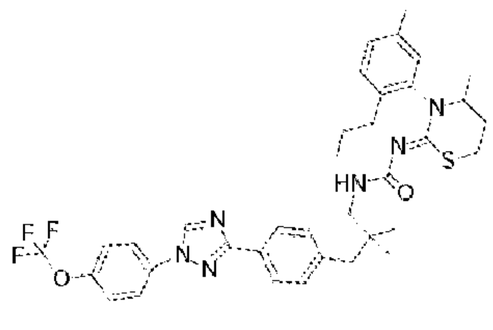
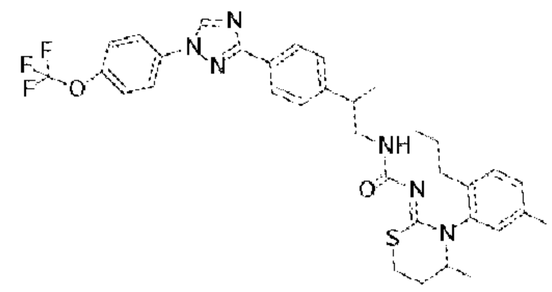
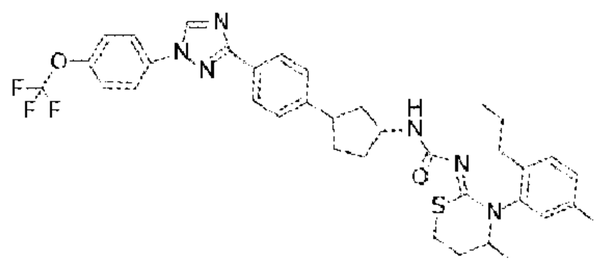
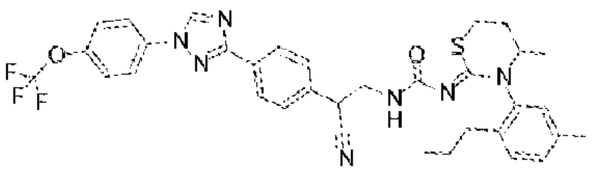
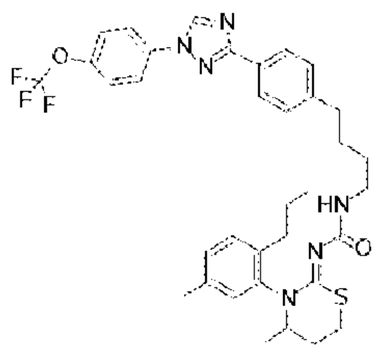
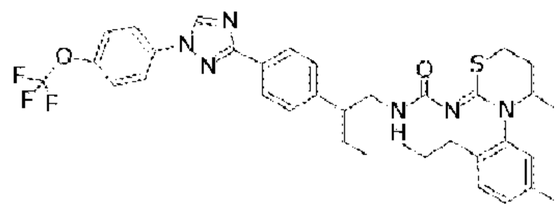
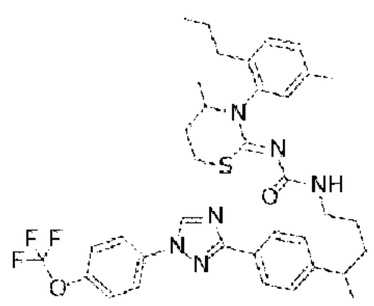
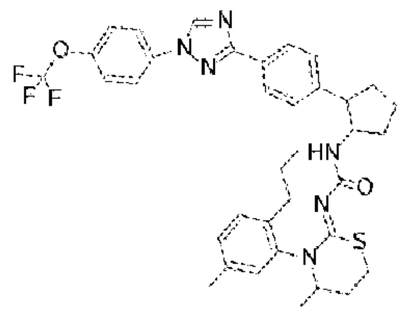
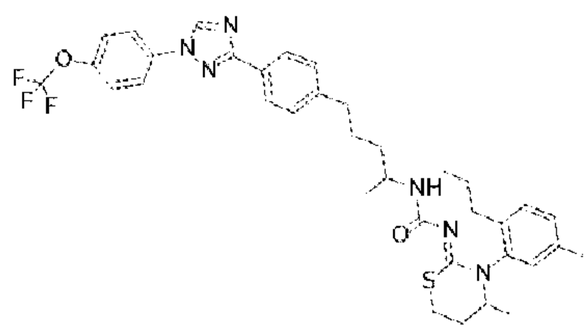
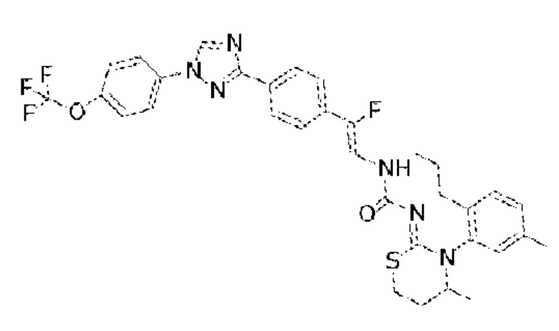
 P916	 P917
 P918	 P919
 P920	 P921
 P922	 P923
 P924	 P925

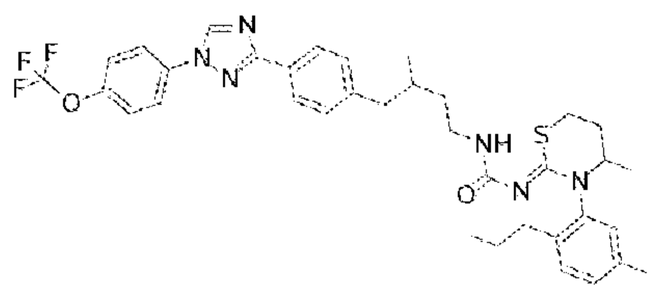
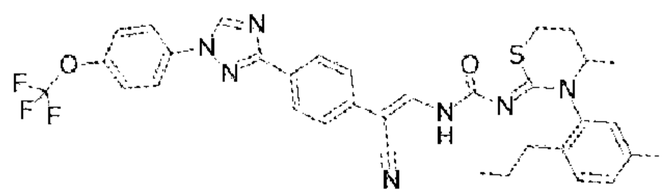
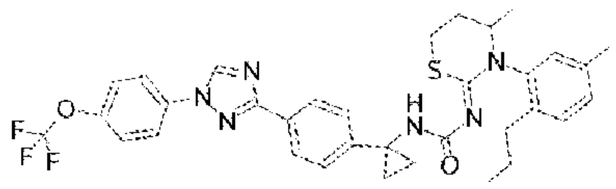
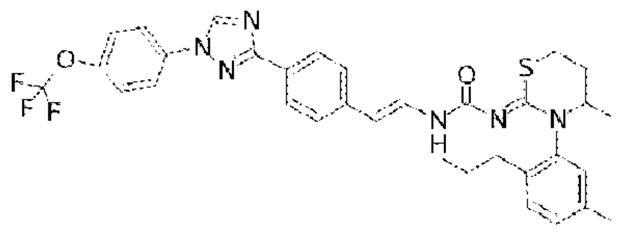
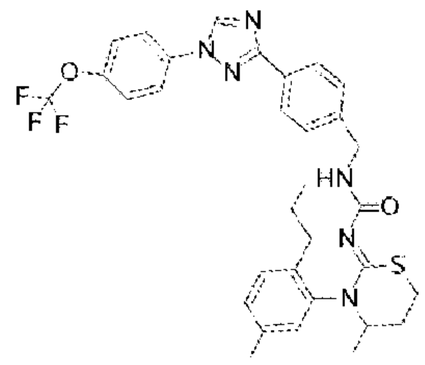
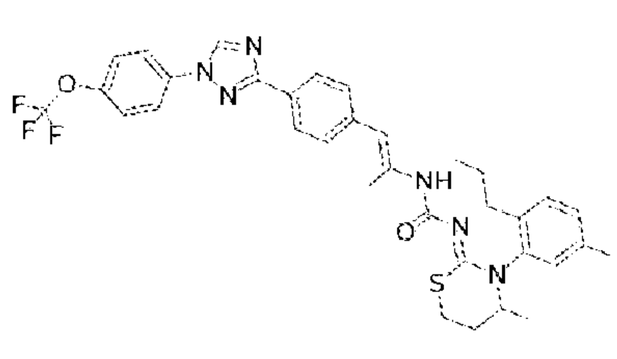
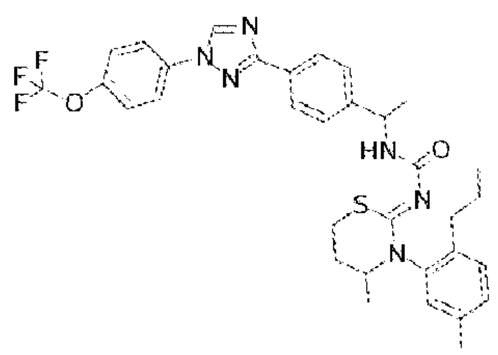
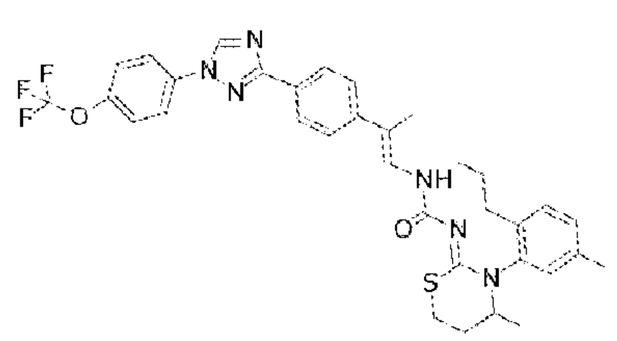
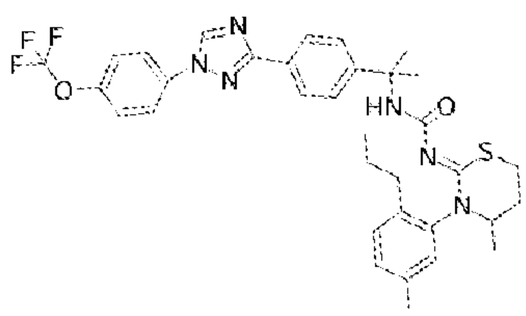
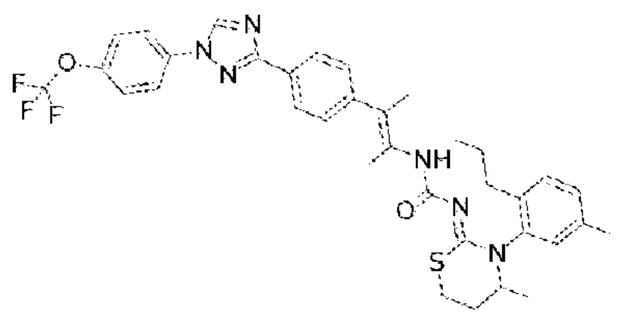
	
P926	P927
	
P928	P929
	
P930	P931
	
P932	P933
	
P934	P935

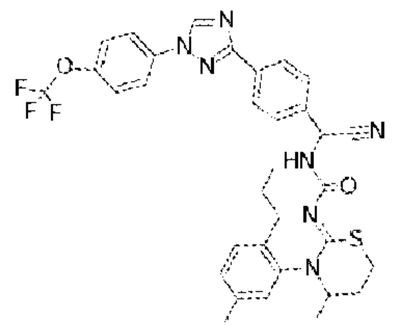
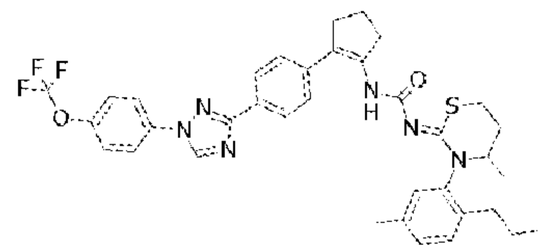
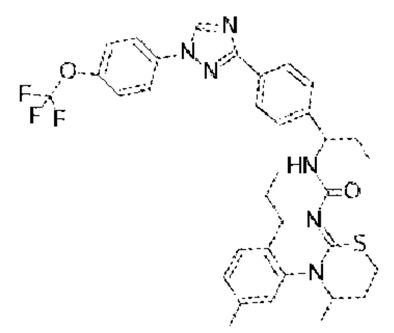
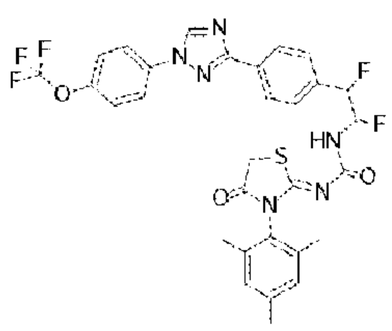
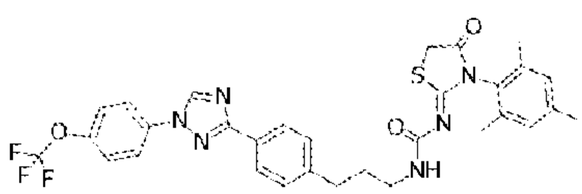
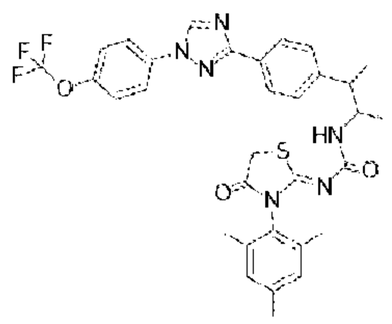
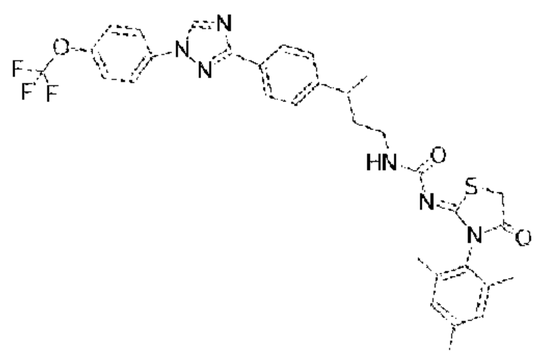
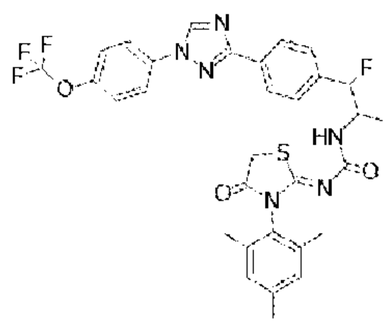
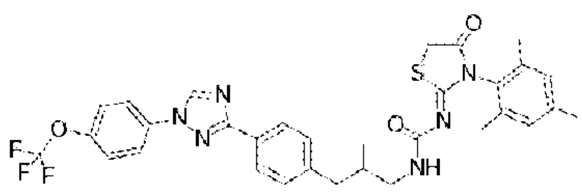
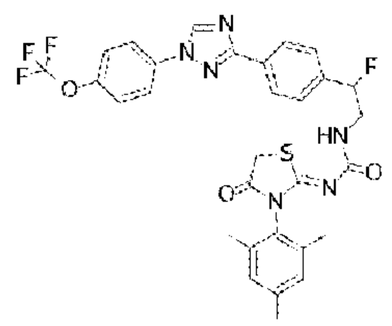
 P936	 P937
 P938	 P939
 P940	 P941
 P942	 P943
 P944	 P945

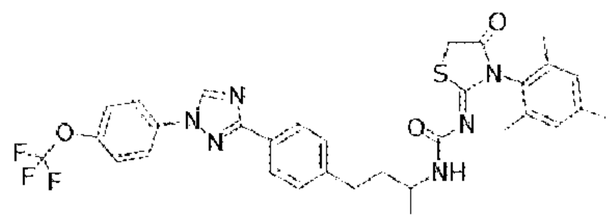
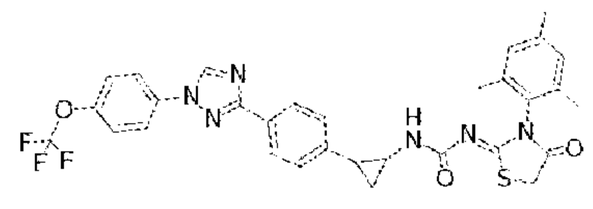
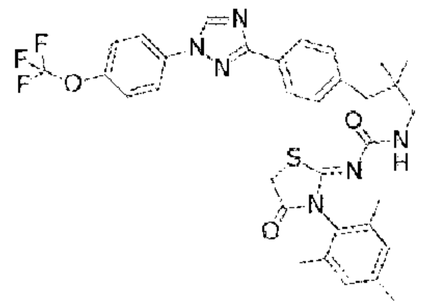
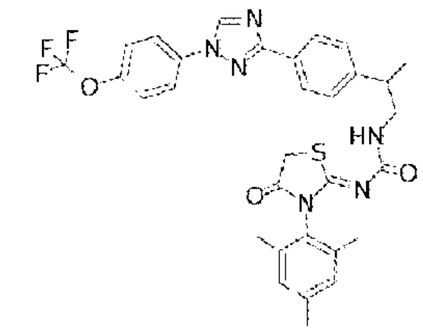
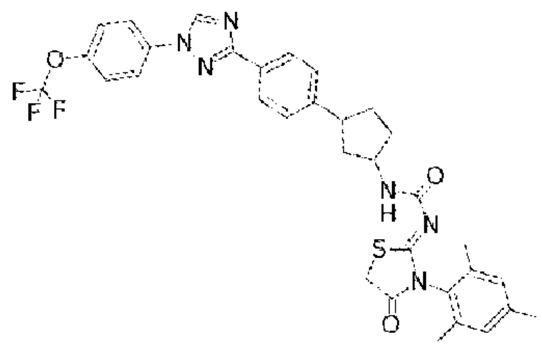
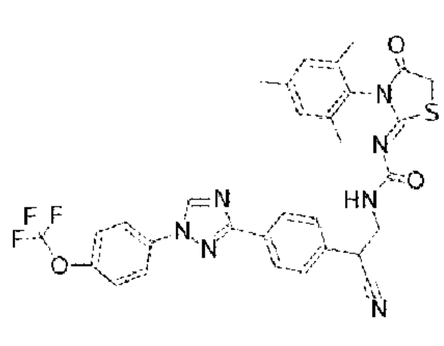
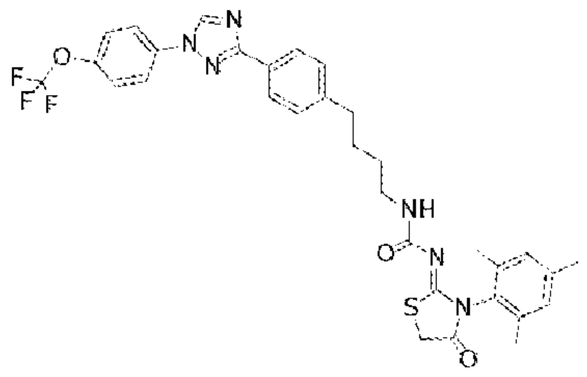
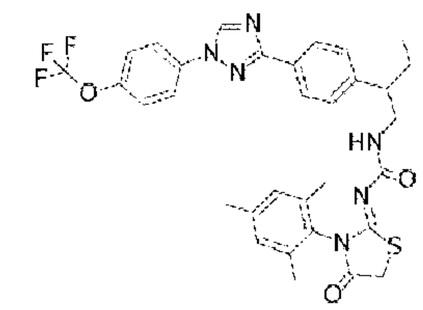
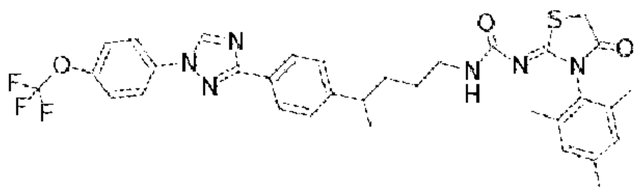
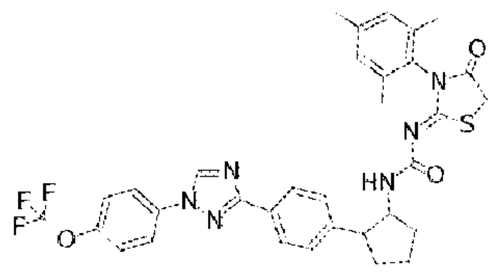
	
P946	P947
	
P948	P949
	
P950	P951
	
P952	P953
	
P954	P955

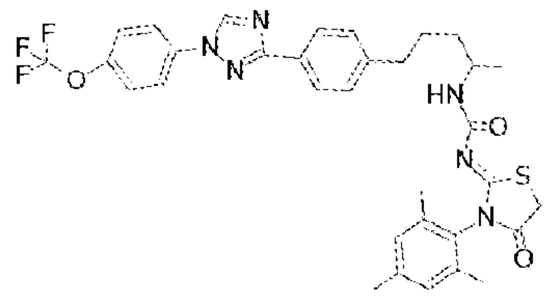
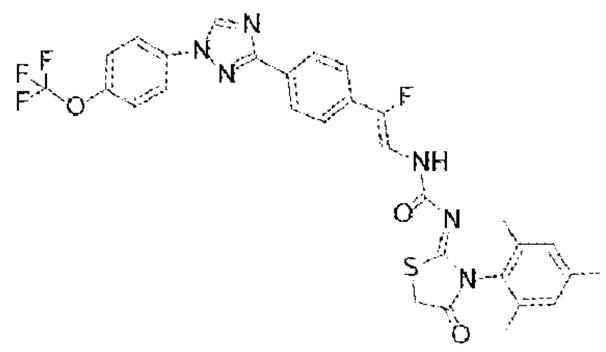
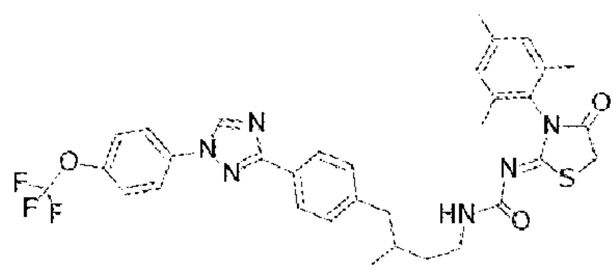
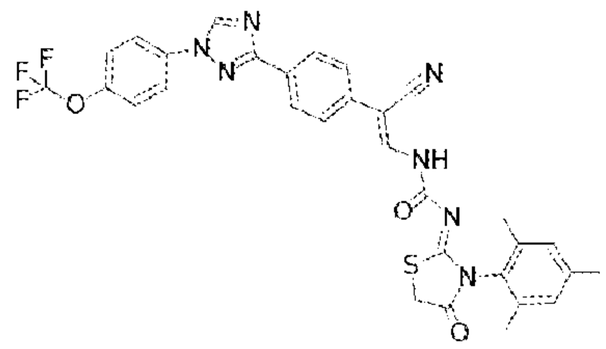
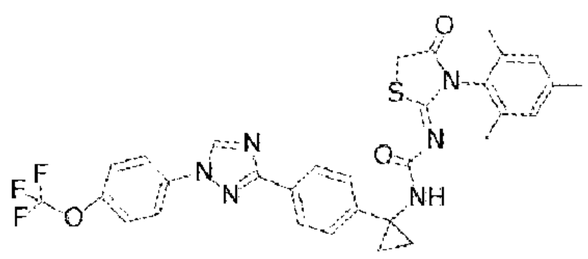
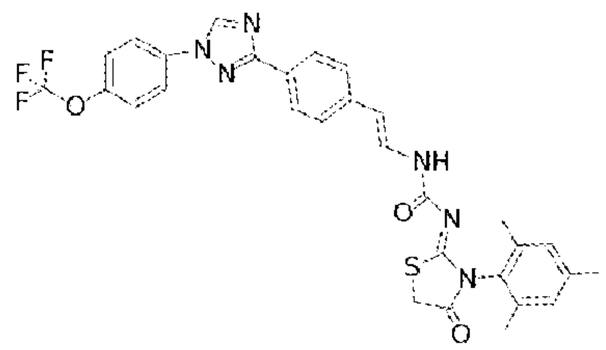
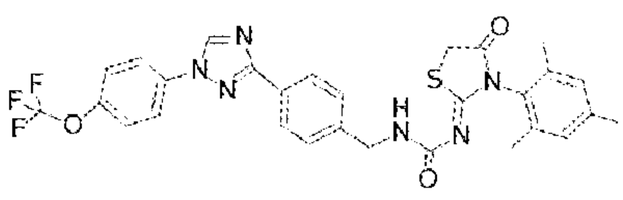
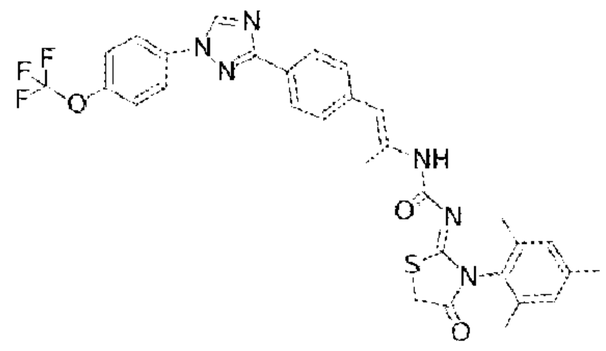
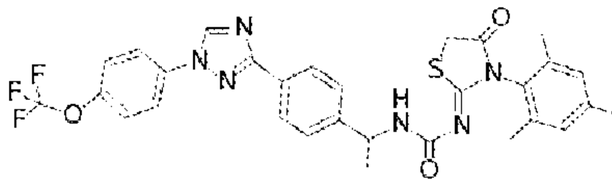
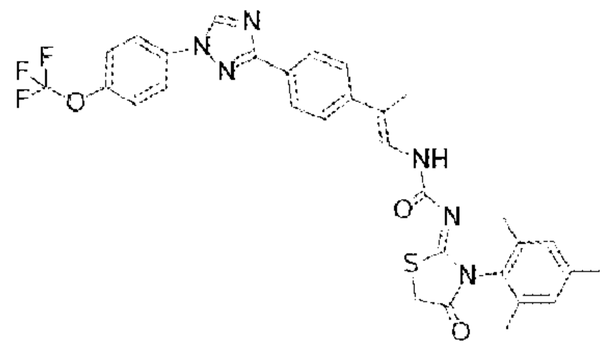
	
P956	P957
	
P958	P959
	
P960	P961
	
P962	P963
	
P964	P965

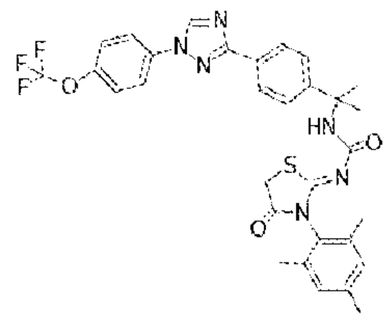
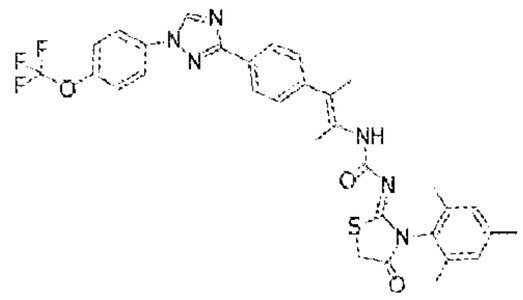
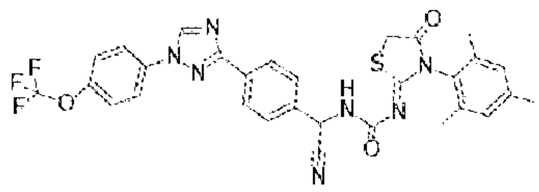
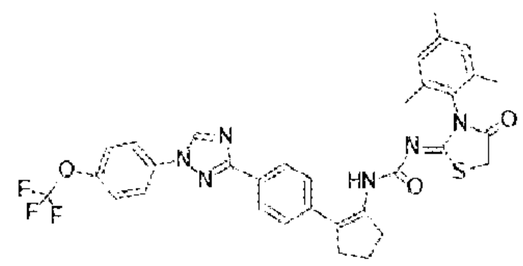
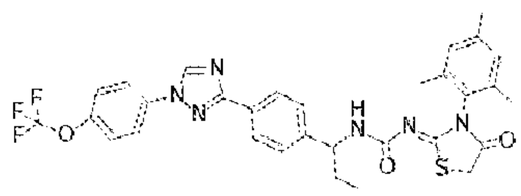
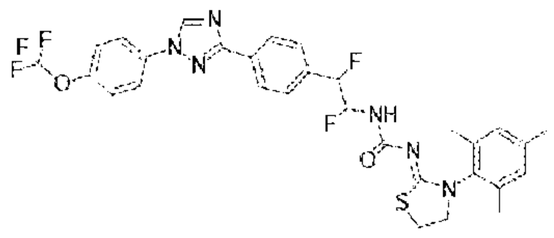
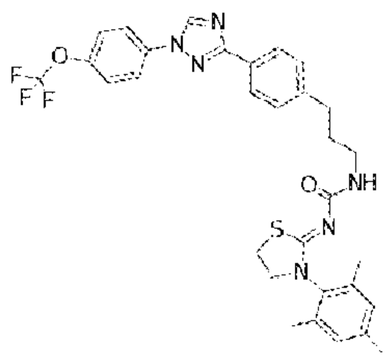
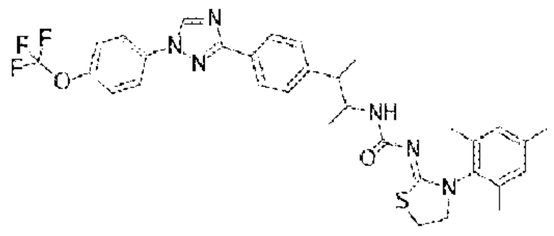
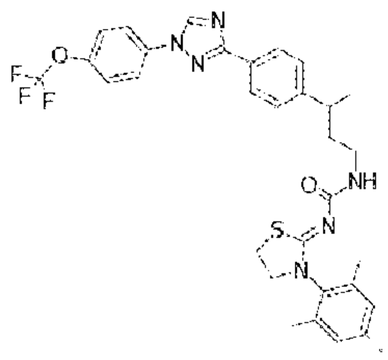
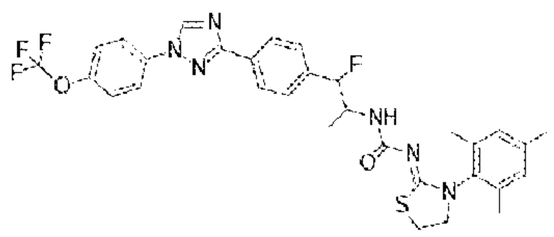
 P966	 P967
 P968	 P969
 P970	 P971
 P972	 P973
 P974	 P975

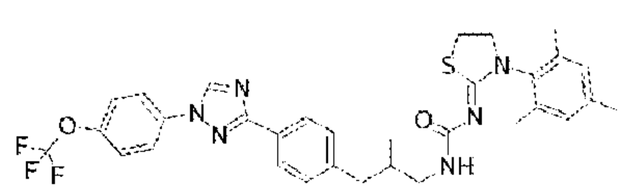
 P976	 P977
 P978	 P979
 P980	 P981
 P982	 P983
 P984	 P985

 P986	 P987
 P988	 P989
 P990	 P991
 P992	 P993
 P994	 P995

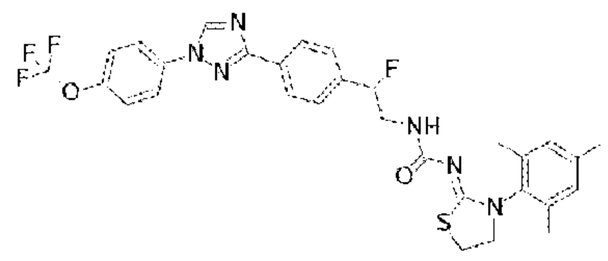
 P996	 P997
 P998	 P999
 P1000	 P1001
 P1002	 P1003
 P1004	 P1005

 P1006	 P1007
 P1008	 P1009
 P1010	 P1011
 P1012	 P1013
 P1014	 P1015

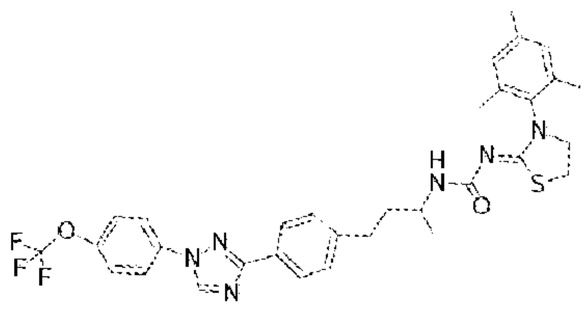
 P1016	 P1017
 P1018	 P1019
 P1020	 P1021
 P1022	 P1023
 P1024	 P1025



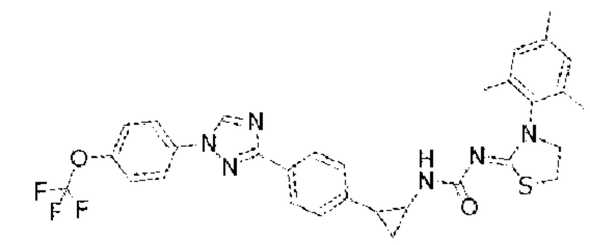
P1026



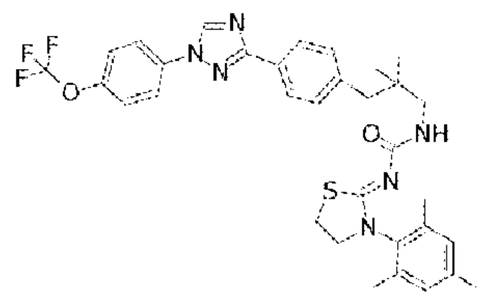
P1027



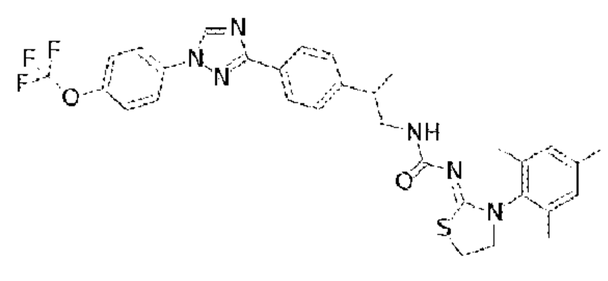
P1028



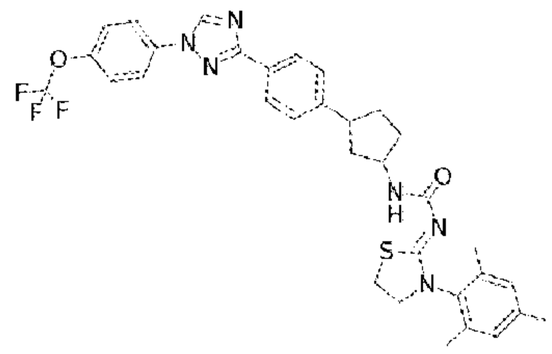
P1029



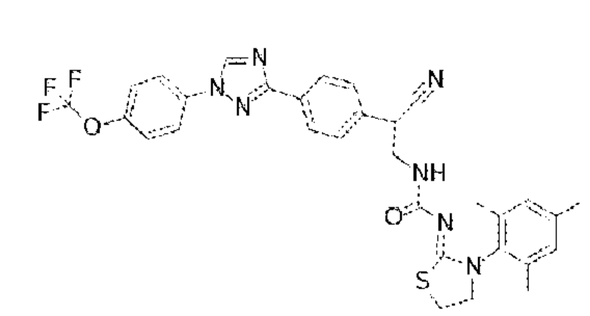
P1030



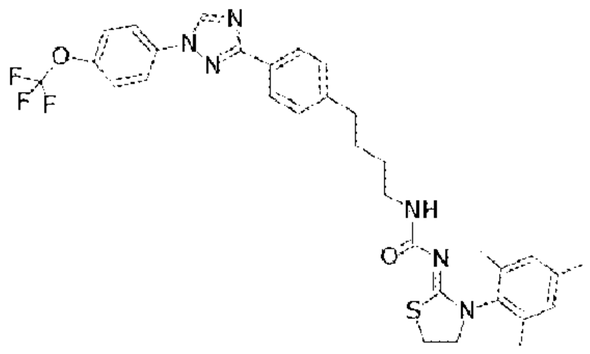
P1031



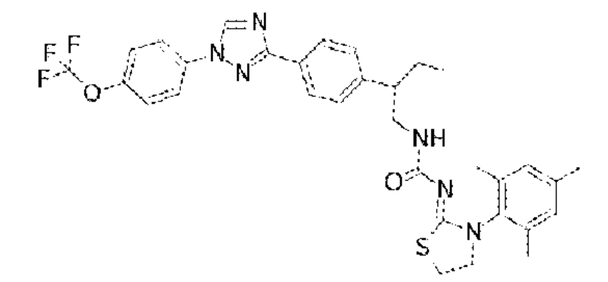
P1032



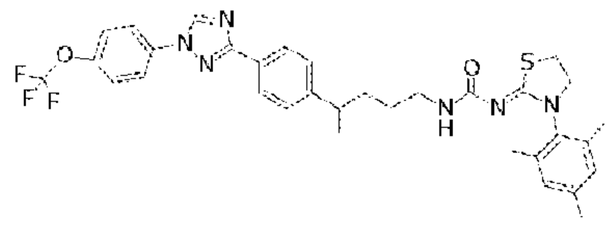
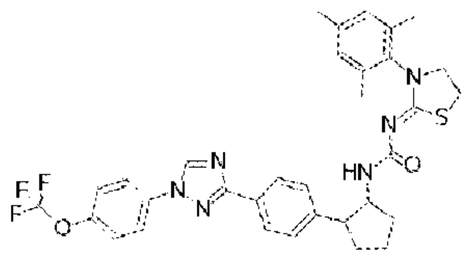
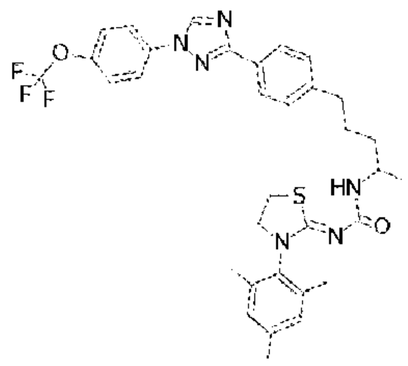
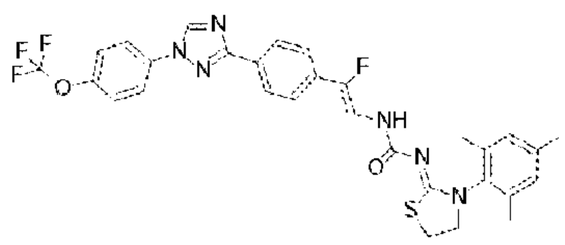
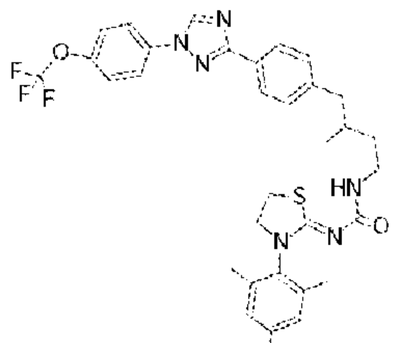
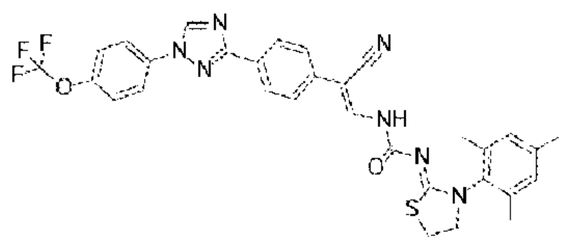
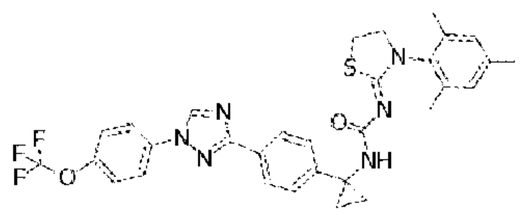
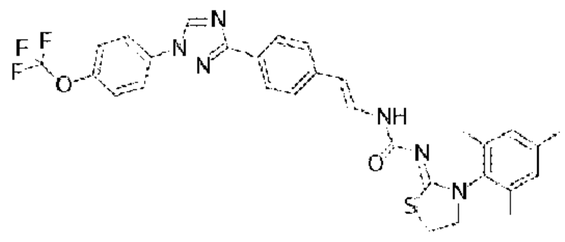
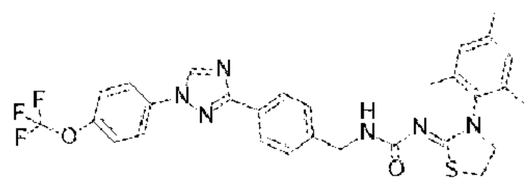
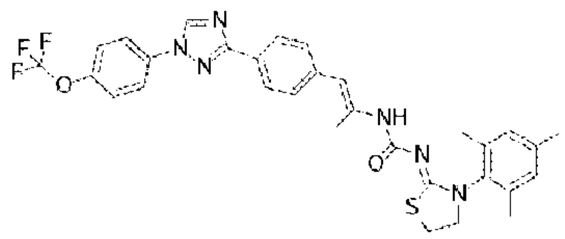
P1033

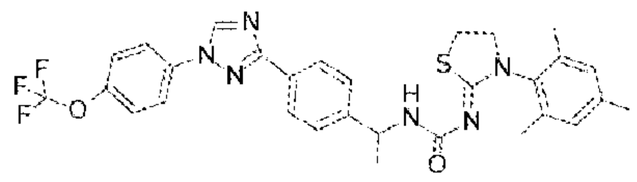
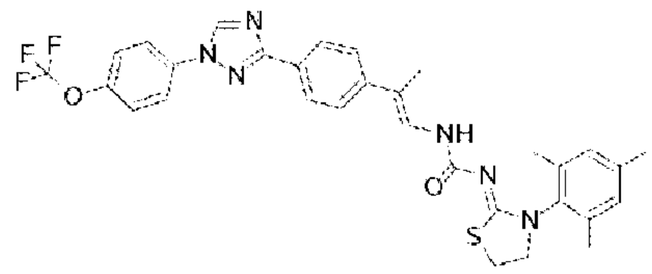
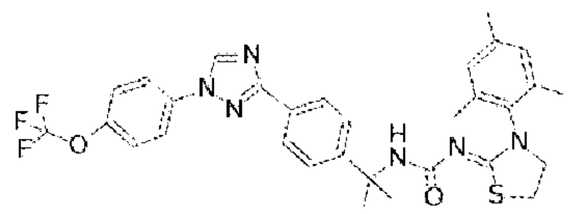
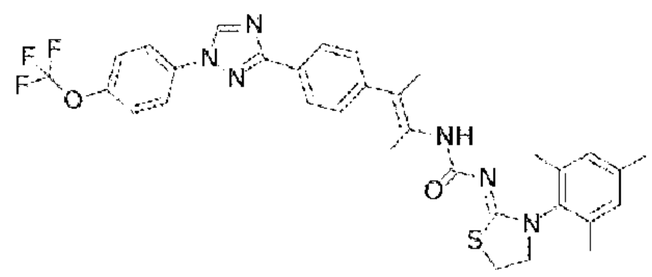
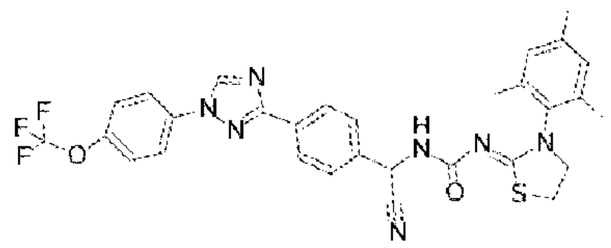
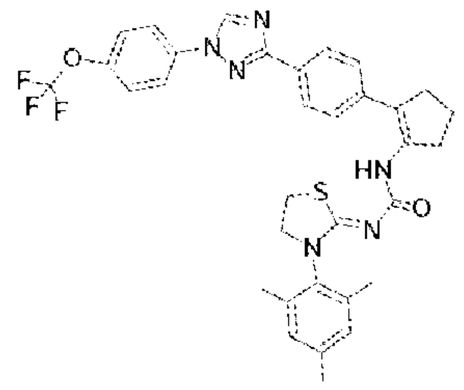
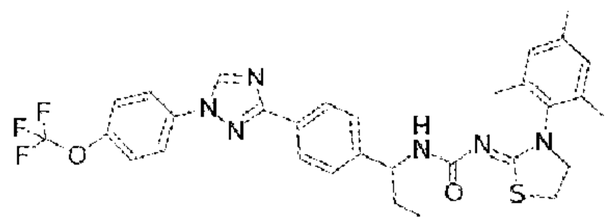
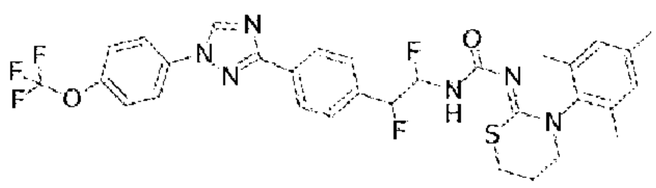
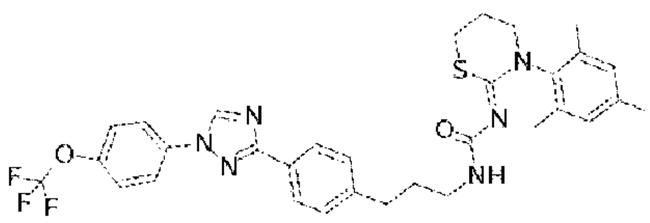
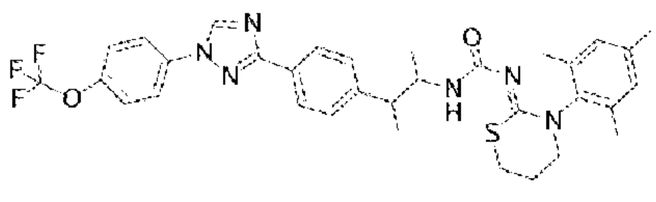


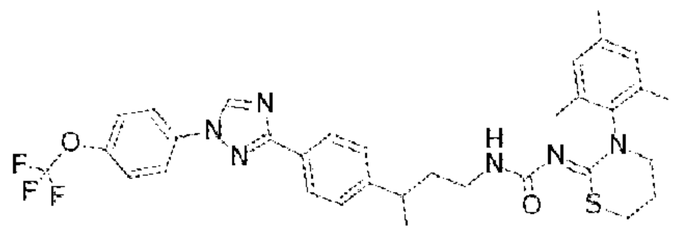
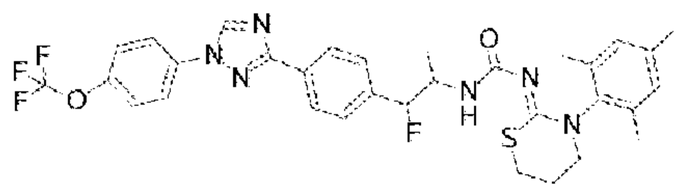
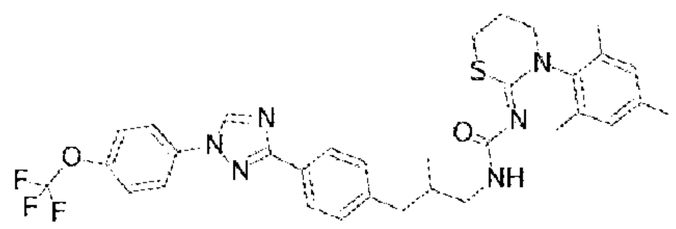
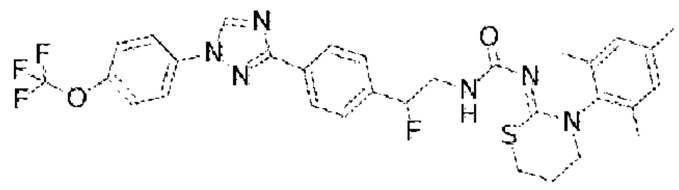
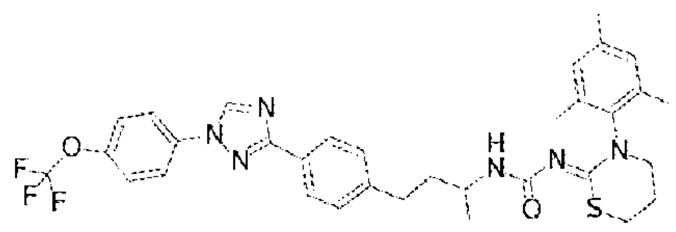
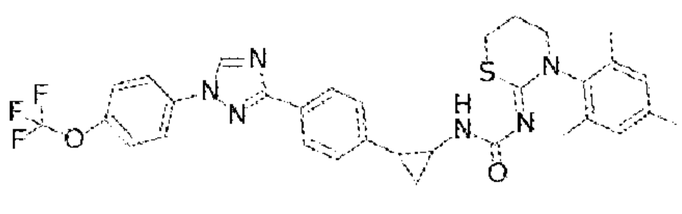
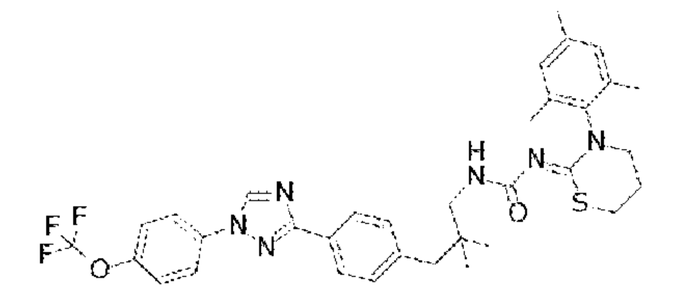
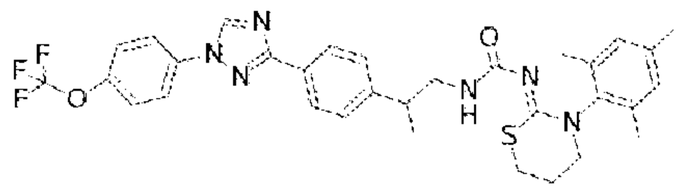
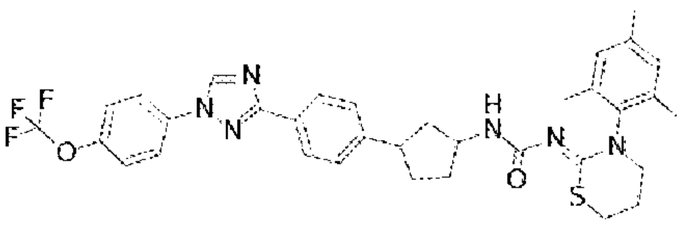
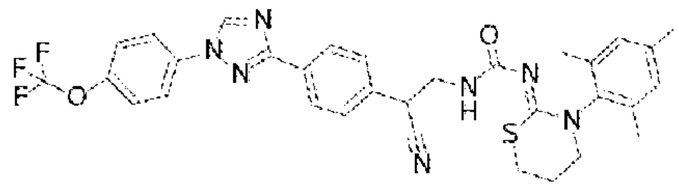
P1034

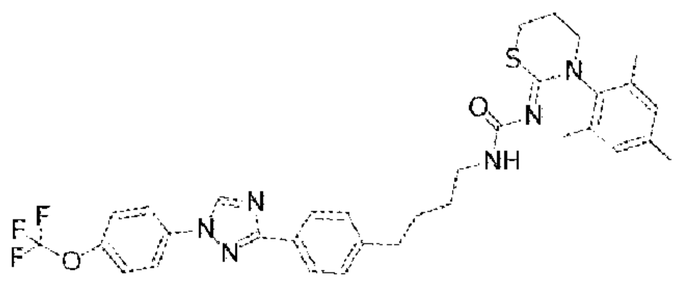
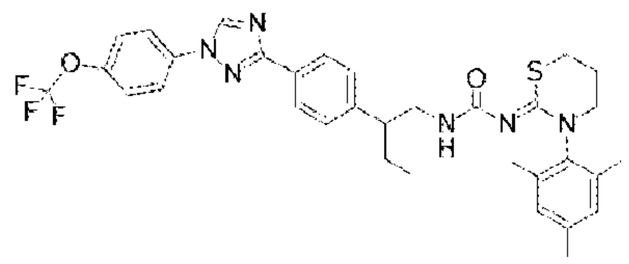
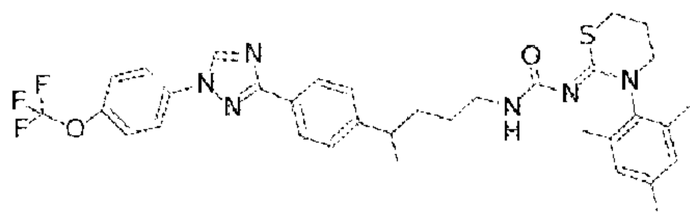
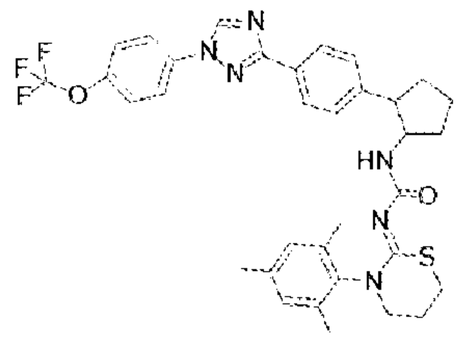
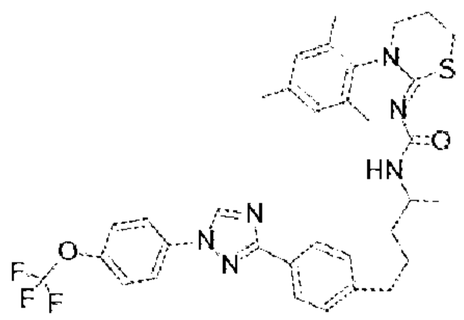
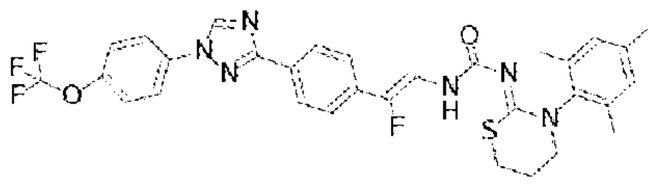
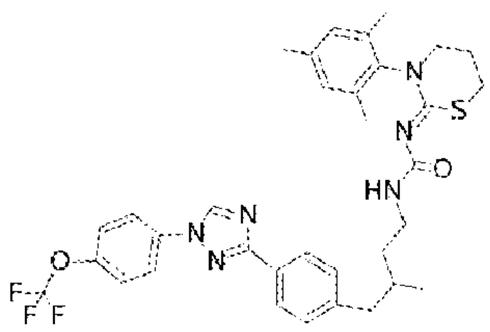
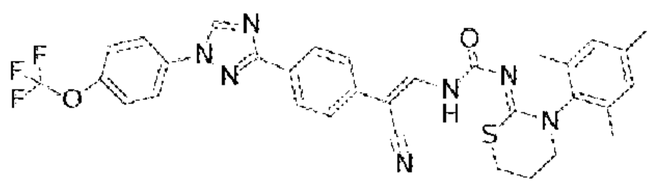
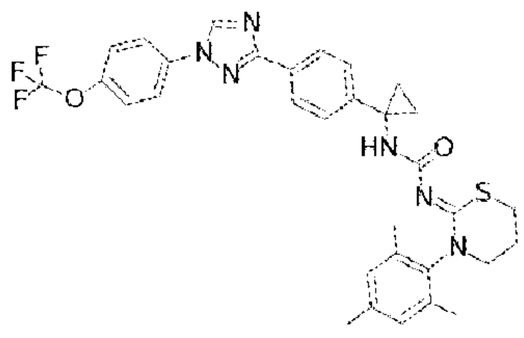
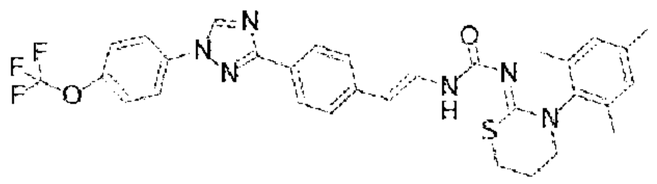


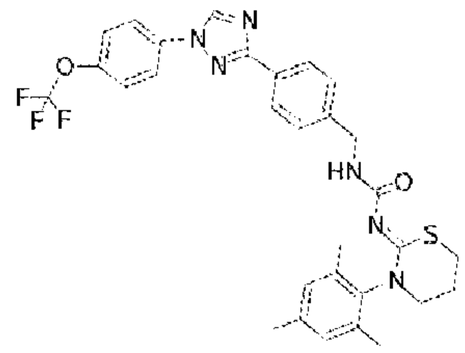
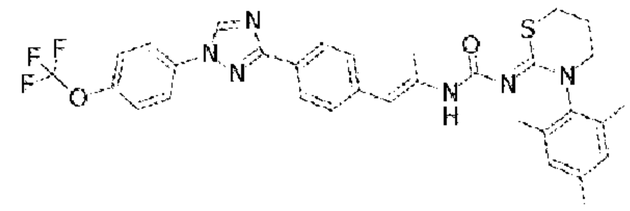
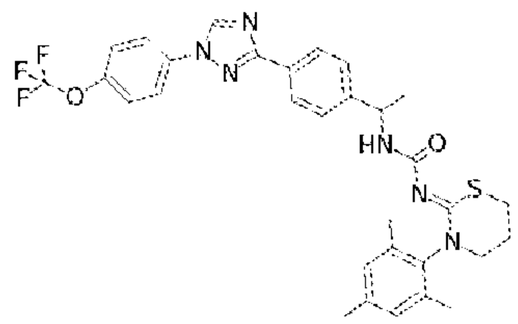
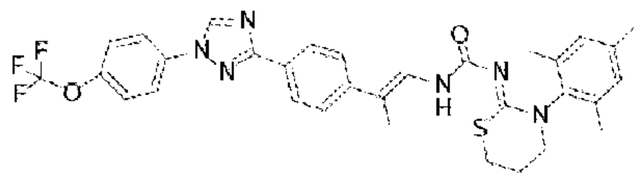
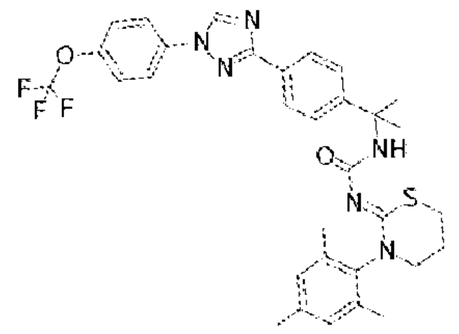
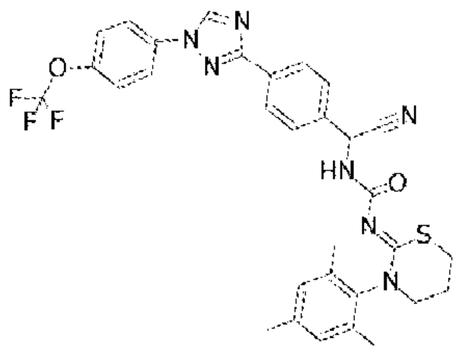
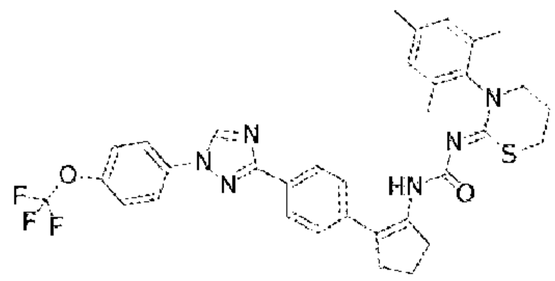
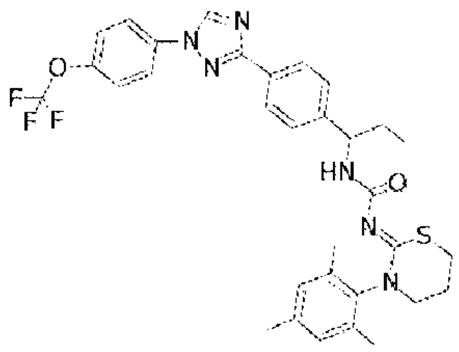
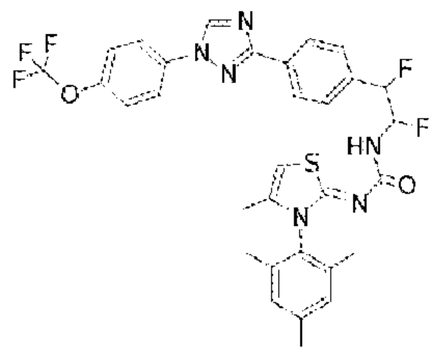
P1035

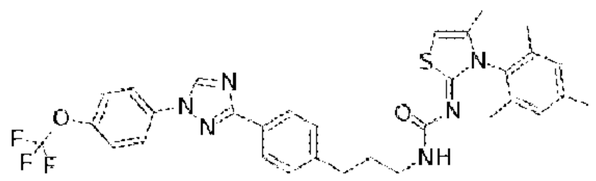
	
P1036	P1037
	
P1038	P1039
	
P1040	P1041
	
P1042	P1043
	
P1044	P1045

	
P1046	P1047
	
P1048	P1049
	
P1050	P1051
	
P1052	P1053
	
P1054	P1055

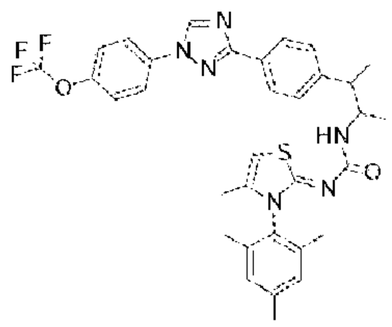
	
P1056	P1057
	
P1058	P1059
	
P1060	P1061
	
P1062	P1063
	
P1064	P1065

 P1066	 P1067
 P1068	 P1069
 P1070	 P1071
 P1072	 P1073
 P1074	 P1075

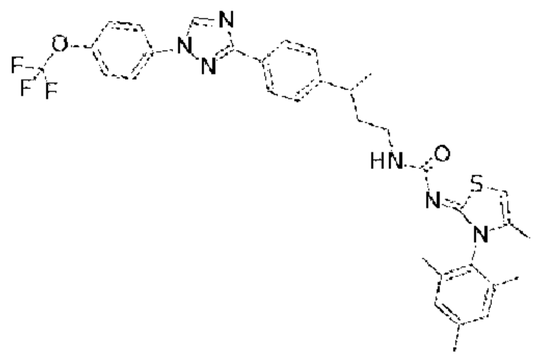
 P1076	 P1077
 P1078	 P1079
 P1080	P1081
 P1082	 P1083
 P1084	 P1085



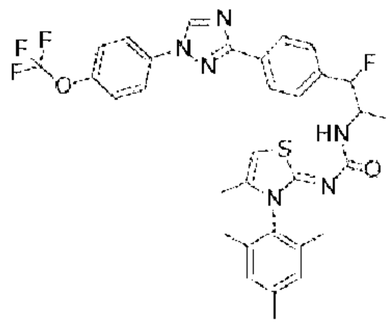
P1086



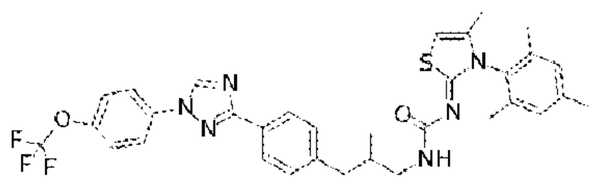
P1087



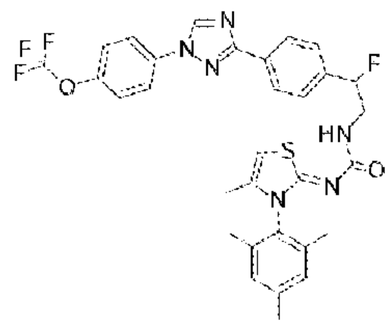
P1088



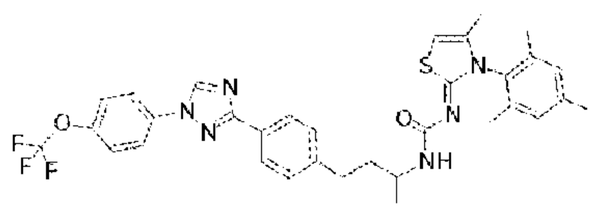
P1089



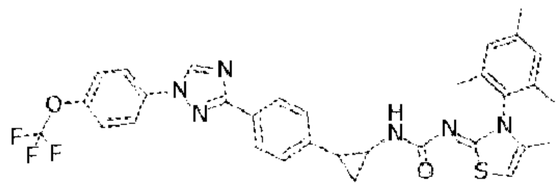
P1090



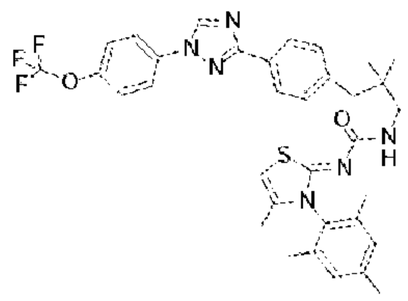
P1091



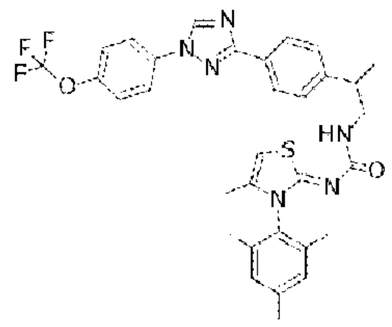
P1092



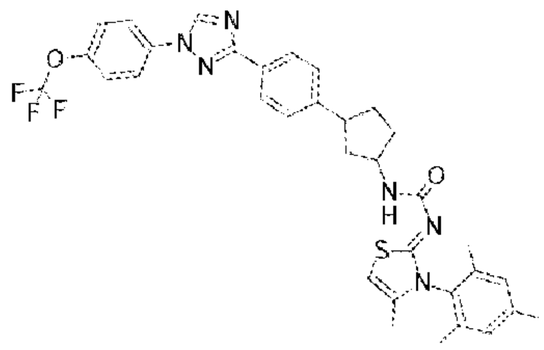
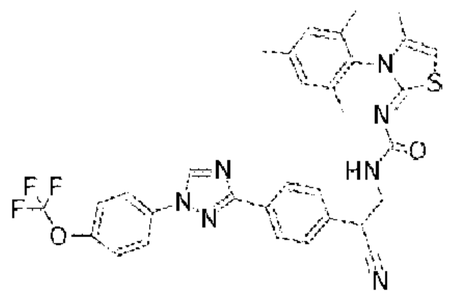
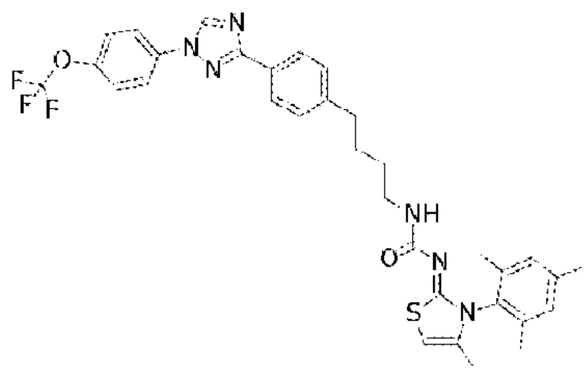
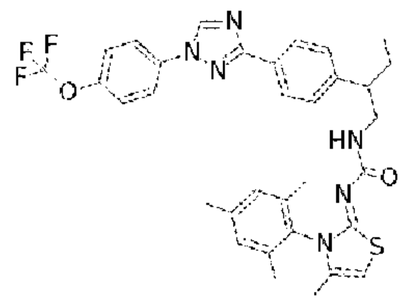
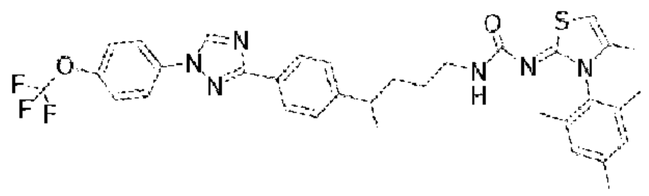
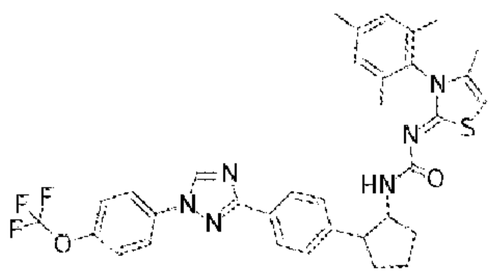
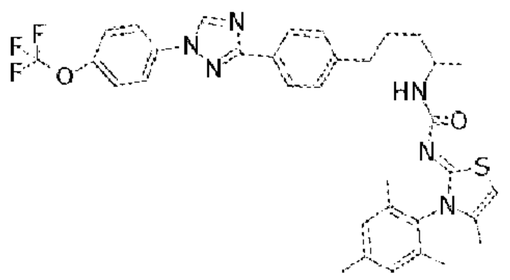
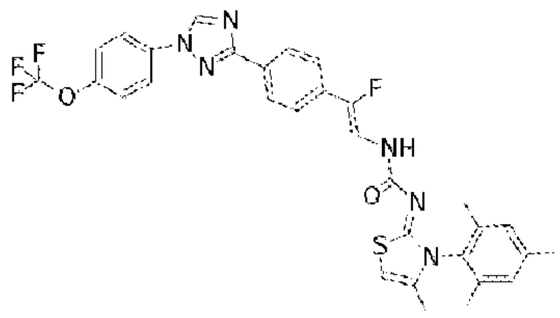
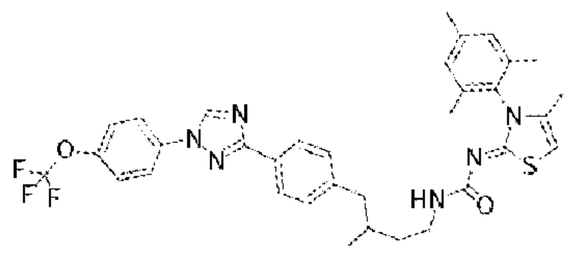
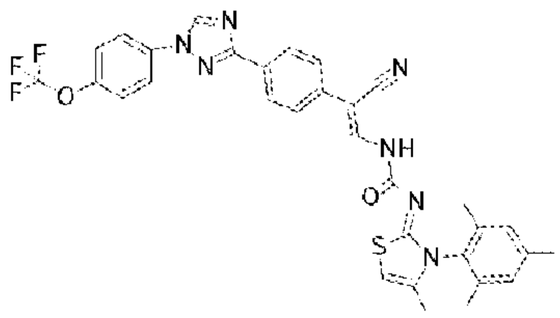
P1093

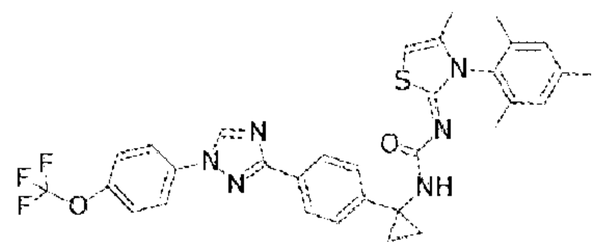
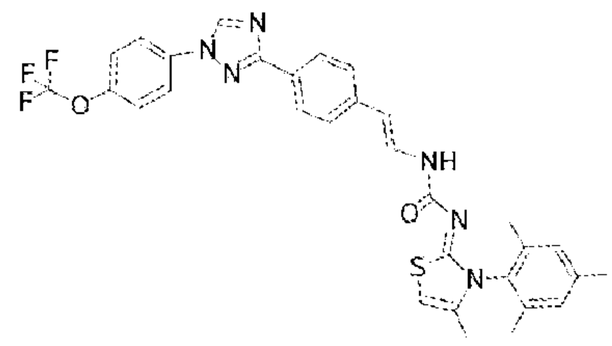
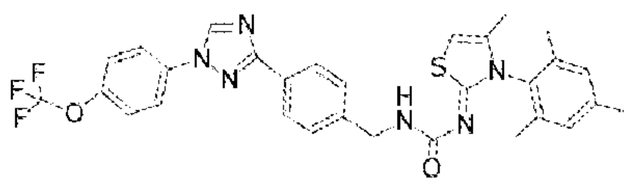
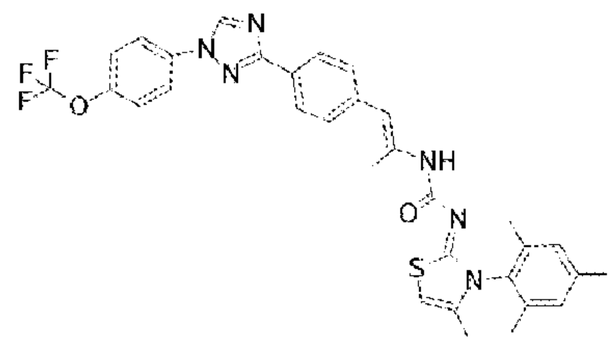
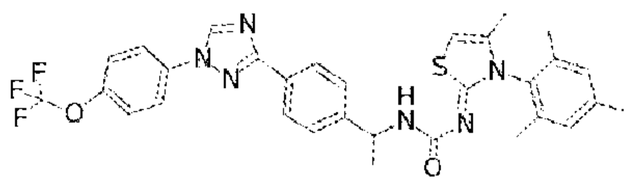
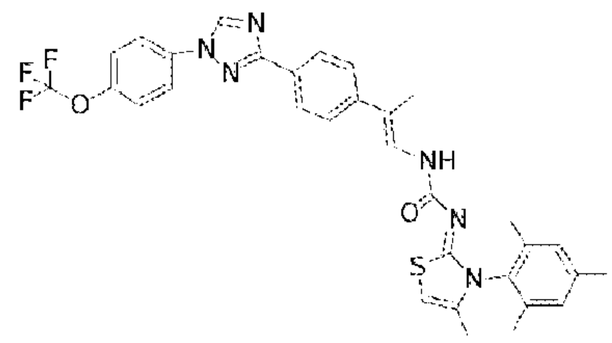
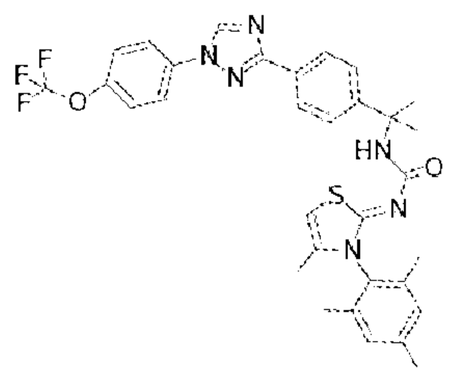
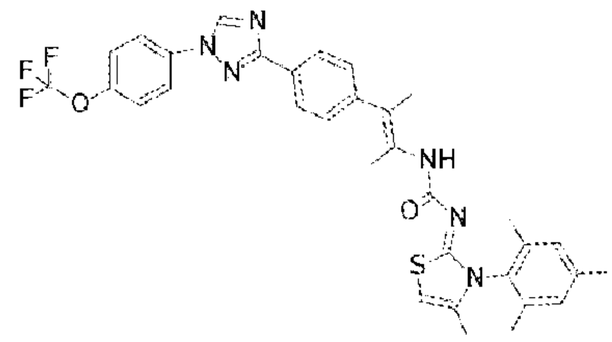
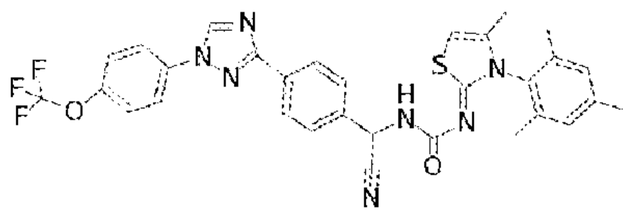
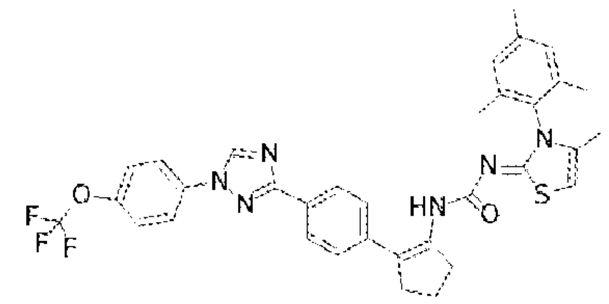


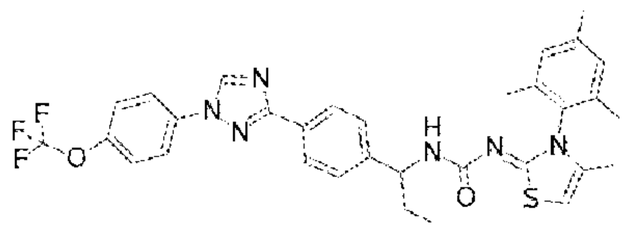
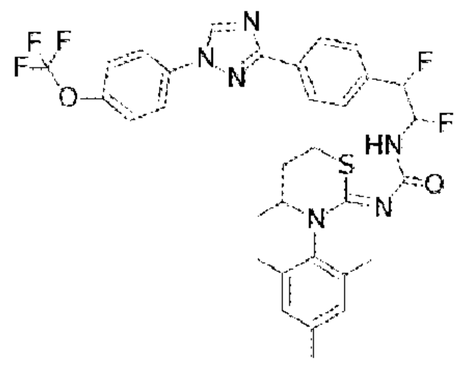
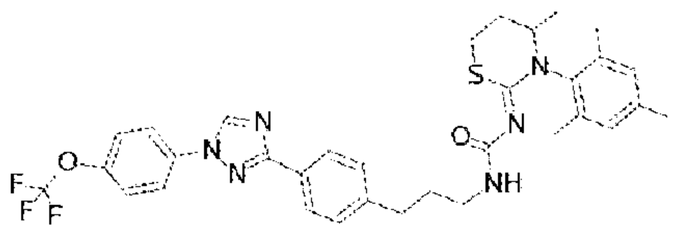
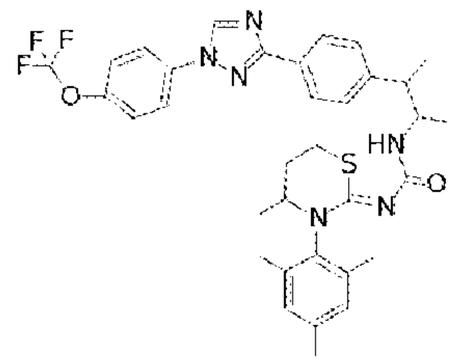
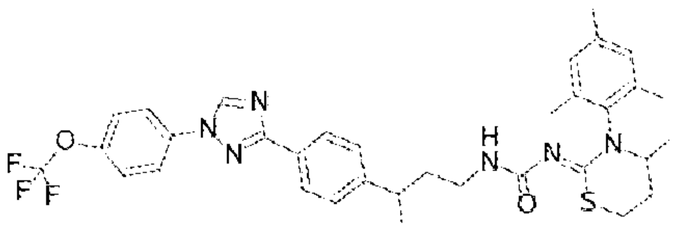
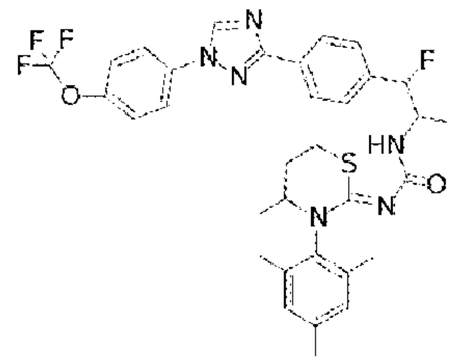
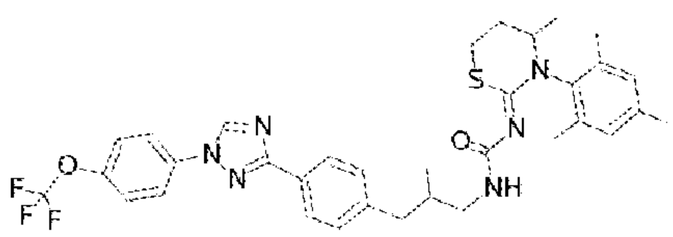
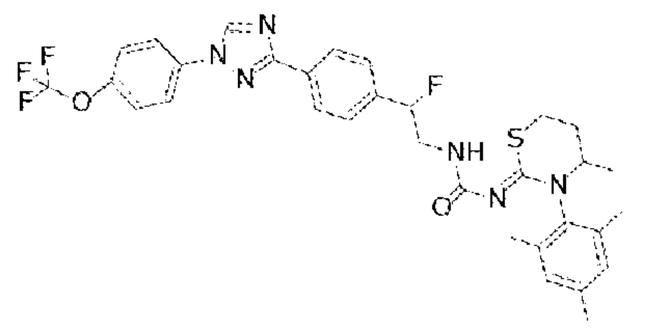
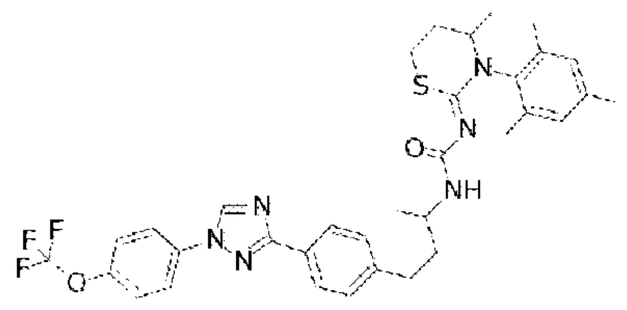
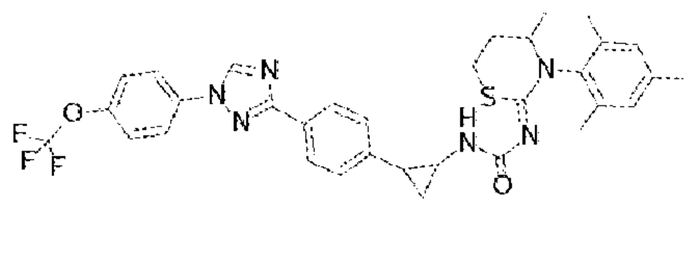
P1094

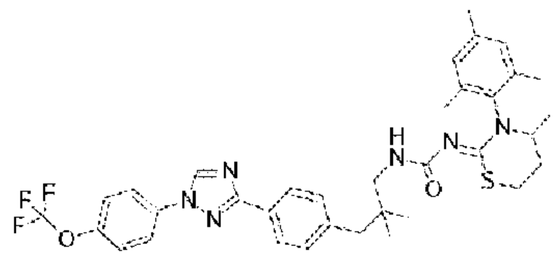
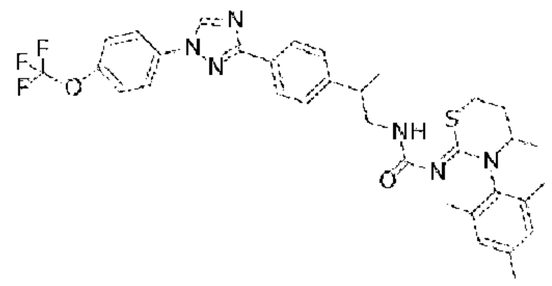
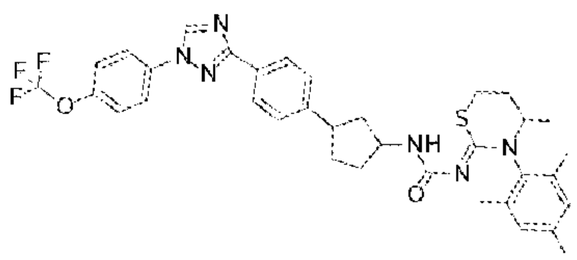
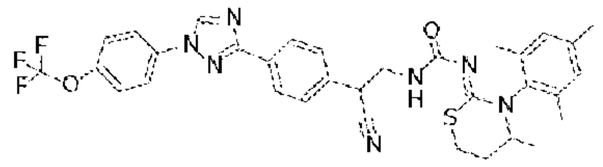
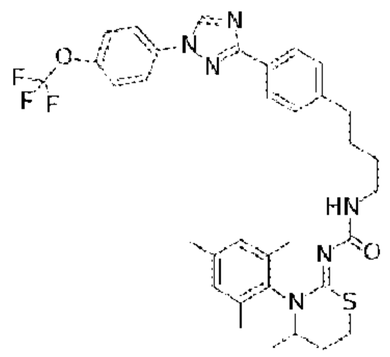
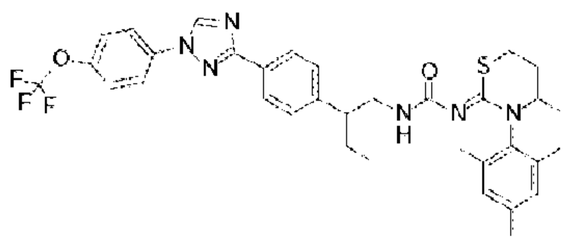
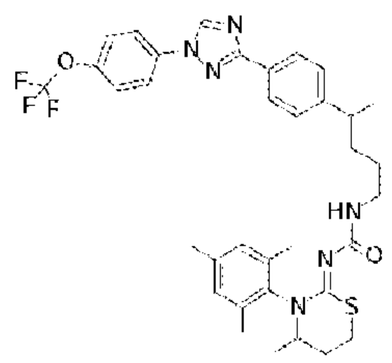
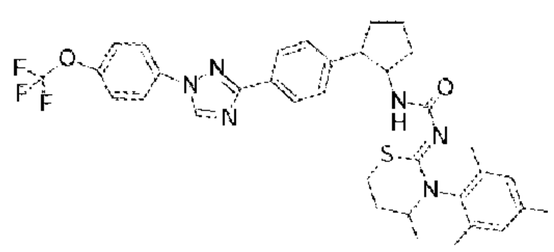
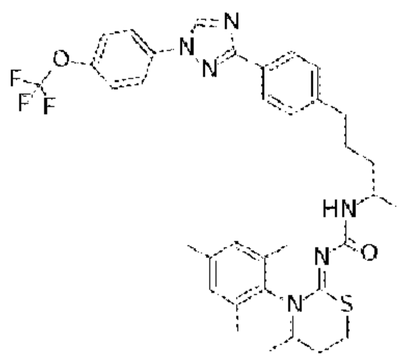
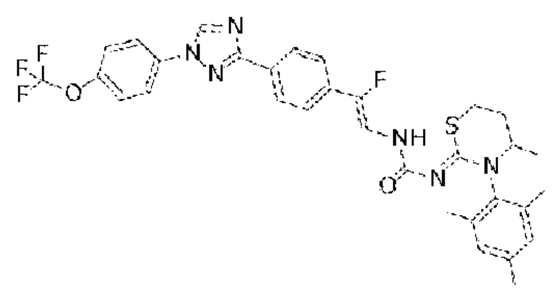


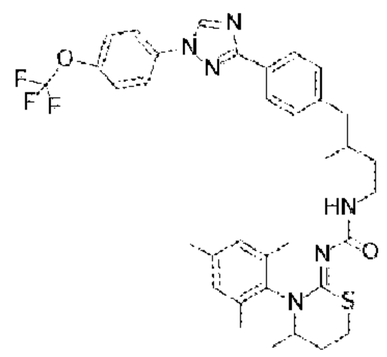
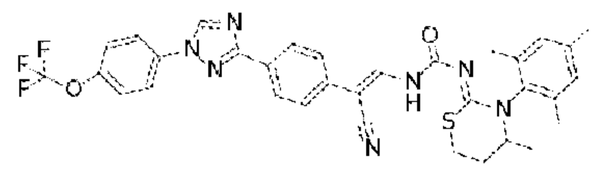
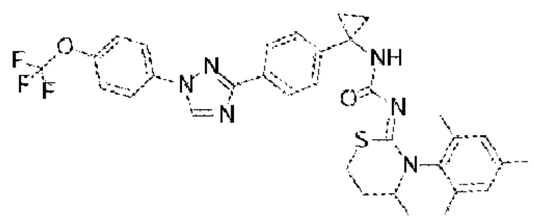
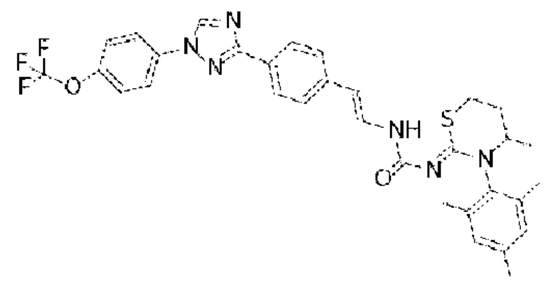
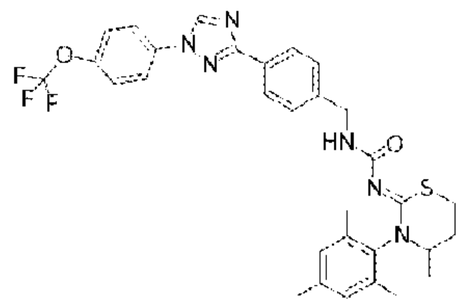
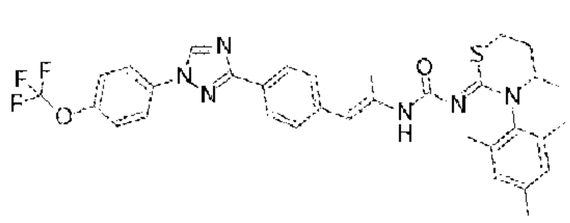
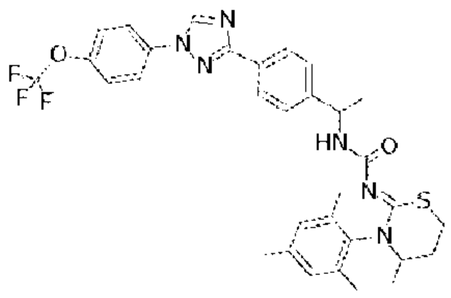
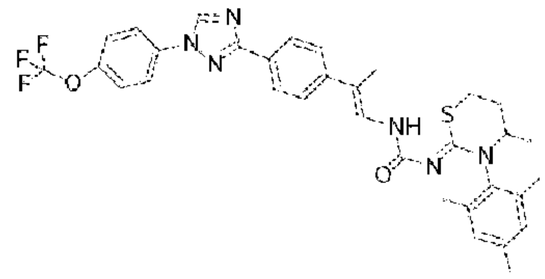
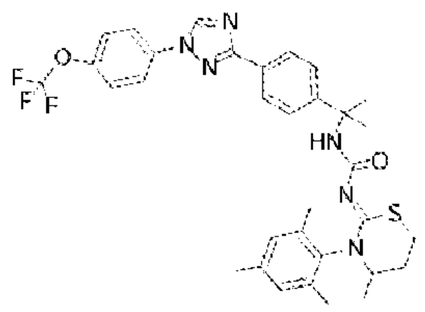
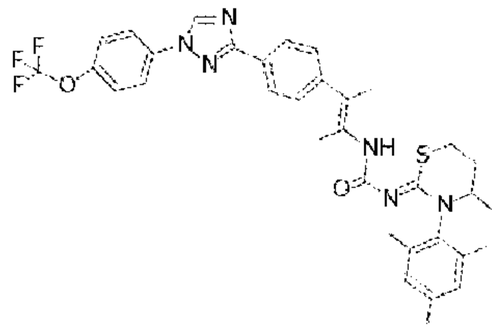
P1095

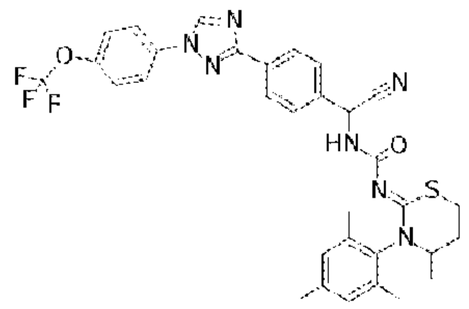
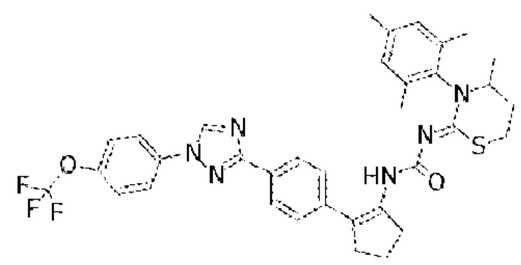
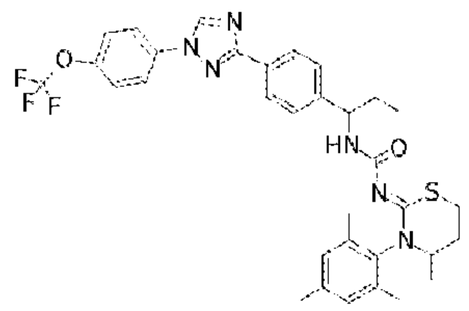
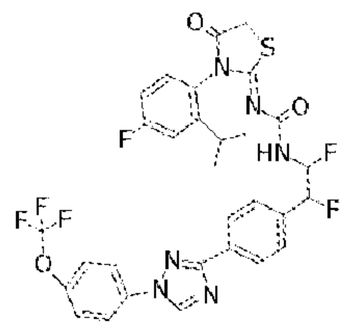
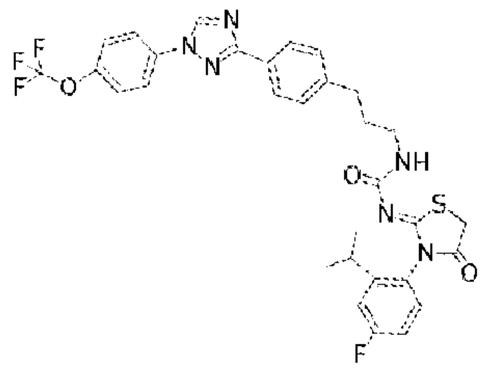
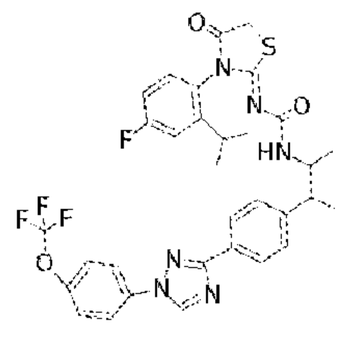
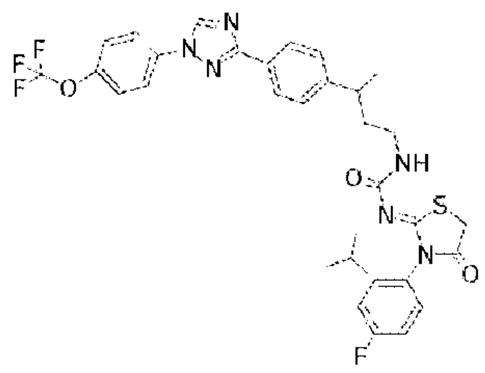
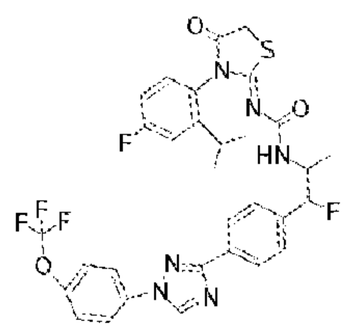
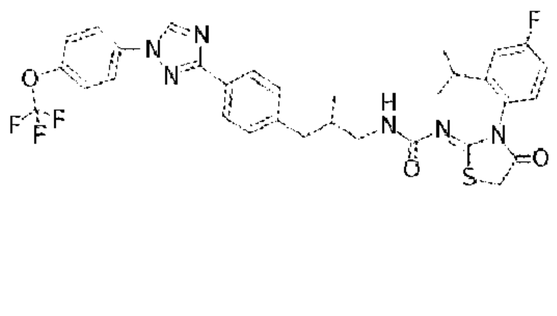
 P1096	 P1097
 P1098	 P1099
 P1100	 P1101
 P1102	 P1103
 P1104	 P1105

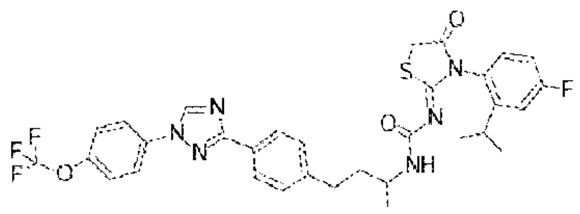
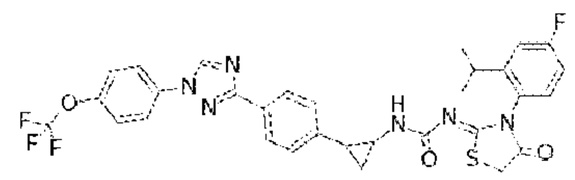
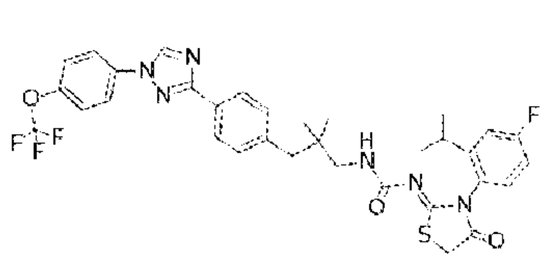
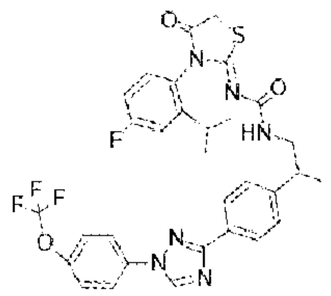
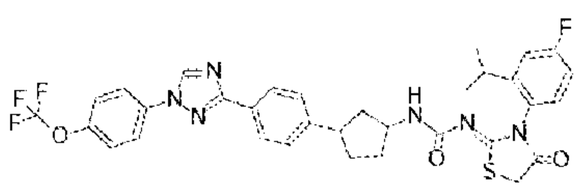
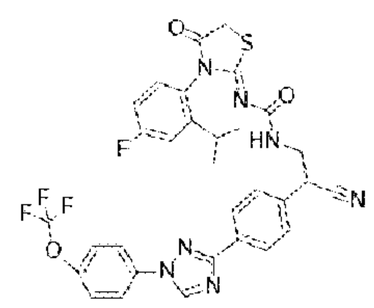
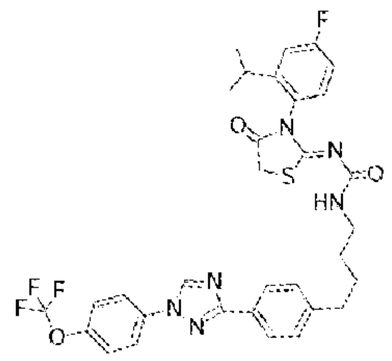
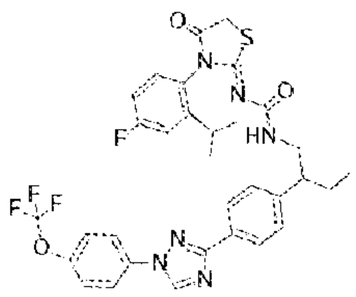
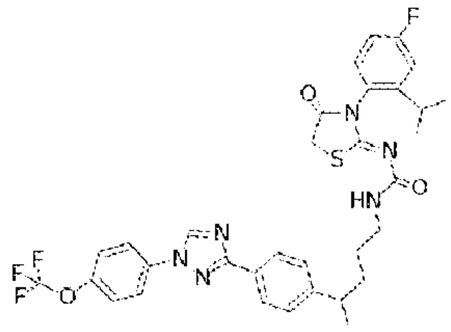
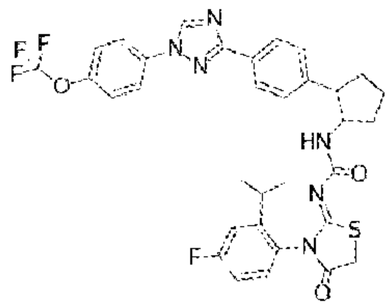
 P1106	 P1107
 P1108	 P1109
 P1110	 P1111
 P1112	 P1113
 P1114	 P1115

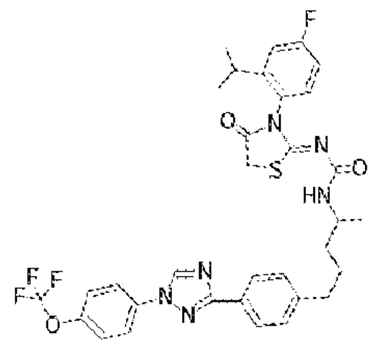
 P1116	 P1117
 P1118	 P1119
 P1120	 P1121
 P1122	 P1123
 P1124	 P1125

 P1126	 P1127
 P1128	 P1129
 P1130	 P1131
 P1132	 P1133
 P1134	 P1135

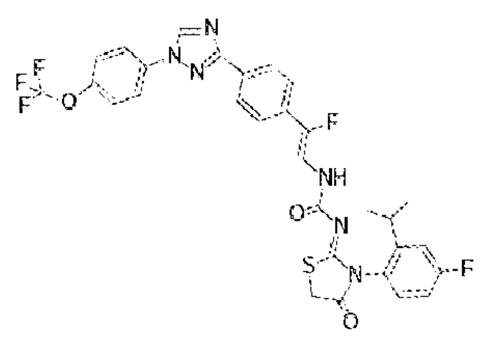
 P1136	 P1137
 P1138	 P1139
 P1140	 P1141
 P1142	 P1143
 P1144	 P1145

 P1146	 P1147
 P1148	 P1149
 P1150	 P1151
 P1152	 P1153
 P1154	P1155

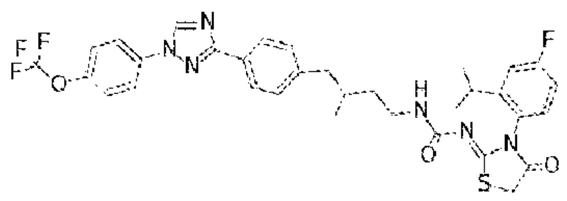
	
P1156	P1157
	
P1158	P1159
	
P1160	P1161
	
P1162	P1163
	
P1164	P1165



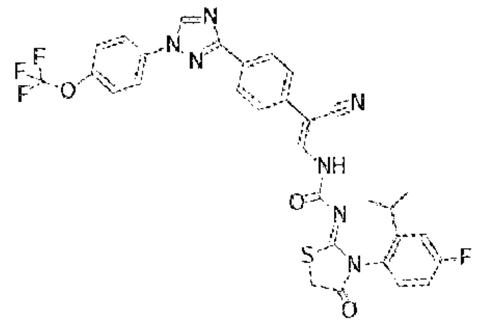
P1166



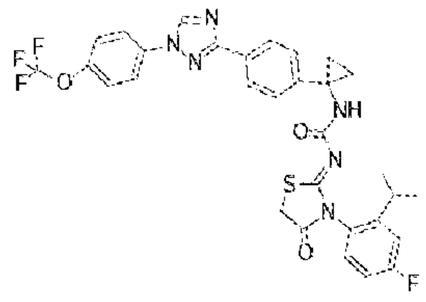
P1167



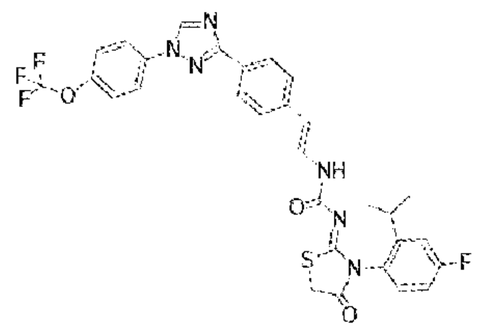
P1168



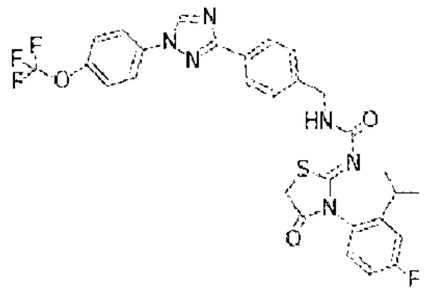
P1169



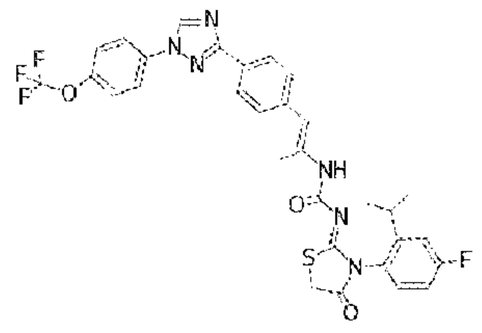
P1170



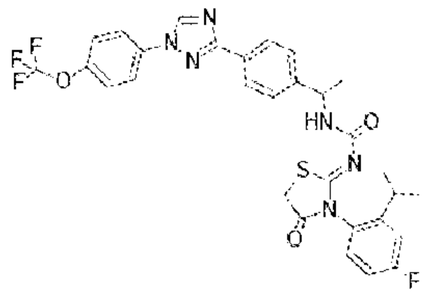
P1171



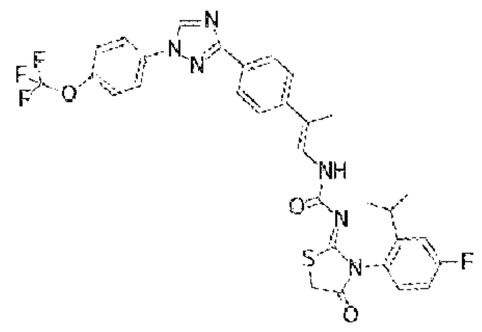
P1172



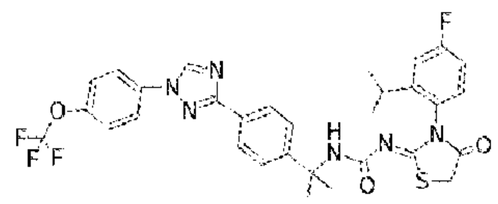
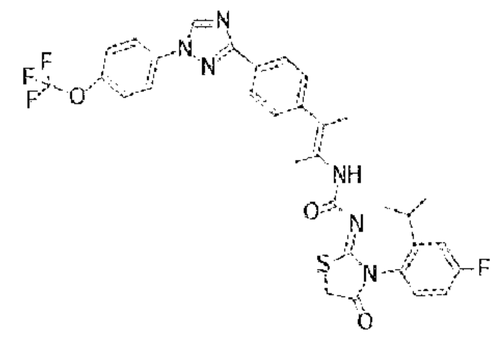
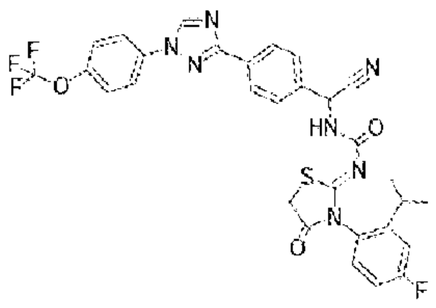
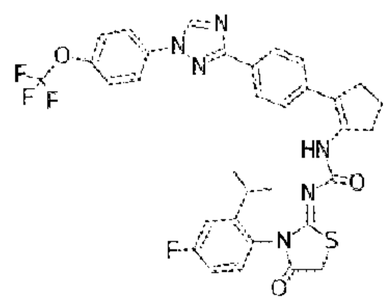
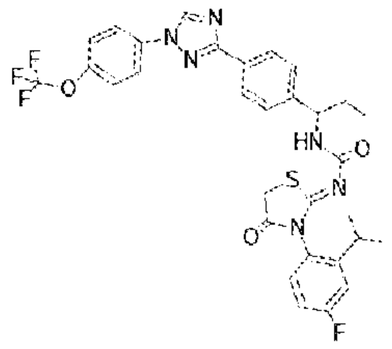
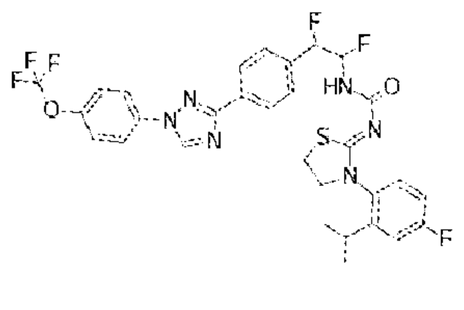
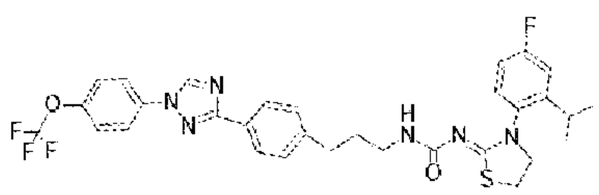
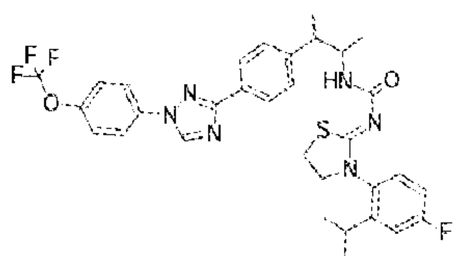
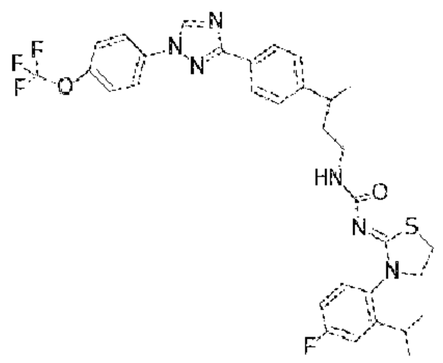
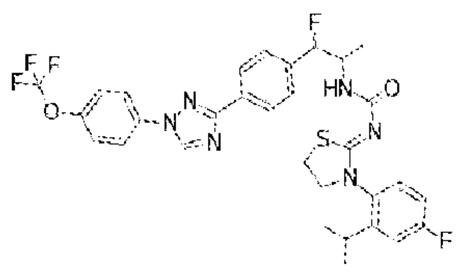
P1173

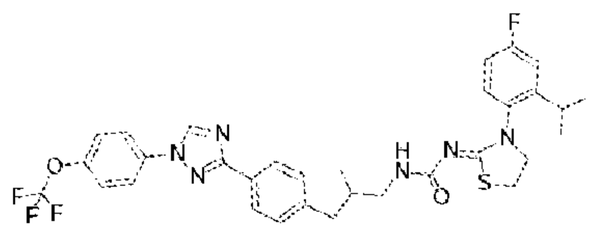
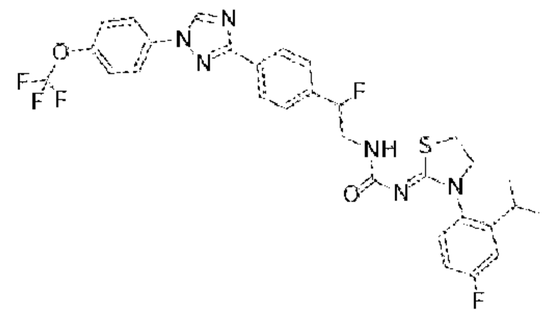
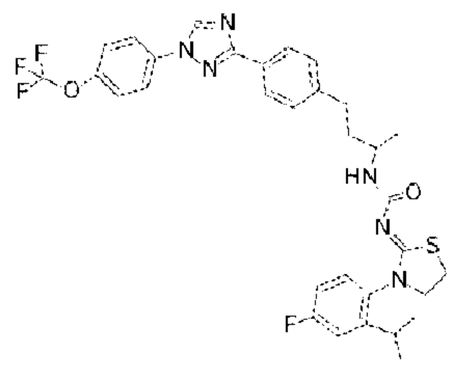
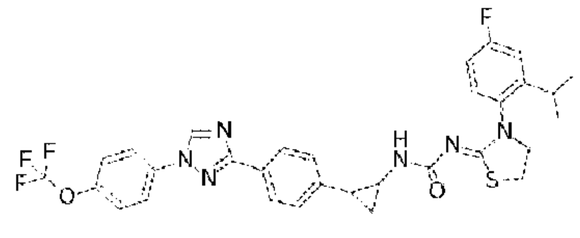
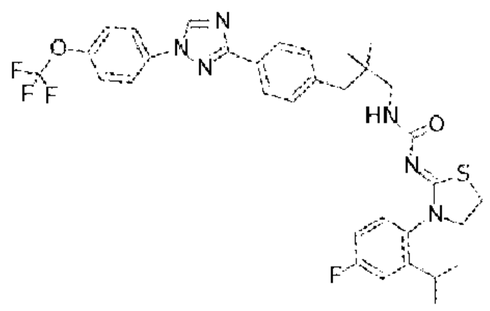
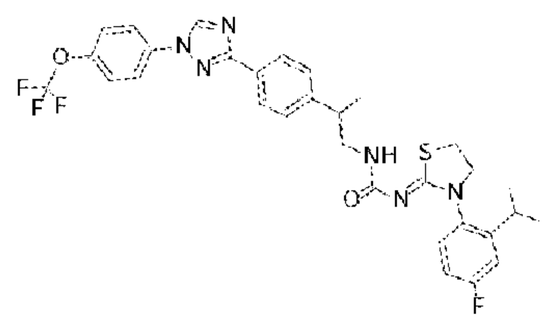
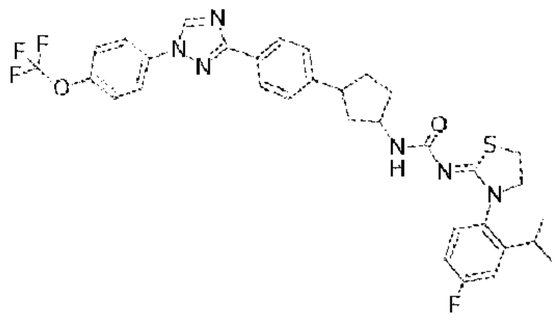
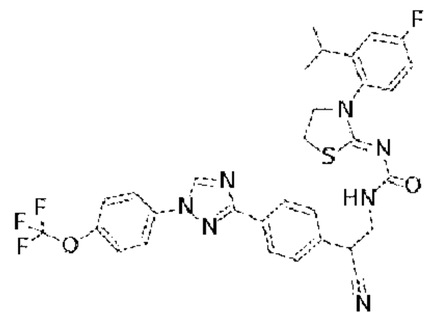
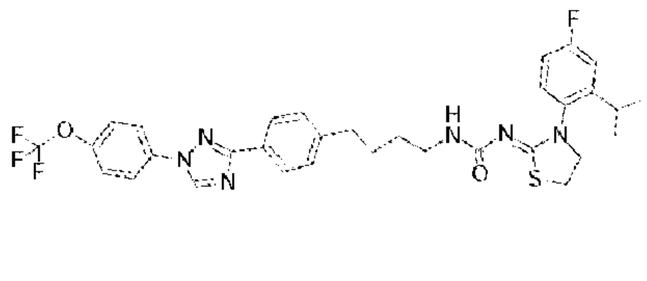
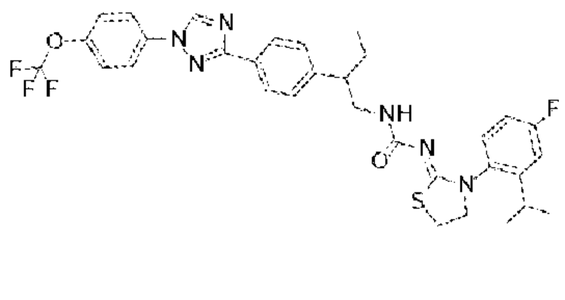


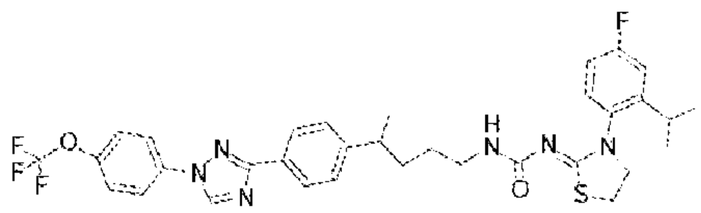
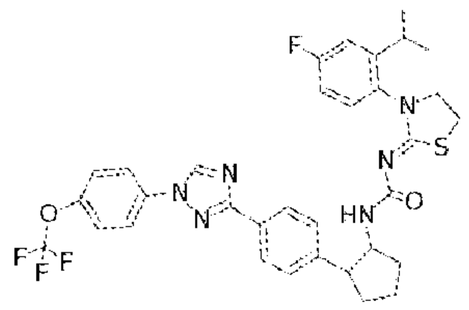
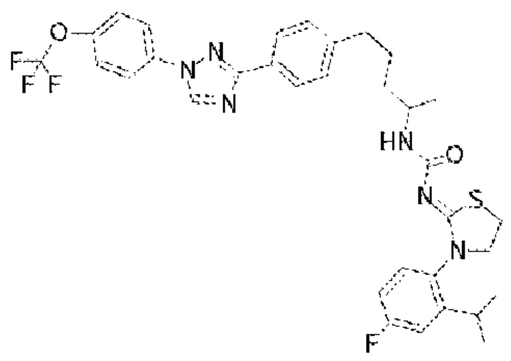
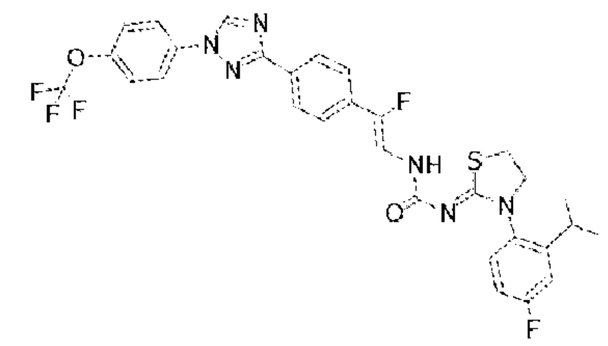
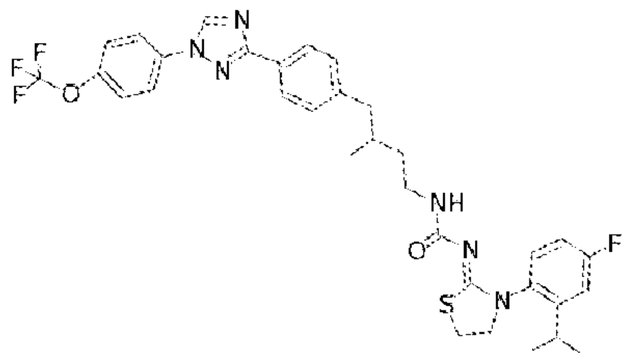
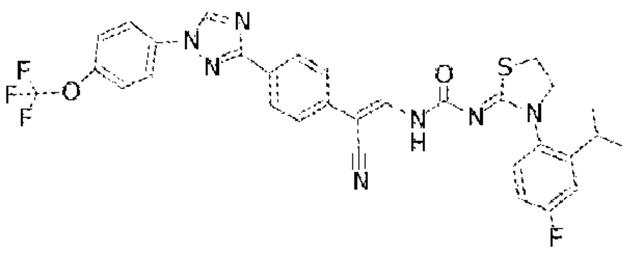
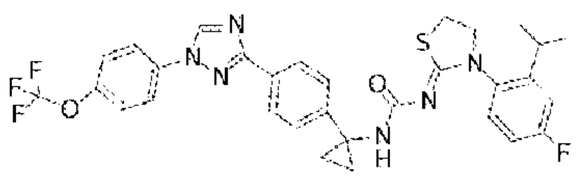
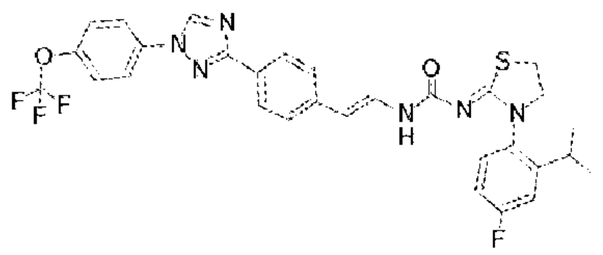
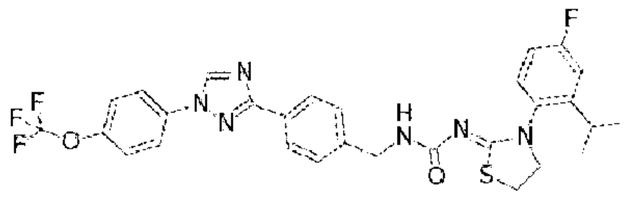
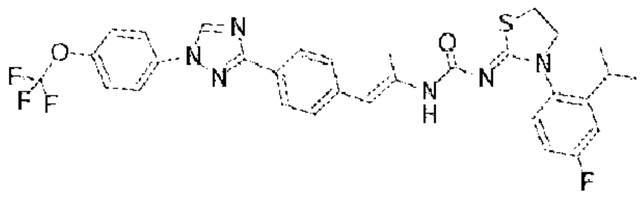
P1174

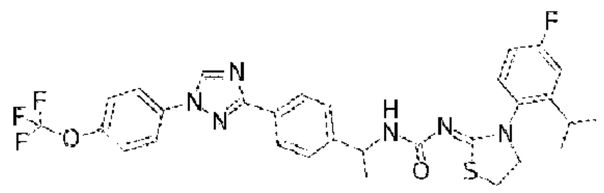
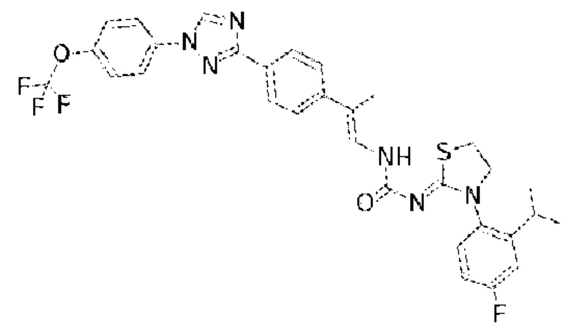
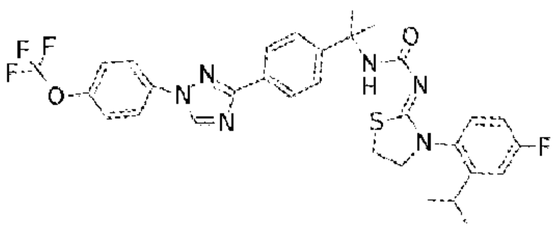
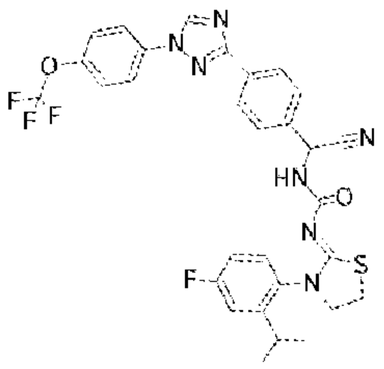
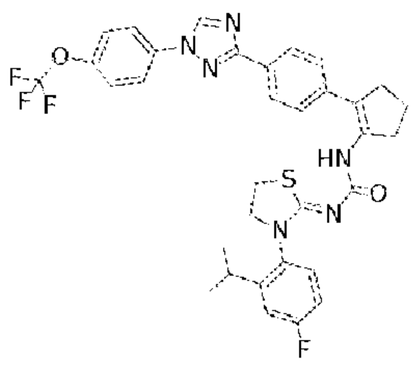
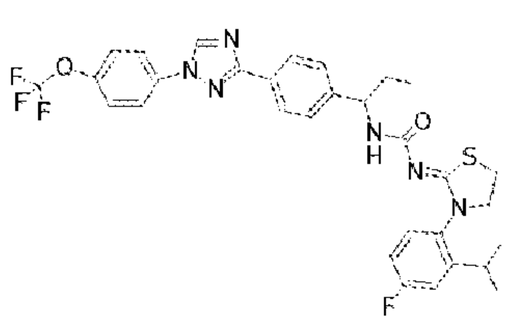
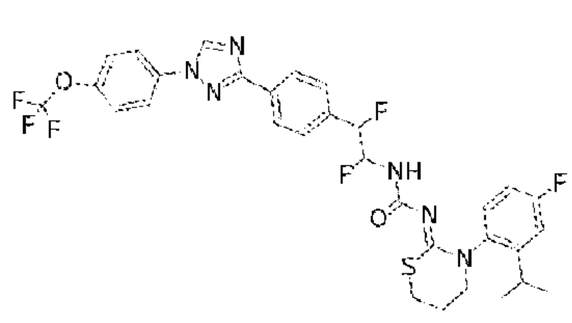
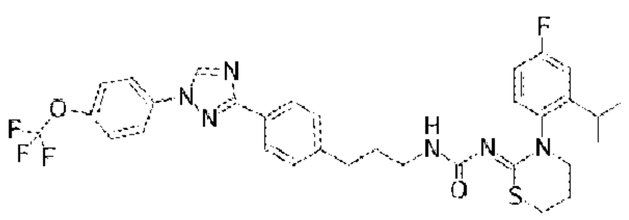
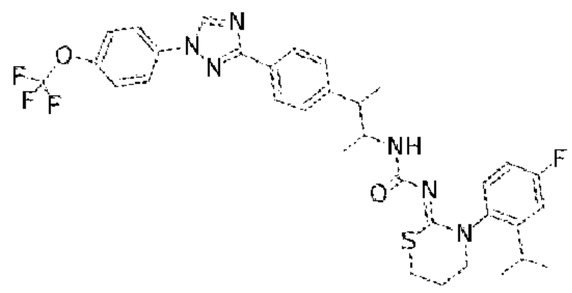


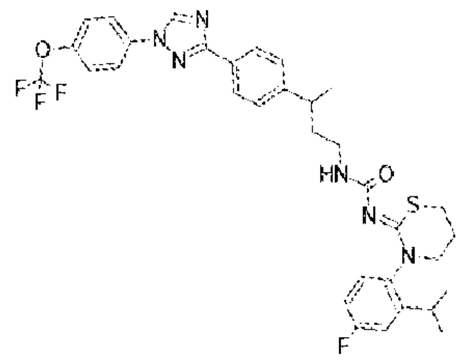
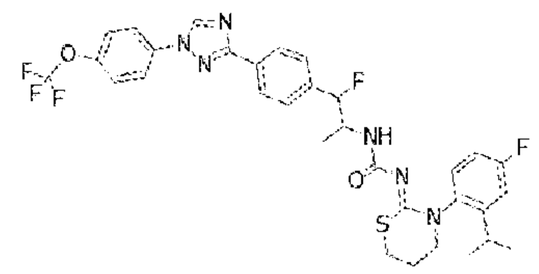
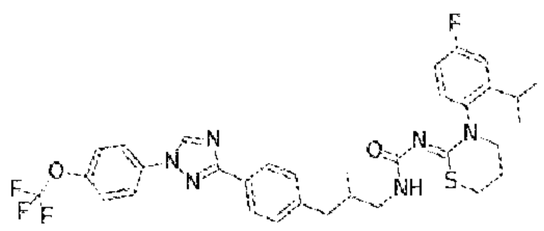
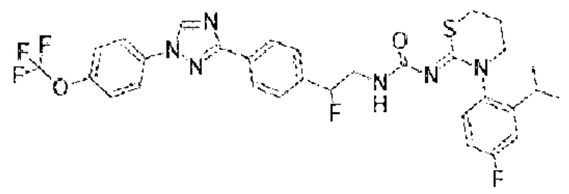
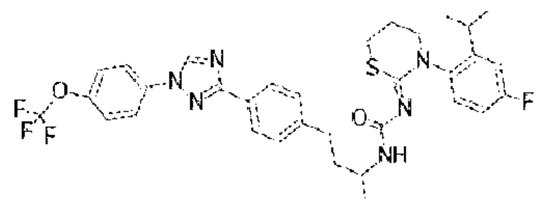
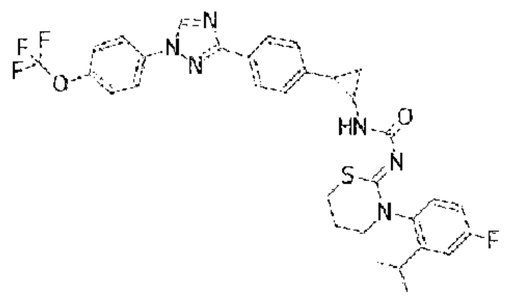
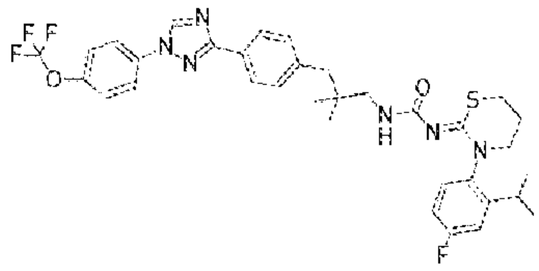
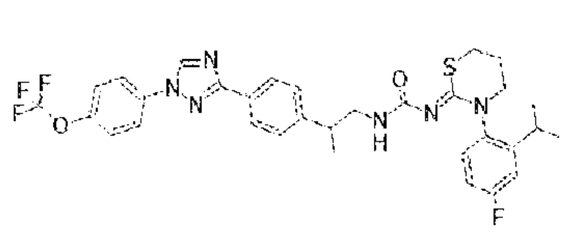
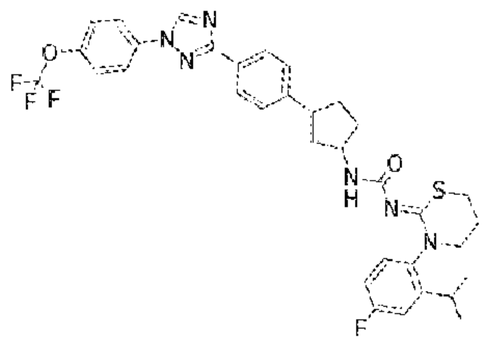
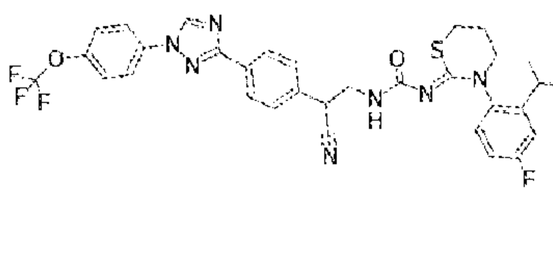
P1175

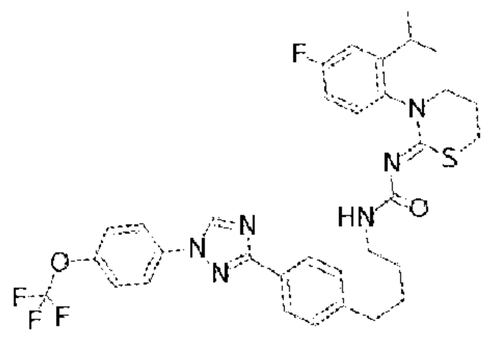
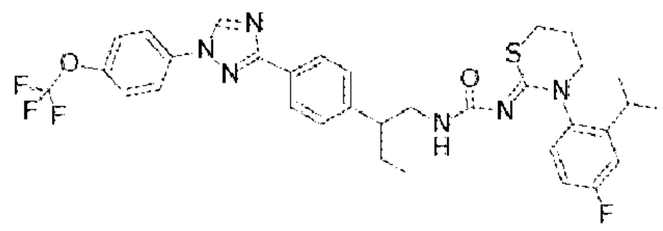
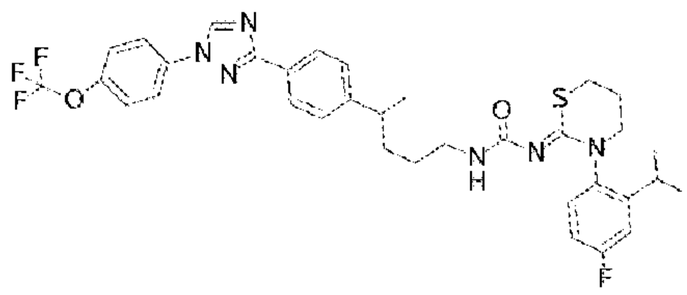
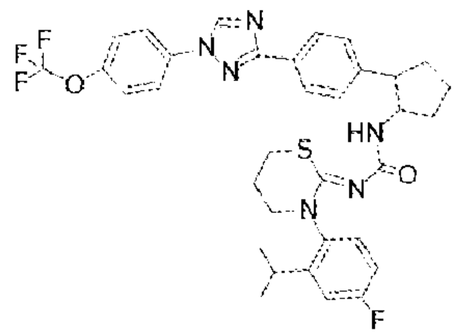
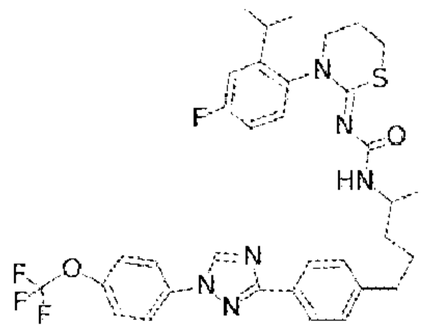
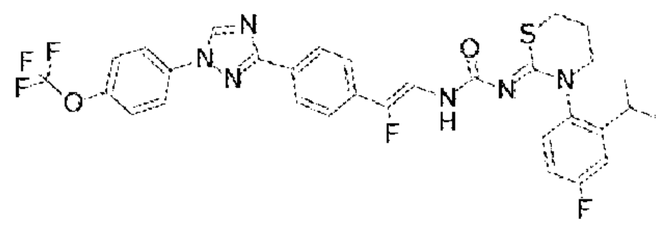
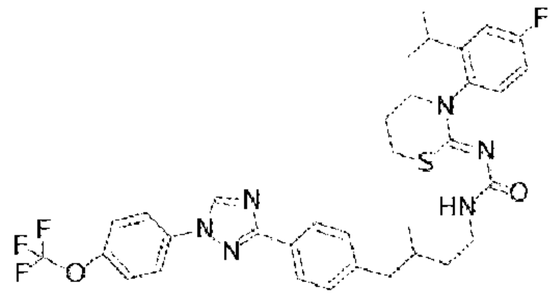
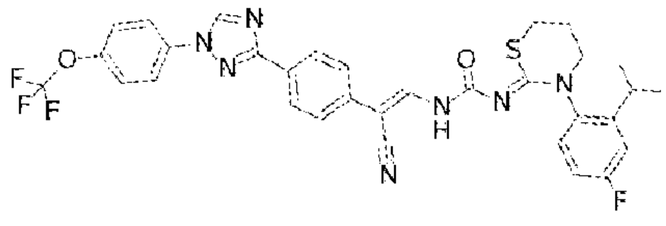
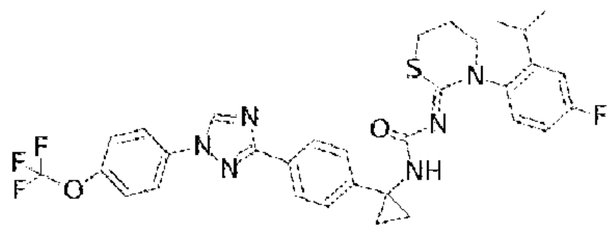
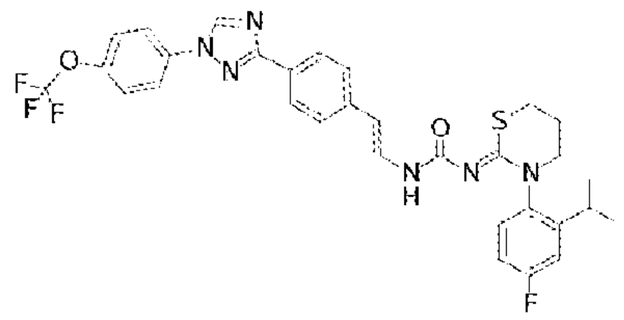
 P1176	 P1177
 P1178	 P1179
 P1180	 P1181
 P1182	 P1183
 P1184	 P1185

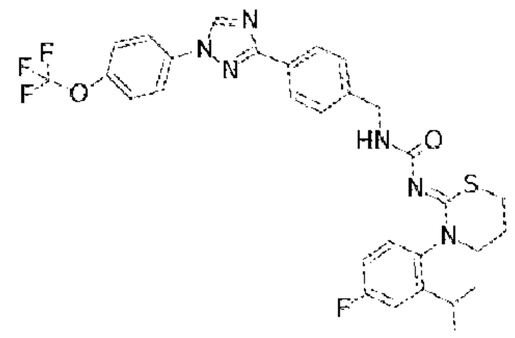
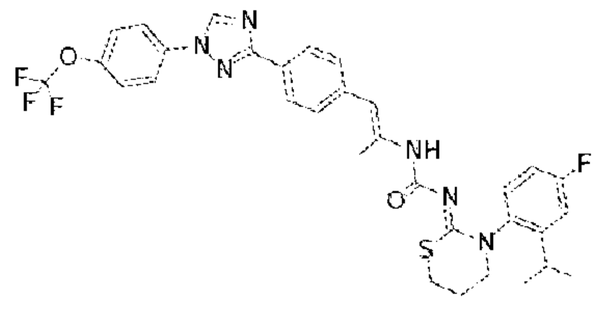
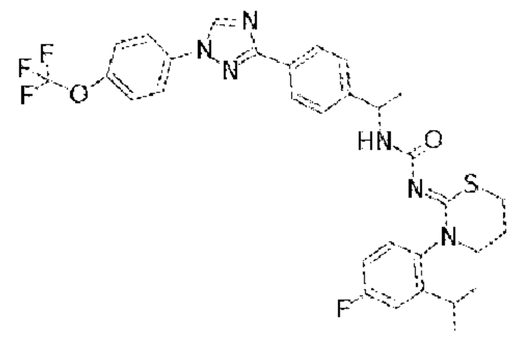
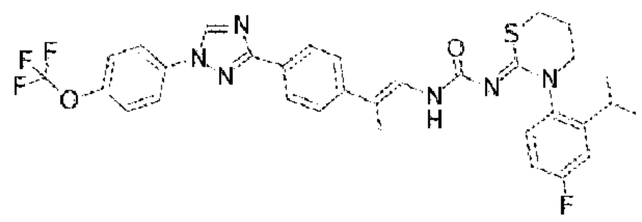
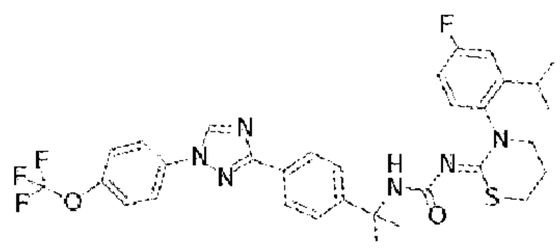
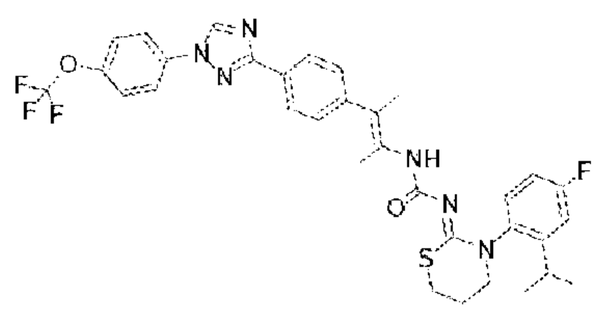
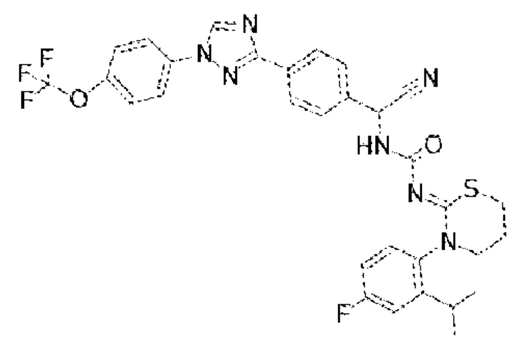
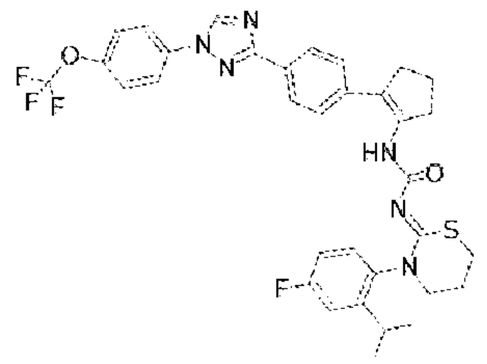
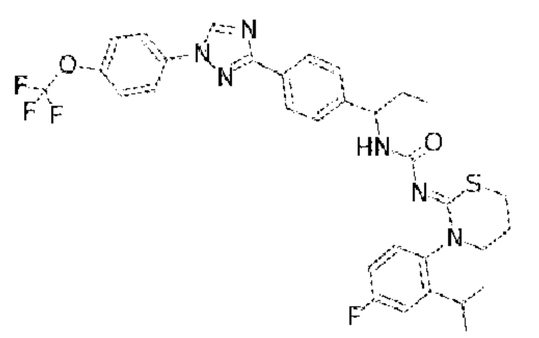
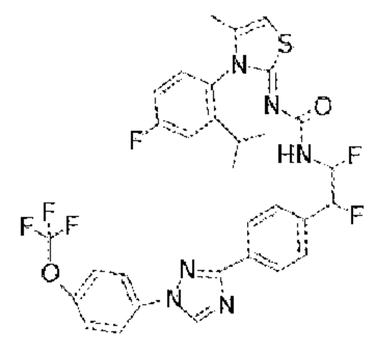
 P1186	 P1187
 P1188	 P1189
 P1190	 P1191
 P1192	 P1193
 P1194	 P1195

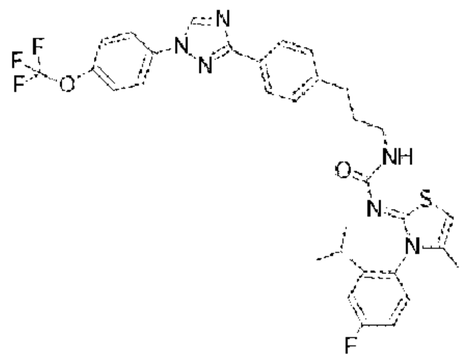
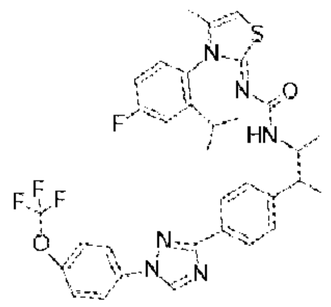
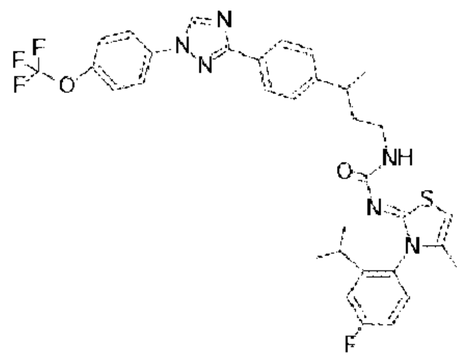
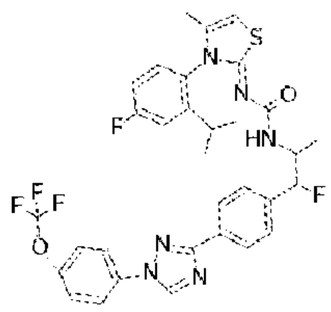
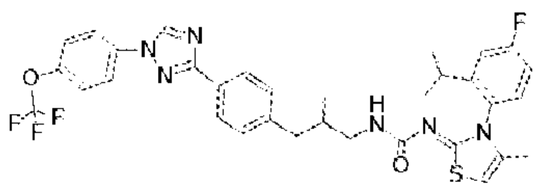
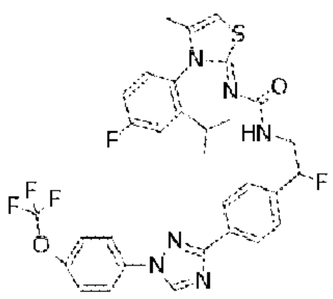
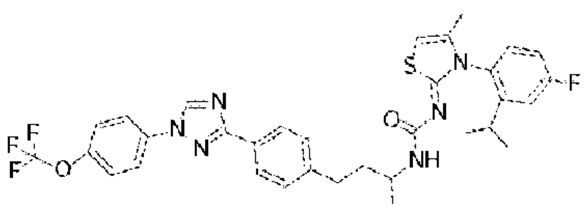
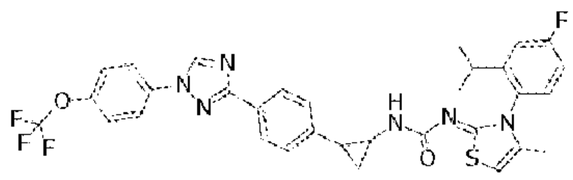
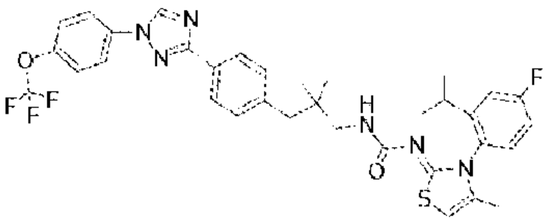
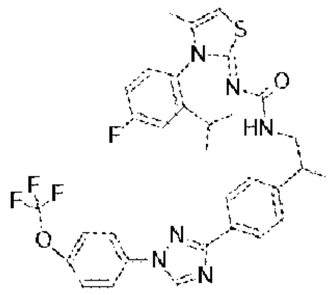
 P1196	 P1197
 P1198	 P1199
 P1200	 P1201
 P1202	 P1203
 P1204	 P1205

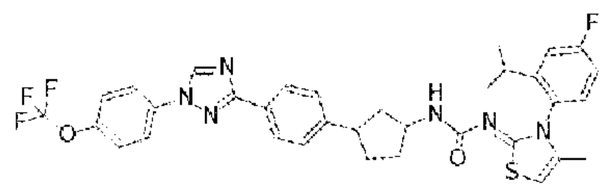
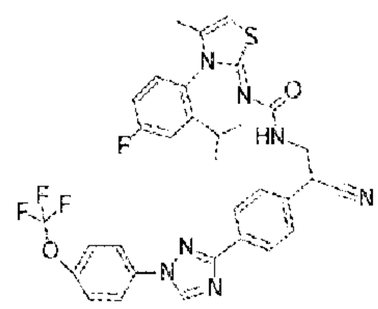
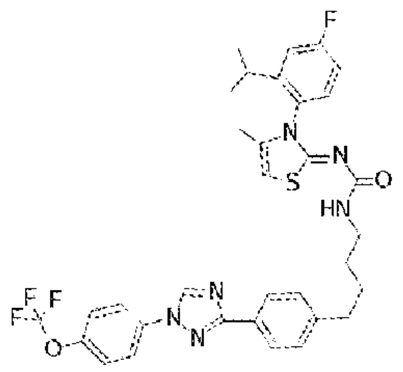
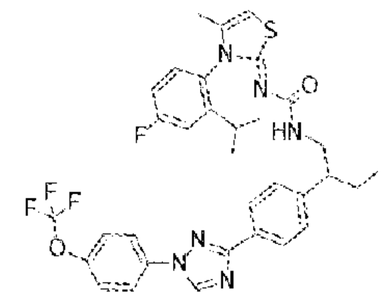
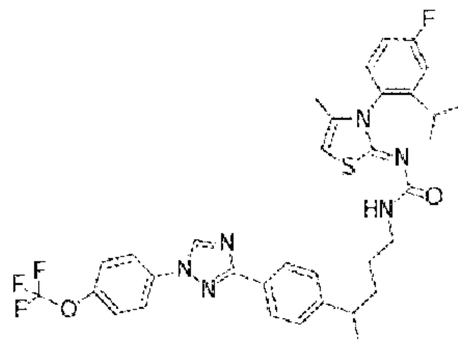
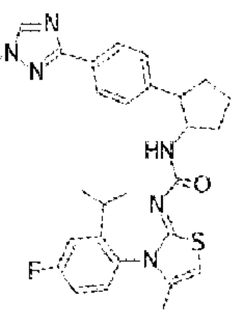
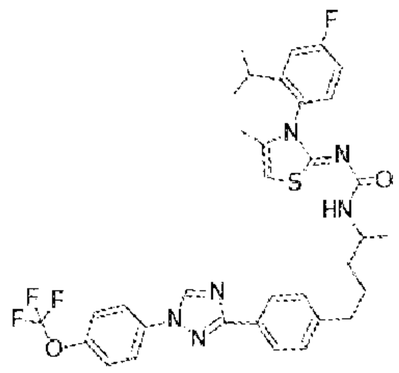
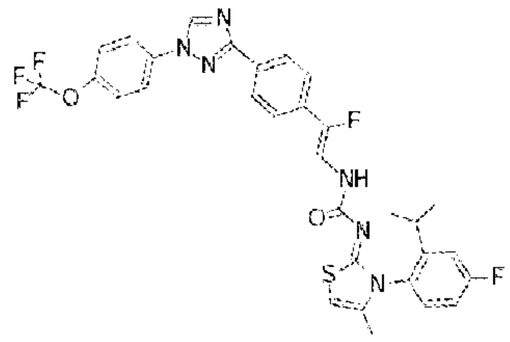
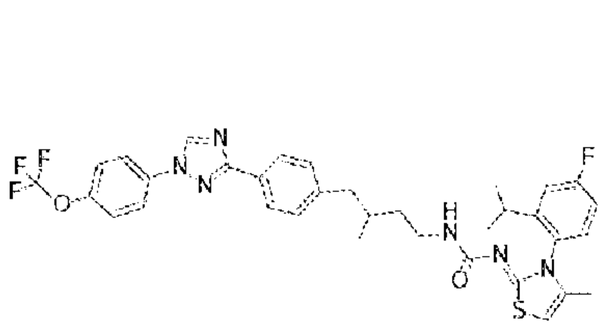
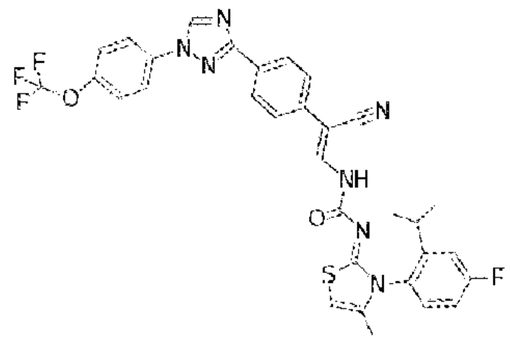
 P1206	 P1207
 P1208	 P1209
 P1210	 P1211
 P1212	 P1213
 P1214	P1215

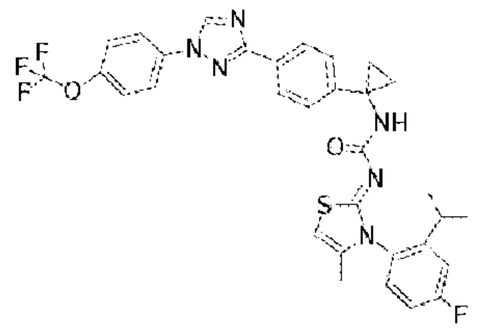
 P1216	 P1217
 P1218	 P1219
 P1220	 P1221
 P1222	 P1223
 P1224	 P1225

 P1226	 P1227
 P1228	 P1229
 P1230	 P1231
 P1232	 P1233
 P1234	 P1235

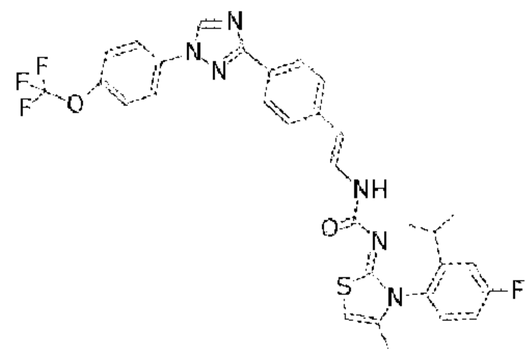
 P1236	 P1237
 P1238	 P1239
 P1240	 P1241
 P1242	 P1243
 P1244	 P1245

 P1246	 P1247
 P1248	 P1249
 P1250	 P1251
 P1252	 P1253
 P1254	 P1255

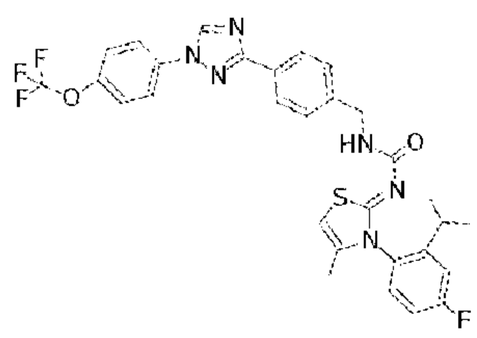
 P1256	 P1257
 P1258	 P1259
 P1260	 P1261
 P1262	 P1263
 P1264	 P1265



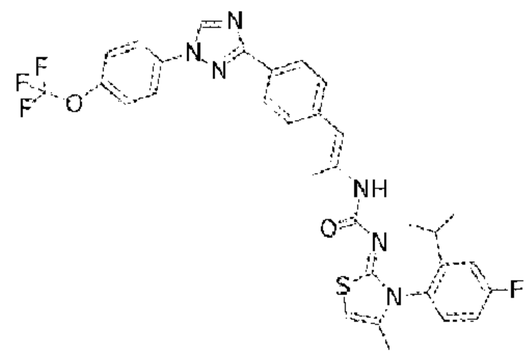
P1266



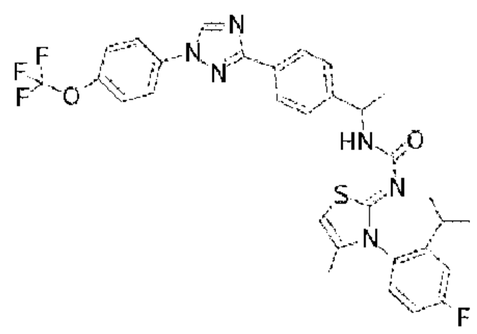
P1267



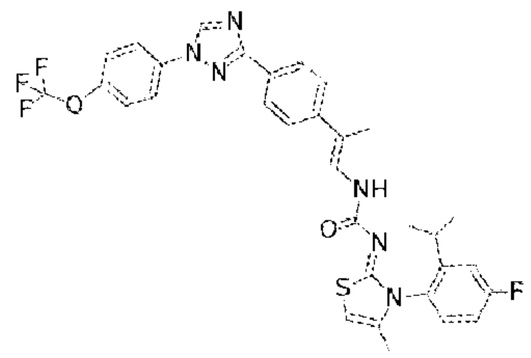
P1268



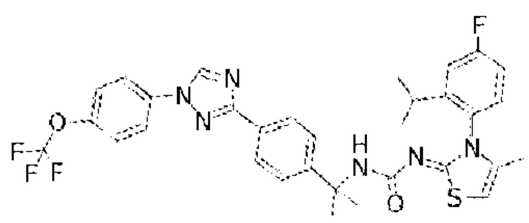
P1269



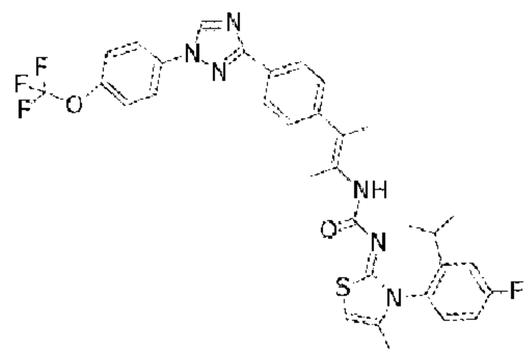
P1270



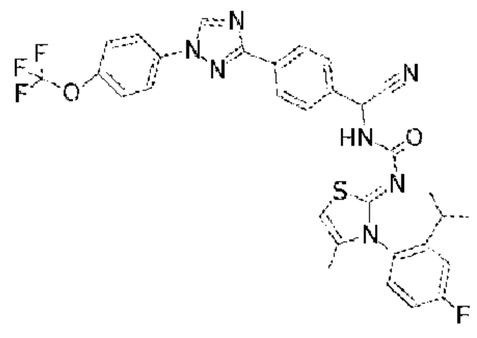
P1271



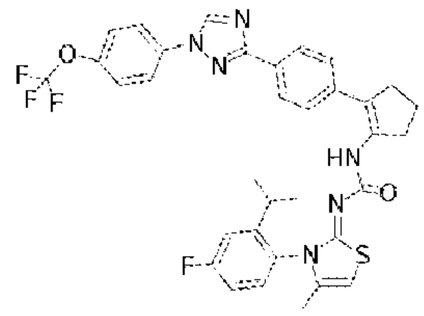
P1272



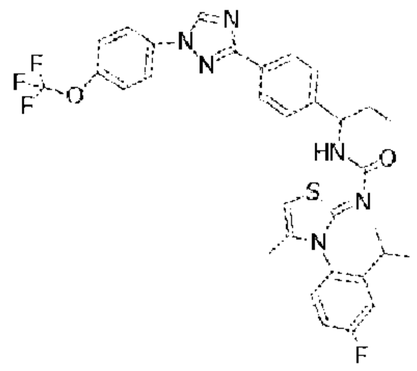
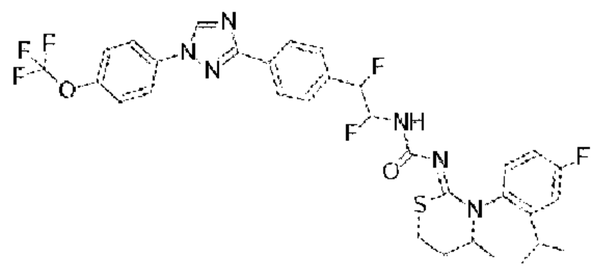
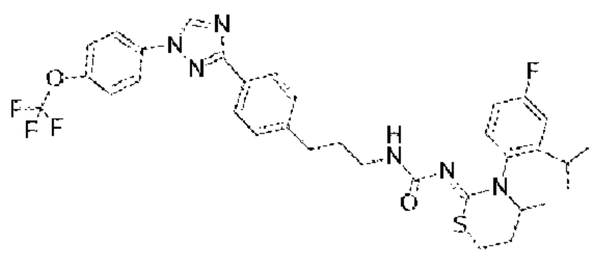
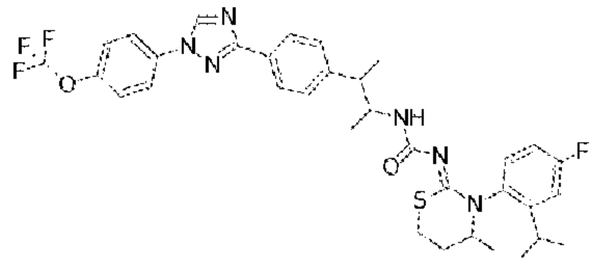
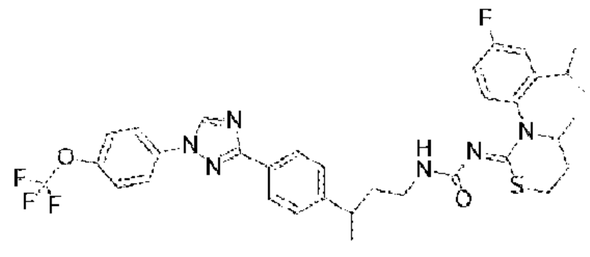
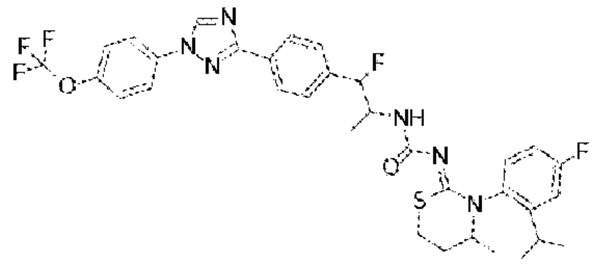
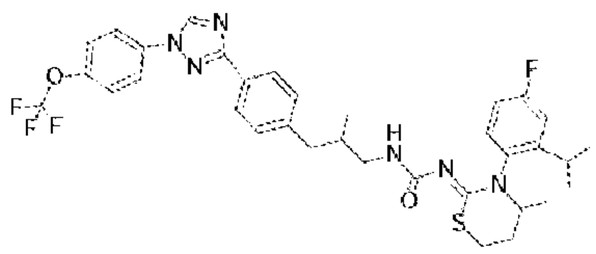
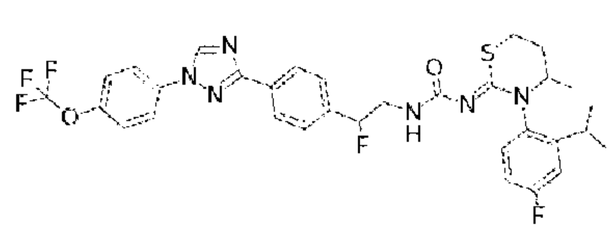
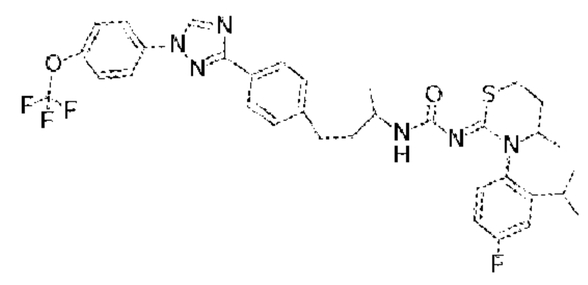
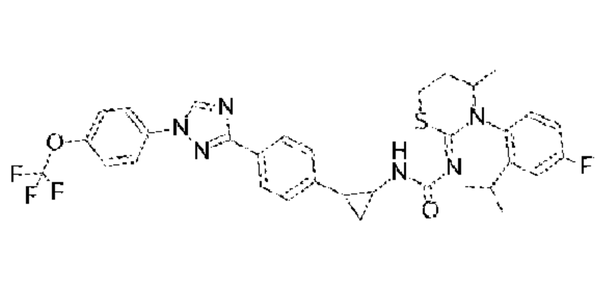
P1273

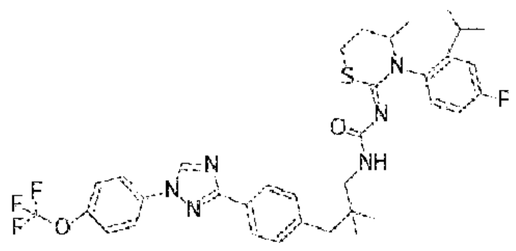
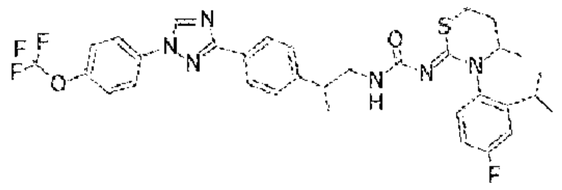
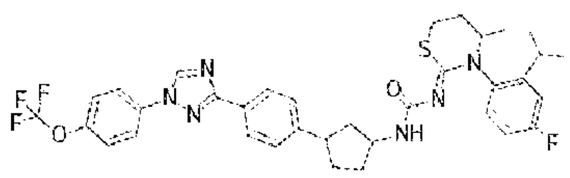
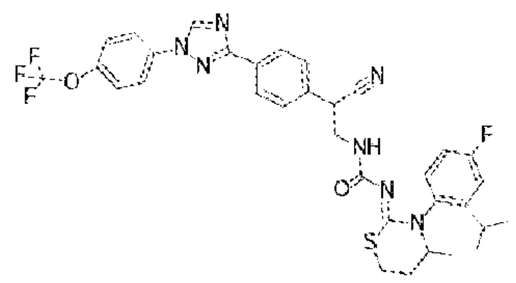
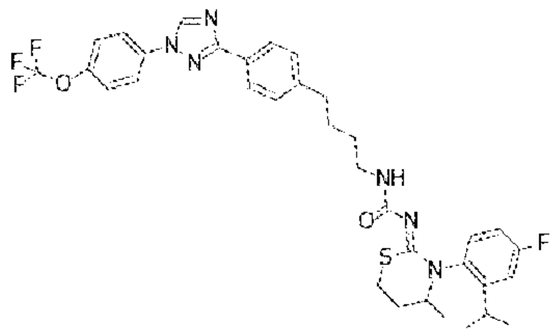
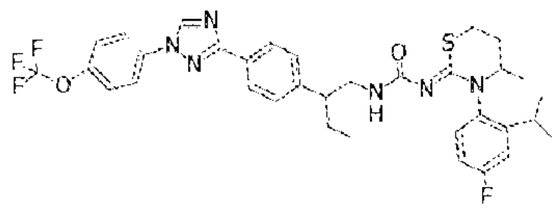
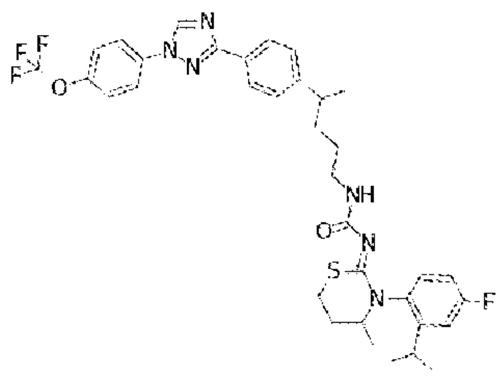
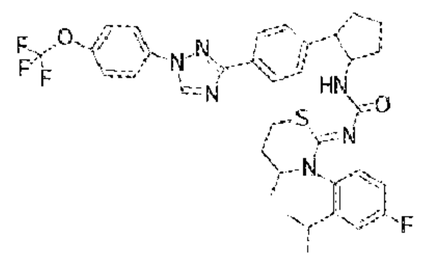
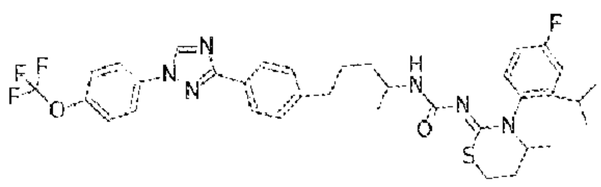
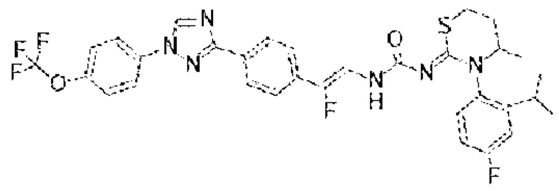


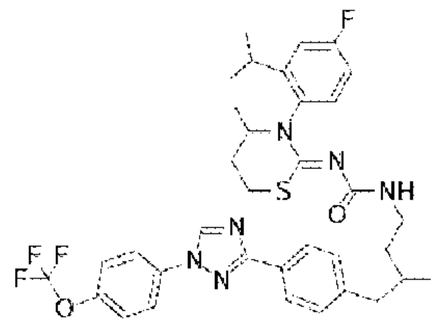
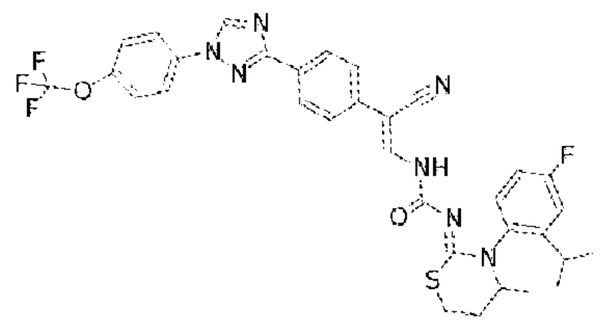
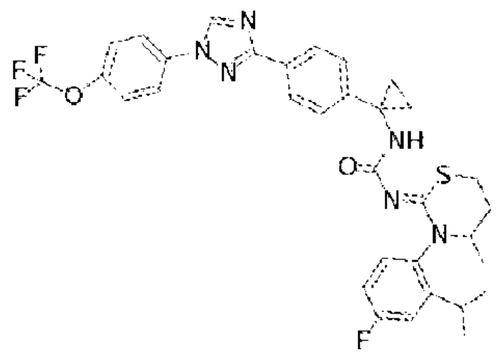
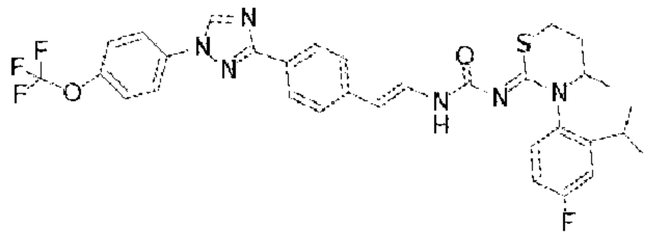
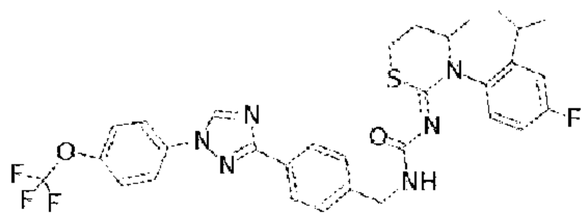
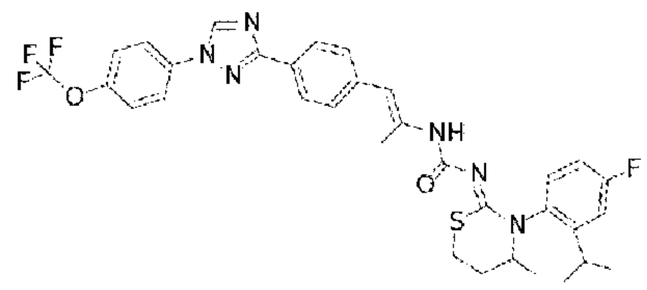
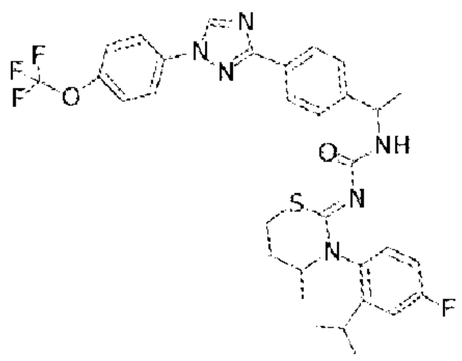
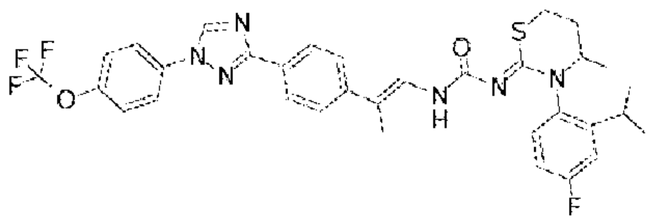
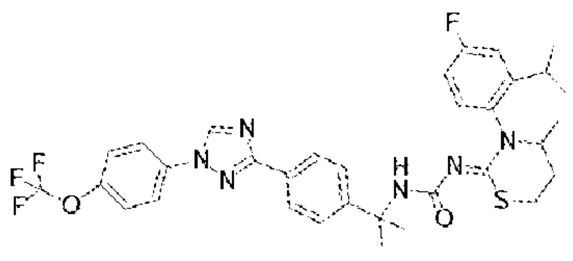
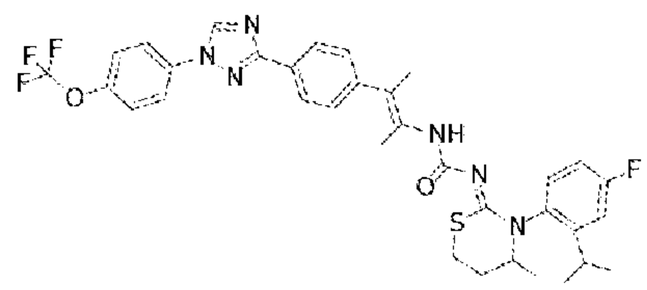
P1274

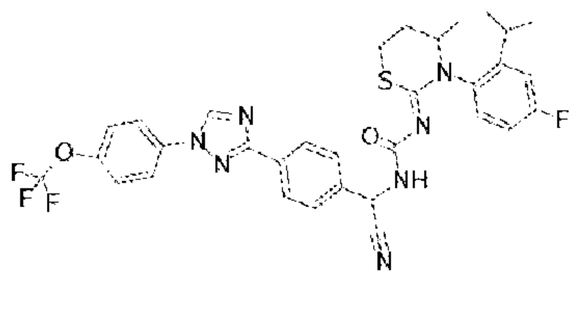


P1275

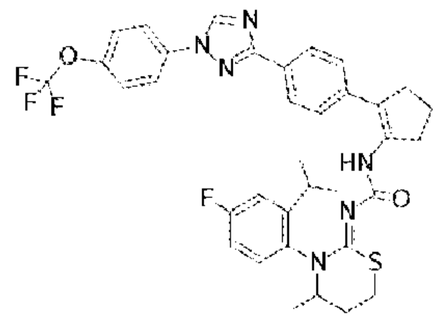
 P1276	 P1277
 P1278	 P1279
 P1280	 P1281
 P1282	 P1283
 P1284	 P1285

	
P1286	P1287
	
P1288	P1289
	
P1290	P1291
	
P1292	P1293
	
P1294	P1295

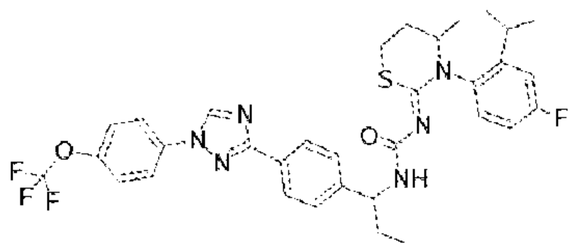
 P1296	 P1297
 P1298	 P1299
 P1300	 P1301
 P1302	 P1303
 P1304	 P1305



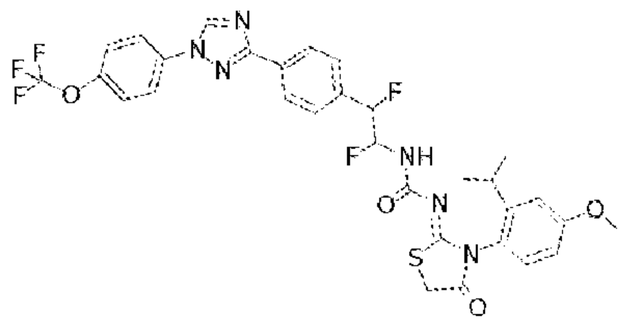
P1306



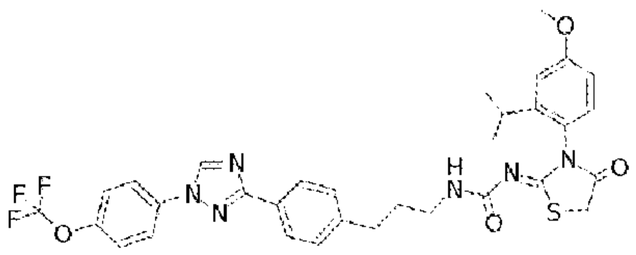
P1307



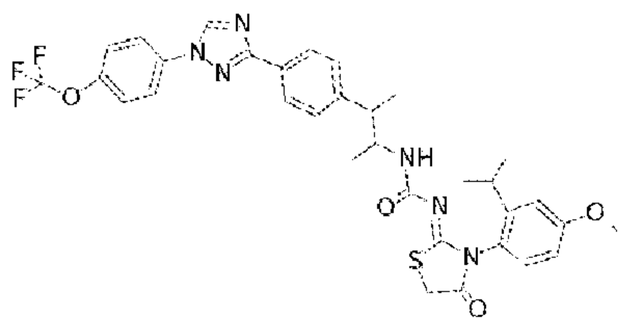
P1308



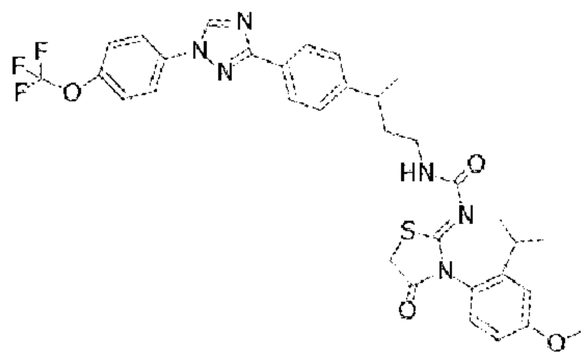
P1309



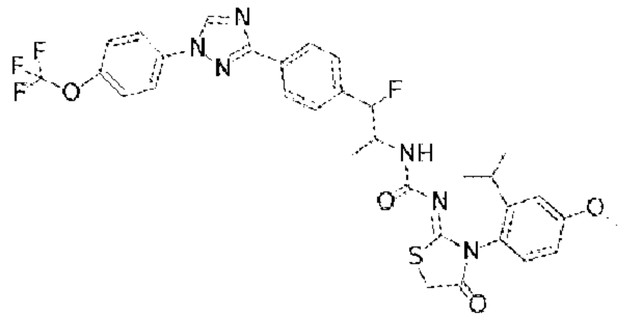
P1310



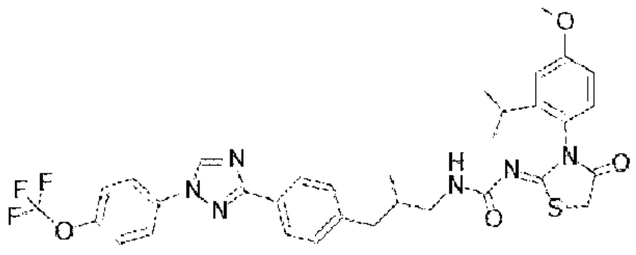
P1311



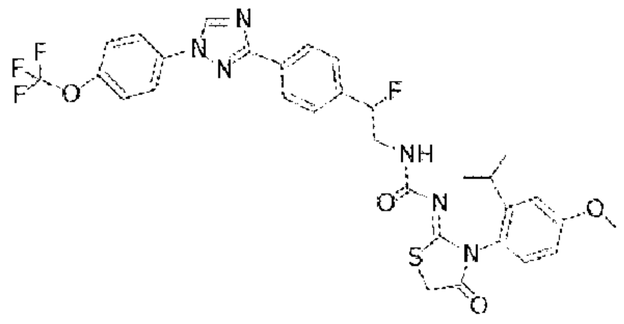
P1312



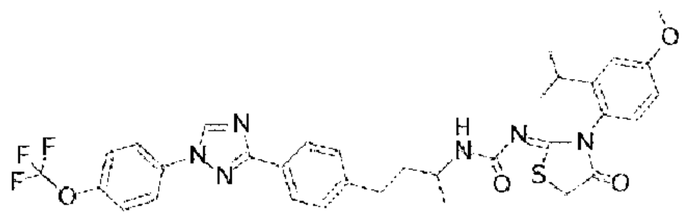
P1313



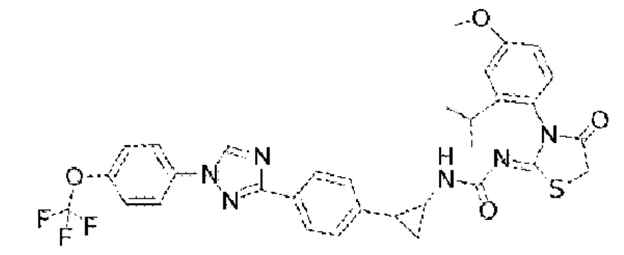
P1314



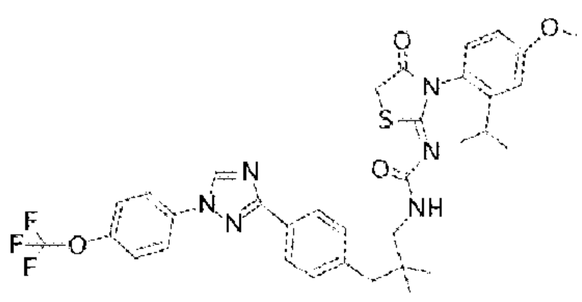
P1315



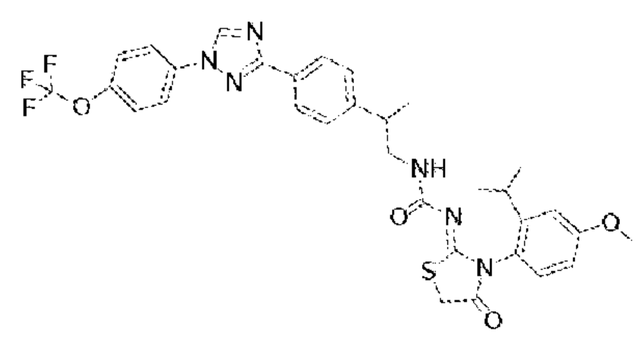
P1316



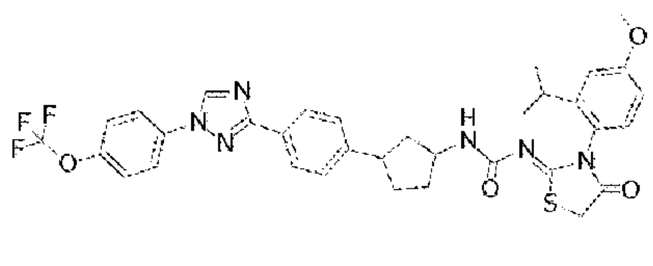
P1317



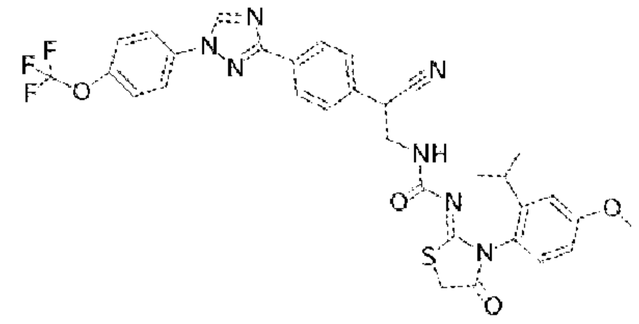
P1318



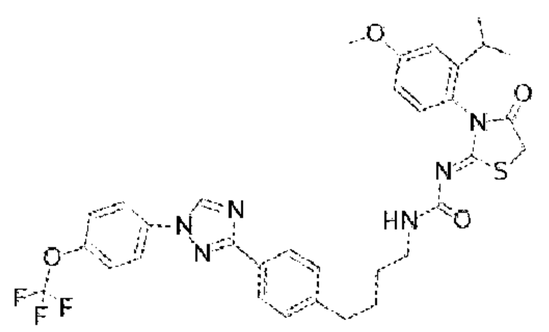
P1319



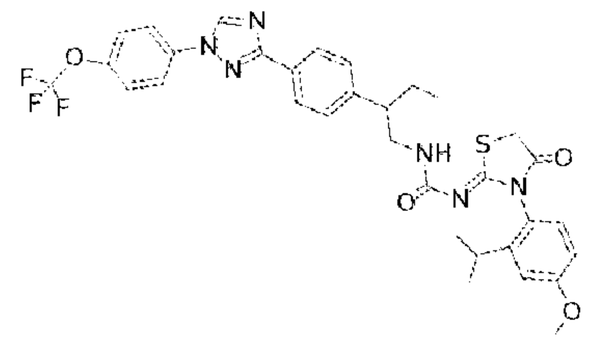
P1320



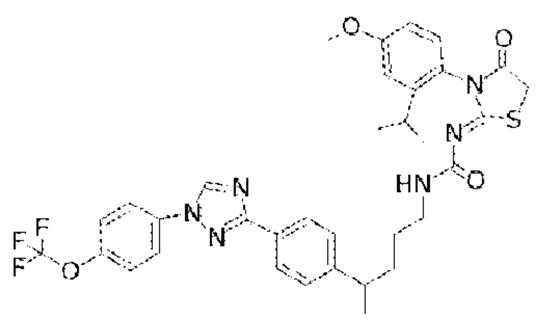
P1321



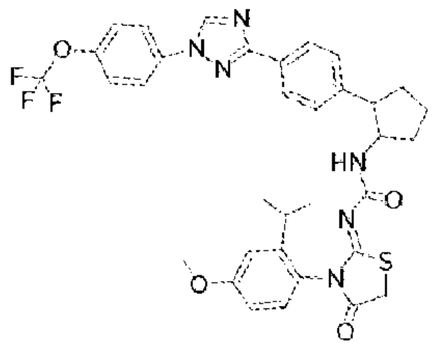
P1322



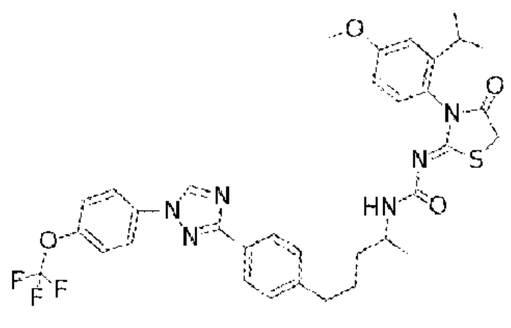
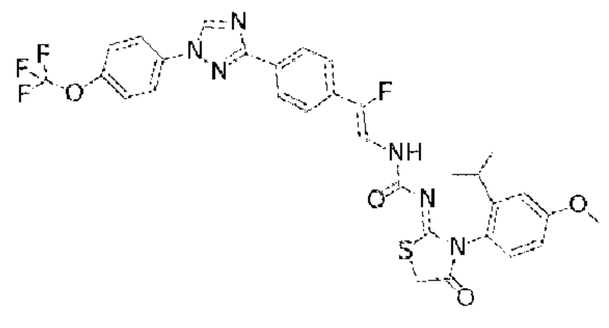
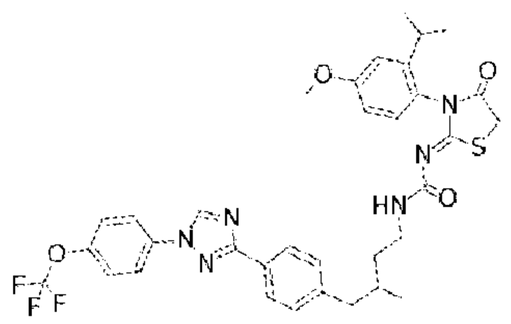
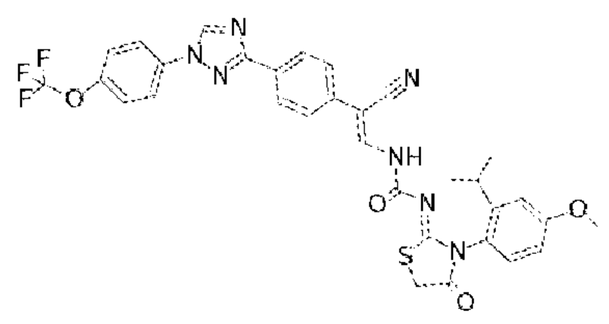
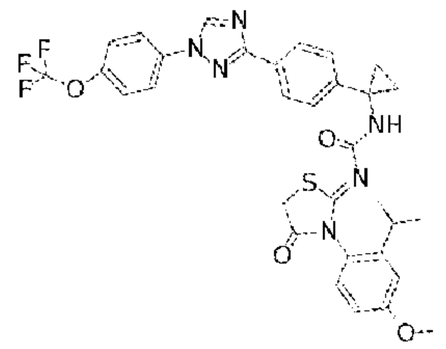
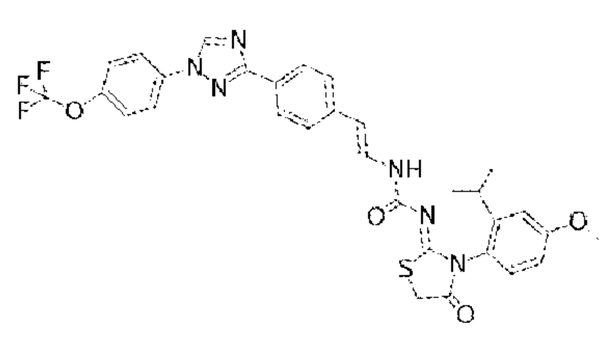
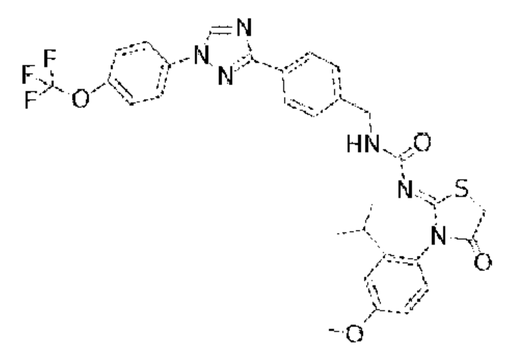
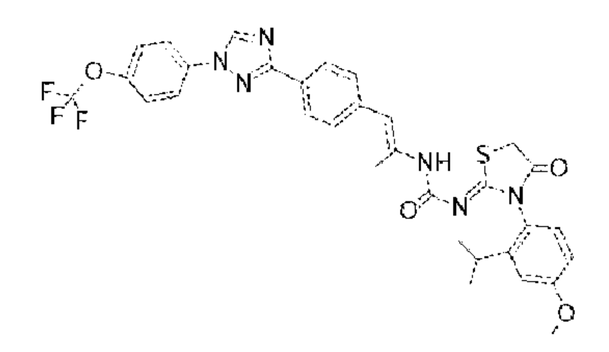
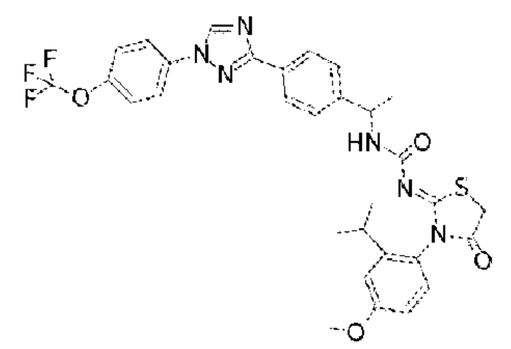
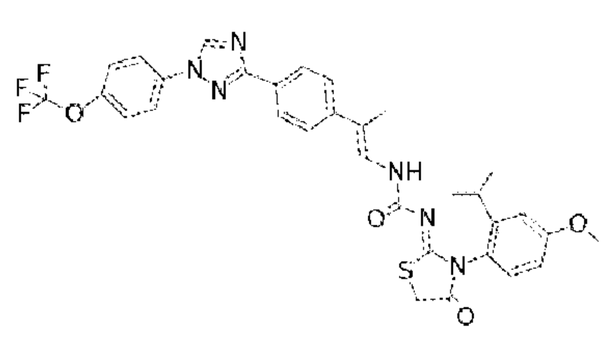
P1323

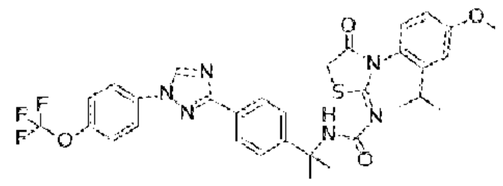
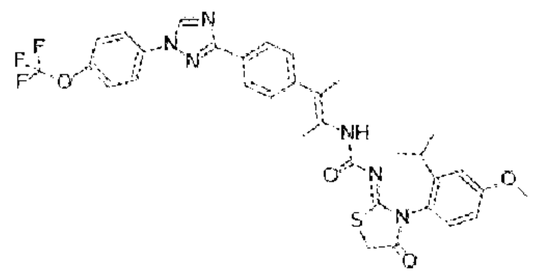
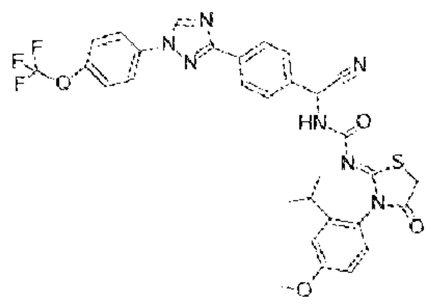
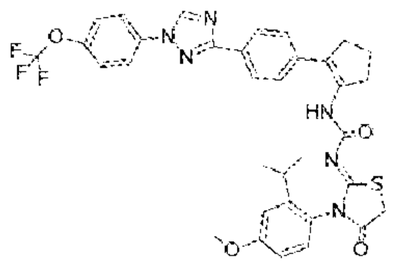
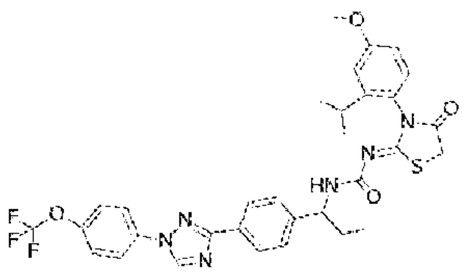
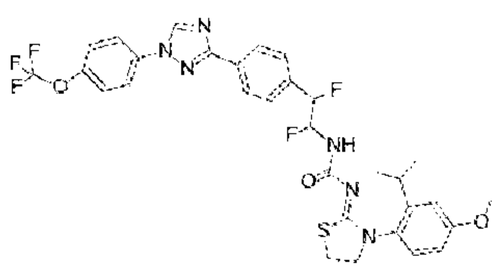
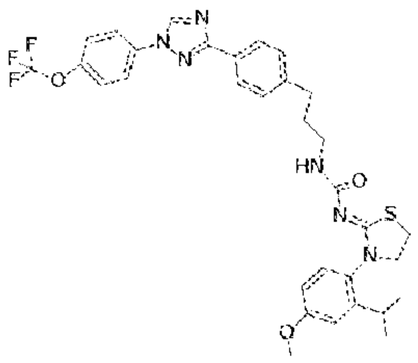
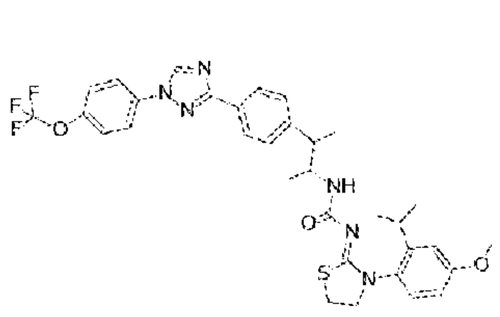
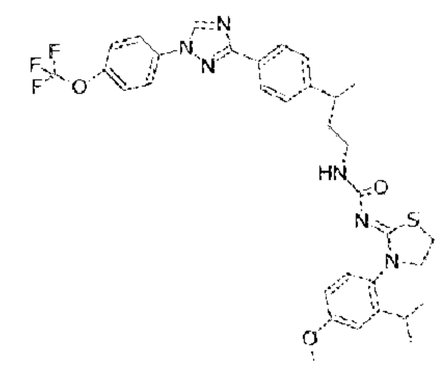
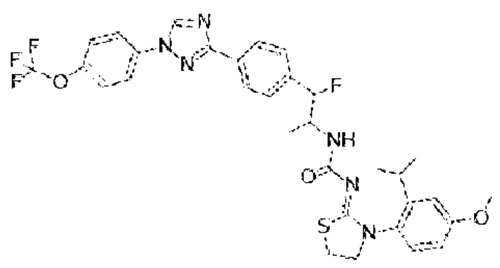


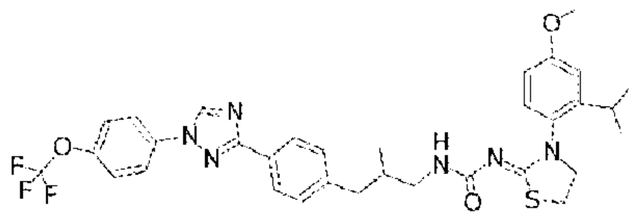
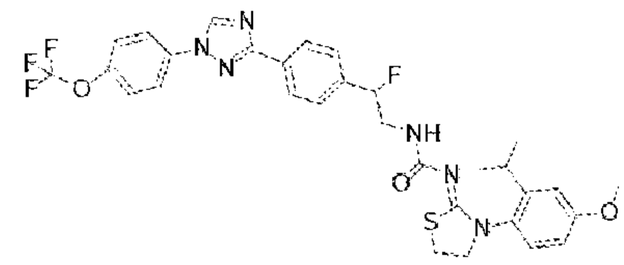
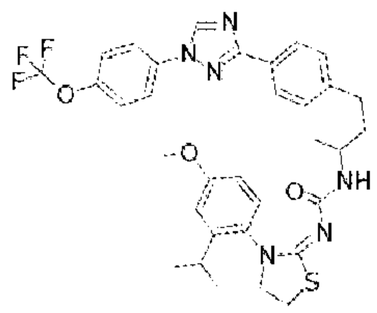
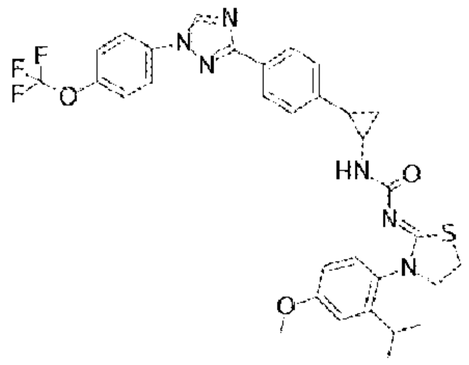
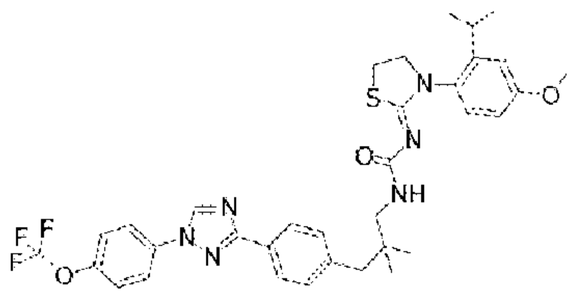
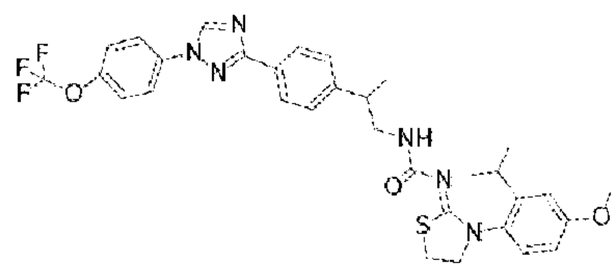
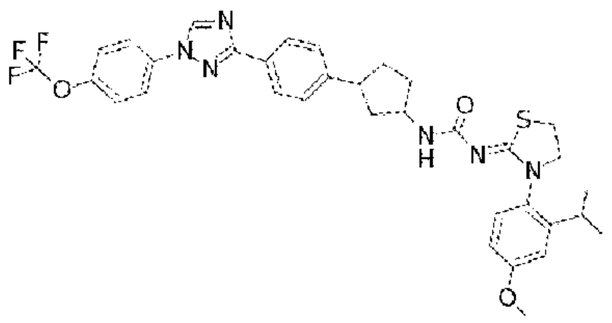
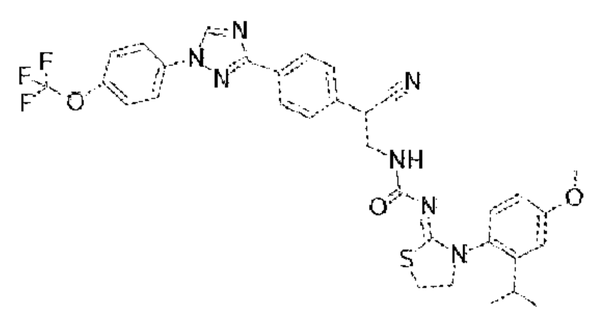
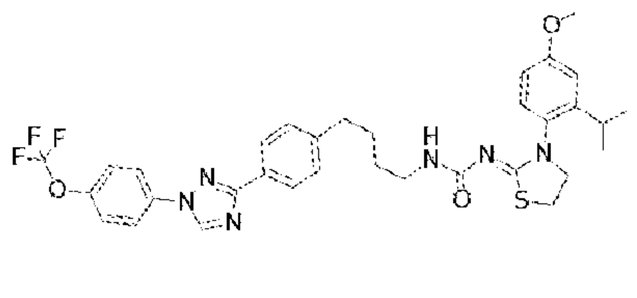
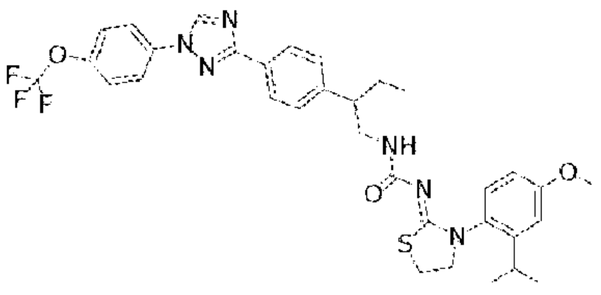
P1324

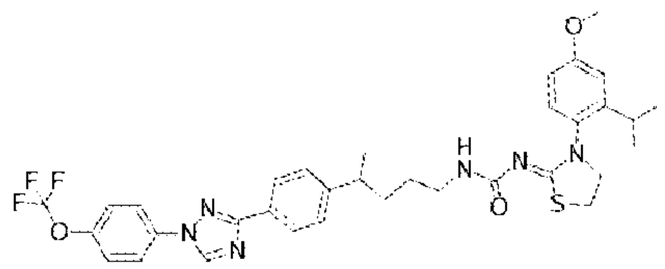
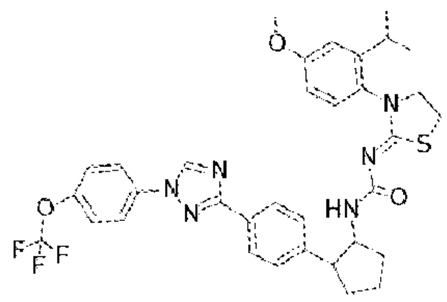
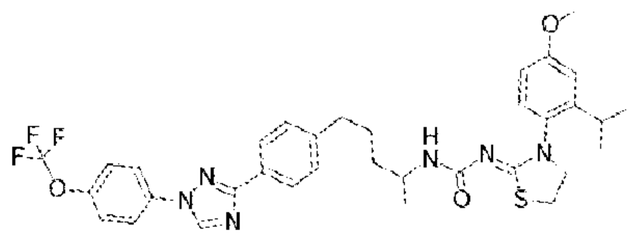
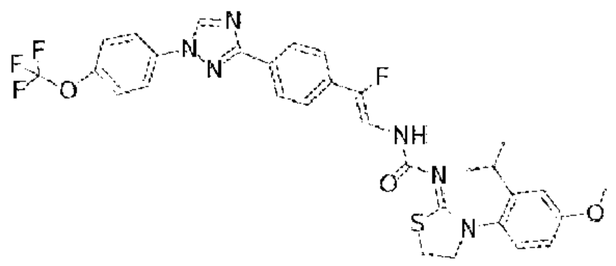
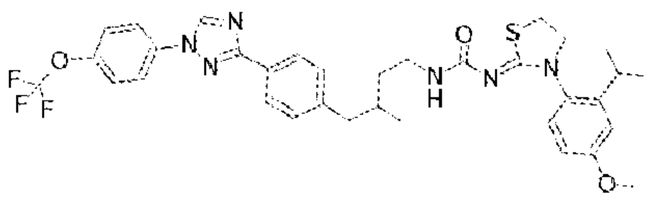
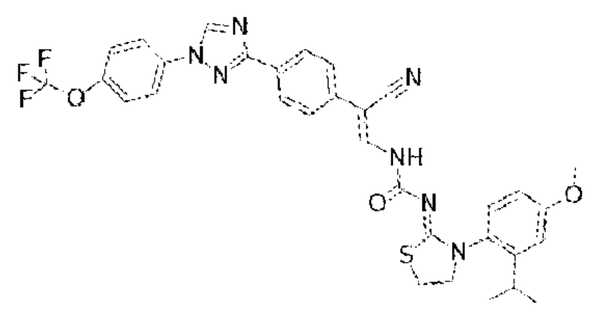
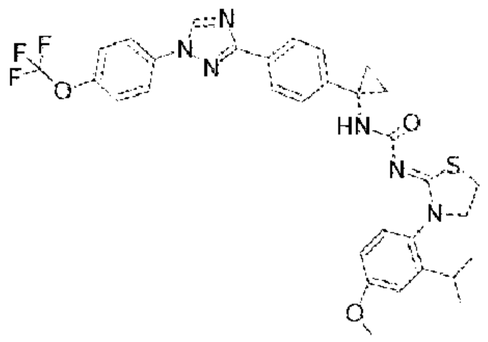
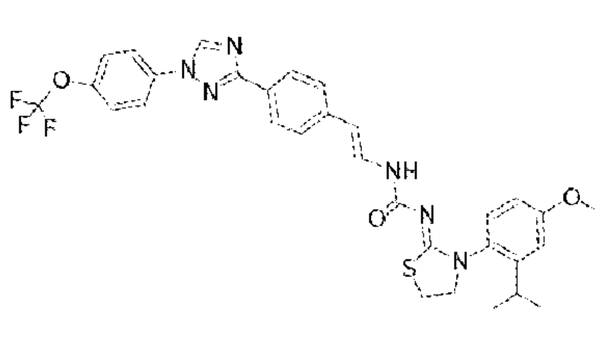
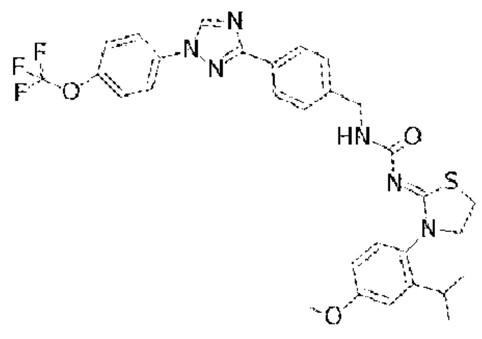
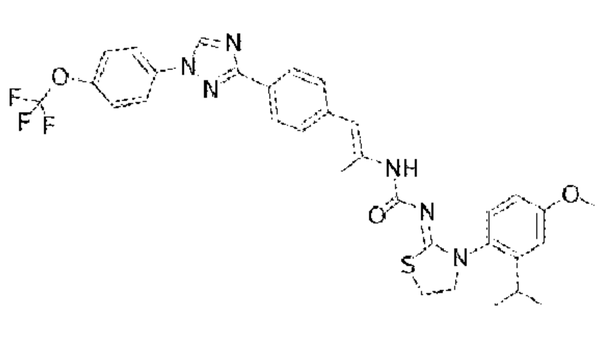


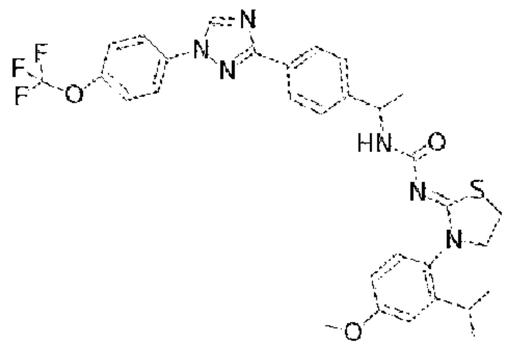
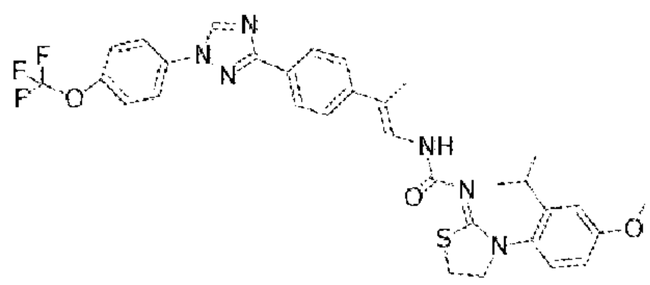
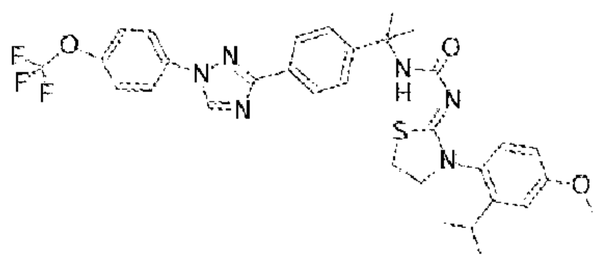
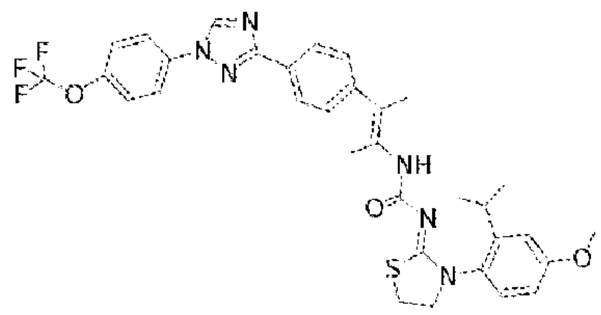
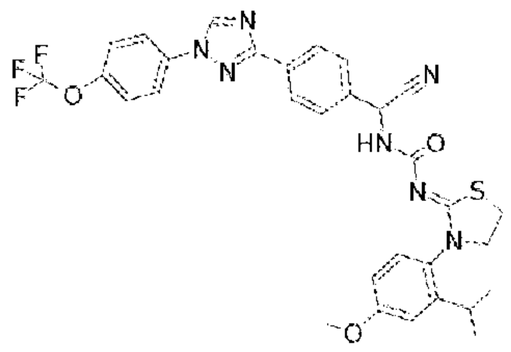
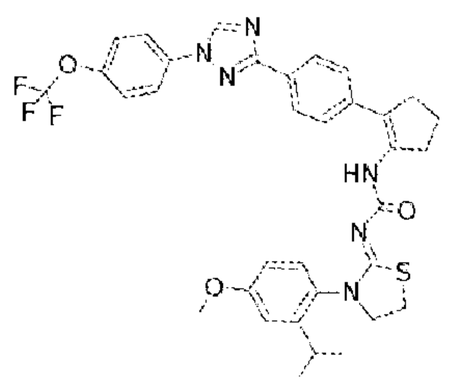
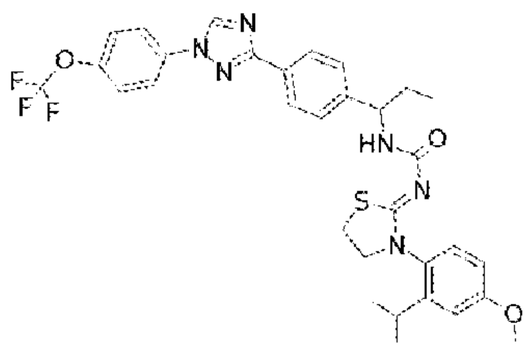
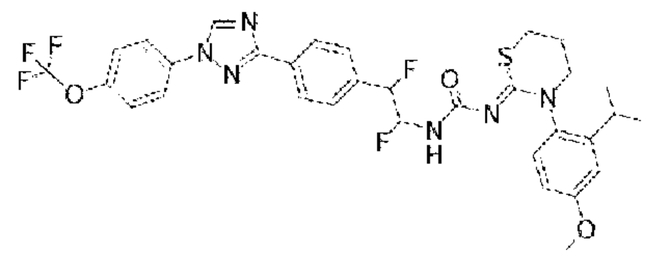
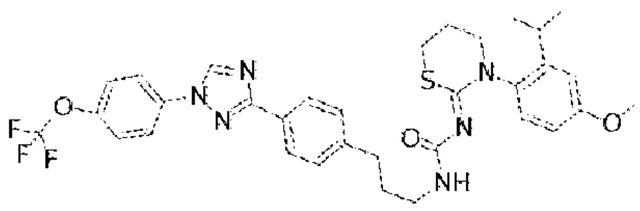
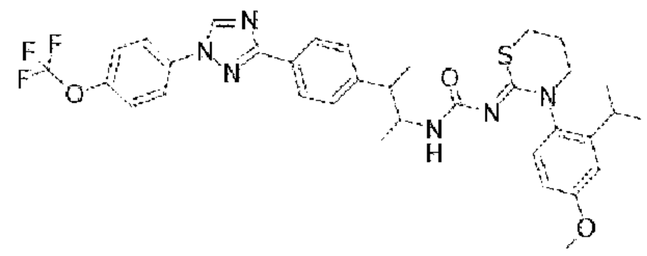
P1325

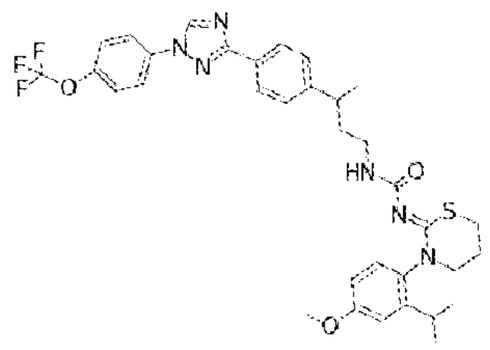
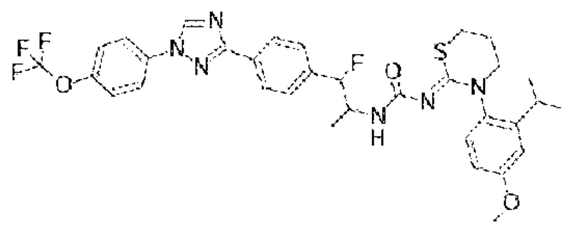
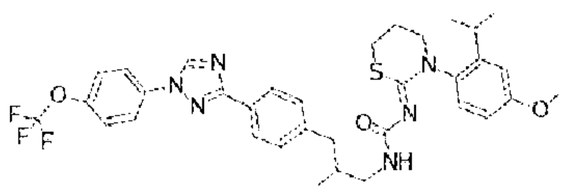
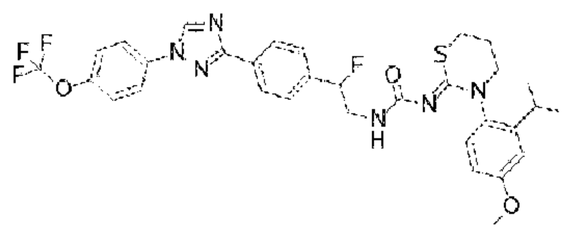
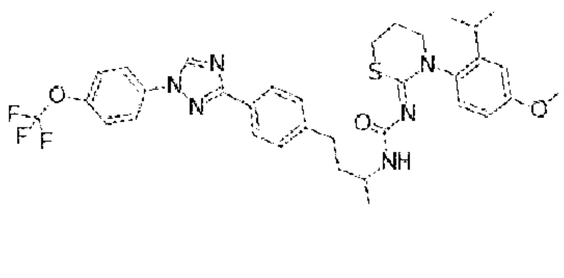
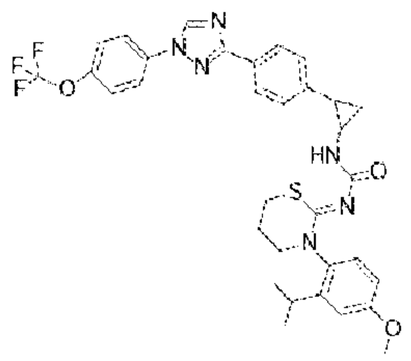
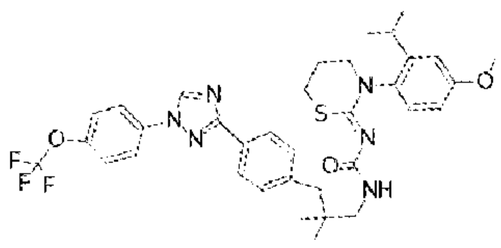
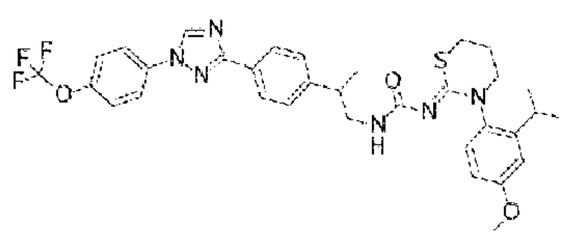
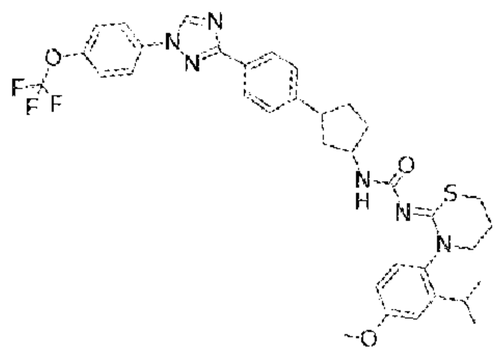
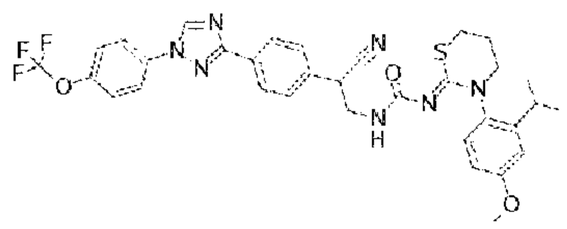
 P1326	 P1327
 P1328	 P1329
 P1330	 P1331
 P1332	 P1333
 P1334	 P1335

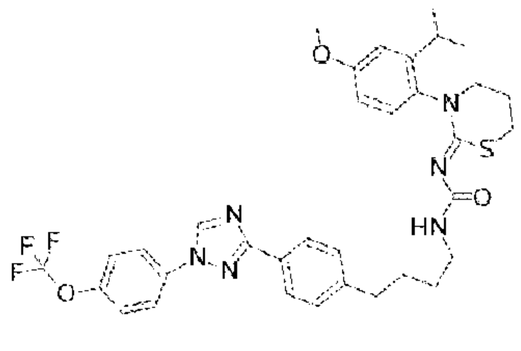
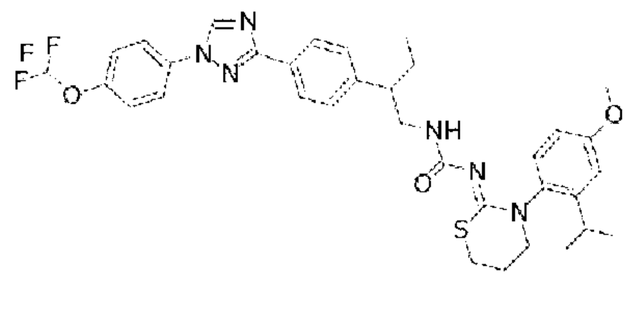
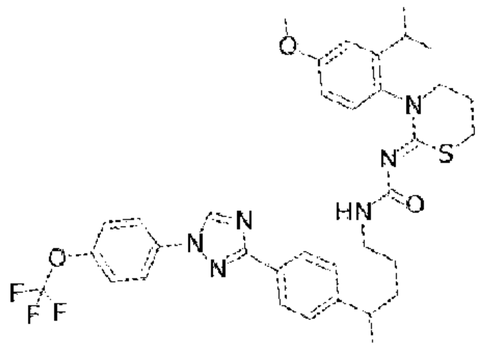
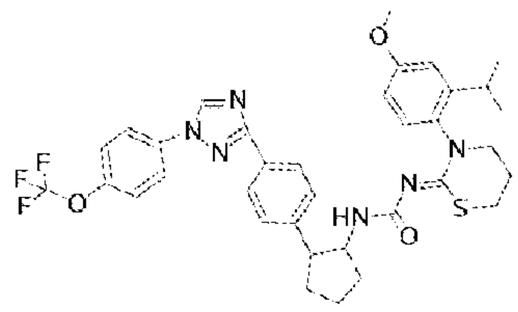
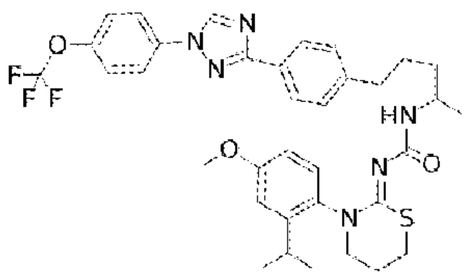
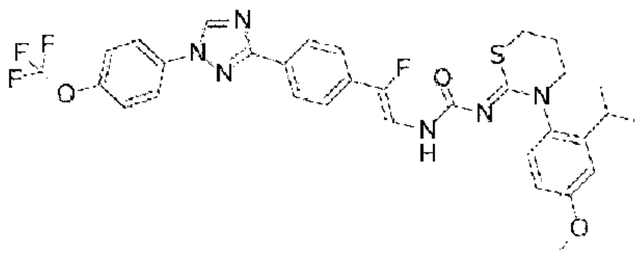
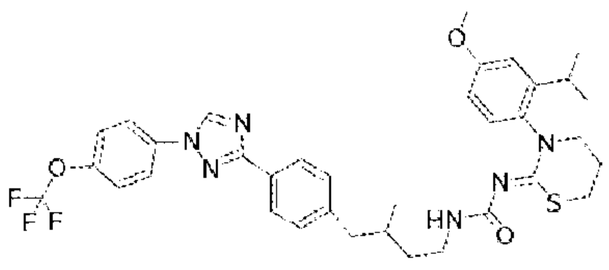
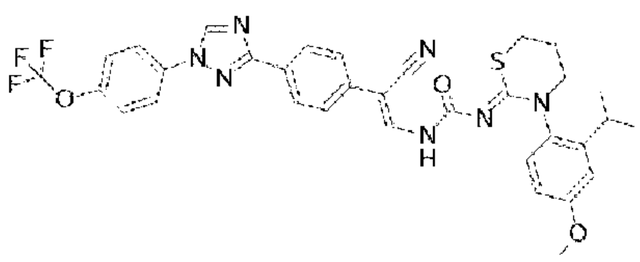
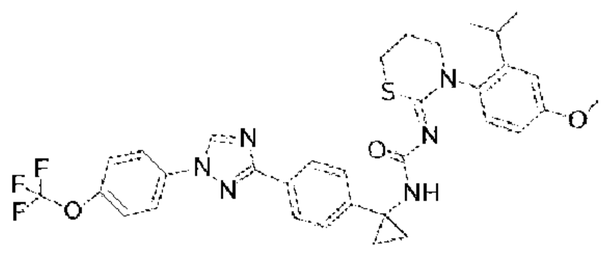
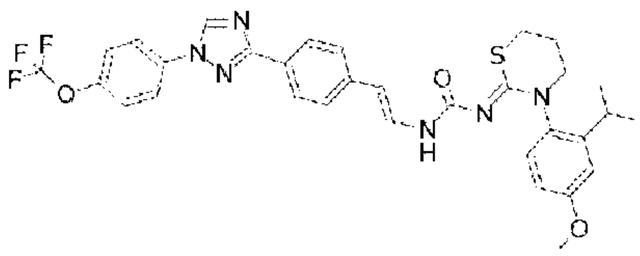
 P1336	 P1337
 P1338	 P1339
 P1340	 P1341
 P1342	 P1343
 P1344	 P1345

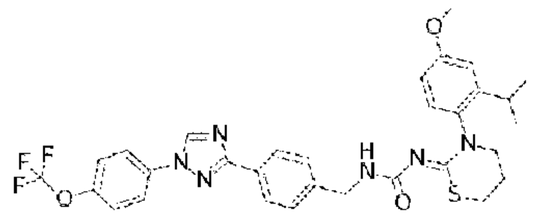
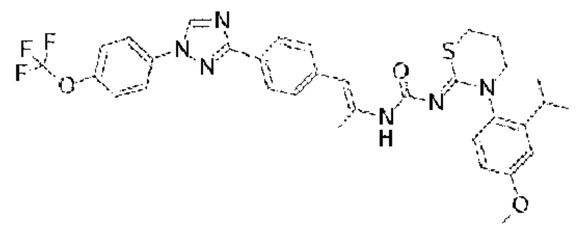
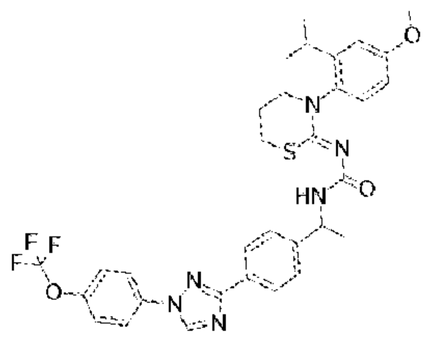
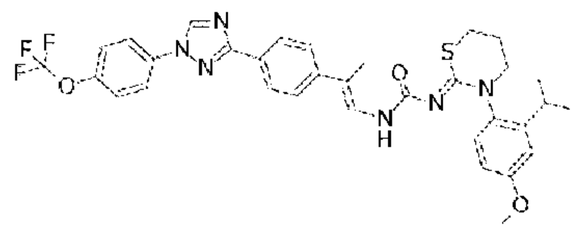
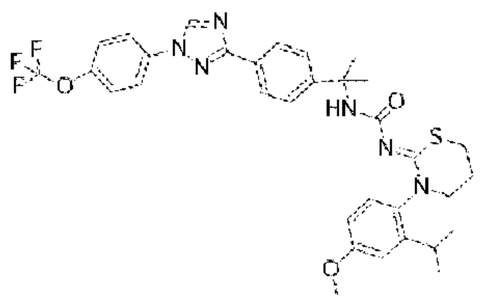
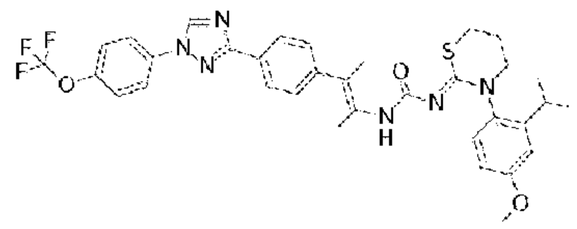
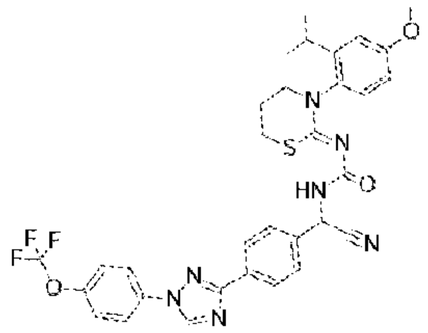
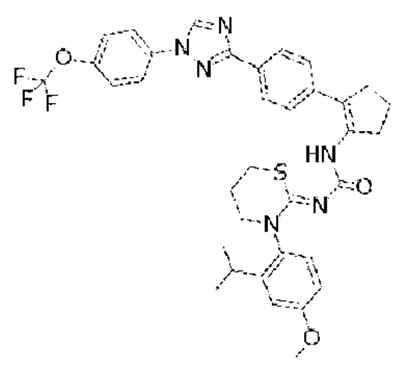
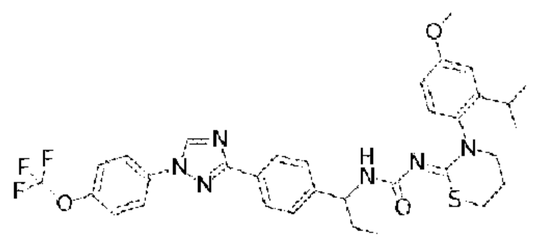
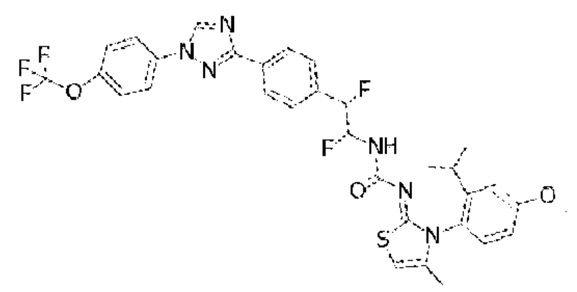
 P1346	 P1347
 P1348	 P1349
 P1350	 P1351
 P1352	 P1353
 P1354	 P1355

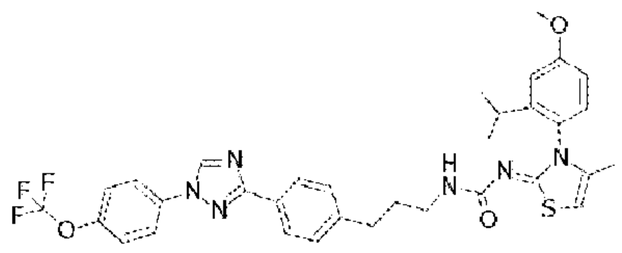
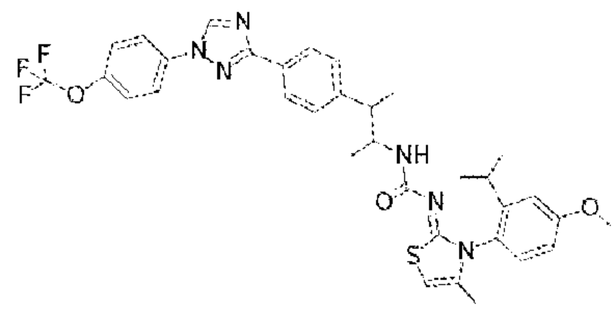
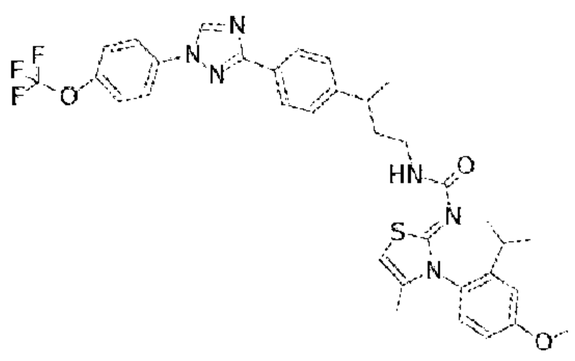
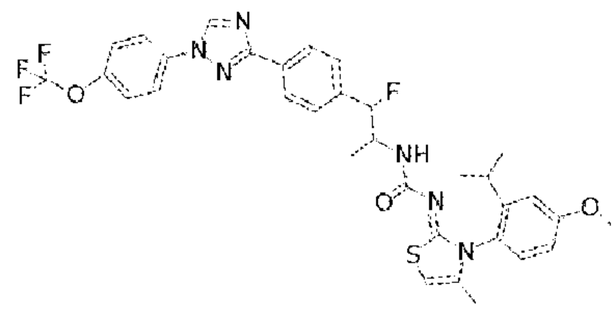
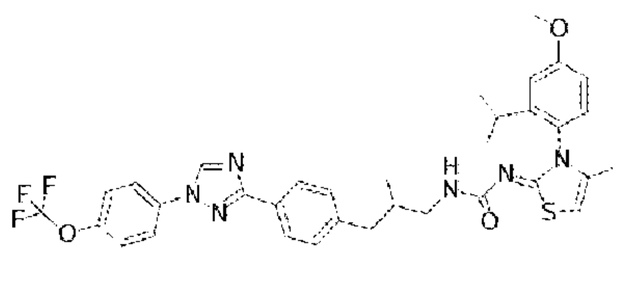
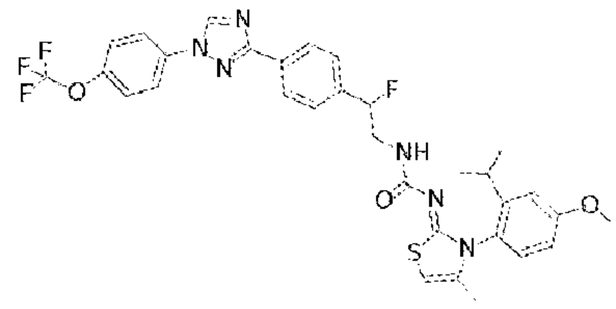
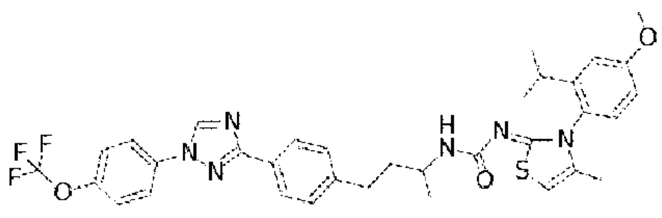
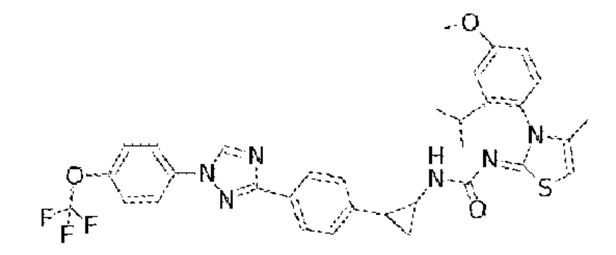
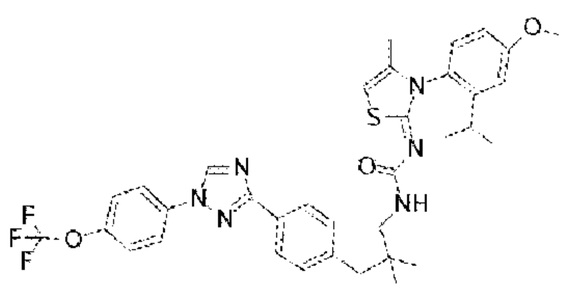
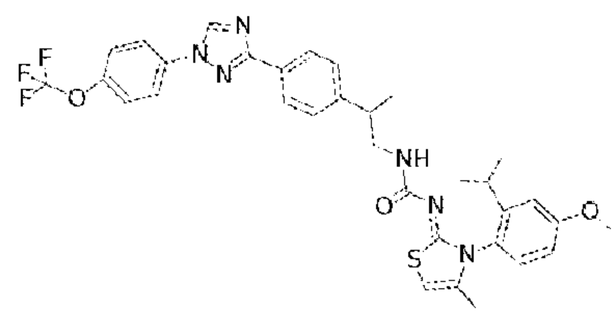
 P1356	 P1357
 P1358	 P1359
 P1360	 P1361
 P1362	 P1363
 P1364	 P1365

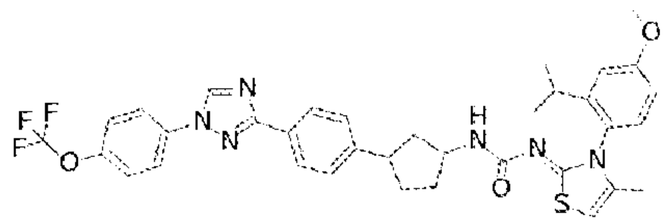
	
P1366	P1367
	
P1368	P1369
	
P1370	P1371
	
P1372	P1373
	
P1374	P1375

 P1376	 P1377
 P1378	 P1379
 P1380	 P1381
 P1382	 P1383
 P1384	 P1385

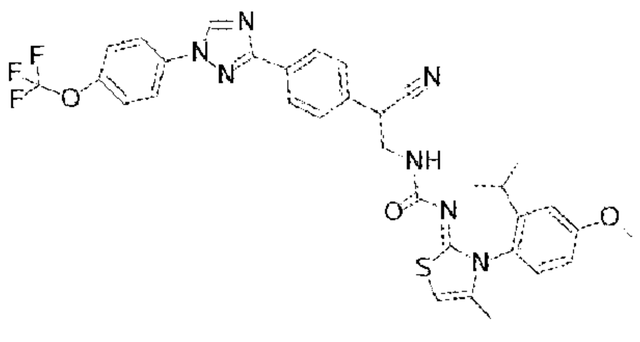
 P1386	 P1387
 P1388	 P1389
 P1390	 P1391
 P1392	 P1393
 P1394	 P1395

 P1396	 P1397
 P1398	 P1399
 P1400	 P1401
 P1402	 P1403
 P1404	 P1405

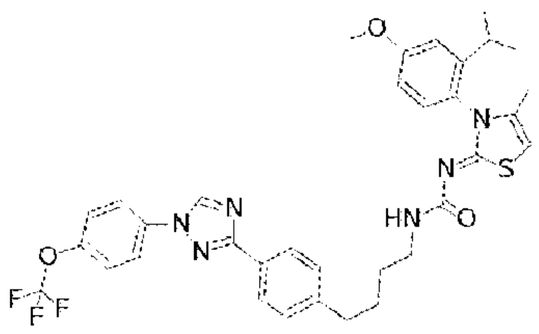
 P1406	 P1407
 P1408	 P1409
 P1410	 P1411
 P1412	 P1413
 P1414	 P1415



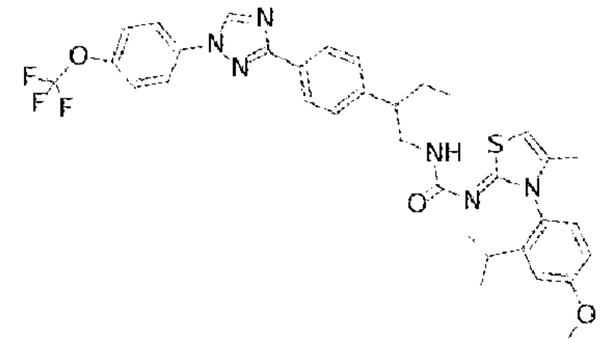
P1416



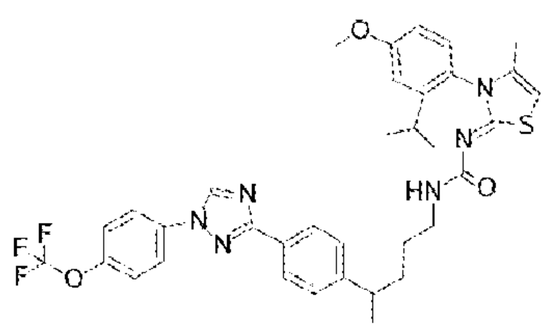
P1417



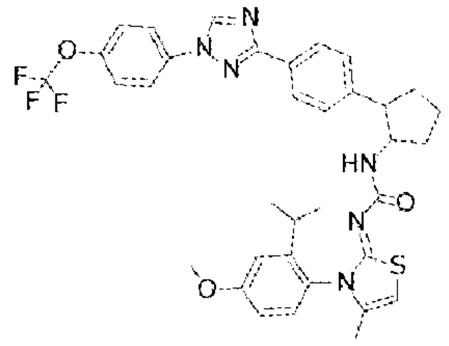
P1418



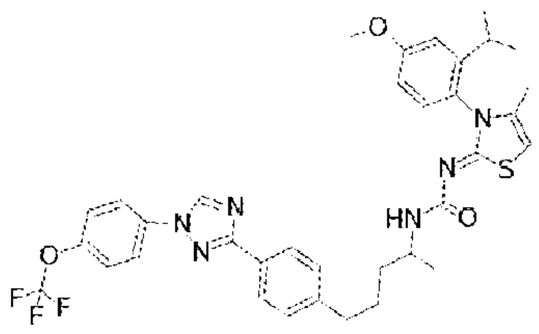
P1419



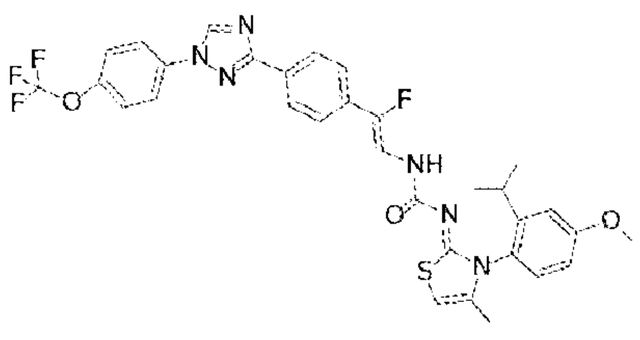
P1420



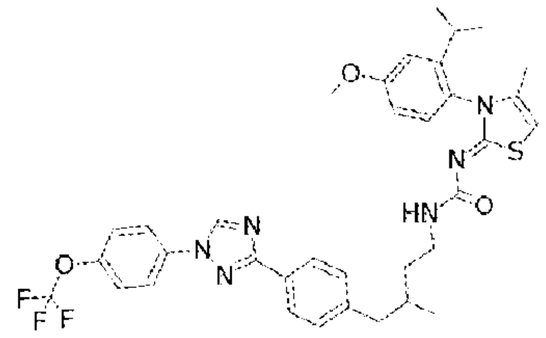
P1421



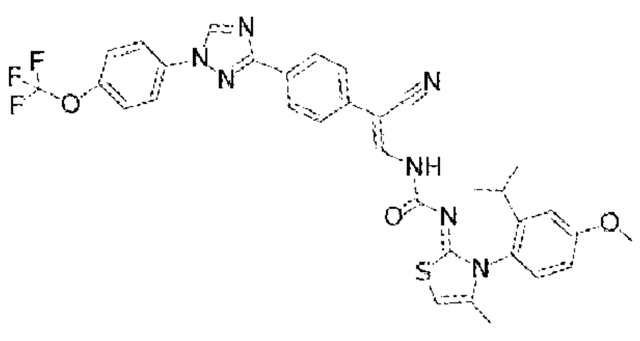
P1422



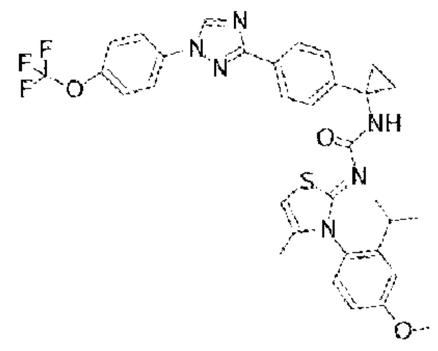
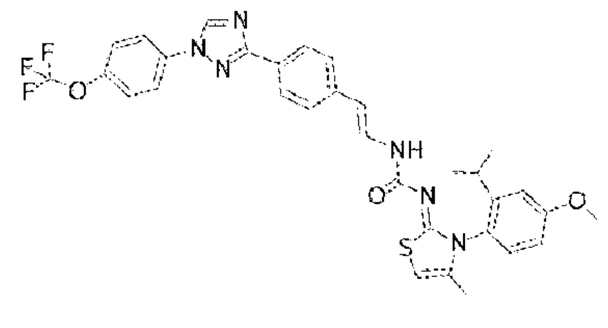
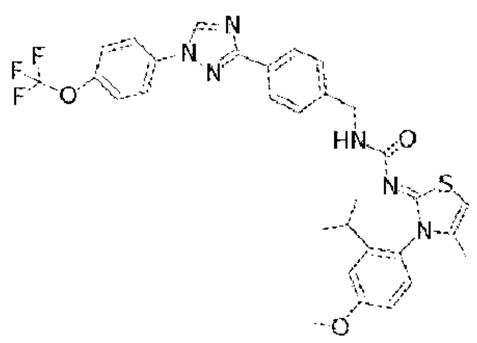
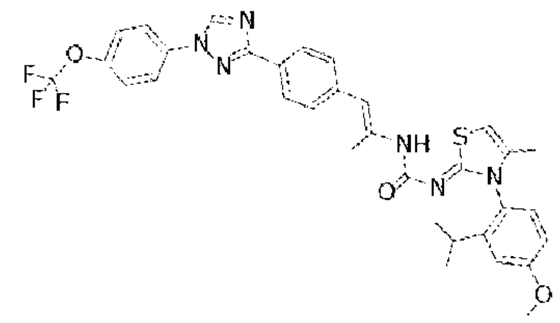
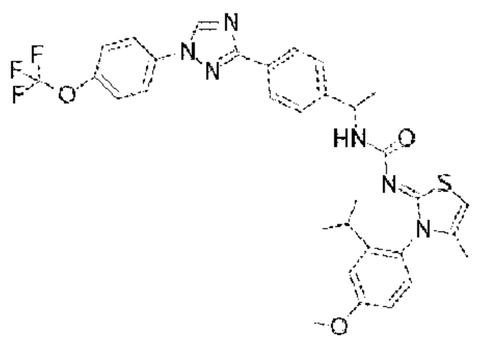
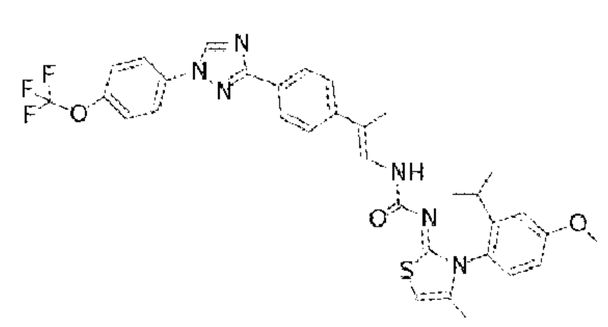
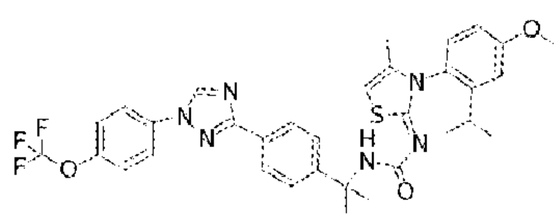
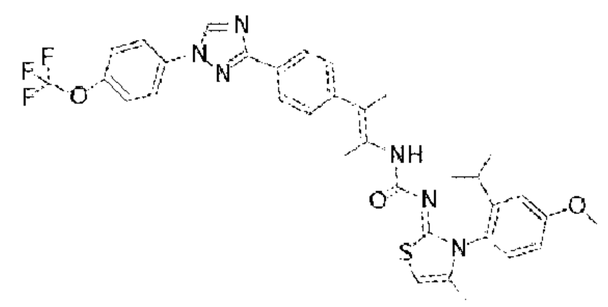
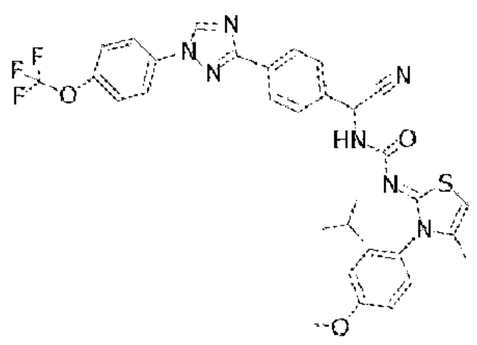
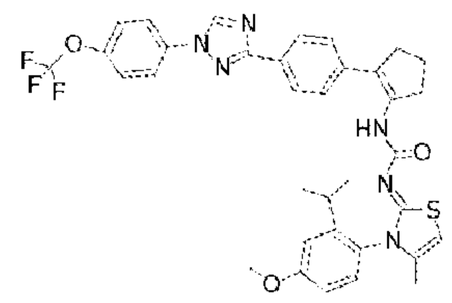
P1423

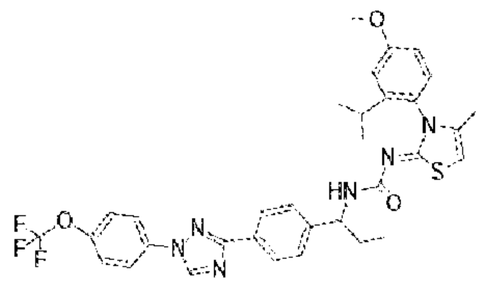
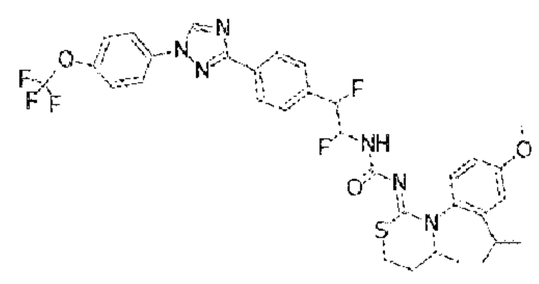
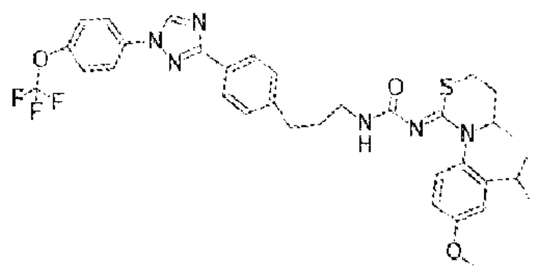
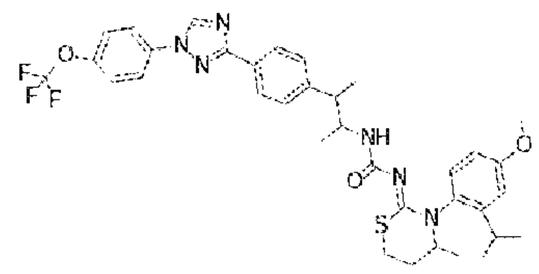
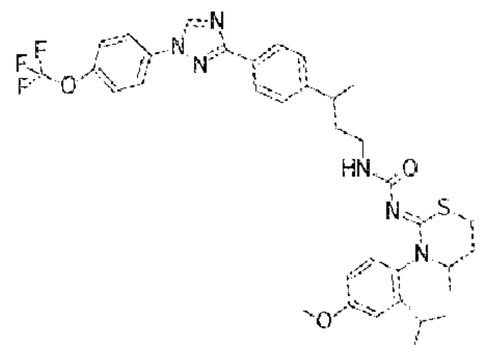
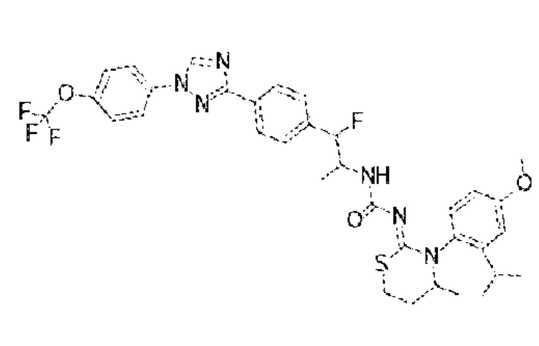
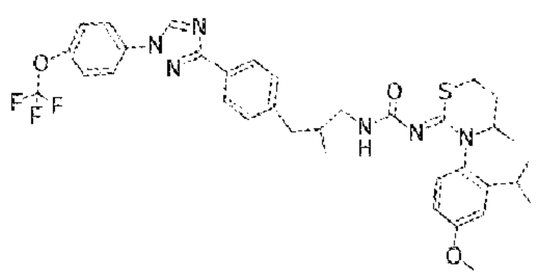
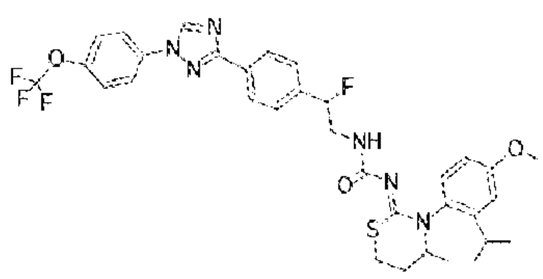
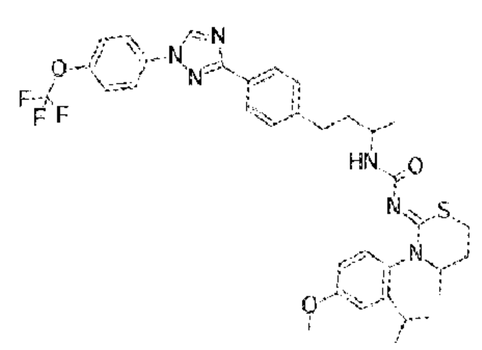
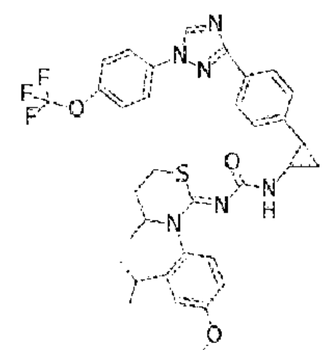


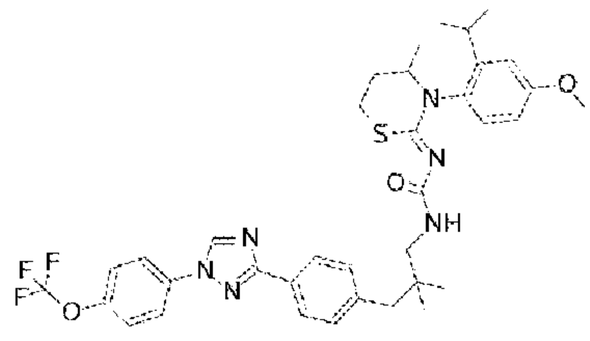
P1424



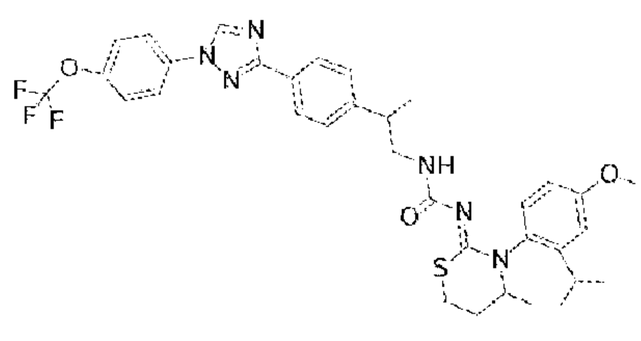
P1425

 P1426	 P1427
 P1428	 P1429
 P1430	 P1431
 P1432	 P1433
 P1434	 P1435

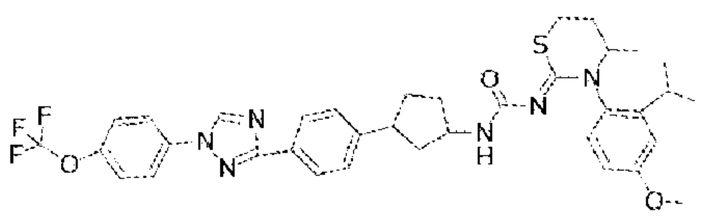
 P1436	 P1437
 P1438	 P1439
 P1440	 P1441
 P1442	 P1443
 P1444	 P1445



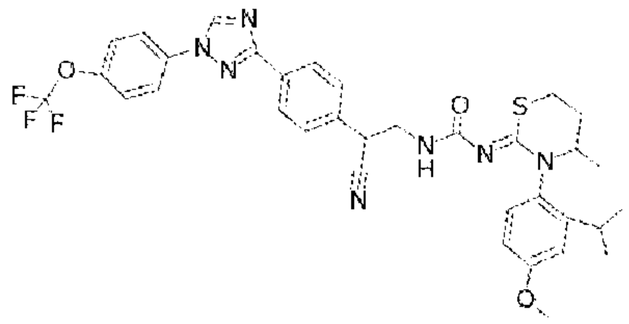
P1446



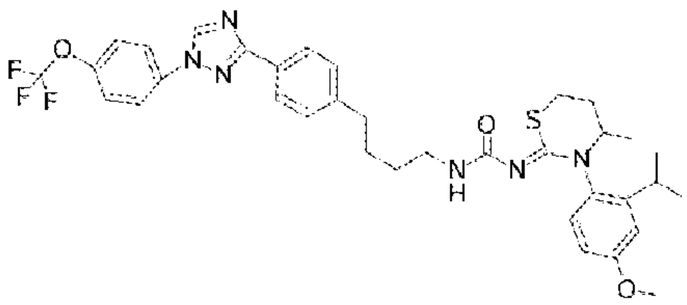
P1447



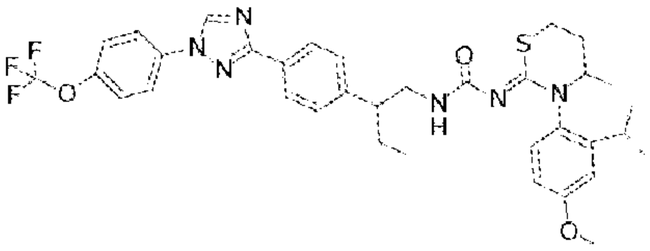
P1448



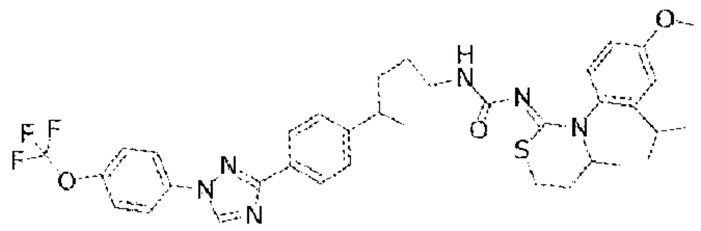
P1449



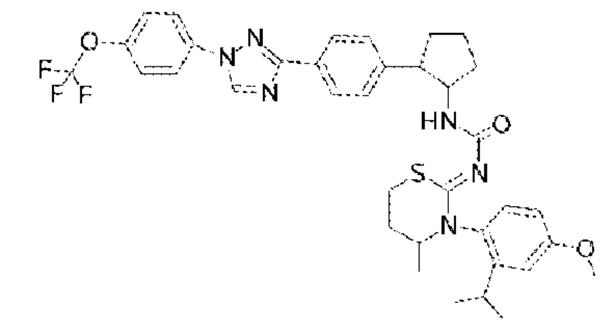
P1450



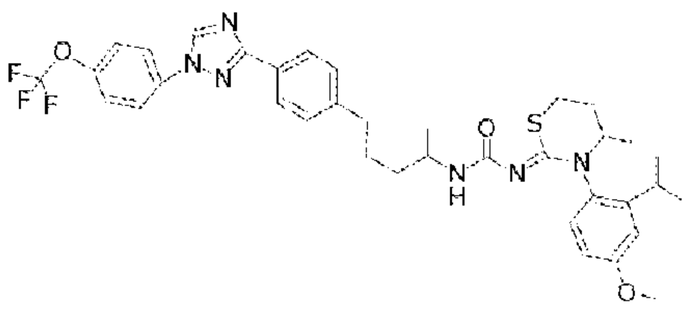
P1451



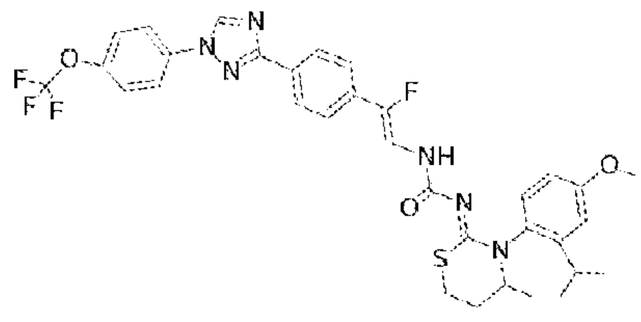
P1452



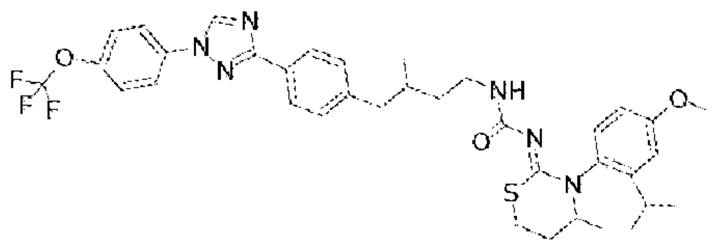
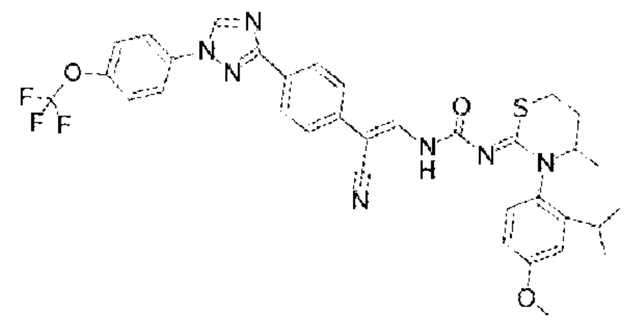
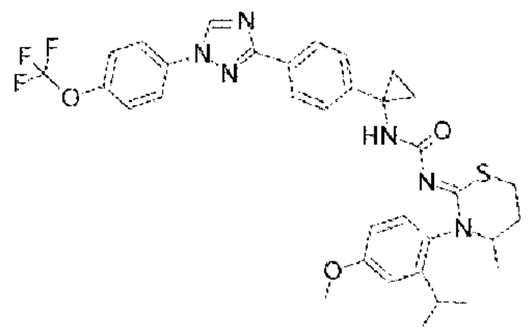
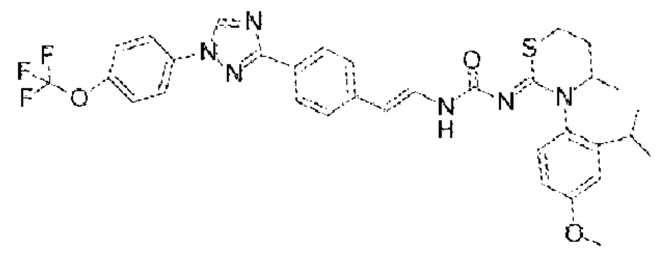
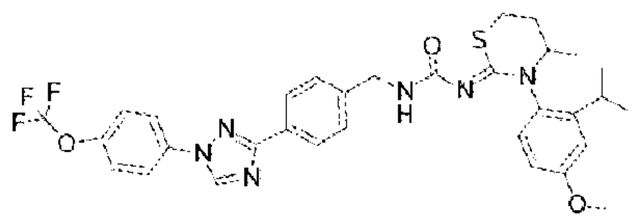
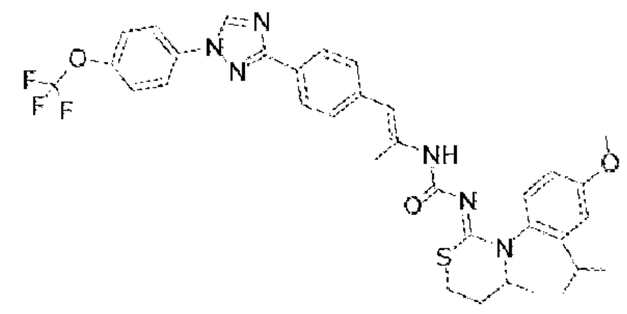
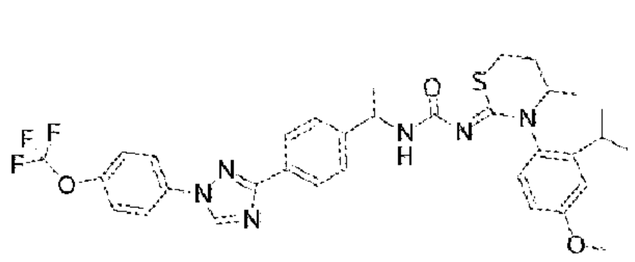
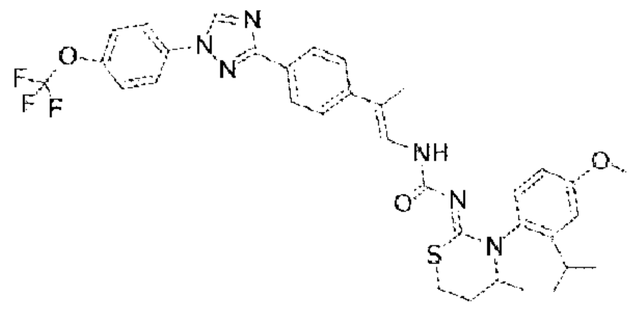
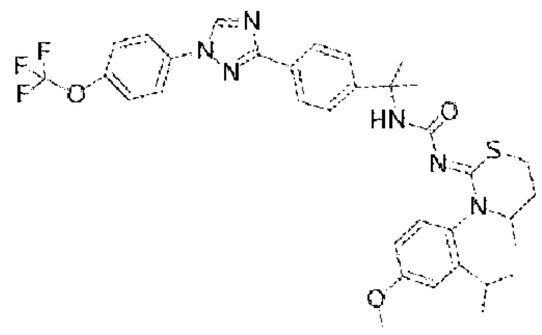
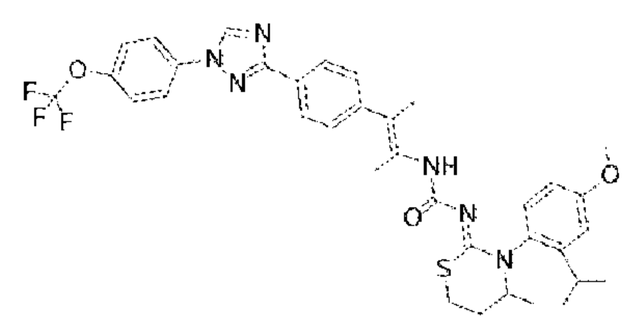
P1453

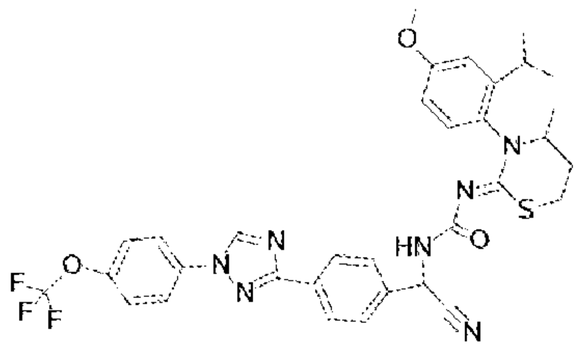


P1454

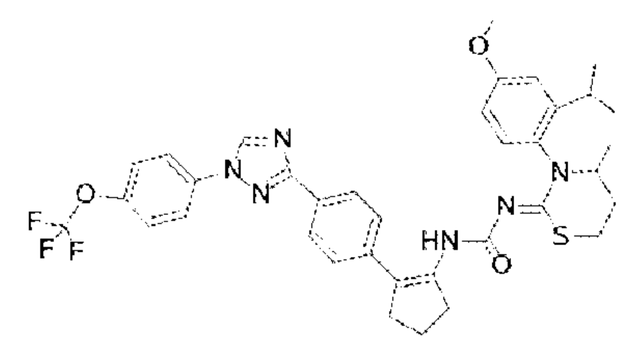


P1455

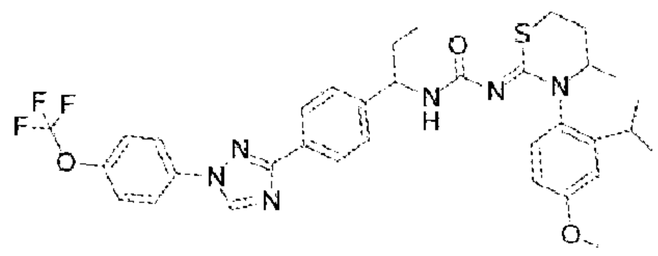
 P1456	 P1457
 P1458	 P1459
 P1460	 P1461
 P1462	 P1463
 P1464	 P1465



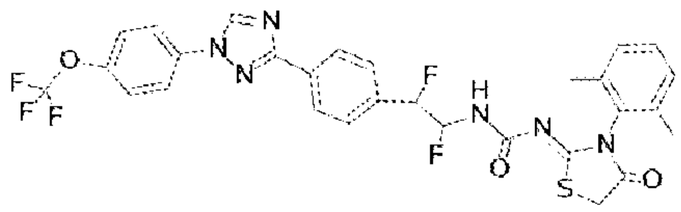
P1466



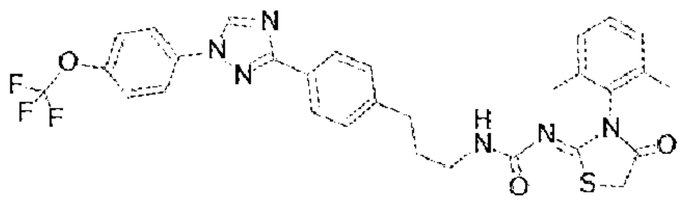
P1467



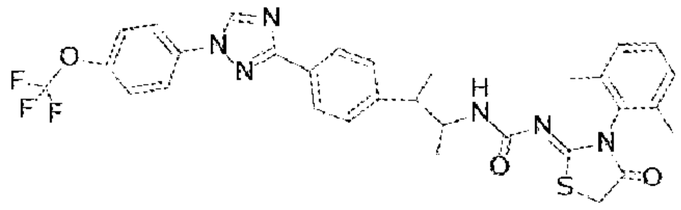
P1468



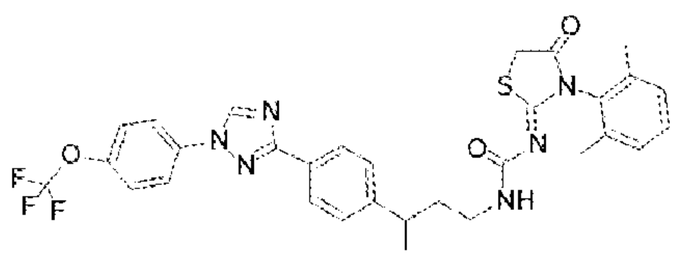
P1469



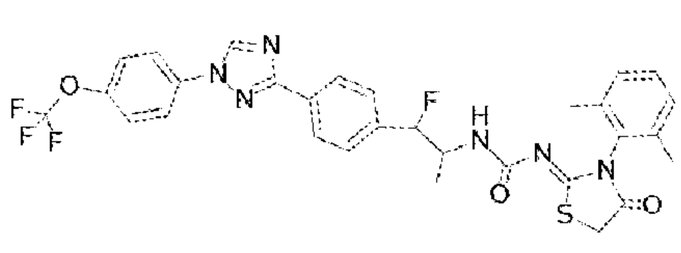
P1470



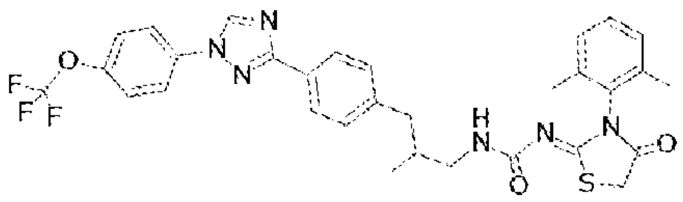
P1471



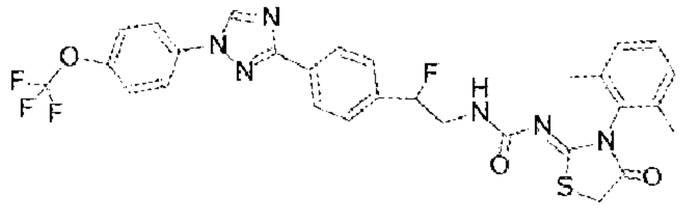
P1472



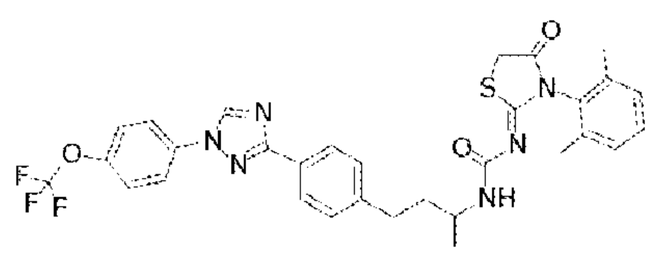
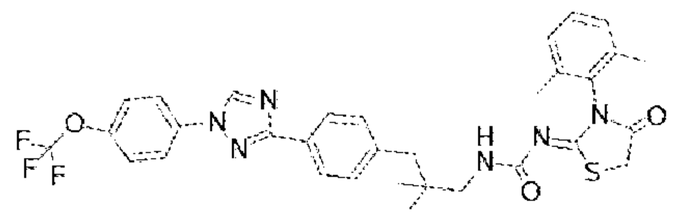
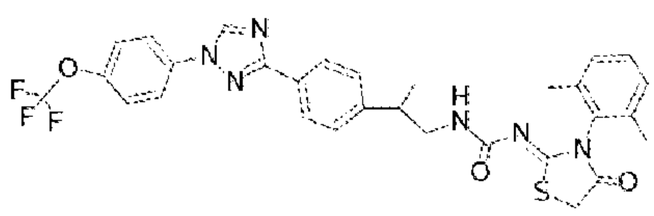
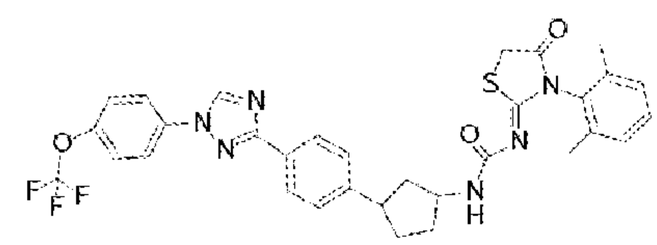
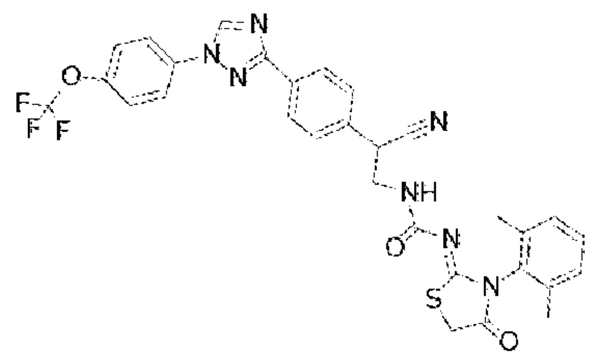
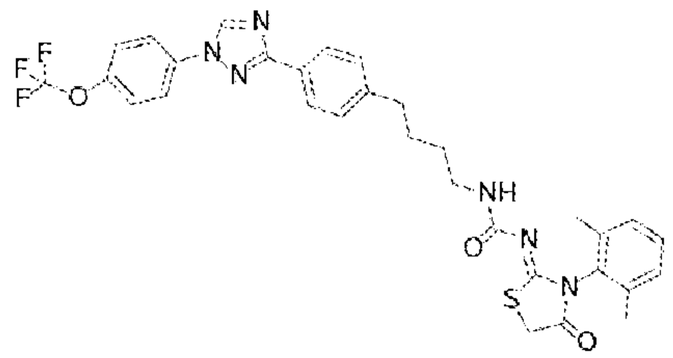
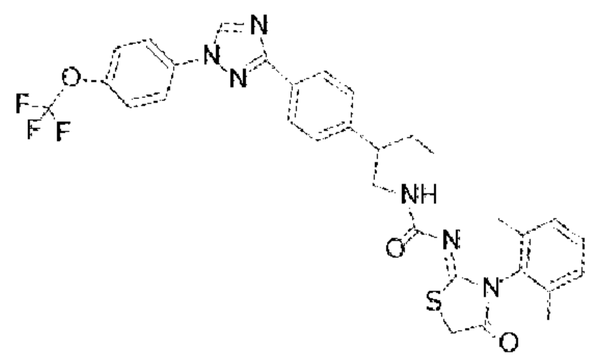
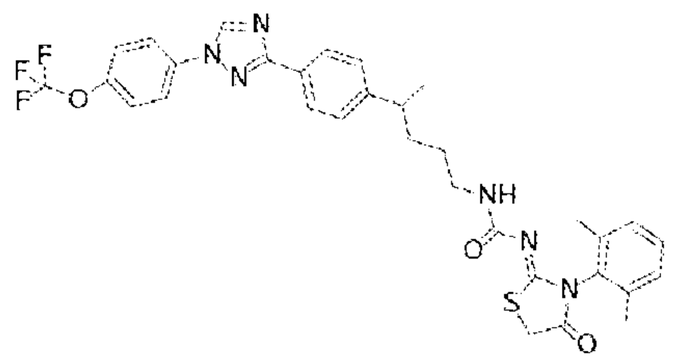
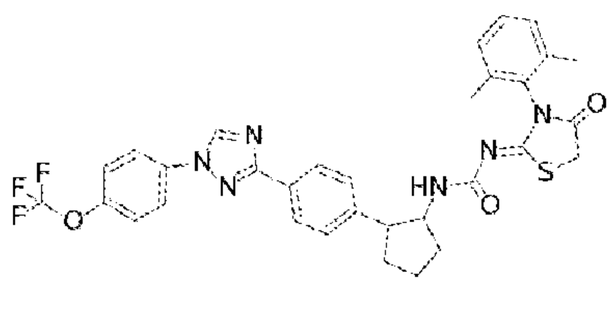
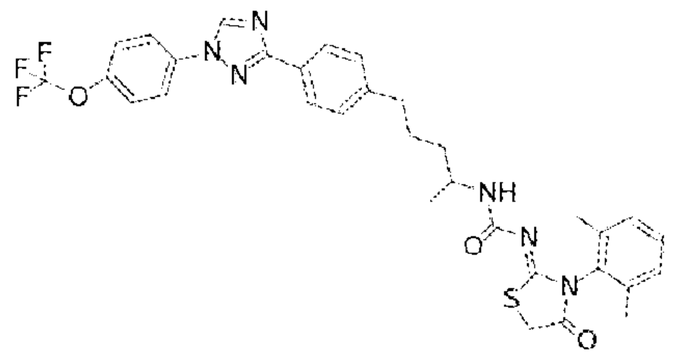
P1473

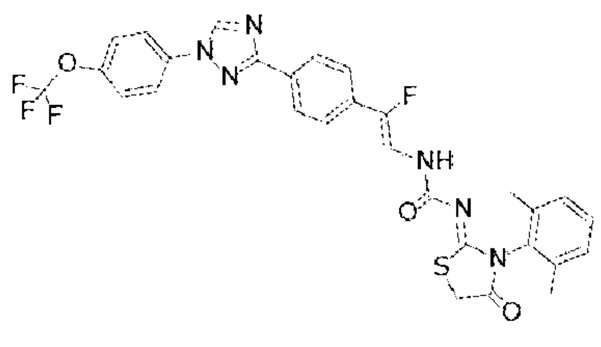
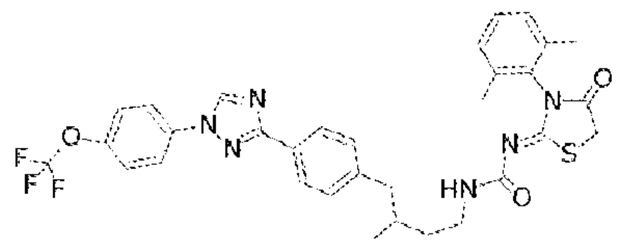
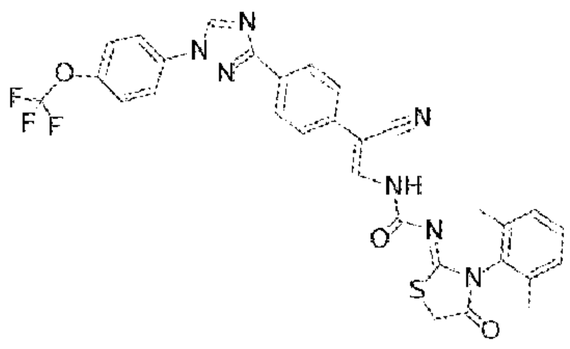
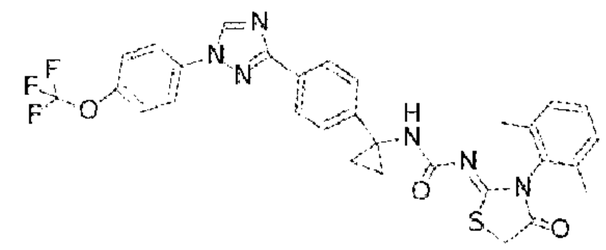
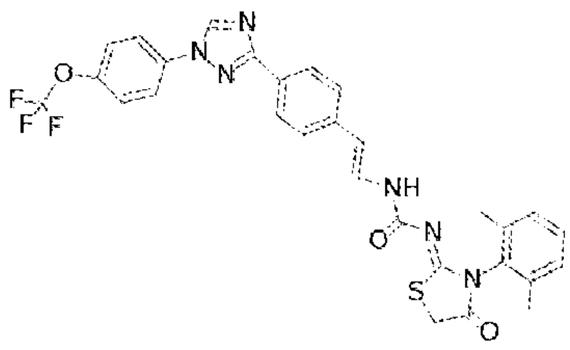
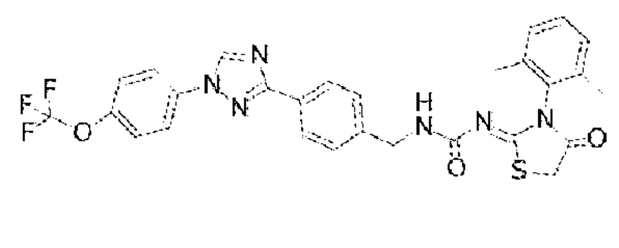
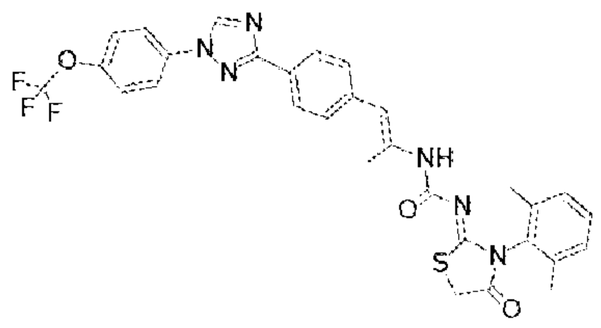
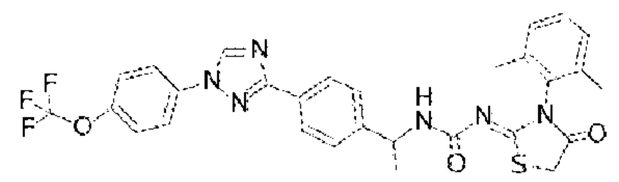
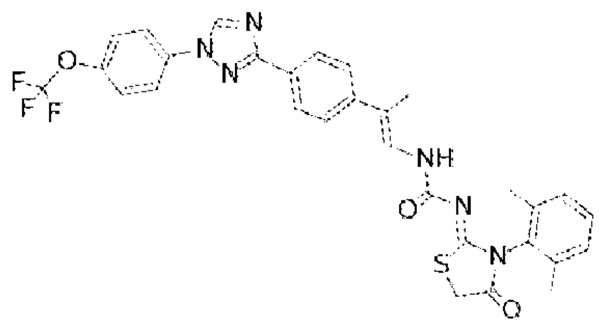
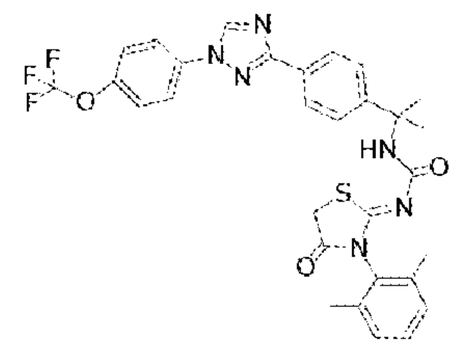


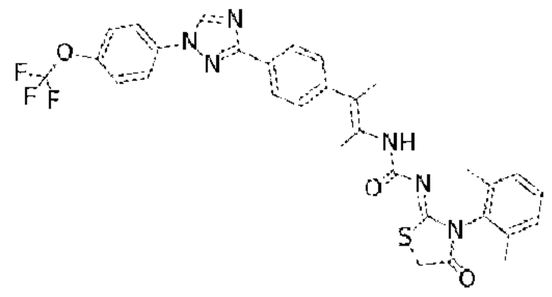
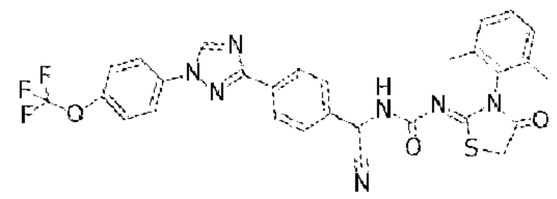
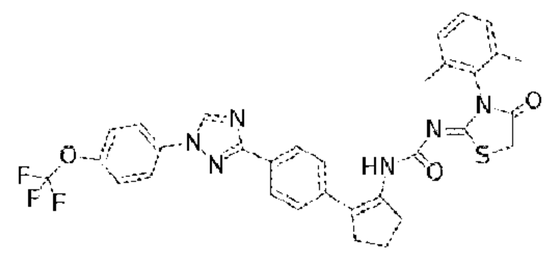
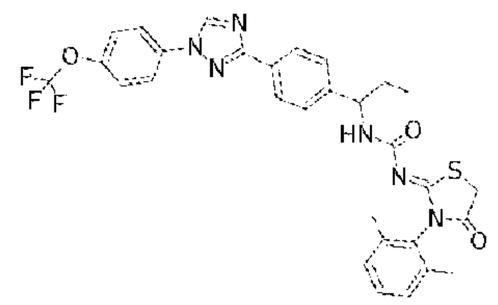
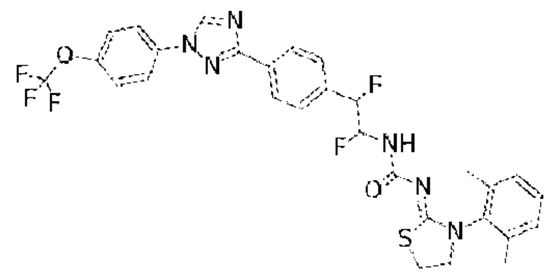
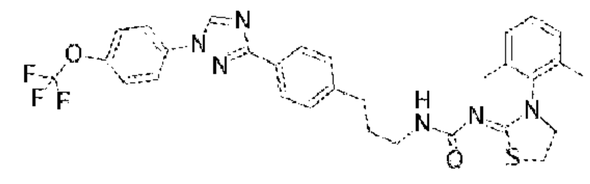
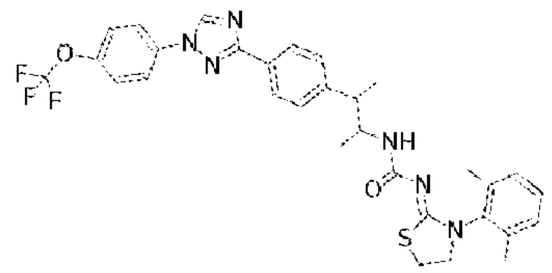
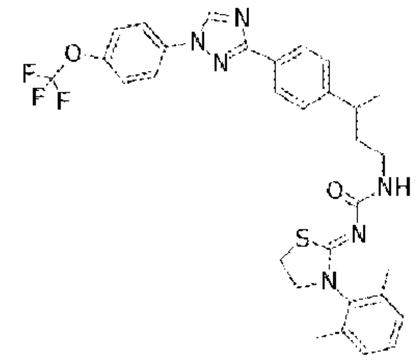
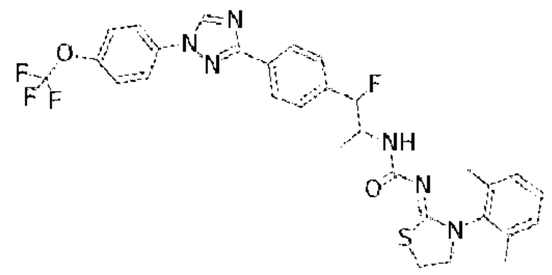
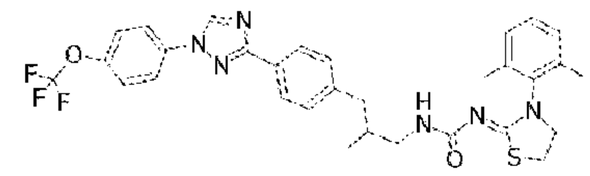
P1474

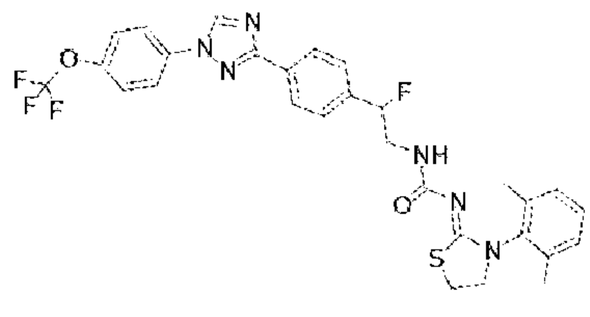
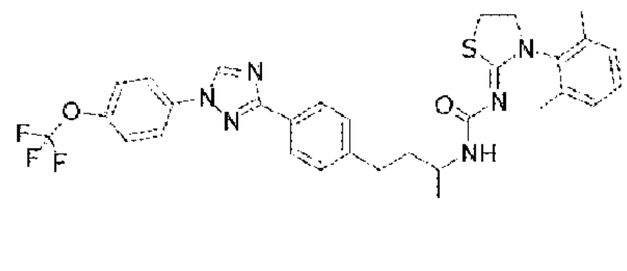
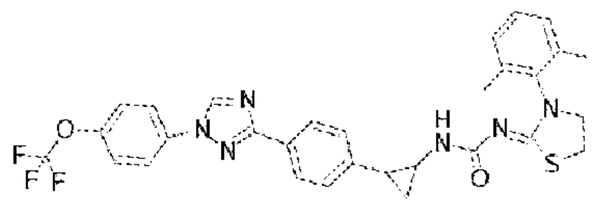
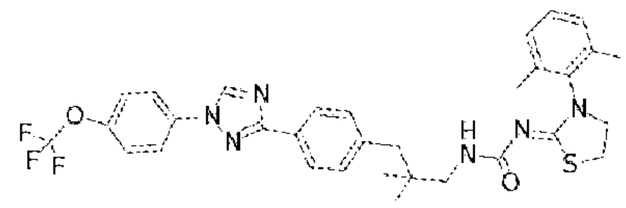
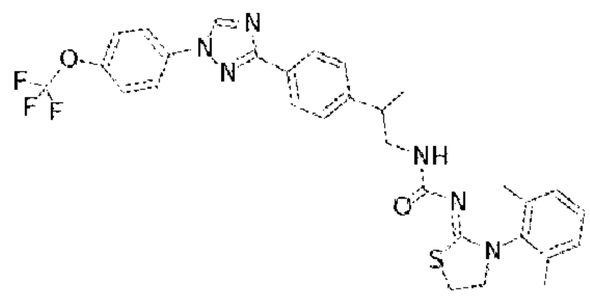
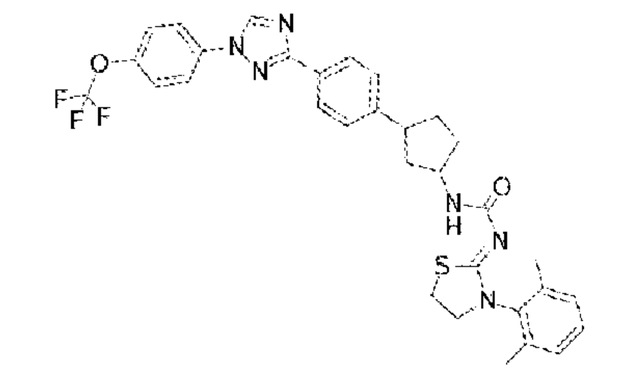
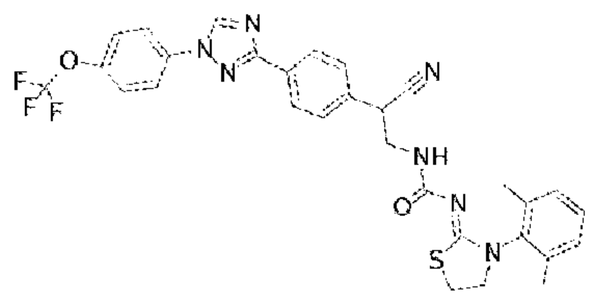
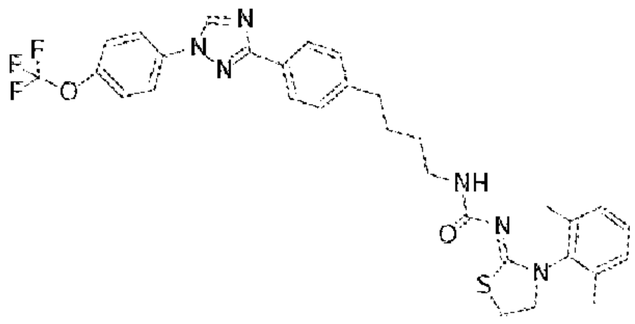
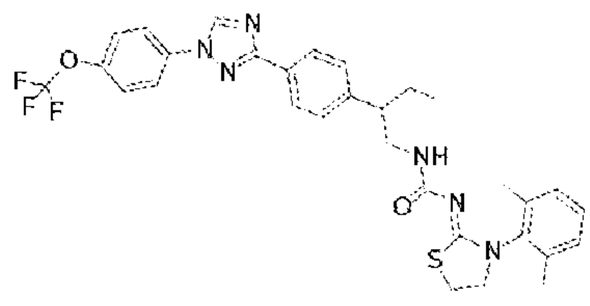
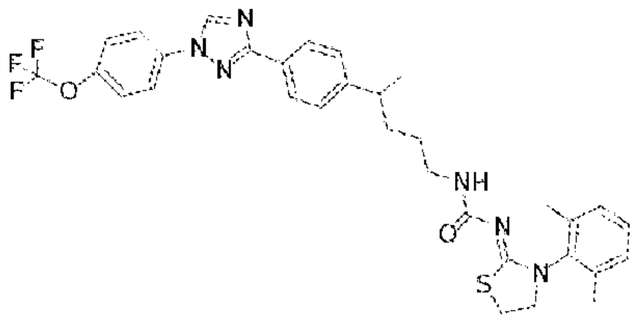


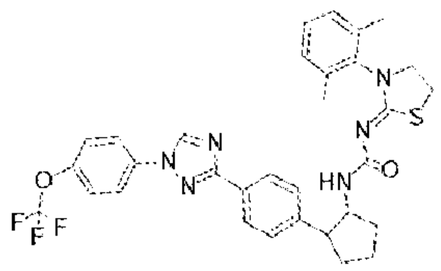
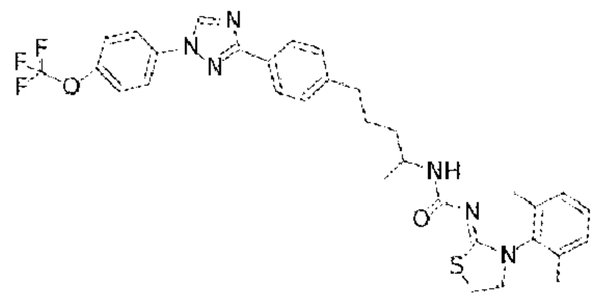
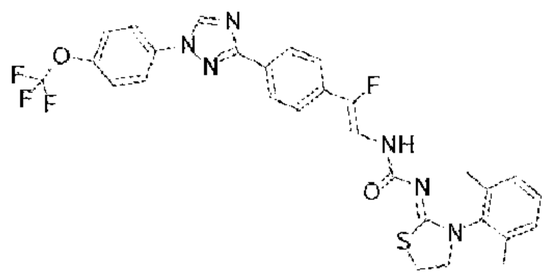
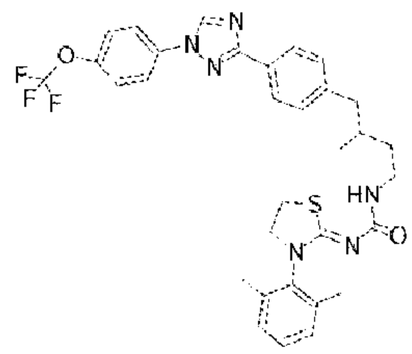
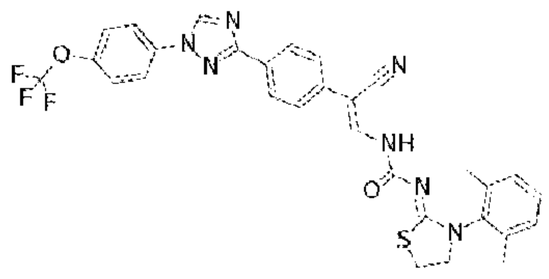
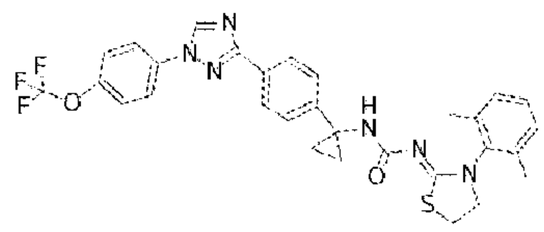
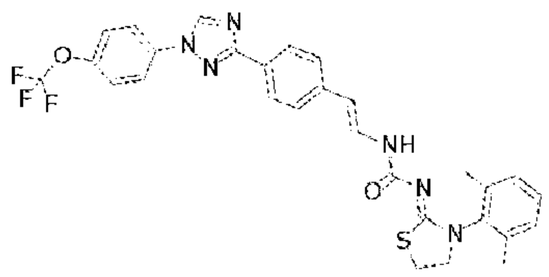
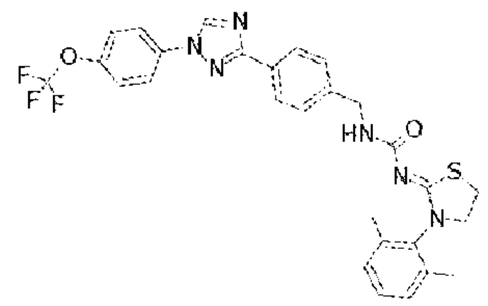
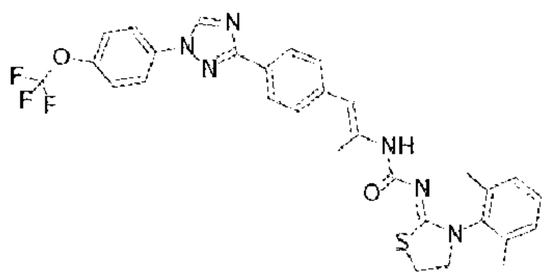
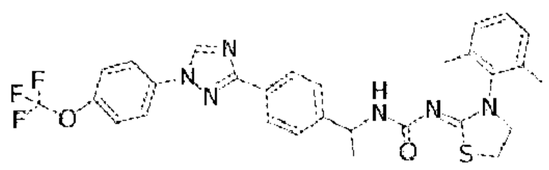
P1475

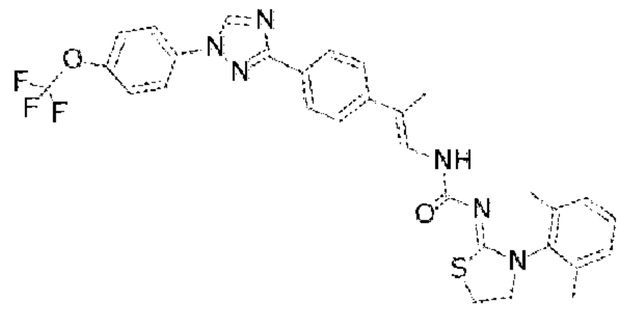
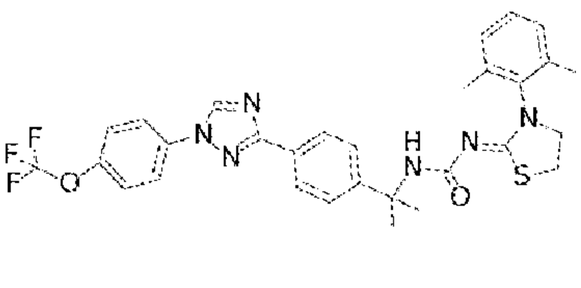
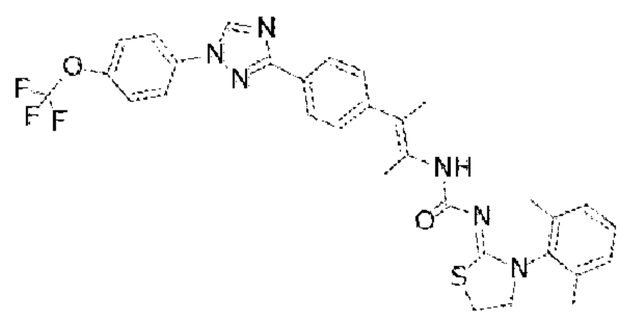
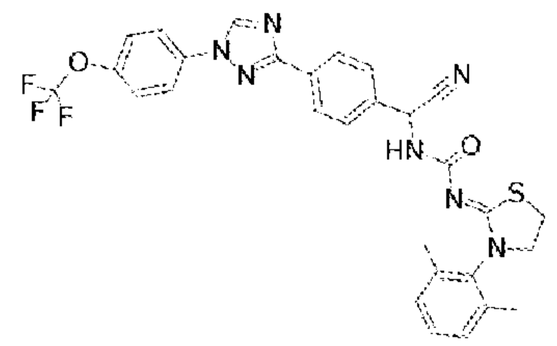
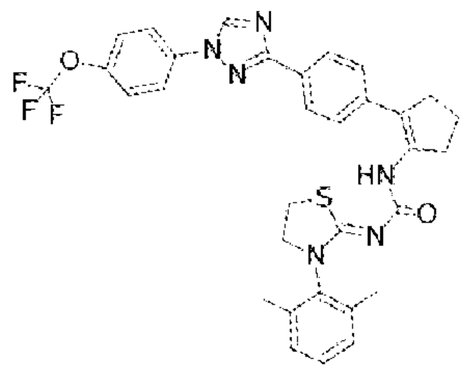
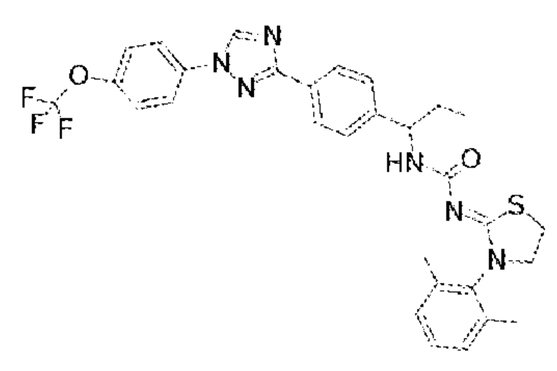
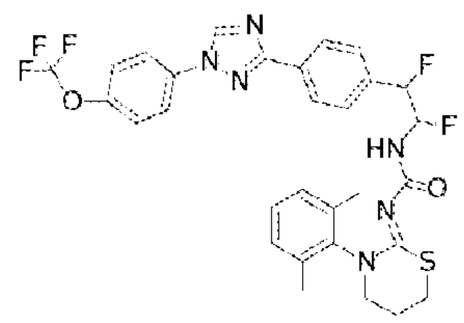
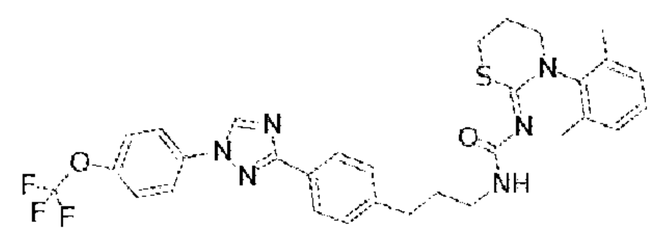
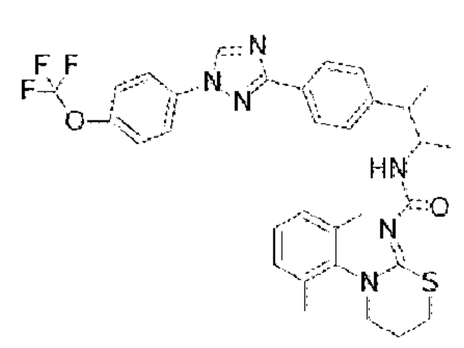
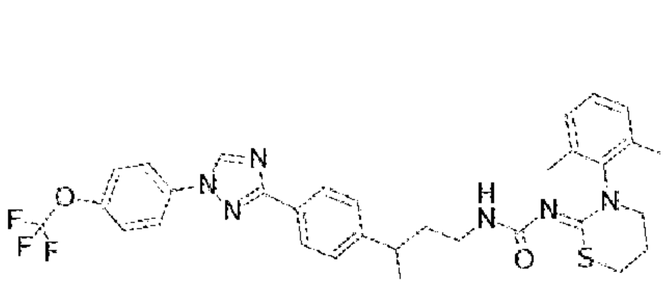
 P1476	 P1477
 P1478	 P1479
 P1480	 P1481
 P1482	 P1483
 P1484	 P1485

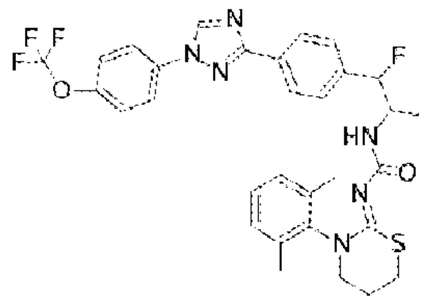
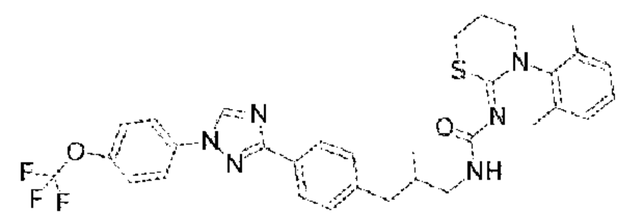
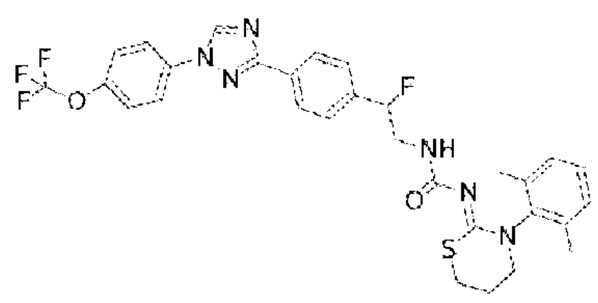
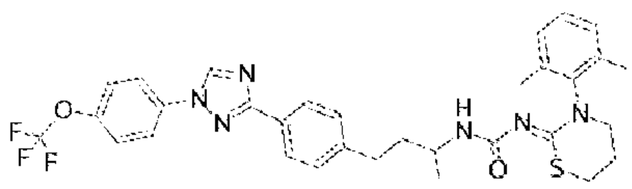
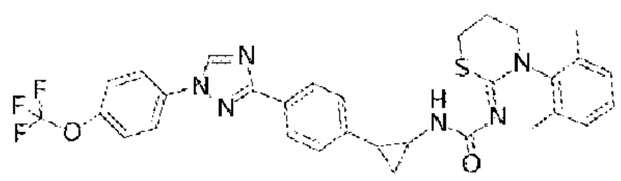
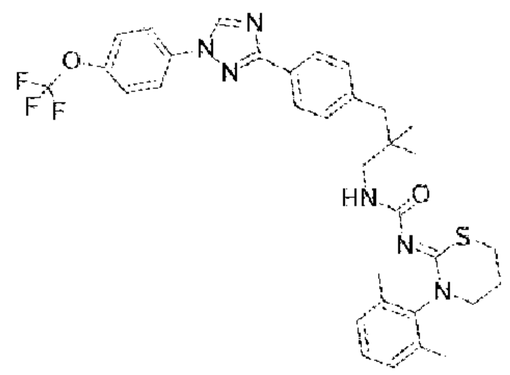
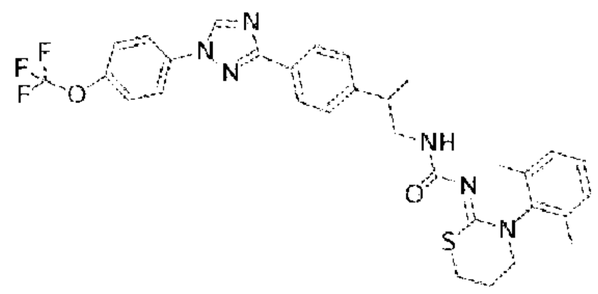
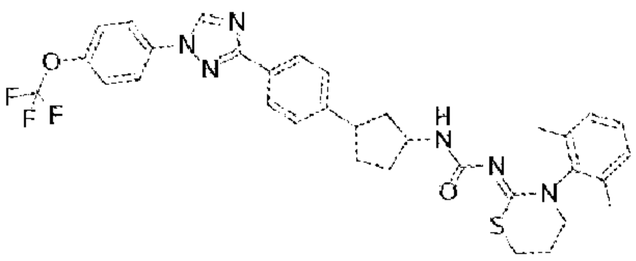
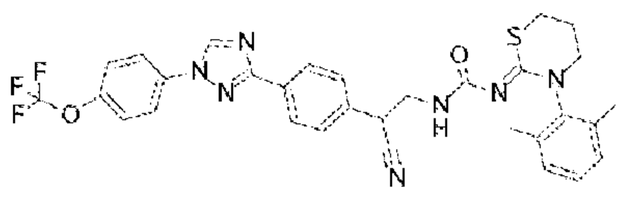
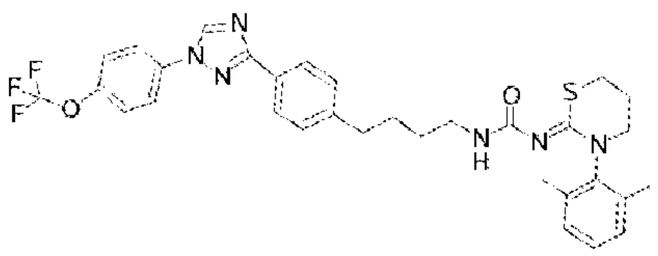
	
P1486	P1487
	
P1488	P1489
	
P1490	P1491
	
P1492	P1493
	
P1494	P1495

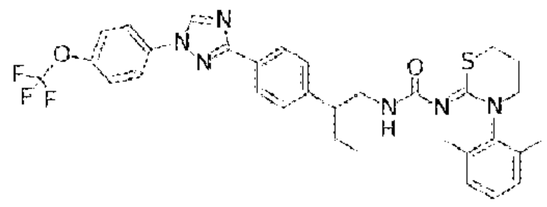
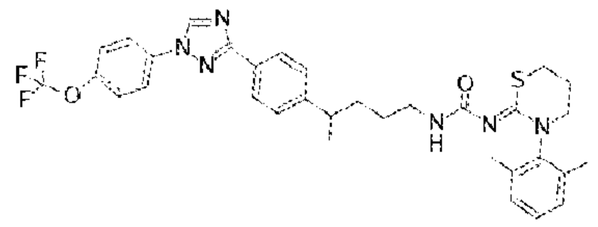
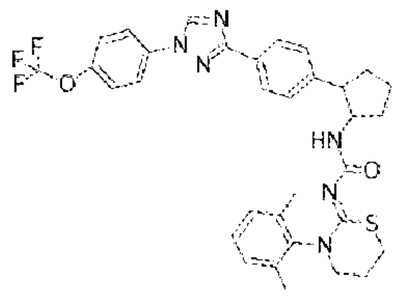
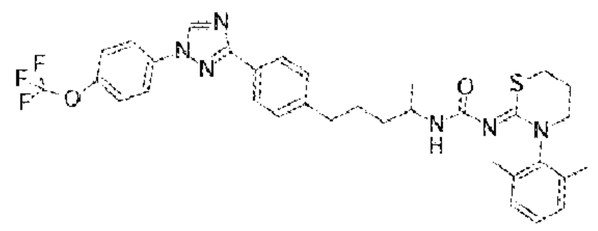
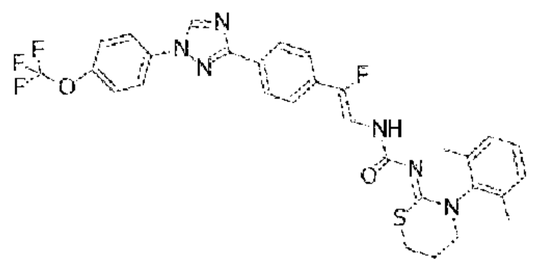
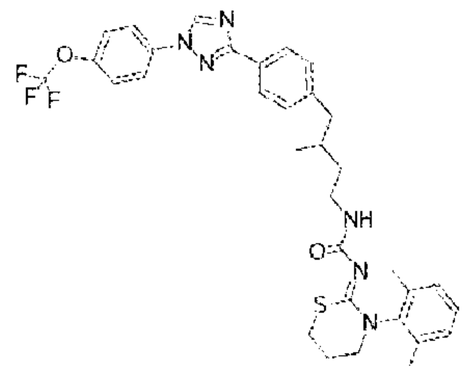
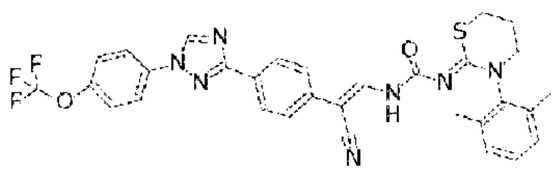
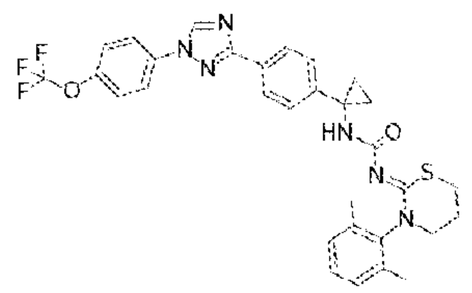
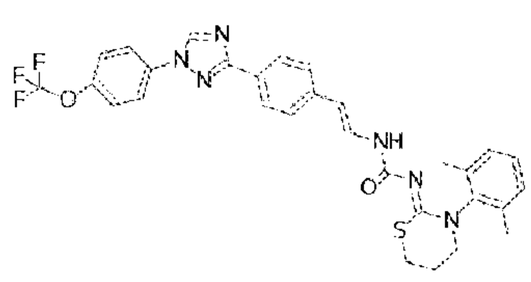
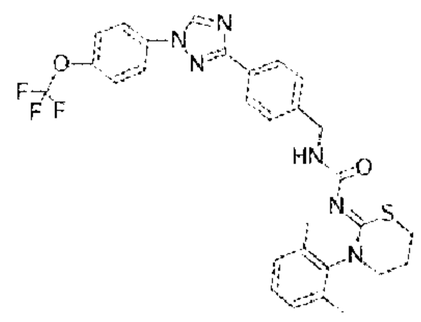
	
P1496	P1497
	
P1498	P1499
	
P1500	P1501
	
P1502	P1503
	
P1504	P1505

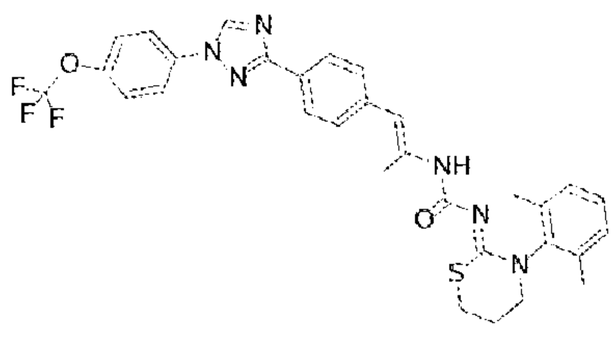
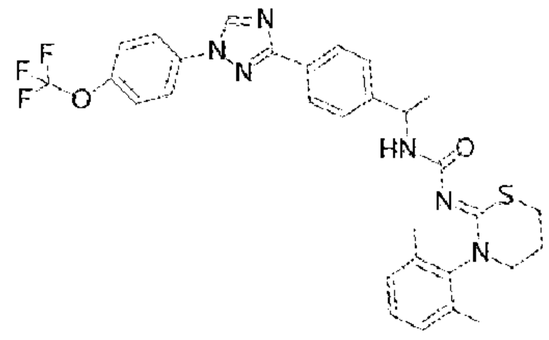
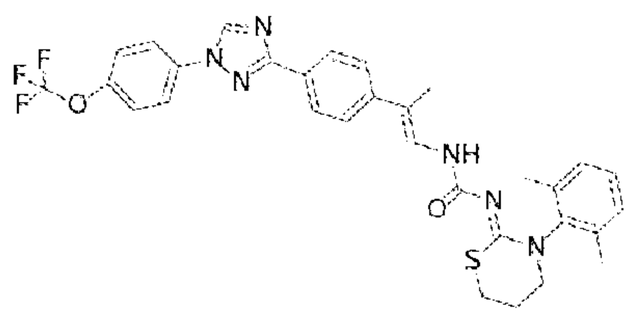
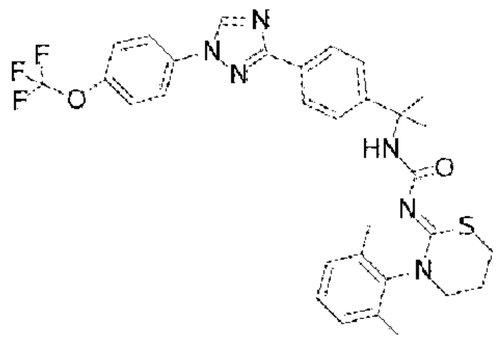
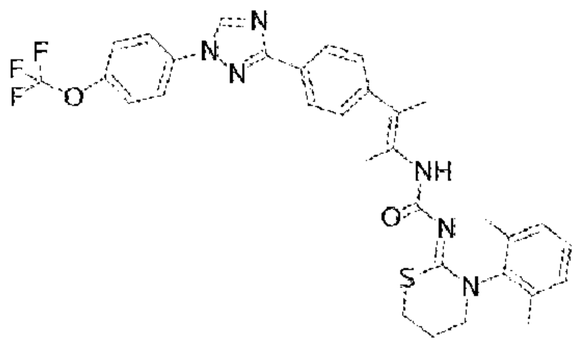
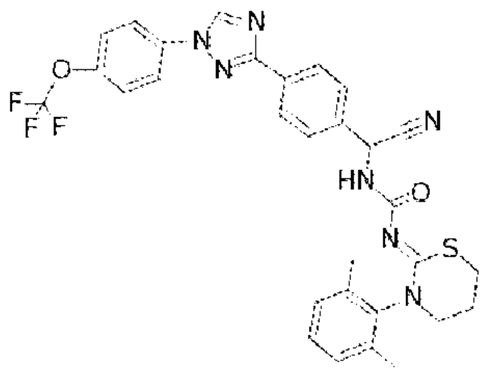
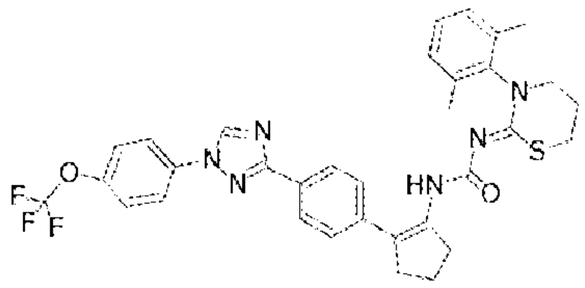
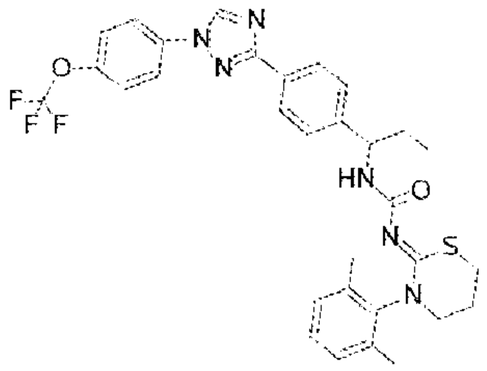
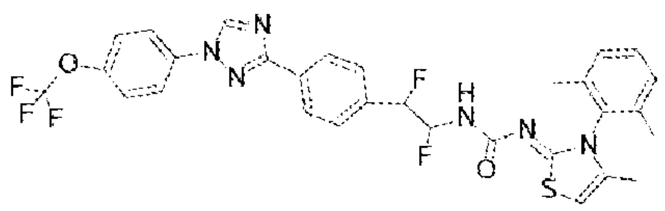
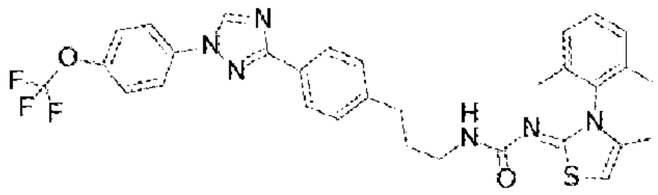
 P1506	 P1507
 P1508	 P1509
 P1510	 P1511
 P1512	 P1513
 P1514	 P1515

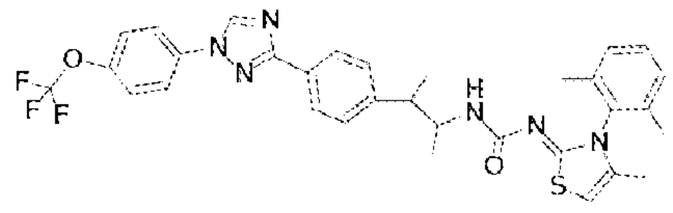
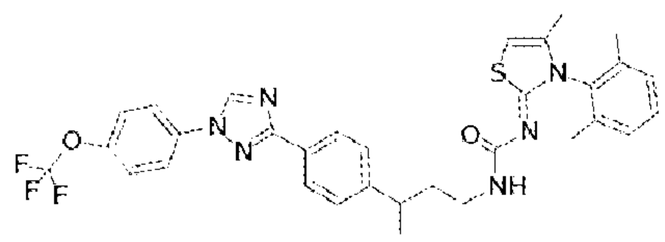
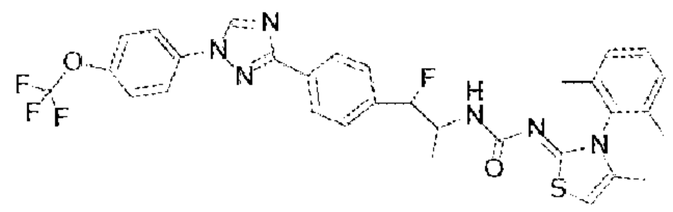
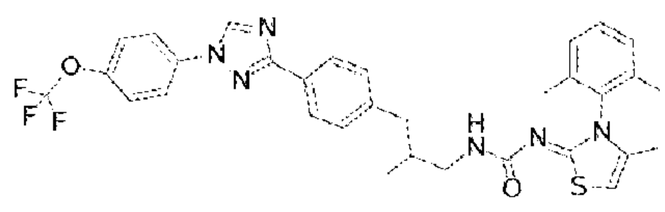
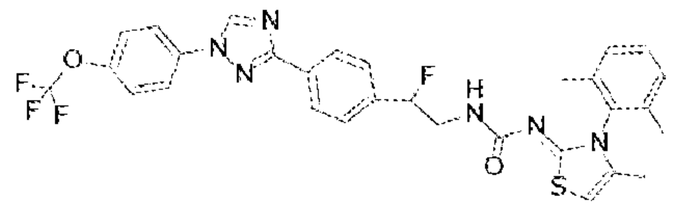
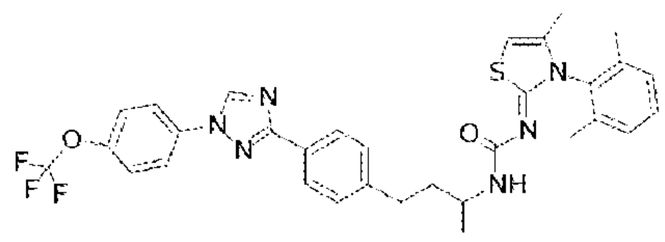
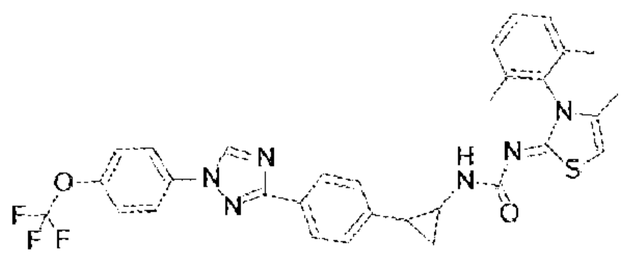
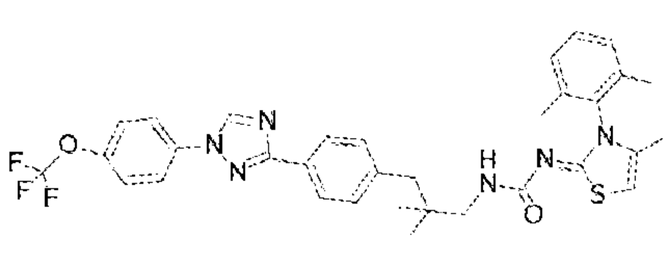
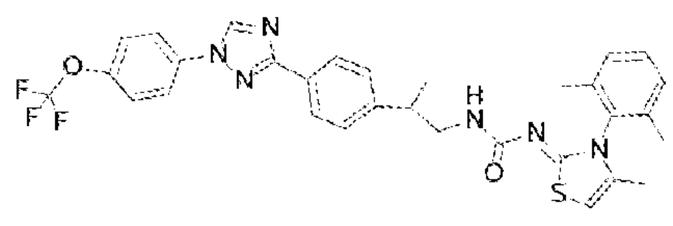
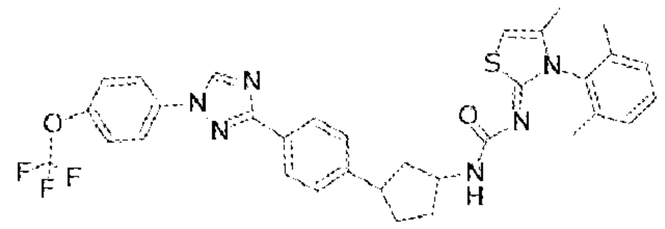
	
P1516	P1517
	
P1518	P1519
	
P1520	P1521
	
P1522	P1523
	
P1524	P1525

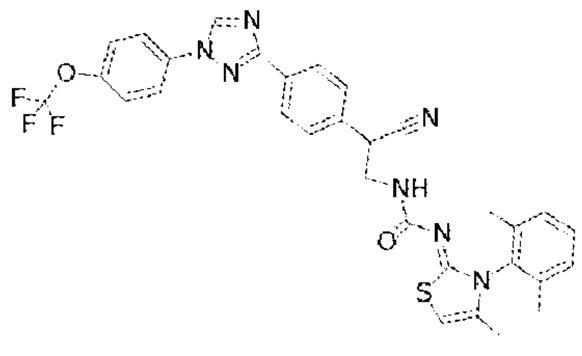
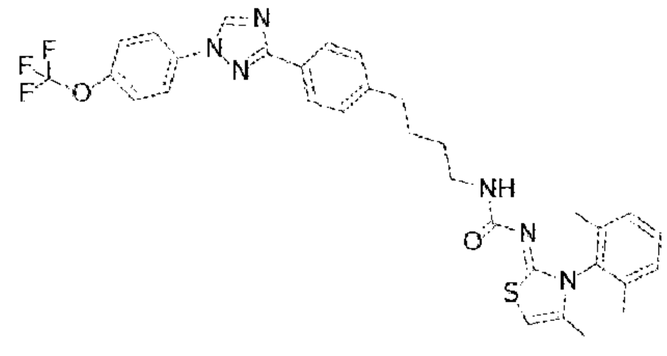
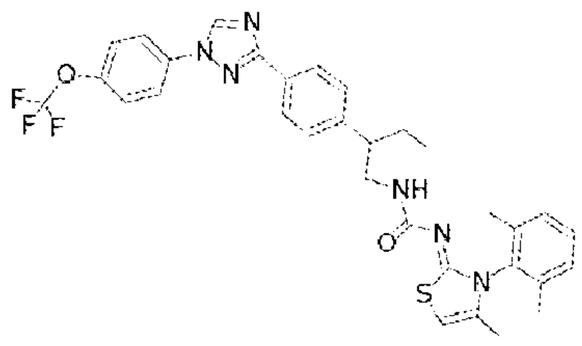
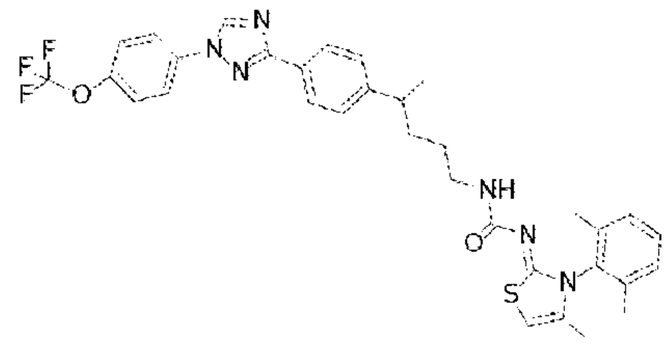
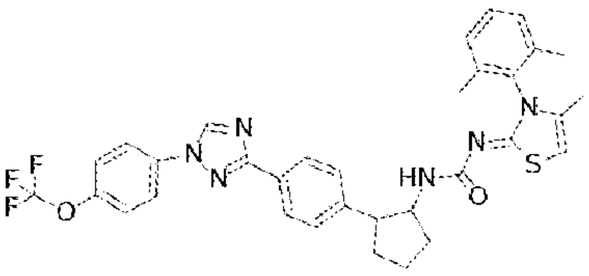
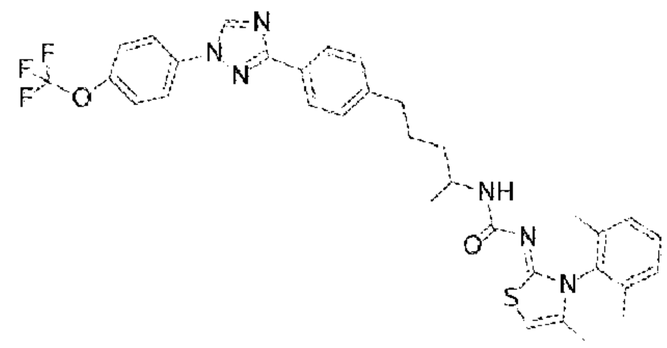
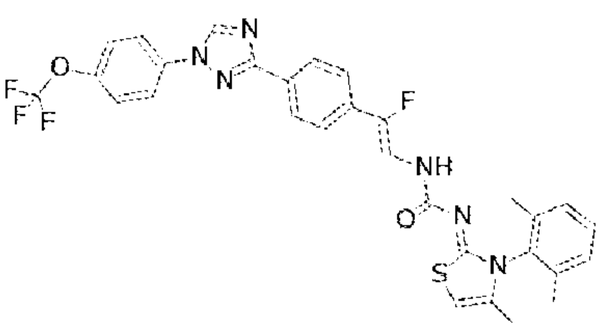
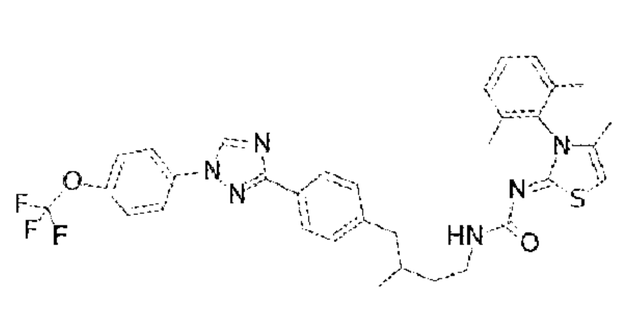
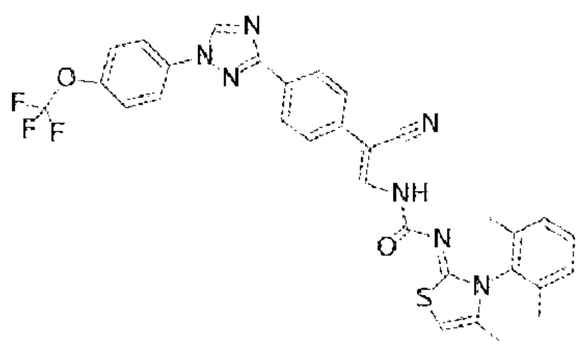
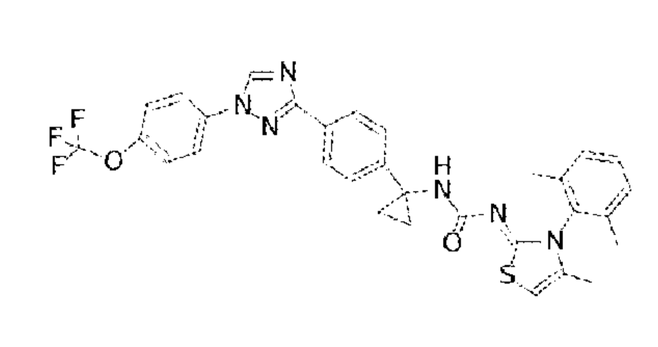
 P1526	 P1527
 P1528	 P1529
 P1530	 P1531
 P1532	 P1533
 P1534	 P1535

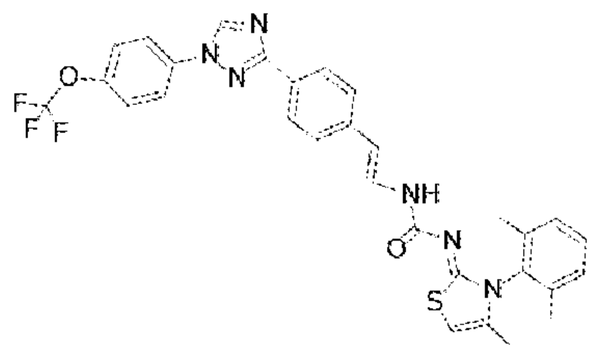
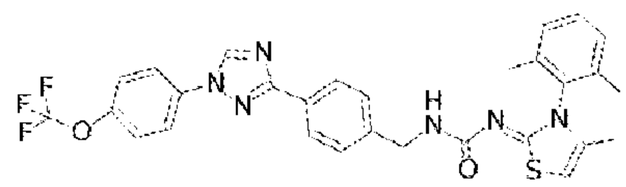
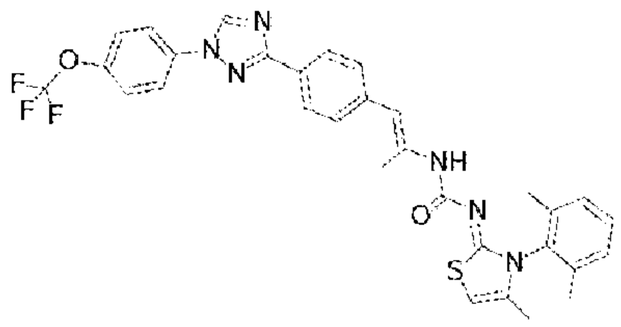
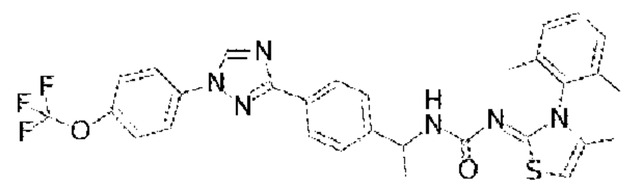
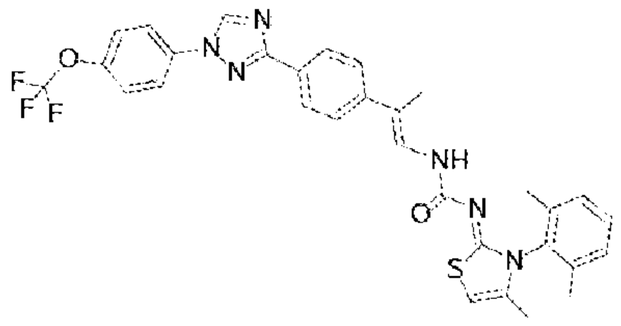
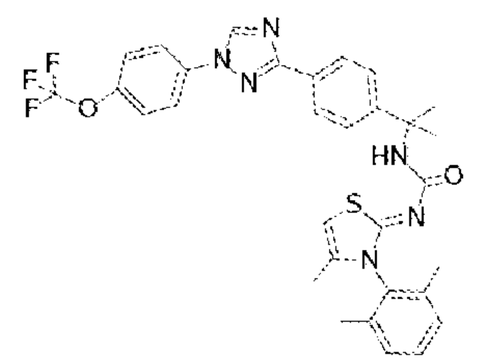
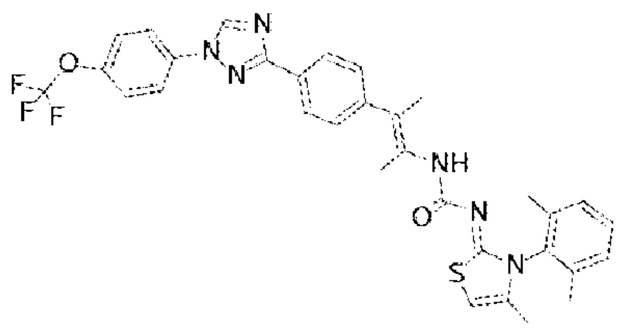
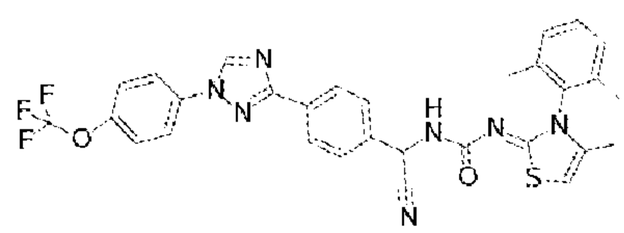
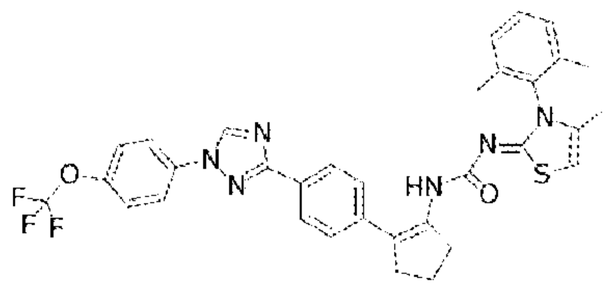
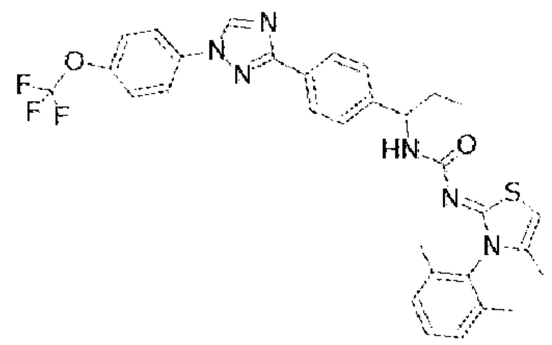
 P1536	 P1537
 P1538	 P1539
 P1540	 P1541
 P1542	 P1543
 P1544	 P1545

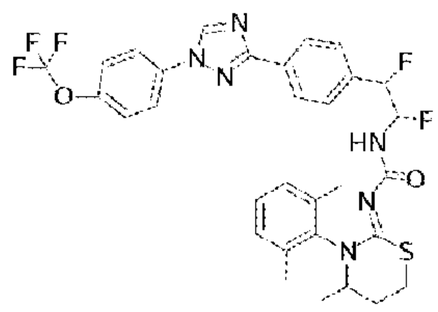
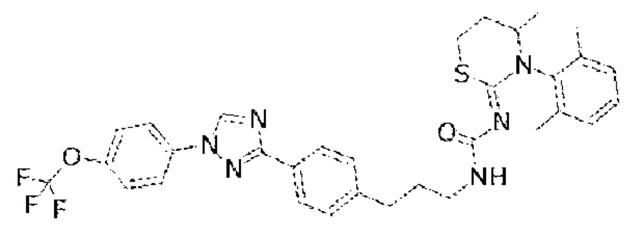
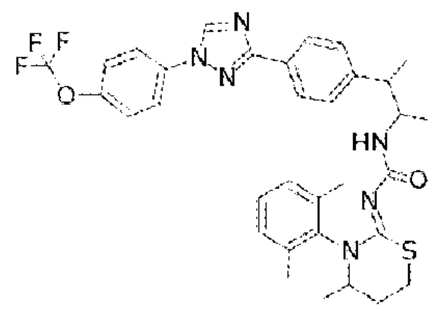
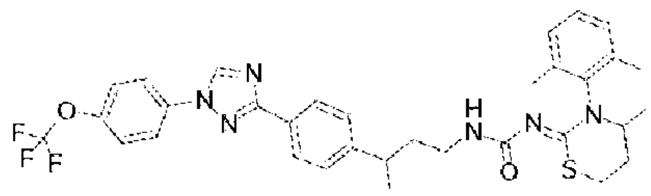
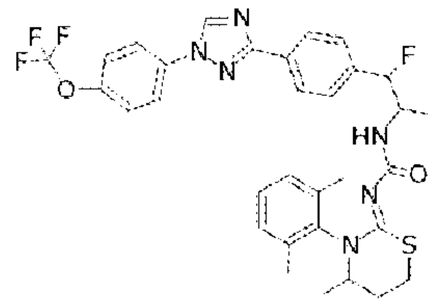
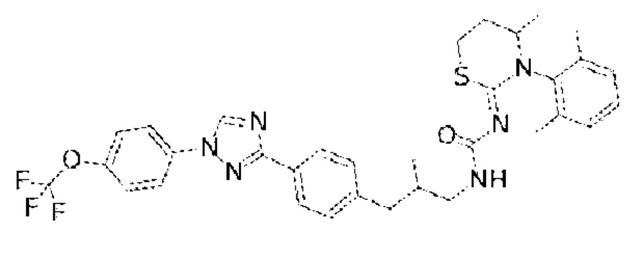
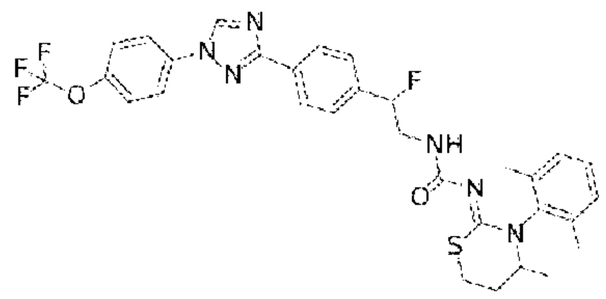
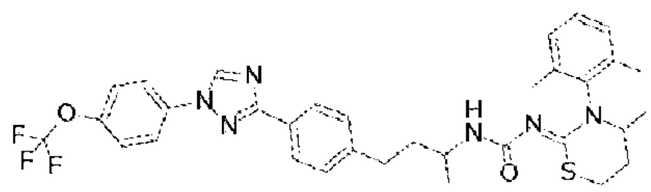
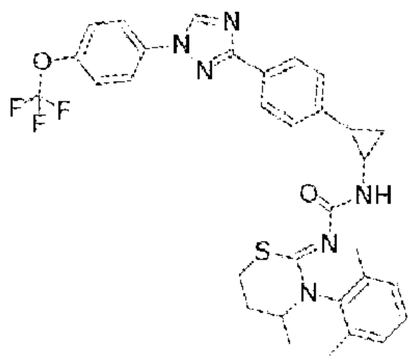
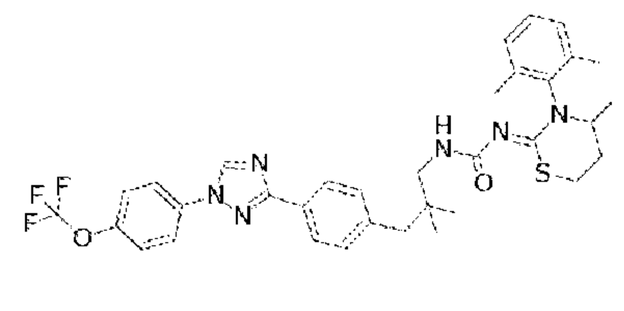
	
P1546	P1547
	
P1548	P1549
	
P1550	P1551
	
P1552	P1553
	
P1554	P1555

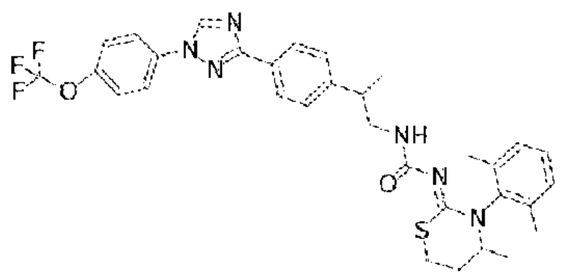
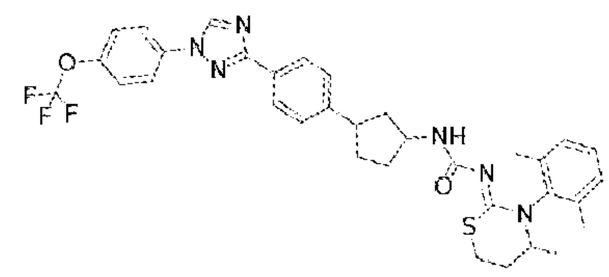
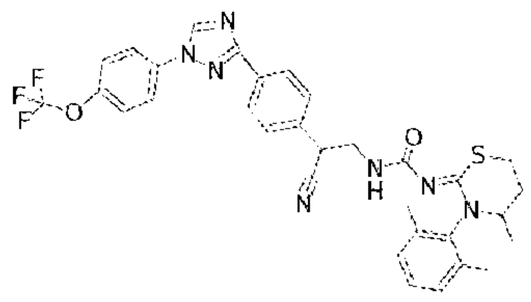
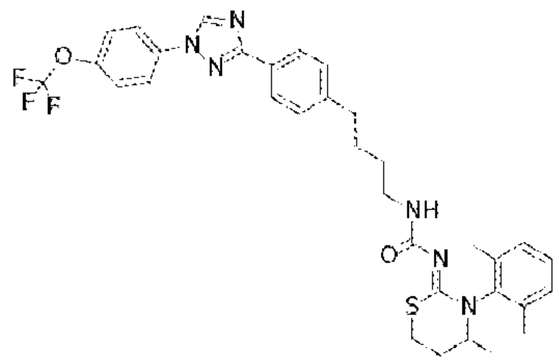
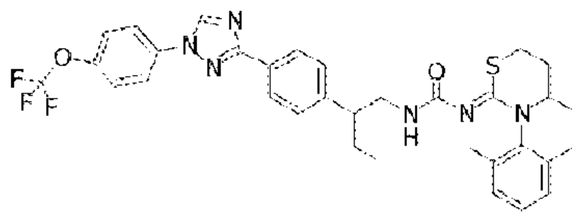
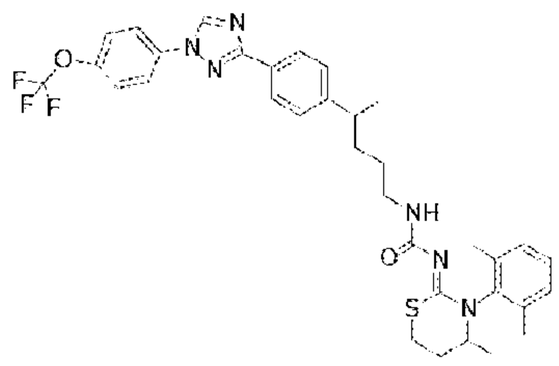
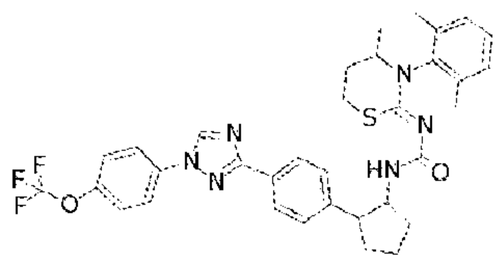
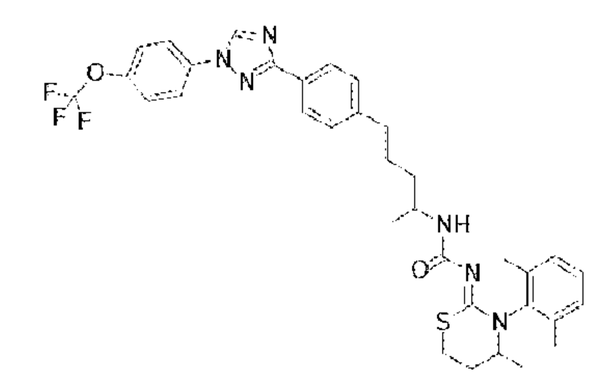
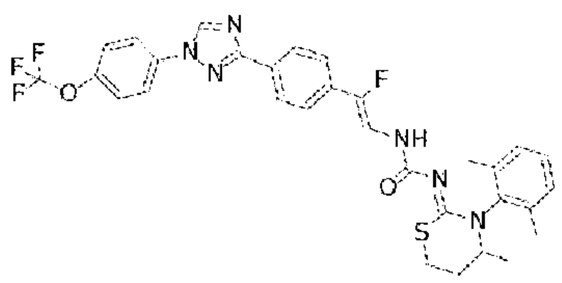
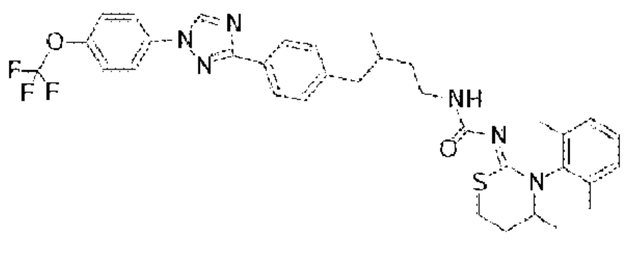
 P1556	 P1557
 P1558	 P1559
 P1560	 P1561
 P1562	 P1563
 P1564	 P1565

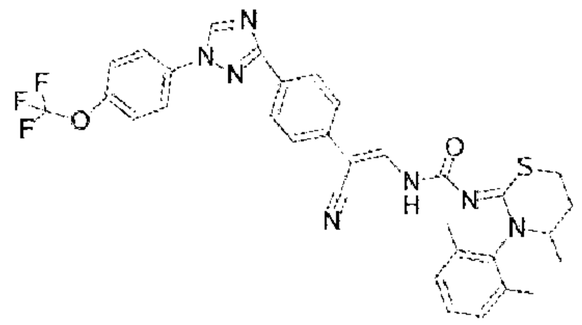
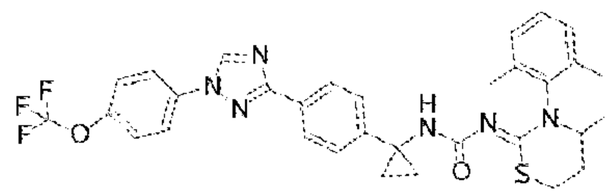
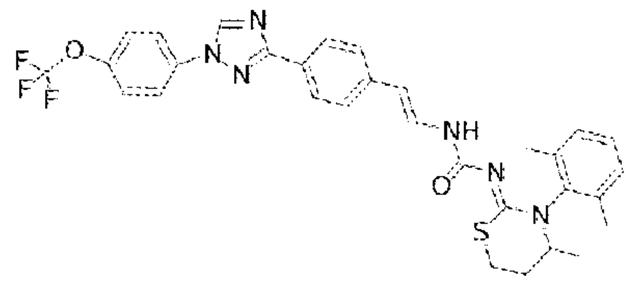
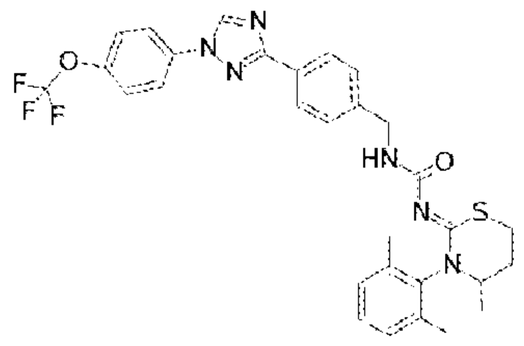
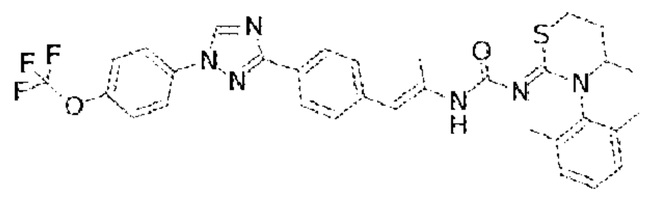
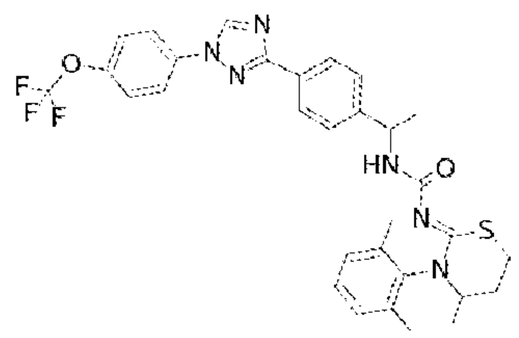
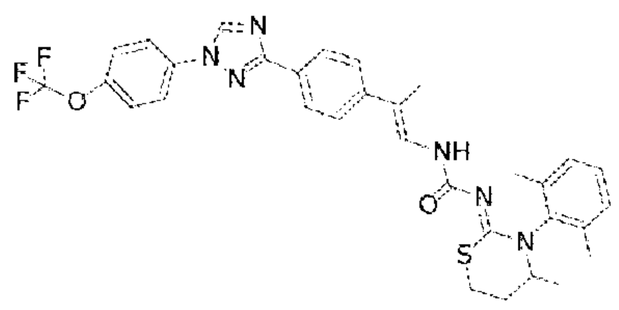
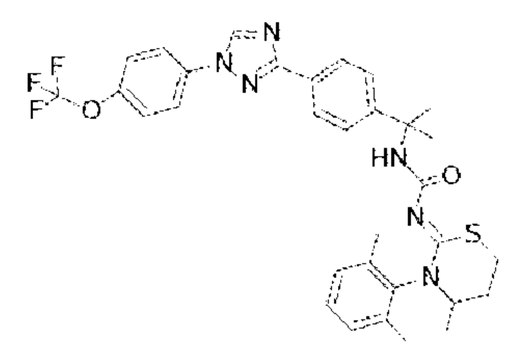
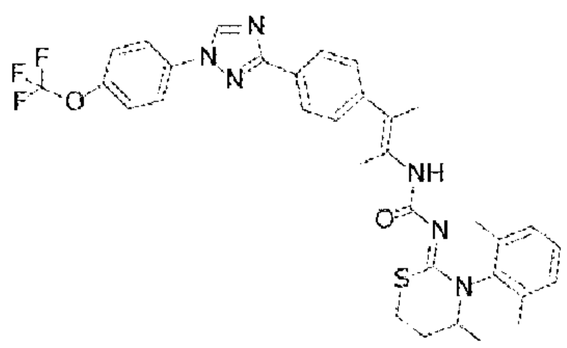
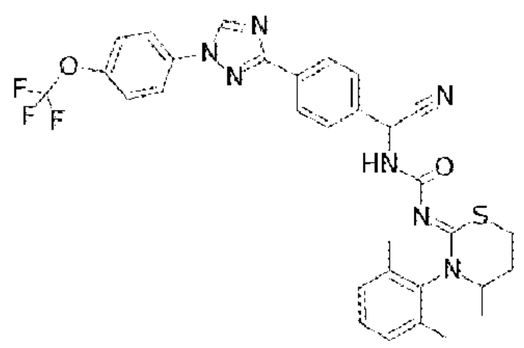
 P1566	 P1567
 P1568	 P1569
 P1570	 P1571
 P1572	 P1573
 P1574	 P1575

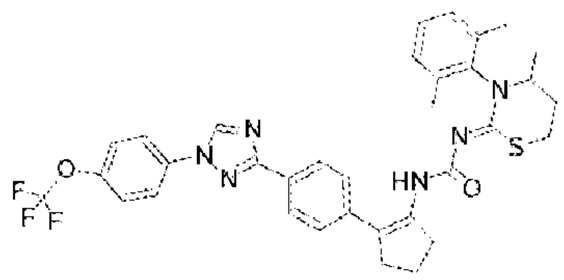
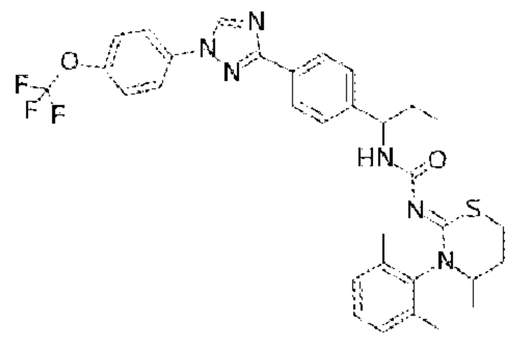
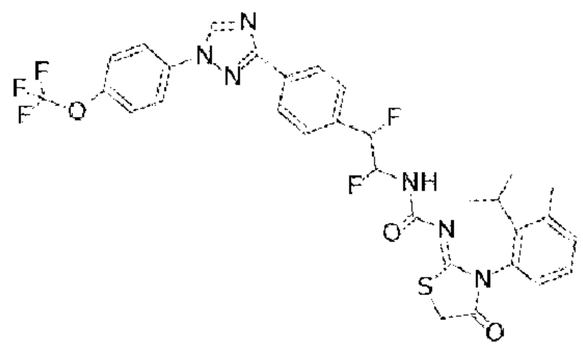
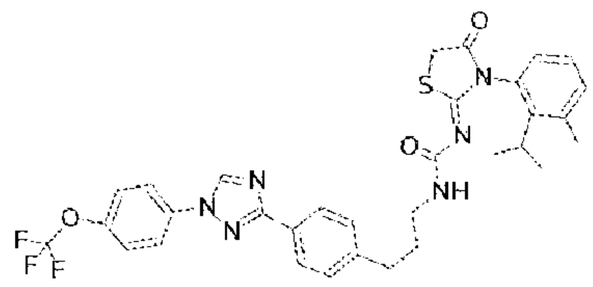
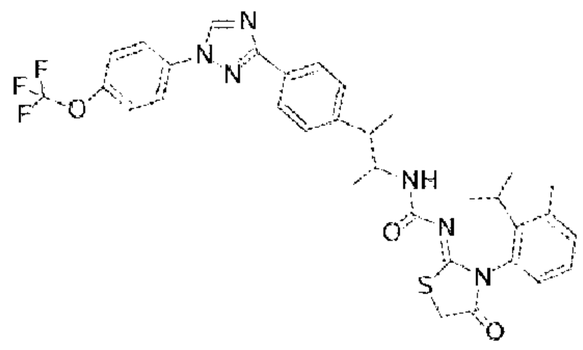
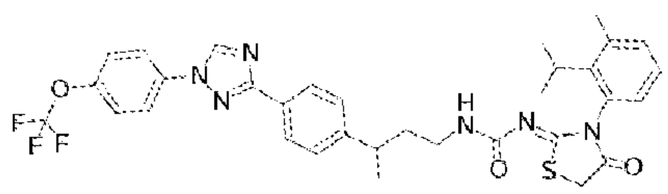
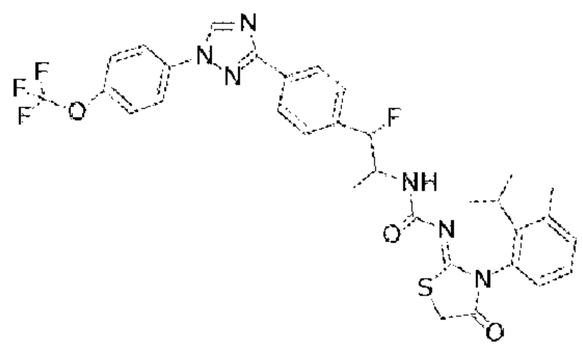
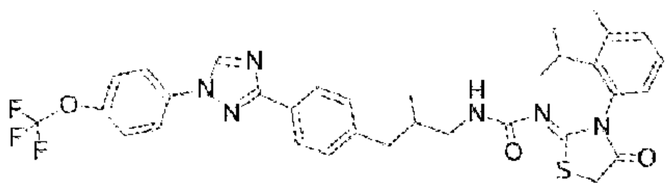
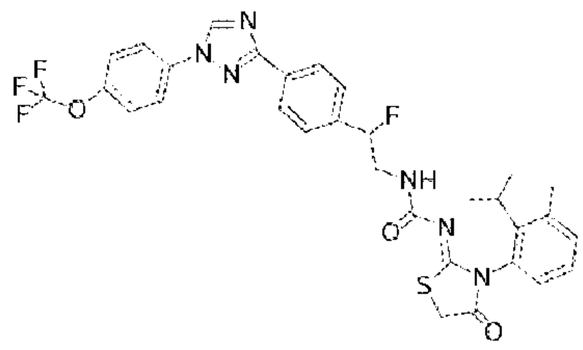
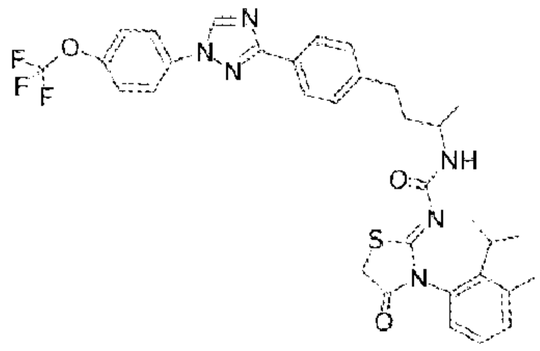
 P1576	 P1577
 P1578	 P1579
 P1580	 P1581
 P1582	 P1583
 P1584	 P1585

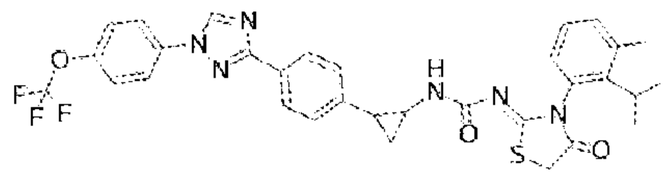
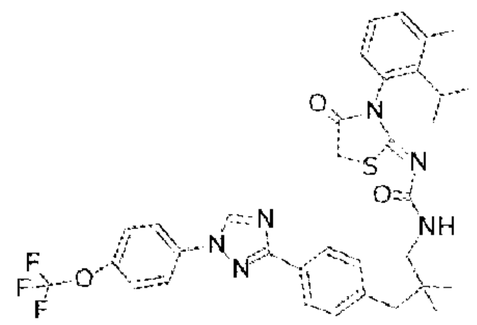
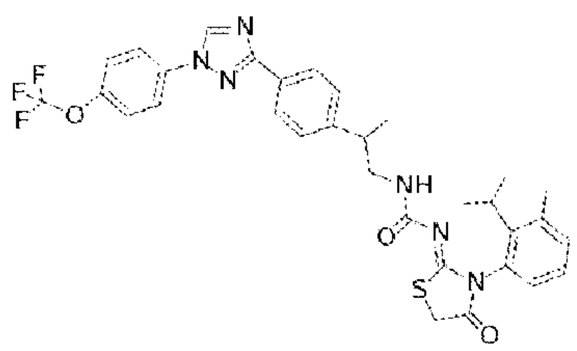
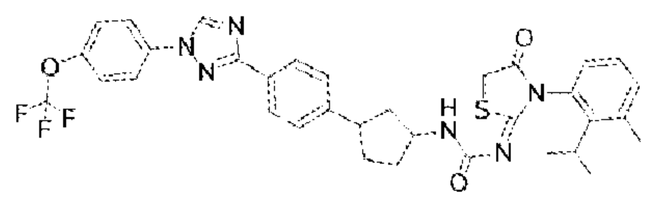
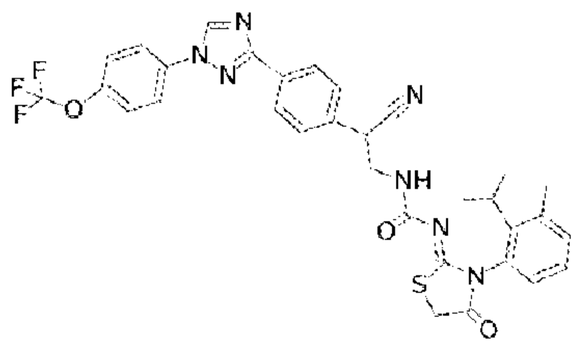
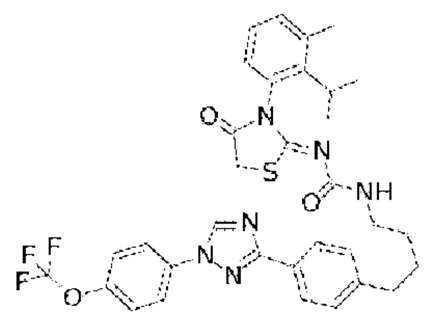
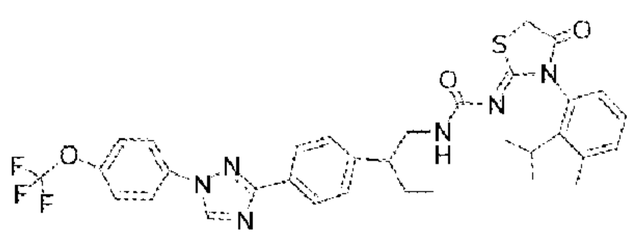
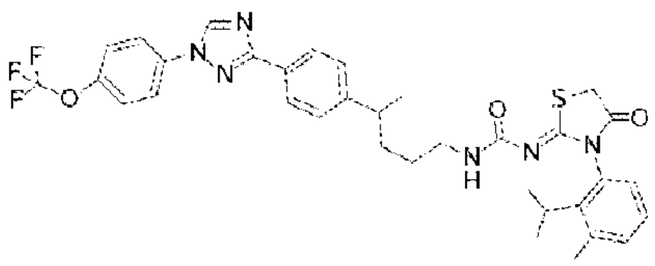
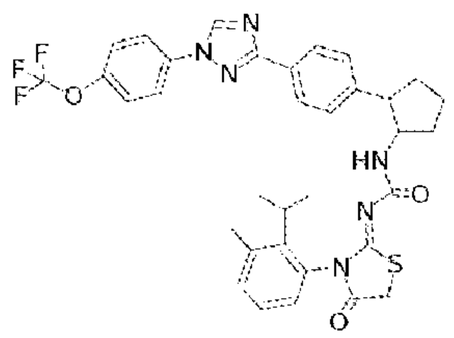
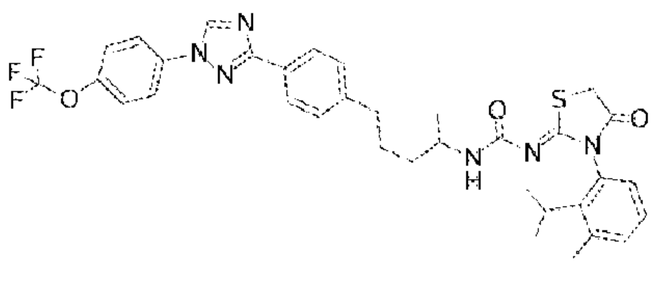
 P1586	 P1587
 P1588	 P1589
 P1590	 P1591
 P1592	 P1593
 P1594	 P1595

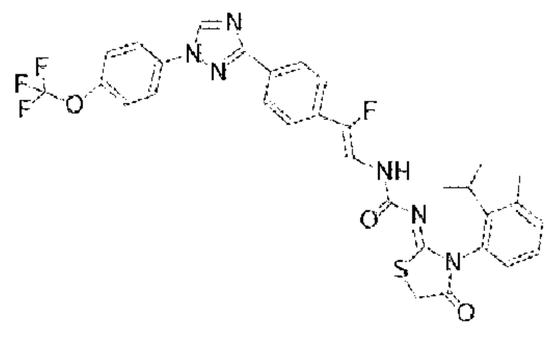
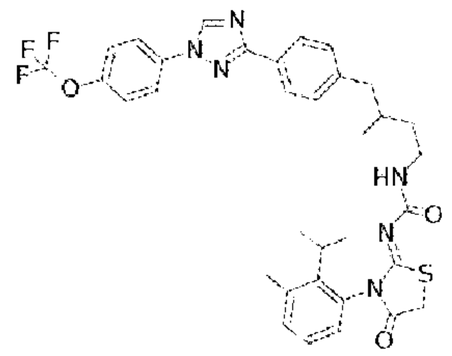
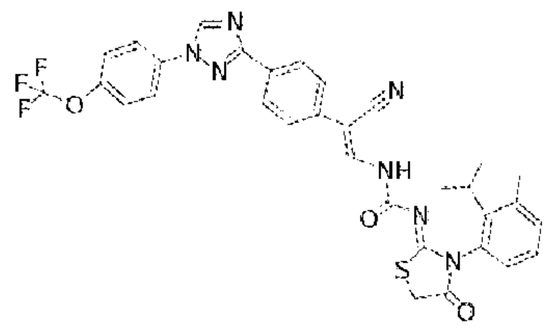
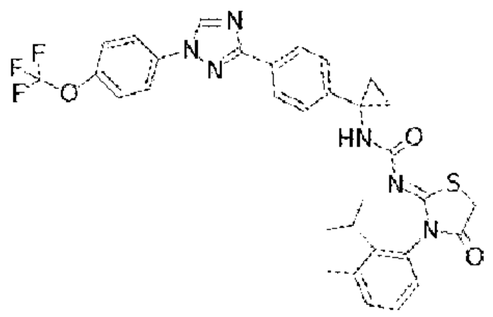
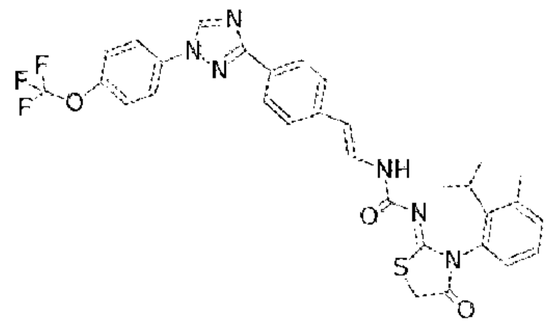
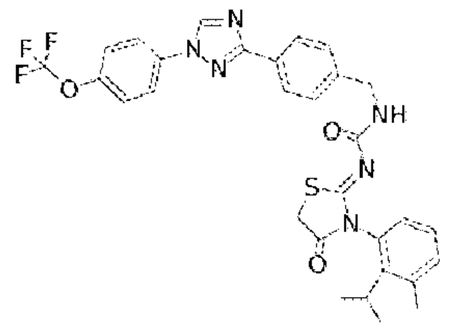
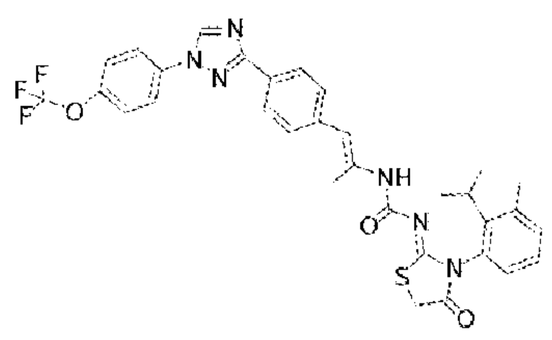
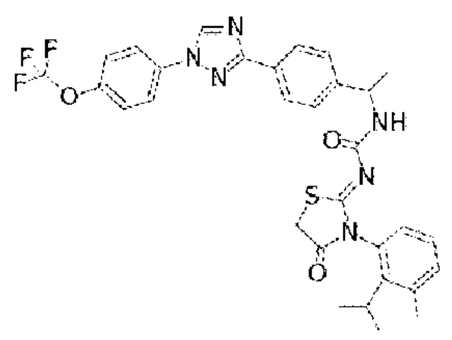
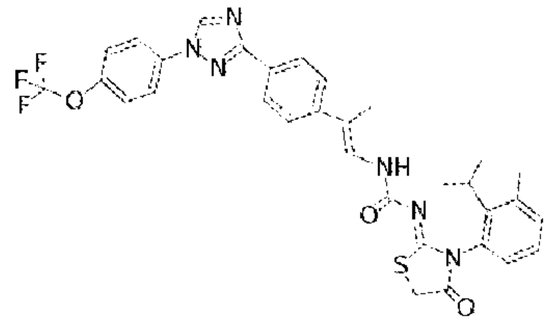
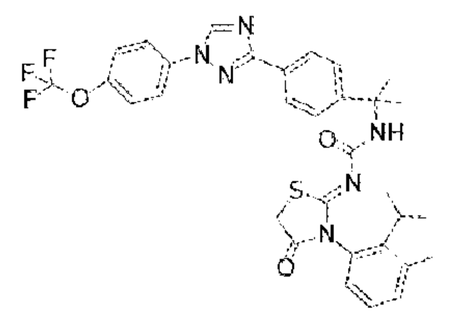
 P1596	 P1597
 P1598	 P1599
 P1600	 P1601
 P1602	 P1603
 P1604	 P1605

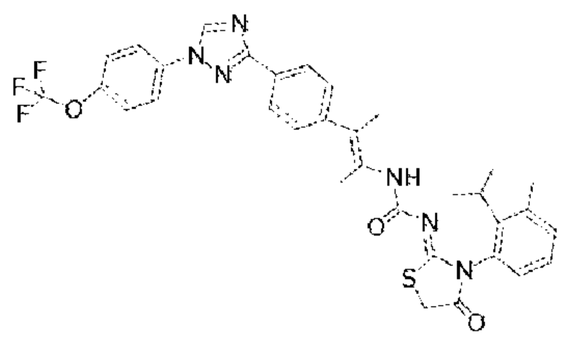
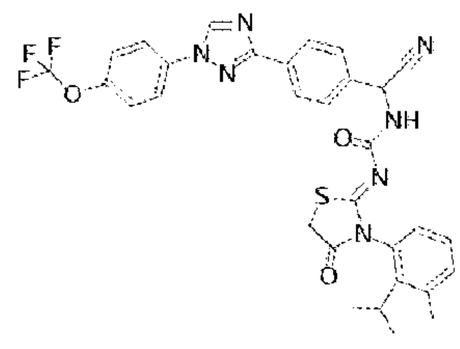
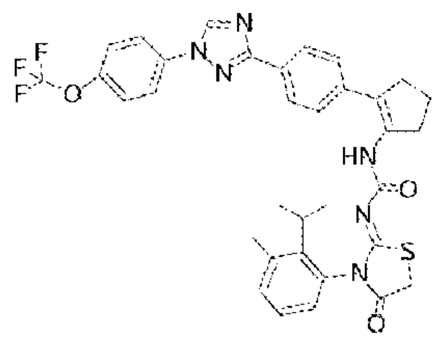
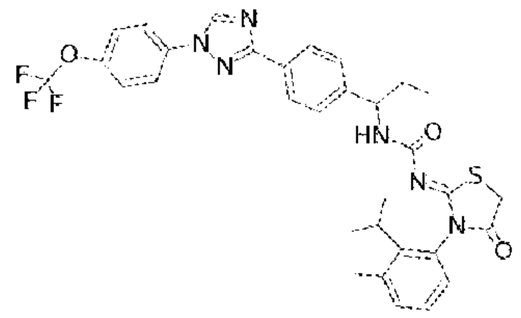
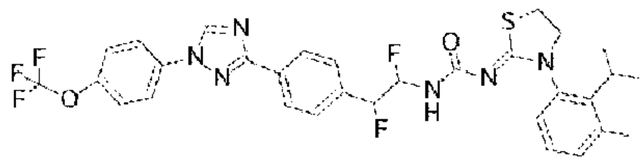
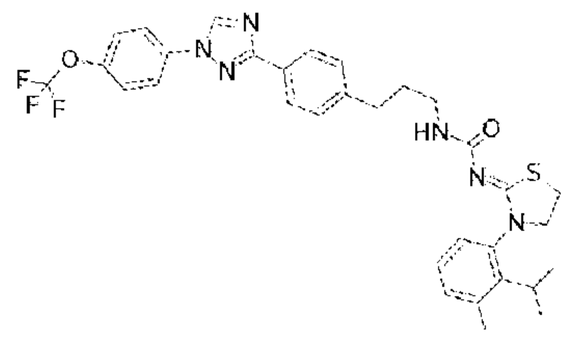
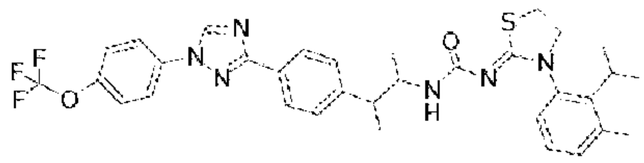
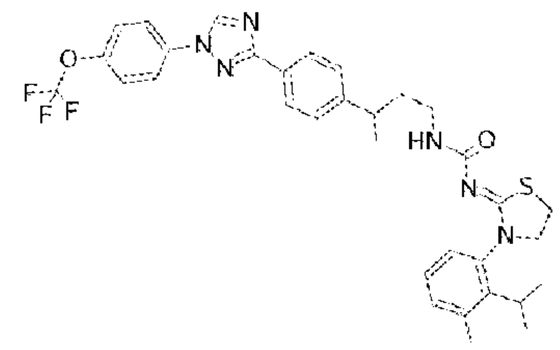
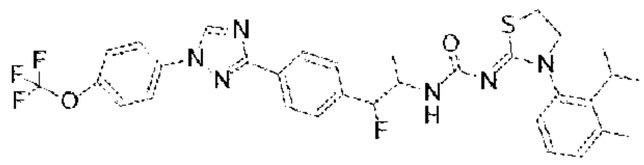
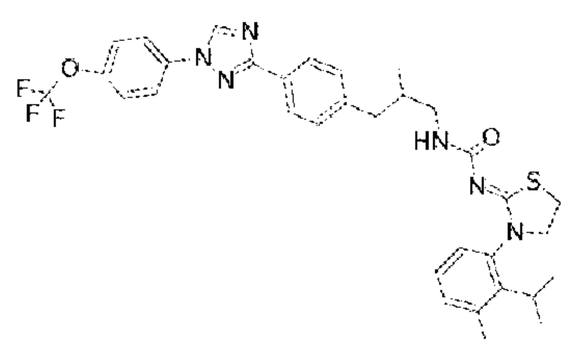
 P1606	 P1607
 P1608	 P1609
 P1610	 P1611
 P1612	 P1613
 P1614	 P1615

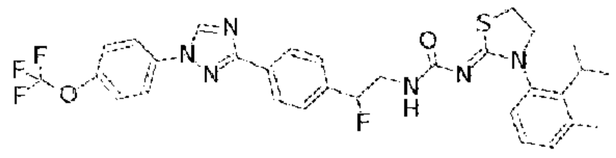
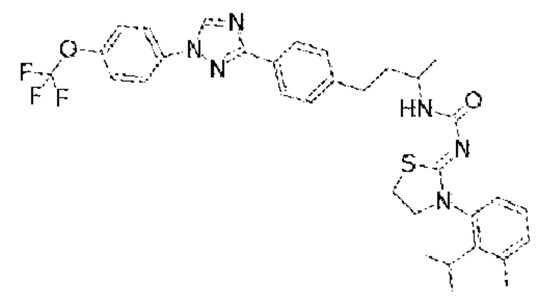
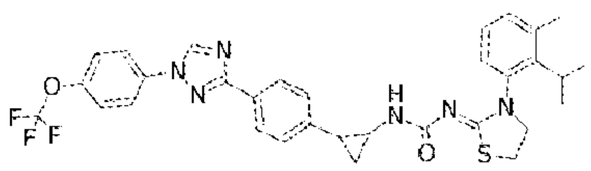
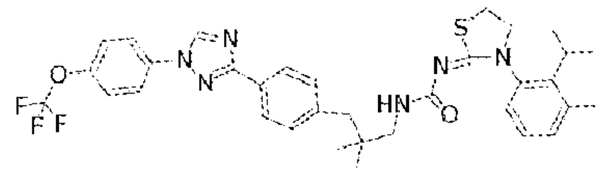
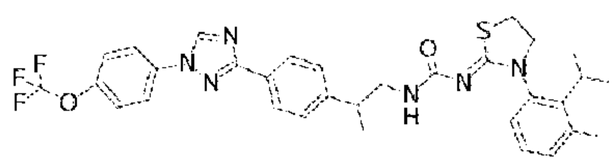
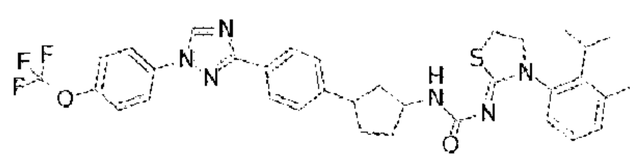
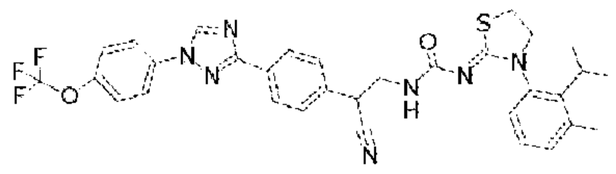
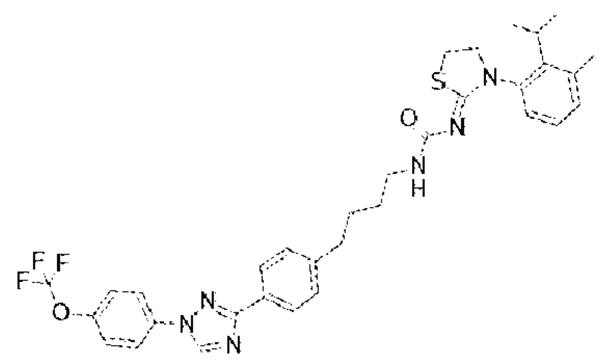
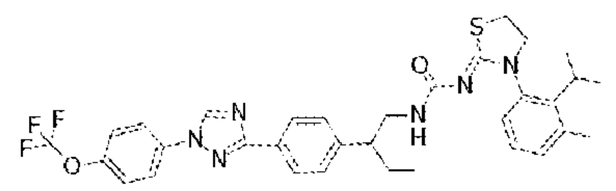
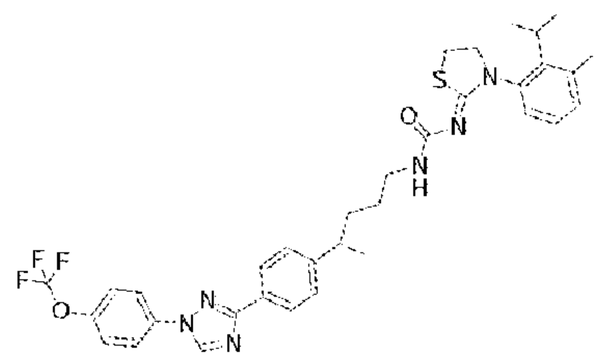
 P1616	 P1617
 P1618	 P1619
 P1620	 P1621
 P1622	 P1623
 P1624	 P1625

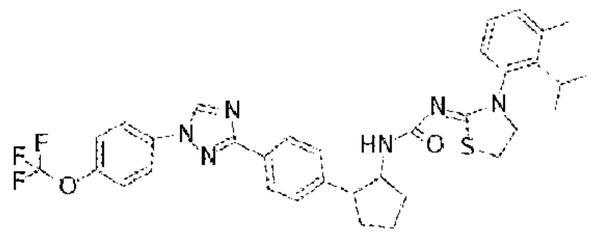
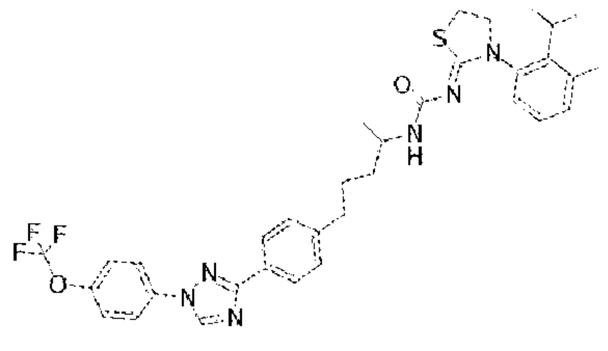
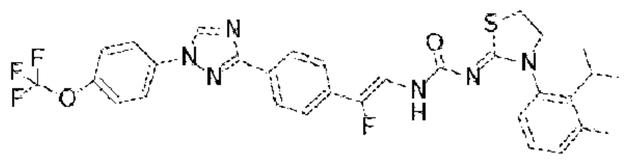
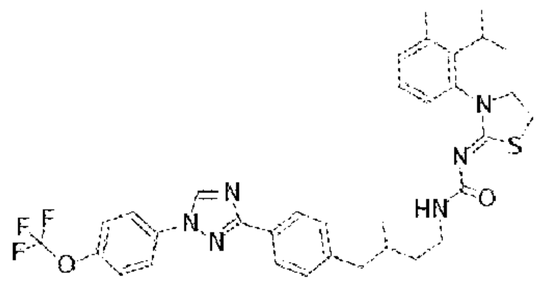
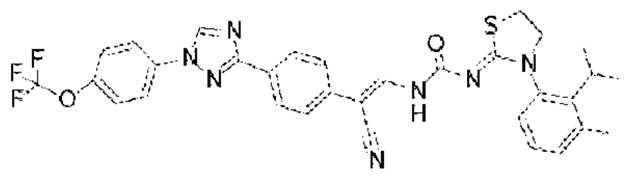
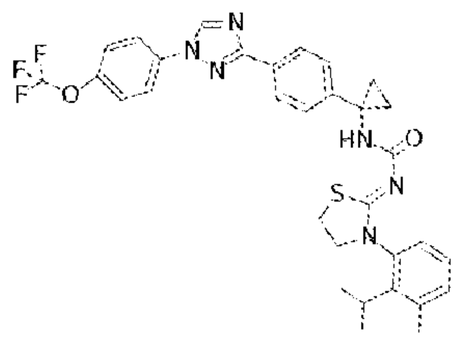
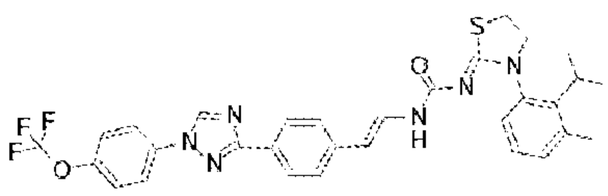
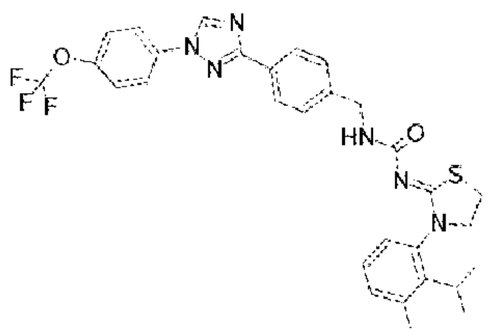
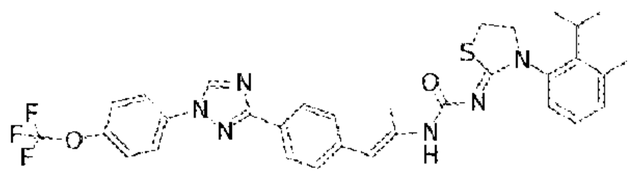
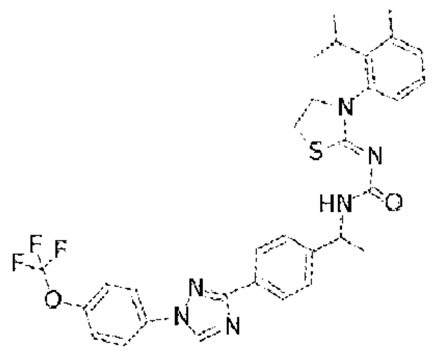
 P1626	 P1627
 P1628	 P1629
 P1630	 P1631
 P1632	 P1633
 P1634	 P1635

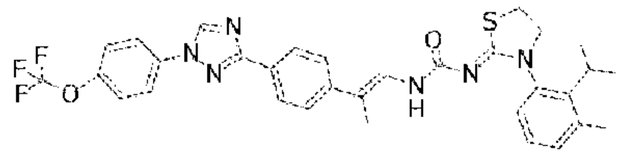
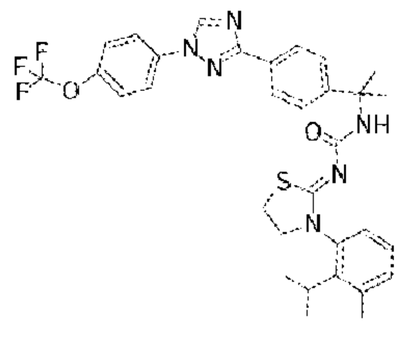
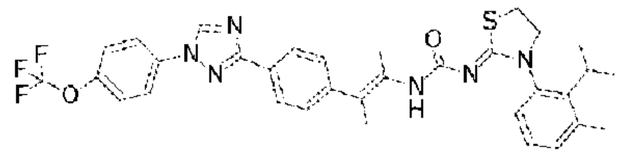
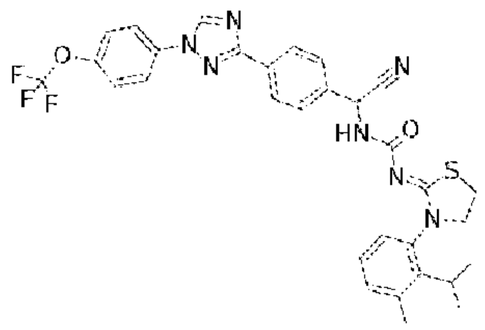
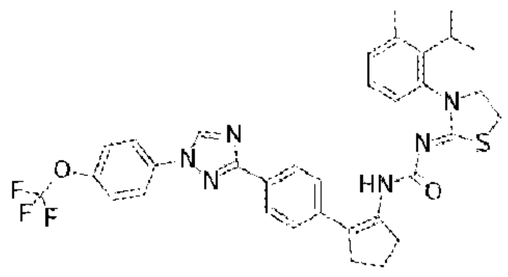
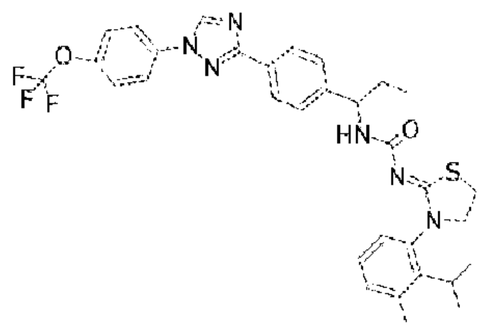
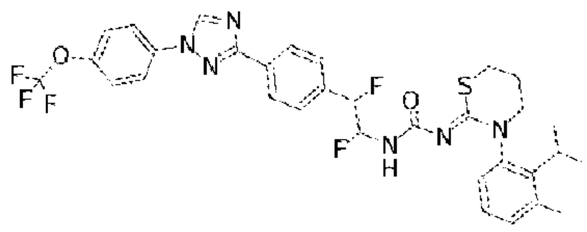
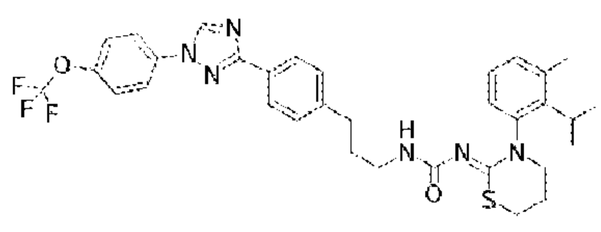
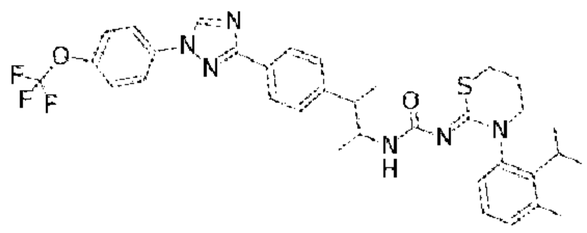
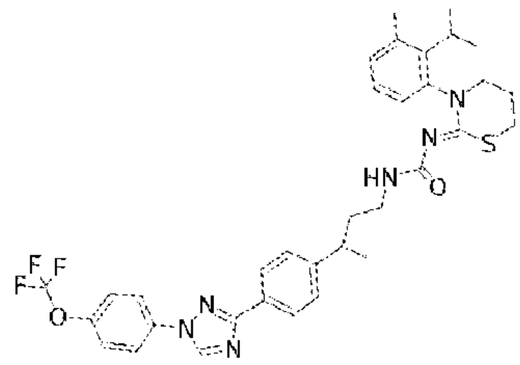
 P1636	 P1637
 P1638	 P1639
 P1640	 P1641
 P1642	 P1643
 P1644	 P1645

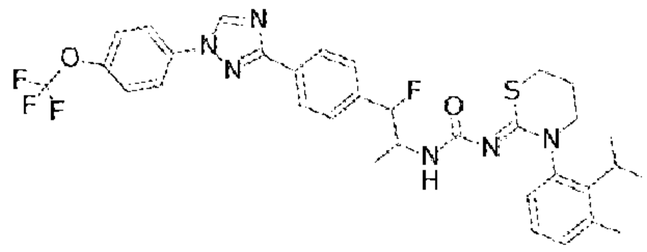
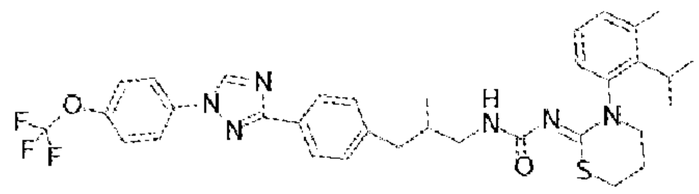
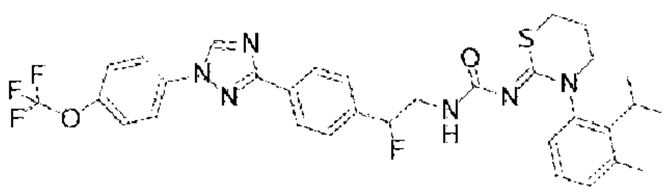
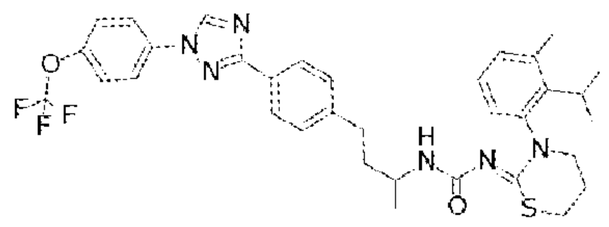
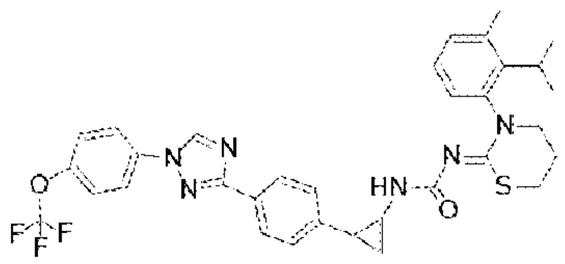
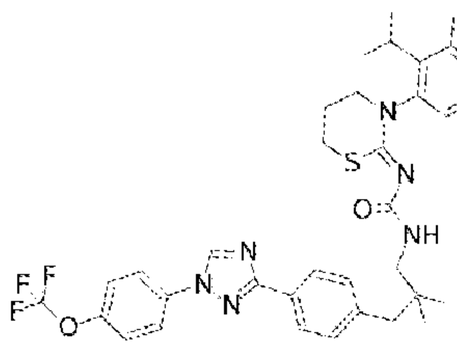
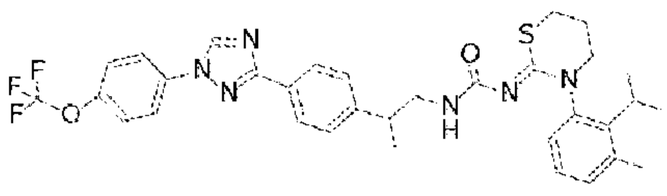
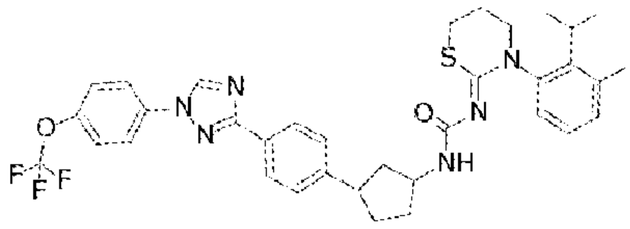
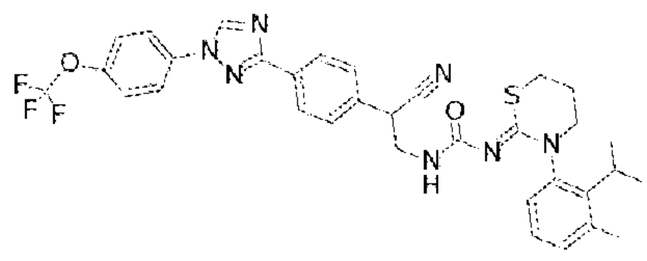
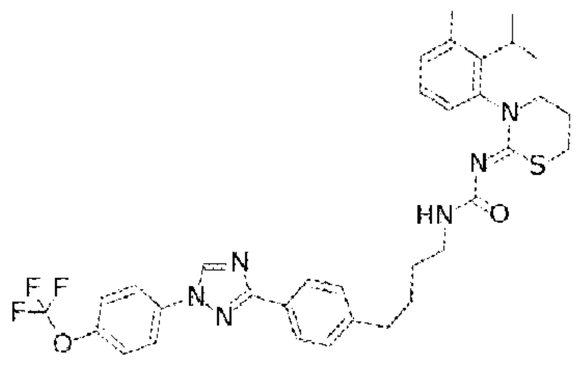
 P1646	 P1647
 P1648	 P1649
 P1650	 P1651
 P1652	 P1653
 P1654	 P1655

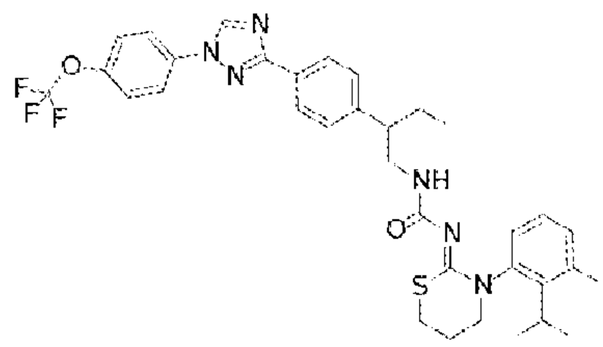
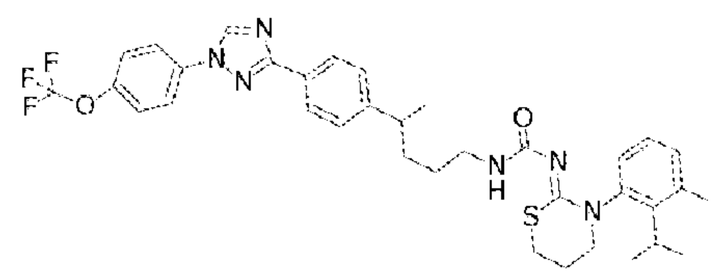
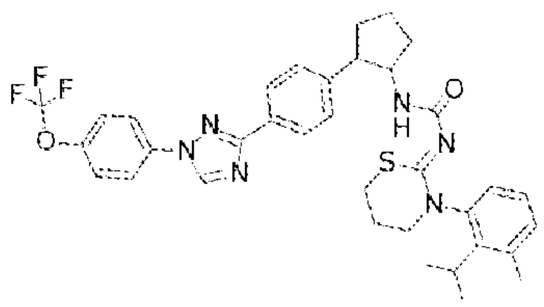
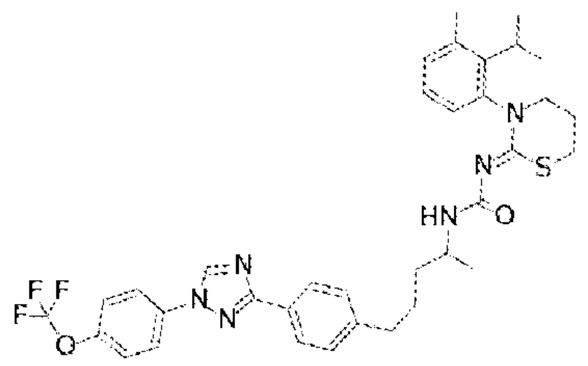
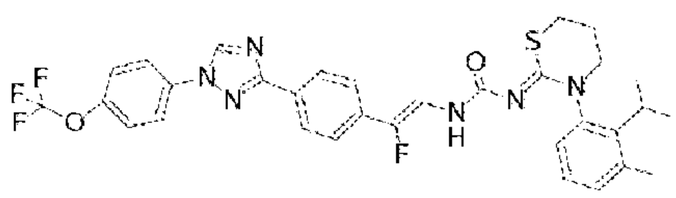
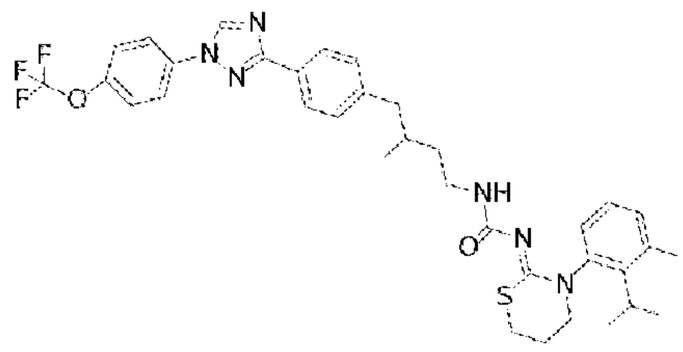
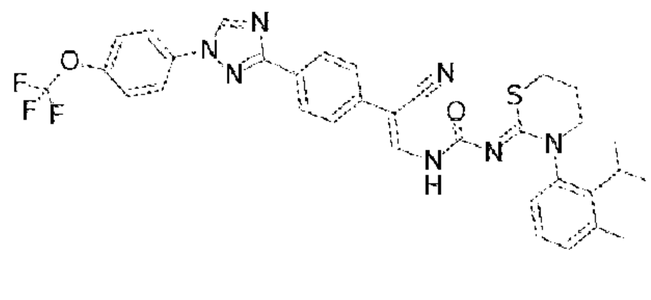
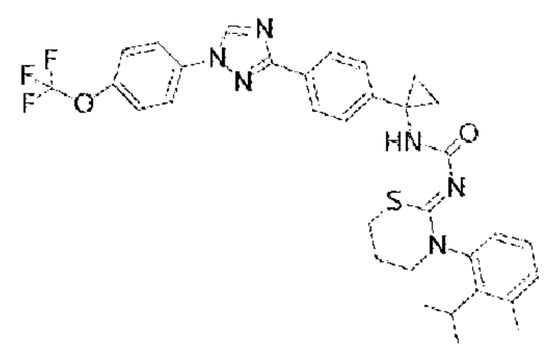
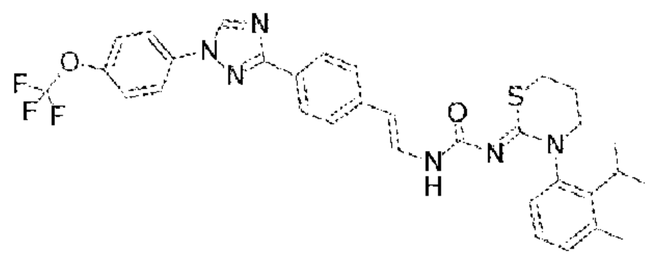
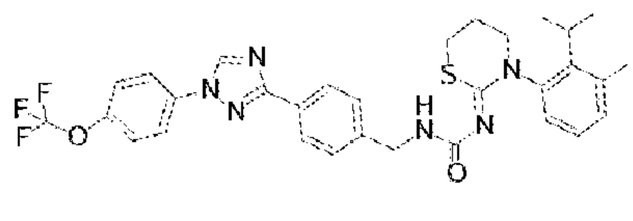
 P1656	 P1657
 P1658	 P1659
 P1660	 P1661
 P1662	 P1663
 P1664	 P1665

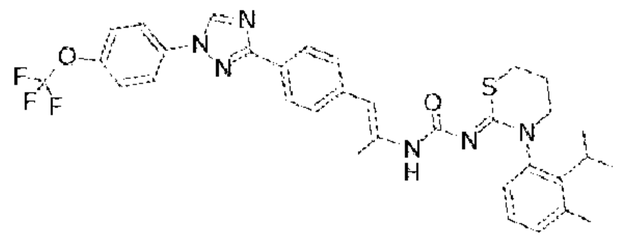
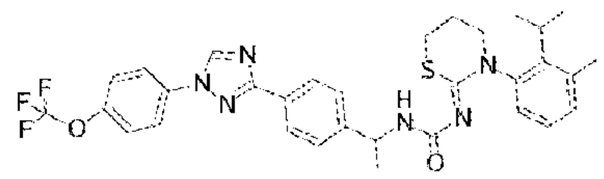
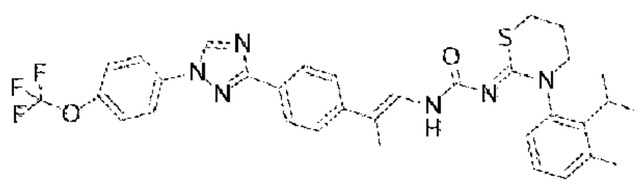
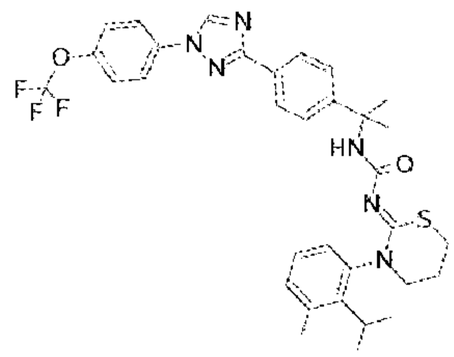
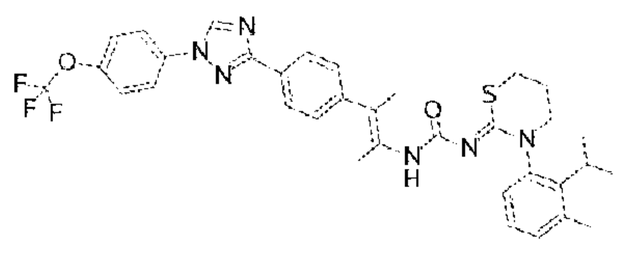
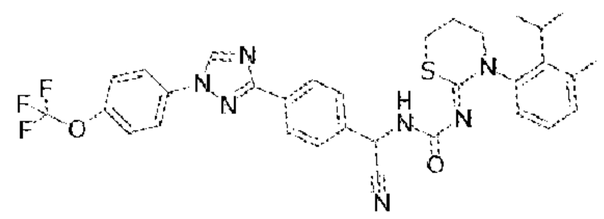
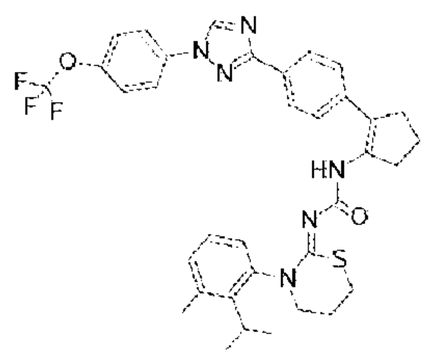
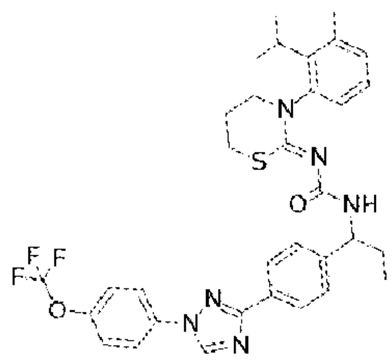
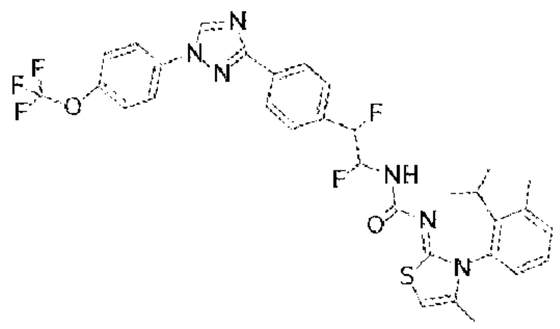
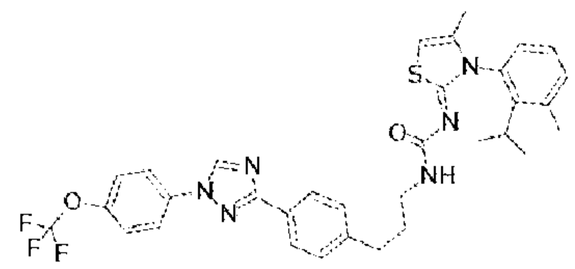
 P1666	 P1667
 P1668	 P1669
 P1670	 P1671
 P1672	 P1673
 P1674	 P1675

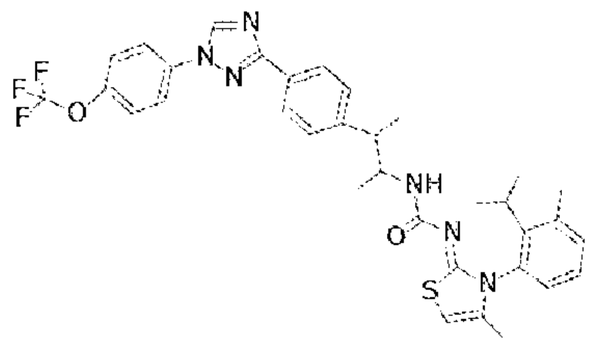
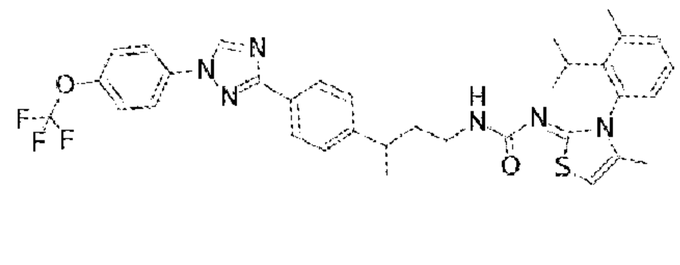
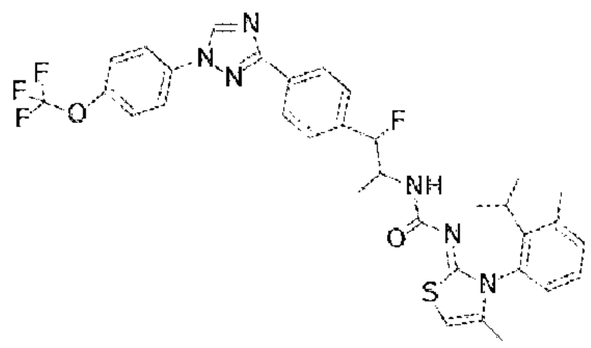
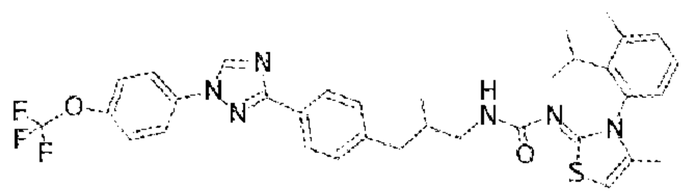
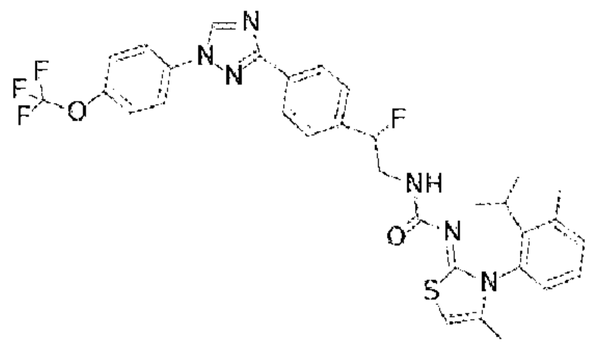
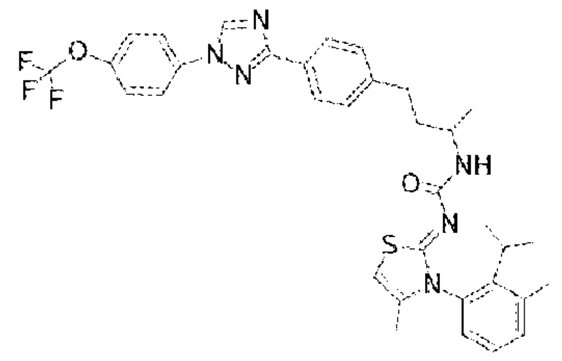
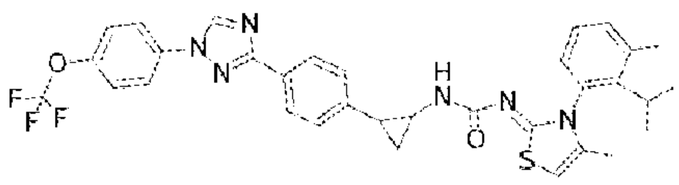
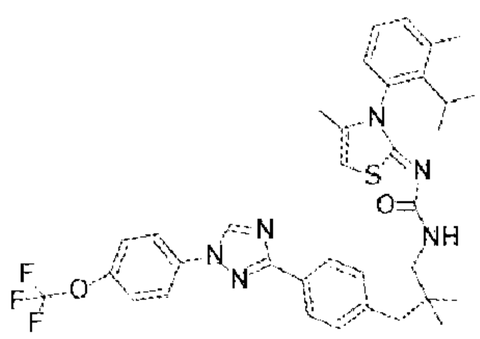
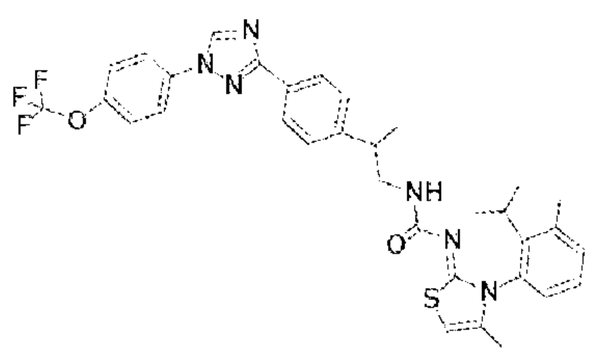
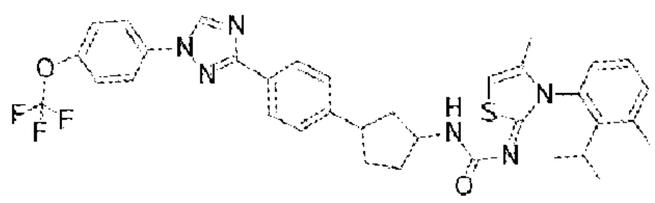
 P1676	 P1677
 P1678	 P1679
 P1680	 P1681
 P1682	 P1683
 P1684	 P1685

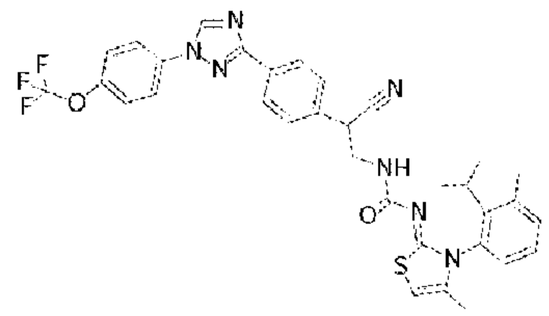
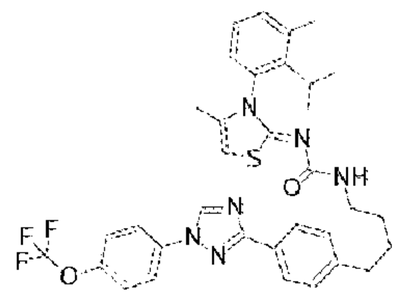
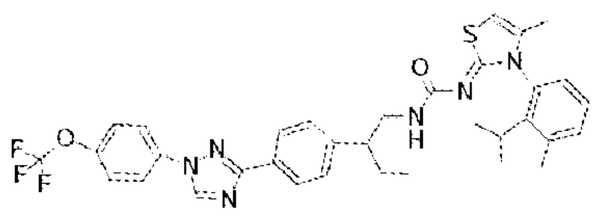
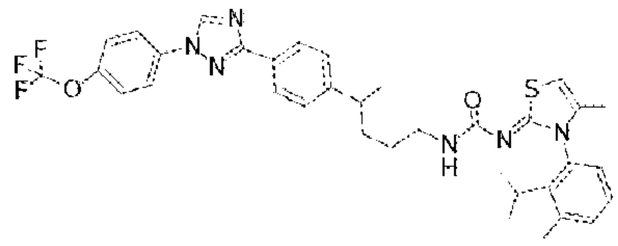
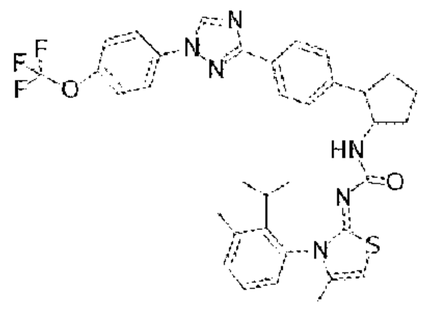
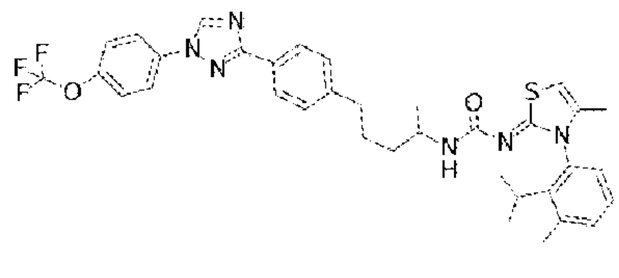
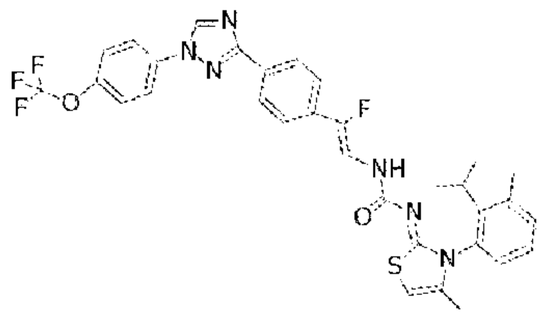
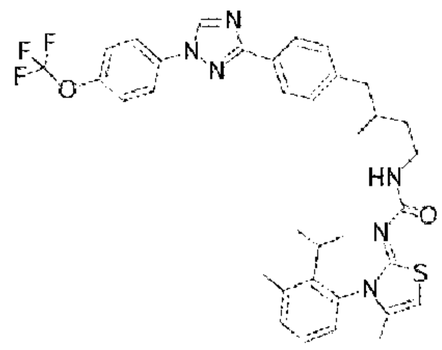
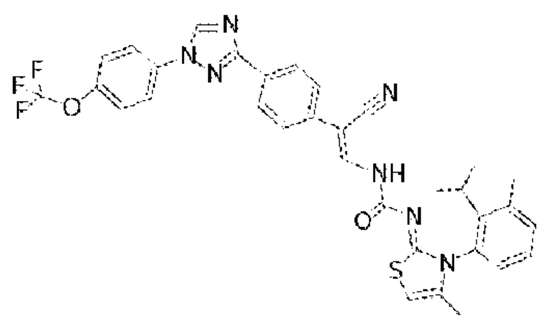
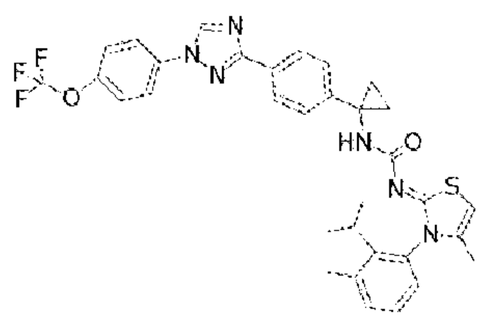
 P1686	 P1687
 P1688	 P1689
 P1690	 P1691
 P1692	 P1693
 P1694	 P1695

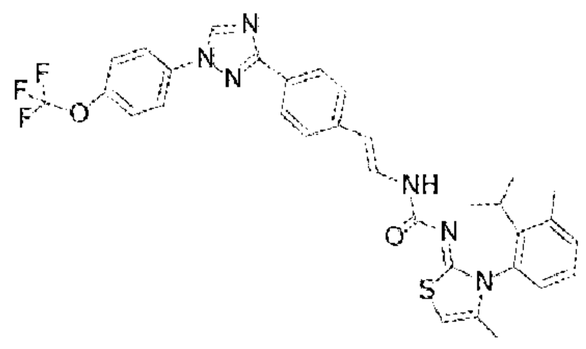
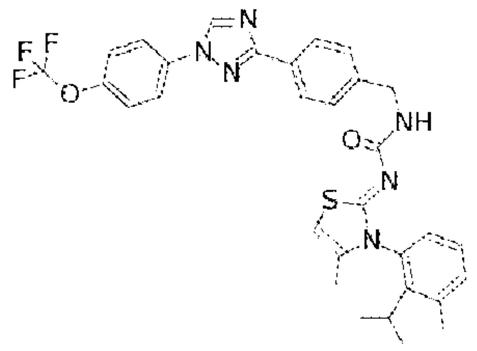
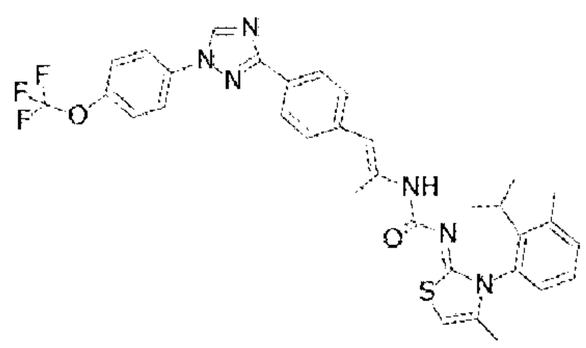
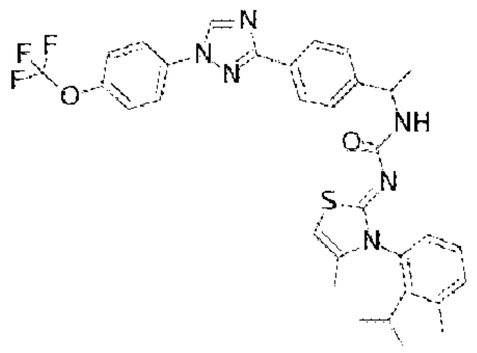
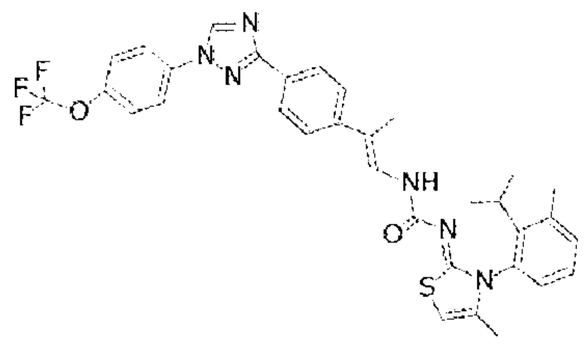
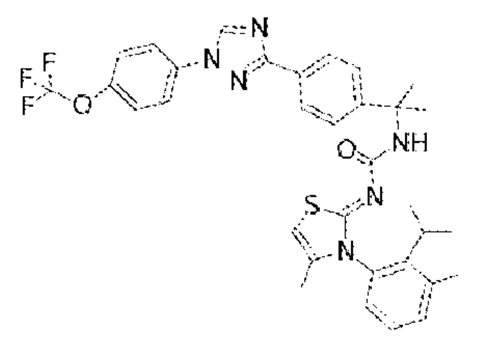
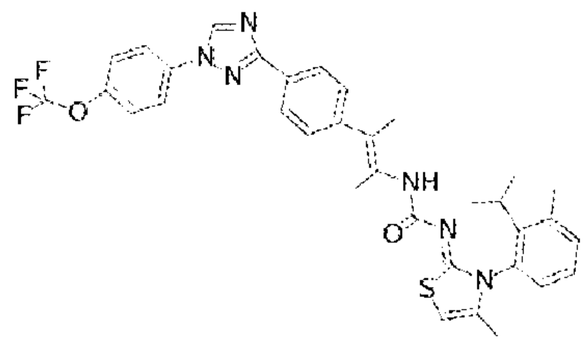
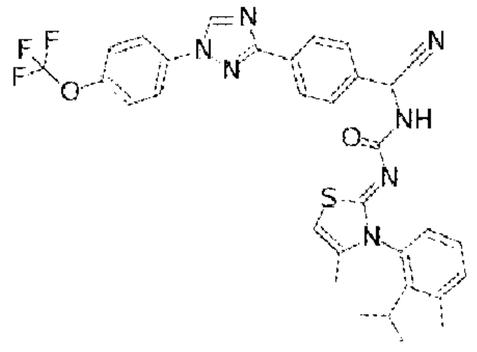
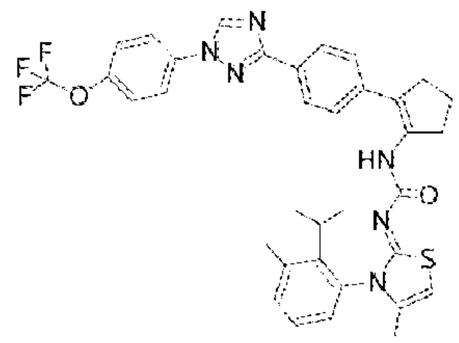
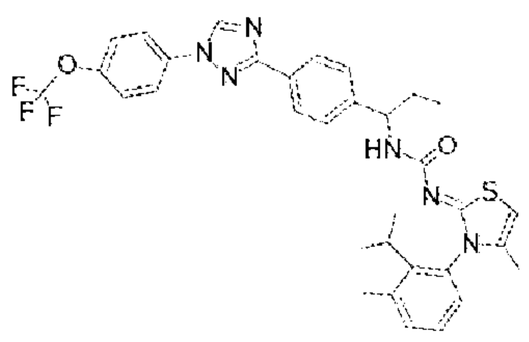
 P1696	 P1697
 P1698	 P1699
 P1700	 P1701
 P1702	 P1703
 P1704	 P1705

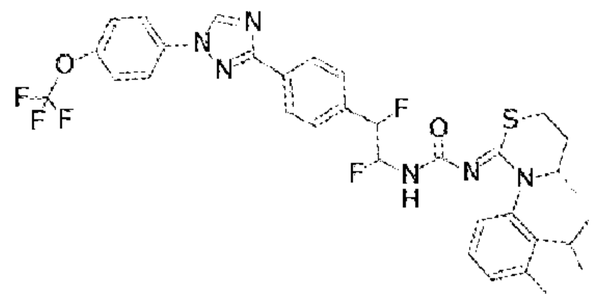
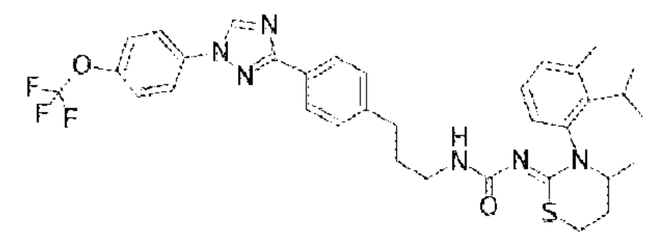
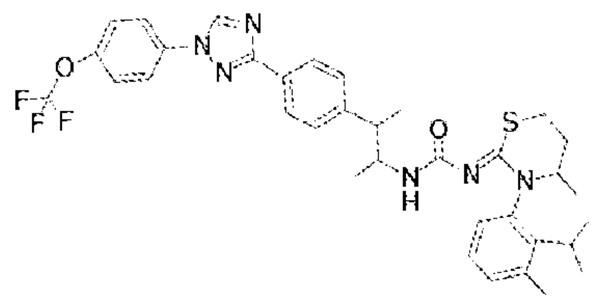
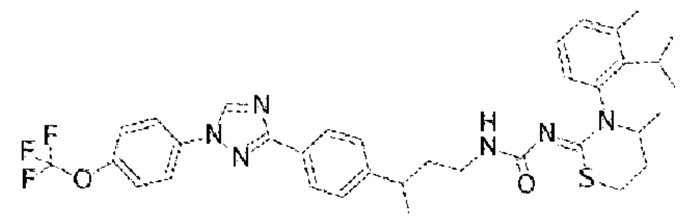
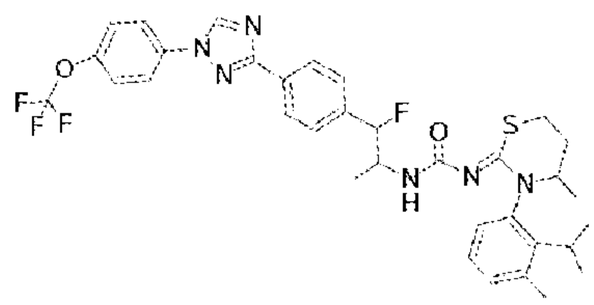
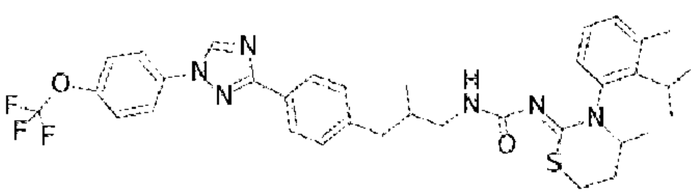
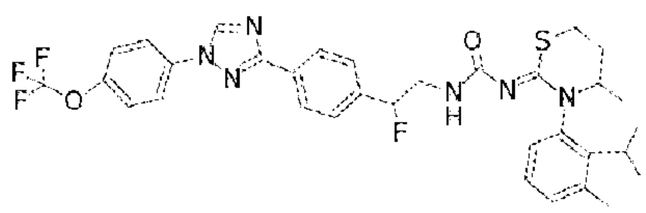
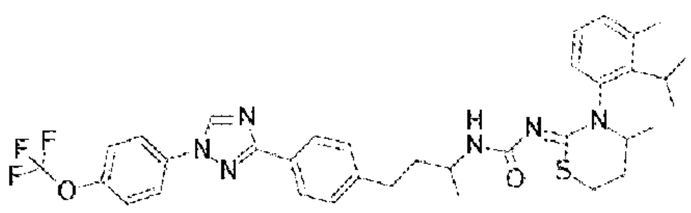
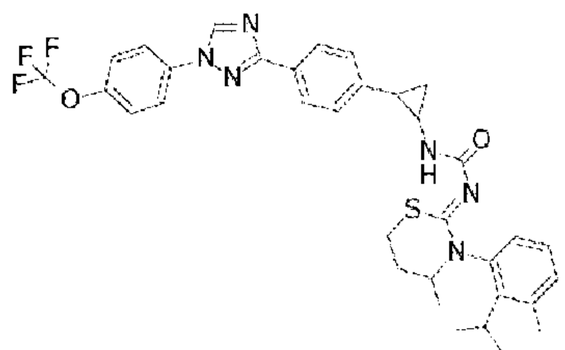
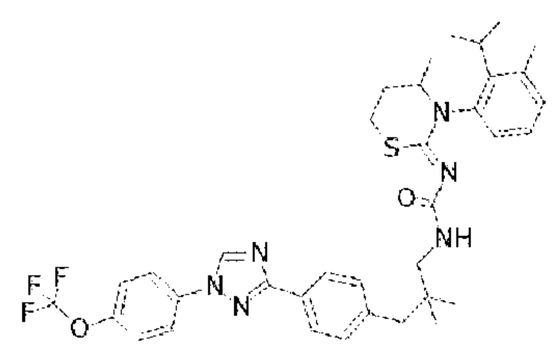
 P1706	 P1707
 P1708	 P1709
 P1710	 P1711
 P1712	 P1713
 P1714	 P1715

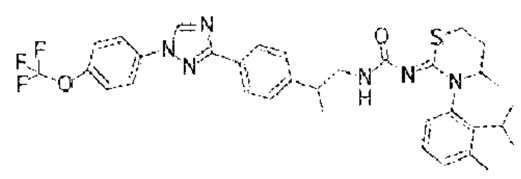
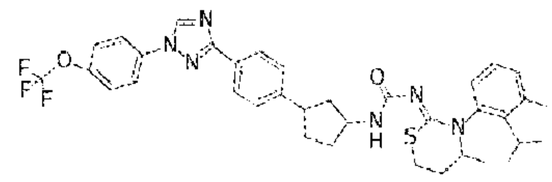
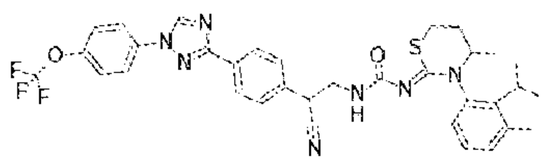
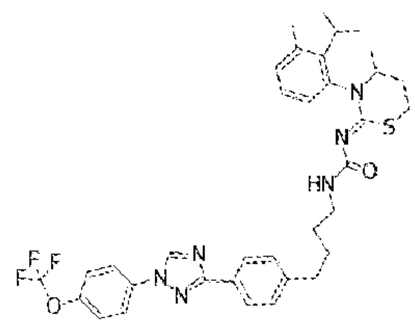
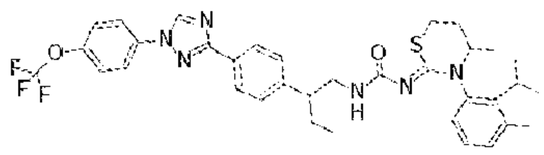
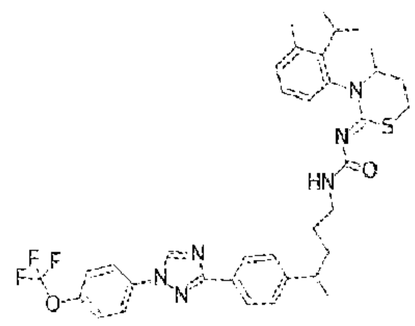
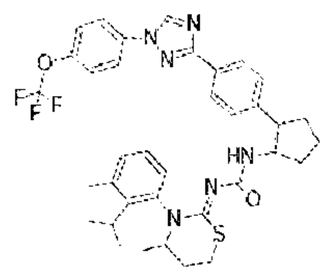
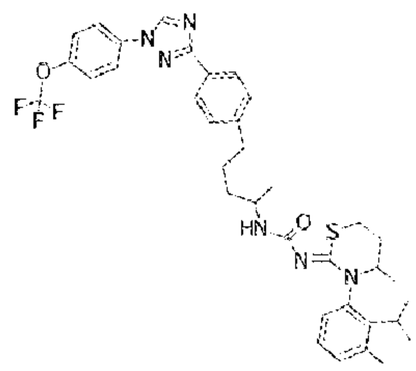
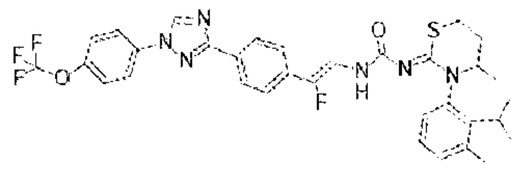
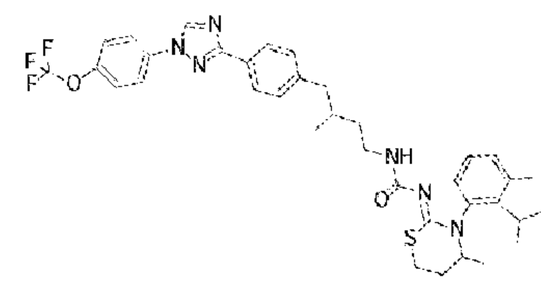
	
P1716	P1717
	
P1718	P1719
	
P1720	P1721
	
P1722	P1723
	
P1724	P1725

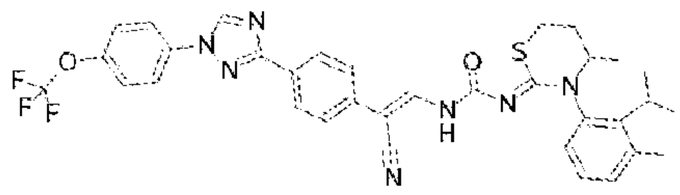
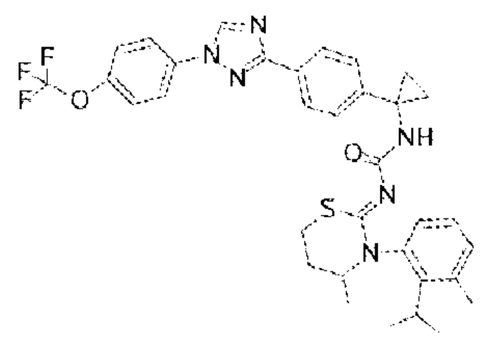
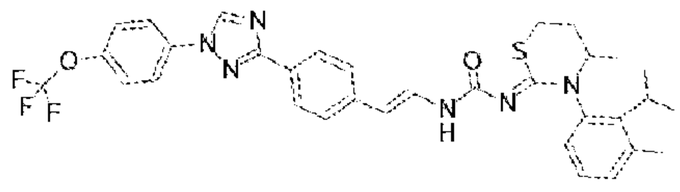
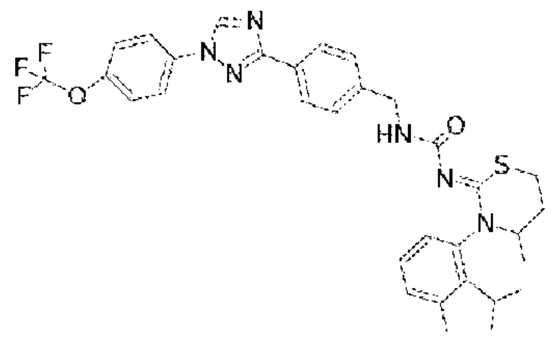
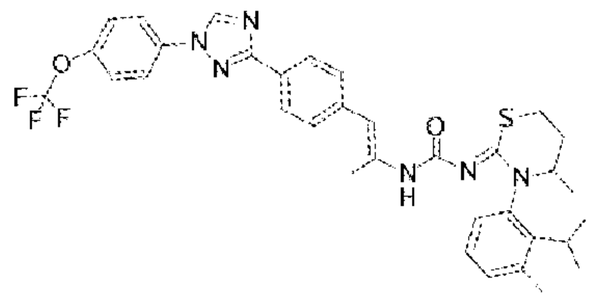
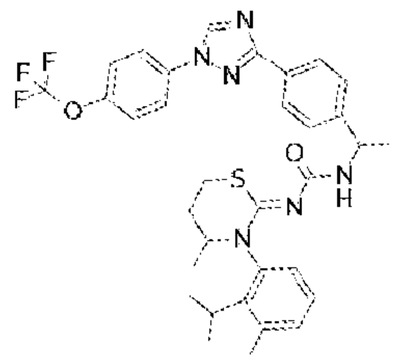
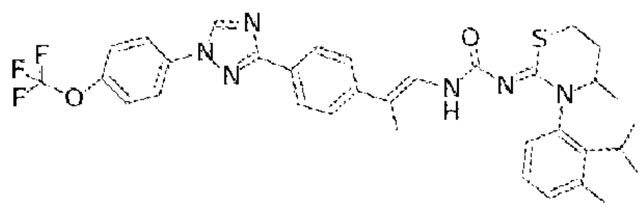
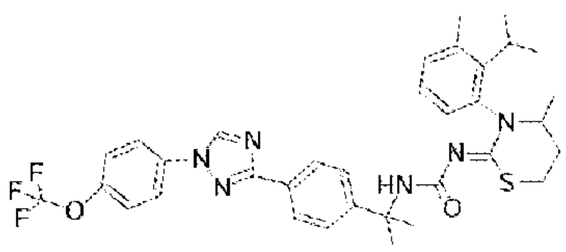
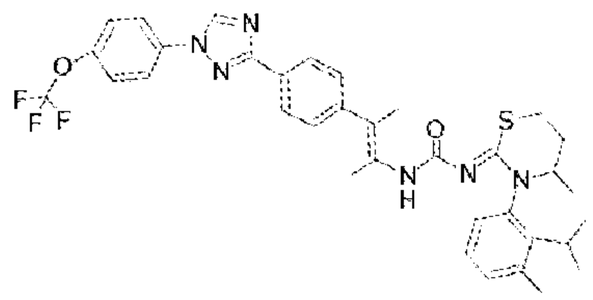
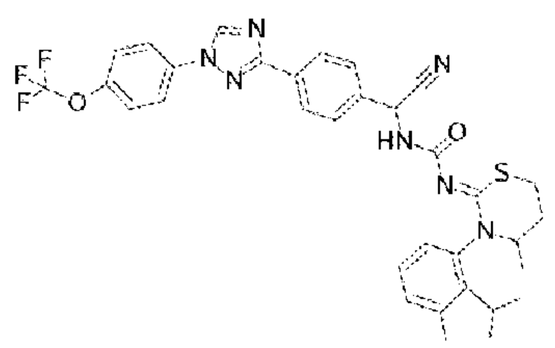
 P1726	 P1727
 P1728	 P1729
 P1730	 P1731
 P1732	 P1733
 P1734	 P1735

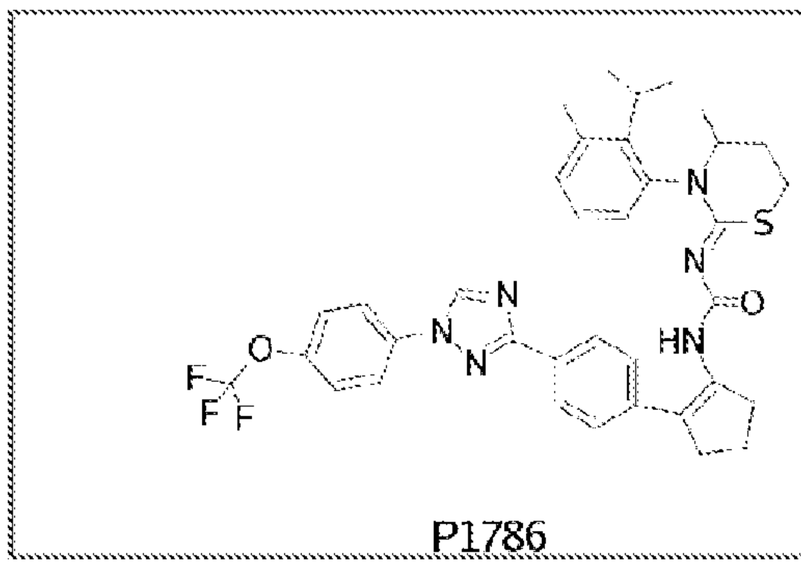
 P1736	 P1737
 P1738	 P1739
 P1740	 P1741
 P1742	 P1743
 P1744	 P1745

 P1746	 P1747
 P1748	 P1749
 P1750	 P1751
 P1752	 P1753
 P1754	 P1755

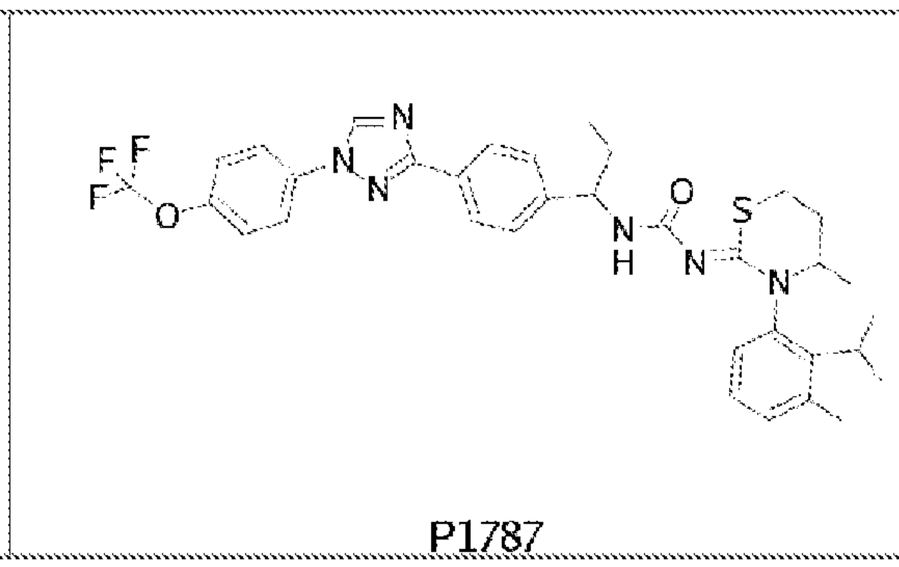
 P1756	 P1757
 P1758	 P1759
 P1760	 P1761
 P1762	 P1763
 P1764	 P1765

 P1766	 P1767
 P1768	 P1769
 P1770	 P1771
 P1772	 P1773
 P1774	 P1775

 P1776	 P1777
 P1778	 P1779
 P1780	 P1781
 P1782	 P1783
 P1784	 P1785



P1786



P1787

Example A: BIOASSAYS ON BEET ARMYWORM (*Spodoptera exigua*) ("BAW") AND Cabbage Looper (*Trichoplusia ni*) **("CL")**

BAW has few effective parasites, diseases, or predators to lower its population. BAW infests many weeds, trees, grasses, legumes, and field crops. In various places, it is of economic concern upon asparagus, cotton, corn, soybeans, tobacco, alfalfa, sugar beets, peppers, tomatoes, potatoes, onions, peas, sunflowers, and citrus, among other plants. The Cabbage Looper is a member of the moth family Noctuidae. It is found throughout the world. It is attacks cabbage, cauliflower, broccoli, Brussel sprouts, tomatoes, cucumbers, potatoes, kale, turnips, mustard, peppers, eggplant, watermelons, melons, squash, cantaloupe, peas, beans, collards, lettuce, spinach, celery, parsley, beets, peas, alfalfa, soybeans, and cotton. This species is very destructive to plants due to its voracious consumption of leaves. In the case of cabbage, however, they feed not only on the wrapper leaves, but also may bore into the developing head. The larvae consume three times their weight in plant material daily. The feeding sites are marked by large accumulations of sticky, wet fecal material.

Consequently, because of the above factors control of these pests is important. Furthermore, molecules that control these pests (BAW and CL), which are known as chewing pests, are useful in controlling other pests that chew on plants.

Certain molecules disclosed in this document were tested against BAW and CEW using procedures described in the following examples. In the reporting of the results, the "**BAW & CL Rating Table**" was used (See Table Section).

BIOASSAYS ON BAW

Bioassays on BAW were conducted using a 128-well diet tray assay. one to five second instar BAW larvae were placed in each well (3 mL) of the diet tray that had been previously filled with 1 mL of artificial diet to which 50 µg/cm^2 of the test compound (dissolved in 50 µL of 90:10 acetone-water mixture) had been applied (to each of eight wells) and then allowed to dry. Trays were covered with a clear self-adhesive cover and held at 25 ℃, 14:10 light-dark for five to seven days. Percent mortality was recorded for the larvae in each well; activity in the eight wells was then averaged. The results are indicated in the table entitled **"Table ABC: Biological Results**" (See Table Section).

Bioassays on Cabbage Looper in CL

Bioassays on CL were conducted using a 128-well diet tray assay. one to five second instar CL larvae were placed in each well (3 mL) of the diet tray that had been previously filled with 1 mL of artificial diet to which 50 µg/cm^2 of the test compound (dissolved in 50 µL of 90:10 acetone–water mixture) had been applied (to each of eight wells) and then allowed to dry. Trays were covered with a clear self-adhesive cover and held at 25 ℃, 14:10 light-dark for five to seven days. Percent mortality was recorded for the larvae in each well; activity in the eight wells was then averaged. The results are indicated in the table entitled "**Table ABC: Biological Results**" (See Table Section).

Example B: BIOASSAYS ON GREEN PEACH APHID ("GPA") (*Myzus persicae*).

GPA is the most significant aphid pest of peach trees, causing decreased growth, shriveling of the leaves, and the death of various tissues. It is also hazardous because it acts as a vector for the transport of plant viruses, such as potato virus Y and potato leafroll virus to members of the nightshade/potato family *Solanaceae*, and various mosaic viruses to many other food crops. GPA attacks such plants as broccoli, burdock, cabbage, carrot, cauliflower, daikon, eggplant, green beans, lettuce, macadamia, papaya, peppers, sweet potatoes, tomatoes, watercress, and zucchini, among other plants. GPA also attacks many ornamental crops such as carnation, chrysanthemum, flowering white cabbage, poinsettia, and roses. GPA has developed resistance to many pesticides. Consequently, because of the above factors control of this pest is important. Furthermore, molecules that control this pest

(GPA), which is known as a sucking pest, are useful in controlling other pests that suck on plants.

Certain molecules disclosed in this document were tested against GPA using procedures described in the following example. In the reporting of the results, the "**GPA Rating Table**" was used (See Table Section).

Cabbage seedlings grown in 3-inch pots, with 2-3 small (3-5 cm) true leaves, were used as test substrate. The seedlings were infested with 20-50 GPA (wingless adult and nymph stages) one day prior to chemical application. Four pots with individual seedlings were used for each treatment. Test compounds (2 mg) were dissolved in 2 mL of acetone/methanol (1:1) solvent, forming stock solutions of 1000 ppm test compound. The stock solutions were diluted 5X with 0.025% Tween 20 in water to obtain the solution at 200 ppm test compound. A hand-held aspirator-type sprayer was used for spraying a solution to both sides of cabbage leaves until runoff. Reference plants (solvent check) were sprayed with the diluent only containing 20% by volume of acetone/methanol (1:1) solvent. Treated plants were held in a holding room for three days at approximately 25 ℃ and ambient relative humidity (RH) prior to grading. Evaluation was conducted by counting the number of live aphids per plant under a microscope. Percent Control was measured by using Abbott's correction formula (W.S. Abbott, "A Method of Computing the Effectiveness of an Insecticide" J. Econ. Entomol. 18 (1925), pp.265-267) as follows.

Corrected % Control = 100 * (X - Y) / X

where

X = No. of live aphids on solvent check plants and

Y = No. of live aphids on treated plants

The results are indicated in the table entitled "**Table ABC: Biological Results**" (See Table Section).

Example C: BIOASSAYS ON Yellow Fever Mosquito "YFM" (*Aedes aegypti*).

YFM prefers to feed on humans during the daytime and is most frequently found in or near human habitations. YFM is a vector for transmitting several diseases. It is a mosquito that can spread the dengue fever and yellow fever viruses. Yellow fever is the second most dangerous mosquito-borne disease after malaria.

Yellow fever is an acute viral hemorrhagic disease and up to 50% of severely affected persons without treatment will die from yellow fever. There are an estimated 200,000 cases of yellow fever, causing 30,000 deaths, worldwide each year. Dengue fever is a nasty, viral disease; it is sometimes called "breakbone fever" or "break-heart fever" because of the intense pain it can produce. Dengue fever kills about 20,000 people annually. Consequently, because of the above factors control of this pest is important. Furthermore, molecules that control this pest (YFM), which is known as a sucking pest, are useful in controlling other pests that cause human and animal suffering.

Certain molecules disclosed in this document were tested against YFM using procedures described in the following paragraph. In the reporting of the results, the "**YFM Rating Table**" was used (See Table Section).

Master plates containing 400 µg of a molecule dissolved in 100 µL of dimethyl sulfoxide (DMSO) (equivalent to a 4000 ppm solution) are used. A master plate of assembled molecules contains 15 µL per well. To this plate, 135 µL of a 90:10 water:acetone mixture is added to each well. A robot (Biomek® NXP Laboratory Automation Workstation) is programmed to dispense 15 µL aspirations from the master plate into an empty 96-well shallow plate ("daughter" plate). There are 6 reps ("daughter" plates) created per master. The created daughter plates are then immediately infested with YFM larvae.

The day before plates are to be treated, mosquito eggs are placed in Millipore water containing liver powder to begin hatching (4 g. into 400 mL). After the daughter plates are created using the robot, they are infested with 220 µL of the liver powder/larval mosquito mixture (about 1 day-old larvae). After plates are infested with mosquito larvae, a non-evaporative lid is used to cover the plate to reduce drying. Plates are held at room temperature for 3 days prior to grading. After 3 days, each well is observed and scored based on mortality.

The results are indicated in the table entitled "**Table ABC: Biological Results**" (See Table Section).

AGRICULTURALLY ACCEPTABLE ACID ADDITION SALTS, SALT DERIVATIVES, SOLVATES, ESTER DERIVATIVES, POLYMORPHS, ISOTOPES, AND RADIONUCLIDES

Molecules of Formula One may be formulated into agriculturally acceptable acid addition salts. By way of a non-limiting example, an amine function can form salts with hydrochloric, hydrobromic, sulfuric, phosphoric, acetic, benzoic, citric, malonic, salicylic, malic, fumaric, oxalic, succinic, tartaric, lactic, gluconic, ascorbic, maleic, aspartic, benzenesulfonic, methanesulfonic, ethanesulfonic, hydroxyl-methanesulfonic, and hydroxyethanesulfonic acids. Additionally, by way of a non-limiting example, an acid function can form salts including those derived from alkali or alkaline earth metals and those derived from ammonia and amines. Examples of preferred cations include sodium, potassium, and magnesium.

Molecules of Formula One may be formulated into salt derivatives. By way of a non-limiting example, a salt derivative can be prepared by contacting a free base with a sufficient amount of the desired acid to produce a salt. A free base may be regenerated by treating the salt with a suitable dilute aqueous base solution such as dilute aqueous sodium hydroxide, potassium carbonate, ammonia, and sodium bicarbonate. As an example, in many cases, a pesticide, such as 2,4-D, is made more water-soluble by converting it to its dimethylamine salt..

Molecules of Formula One may be formulated into stable complexes with a solvent, such that the complex remains intact after the non-complexed solvent is removed. These complexes are often referred to as "solvates." However, it is particularly desirable to form stable hydrates with water as the solvent.

Molecules of Formula One may be made into ester derivatives. These ester derivatives can then be applied in the same manner as the molecules disclosed in this document is applied.

Molecules of Formula One may be made as various crystal polymorphs. Polymorphism is important in the development of agrochemicals since different crystal polymorphs or structures of the same molecule can have vastly different physical properties and biological performances.

Molecules of Formula One may be made with different isotopes. Of particular importance are molecules having ^{2}H (also known as deuterium) in place of ^{1}H.

Molecules of Formula One may be made with different radionuclides. Of particular importance are molecules having ^{14}C.

STEREOISOMERS

Molecules of Formula One may exist as one or more stereoisomers. Thus, certain molecules can be produced as racemic mixtures. It will be appreciated by those skilled in the art that one stereoisomer may be more active than the other stereoisomers. Individual stereoisomers may be obtained by known selective synthetic procedures, by conventional synthetic procedures using resolved starting materials, or by conventional resolution procedures. Certain molecules disclosed in this document can exist as two or more isomers. The various isomers include geometric isomers, diastereomers, and enantiomers. Thus, the molecules disclosed in this document include geometric isomers, racemic mixtures, individual stereoisomers, and optically active mixtures. It will be appreciated by those skilled in the art that one isomer may be more active than the others. The structures disclosed in the present disclosure are drawn in only one geometric form for clarity, but are intended to represent all geometric forms of the molecule.

COMBINATIONS

In another embodiment, molecules of Formula One may be used in combination (such as, in a compositional mixture, or a simultaneous or sequential application) with one or more compounds each having a mode of action that is the same as, similar to, or different from, the mode of action ("MoA") of the molecules of Formula One. Modes of action include, for example the following: Acetylcholinesterase (AChE) inhibitors; GABA-gated chloride channel antagonists; Sodium channel modulators; Nicotinic acetylcholine (nAChR) agonists; Nicotinic acetylcholine receptor (nAChR) allosteric activators; Chloride channel activators; Juvenile hormone mimics; Miscellaneous non-specific (multi-site) inhibitors; Selective homopteran feeding blockers; Mite growth inhibitors; Microbial disruptors of insect midgut membranes; Inhibitors of mitochondrial ATP synthase; Uncouplers of oxidative phosphorylation via disruption of the proton gradient; Nicotinic

acetylcholine receptor (nAChR) channel blockers; Inhibitors of chitin biosynthesis, type 0; Inhibitors of chitin biosynthesis, type 1; Moulting disruptor, Dipteran; Ecdysone receptor agonists; Octopamine receptor agonists; Mitochondrial complex III electron transport inhibitors; Mitochondrial complex I electron transport inhibitors; Voltage-dependent sodium channel blockers; Inhibitors of acetyl CoA carboxylase; Mitochondrial complex IV electron transport inhibitors; Mitochondrial complex II electron transport inhibitors; and Ryanodine receptor modulators.

In another embodiment, molecules of Formula One may be used in combination (such as, in a compositional mixture, or a simultaneous or sequential application) with one or more compounds having acaricidal, algicidal, avicidal, bactericidal, fungicidal, herbicidal, insecticidal, molluscicidal, nematicidal, rodenticidal, and/or virucidal properties.

In another embodiment, the molecules of Formula One may be used in combination (such as, in a compositional mixture, or a simultaneous or sequential application) with one or more compounds that are antifeedants, bird repellents, chemosterilants, herbicide safeners, insect attractants, insect repellents, mammal repellents, mating disrupters, plant activators, plant growth regulators, and/or synergists.

In another embodiment, the molecules of Formula One may be used in combination (such as, in a compositional mixture, or a simultaneous or sequential application) with one or more of the following compounds – (3-ethoxypropyl)mercury bromide, 1,2-dichloropropane, 1,3-dichloropropene, 1-methylcyclopropene, 1-naphthol, 2-(octylthio)ethanol, 2,3,5-tri-iodobenzoic acid, 2,3,6-TBA, 2,3,6-TBA-dimethylammonium, 2,3,6-TBA-lithium, 2,3,6-TBA-potassium, 2,3,6-TBA-sodium, 2,4,5-T, 2,4,5-T-2-butoxypropyl, 2,4,5-T-2-ethylhexyl, 2,4,5-T-3-butoxypropyl, 2,4,5-TB, 2,4,5-T-butometyl, 2,4,5-T-butotyl, 2,4,5-T-butyl, 2,4,5-T-isobutyl, 2,4,5-T-isoctyl, 2,4,5-T-isopropyl, 2,4,5-T-methyl, 2,4,5-T-pentyl, 2,4,5-T-sodium, 2,4,5-T-triethylammonium, 2,4,5-T-trolamine, 2,4-D, 2,4-D-2-butoxypropyl, 2,4-D-2-ethylhexyl, 2,4-D-3-butoxypropyl, 2,4-D-ammonium, 2,4-DB, 2,4-DB-butyl, 2,4-DB-dimethylammonium, 2,4-DB-isoctyl, 2,4-DB-potassium, 2,4-DB-sodium, 2,4-D-butotyl, 2,4-D-butyl, 2,4-D-diethylammonium, 2,4-D-dimethylammonium, 2,4-D-

diolamine, 2,4-D-dodecylammonium, 2,4-DEB, 2,4-DEP, 2,4-D-ethyl, 2,4-D-heptylammonium, 2,4-D-isobutyl, 2,4-D-isoctyl, 2,4-D-isopropyl, 2,4-D-isopropylammonium, 2,4-D-lithium, 2,4-D-meptyl, 2,4-D-methyl, 2,4-D-octyl, 2,4-D-pentyl, 2,4-D-potassium, 2,4-D-propyl, 2,4-D-sodium, 2,4-D-tefuryl, 2,4-D-tetradecylammonium, 2,4-D-triethylammonium, 2,4-D-tris(2-hydroxypropyl)ammonium, 2,4-D-trolamine, 2iP, 2-methoxyethylmercury chloride, 2-phenylphenol, 3,4-DA, 3,4-DB, 3,4-DP, 4-aminopyridine, 4-CPA, 4-CPA-diolamine, 4-CPA-potassium, 4-CPA-sodium, 4-CPB, 4-CPP, 4-hydroxyphenethyl alcohol, 8-hydroxyquinoline sulfate, 8-phenylmercurioxyquinoline, abamectin, abscisic acid, ACC, acephate, acequinocyl, acetamiprid, acethion, acetochlor, acetophos, acetoprole, acibenzolar, acibenzolar-S-methyl, acifluorfen, acifluorfen-methyl, acifluorfen-sodium, aclonifen, acrep, acrinathrin, acrolein, acrylonitrile, acypetacs, acypetacs-copper, acypetacs-zinc, afidopyropen, alachlor, alanycarb, albendazole, aldicarb, aldimorph, aldoxycarb, aldrin, allethrin, allicin, allidochlor, allosamidin, alloxydim, alloxydim-sodium, allyl alcohol, allyxycarb, alorac, *alpha*-cypermethrin, *alpha*-endosulfan, ametoctradin, ametridione, ametryn, amibuzin, amicarbazone, amicarthiazol, amidithion, amidoflumet, amidosulfuron, aminocarb, aminocyclopyrachlor, aminocyclopyrachlor-methyl, aminocyclopyrachlor-potassium, aminopyralid, aminopyralid-potassium, aminopyralid-tris(2-hydroxypropyl)ammonium, amiprofos-methyl, amiprophos, amisulbrom, amiton, amiton oxalate, amitraz, amitrole, ammonium sulfamate, ammonium α-naphthaleneacetate, amobam, ampropylfos, anabasine, anabasine sulfate, ancymidol, anilazine, anilofos, anisuron, anthraquinone, antu, apholate, aramite, arsenous oxide, asomate, aspirin, asulam, asulam-potassium, asulam-sodium, athidathion, atraton, atrazine, aureofungin, aviglycine, aviglycine hydrochloride, azaconazole, azadirachtin, azafenidin, azamethiphos, azimsulfuron, azinphos-ethyl, azinphos-methyl, aziprotryne, azithiram, azobenzene, azocyclotin, azothoate, azoxystrobin, bachmedesh, barban, barium hexafluorosilicate, barium polysulfide, barthrin, BCPC, beflubutamid, benalaxyl, benalaxyl-M, benazolin, benazolin-dimethylammonium, benazolin-ethyl, benazolin-potassium, bencarbazone, benclothiaz, bendiocarb, benfluralin, benfuracarb, benfuresate, benodanil, benomyl,

benoxacor, benoxafos, benquinox, bensulfuron, bensulfuron-methyl, bensulide, bensultap, bentaluron, bentazone, bentazone-sodium, benthiavalicarb, benthiavalicarb-isopropyl, benthiazole, bentranil, benzadox, benzadox-ammonium, benzalkonium chloride, benzamacril, benzamacril-isobutyl, benzamorf, benzfendizone, benzipram, benzobicyclon, benzofenap, benzofluor, benzohydroxamic acid, benzovindiflupyr, benzoximate, benzoylprop, benzoylprop-ethyl, benzthiazuron, benzyl benzoate, benzyladenine, berberine, berberine chloride, *beta*-cyfluthrin, *beta*-cypermethrin, bethoxazin, bicyclopyrone, bifenazate, bifenox, bifenthrin, bifujunzhi, bilanafos, bilanafos-sodium, binapacryl, bingqingxiao, bioallethrin, bioethanomethrin, biopermethrin, bioresmethrin, biphenyl, bisazir, bismerthiazol, bispyribac, bispyribac-sodium, bistrifluron, bitertanol, bithionol, bixafen, blasticidin-S, borax, Bordeaux mixture, boric acid, boscalid, brassinolide, brassinolide-ethyl, brevicomin, brodifacoum, brofenvalerate, brofluthrinate, bromacil, bromacil-lithium, bromacil-sodium, bromadiolone, bromethalin, bromethrin, bromfenvinfos, bromoacetamide, bromobonil, bromobutide, bromocyclen, bromo-DDT, bromofenoxim, bromophos, bromophos-ethyl, bromopropylate, bromothalonil, bromoxynil, bromoxynil butyrate, bromoxynil heptanoate, bromoxynil octanoate, bromoxynil-potassium, brompyrazon, bromuconazole, bronopol, bucarpolate, bufencarb, buminafos, bupirimate, buprofezin, Burgundy mixture, busulfan, butacarb, butachlor, butafenacil, butamifos, butathiofos, butenachlor, butethrin, buthidazole, buthiobate, buthiuron, butocarboxim, butonate, butopyronoxyl, butoxycarboxim, butralin, butroxydim, buturon, butylamine, butylate, cacodylic acid, cadusafos, cafenstrole, calcium arsenate, calcium chlorate, calcium cyanamide, calcium polysulfide, calvinphos, cambendichlor, camphechlor, camphor, captafol, captan, carbamorph, carbanolate, carbaryl, carbasulam, carbendazim, carbendazim benzenesulfonate, carbendazim sulfite, carbetamide, carbofuran, carbon disulfide, carbon tetrachloride, carbophenothion, carbosulfan, carboxazole, carboxide, carboxin, carfentrazone, carfentrazone-ethyl, carpropamid, cartap, cartap hydrochloride, carvacrol, carvone, CDEA, cellocidin, CEPC, ceralure, Cheshunt mixture, chinomethionat, chitosan, chlobenthiazone, chlomethoxyfen, chloralose, chloramben, chloramben-ammonium, chloramben-diolamine, chloramben-methyl,

chloramben-methylammonium, chloramben-sodium, chloramine phosphorus, chloramphenicol, chloraniformethan, chloranil, chloranocryl, chlorantraniliprole, chlorazifop, chlorazifop-propargyl, chlorazine, chlorbenside, chlorbenzuron, chlorbicyclen, chlorbromuron, chlorbufam, chlordane, chlordecone, chlordimeform, chlordimeform hydrochloride, chlorempenthrin, chlorethoxyfos, chloreturon, chlorfenac, chlorfenac-ammonium, chlorfenac-sodium, chlorfenapyr, chlorfenazole, chlorfenethol, chlorfenprop, chlorfenson, chlorfensulphide, chlorfenvinphos, chlorfluazuron, chlorflurazole, chlorfluren, chlorfluren-methyl, chlorflurenol, chlorflurenol-methyl, chloridazon, chlorimuron, chlorimuron-ethyl, chlormephos, chlormequat, chlormequat chloride, chlornidine, chlornitrofen, chlorobenzilate, chlorodinitronaphthalenes, chloroform, chloromebuform, chloromethiuron, chloroneb, chlorophacinone, chlorophacinone-sodium, chloropicrin, chloropon, chloropropylate, chlorothalonil, chlorotoluron, chloroxuron, chloroxynil, chlorphonium, chlorphonium chloride, chlorphoxim, chlorprazophos, chlorprocarb, chlorpropham, chlorpyrifos, chlorpyrifos-methyl, chlorquinox, chlorsulfuron, chlorthal, chlorthal-dimethyl, chlorthal-monomethyl, chlorthiamid, chlorthiophos, chlozolinate, choline chloride, chromafenozide, cinerin I, cinerin II, cinerins, cinidon-ethyl, cinmethylin, cinosulfuron, ciobutide, cisanilide, cismethrin, clacyfos, clethodim, climbazole, cliodinate, clodinafop, clodinafop-propargyl, cloethocarb, clofencet, clofencet-potassium, clofentezine, clofibric acid, clofop, clofop-isobutyl, clomazone, clomeprop, cloprop, cloproxydim, clopyralid, clopyralid-methyl, clopyralid-olamine, clopyralid-potassium, clopyralid-tris(2-hydroxypropyl)ammonium, cloquintocet, cloquintocet-mexyl, cloransulam, cloransulam-methyl, closantel, clothianidin, clotrimazole, cloxyfonac, cloxyfonac-sodium, CMA, codlelure, colophonate, copper acetate, copper acetoarsenite, copper arsenate, copper carbonate, basic, copper hydroxide, copper naphthenate, copper oleate, copper oxychloride, copper silicate, copper sulfate, copper zinc chromate, coumachlor, coumafuryl, coumaphos, coumatetralyl, coumithoate, coumoxystrobin, coumoxystrobin, CPMC, CPMF, CPPC, credazine, cresol, crimidine, crotamiton, crotoxyphos, crufomate, cryolite, cue-lure, cufraneb, cumyluron, cuprobam, cuprous oxide, curcumenol, cyanamide, cyanatryn, cyanazine, cyanofenphos, cyanophos, cyanthoate, cyantraniliprole, cyazofamid,

cybutryne, cyclafuramid, cyclanilide, cyclethrin, cycloate, cycloheximide, cycloprate, cycloprothrin, cyclopyrimorate, cyclosulfamuron, cycloxydim, cycluron, cyenopyrafen, cyflufenamid, cyflumetofen, cyfluthrin, cyhalofop, cyhalofop-butyl, cyhalothrin, cyhexatin, cymiazole, cymiazole hydrochloride, cymoxanil, cyometrinil, cypendazole, cypermethrin, cyperquat, cyperquat chloride, cyphenothrin, cyprazine, cyprazole, cyproconazole, cyprodinil, cyprofuram, cypromid, cyprosulfamide, cyromazine, cythioate, daimuron, dalapon, dalapon-calcium, dalapon-magnesium, dalapon-sodium, daminozide, dayoutong, dazomet, dazomet-sodium, DBCP, *d*-camphor, DCIP, DCPTA, DDT, debacarb, decafentin, decarbofuran, dehydroacetic acid, delachlor, deltamethrin, demephion, demephion-O, demephion-S, demeton, demeton-methyl, demeton-O, demeton-O-methyl, demeton-S, demeton-S-methyl, demeton-S-methylsulphon, desmedipham, desmetryn, *d*-fanshiluquebingjuzhi, diafenthiuron, dialifos, di-allate, diamidafos, diatomaceous earth, diazinon, dibutyl phthalate, dibutyl succinate, dicamba, dicamba-diglycolamine, dicamba-dimethylammonium, dicamba-diolamine, dicamba-isopropylammonium, dicamba-methyl, dicamba-olamine, dicamba-potassium, dicamba-sodium, dicamba-trolamine, dicapthon, dichlobenil, dichlofenthion, dichlofluanid, dichlone, dichloralurea, dichlorbenzuron, dichlorflurenol, dichlorflurenol-methyl, dichlormate, dichlormid, dichlorophen, dichlorprop, dichlorprop-2-ethylhexyl, dichlorprop-butotyl, dichlorprop-dimethylammonium, dichlorprop-ethylammonium, dichlorprop-isoctyl, dichlorprop-methyl, dichlorprop-P, dichlorprop-P-2-ethylhexyl, dichlorprop-P-dimethylammonium, dichlorprop-potassium, dichlorprop-P-potassium, dichlorprop-P-sodium, dichlorprop-sodium, dichlorvos, dichlozoline, diclobutrazol, diclocymet, diclofop, diclofop-methyl, diclomezine, diclomezine-sodium, dicloran, diclosulam, dicofol, dicoumarol, dicresyl, dicrotophos, dicyclanil, dicyclonon, dieldrin, dienochlor, diethamquat, diethamquat dichloride, diethatyl, diethatyl-ethyl, diethofencarb, dietholate, diethyl pyrocarbonate, diethyltoluamide, difenacoum, difenoconazole, difenopenten, difenopenten-ethyl, difenoxuron, difenzoquat, difenzoquat metilsulfate, difethialone, diflovidazin, diflubenzuron, diflufenican, diflufenzopyr, diflufenzopyr-sodium, diflumetorim, dikegulac, dikegulac-sodium, dilor, dimatif, dimefluthrin, dimefox, dimefuron, dimepiperate, dimetachlone, dimetan, dimethacarb, dimethachlor, dimethametryn,

dimethenamid, dimethenamid-P, dimethipin, dimethirimol, dimethoate, dimethomorph, dimethrin, dimethyl carbate, dimethyl phthalate, dimethylvinphos, dimetilan, dimexano, dimidazon, dimoxystrobin, dinex, dinex-diclexine, dingjunezuo, diniconazole, diniconazole-M, dinitramine, dinobuton, dinocap, dinocap-4, dinocap-6, dinocton, dinofenate, dinopenton, dinoprop, dinosam, dinoseb, dinoseb acetate, dinoseb-ammonium, dinoseb-diolamine, dinoseb-sodium, dinoseb-trolamine, dinosulfon, dinotefuran, dinoterb, dinoterb acetate, dinoterbon, diofenolan, dioxabenzofos, dioxacarb, dioxathion, diphacinone, diphacinone-sodium, diphenamid, diphenyl sulfone, diphenylamine, dipropalin, dipropetryn, dipyrithione, diquat, diquat dibromide, disparlure, disul, disulfiram, disulfoton, disul-sodium, ditalimfos, dithianon, dithicrofos, dithioether, dithiopyr, diuron, d-limonene, DMPA, DNOC, DNOC-ammonium, DNOC-potassium, DNOC-sodium, dodemorph, dodemorph acetate, dodemorph benzoate, dodicin, dodicin hydrochloride, dodicin-sodium, dodine, dofenapyn, dominicalure, doramectin, drazoxolon, DSMA, dufulin, EBEP, EBP, ecdysterone, edifenphos, eglinazine, eglinazine-ethyl, emamectin, emamectin benzoate, EMPC, empenthrin, endosulfan, endothal, endothal-diammonium, endothal-dipotassium, endothal-disodium, endothion, endrin, enestroburin, enoxastrobin, EPN, epocholeone, epofenonane, epoxiconazole, eprinomectin, epronaz, EPTC, erbon, ergocalciferol, erlujixiancaoan, esdépalléthrine, esfenvalerate, esprocarb, etacelasil, etaconazole, etaphos, etem, ethaboxam, ethachlor, ethalfluralin, ethametsulfuron, ethametsulfuron-methyl, ethaprochlor, ethephon, ethidimuron, ethiofencarb, ethiolate, ethion, ethiozin, ethiprole, ethirimol, ethoate-methyl, ethofumesate, ethohexadiol, ethoprophos, ethoxyfen, ethoxyfen-ethyl, ethoxyquin, ethoxysulfuron, ethychlozate, ethyl formate, ethyl α-naphthaleneacetate, ethyl-DDD, ethylene, ethylene dibromide, ethylene dichloride, ethylene oxide, ethylicin, ethylmercury 2,3-dihydroxypropyl mercaptide, ethylmercury acetate, ethylmercury bromide, ethylmercury chloride, ethylmercury phosphate, etinofen, etnipromid, etobenzanid, etofenprox, etoxazole, etridiazole, etrimfos, eugenol, EXD, famoxadone, famphur, fenamidone, fenaminosulf, fenaminstrobin, fenamiphos, fenapanil, fenarimol, fenasulam, fenazaflor, fenazaquin, fenbuconazole, fenbutatin oxide, fenchlorazole, fenchlorazole-ethyl, fenchlorphos, fenclorim,

fenethacarb, fenfluthrin, fenfuram, fenhexamid, fenitropan, fenitrothion, fenjuntong, fenobucarb, fenoprop, fenoprop-3-butoxypropyl, fenoprop-butometyl, fenoprop-butotyl, fenoprop-butyl, fenoprop-isoctyl, fenoprop-methyl, fenoprop-potassium, fenothiocarb, fenoxacrim, fenoxanil, fenoxaprop, fenoxaprop-ethyl, fenoxaprop-P, fenoxaprop-P-ethyl, fenoxasulfone, fenoxycarb, fenpiclonil, fenpirithrin, fenpropathrin, fenpropidin, fenpropimorph, fenpyrazamine, fenpyroximate, fenridazon, fenridazon-potassium, fenridazon-propyl, fenson, fensulfothion, fenteracol, fenthiaprop, fenthiaprop-ethyl, fenthion, fenthion-ethyl, fentin, fentin acetate, fentin chloride, fentin hydroxide, fentrazamide, fentrifanil, fenuron, fenuron TCA, fenvalerate, ferbam, ferimzone, ferrous sulfate, fipronil, flamprop, flamprop-isopropyl, flamprop-M, flamprop-methyl, flamprop-M-isopropyl, flamprop-M-methyl, flazasulfuron, flocoumafen, flometoquin, flonicamid, florasulam, fluacrypyrim, fluazifop, fluazifop-butyl, fluazifop-methyl, fluazifop-P, fluazifop-P-butyl, fluazinam, fluazolate, fluazuron, flubendiamide, flubenzimine, flucarbazone, flucarbazone-sodium, flucetosulfuron, fluchloralin, flucofuron, flucycloxuron, flucythrinate, fludioxonil, fluenetil, fluensulfone, flufenacet, flufenerim, flufenican, flufenoxuron, flufenoxystrobin, flufenprox, flufenpyr, flufenpyr-ethyl, flufiprole, flumethrin, flumetover, flumetralin, flumetsulam, flumezin, flumiclorac, flumiclorac-pentyl, flumioxazin, flumipropyn, flumorph, fluometuron, fluopicolide, fluopyram, fluorbenside, fluoridamid, fluoroacetamide, fluorodifen, fluoroglycofen, fluoroglycofen-ethyl, fluoroimide, fluoromidine, fluoronitrofen, fluothiuron, fluotrimazole, fluoxastrobin, flupoxam, flupropacil, flupropadine, flupropanate, flupropanate-sodium, flupyradifurone, flupyrsulfuron, flupyrsulfuron-methyl, flupyrsulfuron-methyl-sodium, fluquinconazole, flurazole, flurenol, flurenol-butyl, flurenol-methyl, fluridone, flurochloridone, fluroxypyr, fluroxypyr-butometyl, fluroxypyr-meptyl, flurprimidol, flursulamid, flurtamone, flusilazole, flusulfamide, fluthiacet, fluthiacet-methyl, flutianil, flutolanil, flutriafol, fluvalinate, fluxapyroxad, fluxofenim, folpet, fomesafen, fomesafen-sodium, fonofos, foramsulfuron, forchlorfenuron, formaldehyde, formetanate, formetanate hydrochloride, formothion, formparanate, formparanate hydrochloride, fosamine, fosamine-ammonium, fosetyl, fosetyl-aluminium, fosmethilan, fospirate, fosthiazate, fosthietan, frontalin,

fuberidazole, fucaojing, fucaomi, funaihecaoling, fuphenthiourea, furalane, furalaxyl, furamethrin, furametpyr, furathiocarb, furcarbanil, furconazole, furconazole-cis, furethrin, furfural, furilazole, furmecyclox, furophanate, furyloxyfen, *gamma*-cyhalothrin, *gamma*-HCH, genit, gibberellic acid, gibberellins, gliftor, glufosinate, glufosinate-ammonium, glufosinate-P, glufosinate-P-ammonium, glufosinate-P-sodium, glyodin, glyoxime, glyphosate, glyphosate-diammonium, glyphosate-dimethylammonium, glyphosate-isopropylammonium, glyphosate-monoammonium, glyphosate-potassium, glyphosate-sesquisodium, glyphosate-trimesium, glyphosine, gossyplure, grandlure, griseofulvin, guazatine, guazatine acetates, halacrinate, halauxifen, halauxifen-methyl, halfenprox, halofenozide, halosafen, halosulfuron, halosulfuron-methyl, haloxydine, haloxyfop, haloxyfop-etotyl, haloxyfop-methyl, haloxyfop-P, haloxyfop-P-etotyl, haloxyfop-P-methyl, haloxyfop-sodium, HCH, hemel, hempa, HEOD, heptachlor, heptafluthrin, heptenophos, heptopargil, herbimycin, heterophos, hexachloroacetone, hexachlorobenzene, hexachlorobutadiene, hexachlorophene, hexaconazole, hexaflumuron, hexaflurate, hexalure, hexamide, hexazinone, hexylthiofos, hexythiazox, HHDN, holosulf, huancaiwo, huangcaoling, huanjunzuo, hydramethylnon, hydrargaphen, hydrated lime, hydrogen cyanide, hydroprene, hymexazol, hyquincarb, IAA, IBA, icaridin, imazalil, imazalil nitrate, imazalil sulfate, imazamethabenz, imazamethabenz-methyl, imazamox, imazamox-ammonium, imazapic, imazapic-ammonium, imazapyr, imazapyr-isopropylammonium, imazaquin, imazaquin-ammonium, imazaquin-methyl, imazaquin-sodium, imazethapyr, imazethapyr-ammonium, imazosulfuron, imibenconazole, imicyafos, imidacloprid, imidaclothiz, iminoctadine, iminoctadine triacetate, iminoctadine trialbesilate, imiprothrin, inabenfide, indanofan, indaziflam, indoxacarb, inezin, iodobonil, iodocarb, iodomethane, iodosulfuron, iodosulfuron-methyl, iodosulfuron-methyl-sodium, iofensulfuron, iofensulfuron-sodium, ioxynil, ioxynil octanoate, ioxynil-lithium, ioxynil-sodium, ipazine, ipconazole, ipfencarbazone, iprobenfos, iprodione, iprovalicarb, iprymidam, ipsdienol, ipsenol, IPSP, isamidofos, isazofos, isobenzan, isocarbamid, isocarbophos, isocil, isodrin, isofenphos, isofenphos-methyl, isofetamid, isolan, isomethiozin, isonoruron, isopolinate, isoprocarb, isopropalin, isoprothiolane, isoproturon, isopyrazam,

isopyrimol, isothioate, isotianil, isouron, isovaledione, isoxaben, isoxachlortole, isoxadifen, isoxadifen-ethyl, isoxaflutole, isoxapyrifop, isoxathion, ivermectin, izopamfos, japonilure, japothrins, jasmolin I, jasmolin II, jasmonic acid, jiahuangchongzong, jiajizengxiaolin, jiaxiangjunzhi, jiecaowan, jiecaoxi, jodfenphos, juvenile hormone I, juvenile hormone II, juvenile hormone III, kadethrin, karbutilate, karetazan, karetazan-potassium, kasugamycin, kasugamycin hydrochloride, kejunlin, kelevan, ketospiradox, ketospiradox-potassium, kinetin, kinoprene, kresoxim-methyl, kuicaoxi, lactofen, lambda-cyhalothrin, latilure, lead arsenate, lenacil, lepimectin, leptophos, lindane, lineatin, linuron, lirimfos, litlure, looplure, lufenuron, lvdingjunzhi, lvxiancaolin, lythidathion, MAA, malathion, maleic hydrazide, malonoben, maltodextrin, MAMA, mancopper, mancozeb, mandipropamid, maneb, matrine, mazidox, MCPA, MCPA-2-ethylhexyl, MCPA-butotyl, MCPA-butyl, MCPA-dimethylammonium, MCPA-diolamine, MCPA-ethyl, MCPA-isobutyl, MCPA-isoctyl, MCPA-isopropyl, MCPA-methyl, MCPA-olamine, MCPA-potassium, MCPA-sodium, MCPA-thioethyl, MCPA-trolamine, MCPB, MCPB-ethyl, MCPB-methyl, MCPB-sodium, mebenil, mecarbam, mecarbinzid, mecarphon, mecoprop, mecoprop-2-ethylhexyl, mecoprop-dimethylammonium, mecoprop-diolamine, mecoprop-ethadyl, mecoprop-isoctyl, mecoprop-methyl, mecoprop-P, mecoprop-P-2-ethylhexyl, mecoprop-P-dimethylammonium, mecoprop-P-isobutyl, mecoprop-potassium, mecoprop-P-potassium, mecoprop-sodium, mecoprop-trolamine, medimeform, medinoterb, medinoterb acetate, medlure, mefenacet, mefenpyr, mefenpyr-diethyl, mefluidide, mefluidide-diolamine, mefluidide-potassium, megatomoic acid, menazon, mepanipyrim, meperfluthrin, mephenate, mephosfolan, mepiquat, mepiquat chloride, mepiquat pentaborate, mepronil, meptyldinocap, mercuric chloride, mercuric oxide, mercurous chloride, merphos, mesoprazine, mesosulfuron, mesosulfuron-methyl, mesotrione, mesulfen, mesulfenfos, metaflumizone, metalaxyl, metalaxyl-M, metaldehyde, metam, metam-ammonium, metamifop, metamitron, metam-potassium, metam-sodium, metazachlor, metazosulfuron, metazoxolon, metconazole, metepa, metflurazon, methabenzthiazuron, methacrifos, methalpropalin, methamidophos, methasulfocarb, methazole, methfuroxam, methidathion, methiobencarb, methiocarb, methiopyrisulfuron, methiotepa,

methiozolin, methiuron, methocrotophos, methometon, methomyl, methoprene, methoprotryne, methoquin-butyl, methothrin, methoxychlor, methoxyfenozide, methoxyphenone, methyl apholate, methyl bromide, methyl eugenol, methyl iodide, methyl isothiocyanate, methylacetophos, methylchloroform, methyldymron, methylene chloride, methylmercury benzoate, methylmercury dicyandiamide, methylmercury pentachlorophenoxide, methylneodecanamide, metiram, metobenzuron, metobromuron, metofluthrin, metolachlor, metolcarb, metominostrobin, metosulam, metoxadiazone, metoxuron, metrafenone, metribuzin, metsulfovax, metsulfuron, metsulfuron-methyl, mevinphos, mexacarbate, mieshuan, milbemectin, milbemycin oxime, milneb, mipafox, mirex, MNAF, moguchun, molinate, molosultap, monalide, monisouron, monochloroacetic acid, monocrotophos, monolinuron, monosulfuron, monosulfuron-ester, monuron, monuron TCA, morfamquat, morfamquat dichloride, moroxydine, moroxydine hydrochloride, morphothion, morzid, moxidectin, MSMA, muscalure, myclobutanil, myclozolin, N-(ethylmercury)-p-toluenesulphonanilide, nabam, naftalofos, naled, naphthalene, naphthaleneacetamide, naphthalic anhydride, naphthoxyacetic acids, naproanilide, napropamide, naptalam, naptalam-sodium, natamycin, neburon, niclosamide, niclosamide-olamine, nicosulfuron, nicotine, nifluridide, nipyraclofen, nitenpyram, nithiazine, nitralin, nitrapyrin, nitrilacarb, nitrofen, nitrofluorfen, nitrostyrene, nitrothal-isopropyl, norbormide, norflurazon, nornicotine, noruron, novaluron, noviflumuron, nuarimol, OCH, octachlorodipropyl ether, octhilinone, ofurace, omethoate, orbencarb, orfralure, ortho-dichlorobenzene, orthosulfamuron, oryctalure, orysastrobin, oryzalin, osthol, ostramone, oxabetrinil, oxadiargyl, oxadiazon, oxadixyl, oxamate, oxamyl, oxapyrazon, oxapyrazon-dimolamine, oxapyrazon-sodium, oxasulfuron, oxathiapiprolin, oxaziclomefone, oxine-copper, oxolinic acid, oxpoconazole, oxpoconazole fumarate, oxycarboxin, oxydemeton-methyl, oxydeprofos, oxydisulfoton, oxyfluorfen, oxymatrine, oxytetracycline, oxytetracycline hydrochloride, paclobutrazol, paichongding, para-dichlorobenzene, parafluron, paraquat, paraquat dichloride, paraquat dimetilsulfate, parathion, parathion-methyl, parinol, pebulate, pefurazoate, pelargonic acid, penconazole, pencycuron, pendimethalin, penflufen, penfluron, penoxsulam, pentachlorophenol,

pentachlorophenyl laurate, pentanochlor, penthiopyrad, pentmethrin, pentoxazone, perfluidone, permethrin, pethoxamid, phenamacril, phenazine oxide, phenisopham, phenkapton, phenmedipham, phenmedipham-ethyl, phenobenzuron, phenothrin, phenproxide, phenthoate, phenylmercuriurea, phenylmercury acetate, phenylmercury chloride, phenylmercury derivative of pyrocatechol, phenylmercury nitrate, phenylmercury salicylate, phorate, phosacetim, phosalone, phosdiphen, phosfolan, phosfolan-methyl, phosglycin, phosmet, phosnichlor, phosphamidon, phosphine, phosphocarb, phosphorus, phostin, phoxim, phoxim-methyl, phthalide, picloram, picloram-2-ethylhexyl, picloram-isoctyl, picloram-methyl, picloram-olamine, picloram-potassium, picloram-triethylammonium, picloram-tris(2-hydroxypropyl)ammonium, picolinafen, picoxystrobin, pindone, pindone-sodium, pinoxaden, piperalin, piperonyl butoxide, piperonyl cyclonene, piperophos, piproctanyl, piproctanyl bromide, piprotal, pirimetaphos, pirimicarb, pirimioxyphos, pirimiphos-ethyl, pirimiphos-methyl, plifenate, polycarbamate, polyoxins, polyoxorim, polyoxorim-zinc, polythialan, potassium arsenite, potassium azide, potassium cyanate, potassium gibberellate, potassium naphthenate, potassium polysulfide, potassium thiocyanate, potassium α-naphthaleneacetate, *pp'*-DDT, prallethrin, precocene I, precocene II, precocene III, pretilachlor, primidophos, primisulfuron, primisulfuron-methyl, probenazole, prochloraz, prochloraz-manganese, proclonol, procyazine, procymidone, prodiamine, profenofos, profluazol, profluralin, profluthrin, profoxydim, proglinazine, proglinazine-ethyl, prohexadione, prohexadione-calcium, prohydrojasmon, promacyl, promecarb, prometon, prometryn, promurit, propachlor, propamidine, propamidine dihydrochloride, propamocarb, propamocarb hydrochloride, propanil, propaphos, propaquizafop, propargite, proparthrin, propazine, propetamphos, propham, propiconazole, propineb, propisochlor, propoxur, propoxycarbazone, propoxycarbazone-sodium, propyl isome, propyrisulfuron, propyzamide, proquinazid, prosuler, prosulfalin, prosulfocarb, prosulfuron, prothidathion, prothiocarb, prothiocarb hydrochloride, prothioconazole, prothiofos, prothoate, protrifenbute, proxan, proxan-sodium, prynachlor, pydanon, pyflubumide, pymetrozine, pyracarbolid, pyraclofos, pyraclonil, pyraclostrobin, pyraflufen, pyraflufen-ethyl, pyrafluprole, pyramat, pyrametostrobin, pyraoxystrobin,

pyrasulfotole, pyrazolynate, pyrazophos, pyrazosulfuron, pyrazosulfuron-ethyl, pyrazothion, pyrazoxyfen, pyresmethrin, pyrethrin I, pyrethrin II, pyrethrins, pyribambenz-isopropyl, pyribambenz-propyl, pyribencarb, pyribenzoxim, pyributicarb, pyriclor, pyridaben, pyridafol, pyridalyl, pyridaphenthion, pyridate, pyridinitril, pyrifenox, pyrifluquinazon, pyriftalid, pyrimethanil, pyrimidifen, pyriminobac, pyriminobac-methyl, pyriminostrobin, pyrimisulfan, pyrimitate, pyrinuron, pyriofenone, pyriprole, pyripropanol, pyriproxyfen, pyrisoxazole, pyrithiobac, pyrithiobac-sodium, pyrolan, pyroquilon, pyroxasulfone, pyroxsulam, pyroxychlor, pyroxyfur, quassia, quinacetol, quinacetol sulfate, quinalphos, quinalphos-methyl, quinazamid, quinclorac, quinconazole, quinmerac, quinoclamine, quinonamid, quinothion, quinoxyfen, quintiofos, quintozene, quizalofop, quizalofop-ethyl, quizalofop-P, quizalofop-P-ethyl, quizalofop-P-tefuryl, quwenzhi, quyingding, rabenzazole, rafoxanide, rebemide, rescalure, resmethrin, rhodethanil, rhodojaponin-III, ribavirin, rimsulfuron, rotenone, ryania, saflufenacil, saijunmao, saisentong, salicylanilide, sanguinarine, santonin, schradan, scilliroside, sebuthylazine, secbumeton, sedaxane, selamectin, semiamitraz, semiamitraz chloride, sesamex, sesamolin, sethoxydim, shuangjiaancaolin, siduron, siglure, silafluofen, silatrane, silica gel, silthiofam, simazine, simeconazole, simeton, simetryn, sintofen, SMA, S-metolachlor, sodium arsenite, sodium azide, sodium chlorate, sodium fluoride, sodium fluoroacetate, sodium hexafluorosilicate, sodium naphthenate, sodium orthophenylphenoxide, sodium pentachlorophenoxide, sodium polysulfide, sodium thiocyanate, sodium α-naphthaleneacetate, sophamide, spinetoram, spinosad, spirodiclofen, spiromesifen, spirotetramat, spiroxamine, streptomycin, streptomycin sesquisulfate, strychnine, sulcatol, sulcofuron, sulcofuron-sodium, sulcotrione, sulfallate, sulfentrazone, sulfiram, sulfluramid, sulfometuron, sulfometuron-methyl, sulfosulfuron, sulfotep, sulfoxaflor, sulfoxide, sulfoxime, sulfur, sulfuric acid, sulfuryl fluoride, sulglycapin, sulprofos, sultropen, swep, *tau*-fluvalinate, tavron, tazimcarb, TCA, TCA-ammonium, TCA-calcium, TCA-ethadyl, TCA-magnesium, TCA-sodium, TDE, tebuconazole, tebufenozide, tebufenpyrad, tebufloquin, tebupirimfos, tebutam, tebuthiuron, tecloftalam, tecnazene, tecoram, teflubenzuron, tefluthrin, tefuryltrione, tembotrione, temephos, tepa, TEPP, tepraloxydim, terallethrin, terbacil, terbucarb,

terbuchlor, terbufos, terbumeton, terbuthylazine, terbutryn, tetcyclacis, tetrachloroethane, tetrachlorvinphos, tetraconazole, tetradifon, tetrafluron, tetramethrin, tetramethylfluthrin, tetramine, tetranactin, tetrasul, thallium sulfate, thenylchlor, theta-cypermethrin, thiabendazole, thiacloprid, thiadifluor, thiamethoxam, thiapronil, thiazafluron, thiazopyr, thicrofos, thicyofen, thidiazimin, thidiazuron, thiencarbazone, thiencarbazone-methyl, thifensulfuron, thifensulfuron-methyl, thifluzamide, thiobencarb, thiocarboxime, thiochlorfenphim, thiocyclam, thiocyclam hydrochloride, thiocyclam oxalate, thiodiazole-copper, thiodicarb, thiofanox, thiofluoximate, thiohempa, thiomersal, thiometon, thionazin, thiophanate, thiophanate-methyl, thioquinox, thiosemicarbazide, thiosultap, thiosultap-diammonium, thiosultap-disodium, thiosultap-monosodium, thiotepa, thiram, thuringiensin, tiadinil, tiaojiean, tiocarbazil, tioclorim, tioxymid, tirpate, tolclofos-methyl, tolfenpyrad, tolprocarb, tolylfluanid, tolylmercury acetate, topramezone, tralkoxydim, tralocythrin, tralomethrin, tralopyril, transfluthrin, transpermethrin, tretamine, triacontanol, triadimefon, triadimenol, triafamone, tri-allate, triamiphos, triapenthenol, triarathene, triarimol, triasulfuron, triazamate, triazbutil, triaziflam, triazophos, triazoxide, tribenuron, tribenuron-methyl, tribufos, tributyltin oxide, tricamba, trichlamide, trichlorfon, trichlormetaphos-3, trichloronat, triclopyr, triclopyr-butotyl, triclopyr-ethyl, triclopyricarb, triclopyr-triethylammonium, tricyclazole, tridemorph, tridiphane, trietazine, trifenmorph, trifenofos, trifloxystrobin, trifloxysulfuron, trifloxysulfuron-sodium, triflumizole, triflumuron, trifluralin, triflusulfuron, triflusulfuron-methyl, trifop, trifop-methyl, trifopsime, triforine, trihydroxytriazine, trimedlure, trimethacarb, trimeturon, trinexapac, trinexapac-ethyl, triprene, tripropindan, triptolide, tritac, triticonazole, tritosulfuron, trunc-call, uniconazole, uniconazole-P, urbacide, uredepa, valerate, validamycin, valifenalate, valone, vamidothion, vangard, vaniliprole, vernolate, vinclozolin, warfarin, warfarin-potassium, warfarin-sodium, xiaochongliulin, xinjunan, xiwojunan, XMC, xylachlor, xylenols, xylylcarb, yishijing, zarilamid, zeatin, zengxiaoan, zeta-cypermethrin, zinc naphthenate, zinc phosphide, zinc thiazole, zineb, ziram, zolaprofos, zoxamide, zuomihuanglong, α-chlorohydrin, α-ecdysone, α-multistriatin, and α-naphthaleneacetic acid. For more information consult the “**COMPENDIUM OF PESTICIDE**

COMMON NAMES" located at http://www.alanwood.net/pesticides/index.html. Also consult "**THE PESTICIDE MANUAL**" 15th Edition, edited by C D S Tomlin, copyright 2009 by British Crop Production Council, or its prior, or more recent editions.

In another embodiment, molecules of Formula One may also be used in combination (such as in a compositional mixture, or a simultaneous or sequential application) with one or more biopesticides. The term "biopesticide" is used for microbial biological pest control agents that are applied in a similar manner to chemical pesticides. Commonly these are bacterial, but there are also examples of fungal control agents, including *Trichoderma* spp. and *Ampelomyces quisqualis* (a control agent for grape powdery mildew). *Bacillus subtilis* are used to control plant pathogens. Weeds and rodents have also been controlled with microbial agents. One well-known insecticide example is *Bacillus thuringiensis*, a bacterial disease of Lepidoptera, Coleoptera, and Diptera. Because it has little effect on other organisms, it is considered more environmentally friendly than synthetic pesticides. Biological insecticides include products based on: entomopathogenic fungi (*e.g. Metarhizium anisopliae*); entomopathogenic nematodes (*e.g. Steinernema feltiae*); and entomopathogenic viruses (*e.g. Cydia pomonella* granulovirus).

Other examples of entomopathogenic organisms include, but are not limited to, baculoviruses, bacteria and other prokaryotic organisms, fungi, protozoa and Microsproridia. Biologically derived insecticides include, but not limited to, rotenone, veratridine, as well as microbial toxins; insect tolerant or resistant plant varieties; and organisms modified by recombinant DNA technology to either produce insecticides or to convey an insect resistant property to the genetically modified organism. In one embodiment, the molecules of Formula One may be used with one or more biopesticides in the area of seed treatments and soil amendments. *The Manual of Biocontrol Agents* gives a review of the available biological insecticide (and other biology-based control) products. Copping L.G. (ed.) (2004). *The Manual of Biocontrol Agents* (formerly the *Biopesticide Manual*) 3rd Edition. British Crop Production Council (BCPC), Farnham, Surrey UK.

In another embodiment, the above possible combinations may be used in a wide variety of weight ratios. For example, a two component mixture, the weight ratio

of a molecule of Formula One to another compound, can be from about 100:1 to about 1:100; in another example the weight ratio can be about 50:1 to about 1:50; in another example the weight ratio can be about 20:1 to about 1 to 20; in another example the weight ratio can be about 10:1 to about 1 :10; in another example the weight ratio can be about 5:1 to 1:5; in another example the weight ratio can be about 3:1 to about 1:3; and in a final example the weight ratio can be about 1:1. However, preferably, weight ratios less than about 10:1 to about 1:10 are preferred. It is also preferred sometimes to use a three or four component mixture comprising one or more molecules of Formula One and one or more other compounds from the above possible combinations.

FORMULATIONS

A pesticide is rarely suitable for application in its pure form. It is usually necessary to add other substances so that the pesticide can be used at the required concentration and in an appropriate form, permitting ease of application, handling, transportation, storage, and maximum pesticide activity. Thus, pesticides are formulated into, for example, baits, concentrated emulsions, dusts, emulsifiable concentrates, fumigants, gels, granules, microencapsulations, seed treatments, suspension concentrates, suspoemulsions, tablets, water soluble liquids, water dispersible granules or dry flowables, wettable powders, and ultra low volume solutions. For further information on formulation types see “Catalogue of Pesticide Formulation Types and International Coding System” Technical Monograph n°2, 5th Edition by CropLife International (2002).

Pesticides are applied most often as aqueous suspensions or emulsions prepared from concentrated formulations of such pesticides. Such water-soluble, water-suspendable, or emulsifiable formulations are either solids, usually known as wettable powders, or water dispersible granules, or liquids usually known as emulsifiable concentrates, or aqueous suspensions. Wettable powders, which may be compacted to form water dispersible granules, comprise an intimate mixture of the pesticide, a carrier, and surfactants. The concentration of the pesticide is usually from about 10% to about 90% by weight. The carrier is usually selected from among the attapulgite clays, the montmorillonite clays, the diatomaceous earths, or the

purified silicates. Effective surfactants, comprising from about 0.5% to about 10% of the wettable powder, are found among sulfonated lignins, condensed naphthalenesulfonates, naphthalenesulfonates, alkylbenzenesulfonates, alkyl sulfates, and non-ionic surfactants such as ethylene oxide adducts of alkyl phenols.

Emulsifiable concentrates of pesticides comprise a convenient concentration of a pesticide, such as from about 50 to about 500 grams per liter of liquid dissolved in a carrier that is either a water miscible solvent or a mixture of water-immiscible organic solvent and emulsifiers. Useful organic solvents include aromatics, especially xylenes and petroleum fractions, especially the high-boiling naphthalenic and olefinic portions of petroleum such as heavy aromatic naphtha. Other organic solvents may also be used, such as the terpenic solvents including rosin derivatives, aliphatic ketones such as cyclohexanone, and complex alcohols such as 2-ethoxyethanol. Suitable emulsifiers for emulsifiable concentrates are selected from conventional anionic and non-ionic surfactants.

Aqueous suspensions comprise suspensions of water-insoluble pesticides dispersed in an aqueous carrier at a concentration in the range from about 5% to about 50% by weight. Suspensions are prepared by finely grinding the pesticide and vigorously mixing it into a carrier comprised of water and surfactants. Ingredients, such as inorganic salts and synthetic or natural gums may also be added, to increase the density and viscosity of the aqueous carrier. It is often most effective to grind and mix the pesticide at the same time by preparing the aqueous mixture and homogenizing it in an implement such as a sand mill, ball mill, or piston-type homogenizer.

Pesticides may also be applied as granular compositions that are particularly useful for applications to the soil. Granular compositions usually contain from about 0.5% to about 10% by weight of the pesticide, dispersed in a carrier that comprises clay or a similar substance. Such compositions are usually prepared by dissolving the pesticide in a suitable solvent and applying it to a granular carrier which has been pre-formed to the appropriate particle size, in the range of from about 0.5 to about 3 mm. Such compositions may also be formulated by making a dough or paste

of the carrier and compound and crushing and drying to obtain the desired granular particle size.

Dusts containing a pesticide are prepared by intimately mixing the pesticide in powdered form with a suitable dusty agricultural carrier, such as kaolin clay, ground volcanic rock, and the like. Dusts can suitably contain from about 1% to about 10% of the pesticide. They can be applied as a seed dressing or as a foliage application with a dust blower machine.

It is equally practical to apply a pesticide in the form of a solution in an appropriate organic solvent, usually petroleum oil, such as the spray oils, which are widely used in agricultural chemistry.

Pesticides can also be applied in the form of an aerosol composition. In such compositions the pesticide is dissolved or dispersed in a carrier, which is a pressure-generating propellant mixture. The aerosol composition is packaged in a container from which the mixture is dispensed through an atomizing valve.

Pesticide baits are formed when the pesticide is mixed with food or an attractant or both. When the pests eat the bait they also consume the pesticide. Baits may take the form of granules, gels, flowable powders, liquids, or solids. They can be used in pest harborages.

Fumigants are pesticides that have a relatively high vapor pressure and hence can exist as a gas in sufficient concentrations to kill pests in soil or enclosed spaces. The toxicity of the fumigant is proportional to its concentration and the exposure time. They are characterized by a good capacity for diffusion and act by penetrating the pest's respiratory system or being absorbed through the pest's cuticle. Fumigants are applied to control stored product pests under gas proof sheets, in gas sealed rooms or buildings or in special chambers.

Pesticides can be microencapsulated by suspending the pesticide particles or droplets in plastic polymers of various types. By altering the chemistry of the polymer or by changing factors in the processing, microcapsules can be formed of various sizes, solubility, wall thicknesses, and degrees of penetrability. These factors govern the speed with which the active ingredient within is released, which in turn, affects the residual performance, speed of action, and odor of the product.

Oil solution concentrates are made by dissolving pesticide in a solvent that will hold the pesticide in solution. Oil solutions of a pesticide usually provide faster knockdown and kill of pests than other formulations due to the solvents themselves having pesticidal action and the dissolution of the waxy covering of the integument increasing the speed of uptake of the pesticide. Other advantages of oil solutions include better storage stability, better penetration of crevices, and better adhesion to greasy surfaces.

Another embodiment is an oil-in-water emulsion, wherein the emulsion comprises oily globules which are each provided with a lamellar liquid crystal coating and are dispersed in an aqueous phase, wherein each oily globule comprises at least one compound which is agriculturally active, and is individually coated with a monolamellar or oligolamellar layer comprising: (1) at least one non-ionic lipophilic surface-active agent, (2) at least one non-ionic hydrophilic surface-active agent and (3) at least one ionic surface-active agent, wherein the globules having a mean particle diameter of less than 800 nanometers. Further information on the embodiment is disclosed in U.S. patent publication 20070027034 published February 1, 2007, having Patent Application serial number 11/495,228. For ease of use, this embodiment will be referred to as “OIWE”.

For further information consult “Insect Pest Management” 2nd Edition by D. Dent, copyright CAB International (2000). Additionally, for more detailed information consult “Handbook of Pest Control – The Behavior, Life History, and Control of Household Pests” by Arnold Mallis, 9th Edition, copyright 2004 by GIE Media Inc.

OTHER FORMULATION COMPONENTS

Generally, when the molecules disclosed in Formula One are used in a formulation, such formulation can also contain other components. These components include, but are not limited to, (this is a non-exhaustive and non-mutually exclusive list) wetters, spreaders, stickers, penetrants, buffers, sequestering agents, drift reduction agents, compatibility agents, anti-foam agents, cleaning agents, and emulsifiers. A few components are described forthwith.

A wetting agent is a substance that when added to a liquid increases the spreading or penetration power of the liquid by reducing the interfacial tension

between the liquid and the surface on which it is spreading. Wetting agents are used for two main functions in agrochemical formulations: during processing and manufacture to increase the rate of wetting of powders in water to make concentrates for soluble liquids or suspension concentrates; and during mixing of a product with water in a spray tank to reduce the wetting time of wettable powders and to improve the penetration of water into water-dispersible granules. Examples of wetting agents used in wettable powder, suspension concentrate, and water-dispersible granule formulations are: sodium lauryl sulfate; sodium dioctyl sulfosuccinate; alkyl phenol ethoxylates; and aliphatic alcohol ethoxylates.

A dispersing agent is a substance which adsorbs onto the surface of particles and helps to preserve the state of dispersion of the particles and prevents them from reaggregating. Dispersing agents are added to agrochemical formulations to facilitate dispersion and suspension during manufacture, and to ensure the particles redisperse into water in a spray tank. They are widely used in wettable powders, suspension concentrates and water-dispersible granules. Surfactants that are used as dispersing agents have the ability to adsorb strongly onto a particle surface and provide a charged or steric barrier to reaggregation of particles. The most commonly used surfactants are anionic, non-ionic, or mixtures of the two types. For wettable powder formulations, the most common dispersing agents are sodium lignosulfonates. For suspension concentrates, very good adsorption and stabilization are obtained using polyelectrolytes, such as sodium naphthalene sulfonate formaldehyde condensates. Tristyrylphenol ethoxylate phosphate esters are also used. Non-ionics such as alkylarylethylene oxide condensates and EO-PO block copolymers are sometimes combined with anionics as dispersing agents for suspension concentrates. In recent years, new types of very high molecular weight polymeric surfactants have been developed as dispersing agents. These have very long hydrophobic ‘backbones’ and a large number of ethylene oxide chains forming the ‘teeth’ of a ‘comb’ surfactant. These high molecular weight polymers can give very good long-term stability to suspension concentrates because the hydrophobic backbones have many anchoring points onto the particle surfaces. Examples of dispersing agents used in agrochemical formulations are: sodium lignosulfonates;

sodium naphthalene sulfonate formaldehyde condensates; tristyrylphenol ethoxylate phosphate esters; aliphatic alcohol ethoxylates; alkyl ethoxylates; EO-PO block copolymers; and graft copolymers.

An emulsifying agent is a substance which stabilizes a suspension of droplets of one liquid phase in another liquid phase. Without the emulsifying agent the two liquids would separate into two immiscible liquid phases. The most commonly used emulsifier blends contain alkylphenol or aliphatic alcohol with twelve or more ethylene oxide units and the oil-soluble calcium salt of dodecylbenzenesulfonic acid. A range of hydrophile-lipophile balance ("HLB") values from 8 to 18 will normally provide good stable emulsions. Emulsion stability can sometimes be improved by the addition of a small amount of an EO-PO block copolymer surfactant.

A solubilizing agent is a surfactant which will form micelles in water at concentrations above the critical micelle concentration. The micelles are then able to dissolve or solubilize water-insoluble materials inside the hydrophobic part of the micelle. The types of surfactants usually used for solubilization are non-ionics, sorbitan monooleates, sorbitan monooleate ethoxylates, and methyl oleate esters.

Surfactants are sometimes used, either alone or with other additives such as mineral or vegetable oils as adjuvants to spray-tank mixes to improve the biological performance of the pesticide on the target. The types of surfactants used for bioenhancement depend generally on the nature and mode of action of the pesticide. However, they are often non-ionics such as: alkyl ethoxylates; linear aliphatic alcohol ethoxylates; aliphatic amine ethoxylates.

A carrier or diluent in an agricultural formulation is a material added to the pesticide to give a product of the required strength. Carriers are usually materials with high absorptive capacities, while diluents are usually materials with low absorptive capacities. Carriers and diluents are used in the formulation of dusts, wettable powders, granules and water-dispersible granules.

Organic solvents are used mainly in the formulation of emulsifiable concentrates, oil-in-water emulsions, suspoemulsions, and ultra low volume formulations, and to a lesser extent, granular formulations. Sometimes mixtures of solvents are used. The first main groups of solvents are aliphatic paraffinic oils such

as kerosene or refined paraffins. The second main group (and the most common) comprises the aromatic solvents such as xylene and higher molecular weight fractions of C9 and C10 aromatic solvents. Chlorinated hydrocarbons are useful as cosolvents to prevent crystallization of pesticides when the formulation is emulsified into water. Alcohols are sometimes used as cosolvents to increase solvent power. Other solvents may include vegetable oils, seed oils, and esters of vegetable and seed oils.

Thickeners or gelling agents are used mainly in the formulation of suspension concentrates, emulsions and suspoemulsions to modify the rheology or flow properties of the liquid and to prevent separation and settling of the dispersed particles or droplets. Thickening, gelling, and anti-settling agents generally fall into two categories, namely water-insoluble particulates and water-soluble polymers. It is possible to produce suspension concentrate formulations using clays and silicas. Examples of these types of materials, include, but are not limited to, montmorillonite, bentonite, magnesium aluminum silicate, and attapulgite. Water-soluble polysaccharides have been used as thickening-gelling agents for many years. The types of polysaccharides most commonly used are natural extracts of seeds and seaweeds or are synthetic derivatives of cellulose. Examples of these types of materials include, but are not limited to, guar gum; locust bean gum; carrageenam; alginates; methyl cellulose; sodium carboxymethyl cellulose (SCMC); hydroxyethyl cellulose (HEC). Other types of anti-settling agents are based on modified starches, polyacrylates, polyvinyl alcohol and polyethylene oxide. Another good anti-settling agent is xanthan gum.

Microorganisms can cause spoilage of formulated products. Therefore preservation agents are used to eliminate or reduce their effect. Examples of such agents include, but are not limited to: propionic acid and its sodium salt; sorbic acid and its sodium or potassium salts; benzoic acid and its sodium salt; *p*-hydroxybenzoic acid sodium salt; methyl *p*-hydroxybenzoate; and 1,2-benzisothiazolin-3-one (BIT).

The presence of surfactants often causes water-based formulations to foam during mixing operations in production and in application through a spray tank. In

order to reduce the tendency to foam, anti-foam agents are often added either during the production stage or before filling into bottles. Generally, there are two types of anti-foam agents, namely silicones and non-silicones. Silicones are usually aqueous emulsions of dimethyl polysiloxane, while the non-silicone anti-foam agents are water-insoluble oils, such as octanol and nonanol, or silica. In both cases, the function of the anti-foam agent is to displace the surfactant from the air-water interface.

"Green" agents (*e.g.*, adjuvants, surfactants, solvents) can reduce the overall environmental footprint of crop protection formulations. Green agents are biodegradable and generally derived from natural and/or sustainable sources, *e.g.* plant and animal sources. Specific examples are: vegetable oils, seed oils, and esters thereof, also alkoxylated alkyl polyglucosides.

For further information, see "Chemistry and Technology of Agrochemical Formulations" edited by D.A. Knowles, copyright 1998 by Kluwer Academic Publishers. Also see "Insecticides in Agriculture and Environment – Retrospects and Prospects" by A.S. Perry, I. Yamamoto, I. Ishaaya, and R. Perry, copyright 1998 by Springer-Verlag.

PESTS

In general, the molecules of Formula One may be used to control pests *e.g.* ants, aphids, beetles, bristletails, cockroaches, crickets, earwigs, fleas, flies, grasshoppers, leafhoppers, lice, locusts, mites, moths, nematodes, scales, symphylans, termites, thrips, ticks, wasps, and whiteflies.

In another embodiment, the molecules of Formula One may be used to control pests in the **Phyla Nematoda** and/or **Arthropoda**.

In another embodiment, the molecules of Formula One may be used to control pests in the **Subphyla Chelicerata**, **Myriapoda**, and/or **Hexapoda**.

In another embodiment, the molecules of Formula One may be used to control pests in the **Classes** of **Arachnida, Symphyla**, and/or **Insecta**.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Anoplura**. A non-exhaustive list of particular genera includes, but is not limited to, *Haematopinus* spp., *Hoplopleura* spp., *Linognathus*

spp., *Pediculus* spp., and *Polyplax* spp. A non-exhaustive list of particular species includes, but is not limited to, *Haematopinus asini, Haematopinus suis*, *Linognathus setosus*, *Linognathus ovillus*, *Pediculus humanus capitis*, *Pediculus humanus humanus*, and *Pthirus pubis*.

In another embodiment, the molecules of Formula One may be used to control pests in the **Order Coleoptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Acanthoscelides* spp., *Agriotes* spp., *Anthonomus* spp., *Apion* spp., *Apogonia* spp., *Aulacophora* spp., *Bruchus* spp., *Cerosterna* spp., *Cerotoma* spp., *Ceutorhynchus* spp., *Chaetocnema* spp., *Colaspis* spp., *Ctenicera* spp., *Curculio* spp., *Cyclocephala* spp., *Diabrotica* spp., *Hypera* spp., *Ips* spp., *Lyctus* spp., *Megascelis* spp., *Meligethes* spp., *Otiorhynchus* spp., *Pantomorus* spp., *Phyllophaga* spp., *Phyllotreta* spp., *Rhizotrogus* spp., *Rhynchites* spp., *Rhynchophorus* spp., *Scolytus* spp., *Sphenophorus* spp., *Sitophilus* spp., and *Tribolium* spp. A non-exhaustive list of particular species includes, but is not limited to, *Acanthoscelides obtectus, Agrilus planipennis, Anoplophora glabripennis, Anthonomus grandis, Ataenius spretulus, Atomaria linearis, Bothynoderes punctiventris, Bruchus pisorum, Callosobruchus maculatus, Carpophilus hemipterus, Cassida vittata, Cerotoma trifurcata, Ceutorhynchus assimilis, Ceutorhynchus napi, Conoderus scalaris, Conoderus stigmosus, Conotrachelus nenuphar, Cotinis nitida, Crioceris asparagi, Cryptolestes ferrugineus, Cryptolestes pusillus, Cryptolestes turcicus, Cylindrocopturus adspersus, Deporaus marginatus, Dermestes lardarius, Dermestes maculatus, Epilachna varivestis, Faustinus cubae, Hylobius pales, Hypera postica, Hypothenemus hampei, Lasioderma serricorne, Leptinotarsa decemlineata, Liogenys fuscus, Liogenys suturalis, Lissorhoptrus oryzophilus, Maecolaspis joliveti, Melanotus communis, Meligethes aeneus, Melolontha melolontha, Oberea brevis, Oberea linearis, Oryctes rhinoceros, Oryzaephilus mercator, Oryzaephilus surinamensis, Oulema melanopus, Oulema oryzae, Phyllophaga cuyabana, Popillia japonica, Prostephanus truncatus, Rhyzopertha dominica,, Sitona lineatus, Sitophilus granarius, Sitophilus oryzae, Sitophilus zeamais, Stegobium paniceum, Tribolium castaneum, Tribolium confusum, Trogoderma variabile,* and *Zabrus tenebrioides.*

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Dermaptera**.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Blattaria**. A non-exhaustive list of particular species includes, but is not limited to, *Blattella germanica, Blatta orientalis, Parcoblatta pennsylvanica, Periplaneta americana, Periplaneta australasiae, Periplaneta brunnea, Periplaneta fuliginosa, Pycnoscelus surinamensis,* and *Supella longipalpa.*

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Diptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Aedes* spp., *Agromyza* spp., *Anastrepha* spp., *Anopheles* spp., *Bactrocera* spp., *Ceratitis* spp., *Chrysops* spp., *Cochliomyia* spp., *Contarinia* spp., *Culex* spp., *Dasineura* spp., *Delia* spp., *Drosophila* spp., *Fannia* spp., *Hylemyia* spp., *Liriomyza* spp., *Musca* spp., *Phorbia* spp., *Tabanus* spp., and *Tipula* spp. A non-exhaustive list of particular species includes, but is not limited to, *Agromyza frontella*, *Anastrepha suspensa*, *Anastrepha ludens, Anastrepha obliqa, Bactrocera cucurbitae*, *Bactrocera dorsalis*, *Bactrocera invadens, Bactrocera zonata, Ceratitis capitata*, *Dasineura brassicae*, *Delia platura*, *Fannia canicularis*, *Fannia scalaris*, *Gasterophilus intestinalis*, *Gracillia perseae*, *Haematobia irritans*, *Hypoderma lineatum*, *Liriomyza brassicae, Melophagus ovinus*, *Musca autumnalis*, *Musca domestica*, *Oestrus ovis*, *Oscinella frit*, *Pegomya betae, Psila rosae*, *Rhagoletis cerasi*, *Rhagoletis pomonella*, *Rhagoletis mendax, Sitodiplosis mosellana*, and *Stomoxys calcitrans*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Hemiptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Adelges* spp., *Aulacaspis* spp., *Aphrophora* spp., *Aphis* spp., *Bemisia* spp., *Ceroplastes* spp., *Chionaspis* spp., *Chrysomphalus* spp., *Coccus* spp., *Empoasca* spp., *Lepidosaphes* spp., *Lagynotomus* spp., *Lygus* spp., *Macrosiphum* spp., *Nephotettix* spp., *Nezara* spp., *Philaenus* spp., *Phytocoris* spp., *Piezodorus* spp., *Planococcus* spp., *Pseudococcus* spp., *Rhopalosiphum* spp., *Saissetia* spp., *Therioaphis* spp., *Toumeyella* spp., *Toxoptera* spp., *Trialeurodes* spp., *Triatoma* spp. and *Unaspis* spp. A non-exhaustive list of particular species

includes, but is not limited to, *Acrosternum hilare*, *Acyrthosiphon pisum, Aleyrodes proletella, Aleurodicus dispersus, Aleurothrixus floccosus*, *Amrasca biguttula biguttula, Aonidiella aurantii*, *Aphis gossypii*, *Aphis glycines*, *Aphis pomi*, *Aulacorthum solani*, *Bemisia argentifolii, Bemisia tabaci*, *Blissus leucopterus*, *Brachycorynella asparagi*, *Brevennia rehi, Brevicoryne brassicae*, *Calocoris norvegicus*, *Ceroplastes rubens*, *Cimex hemipterus*, *Cimex lectularius*, *Dagbertus fasciatus*, *Dichelops furcatus, Diuraphis noxia, Diaphorina citri, Dysaphis plantaginea*, *Dysdercus suturellus*, *Edessa meditabunda, Eriosoma lanigerum*, *Eurygaster maura*, *Euschistus heros, Euschistus servus*, *Helopeltis antonii, Helopeltis theivora*, *Icerya purchasi*, *Idioscopus nitidulus*, *Laodelphax striatellus*, *Leptocorisa oratorius, Leptocorisa varicornis, Lygus hesperus*, *Maconellicoccus hirsutus, Macrosiphum euphorbiae*, *Macrosiphum granarium*, *Macrosiphum rosae*, *Macrosteles quadrilineatus*, *Mahanarva frimbiolata, Metopolophium dirhodum*, *Mictis longicornis, Myzus persicae*, *Nephotettix cinctipes*, *Neurocolpus longirostris, Nezara viridula, Nilaparvata lugens*, *Parlatoria pergandii*, *Parlatoria ziziphi*, *Peregrinus maidis*, *Phylloxera vitifoliae*, *Physokermes piceae*,, *Phytocoris californicus, Phytocoris relativus, Piezodorus guildinii, Poecilocapsus lineatus*, *Psallus vaccinicola, Pseudacysta perseae, Pseudococcus brevipes*, *Quadraspidiotus perniciosus*, *Rhopalosiphum maidis, Rhopalosiphum padi, Saissetia oleae*, *Scaptocoris castanea*, *Schizaphis graminum*, *Sitobion avenae*, *Sogatella furcifera*, *Trialeurodes vaporariorum*, *Trialeurodes abutiloneus, Unaspis yanonensis*, and *Zulia entrerriana*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Hymenoptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Acromyrmex* spp., *Atta* spp., *Camponotus* spp., *Diprion* spp., *Formica* spp., *Monomorium* spp., *Neodiprion* spp., *Pogonomyrmex* spp., *Polistes* spp., *Solenopsis* spp., *Vespula* spp., and *Xylocopa* spp. A non-exhaustive list of particular species includes, but is not limited to, *Athalia rosae, Atta texana, Iridomyrmex humilis*, *Monomorium minimum, Monomorium pharaonis, Solenopsis invicta, Solenopsis geminata, Solenopsis molesta, Solenopsis richtery, Solenopsis xyloni,* and *Tapinoma sessile*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Isoptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Coptotermes* spp., *Cornitermes* spp., *Cryptotermes* spp., *Heterotermes* spp., *Kalotermes* spp., *Incisitermes* spp., *Macrotermes* spp., *Marginitermes* spp., *Microcerotermes* spp., *Procornitermes* spp., *Reticulitermes* spp., *Schedorhinotermes* spp., and *Zootermopsis* spp. A non-exhaustive list of particular species includes, but is not limited to, *Coptotermes curvignathus, Coptotermes frenchi, Coptotermes formosanus*, *Heterotermes aureus, Microtermes obesi, Reticulitermes banyulensis, Reticulitermes grassei, Reticulitermes flavipes*, *Reticulitermes hageni, Reticulitermes hesperus*, *Reticulitermes santonensis, Reticulitermes speratus, Reticulitermes tibialis,* and *Reticulitermes virginicus.*

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Lepidoptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Adoxophyes* spp., *Agrotis* spp., *Argyrotaenia* spp., *Cacoecia* spp., *Caloptilia* spp., *Chilo* spp., *Chrysodeixis* spp., *Colias* spp., *Crambus* spp., *Diaphania* spp., *Diatraea* spp., *Earias* spp., *Ephestia* spp., *Epimecis* spp., *Feltia* spp., *Gortyna* spp., *Helicoverpa* spp., *Heliothis* spp., *Indarbela* spp., *Lithocolletis* spp., *Loxagrotis* spp., *Malacosoma* spp., *Peridroma* spp., *Phyllonorycter* spp., *Pseudaletia* spp., *Sesamia* spp., *Spodoptera* spp., *Synanthedon* spp., and *Yponomeuta* spp. A non-exhaustive list of particular species includes, but is not limited to, *Achaea janata, Adoxophyes orana, Agrotis ipsilon*, *Alabama argillacea*, *Amorbia cuneana, Amyelois transitella, Anacamptodes defectaria, Anarsia lineatella*, *Anomis sabulifera*, *Anticarsia gemmatalis*, *Archips argyrospila*, *Archips rosana*, *Argyrotaenia citrana*, *Autographa gamma, Bonagota cranaodes, Borbo cinnara*, *Bucculatrix thurberiella*, *Capua reticulana, Carposina niponensis*, *Chlumetia transversa*, *Choristoneura rosaceana, Cnaphalocrocis medinalis, Conopomorpha cramerella, Cossus cossus*, *Cydia caryana, Cydia funebrana*, *Cydia molesta*, *Cydia nigricana, Cydia pomonella*, *Darna diducta, Diatraea saccharalis*, *Diatraea grandiosella, Earias insulana, Earias vittella, Ecdytolopha aurantianum, Elasmopalpus lignosellus*, *Ephestia cautella*, *Ephestia elutella*, *Ephestia kuehniella*, *Epinotia aporema, Epiphyas postvittana, Erionota thrax*, *Eupoecilia ambiguella*,

Euxoa auxiliaris, *Grapholita molesta*, *Hedylepta indicata*, *Helicoverpa armigera*, *Helicoverpa zea*, *Heliothis virescens, Hellula undalis*, *Keiferia lycopersicella*, *Leucinodes orbonalis*, *Leucoptera coffeella, Leucoptera malifoliella, Lobesia botrana*, *Loxagrotis albicosta*, *Lymantria dispar*, *Lyonetia clerkella*, *Mahasena corbetti*, *Mamestra brassicae*, *Maruca testulalis*, *Metisa plana*, *Mythimna unipuncta*, *Neoleucinodes elegantalis*, *Nymphula depunctalis*, *Operophtera brumata, Ostrinia nubilalis*, *Oxydia vesulia, Pandemis cerasana*, *Pandemis heparana*, *Papilio demodocus, Pectinophora gossypiella*, *Peridroma saucia*, *Perileucoptera coffeella*, *Phthorimaea operculella*, *Phyllocnistis citrella, Pieris rapae*, *Plathypena scabra, Plodia interpunctella*, *Plutella xylostella*, *Polychrosis viteana*, *Prays endocarpa, Prays oleae*, *Pseudaletia unipuncta, Pseudoplusia includens*, *Rachiplusia nu, Scirpophaga incertulas, Sesamia inferens*, *Sesamia nonagrioides, Setora nitens, Sitotroga cerealella*, *Sparganothis pilleriana, Spodoptera exigua*, *Spodoptera frugiperda, Spodoptera eridania, Thecla basilides, Tineola bisselliella*, *Trichoplusia ni*, *Tuta absoluta, Zeuzera coffeae*, and *Zeuzera pyrina*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Mallophaga**. A non-exhaustive list of particular genera includes, but is not limited to, *Anaticola* spp., *Bovicola* spp., *Chelopistes* spp., *Goniodes* spp., *Menacanthus* spp., and *Trichodectes* spp. A non-exhaustive list of particular species includes, but is not limited to, *Bovicola bovis, Bovicola caprae, Bovicola ovis*, *Chelopistes meleagridis, Goniodes dissimilis, Goniodes gigas, Menacanthus stramineus*, *Menopon gallinae,* and *Trichodectes canis*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Orthoptera**. A non-exhaustive list of particular genera includes, but is not limited to, *Melanoplus* spp., and *Pterophylla* spp. A non-exhaustive list of particular species includes, but is not limited to, *Anabrus simplex*, *Gryllotalpa africana, Gryllotalpa australis, Gryllotalpa brachyptera, Gryllotalpa hexadactyla*, *Locusta migratoria, Microcentrum retinerve*, *Schistocerca gregaria,* and *Scudderia furcata*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Siphonaptera**. A non-exhaustive list of particular species

includes, but is not limited to, *Ceratophyllus gallinae, Ceratophyllus niger, Ctenocephalides canis*, *Ctenocephalides felis*, and *Pulex irritans*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Thysanoptera**. A non-exhaustive list of particular genera includes, but is not limited to, Caliothrips spp., Frankliniella spp., *Scirtothrips* spp., and *Thrips* spp. A non-exhaustive list of particular sp. includes, but is not limited to, *Frankliniella fusca*, *Frankliniella occidentalis*, *Frankliniella schultzei, Frankliniella williamsi*, *Heliothrips haemorrhoidalis, Rhipiphorothrips cruentatus, Scirtothrips citri*, *Scirtothrips dorsalis*, and *Taeniothrips rhopalantennalis, Thrips hawaiiensis, Thrips nigropilosus, Thrips orientalis, Thrips tabaci*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Thysanura**. A non-exhaustive list of particular genera includes, but is not limited to, *Lepisma* spp. and *Thermobia* spp.

In another embodiment, the molecules of Formula One may be used to control pests of the **Order Acarina**. A non-exhaustive list of particular genera includes, but is not limited to, *Acarus* spp., *Aculops* spp., *Boophilus* spp., *Demodex* spp., *Dermacentor* spp., *Epitrimerus* spp., *Eriophyes* spp., *Ixodes* spp., *Oligonychus* spp., *Panonychus* spp., *Rhizoglyphus* spp., and *Tetranychus* spp. A non-exhaustive list of particular species includes, but is not limited to, *Acarapis woodi, Acarus siro*, *Aceria mangiferae*, *Aculops lycopersici*, *Aculus pelekassi, Aculus schlechtendali*, *Amblyomma americanum*, *Brevipalpus obovatus*, *Brevipalpus phoenicis*, *Dermacentor variabilis*, *Dermatophagoides pteronyssinus*, *Eotetranychus carpini*, *Notoedres cati, Oligonychus coffeae, Oligonychus ilicis, Panonychus citri*, *Panonychus ulmi*, *Phyllocoptruta oleivora*, *Polyphagotarsonemus latus, Rhipicephalus sanguineus*, *Sarcoptes scabiei*, *Tegolophus perseaflorae, Tetranychus urticae*, and *Varroa destructor*.

In another embodiment, the molecules of Formula One may be used to control pest of the **Order Symphyla**. A non-exhaustive list of particular sp. includes, but is not limited to, *Scutigerella immaculata*.

In another embodiment, the molecules of Formula One may be used to control pests of the **Phylum Nematoda**. A non-exhaustive list of particular genera

includes, but is not limited to, *Aphelenchoides* spp., *Belonolaimus* spp., *Criconemella* spp., *Ditylenchus* spp., *Heterodera* spp., *Hirschmanniella* spp., *Hoplolaimus* spp., *Meloidogyne* spp., *Pratylenchus* spp., and *Radopholus* spp. A non-exhaustive list of particular sp. includes, but is not limited to, *Dirofilaria immitis*, *Heterodera zeae, Meloidogyne incognita, Meloidogyne javanica, Onchocerca volvulus*, *Radopholus similis, and Rotylenchulus reniformis*.

For additional information consult "**HANDBOOK OF PEST CONTROL – THE BEHAVIOR, LIFE HISTORY, AND CONTROL OF HOUSEHOLD PESTS**" by Arnold Mallis, 9th Edition, copyright 2004 by GIE Media Inc.

APPLICATIONS

Controlling pests of Phyla Nematoda, Arthropoda, and/or Mollusca generally means that pest populations, pest activity, or both, are reduced in an locus. This can come about when:

(a) pest populations are repulsed from a locus;

(b) pests are incapacitated in, or around, a locus; or

(c) pests are exterminated in, or around, a locus.

Of course, a combination of these results can occur. Generally, pest populations, activity, or both are desirably reduced more than fifty percent, preferably more than 90 percent, and most preferably more than 98 percent. Generally, the locus is not in, or on, a human; consequently, the locus is generally a non-human locus.

In another embodiment, the locus to which a molecule of Formula One is applied can be any locus that is inhabited, or that may become inhabited, or that may be traversed, by a pest of Phyla Nematoda, Arthropoda, and/or Mollusca. For example, the locus can be:

(a) where crops, trees, fruits, cereals, fodder species, vines, turf, and/or ornamental plants, are growing;

(b) where domesticated animals are residing;

(c) the interior or exterior surfaces of buildings (such as places where grains are stored);

(d) the materials of construction used in buildings (such as impregnated wood); and

(e) the soil around buildings.

Particular crop areas to use a molecule of Formula One include areas where apples, corn, sunflowers, cotton, soybeans, canola, wheat, rice, sorghum, barley, oats, potatoes, oranges, alfalfa, lettuce, strawberries, tomatoes, peppers, crucifers, pears, tobacco, almonds, sugar beets, beans and other valuable crops are growing or the seeds thereof are going to be planted. It is also advantageous to use ammonium sulfate with a molecule of Formula One when growing various plants.

In another embodiment, molecules of Formula One are generally used in amounts from about 0.0001 grams per hectare to about 5000 grams per hectare to provide control. In another embodiment, it is preferred that molecules of Formula One are used in amounts from about 0.001 grams per hectare to about 500 grams per hectare. In another embodiment, it is more preferred that molecules of Formula One are used in amounts from about 0.01 gram per hectare to about 50 grams per hectare.

The molecules of Formula One may be used in mixtures, applied simultaneously or sequentially, alone or with other compounds to enhance plant vigor (*e.g.* to grow a better root system, to better withstand stressful growing conditions). Such other compounds are, for example, compounds that modulate plant ethylene receptors, most notably 1-methylcyclopropene (also known as 1-MCP). Furthermore, such molecules may be used during times when pest activity is low, such as before the plants that are growing begin to produce valuable agricultural commodities. Such times include the early planting season when pest pressure is usually low.

The molecules of Formula One can be applied to the foliar and fruiting portions of plants to control pests. The molecules will either come in direct contact with the pest, or the pest will consume the pesticide when eating leaf, fruit mass, or extracting sap, that contains the pesticide. The molecules of Formula One can also be applied to the soil, and when applied in this manner, root and stem feeding pests can be controlled. The roots can absorb a molecule taking it up into the foliar portions of the plant to control above ground chewing and sap feeding pests.

Generally, with baits, the baits are placed in the ground where, for example, termites can come into contact with, and/or be attracted to, the bait. Baits can also be applied to a surface of a building, (horizontal, vertical, or slant surface) where, for example, ants, termites, cockroaches, and flies, can come into contact with, and/or be attracted to, the bait. Baits can comprise a molecule of Formula One.

The molecules of Formula One can be encapsulated inside, or placed on the surface of a capsule. The size of the capsules can range from nanometer size (about 100-900 nanometers in diameter) to micrometer size (about 10-900 microns in diameter).

Because of the unique ability of the eggs of some pests to resist certain pesticides, repeated applications of the molecules of Formula One may be desirable to control newly emerged larvae.

Systemic movement of pesticides in plants may be utilized to control pests on one portion of the plant by applying (for example by spraying an area) the molecules of Formula One to a different portion of the plant. For example, control of foliar-feeding insects can be achieved by drip irrigation or furrow application, by treating the soil with for example pre- or post-planting soil drench, or by treating the seeds of a plant before planting.

Seed treatment can be applied to all types of seeds, including those from which plants genetically modified to express specialized traits will germinate. Representative examples include those expressing proteins toxic to invertebrate pests, such as *Bacillus thuringiensis* or other insecticidal toxins, those expressing herbicide resistance, such as “Roundup Ready” seed, or those with “stacked” foreign genes expressing insecticidal toxins, herbicide resistance, nutrition-enhancement, drought resistance, or any other beneficial traits. Furthermore, such seed treatments with the molecules of Formula One may further enhance the ability of a plant to better withstand stressful growing conditions. This results in a healthier, more vigorous plant, which can lead to higher yields at harvest time. Generally, about 1 gram of the molecules of Formula One to about 500 grams per 100,000 seeds is expected to provide good benefits, amounts from about 10 grams to about 100 grams per 100,000 seeds is expected to provide better benefits, and amounts from

about 25 grams to about 75 grams per 100,000 seeds is expected to provide even better benefits.

It should be readily apparent that the molecules of Formula One may be used on, in, or around plants genetically modified to express specialized traits, such as *Bacillus thuringiensis* or other insecticidal toxins, or those expressing herbicide resistance, or those with “stacked” foreign genes expressing insecticidal toxins, herbicide resistance, nutrition-enhancement, or any other beneficial traits.

The molecules of Formula One may be used for controlling endoparasites and ectoparasites in the veterinary medicine sector or in the field of non-human animal keeping. The molecules of Formula One are applied, such as by oral administration in the form of, for example, tablets, capsules, drinks, granules, by dermal application in the form of, for example, dipping, spraying, pouring on, spotting on, and dusting, and by parenteral administration in the form of, for example, an injection.

The molecules of Formula One may also be employed advantageously in livestock keeping, for example, cattle, sheep, pigs, chickens, and geese. They may also be employed advantageously in pets such as, horses, dogs, and cats. Particular pests to control would be fleas and ticks that are bothersome to such animals. Suitable formulations are administered orally to the animals with the drinking water or feed. The dosages and formulations that are suitable depend on the species.

The molecules of Formula One may also be used for controlling parasitic worms, especially of the intestine, in the animals listed above.

The molecules of Formula One may also be employed in therapeutic methods for human health care. Such methods include, but are limited to, oral administration in the form of, for example, tablets, capsules, drinks, granules, and by dermal application.

Pests around the world have been migrating to new environments (for such pest) and thereafter becoming a new invasive species in such new environment. The molecules of Formula One may also be used on such new invasive species to control them in such new environment.

The molecules of Formula One may also be used in an area where plants, such as crops, are growing (*e.g.* pre-planting, planting, pre-harvesting) and where

there are low levels (even no actual presence) of pests that can commercially damage such plants. The use of such molecules in such area is to benefit the plants being grown in the area. Such benefits, may include, but are not limited to, improving the health of a plant, improving the yield of a plant *(e.g.* increased biomass and/or increased content of valuable ingredients), improving the vigor of a plant (*e.g.* improved plant growth and/or greener leaves), improving the quality of a plant (*e.g.* improved content or composition of certain ingredients), and improving the tolerance to abiotic and/or biotic stress of the plant.

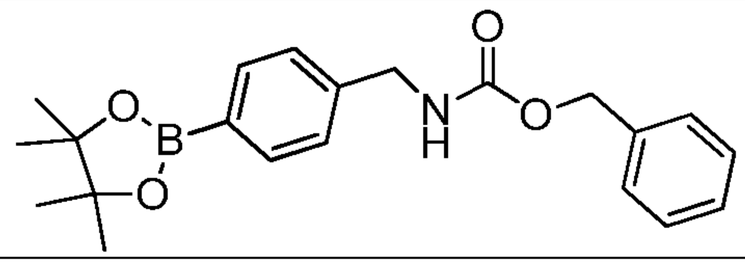
Before a pesticide can be used or sold commercially, such pesticide undergoes lengthy evaluation processes by various governmental authorities (local, regional, state, national, and international). Voluminous data requirements are specified by regulatory authorities and must be addressed through data generation and submission by the product registrant or by a third party on the product registrant's behalf, often using a computer with a connection to the World Wide Web. These governmental authorities then review such data and if a determination of safety is concluded, provide the potential user or seller with product registration approval. Thereafter, in that locality where the product registration is granted and supported, such user or seller may use or sell such pesticide.

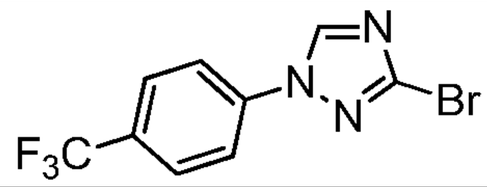
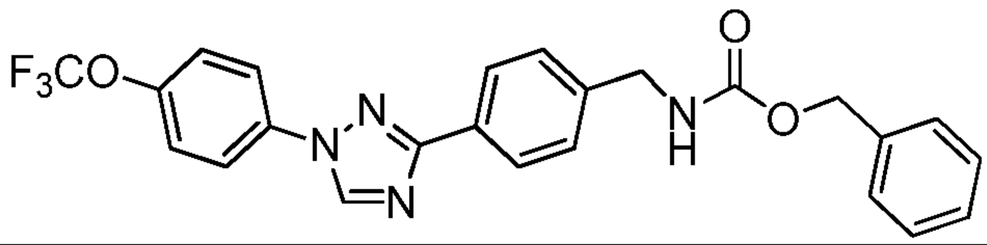
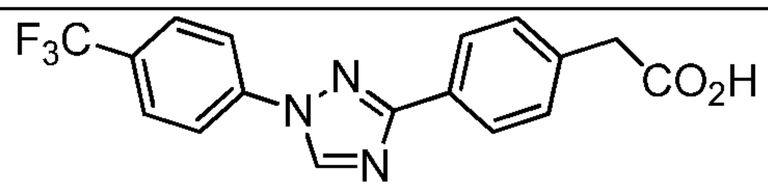
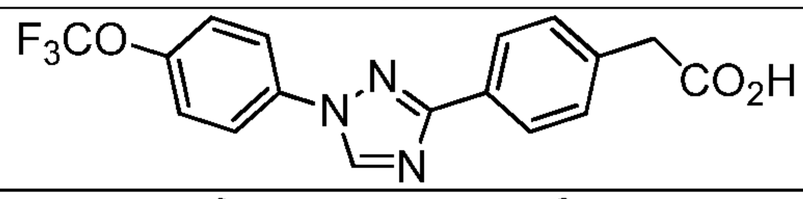
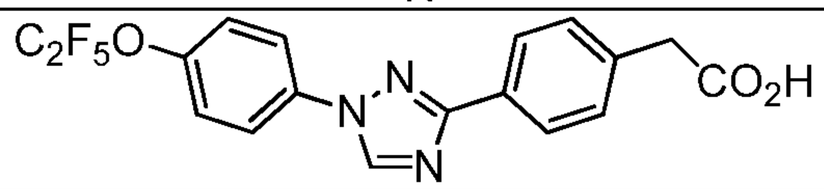
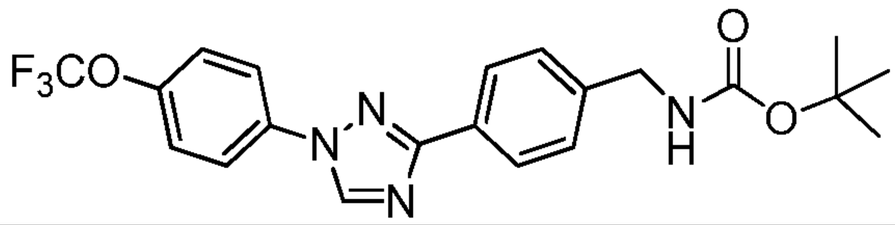
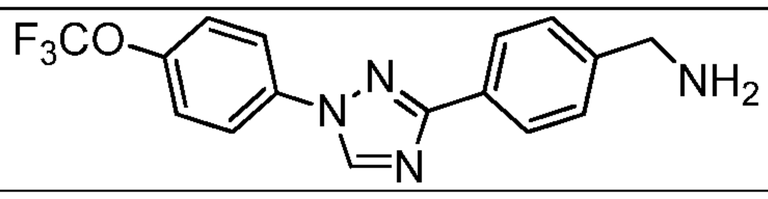
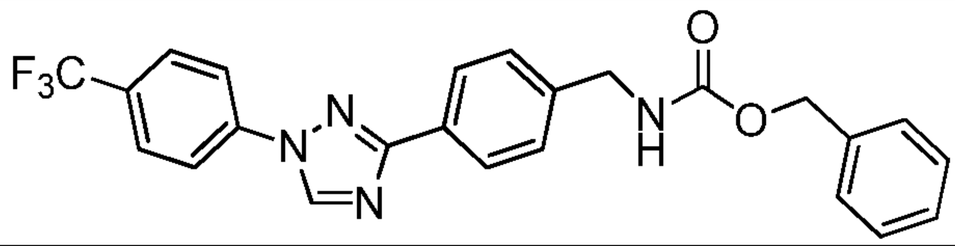
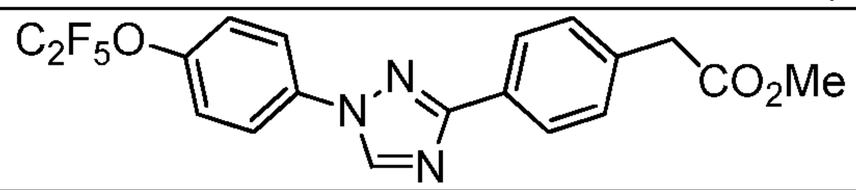
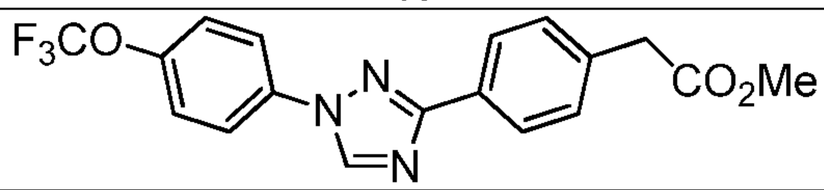
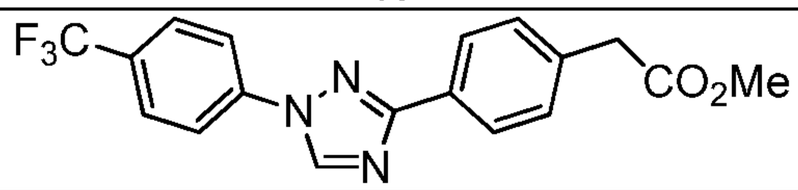
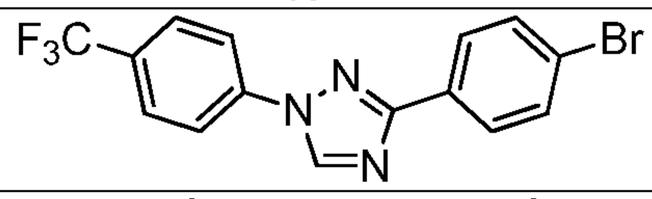
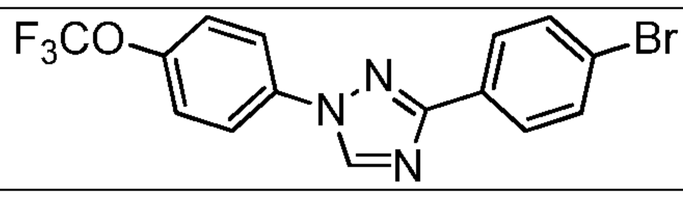
A molecule according to Formula One can be tested to determine its efficacy against pests. Furthermore, mode of action studies can be conducted to determine if said molecule has a different mode of action than other pesticides. Thereafter, such acquired data can be disseminated, such as by the internet, to third parties.

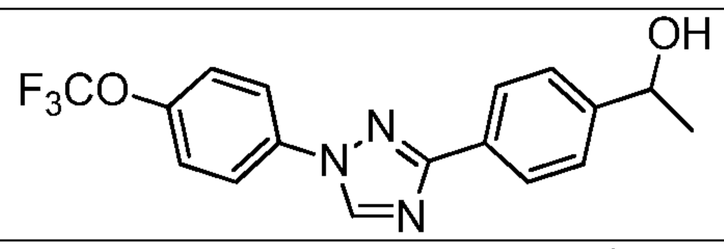
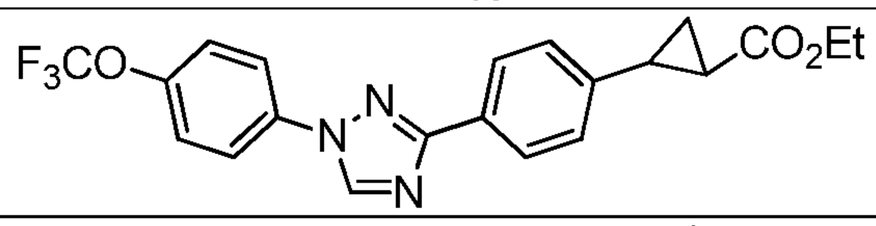
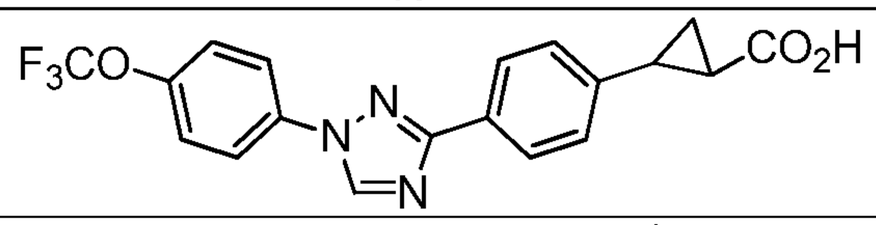
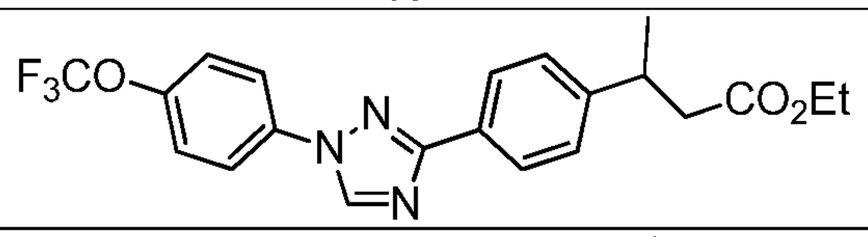
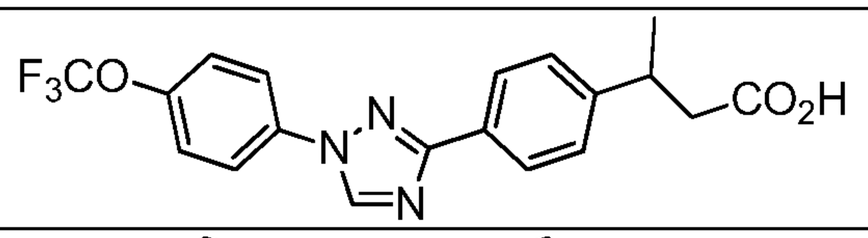
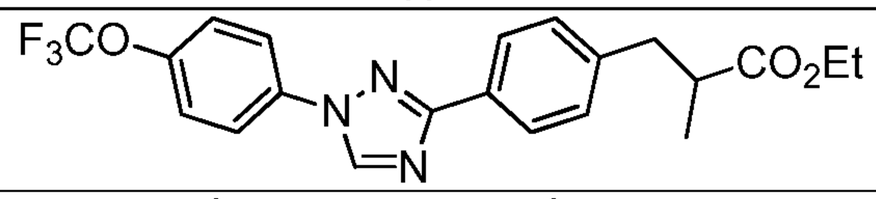
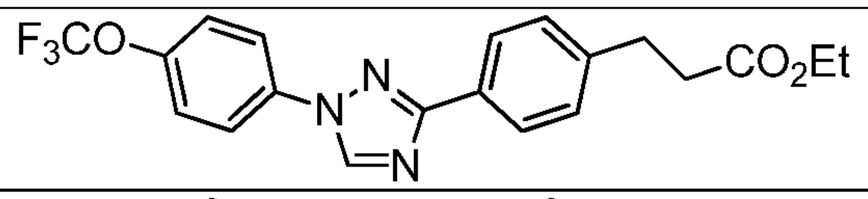
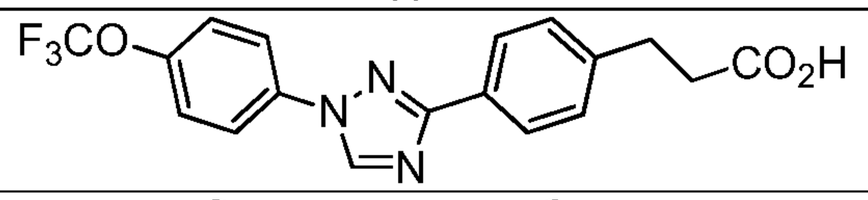
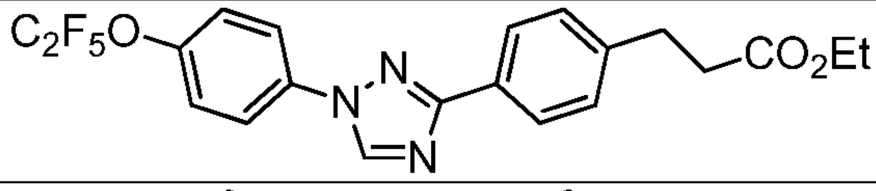
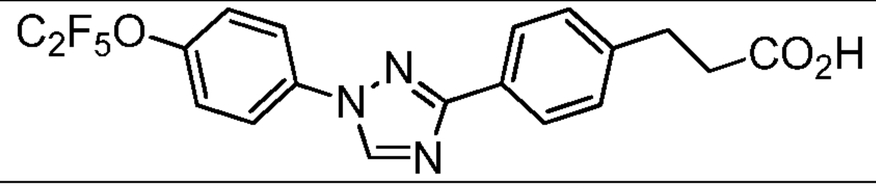
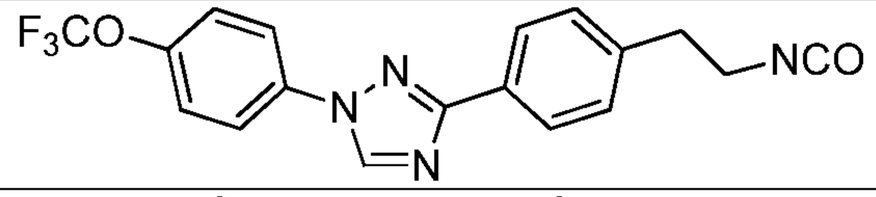
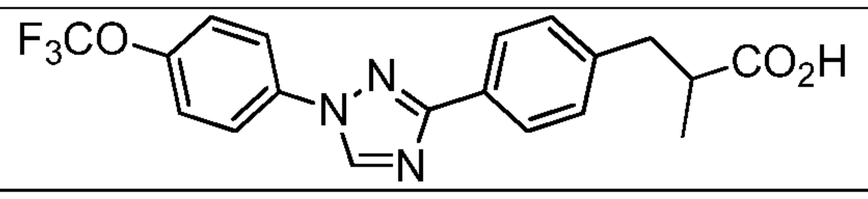
The headings in this document are for convenience only and must not be used to interpret any portion hereof.

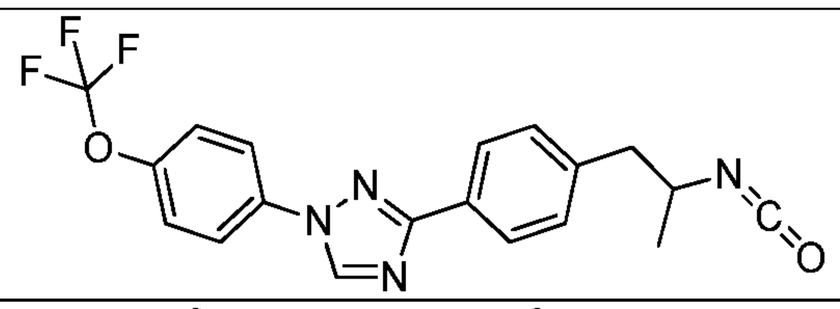
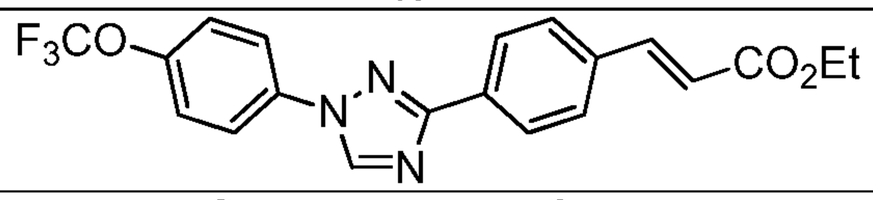
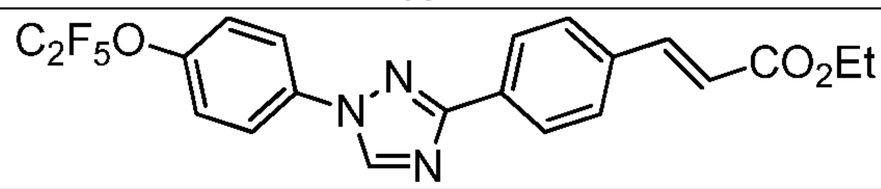
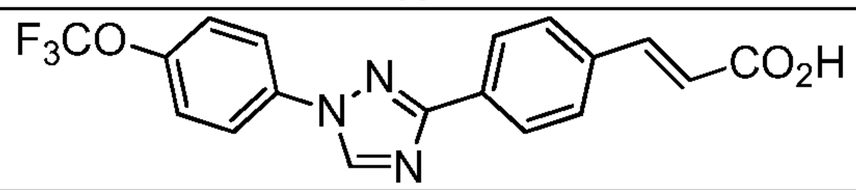
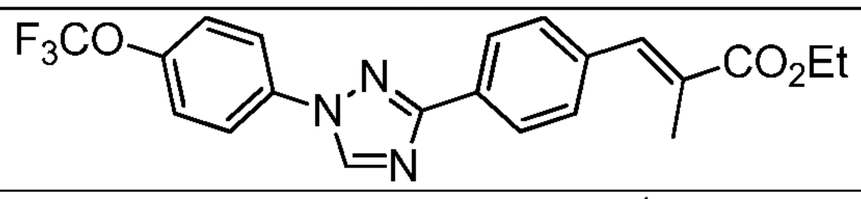
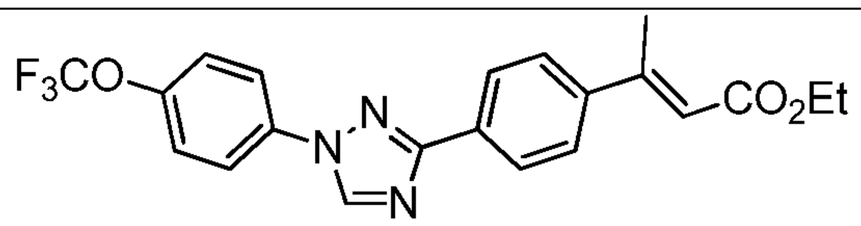
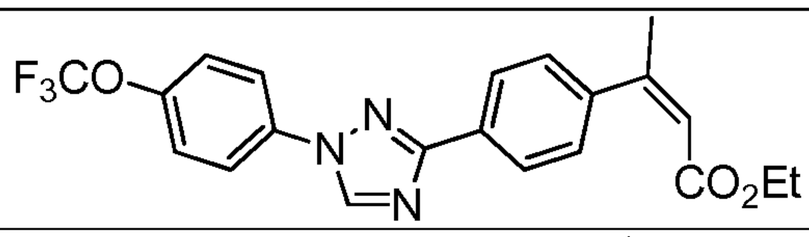
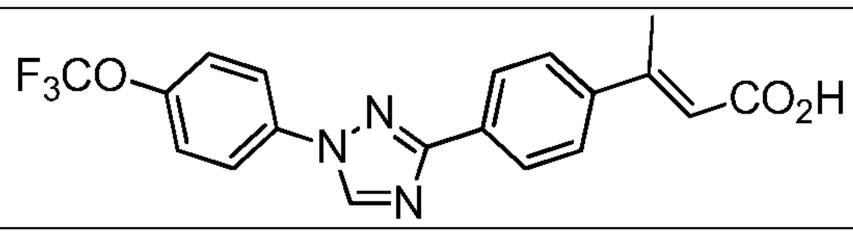
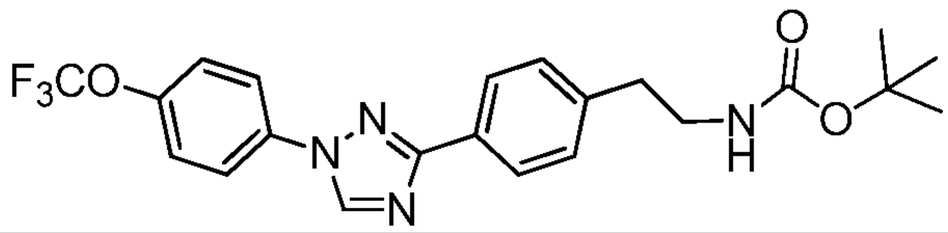
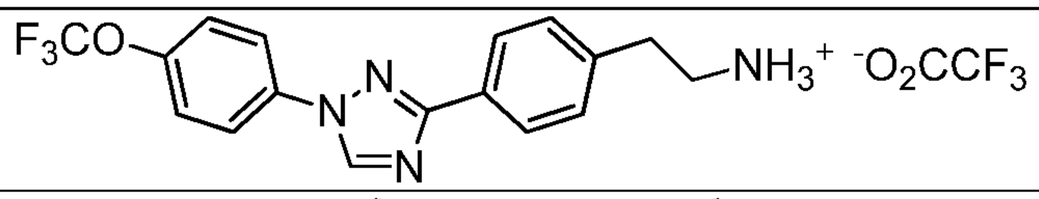
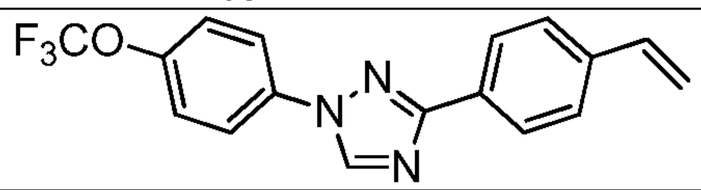
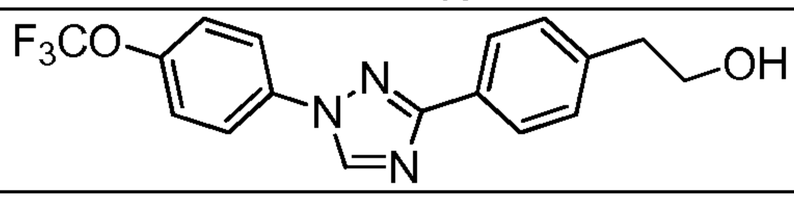
TABLE SECTION

Table 1: Structures for Intermediates

No.	Preparation	Structure
C13	Ex 9	

C1b	**Ex 1**	
C14	**Ex 10**	
C8	**Ex 4**	
C6	**Ex 4**	
C7	**Ex 4**	
C15a	**Ex 10a**	
C16	**Ex 11**	
C15	**Ex 10**	
C4	**Ex 3**	
C3	**Ex 3**	
C5	**Ex 3**	
C53	**Ex 56**	
C52	**Ex 56**	

C24	**Ex 24**	
C19	**Ex 14**	
C20	**Ex 15**	
C40	**Ex 43**	
C41	**Ex 44**	
C37	**Ex 37**	
C30	**Ex 30**	
C32	**Ex 31**	
C31	**Ex 30**	
C33	**Ex 31**	
C34a	**Ex 32a**	
C38	**Ex 38**	

C39	**Ex 39**	
C17	**Ex 13**	
C18	**Ex 13**	
C22	**Ex 20**	
C36	**Ex 36**	
C26	**Ex 26**	
C27	**Ex 26**	
C28	**Ex 27**	
C50	**Ex 54**	
C55	**Ex 58**	
C43	**Ex 47**	
C44	**Ex 48**	

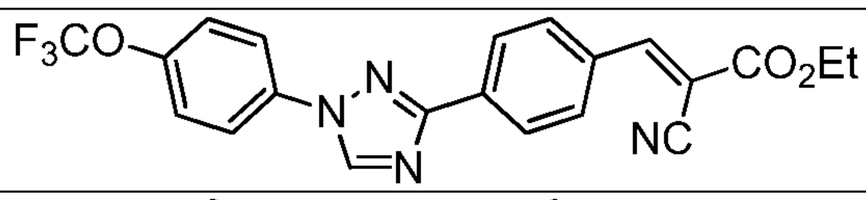
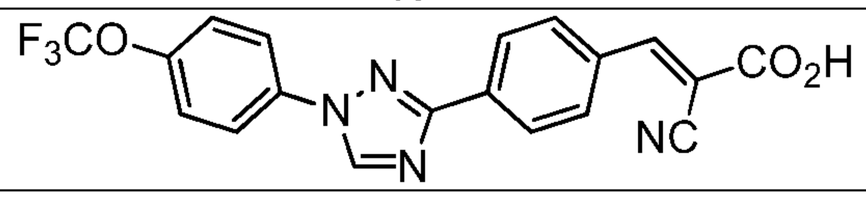
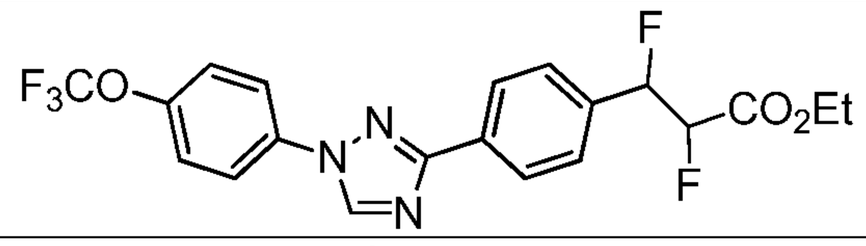
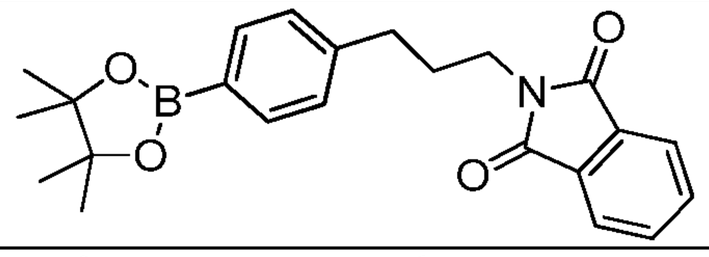
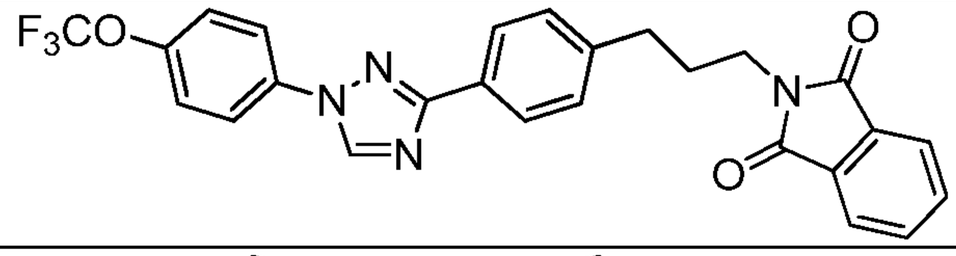
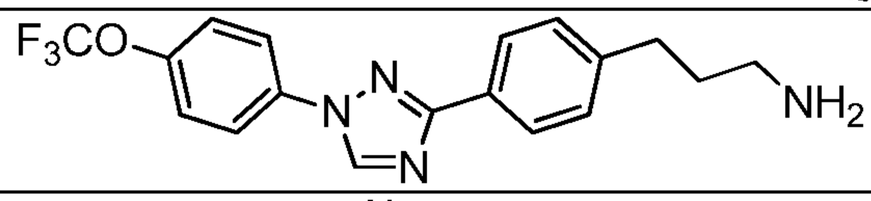
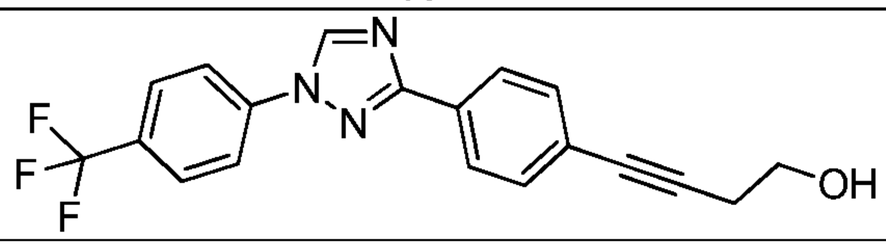
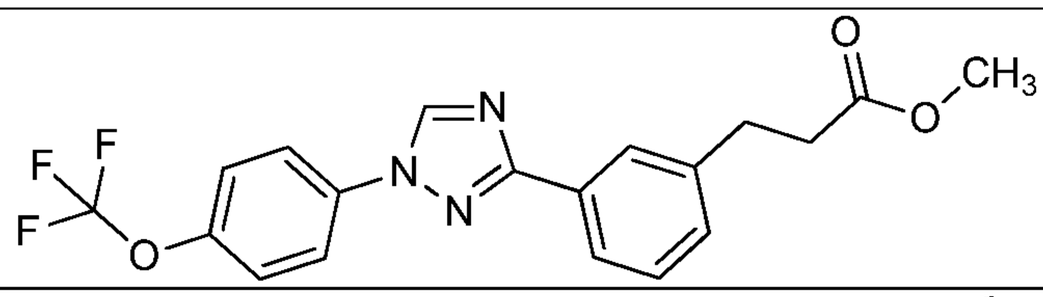
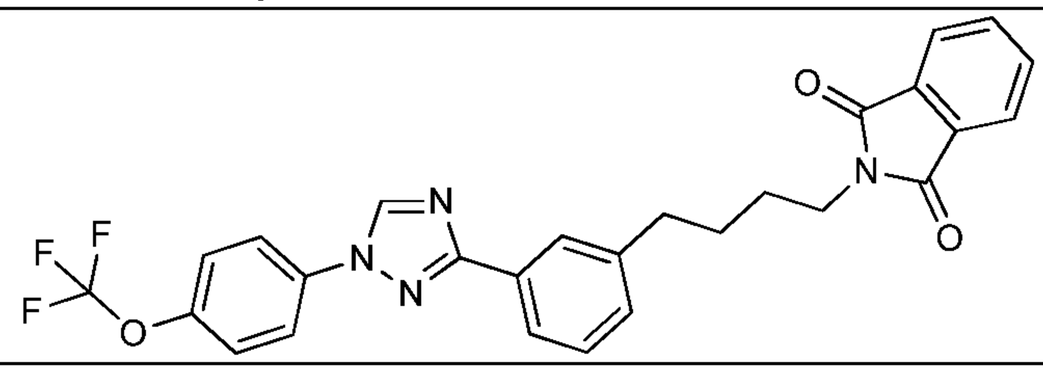
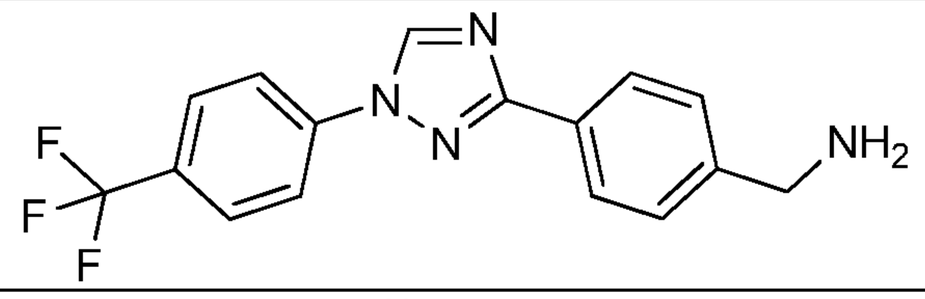
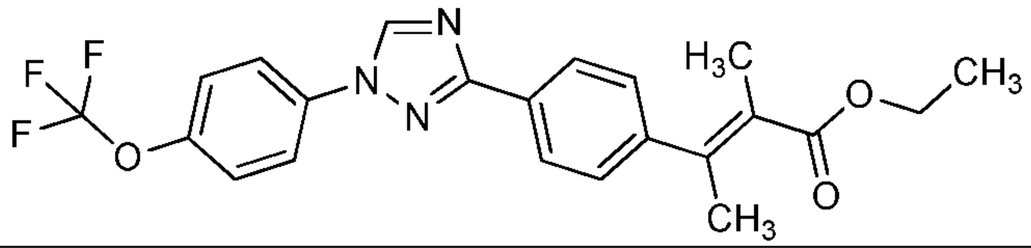
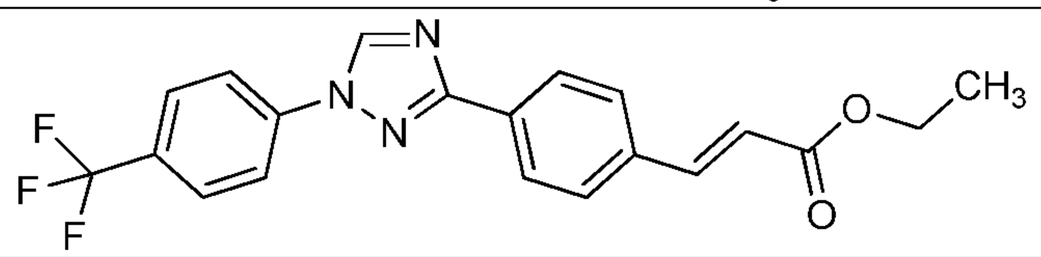
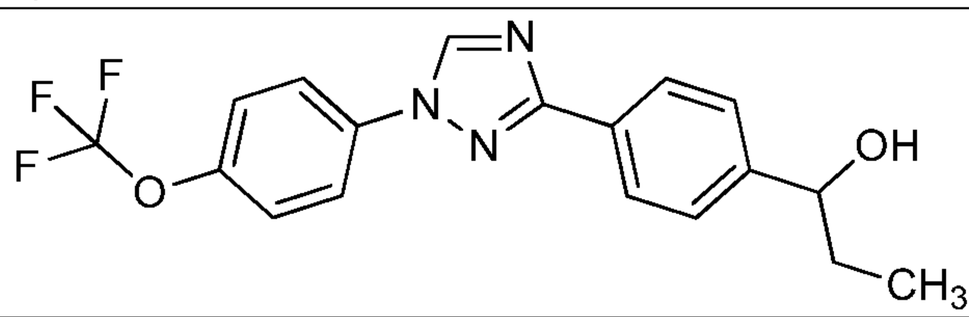
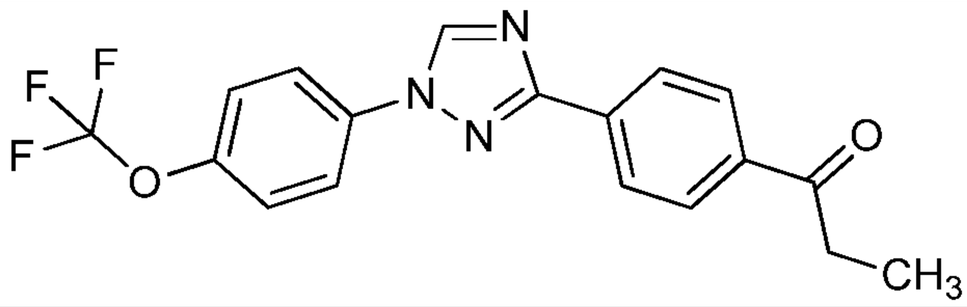
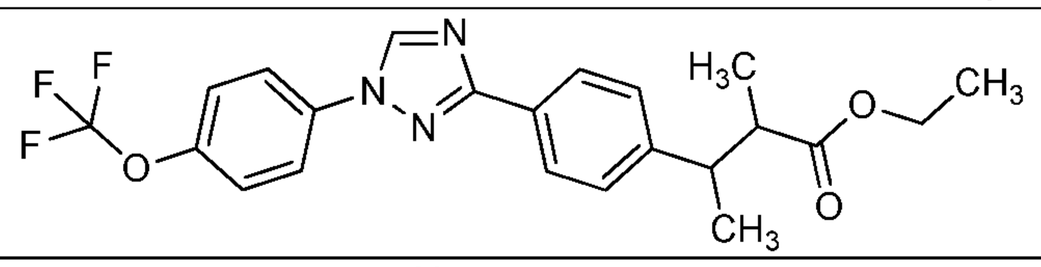
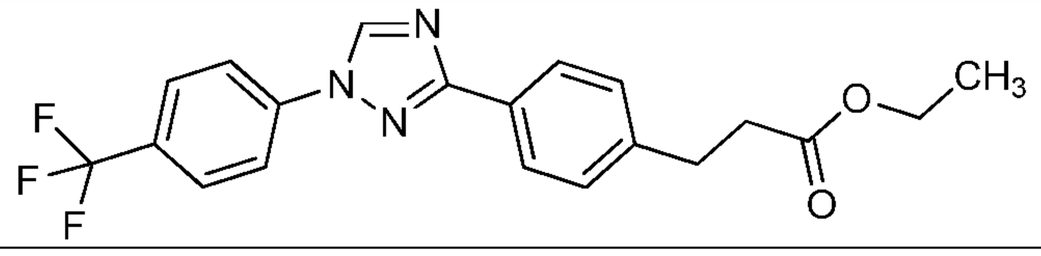
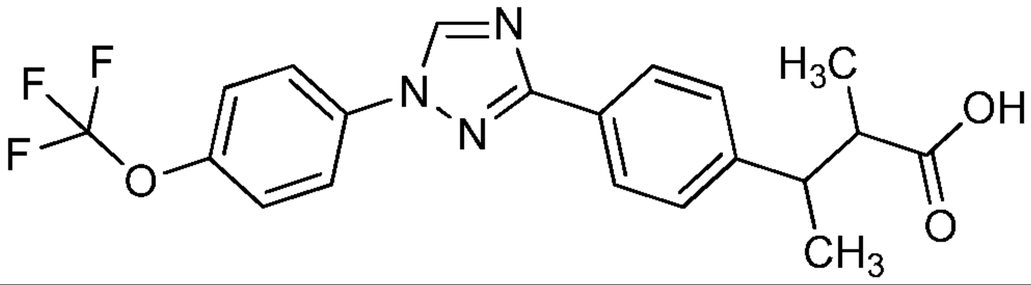
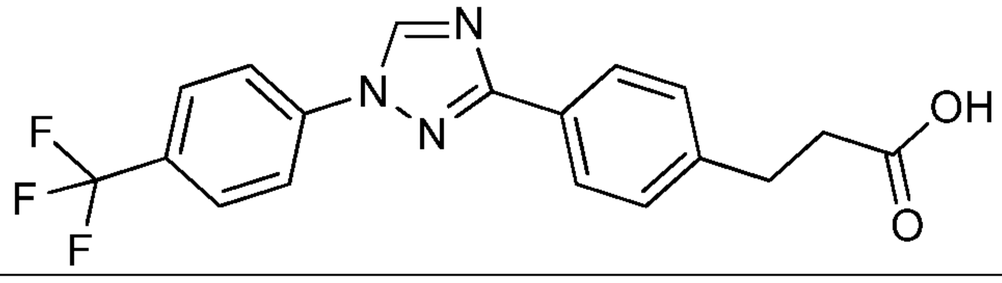
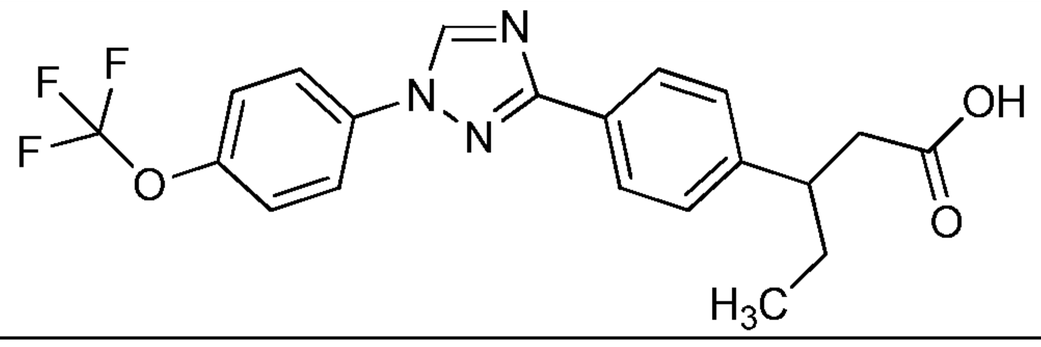
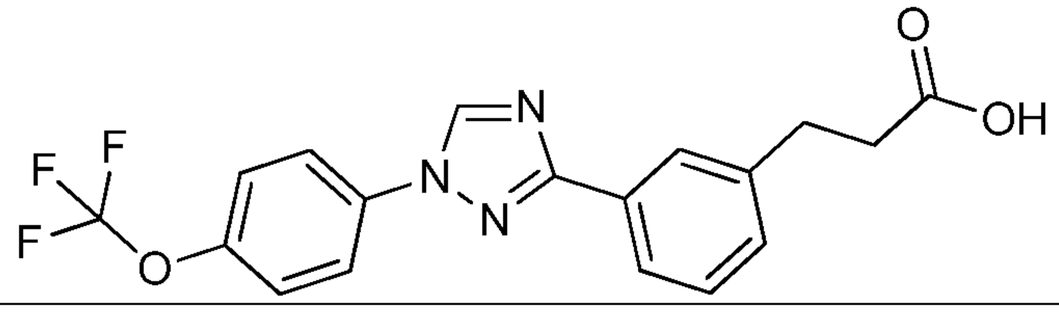
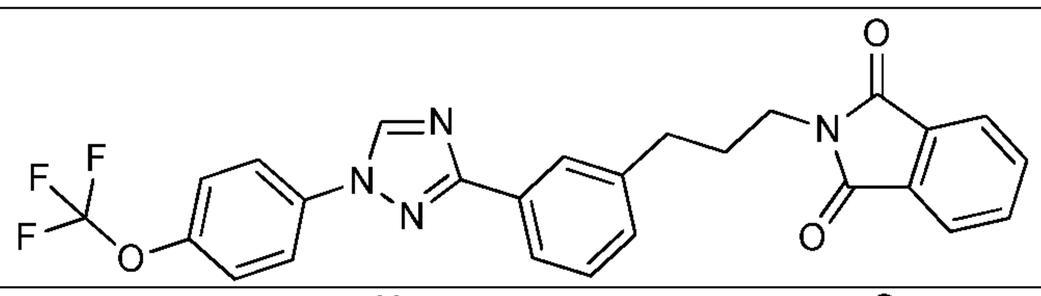
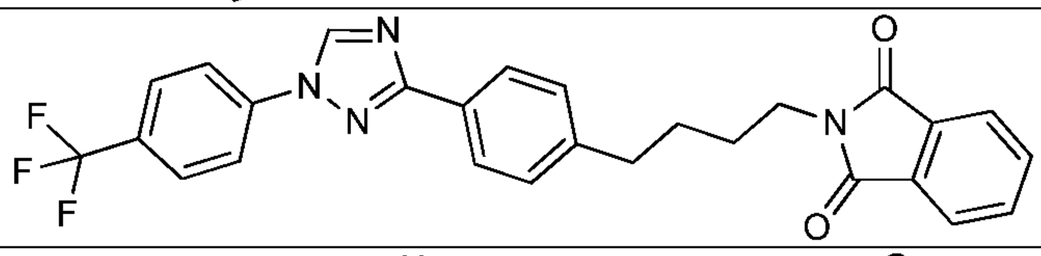
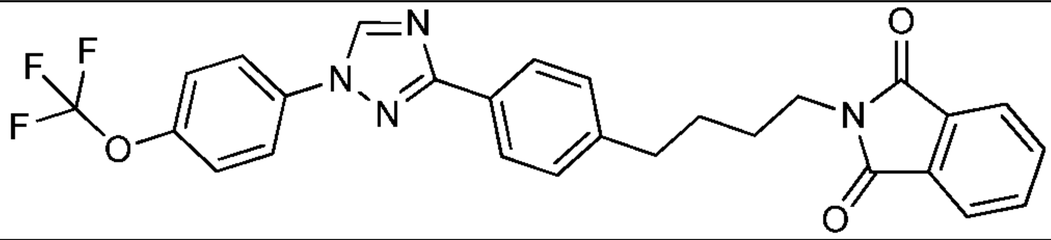
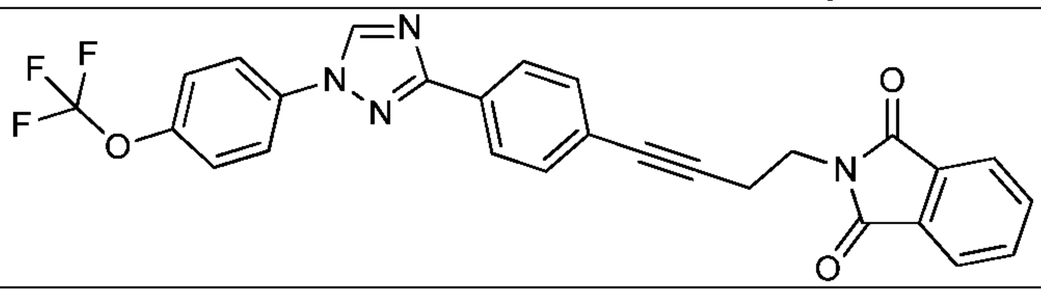
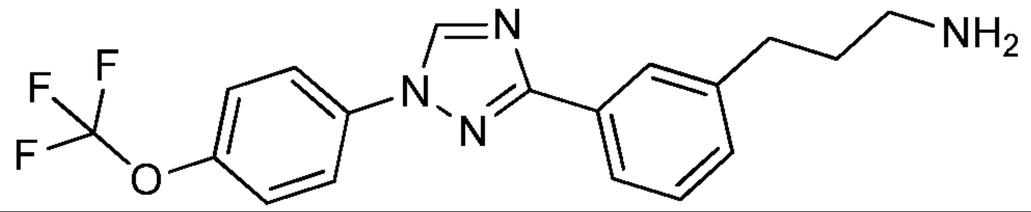
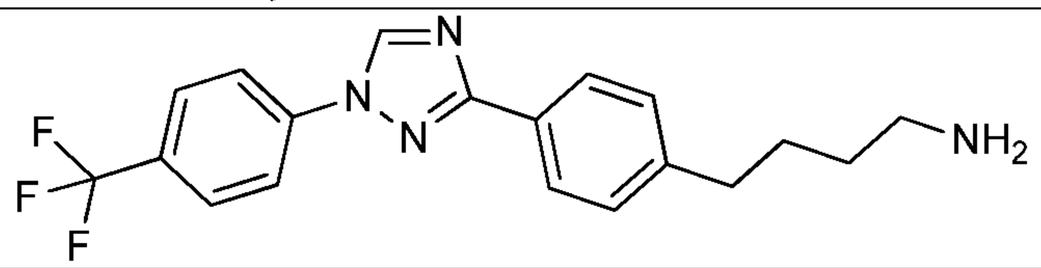
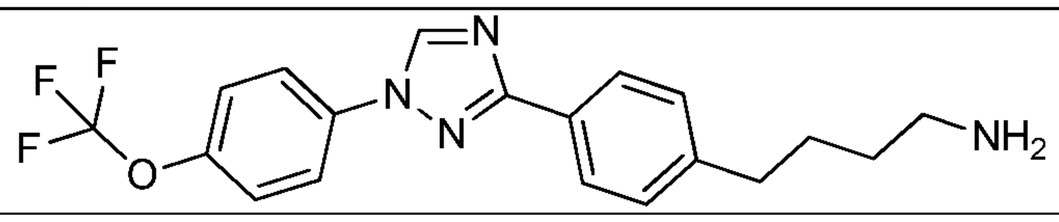
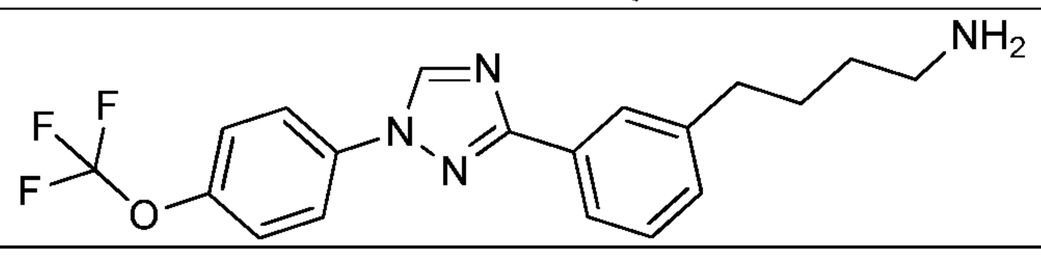
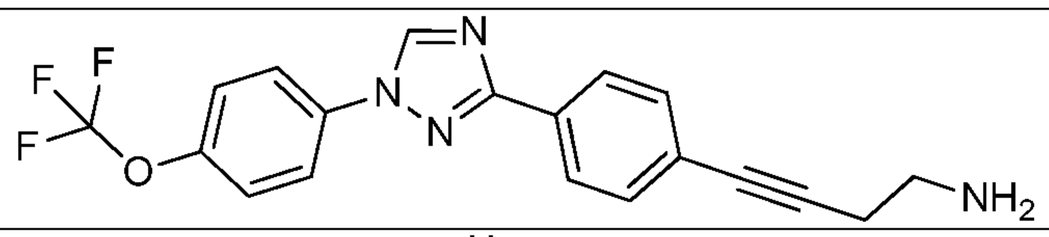
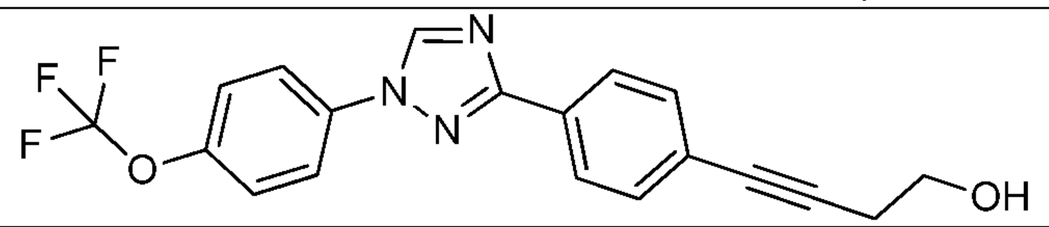
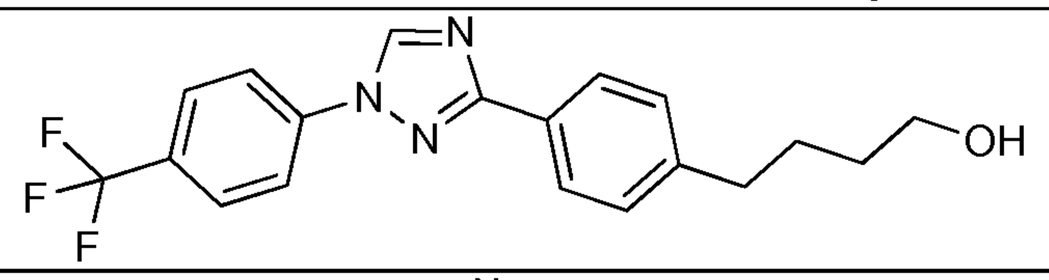
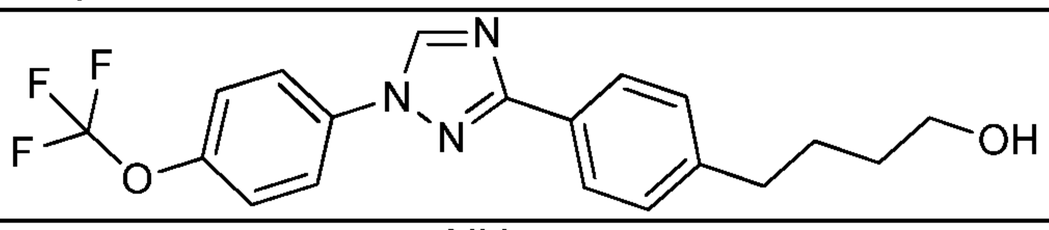
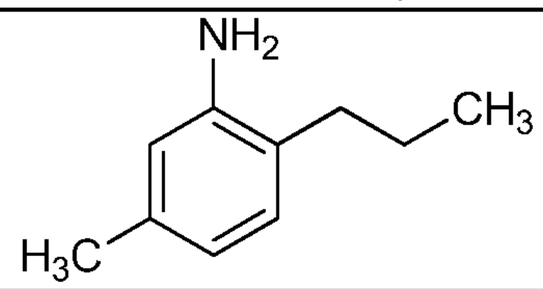
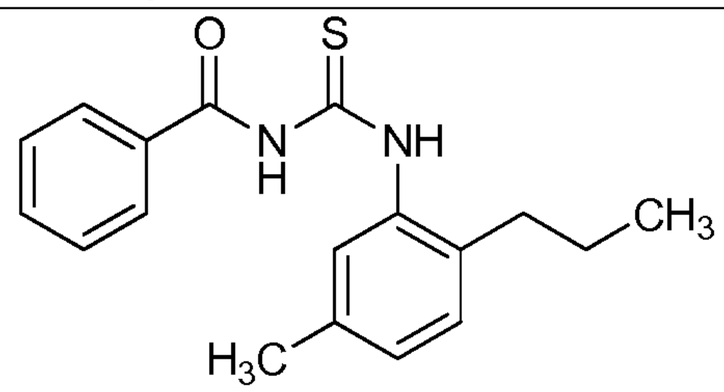
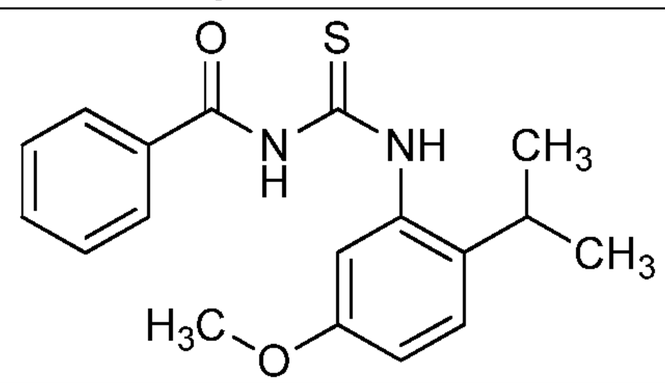
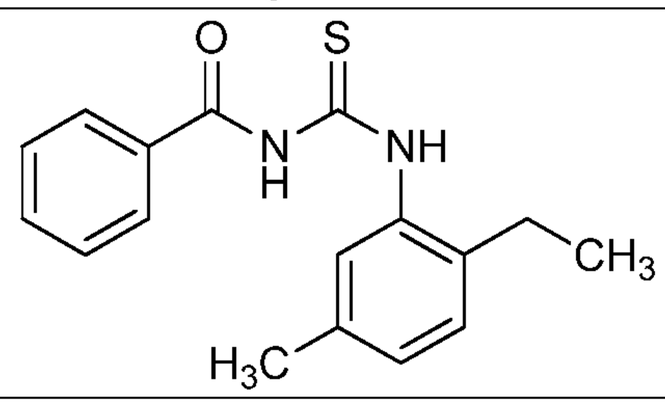
C46	**Ex 50**	
C47	**Ex 51**	
C45	**Ex 49**	
C58	**Ex 60**	
C59	**Ex 61**	
C60	**Ex 62**	
C61	**Ex 65**	

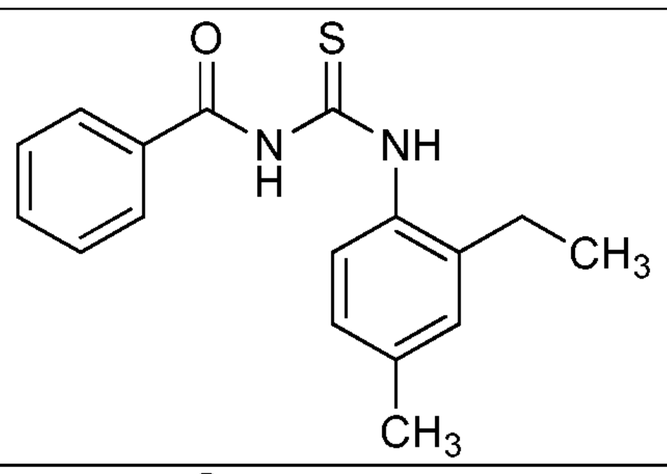
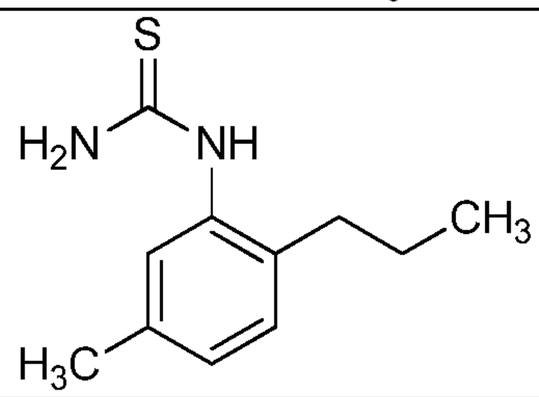
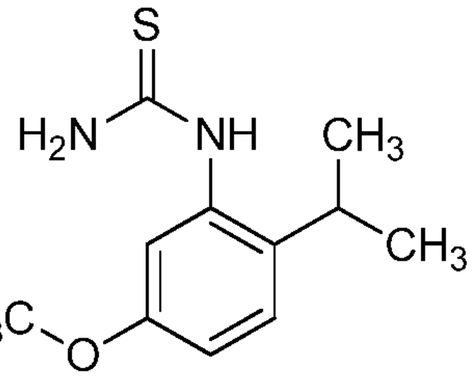
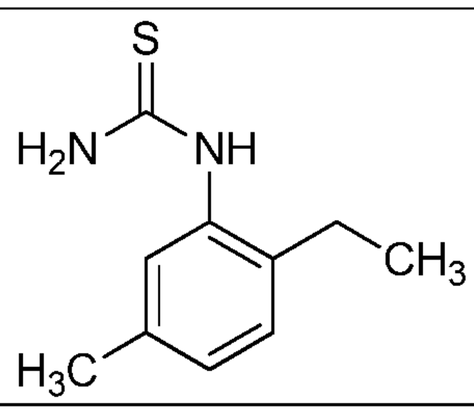
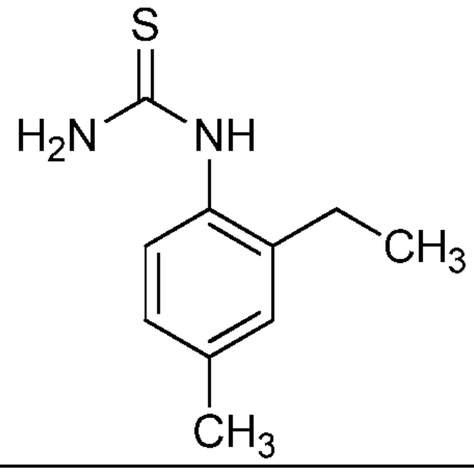
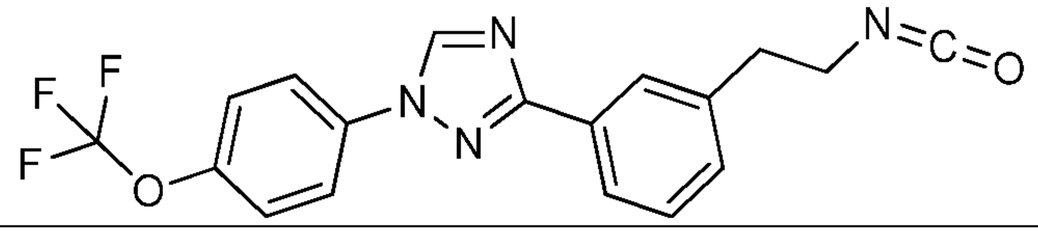
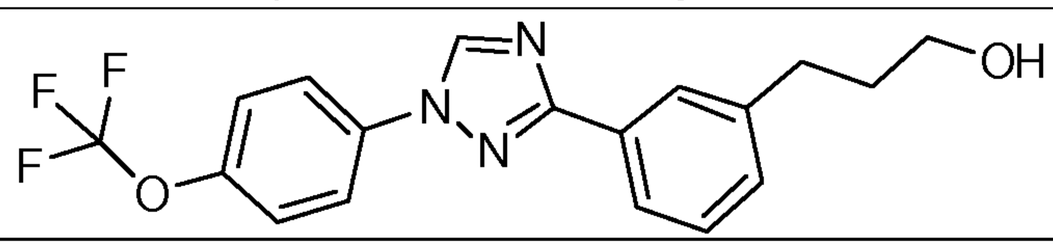
Table 1A: Structures for Intermediates (CA)

No.	Preparation	Structure
CA1	**Ex 10**	
CA2	**Ex 10**	

CA3	**Ex 11**	
CA4	**Ex 13**	
CA5	**Ex 13**	
CA6	**Ex 24**	
CA7	**Ex 25**	
CA8	**Ex 30**	
CA9	**Ex 30**	
CA10	**Ex 31**	
CA11	**Ex 31**	

CA12	**Ex 44**	
CA13	**Ex 51**	
CA14	**Ex 59**	
CA15	**Ex 59**	
CA16	**Ex 59**	
CA17	**Ex 59**	
CA18	**Ex 62**	
CA19	**Ex 62**	
CA20	**Ex 62**	
CA21	**Ex 62**	

CA22	**Ex 62**	
CA23	**Ex 65**	
CA24	**Ex 66**	
CA25	**Ex 66**	
CA26	**Ex 66**	
CA33	**Ex 68**	
CA35	**Ex 68**	
CA36	**Ex 68**	

CA37	**Ex 68**	
CA38	**Ex 69**	
CA40	**Ex 69**	
CA41	**Ex 69**	
CA42	**Ex 69**	
CA44	**Ex 74**	
CA45	**Ex 76**	

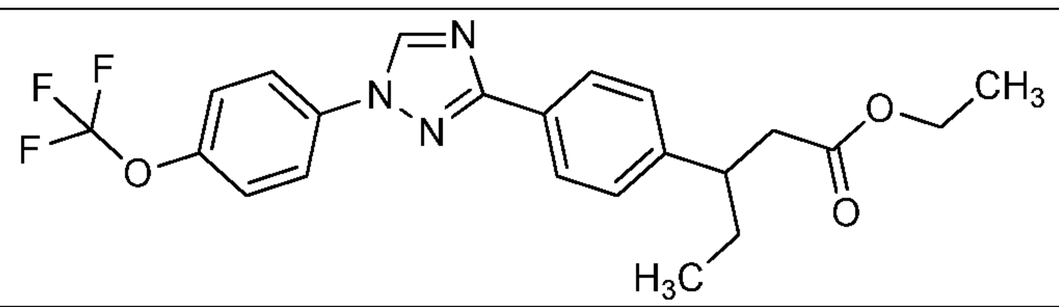
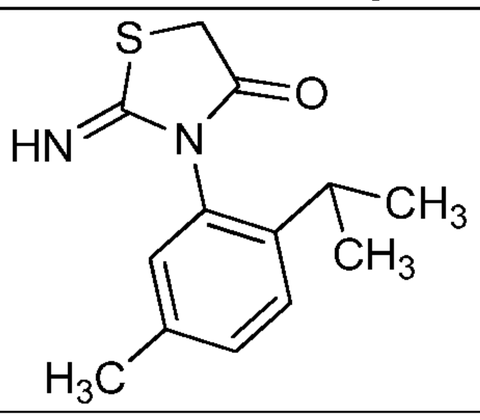
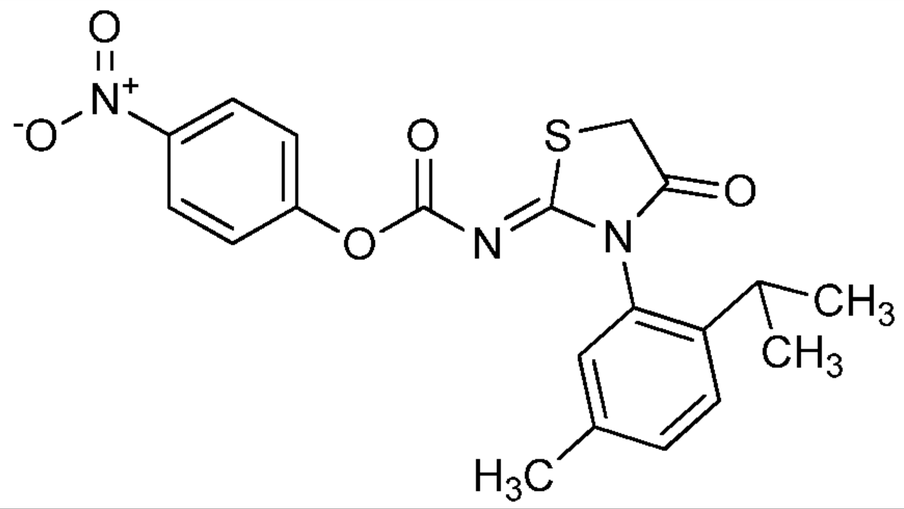
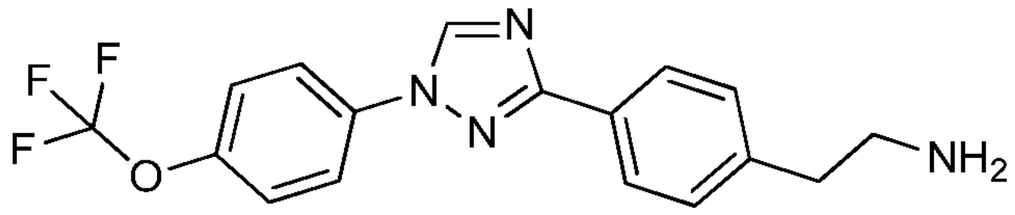
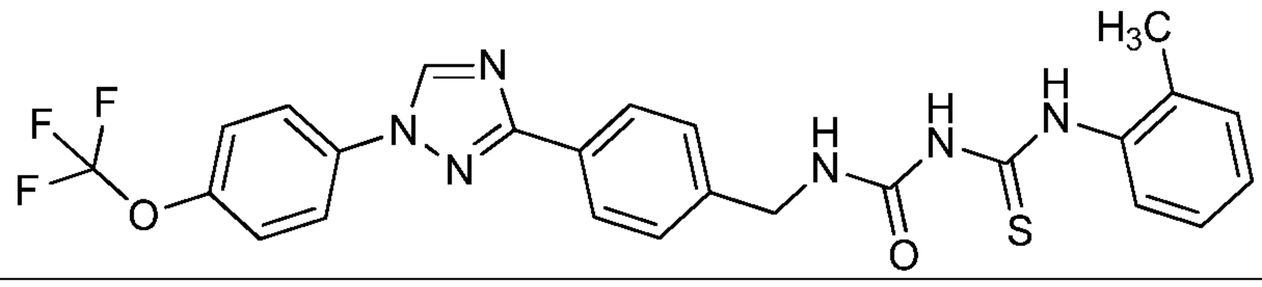
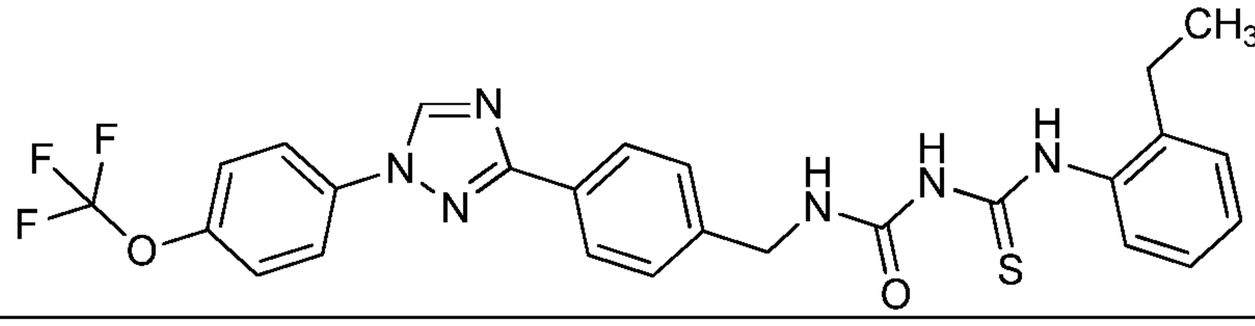
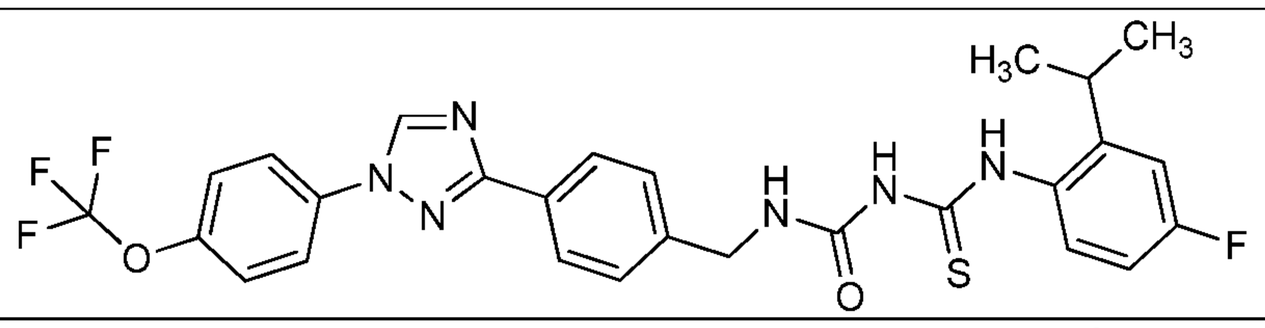
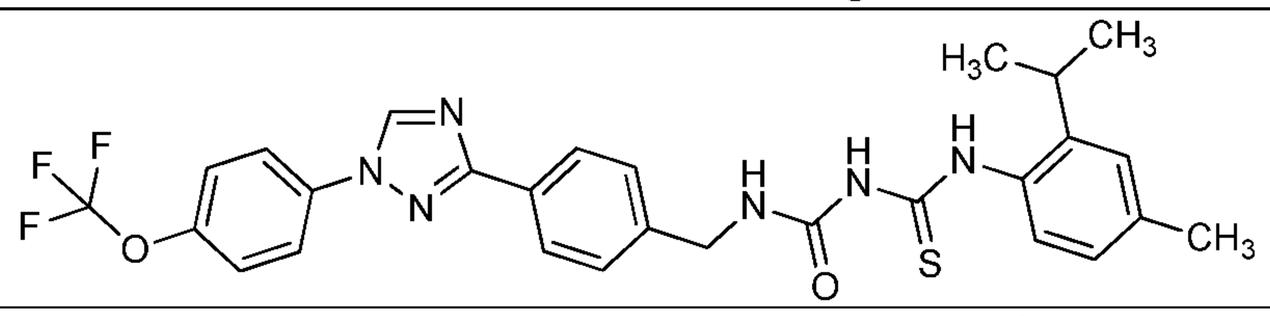
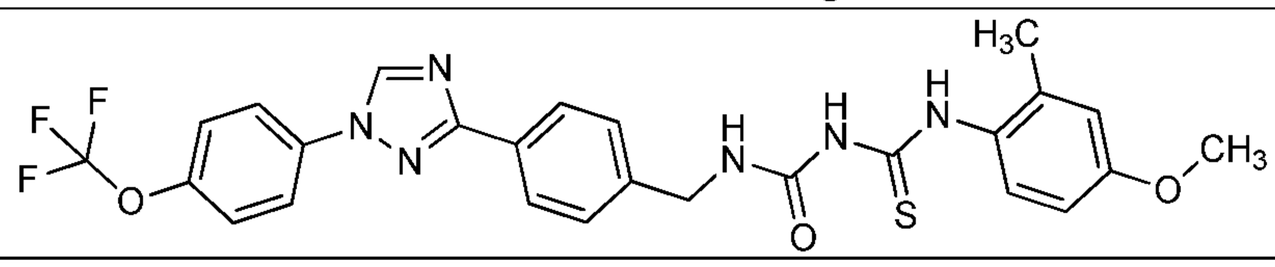
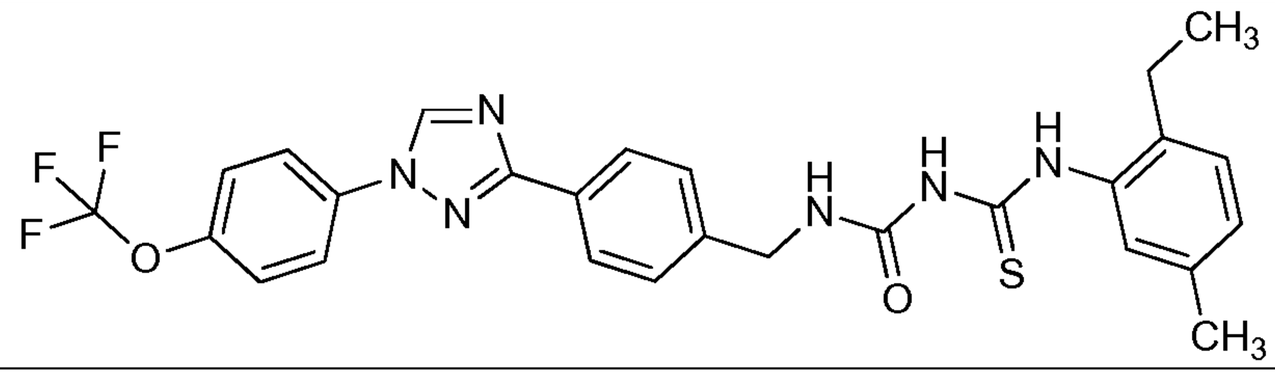
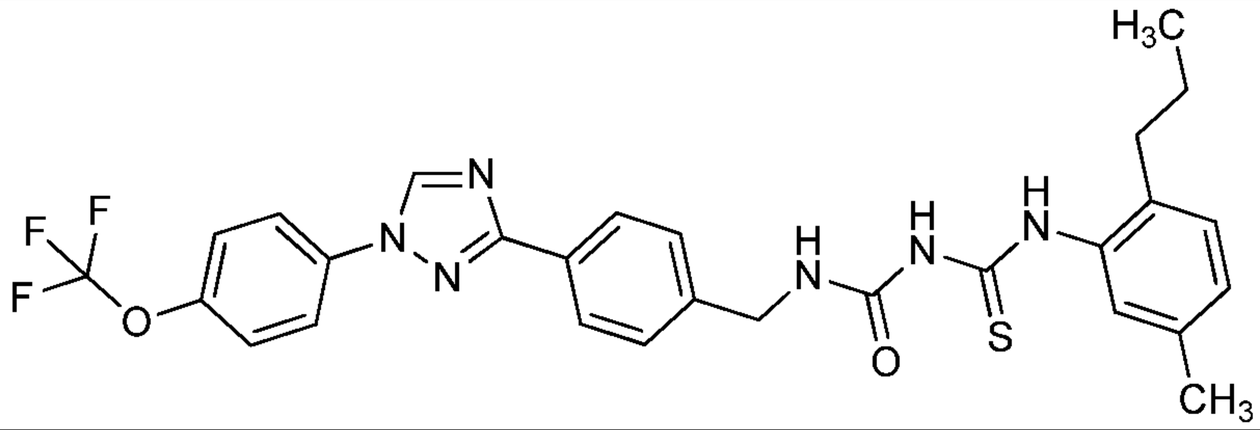
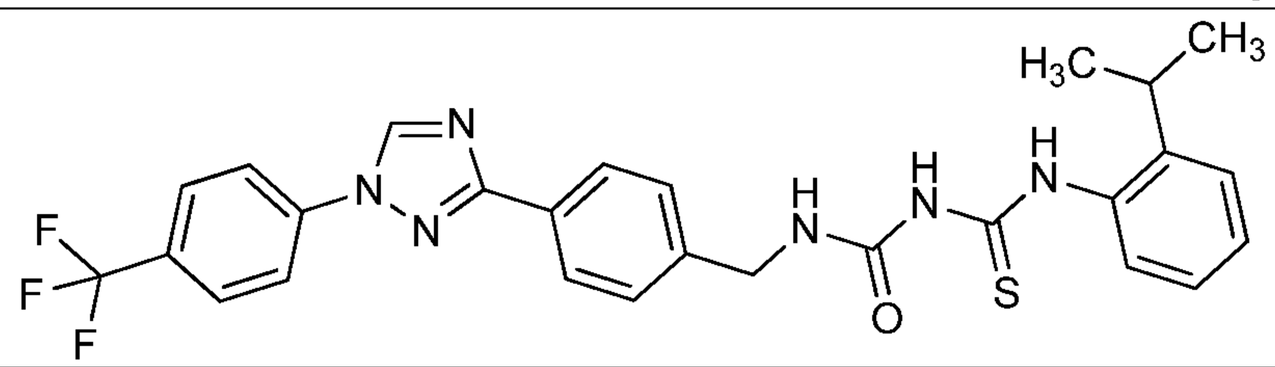
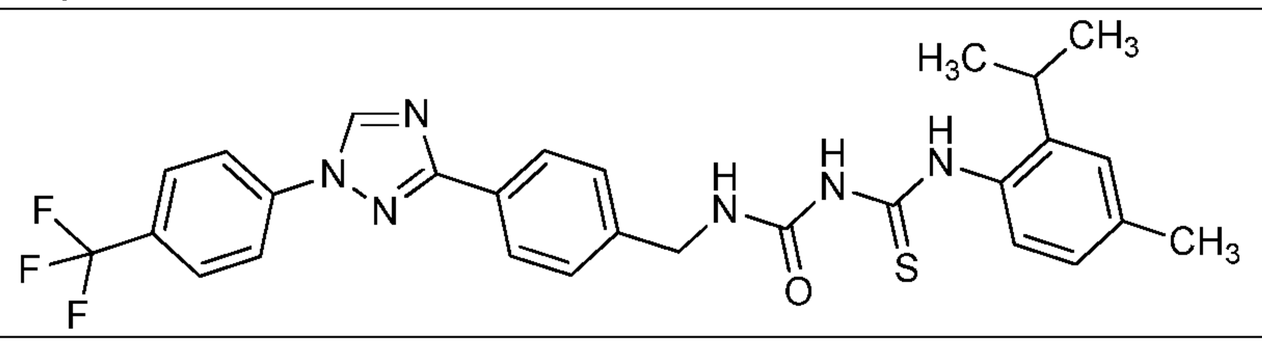
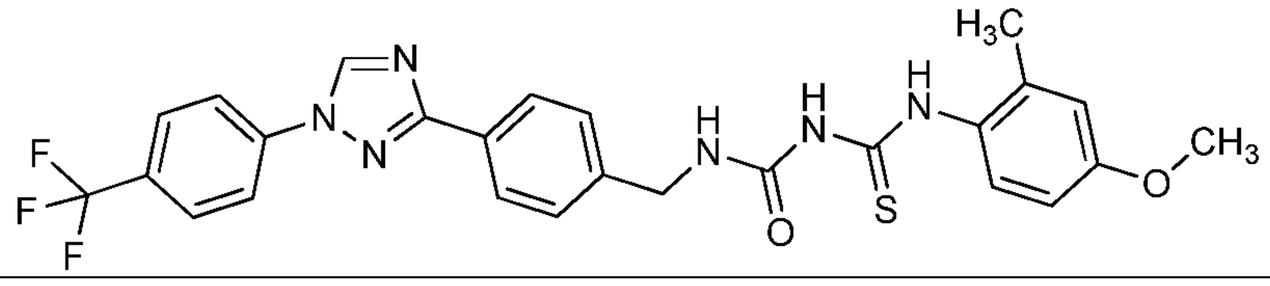
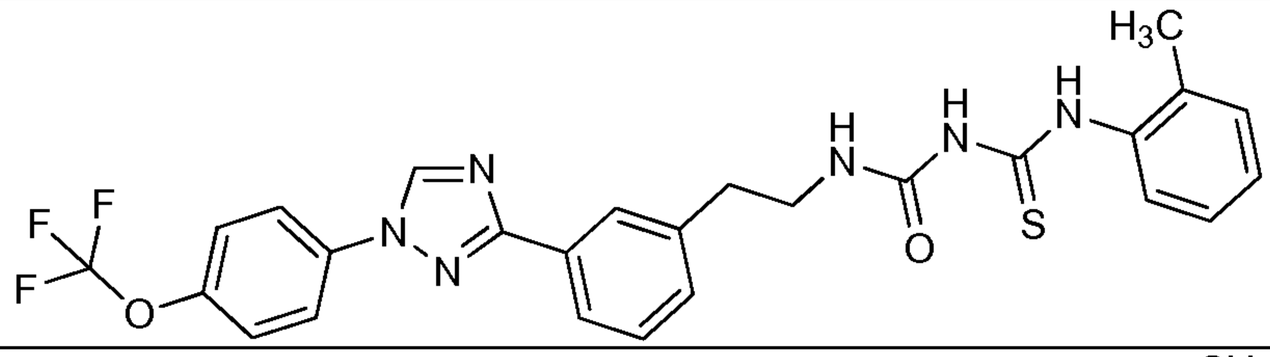
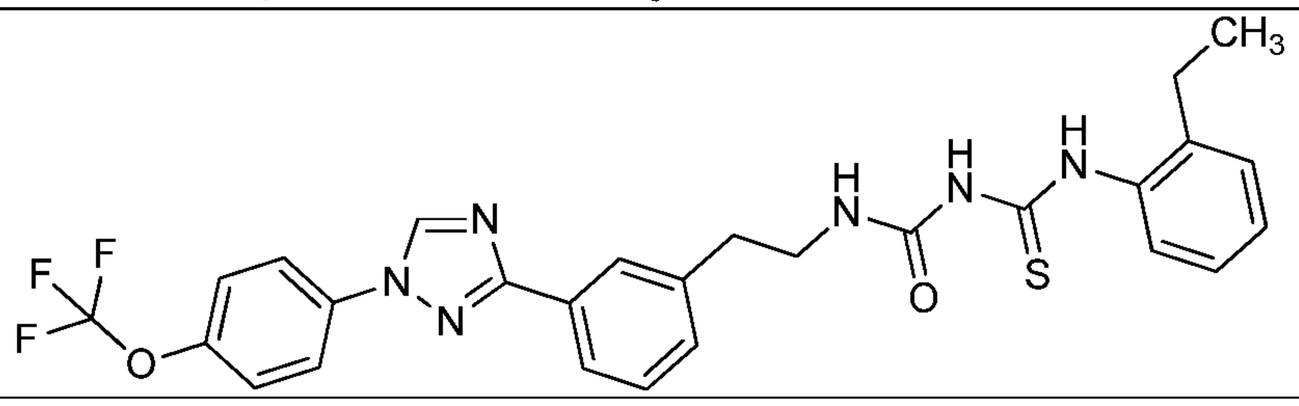
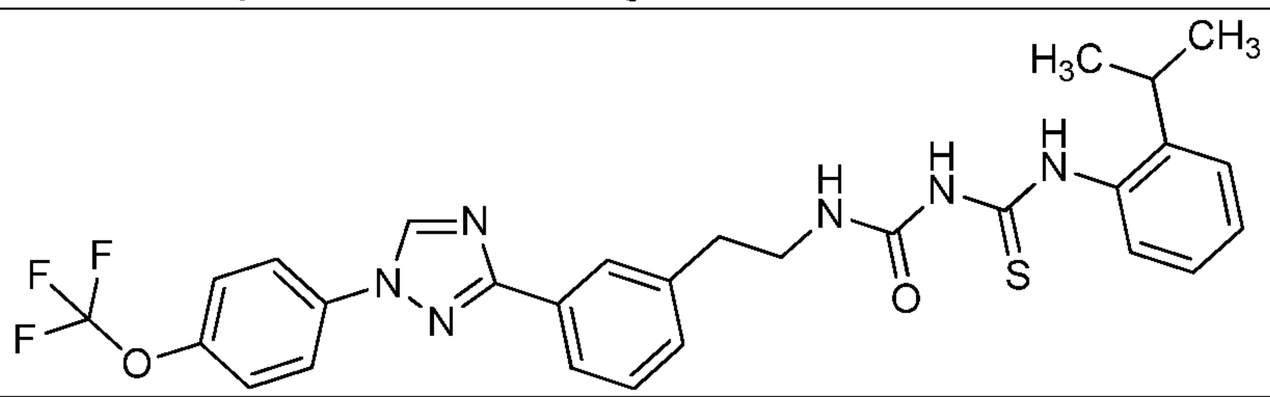
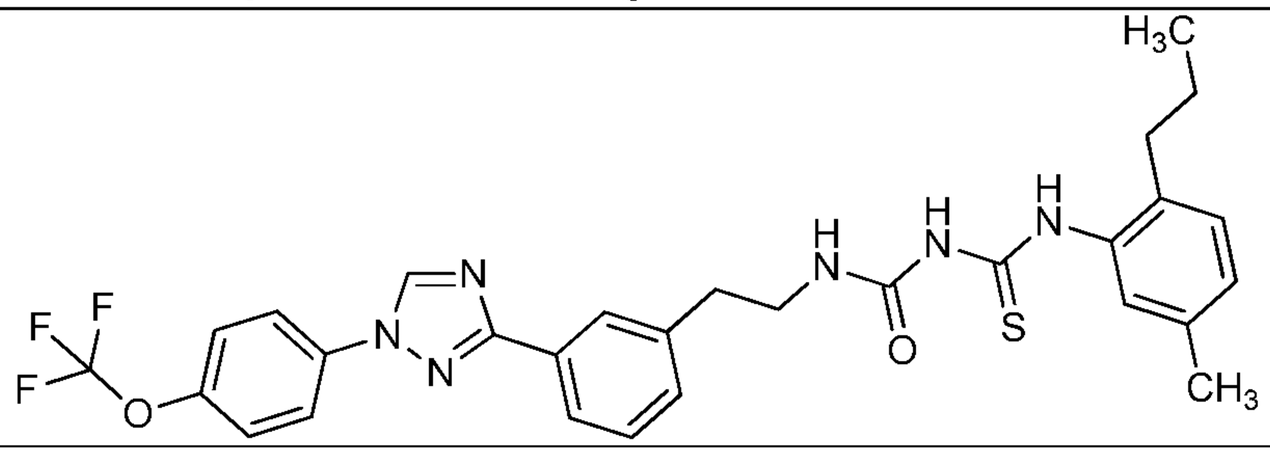
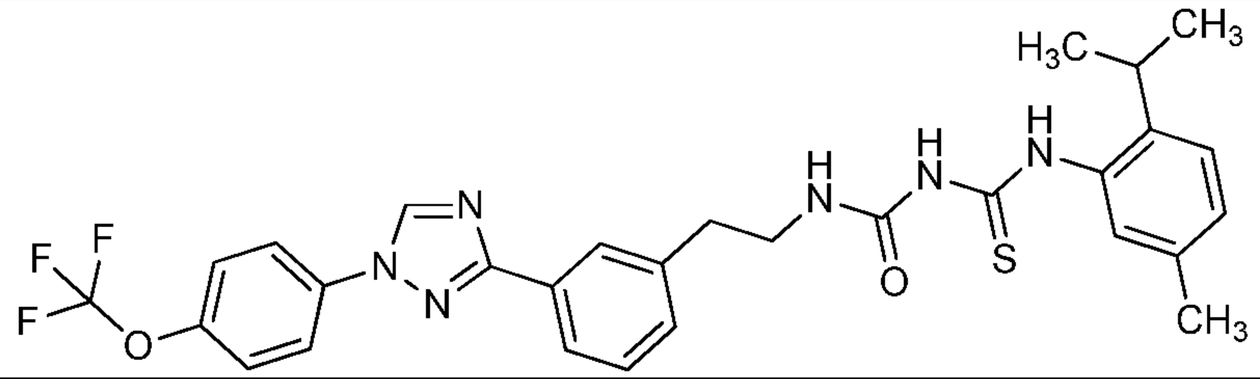
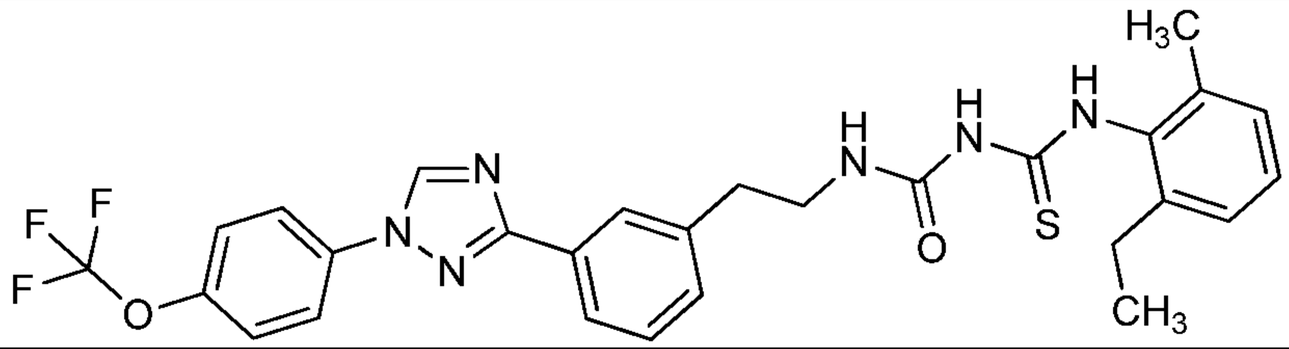
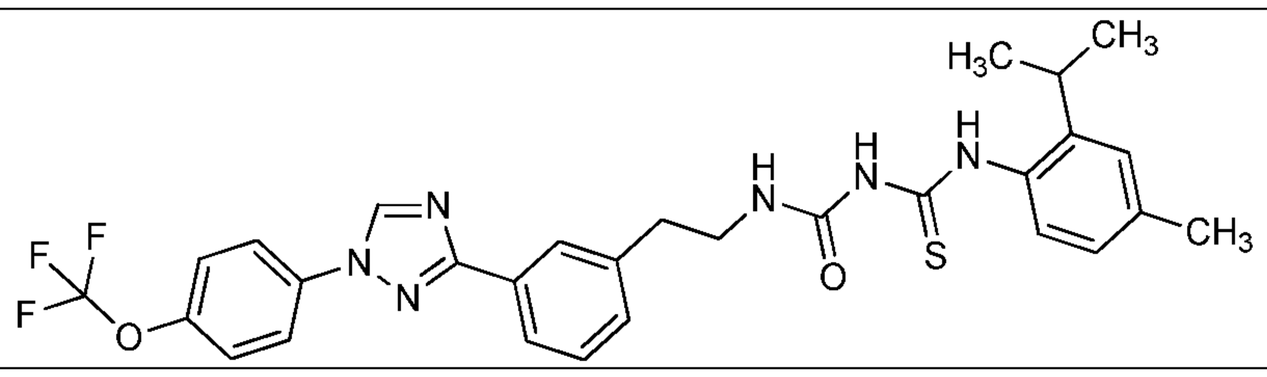
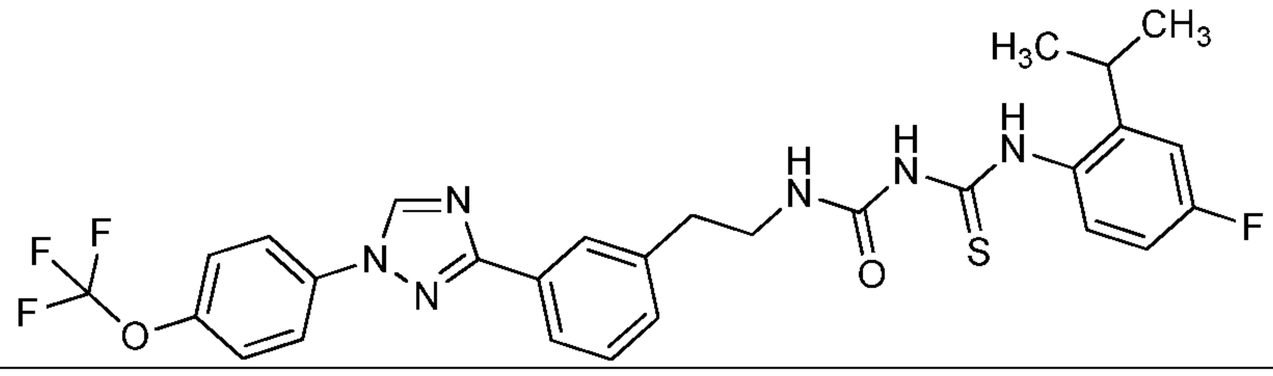
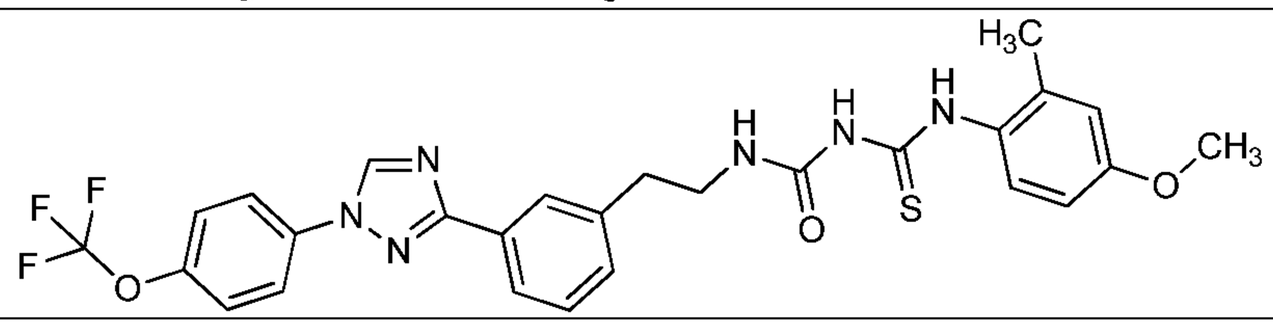
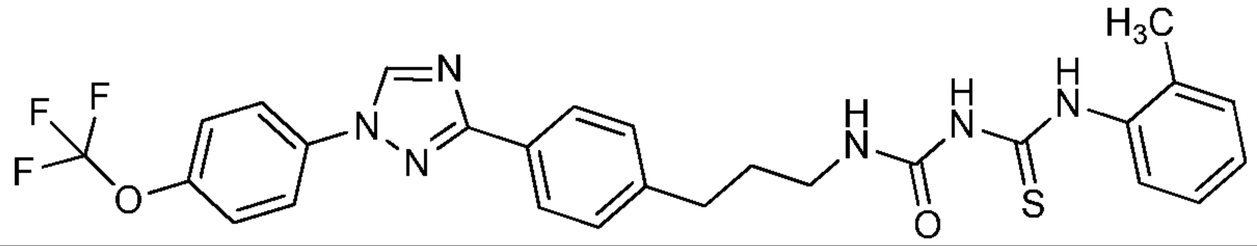
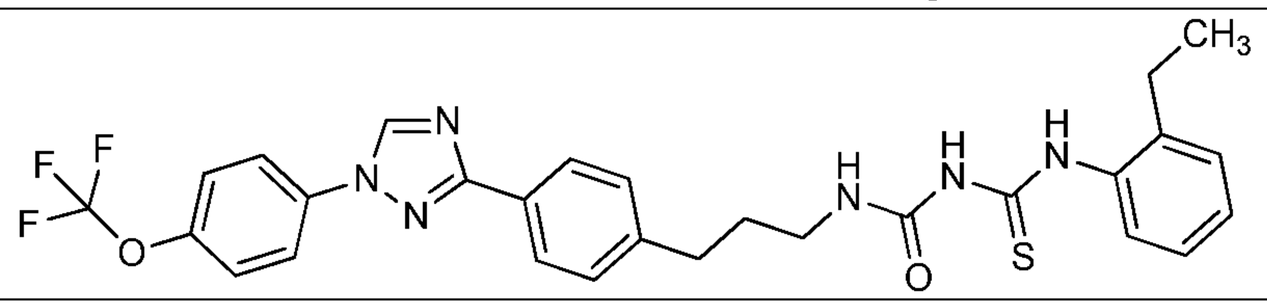
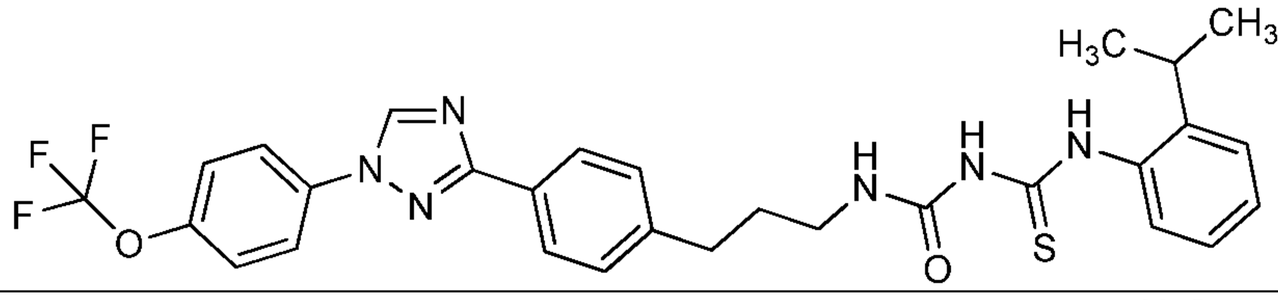
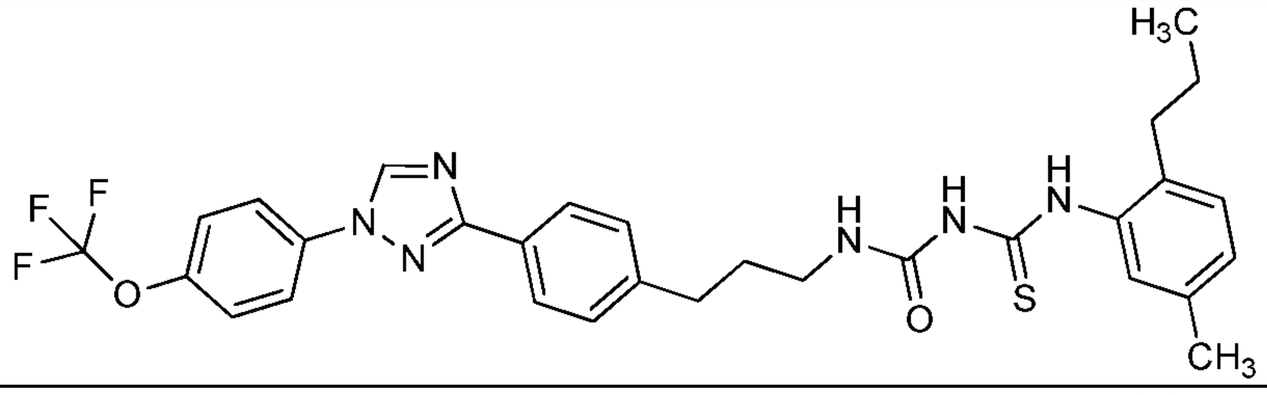
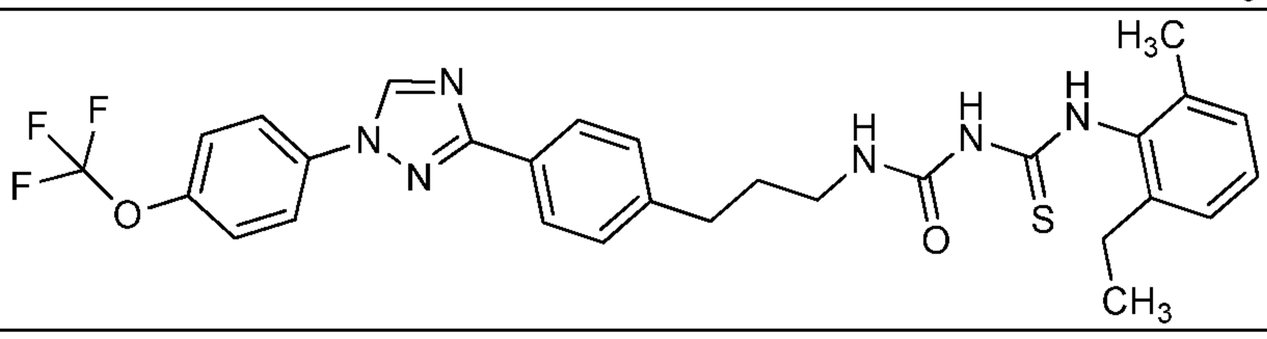
CA48	**Ex 81**	
CA49	**Ex 83**	
CA50	**Ex 84**	
CA51	**Ex 58a**	

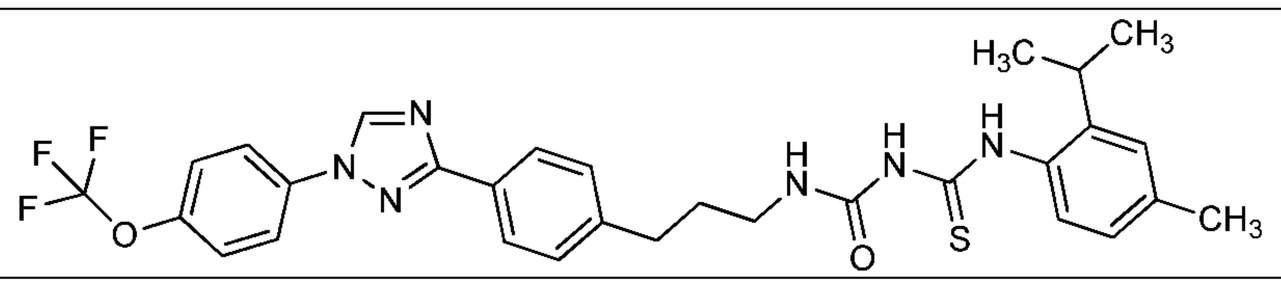
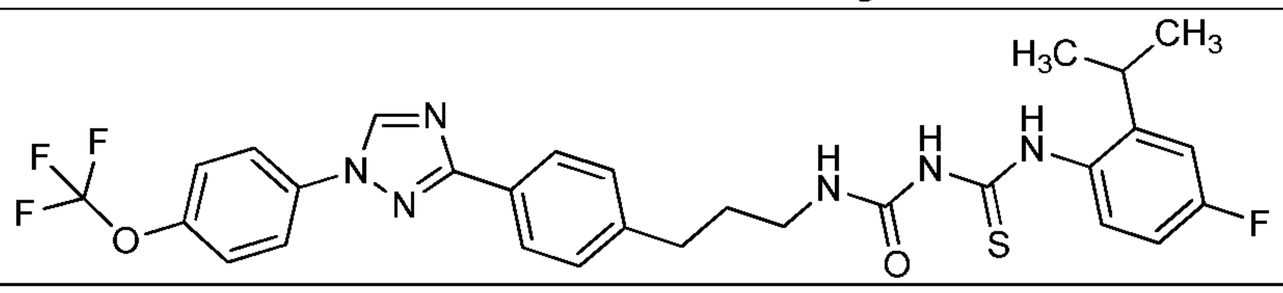
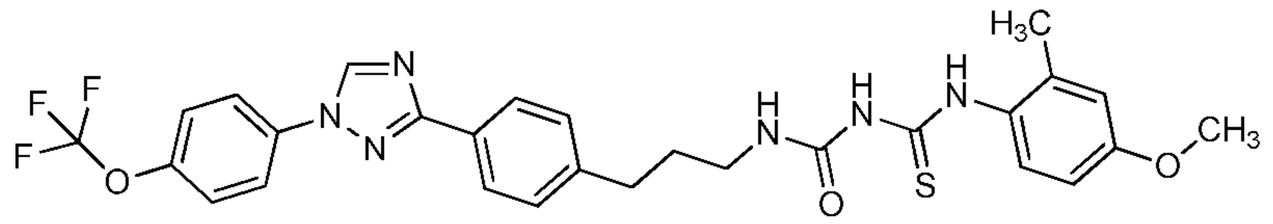
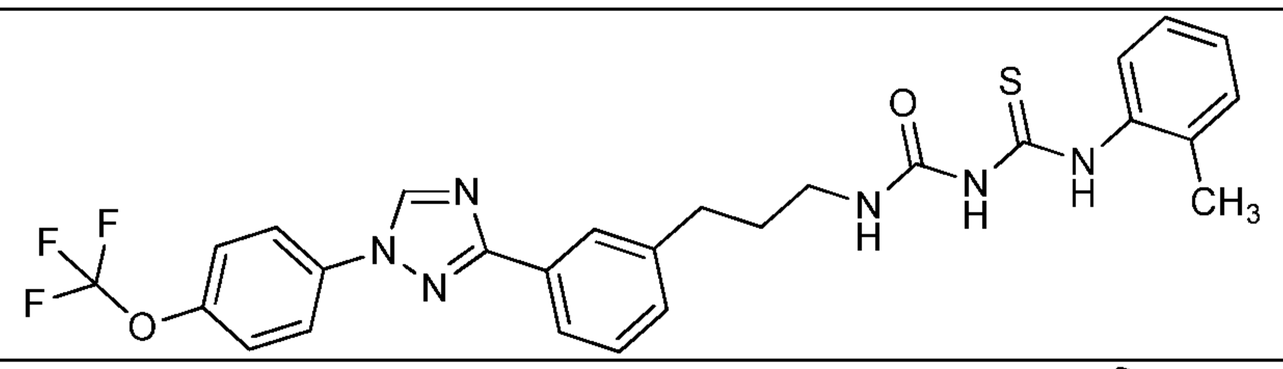
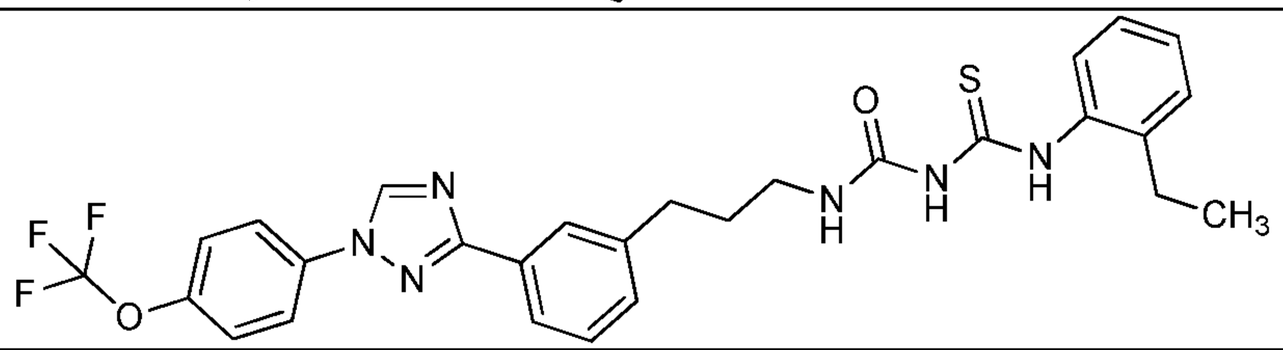
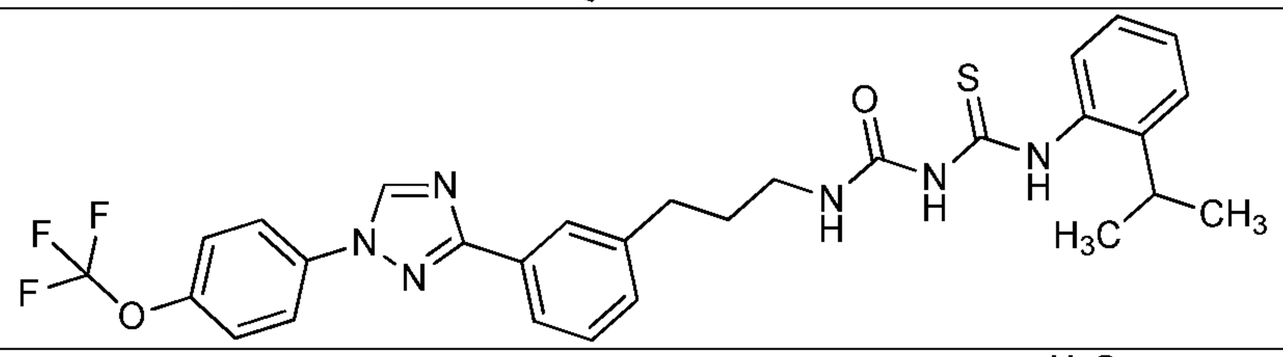
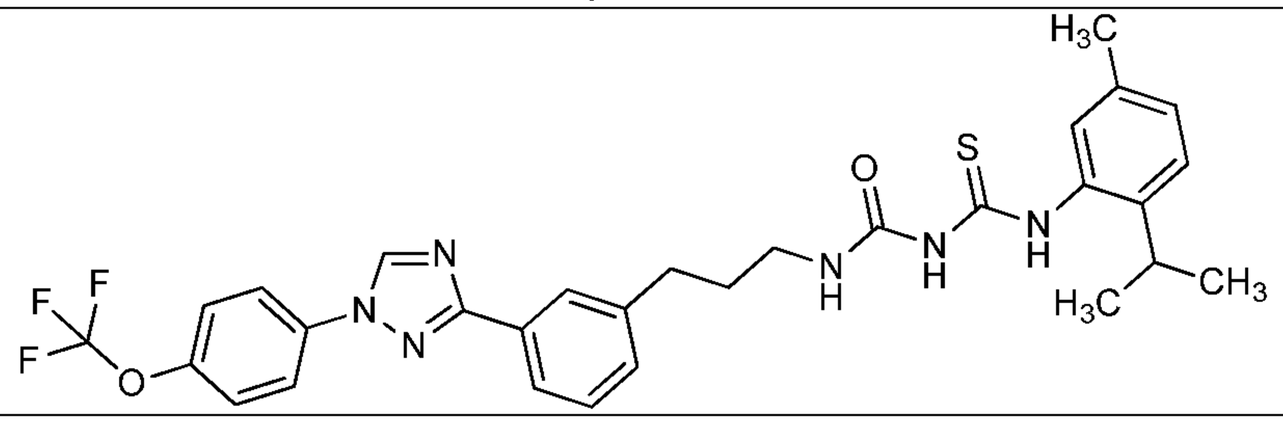
Table 1B: Structures for Intermediates (PC)

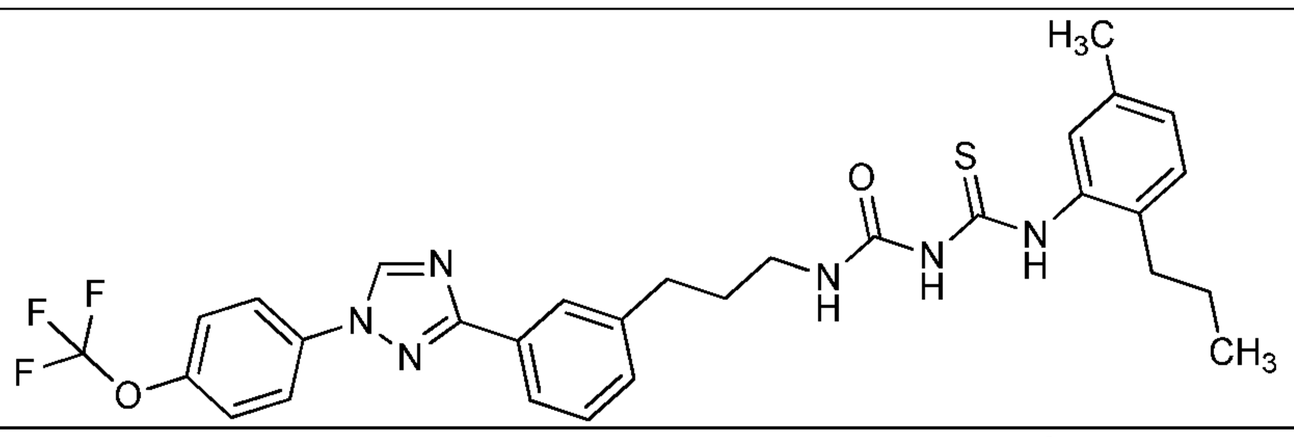
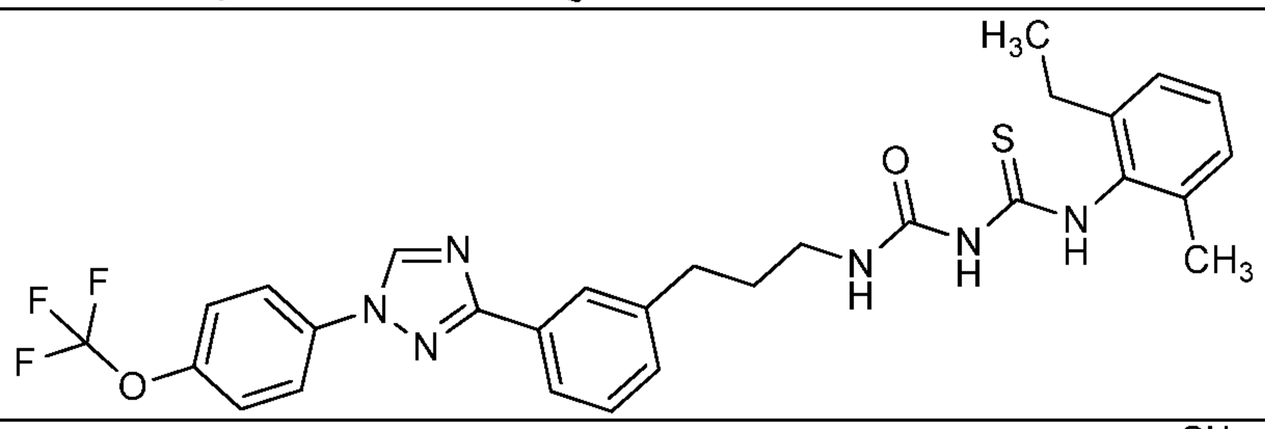
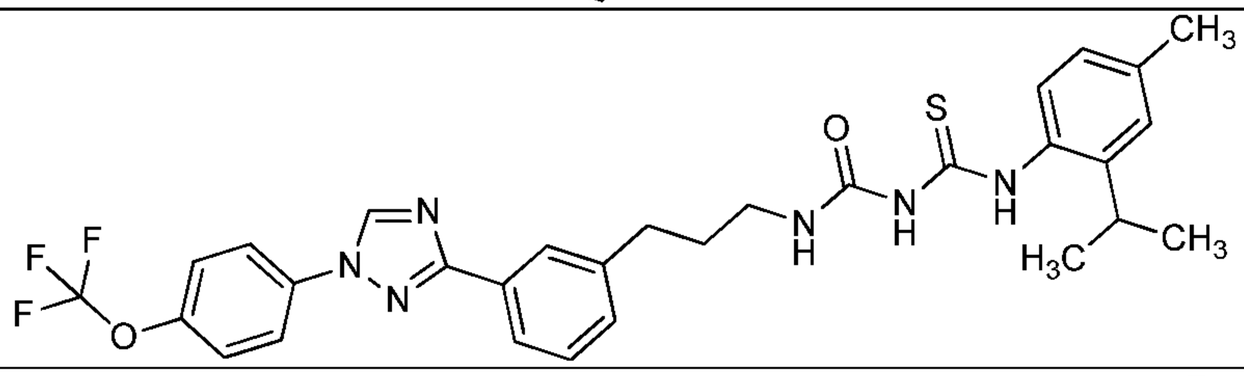
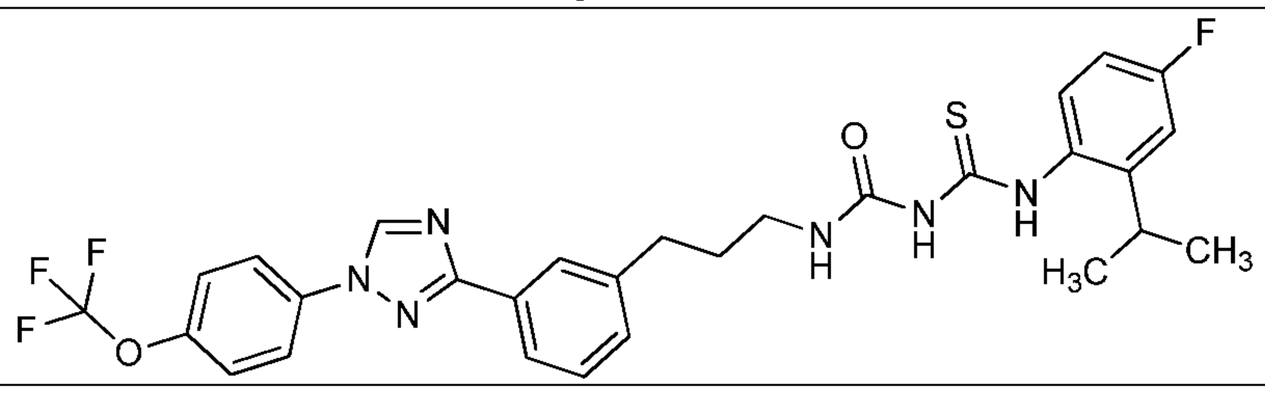
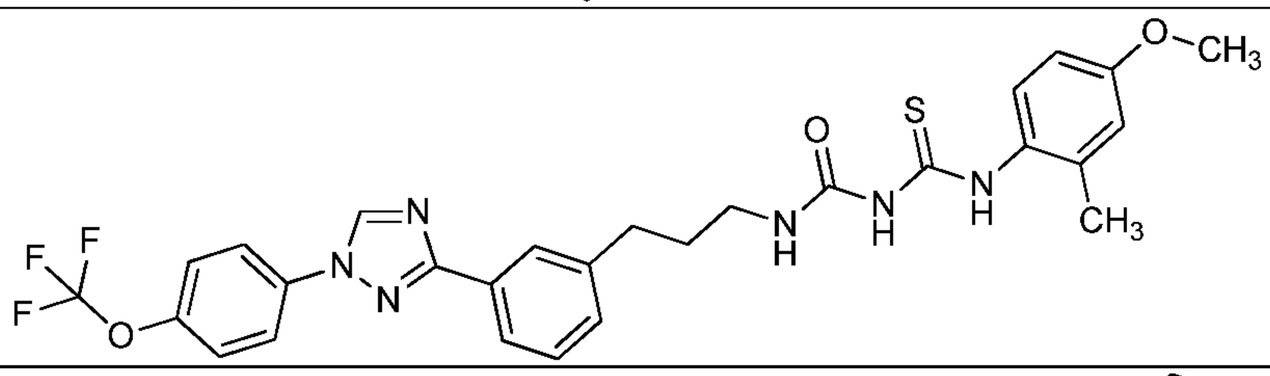
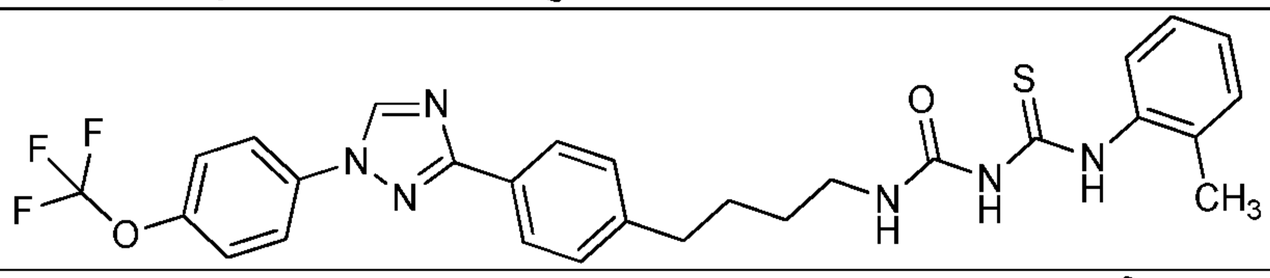
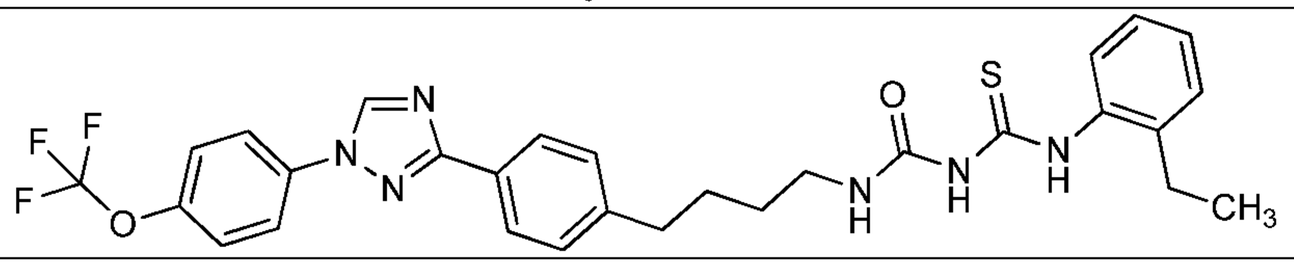
No.	Preparation	Structure
PC1	**Ex 71**	
PC2	**Ex 71**	

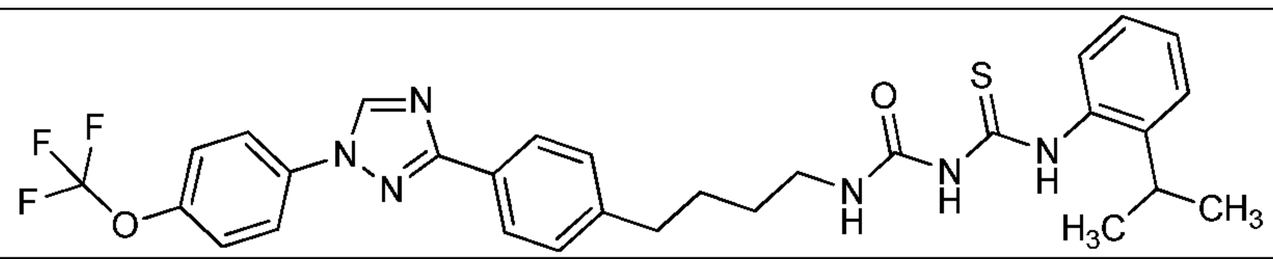
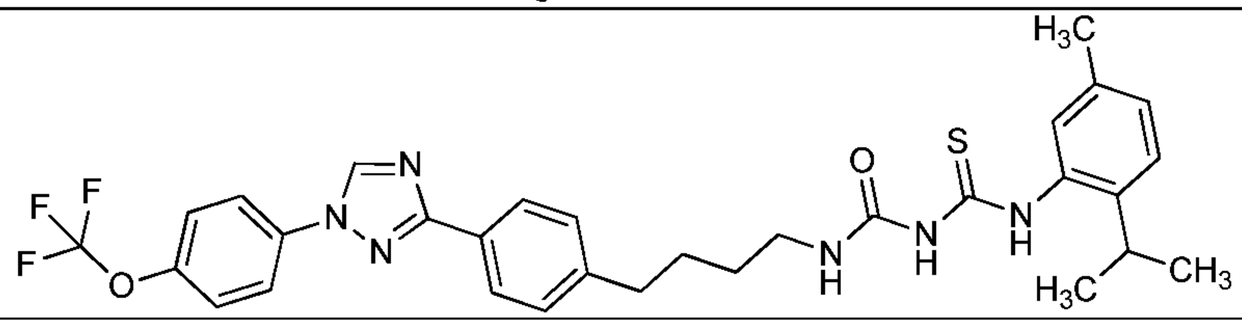
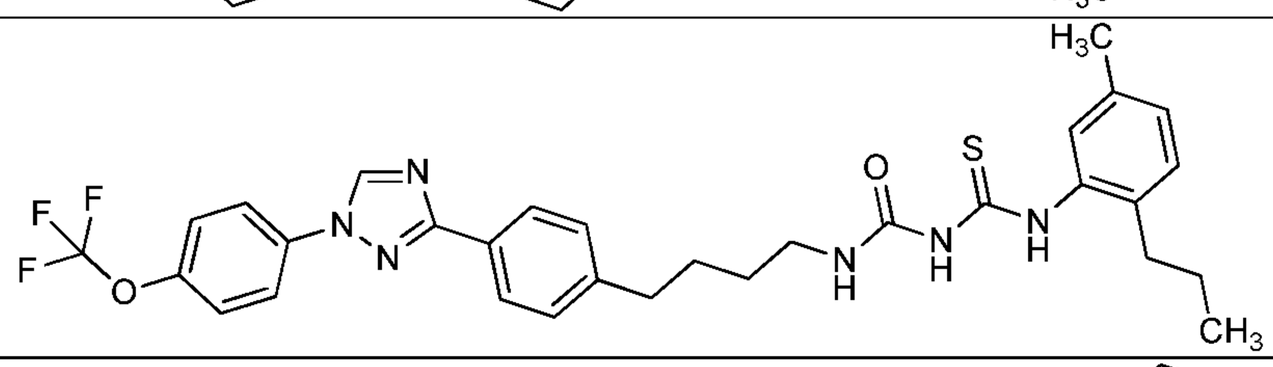
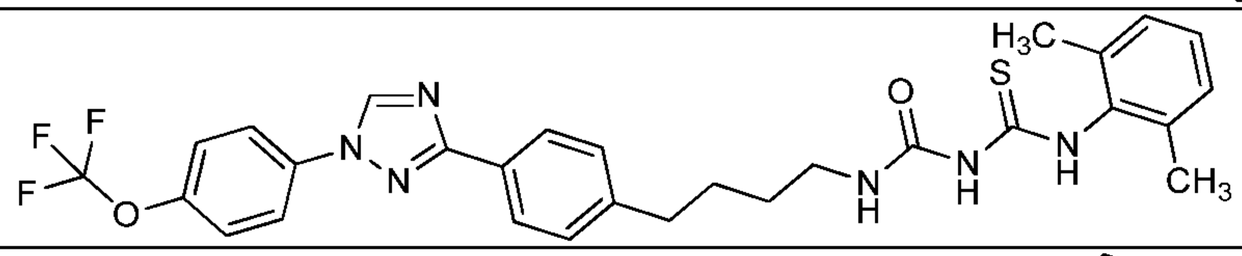
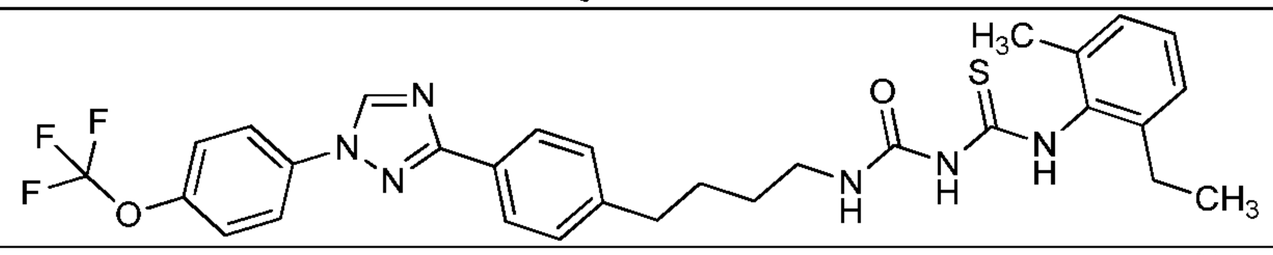
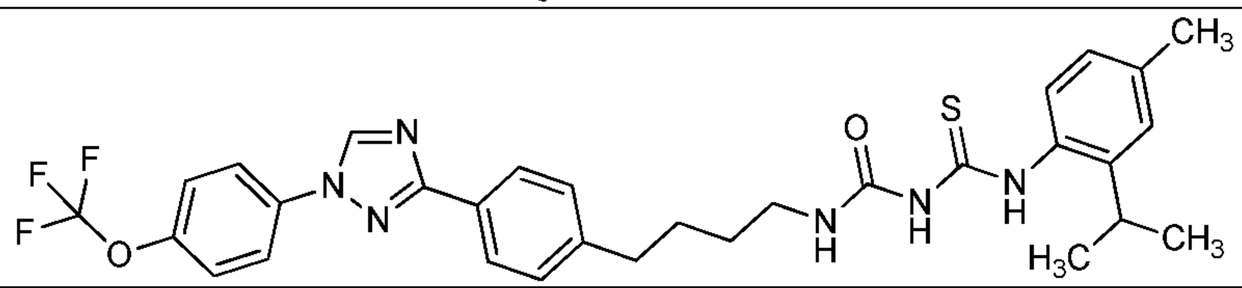
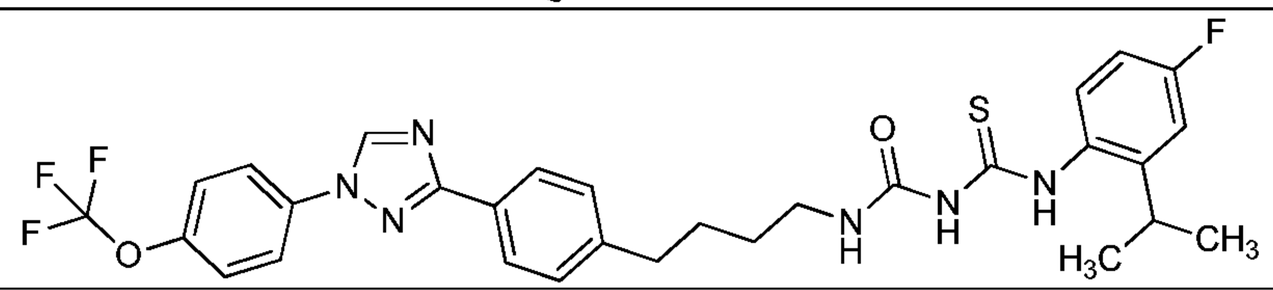
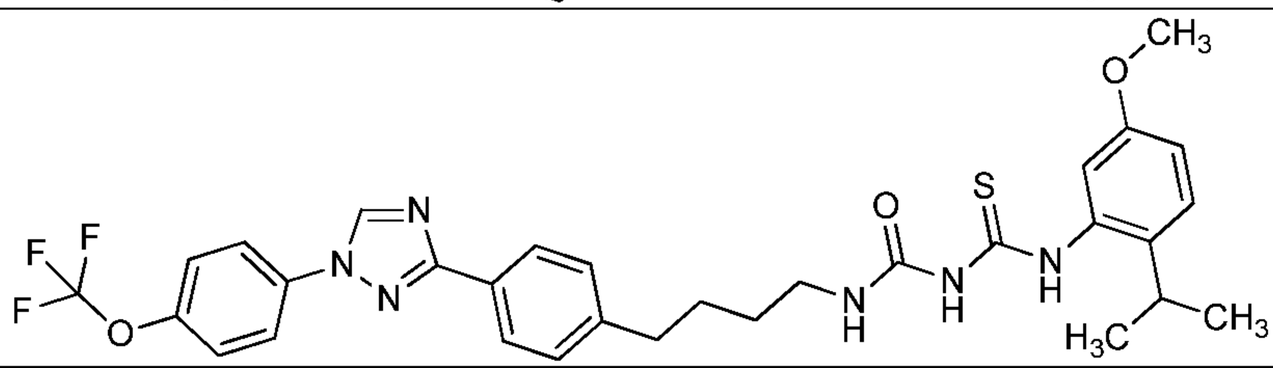
PC3	**Ex 71**	
PC5	**Ex 71**	
PC6	**Ex 71**	
PC7	**Ex 71**	
PC8	**Ex 71**	
PC14	**Ex 71**	
PC15	**Ex 71**	

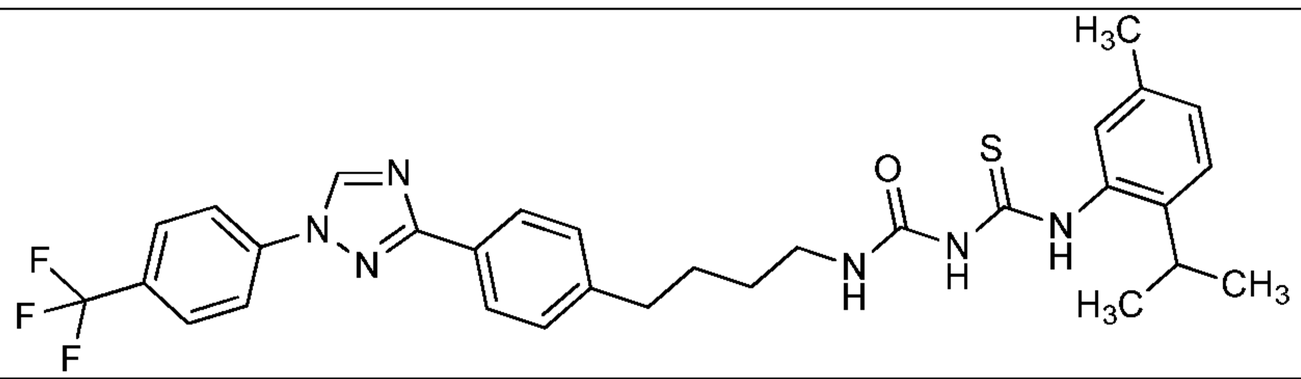
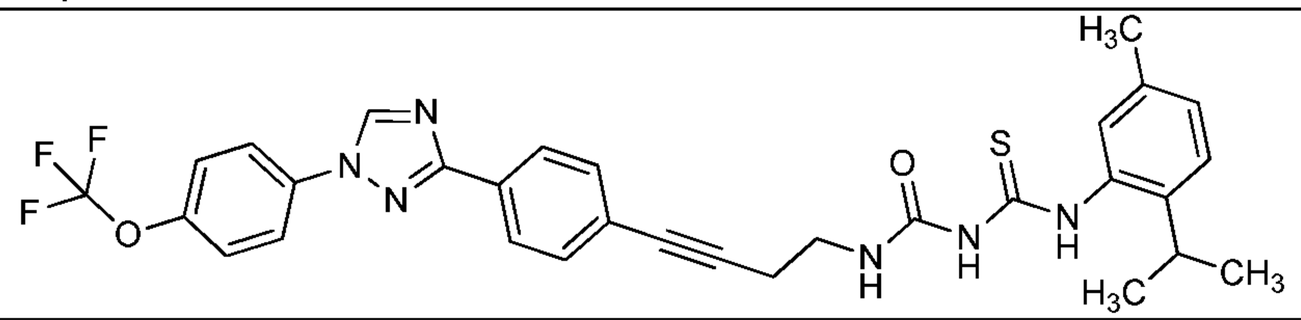
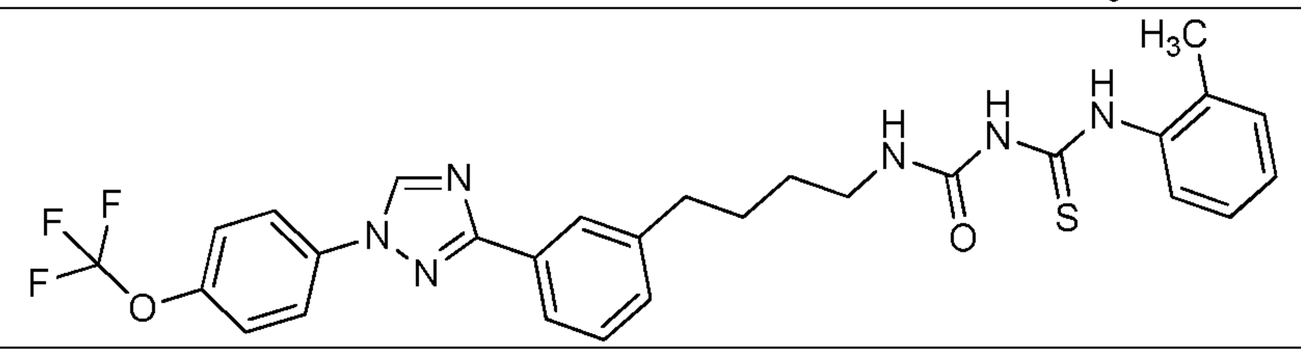
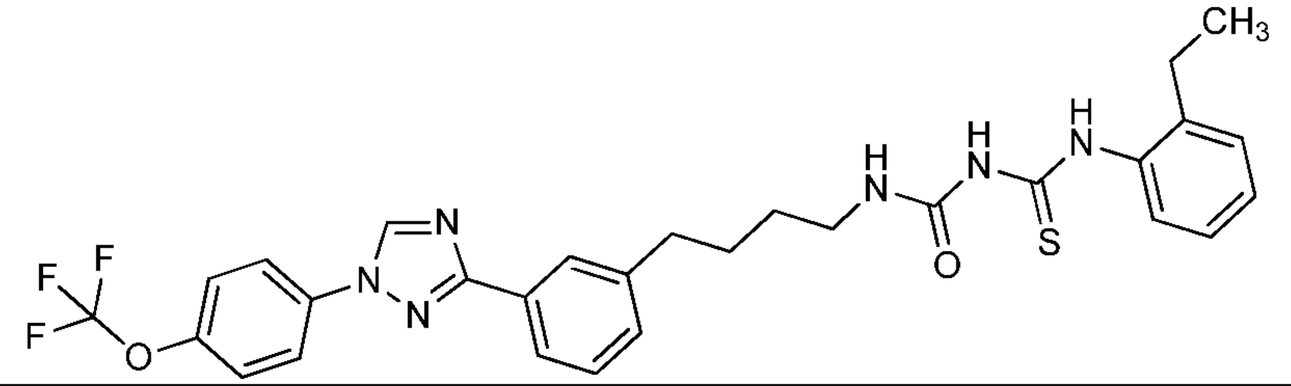
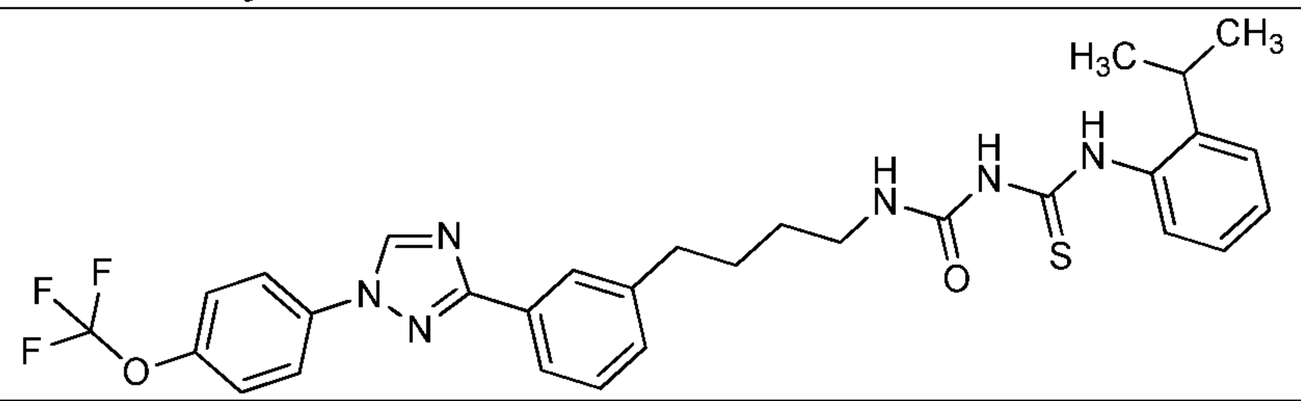
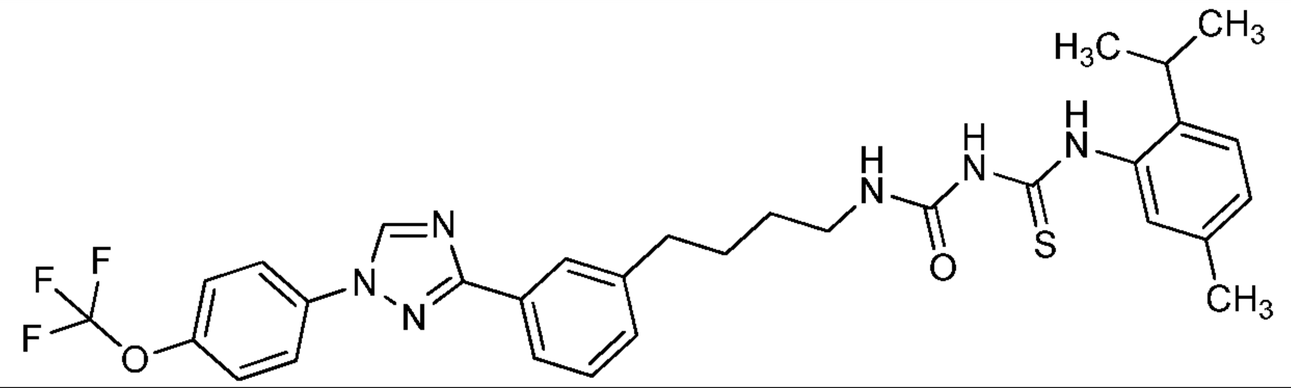
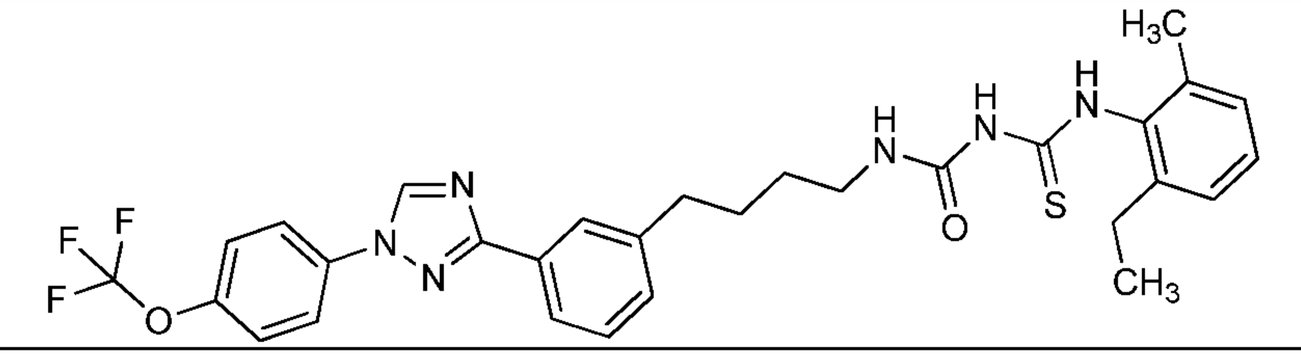
PC16	**Ex 71**	
PC74	**Ex 75**	
PC75	**Ex 75**	
PC76	**Ex 75**	
PC80	**Ex 75**	
PC81	**Ex 75**	
PC83	**Ex 75**	

PC84	**Ex 75**	
PC85	**Ex 75**	
PC87	**Ex 75**	
PC92	**Ex 63**	
PC93	**Ex 63**	
PC94	**Ex 63**	
PC99	**Ex 63**	
PC101	**Ex 63**	

PC102	**Ex 63**	
PC103	**Ex 63**	
PC105	**Ex 63**	
PC118	**Ex 63**	
PC119	**Ex 63**	
PC120	**Ex 63**	
PC124	**Ex 63**	

PC125	**Ex 63**	
PC127	**Ex 63**	
PC128	**Ex 63**	
PC129	**Ex 63**	
PC131	**Ex 63**	
PC144	**Ex 63**	
PC145	**Ex 63**	

PC146	**Ex 63**	
PC150	**Ex 63**	
PC151	**Ex 63**	
PC152	**Ex 63**	
PC153	**Ex 63**	
PC154	**Ex 63**	
PC155	**Ex 63**	
PC156	**Ex 63**	

PC159	**Ex 63**	
PC160	**Ex 63**	
PC170	**Ex 63**	
PC171	**Ex 63**	
PC172	**Ex 63**	
PC176	**Ex 63**	
PC179	**Ex 63**	

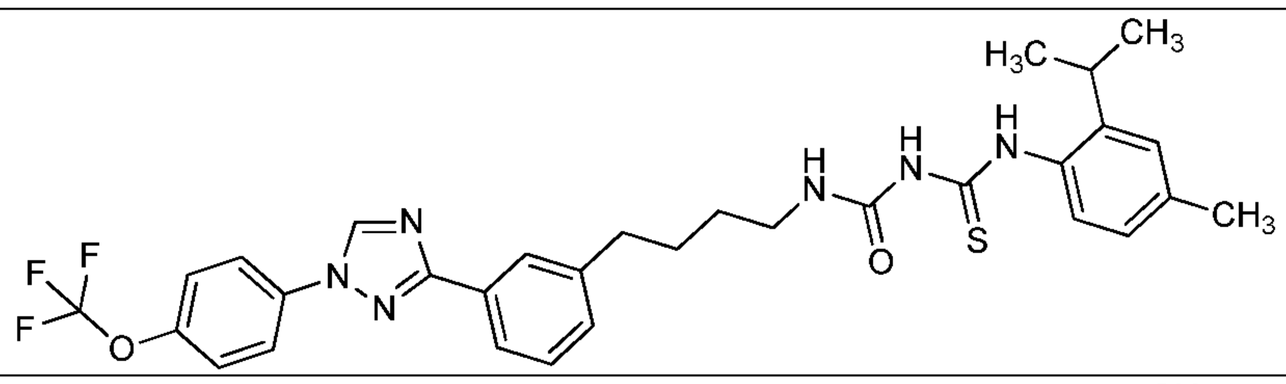
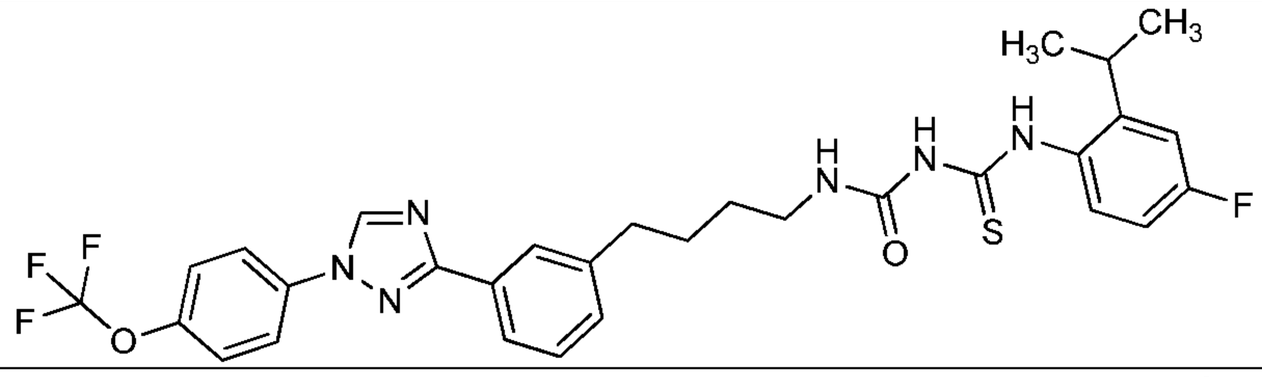
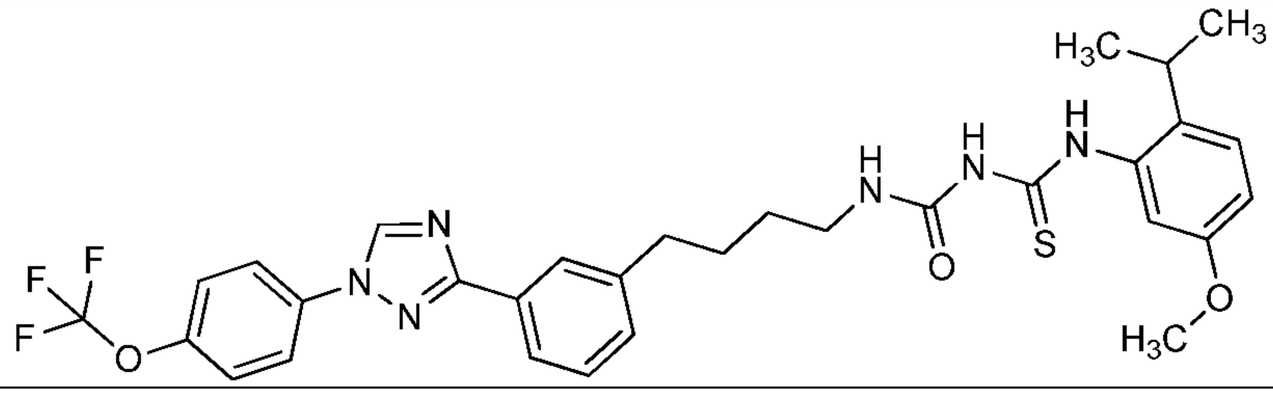
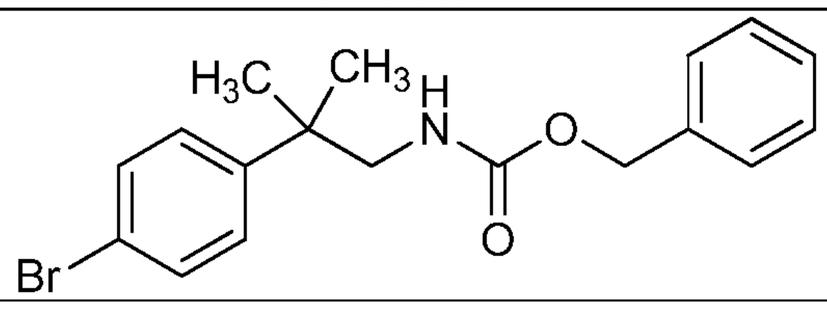
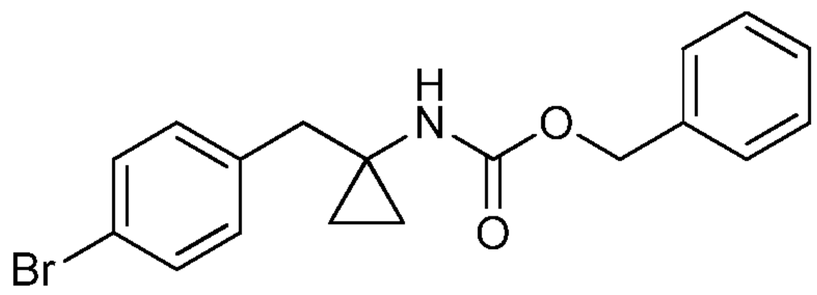
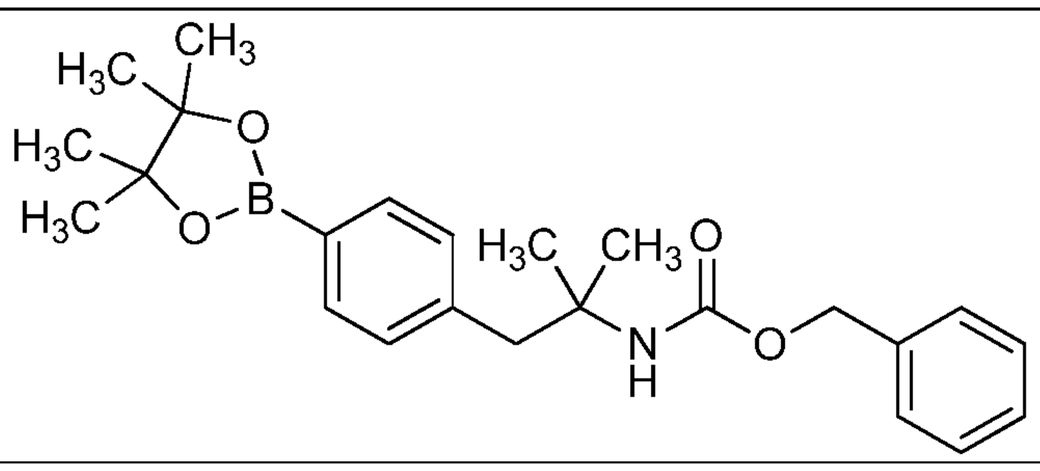
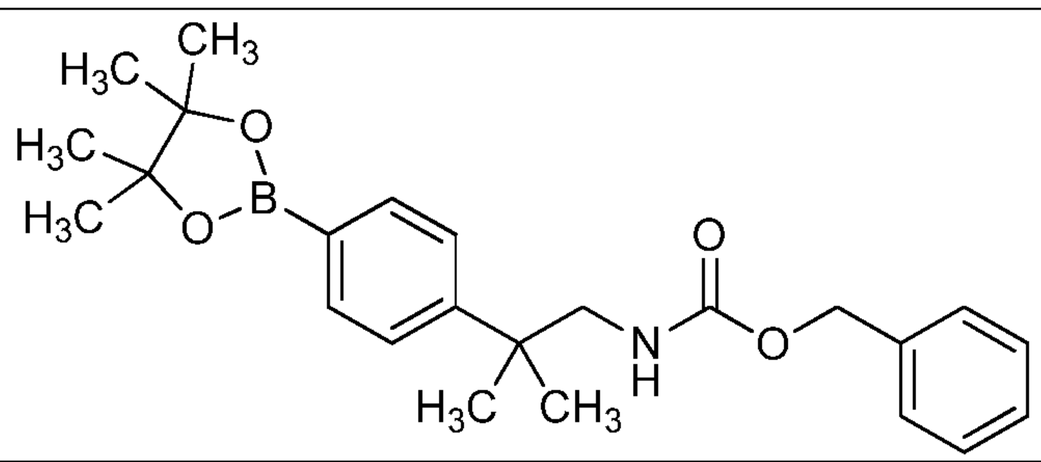
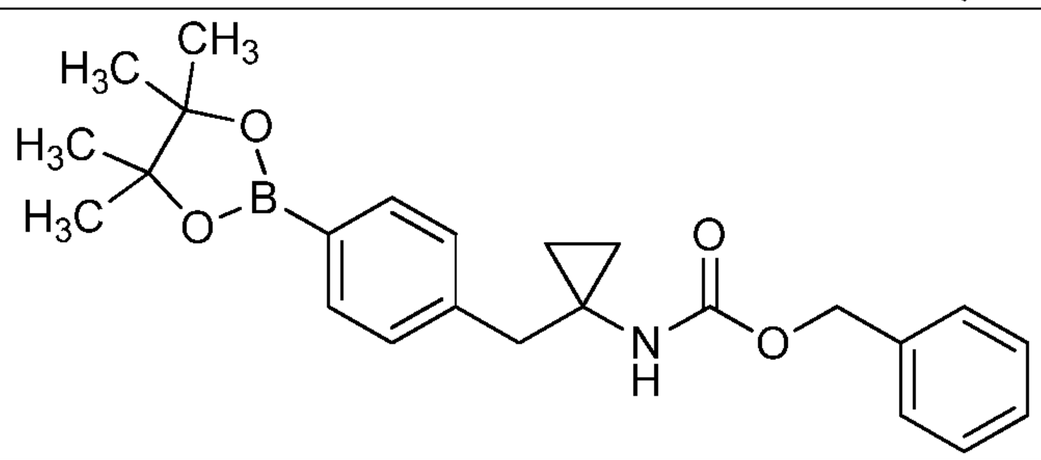
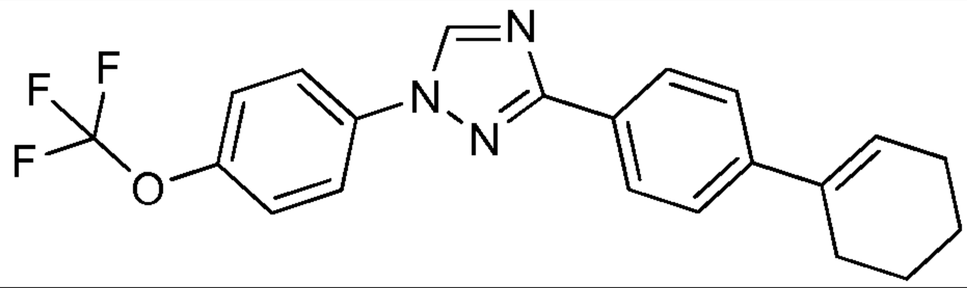
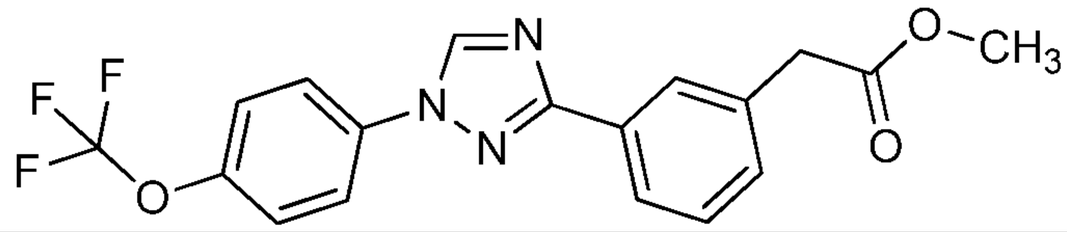
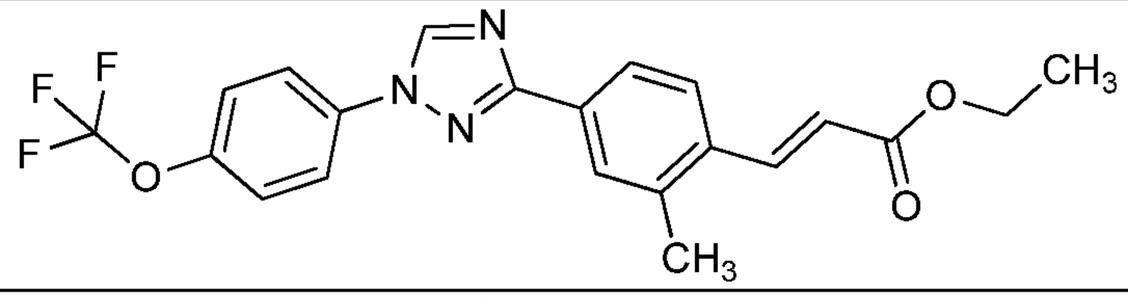
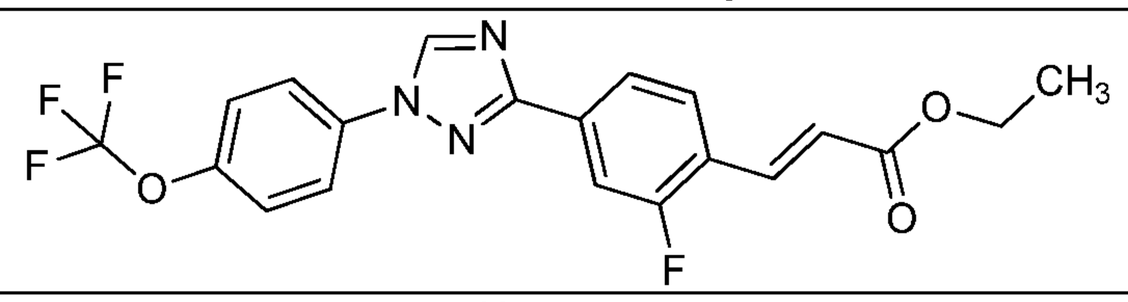
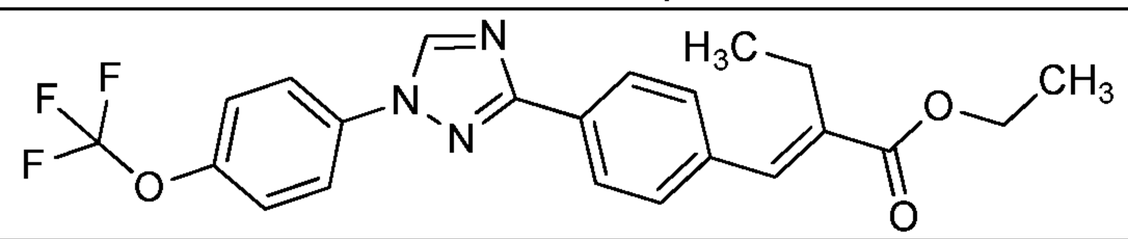
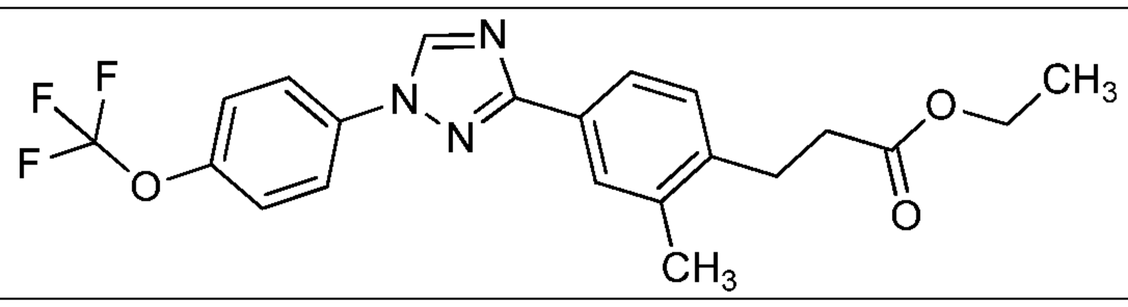
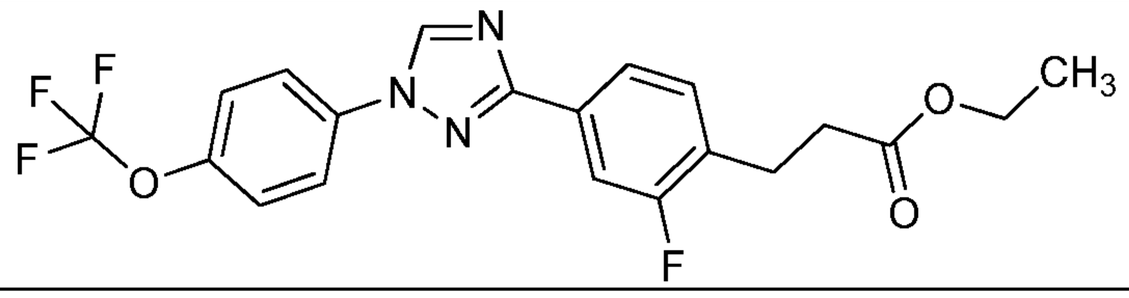
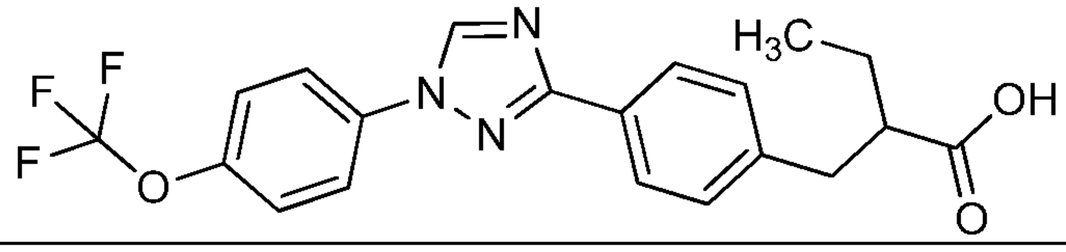
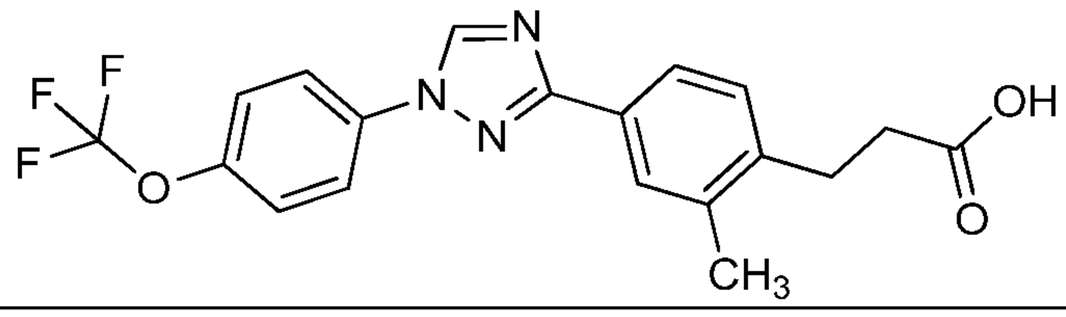
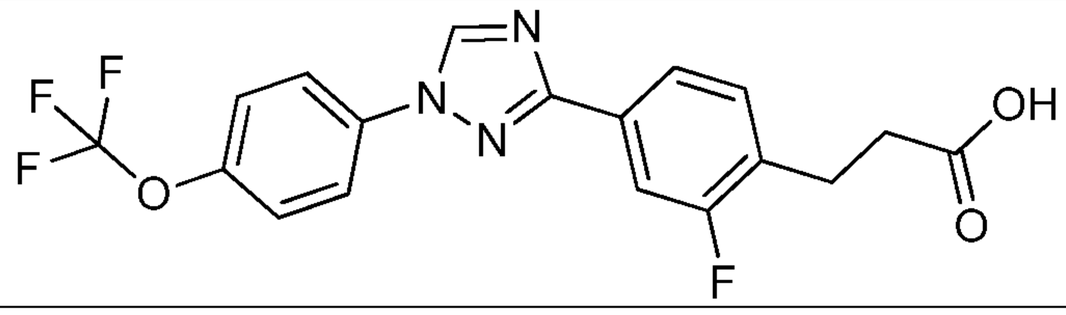
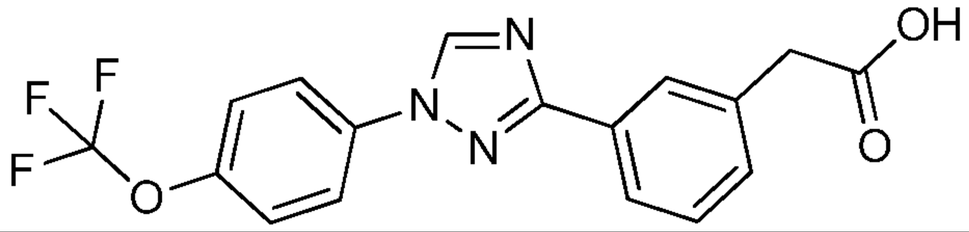
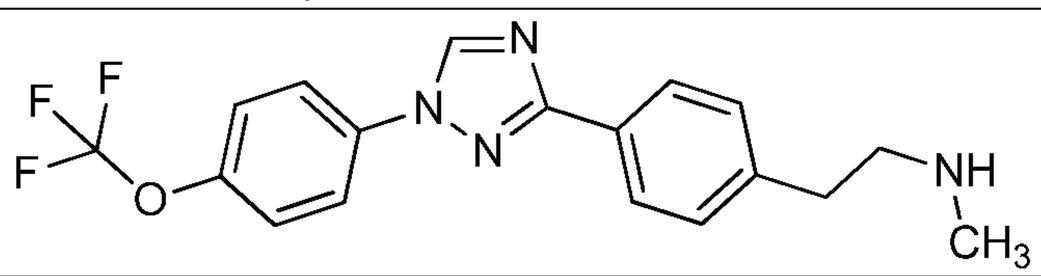
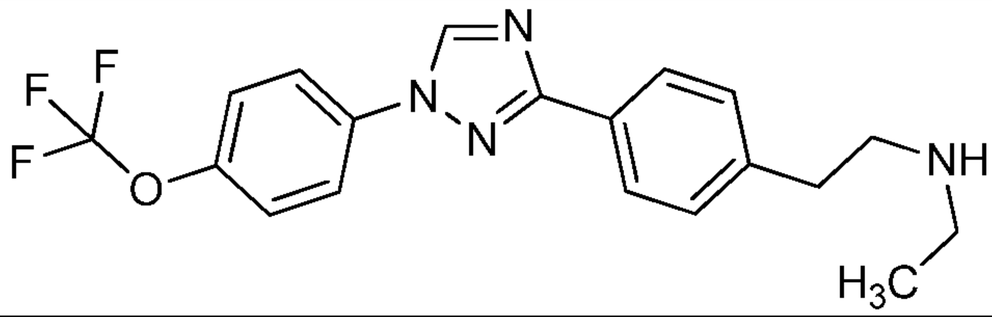
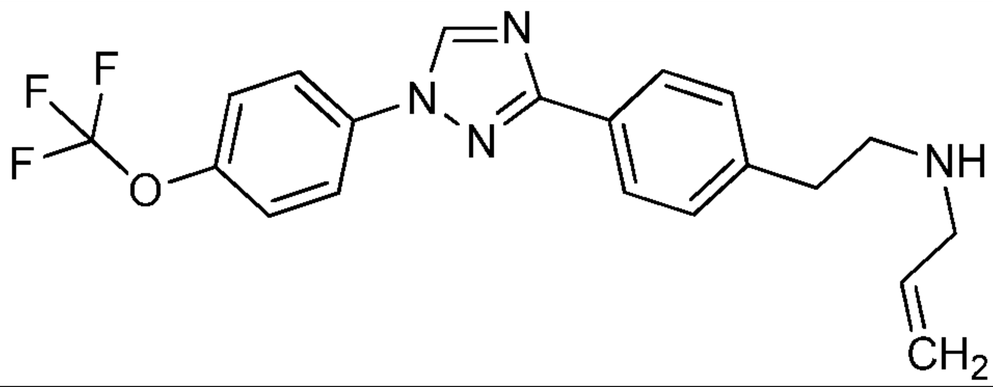
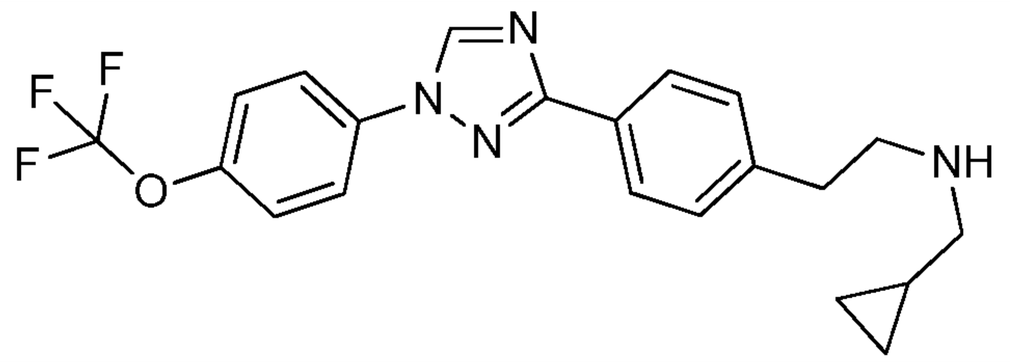
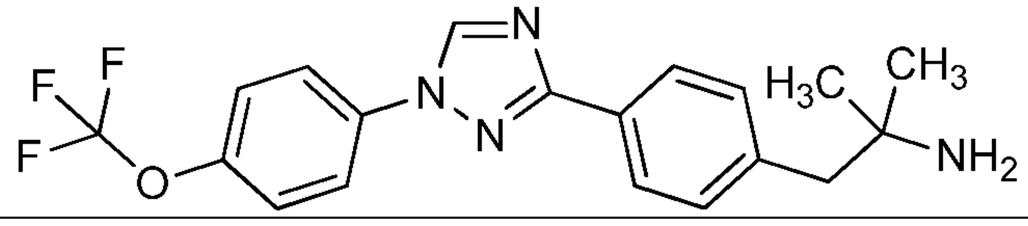
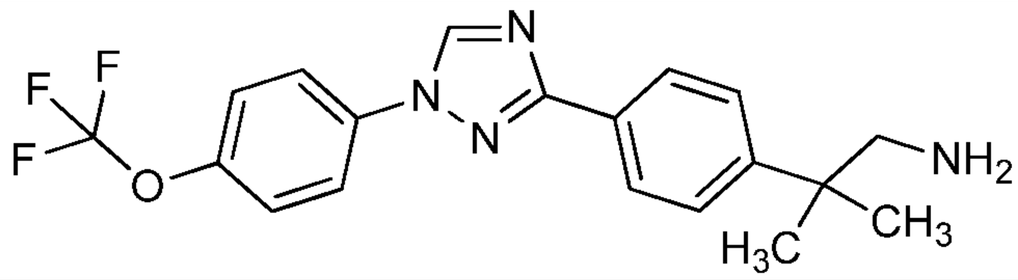
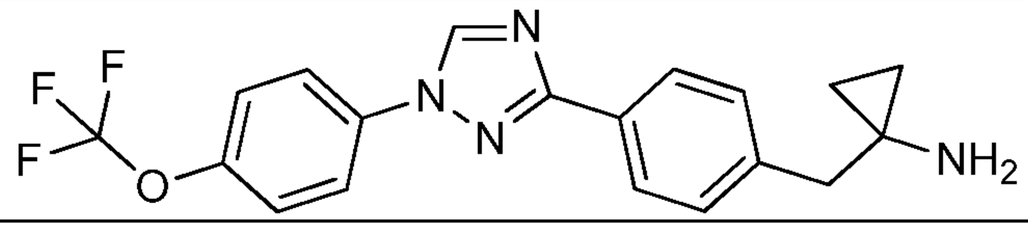
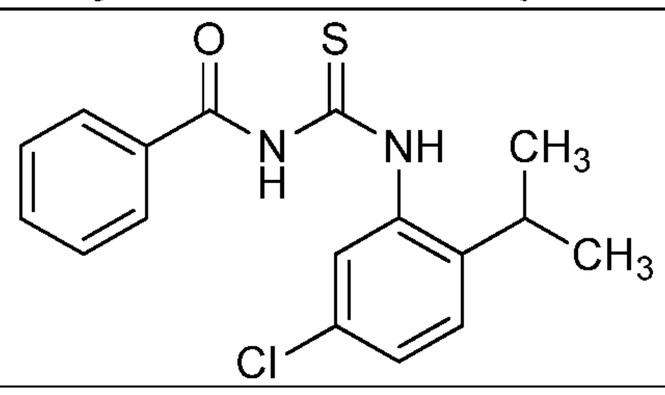
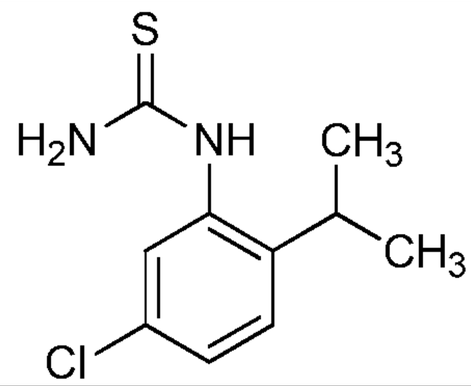
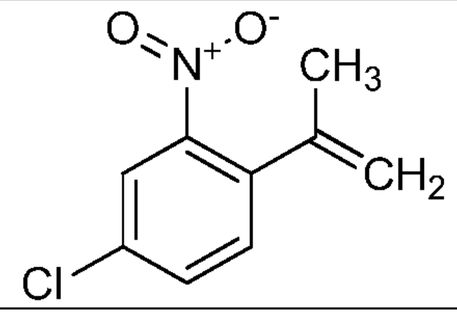
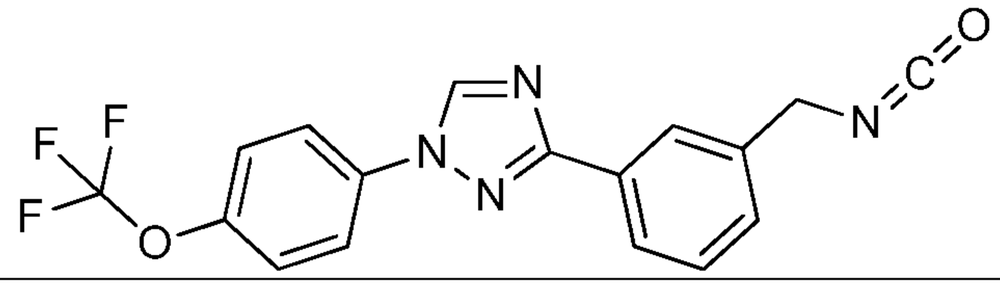
PC180	**Ex 63**	
PC181	**Ex 63**	
PC182	**Ex 63**	

Table 1C: Structures for Intermediates (CB)

No.	Preparation	Structure
CB2	**Ex 8**	
CB3	**Ex 8**	
CB7	**Ex 9**	

CB8	**Ex 9**	
CB9	**Ex 9**	
CB10	**Ex 10**	
CB11	**Ex 10**	
CB12	**Ex 13**	
CB13	**Ex 13**	
CB14	**Ex 13**	
CB15	**Ex 30**	

CB16	**Ex 30**	
CB17	**Ex 30**	
CB18	**Ex 31**	
CB19	**Ex 31**	
CB23	**Ex 51**	
CB24	**Ex 58**	
CB25	**Ex 58**	
CB26	**Ex 58**	

CB27	**Ex 58**	
CB28	**Ex 66**	
CB29	**Ex 66**	
CB30	**Ex 66**	
CB31	**Ex 68**	
CB32	**Ex 69**	
CB33	**Ex 70**	
CB34	**Ex 74**	

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 503

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 503

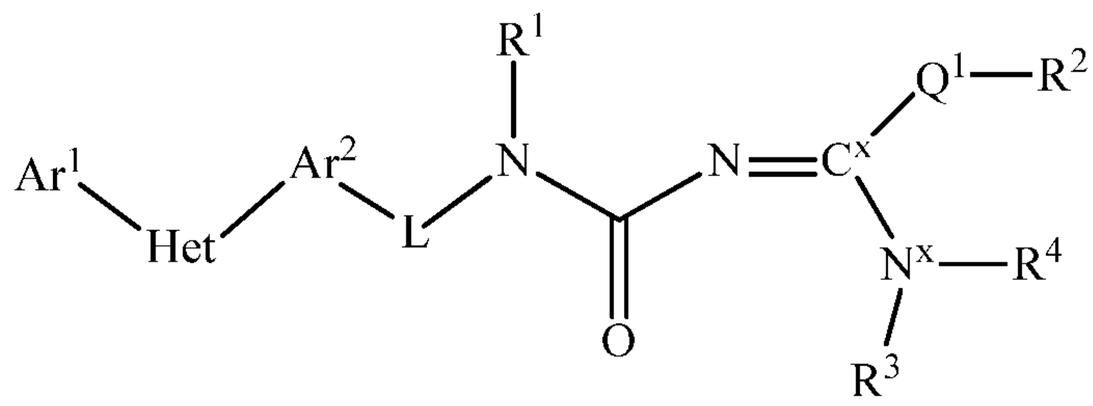
NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

WE CLAIM

1. A molecule having the following formula ("**Formula One**")



Formula One

and tautomers thereof, wherein:

wherein:

(A) Ar^1 is selected from

(1) phenyl, pyridazinyl, pyridyl, pyrimidinyl, or

(2) substituted phenyl, substituted pyridazinyl, substituted pyridyl, or substituted pyrimidinyl,

wherein said substituted phenyl, substituted pyridazinyl, substituted pyridyl, and substituted pyrimidinyl, have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6

alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, and phenoxy;

(B) Het is a 5- or 6-membered, saturated or unsaturated, heterocyclic ring, containing one or more heteroatoms independently selected from nitrogen, sulfur, or oxygen, and where Ar^1 and Ar^2 are not *ortho* to each other (but may be *meta* or *para*, such as, for a five-membered ring they are 1,3 and for a 6-membered ring they are either 1,3 or 1,4) and where said heterocyclic ring may also be substituted with one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n$(C_1-C_6 alkyl), $S(=O)_n$(C_1-C_6 haloalkyl), OSO_2(C_1-C_6 alkyl), OSO_2(C_1-C_6 haloalkyl), C(=O)NR^xR^y, (C_1-C_6 alkyl)NR^xR^y, C(=O)(C_1-C_6 alkyl), C(=O)O(C_1-C_6 alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), C(=O)(C_1-C_6 alkyl)C(=O)O(C_1-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n$(C_1-C_6 alkyl), $S(=O)_n$(C_1-C_6 haloalkyl), OSO_2(C_1-C_6 alkyl), OSO_2(C_1-C_6 haloalkyl), C(=O)H, C(=O)NR^xR^y, (C_1-C_6 alkyl)NR^xR^y, C(=O)(C_1-C_6 alkyl), C(=O)O(C_1-C_6 alkyl), C(=O)(C_1-C_6 haloalkyl), C(=O)O(C_1-C_6 haloalkyl), C(=O)(C_3-C_6 cycloalkyl), C(=O)O(C_3-C_6 cycloalkyl), C(=O)(C_2-C_6 alkenyl), C(=O)O(C_2-C_6 alkenyl), (C_1-C_6 alkyl)O(C_1-C_6 alkyl), (C_1-C_6 alkyl)S(C_1-C_6 alkyl), phenyl, and phenoxy;

(C) Ar^2 is selected from

(1) phenyl, pyridazinyl, pyridyl, pyrimidinyl, or

(2) substituted phenyl, substituted pyridazinyl, substituted pyridyl, or substituted pyrimidinyl,

wherein said substituted phenyl, substituted pyridazinyl, substituted pyridyl, and substituted pyrimidinyl, have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, and phenoxy;

(D) R^1 is selected from H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$OC(=O)(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), and (C_1-C_6 alkyl)$OC(=O)O(C_1$-C_6 alkyl),

wherein each alkyl, cycloalkyl, cycloalkoxy, alkoxy, alkenyl, and alkynyl are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl),

$OSO_2(C_1\text{-}C_6$ haloalkyl), $C(=O)NR^xR^y$, $(C_1\text{-}C_6$ alkyl$)NR^xR^y$, $C(=O)(C_1\text{-}C_6$ alkyl), $C(=O)O(C_1\text{-}C_6$ alkyl), $C(=O)(C_1\text{-}C_6$ haloalkyl), $C(=O)O(C_1\text{-}C_6$ haloalkyl), $C(=O)(C_3\text{-}C_6$ cycloalkyl), $C(=O)O(C_3\text{-}C_6$ cycloalkyl), $C(=O)(C_2\text{-}C_6$ alkenyl), $C(=O)O(C_2\text{-}C_6$ alkenyl), $(C_1\text{-}C_6$ alkyl$)O(C_1\text{-}C_6$ alkyl), $(C_1\text{-}C_6$ alkyl$)S(C_1\text{-}C_6$ alkyl), $C(=O)(C_1\text{-}C_6$ alkyl$)C(=O)O(C_1\text{-}C_6$ alkyl), phenyl, and phenoxy;

(E) R^2 is selected from **(J)**, H, $C_1\text{-}C_6$ alkyl, $C_3\text{-}C_6$ cycloalkyl, $C_2\text{-}C_6$ alkenyl, $C_2\text{-}C_6$ alkynyl, $C(=O)(C_1\text{-}C_6$ alkyl), $(C_1\text{-}C_6$ alkyl$)O(C_1\text{-}C_6$ alkyl), $(C_1\text{-}C_6$ alkyl$)S(C_1\text{-}C_6$ alkyl), $C_1\text{-}C_6$ alkylphenyl, $C_1\text{-}C_6$ alkyl-O-phenyl, C(=O)(Het-1), (Het-1), $(C_1\text{-}C_6$ alkyl)-(Het-1), $C_1\text{-}C_6$ alkyl-O-$C(=O)C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl-O-$C(=O)(C_1\text{-}C_6$ alkyl), $C_1\text{-}C_6$ alkyl-O-$C(=O)OC_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl-O-$C(=O)NR^xR^y$, $C_1\text{-}C_6$ alkyl $C(=O)N(R^x)C_1\text{-}C_6$ alkyl-(Het-1), $C_1\text{-}C_6$ alkyl$C(=O)$(Het-1), $C_1\text{-}C_6$ alkyl$C(=O)N(R^x)C_1\text{-}C_6$ alkyl$(N(R^x)(R^y))(C(=O)OH)$, $C_1\text{-}C_6$ alkyl$C(=O)N(R^x)C_1\text{-}C_6$ alkyl$N(R^x)(R^y)$, $C_1\text{-}C_6$ alkyl$C(=O)N(R^x)C_1\text{-}C_6$ alkyl$N(R^x)C(=O)$-O-$C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl$C(=O)N(R^x)C_1\text{-}C_6$ alkyl$(N(R^x)C(=O)$-O-$C_1\text{-}C_6$ alkyl$)(C(=O)OH)$, $C_1\text{-}C_6$ alkyl$C(=O)$(Het-1)$C(=O)$-O-$C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl-O-$C(=O)$-O-$C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl-O-$C(=O)C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl-O-$C(=O)C_3\text{-}C_6$ cycloalkyl, $C_1\text{-}C_6$ alkyl-O-$C(=O)$(Het-1), $C_1\text{-}C_6$ alkyl-O-$C(=O)C_1\text{-}C_6$ alkyl-$N(R^x)C(=O)$-O-$C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkyl-NR^xR^y, $(C_1\text{-}C_6$ alkyl$)S$-(Het-1) or $C_1\text{-}C_6$ alkyl-O-(Het-1),

wherein each alkyl, cycloalkyl, alkenyl, alkynyl, phenyl, and (Het-1) are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, NR^xR^y, $C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ haloalkyl, $C_3\text{-}C_6$ cycloalkyl, $C_3\text{-}C_6$ halocycloalkyl, $C_3\text{-}C_6$ cycloalkoxy, $C_3\text{-}C_6$ halocycloalkoxy, $C_1\text{-}C_6$ alkoxy, $C_1\text{-}C_6$ haloalkoxy, $C_2\text{-}C_6$ alkenyl, $C_3\text{-}C_6$ cycloalkenyl, $C_2\text{-}C_6$ alkynyl, $S(=O)_n(C_1\text{-}C_6$ alkyl), $S(=O)_n(C_1\text{-}C_6$ haloalkyl), $OSO_2(C_1\text{-}C_6$ alkyl), $OSO_2(C_1\text{-}C_6$ haloalkyl), C(=O)H, C(=O)OH, $C(=O)NR^xR^y$, $(C_1\text{-}C_6$ alkyl$)NR^xR^y$, $C(=O)(C_1\text{-}C_6$ alkyl), $C(=O)O(C_1\text{-}C_6$ alkyl), $C(=O)(C_1\text{-}C_6$ haloalkyl), $C(=O)O(C_1\text{-}C_6$ haloalkyl), $C(=O)(C_3\text{-}C_6$ cycloalkyl), $C(=O)O(C_3\text{-}C_6$ cycloalkyl), $C(=O)(C_2\text{-}C_6$ alkenyl), $C(=O)O(C_2\text{-}C_6$ alkenyl), $(C_1\text{-}C_6$ alkyl$)O(C_1\text{-}C_6$ alkyl), $(C_1\text{-}C_6$ alkyl$)S(C_1\text{-}C_6$ alkyl), $C(=O)(C_1\text{-}C_6$ alkyl$)C(=O)O(C_1\text{-}C_6$ alkyl), phenyl, phenoxy, $Si(C_1\text{-}C_6$ alkyl$)_3$, $S(=O)_nNR^xR^y$, or (Het-1);

(F) R^3 is selected from phenyl, $C_1\text{-}C_6$ alkylphenyl, $C_1\text{-}C_6$ alkyl-O-phenyl, $C_2\text{-}C_6$ alkenyl-O-phenyl, (Het-1), $C_1\text{-}C_6$ alkyl(Het-1), or $C_1\text{-}C_6$ alkyl-O-(Het-1),

wherein each alkyl, cycloalkyl, alkenyl, alkynyl, phenyl, and (Het-1) are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, NR^xR^y, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), $O(C_1$-C_6 alkyl), $S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, and (Het-1);

(G) R^4 is selected from **(J)**, H, or C_1-C_6 alkyl;

(H) Q^1 is selected from O or S,

(I) R^x and R^y are independently selected from H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), and phenyl,

wherein each alkyl, cycloalkyl, cycloalkoxy, alkoxy, alkenyl, alkynyl, phenyl, phenoxy, and (Het-1), are optionally substituted with one or more substituents independently selected from F, Cl, Br, I, CN, NO_2, OH, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, C(=O)OH, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, halophenyl, phenoxy, and (Het-1),

or R^x and R^y together can optionally form a 5- to 7-membered saturated or unsaturated cyclic group which may contain one or more heteroatoms selected from nitrogen, sulfur, and oxygen, and where said cyclic group may be substituted with F, Cl, Br, I, CN, oxo, thioxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, substituted phenyl, phenoxy, and (Het-1);

(J) R^2 and R^4 may be a 1- to 4-membered saturated or unsaturated, hydrocarbyl link, which may contain one or more heteroatoms selected from nitrogen, sulfur, and oxygen, and together with $C^x(Q^1)(N^x)$ forms a cyclic structure, wherein said hydrocarbyl link may optionally be substituted with one or more substituents independently selected from R^5, R^6, and R^7, wherein each R^5, R^6, and R^7 is selected from H, F, Cl, Br, I, CN, OH, C_1-C_6 alkyl, oxo, thioxo, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, substituted phenyl, phenoxy, or (Het-1);

(K) (Het-1) is a 5- or 6-membered, saturated or unsaturated, heterocyclic ring, containing one or more heteroatoms independently selected from nitrogen, sulfur or oxygen, wherein said heterocyclic ring may also be substituted with one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6

halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 alkyl)$C(=O)O(C_1$-C_6 alkyl), phenyl, phenoxy, substituted phenyl and substituted phenoxy,

wherein such substituted phenyl and substituted phenoxy have one or more substituents independently selected from H, F, Cl, Br, I, CN, NO_2, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 halocycloalkyl, C_3-C_6 cycloalkoxy, C_3-C_6 halocycloalkoxy, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $S(=O)_n(C_1$-C_6 alkyl), $S(=O)_n(C_1$-C_6 haloalkyl), $OSO_2(C_1$-C_6 alkyl), $OSO_2(C_1$-C_6 haloalkyl), C(=O)H, $C(=O)NR^xR^y$, (C_1-C_6 alkyl)NR^xR^y, $C(=O)(C_1$-C_6 alkyl), $C(=O)O(C_1$-C_6 alkyl), $C(=O)(C_1$-C_6 haloalkyl), $C(=O)O(C_1$-C_6 haloalkyl), $C(=O)(C_3$-C_6 cycloalkyl), $C(=O)O(C_3$-C_6 cycloalkyl), $C(=O)(C_2$-C_6 alkenyl), $C(=O)O(C_2$-C_6 alkenyl), (C_1-C_6 alkyl)$O(C_1$-C_6 alkyl), (C_1-C_6 alkyl)$S(C_1$-C_6 alkyl), phenyl, and phenoxy;

(L) L is linker selected from

(1) a saturated or unsaturated, substituted or unsubstituted, linear (C_1-C_4)hydrocarbyl linker, or

(2) a saturated or unsaturated, substituted or unsubstituted, cyclic (C_3-C_8)hydrocarbyl group linker,

wherein each of said linkers connects Ar^2 to N^Y and

wherein said substituted linear (C_1-C_4)hydrocarbyl linker and substituted cyclic (C_3-C_8)hydrocarbyl linker has one or more substituents independently selected from R^8, R^9, R^{10}, R^{11}, and R^{12}, wherein each R^8, R^9, R^{10}, R^{11}, and R^{12}, is selected from F, Cl, Br, I, CN, oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 haloalkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, C_3-C_6 halocycloalkyl, or phenyl; and

(M) n is each individually 0, 1, or 2.

2. A molecule according to claim 1 wherein Ar^1 is a substituted phenyl that has one or more substituents selected from C_1-C_6 haloalkyl and C_1-C_6 haloalkoxy.

3. A molecule according to claims 1 or 2 wherein Het is 1,2,4 triazolyl.

4. A molecule according to claims 1, 2, or 3 wherein Ar^2 is phenyl or a substituted phenyl wherein said substituted phenyl has one or more substituents independently selected from F, Cl, Br, I, and C_1-C_6 alkyl .

5. A molecule according to any of the proceeding claims wherein R^1 is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl, wherein said alkyl is optionally substituted with a C_3-C_6 cycloalkyl.

6. A molecule according to any of the proceeding claims wherein R^2 is **(J)**, H, or C_1-C_6 alkyl.

7. A molecule according to any of the proceeding claims wherein R^3 is phenyl, wherein said phenyl is optionally substituted with one or more substituents independently selected from F, Cl, Br, I, C_1-C_6 alkyl, and C_1-C_6 alkoxy.

8. A molecule according to any of the proceeding claims wherein R^4 is **(J),** H, or C_1-C_6 alkyl.

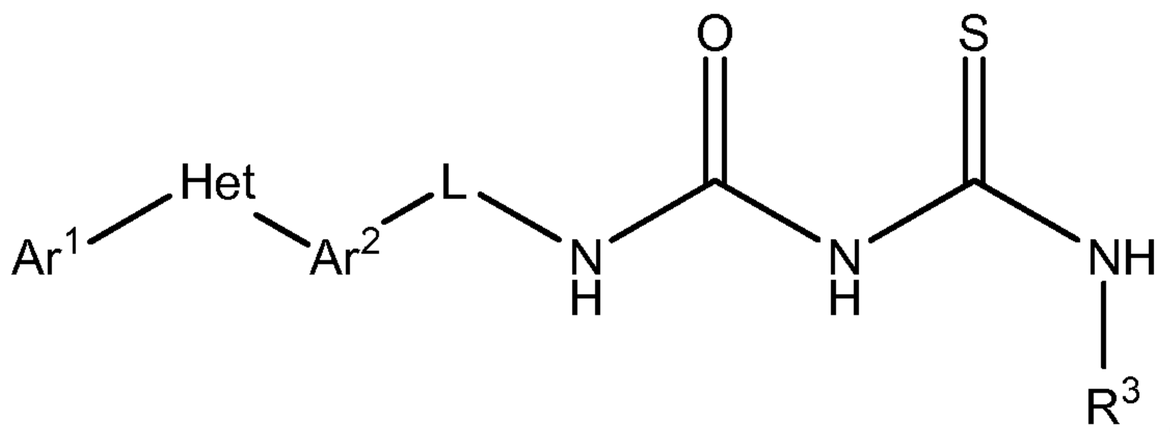
9. A molecule according to any of the proceeding claims wherein Q^1 is S.

10. A molecule according to any of the proceeding claims wherein R^2 and R^4 is a hydrocarbyl link wherein said hydrocarbyl link is substituted with $CH_2C(=O)$, $C(C(OH)(CH_3)_2)C(=O)$, $C(cyclopropyl)C(=O)$, $C(CH_3)_2C(=O)$, $CFHC(=O)$, $CBrHC(=O)$, $CH(CH_3)C(=O)$, CH_2CH_2, $CH_2C(OH)(CH_3)$, $CH_2CH_2CH_2$, $CH_2CH_2C(=O)$, $CH_2CH(CH_3)CH_2$, $N(CH_3)C(=O)$, $N(CH_2CH_3)C(=O)$, $CH=C(CH_3)$, or $CH_2CH(CH_3)$.

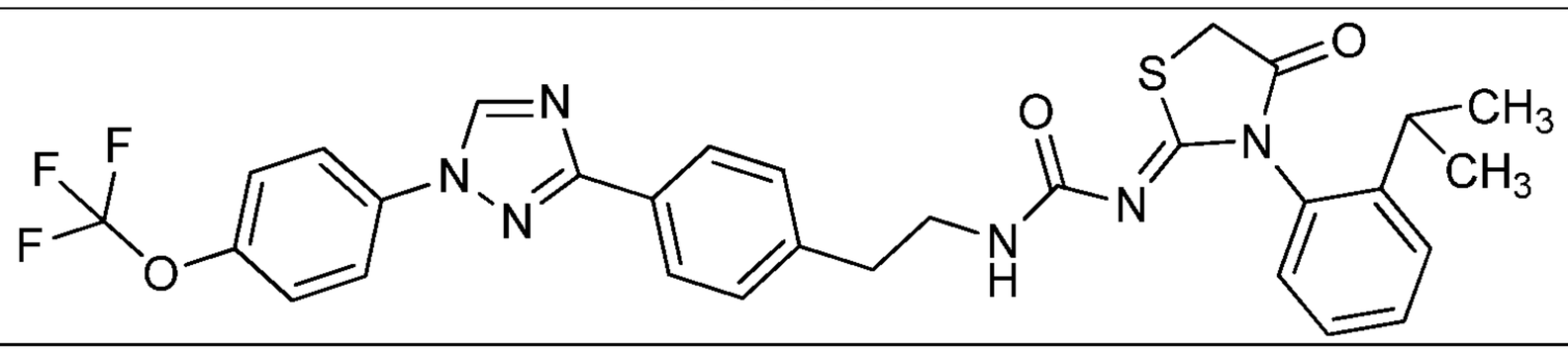
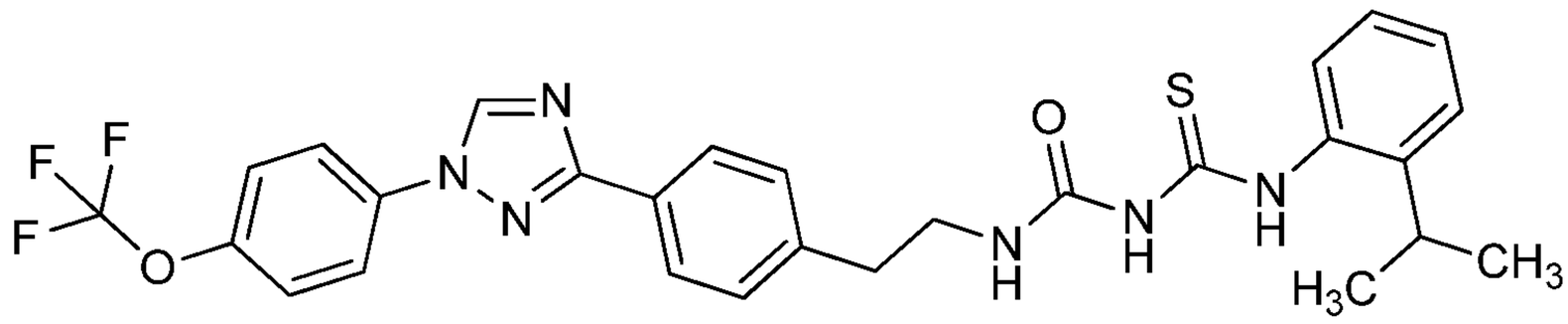
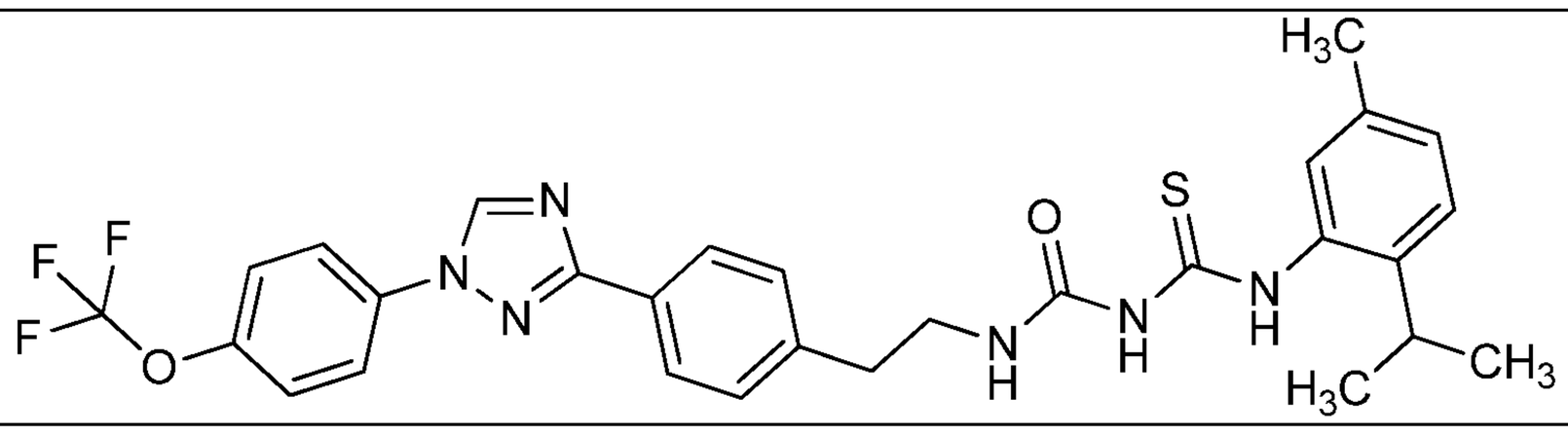
11. A molecule according to any of the proceeding claims wherein L is CH_2, CH_2CH_2, $CH_2CH(CH_3)$, $CH_2C(CH_3)_2$, $CH_2CH(CH_2CH_3)$, $CH=CH$, $CH(CH_3)CH_2$,

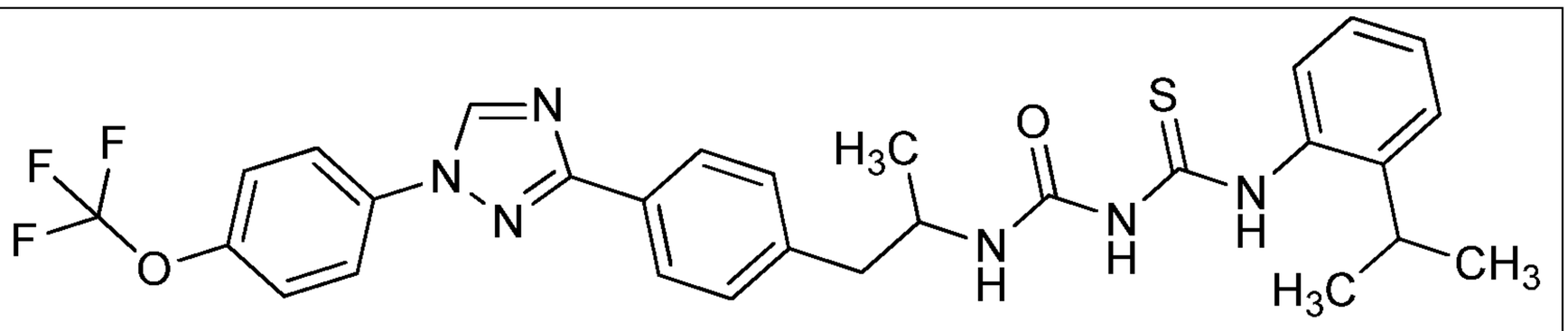
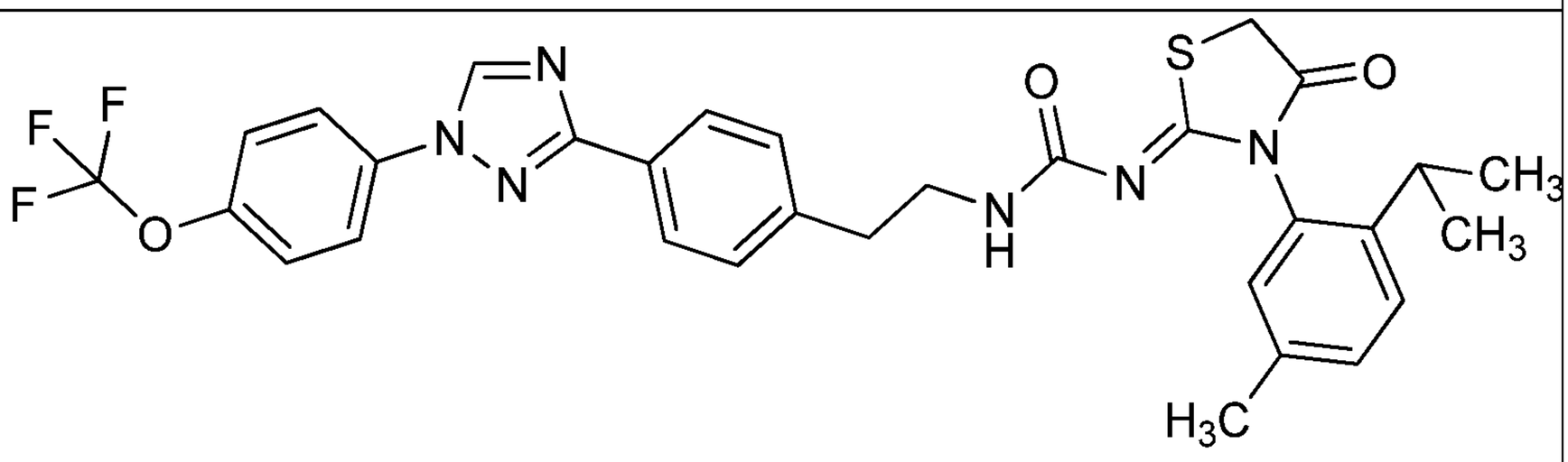
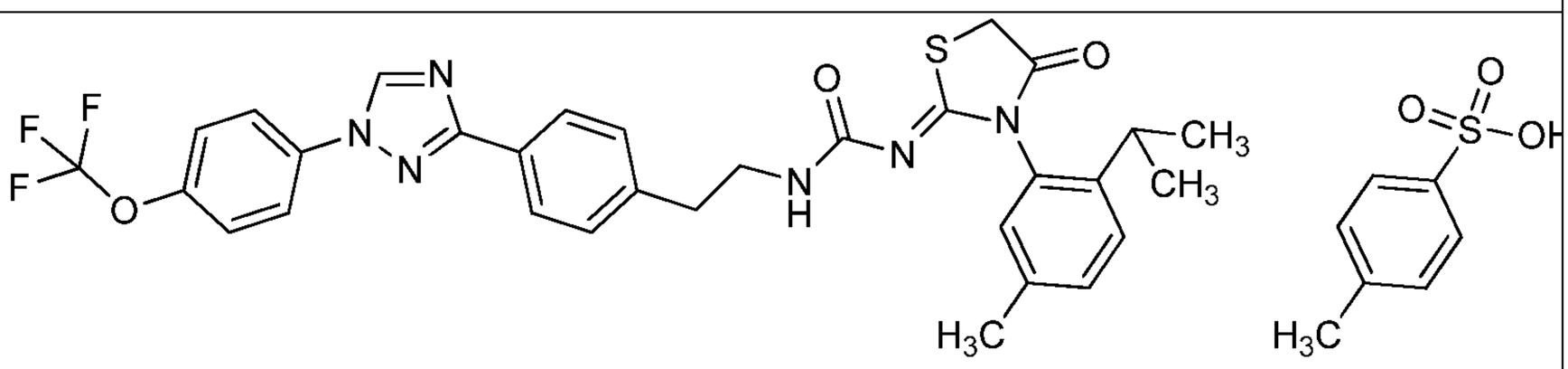
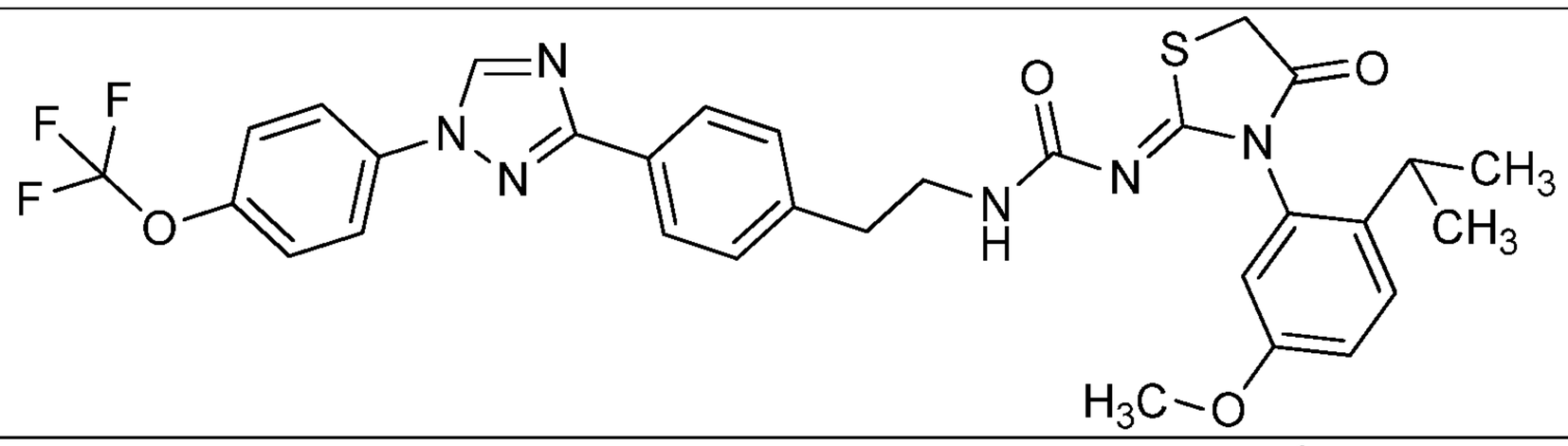
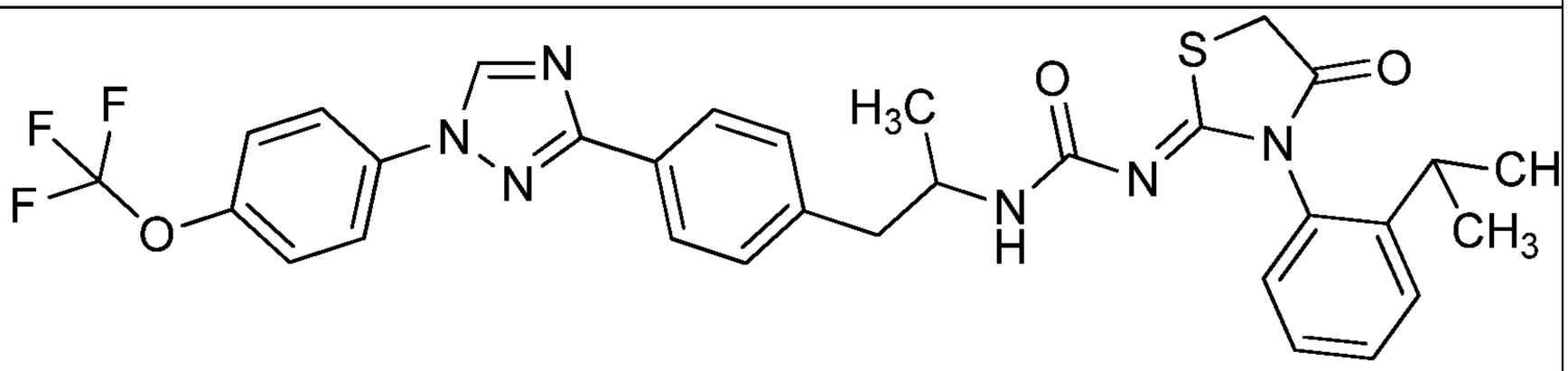
$C(CH_3)_2CH_2$, $CHBrCH_2$, CH_2C(cyclopropyl), $CH(CH_2CH_3)CH_2$, $C(CH_3)=CH$, $CH_2CH_2CH_2$, $CH(CH_3)CH(CH_3)$, $CH_2CH_2CH_2CH_2$, $C\equiv CCH_2CH_2$, cyclopropyl, or cyclohexyl.

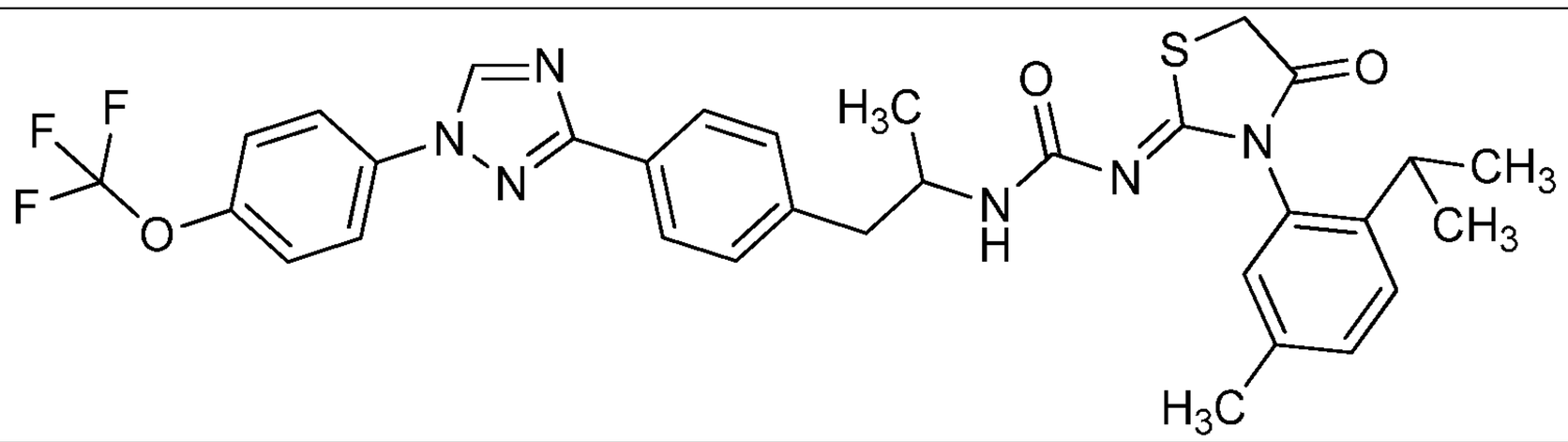
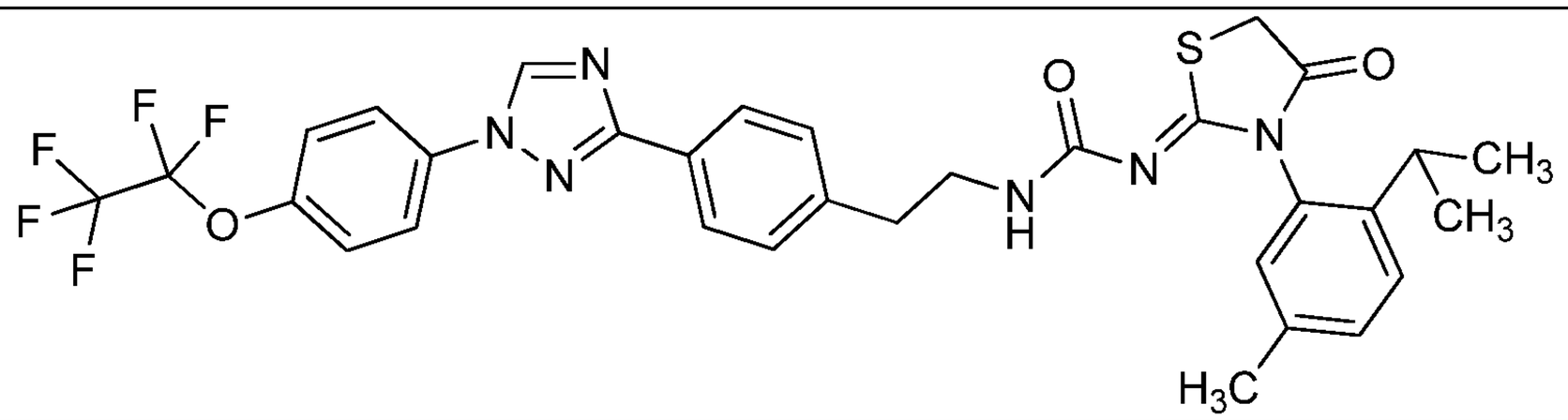
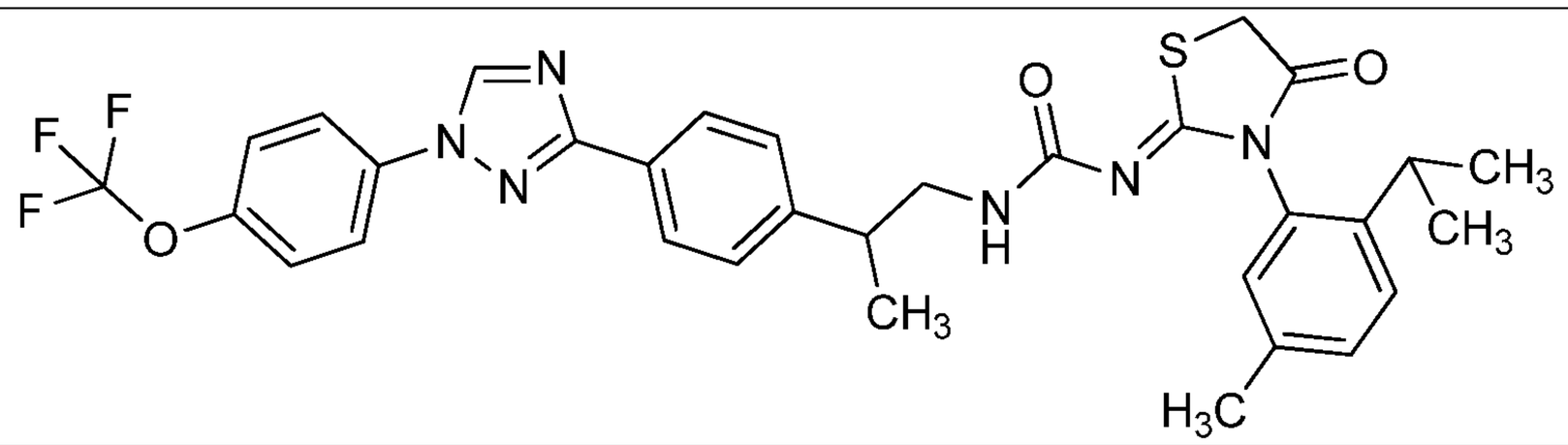
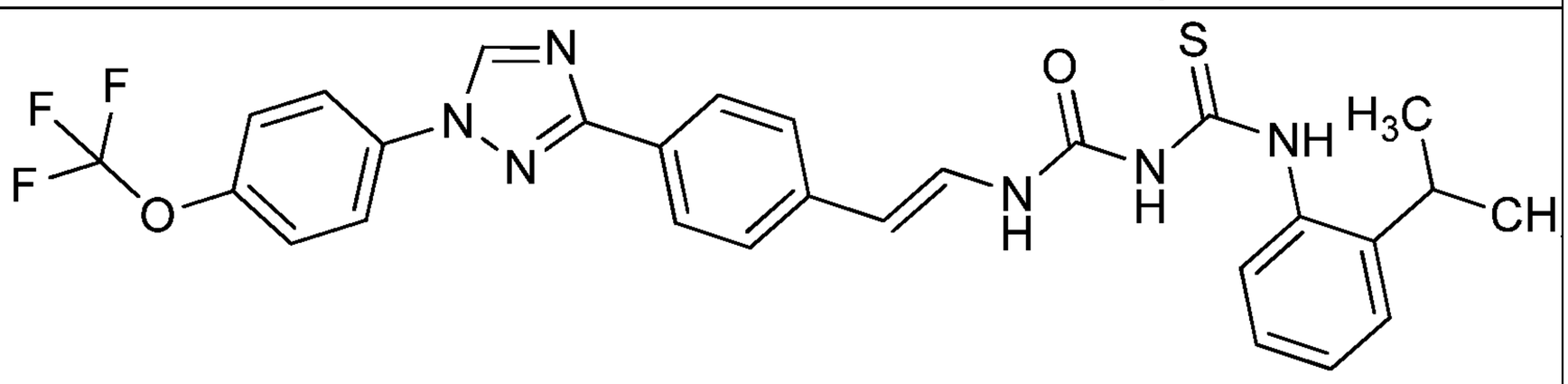
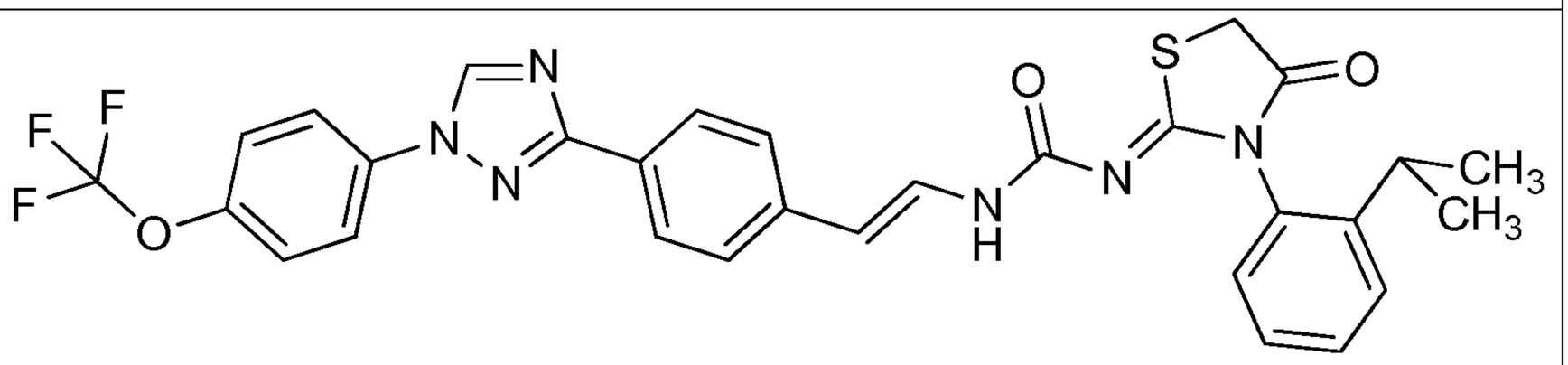
12. A molecule according to claim 1 wherein said molecule is a tautomer having the following formula

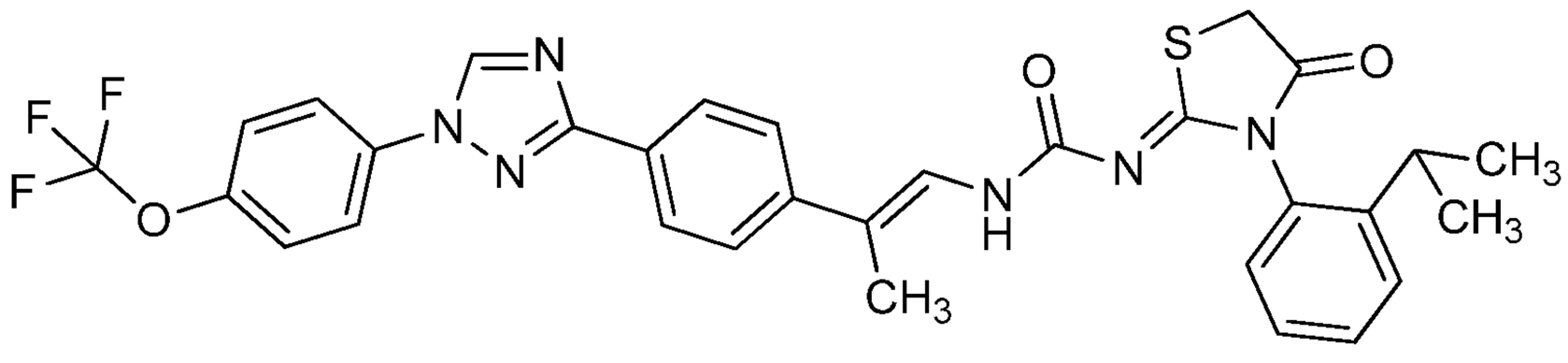
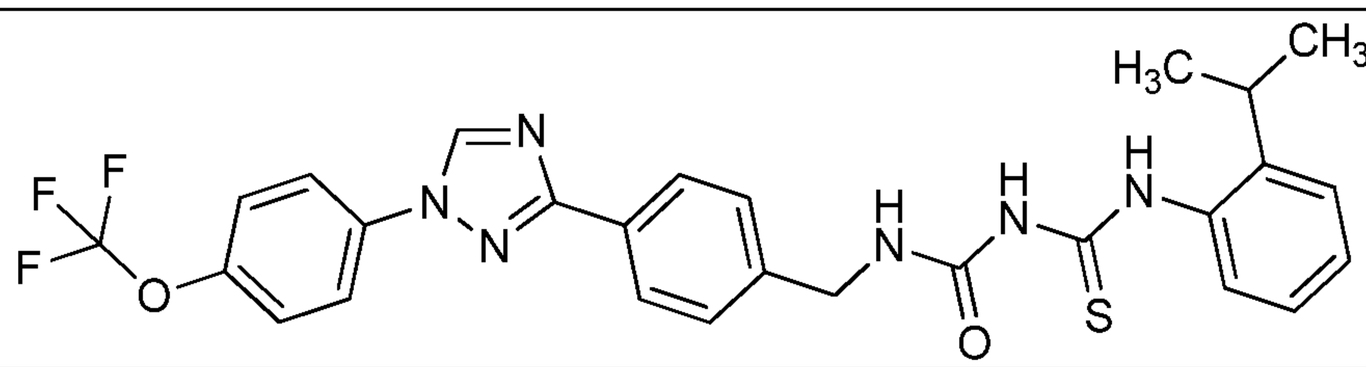
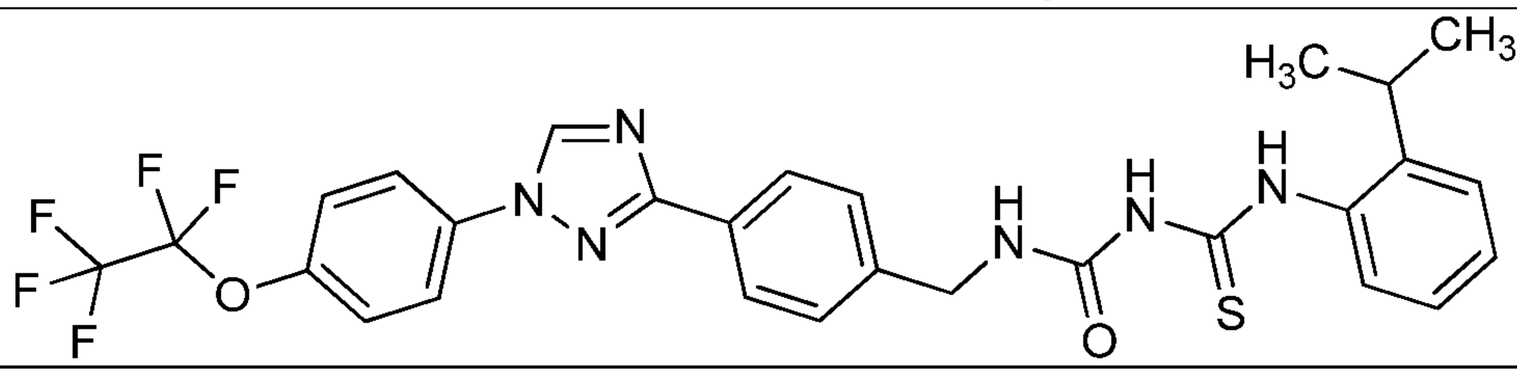
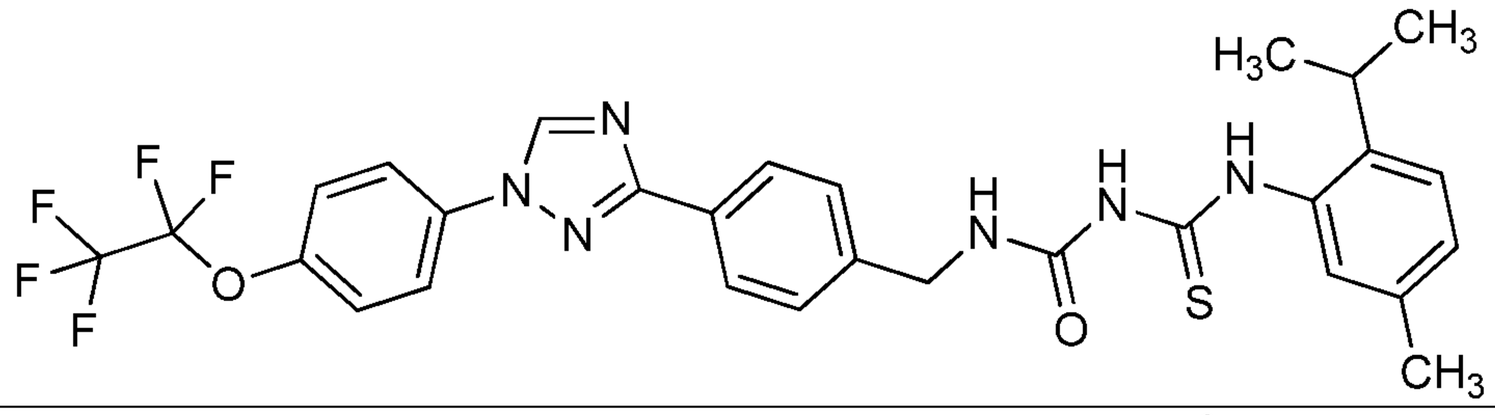
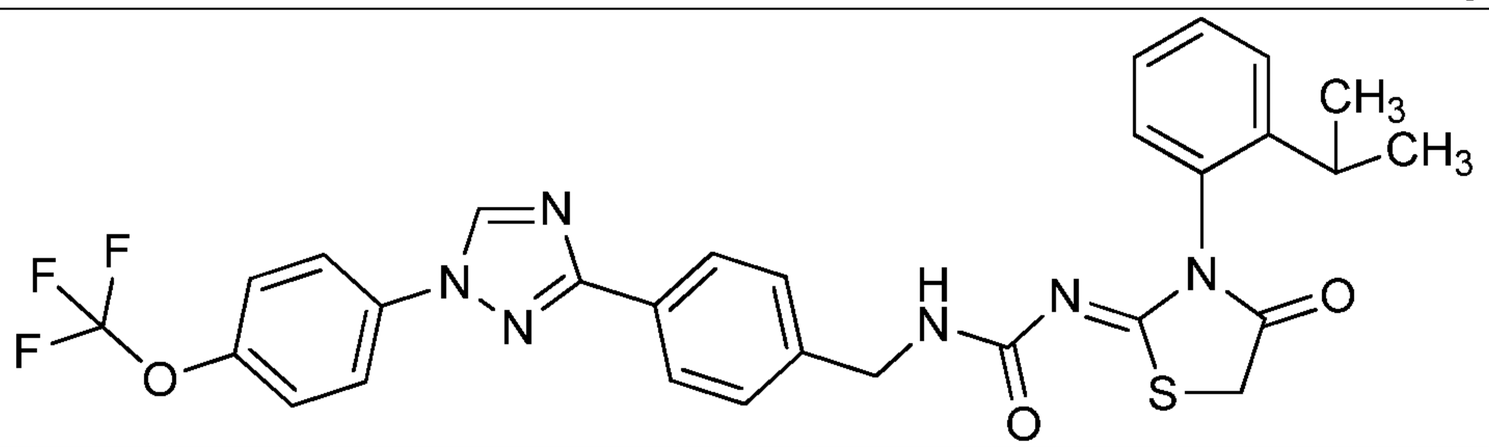
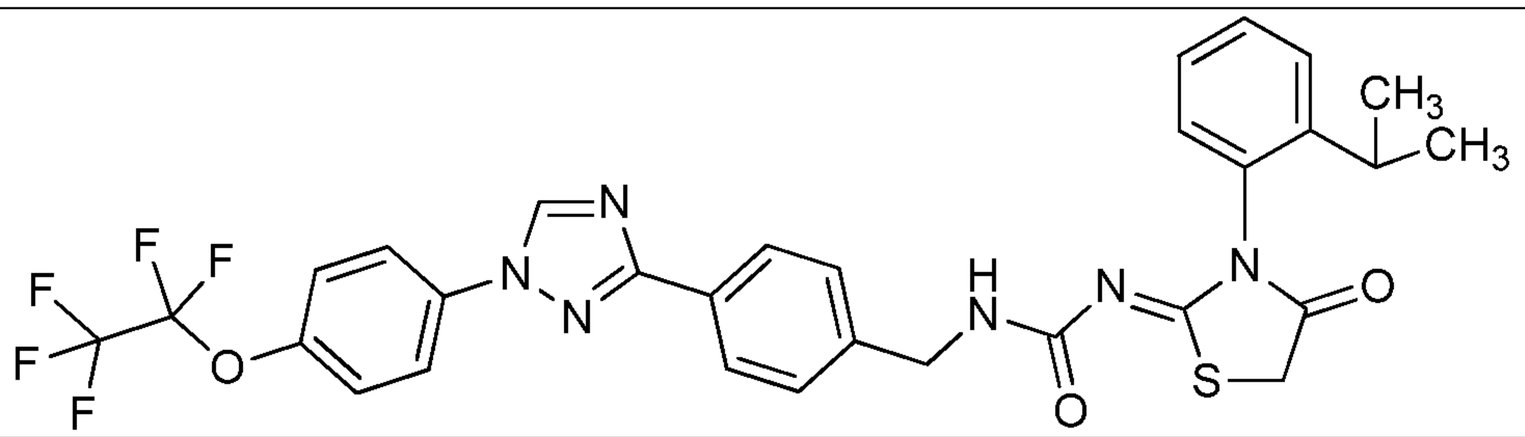


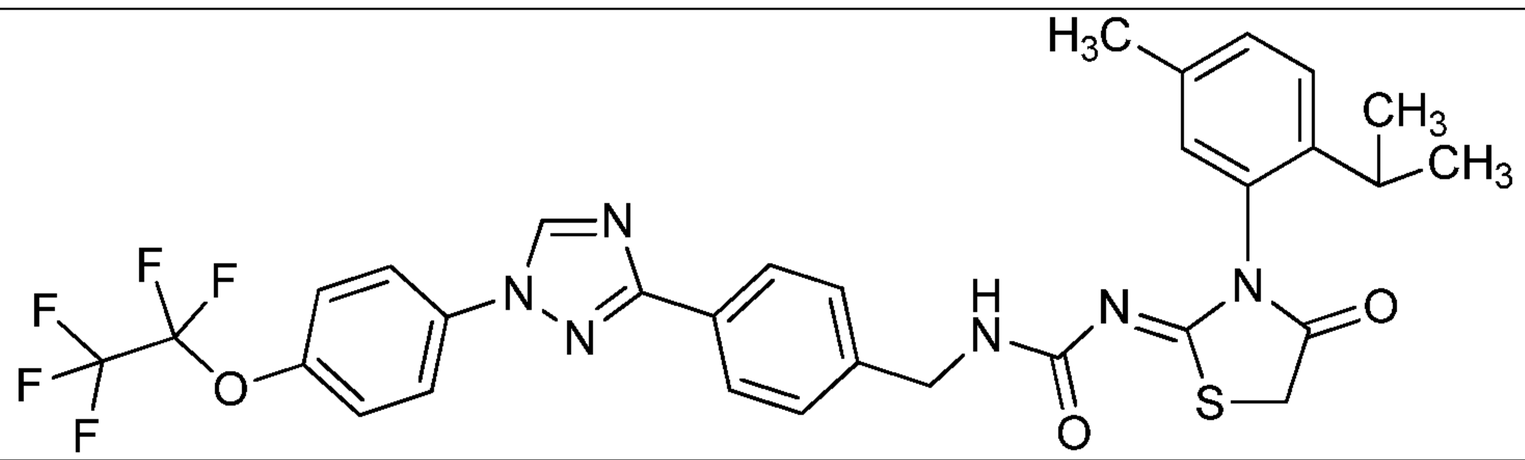
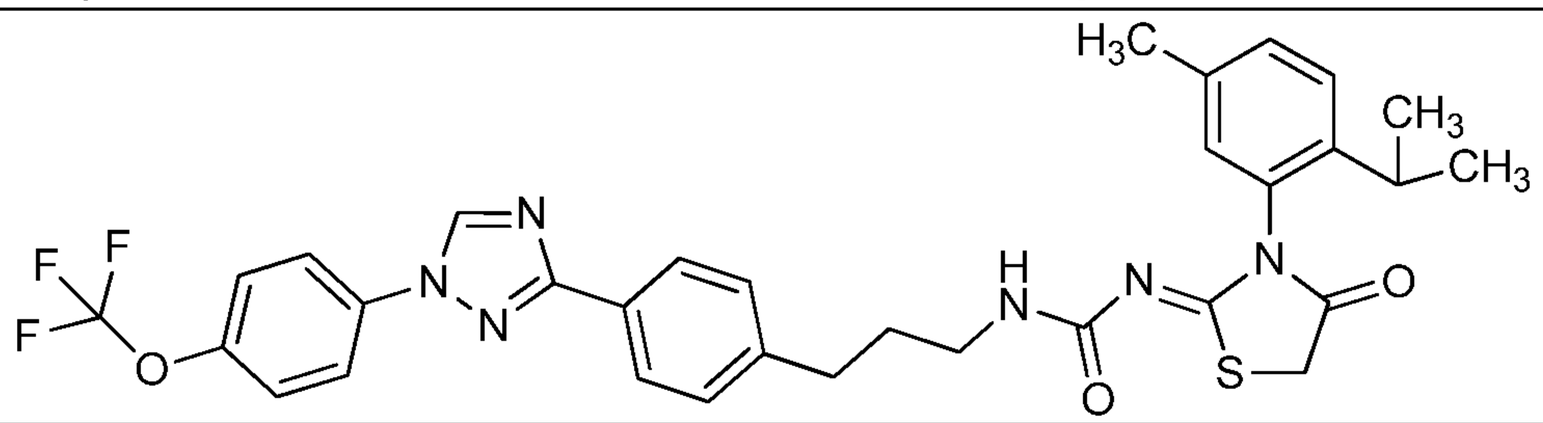
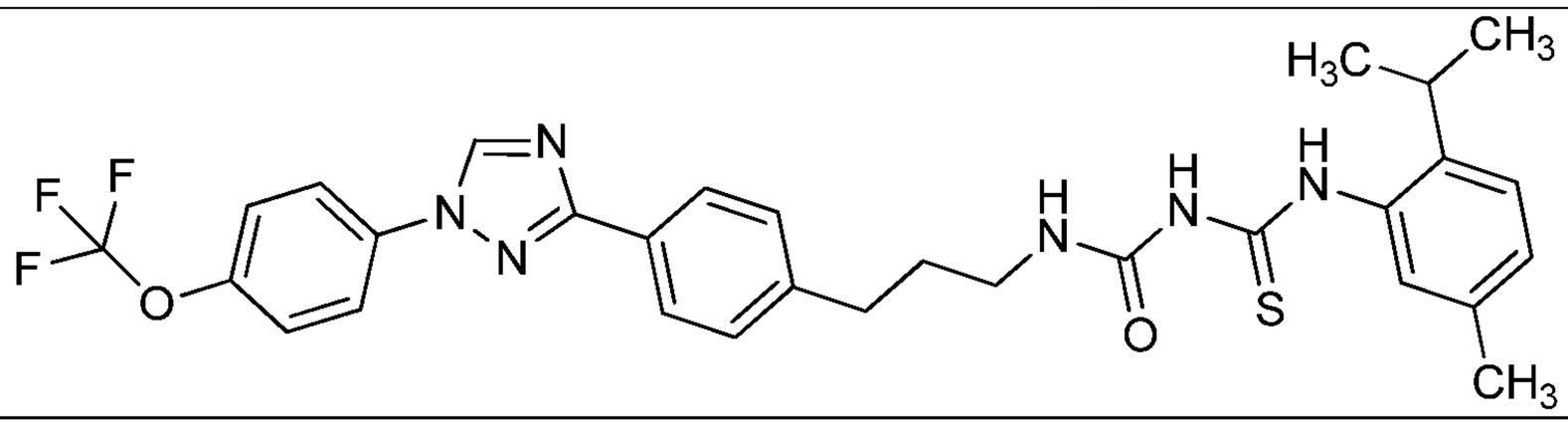
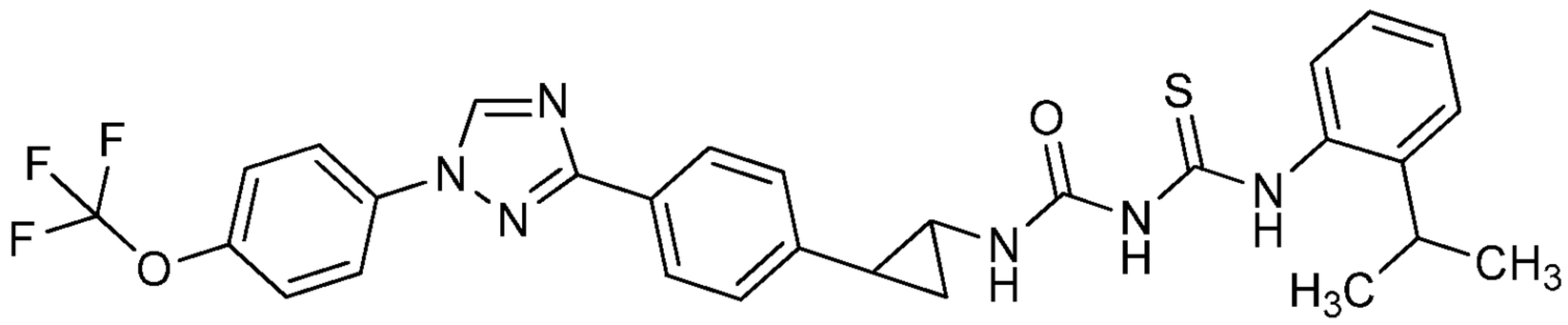
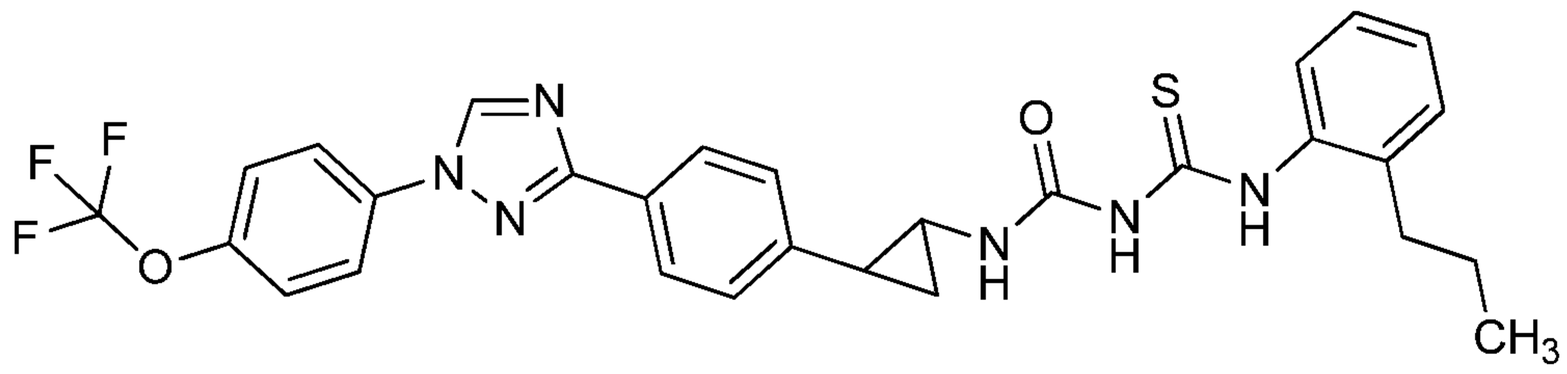
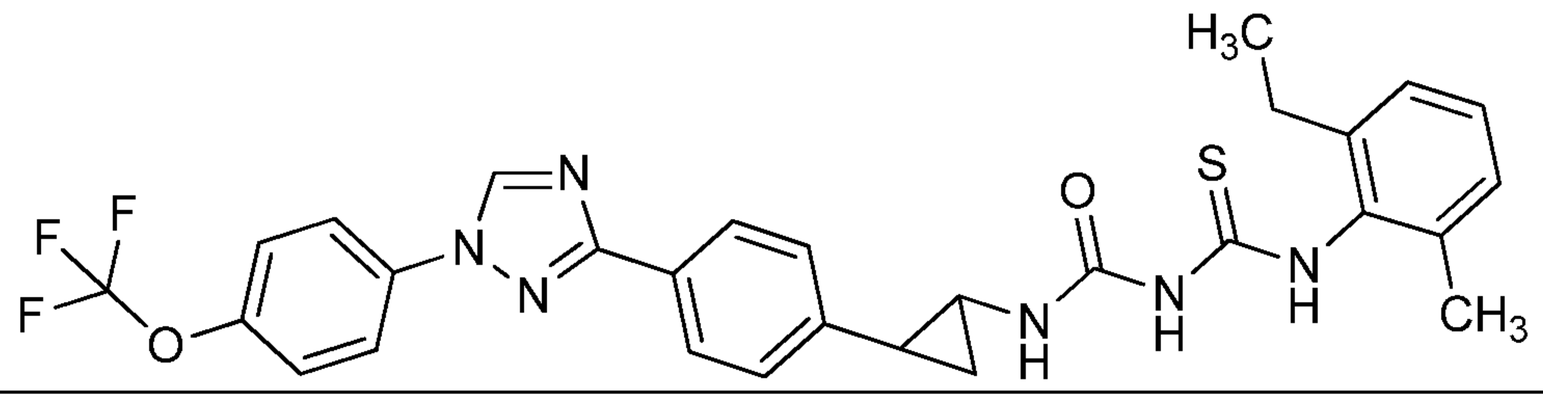
13. A molecule according to claim 1 wherein said molecule is selected from one of the following molecules

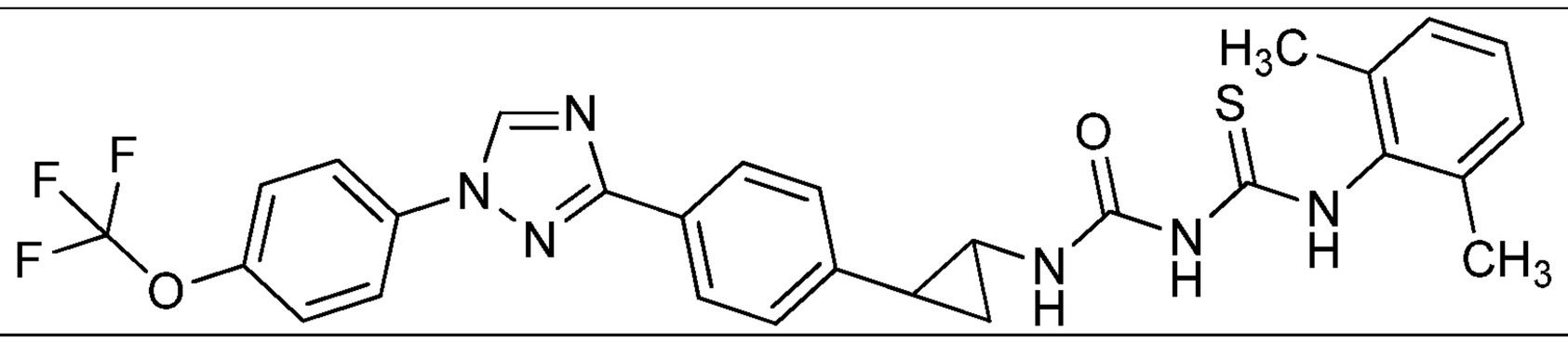
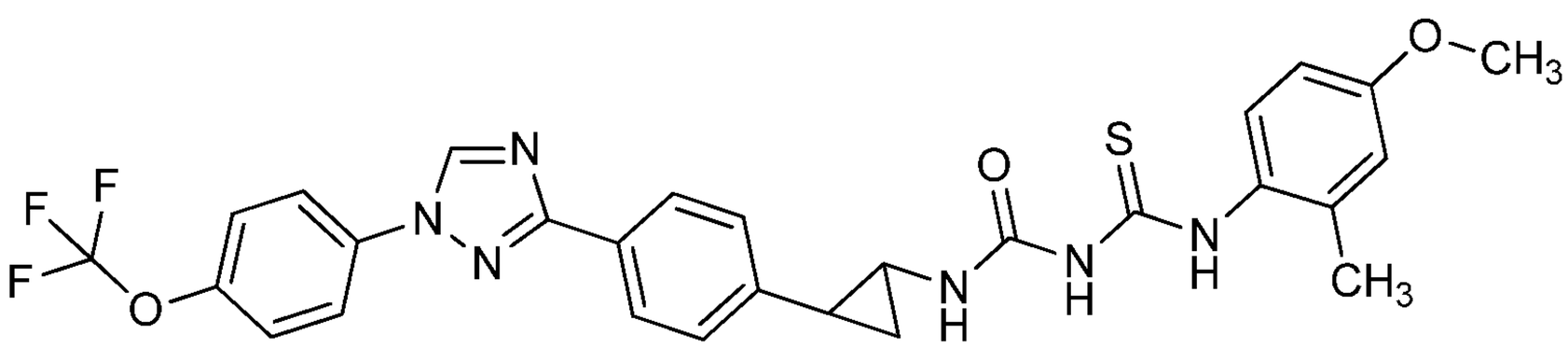
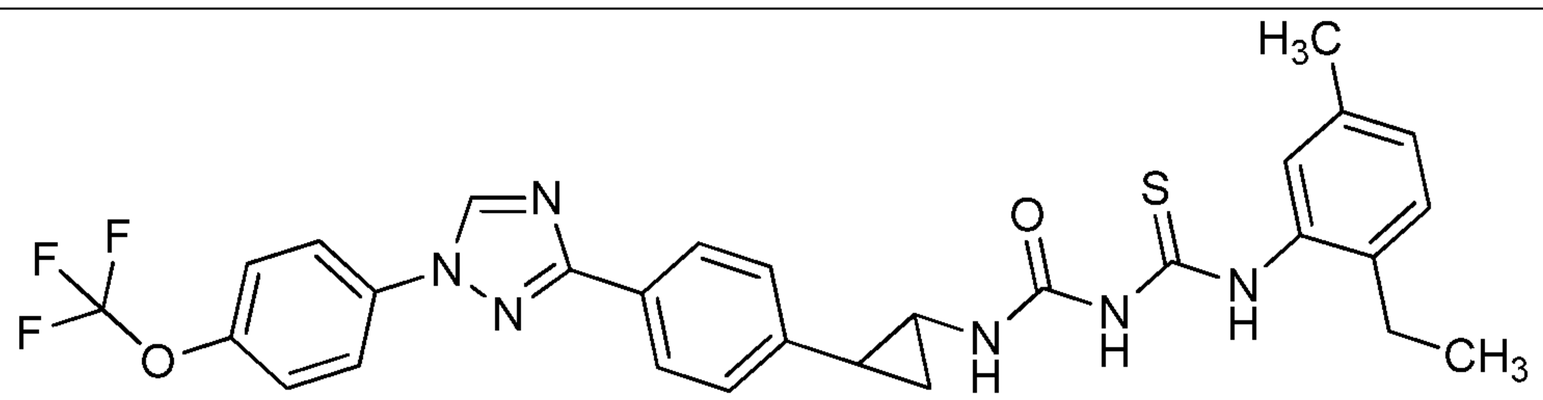
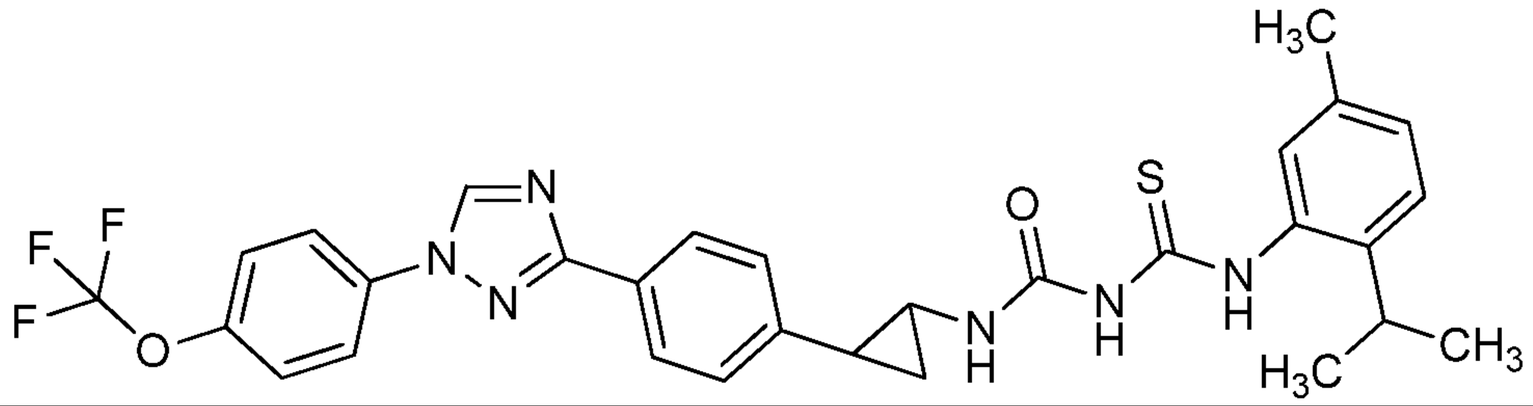
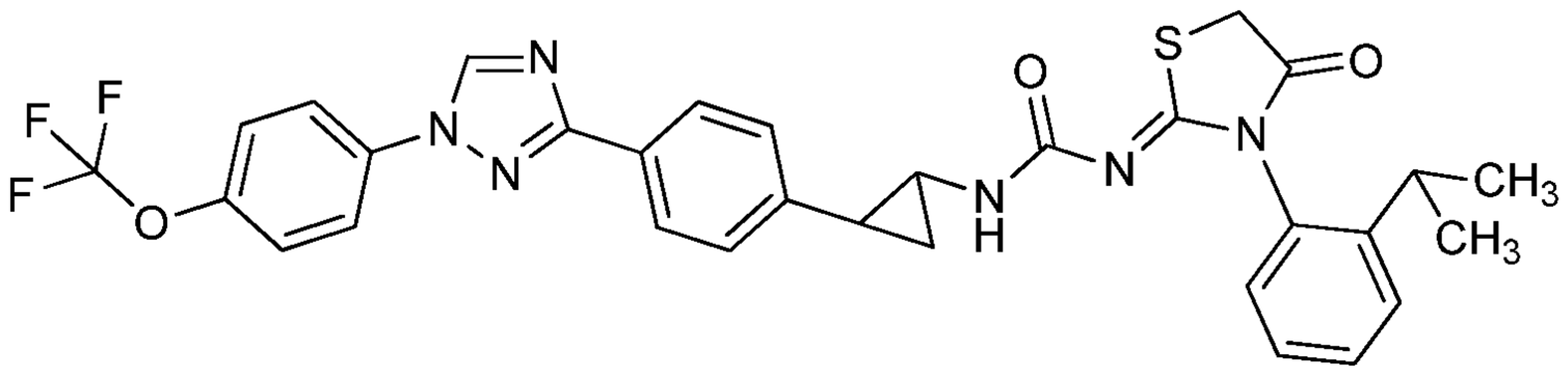
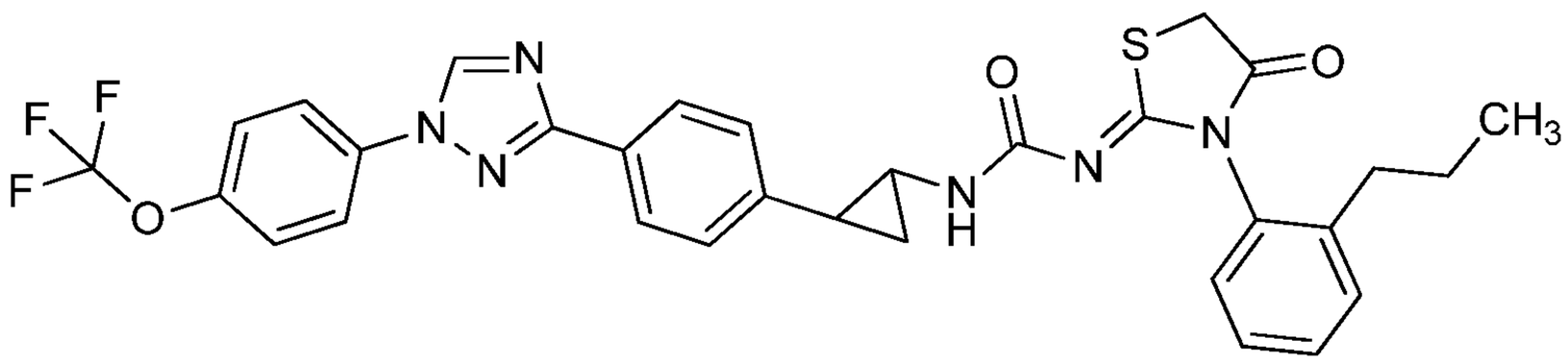
No.	Structure
F1	
F2	
F3	

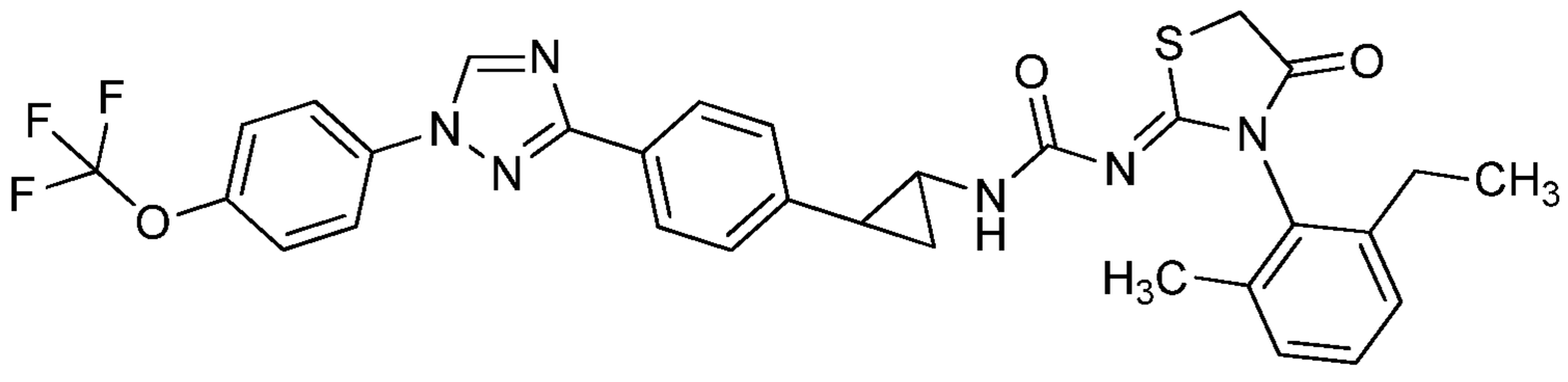
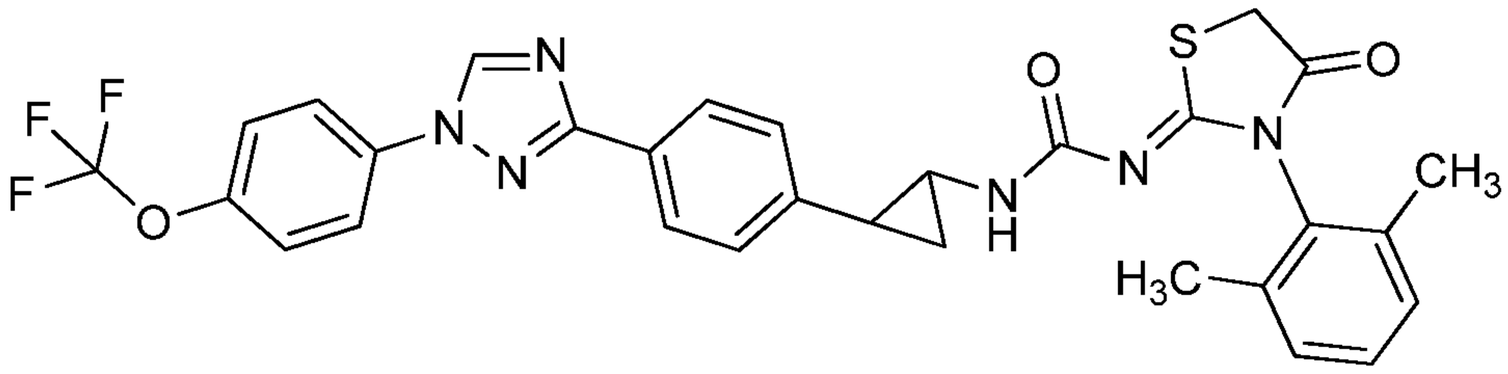
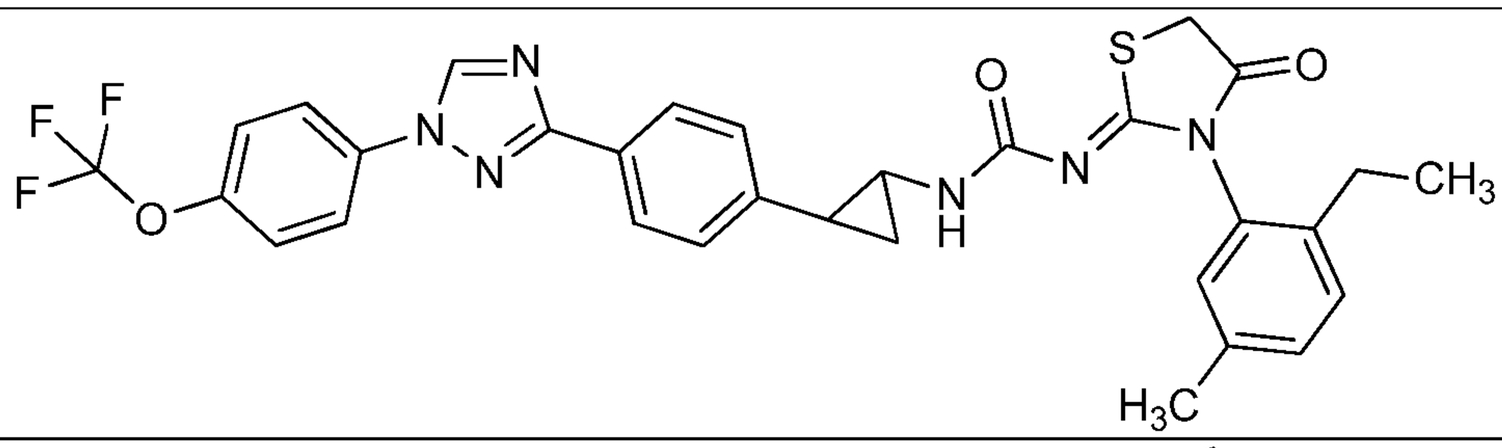
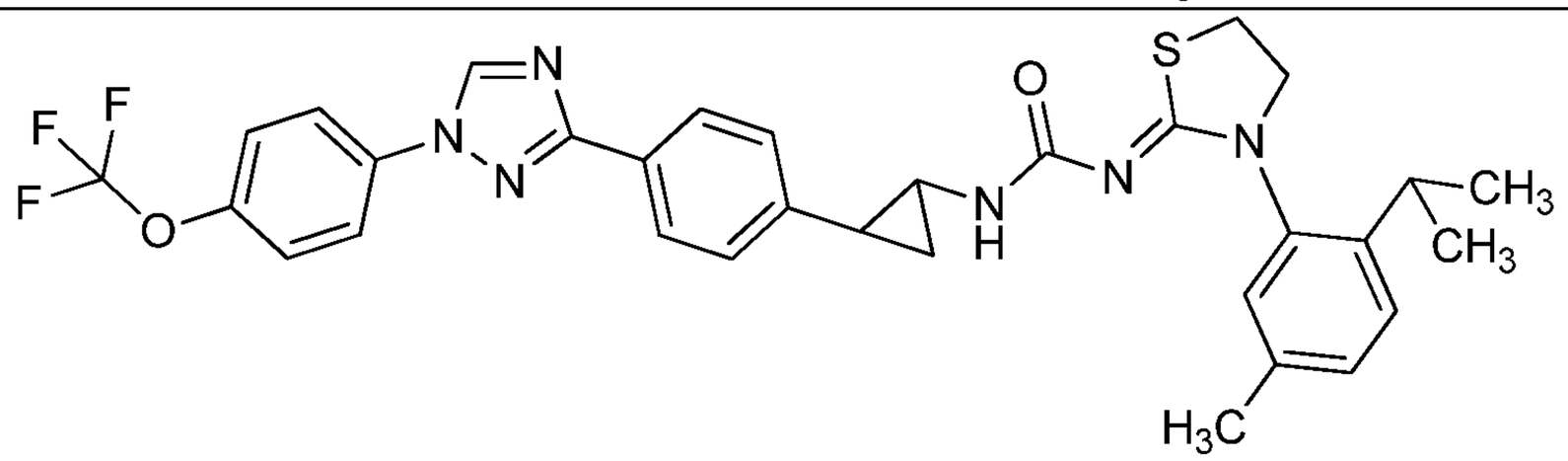
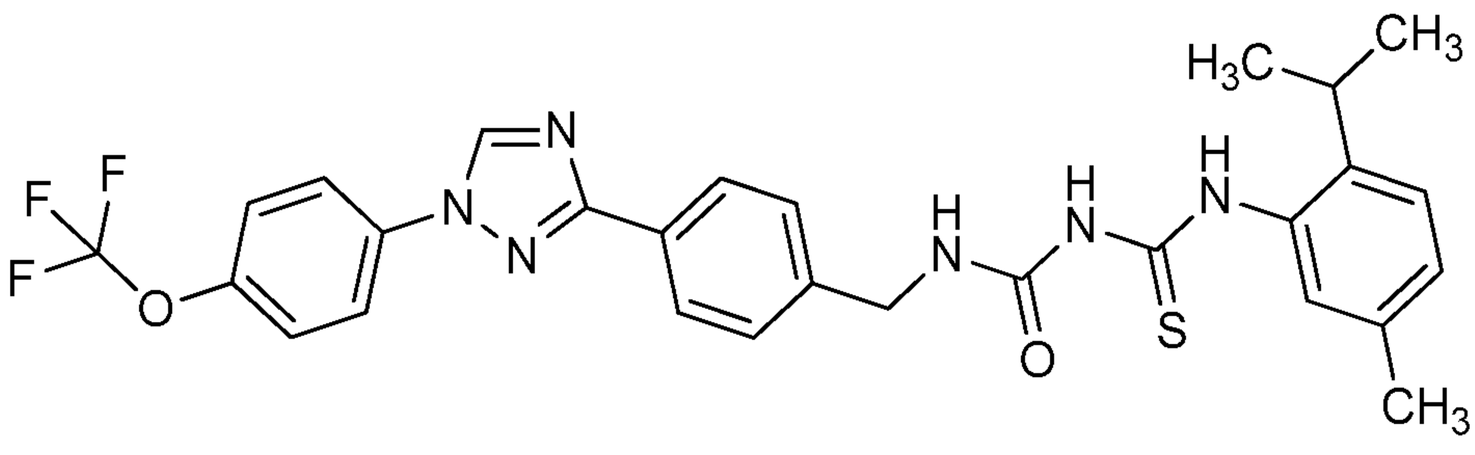
F4	
F5	
F5 A	
F6	
F7	

F8	
F9	
F10	
F11	
F12	

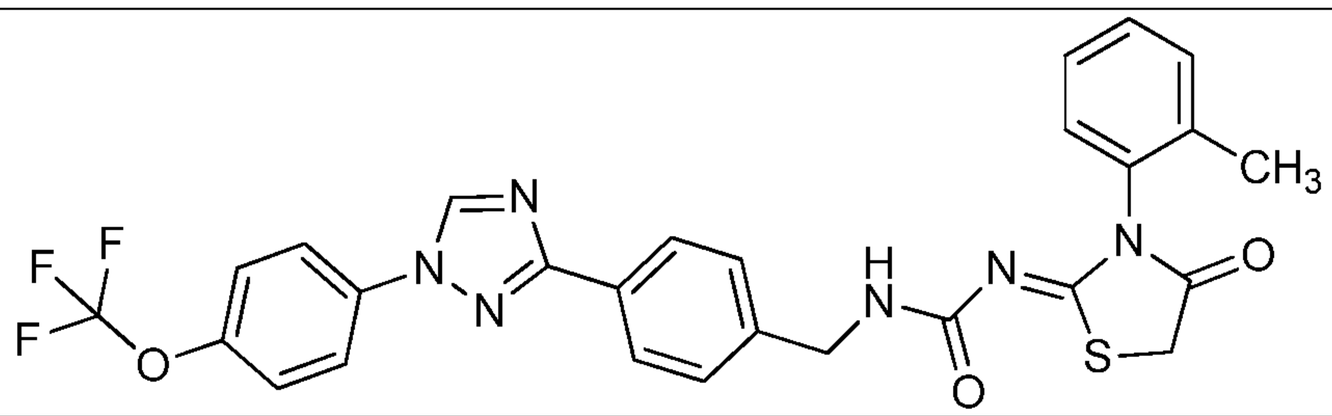
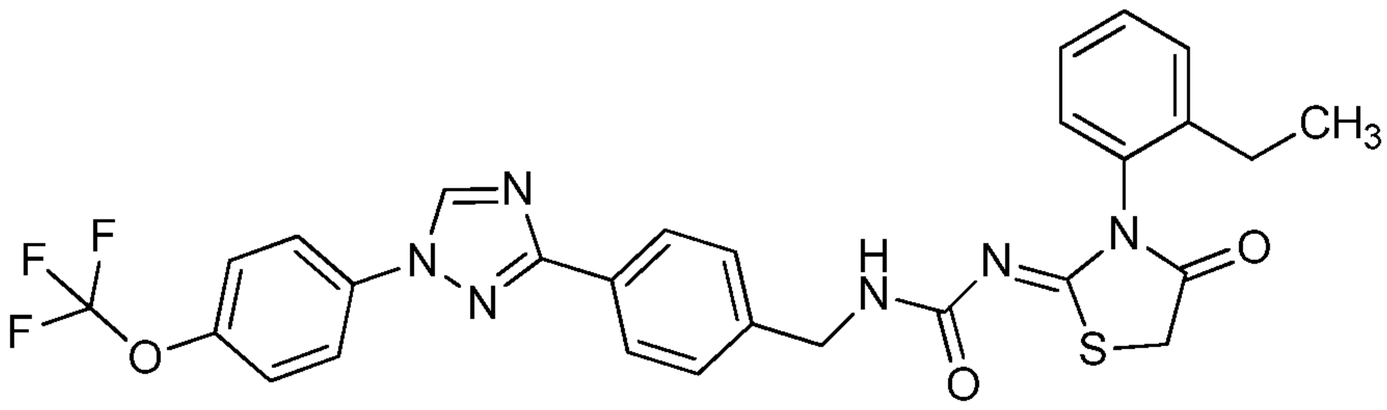
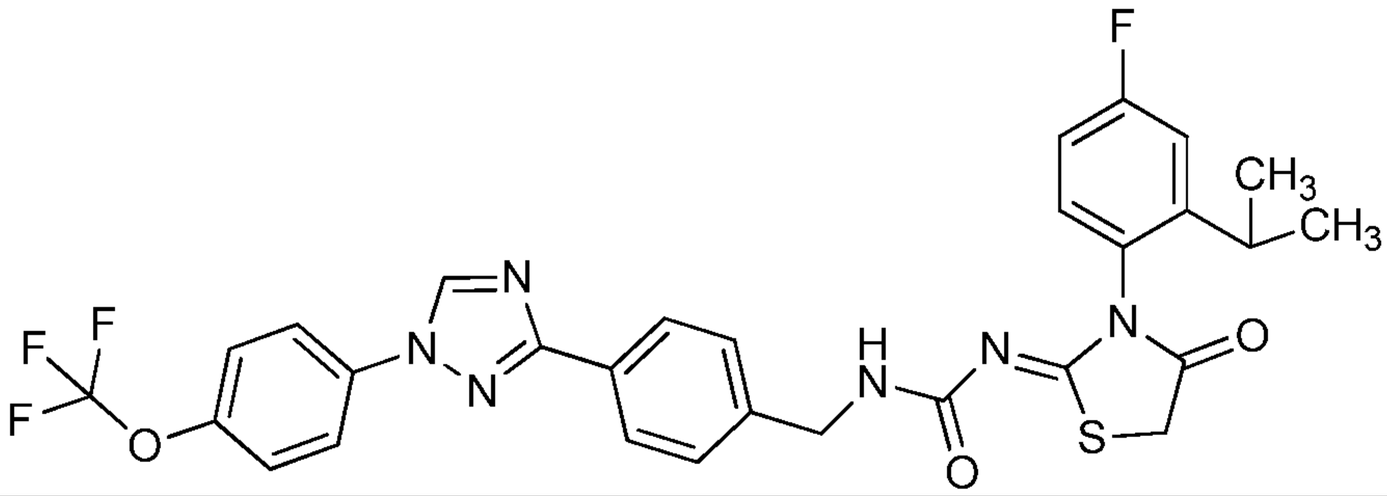
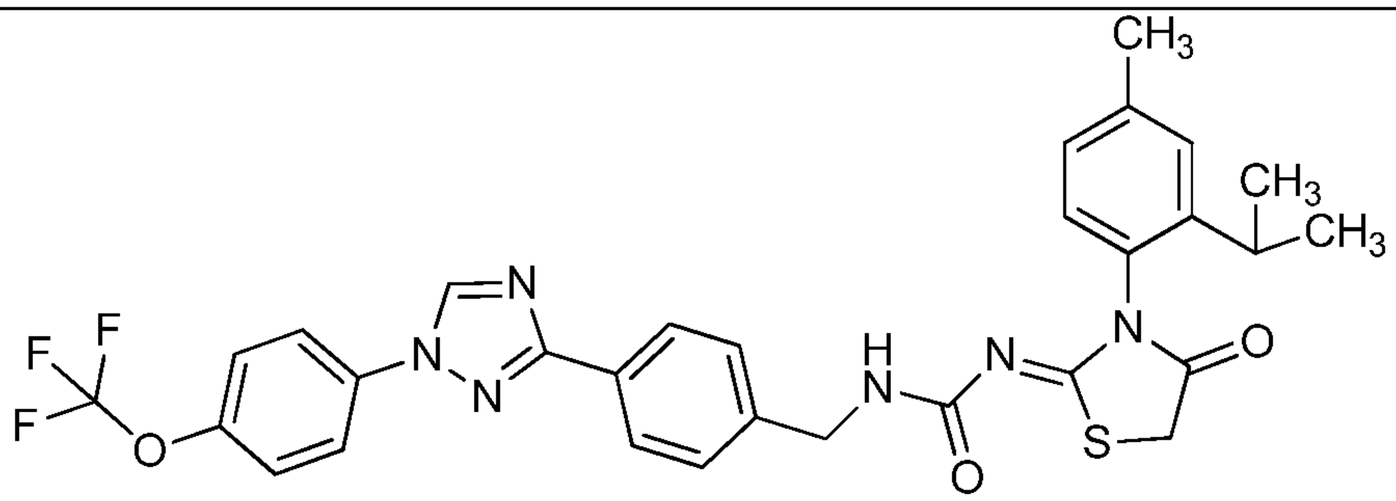
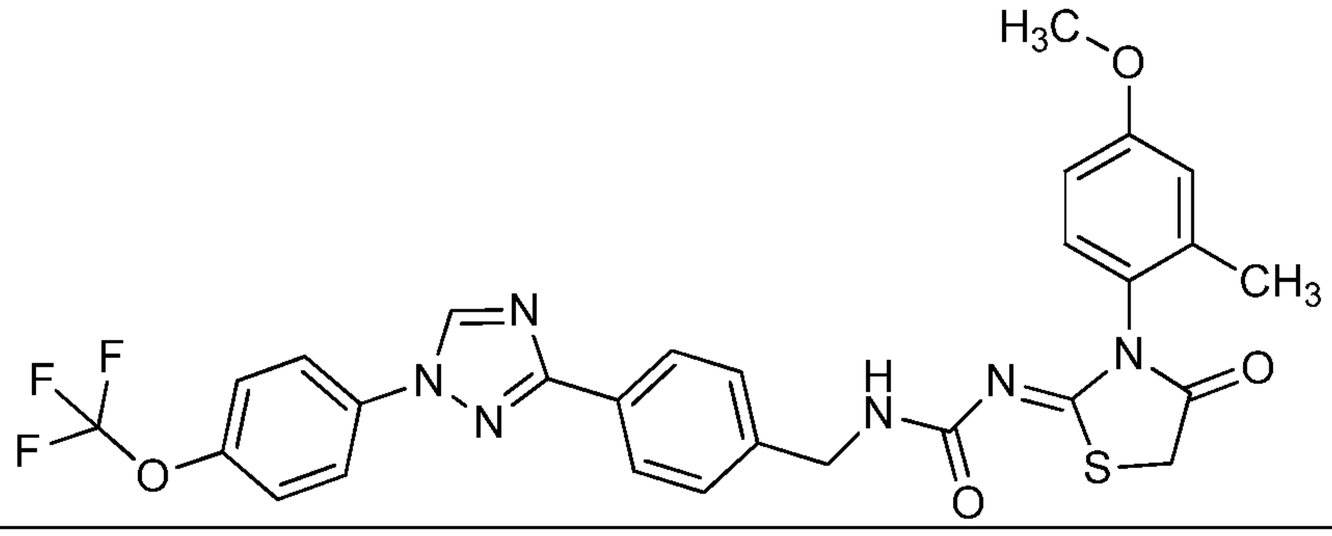
F13	
F14	
F15	
F16	
F17	
F18	

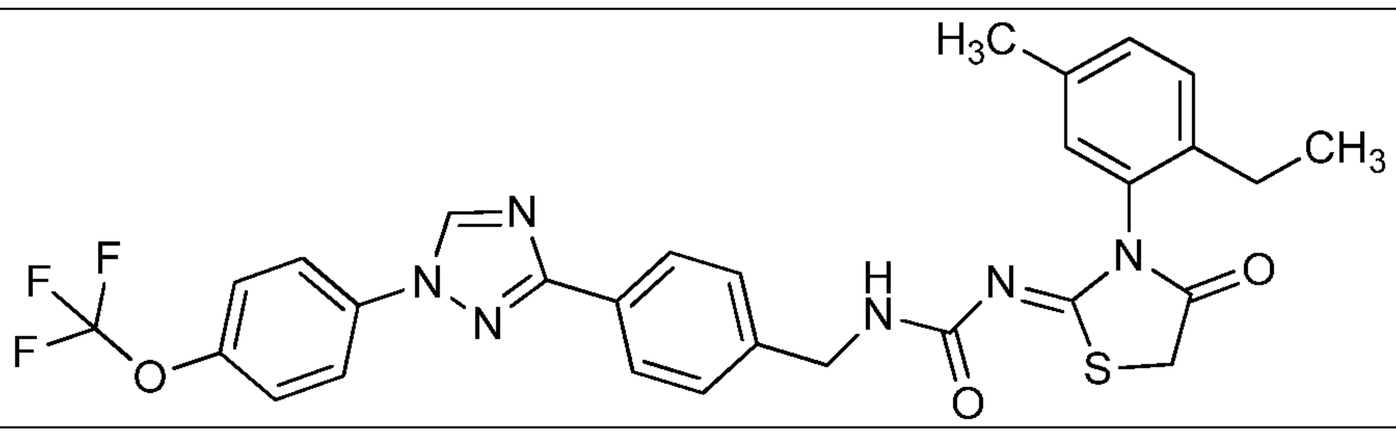
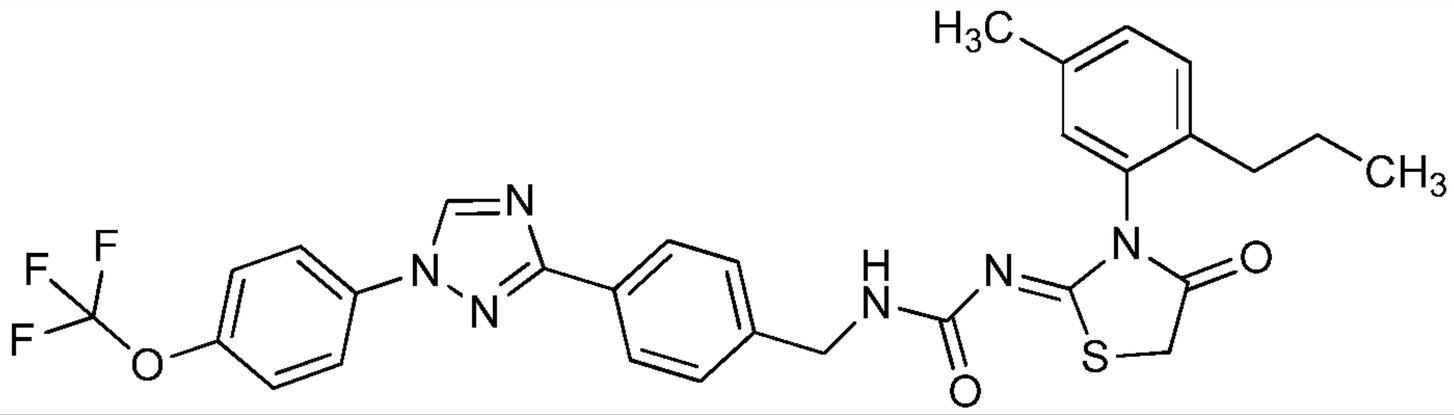
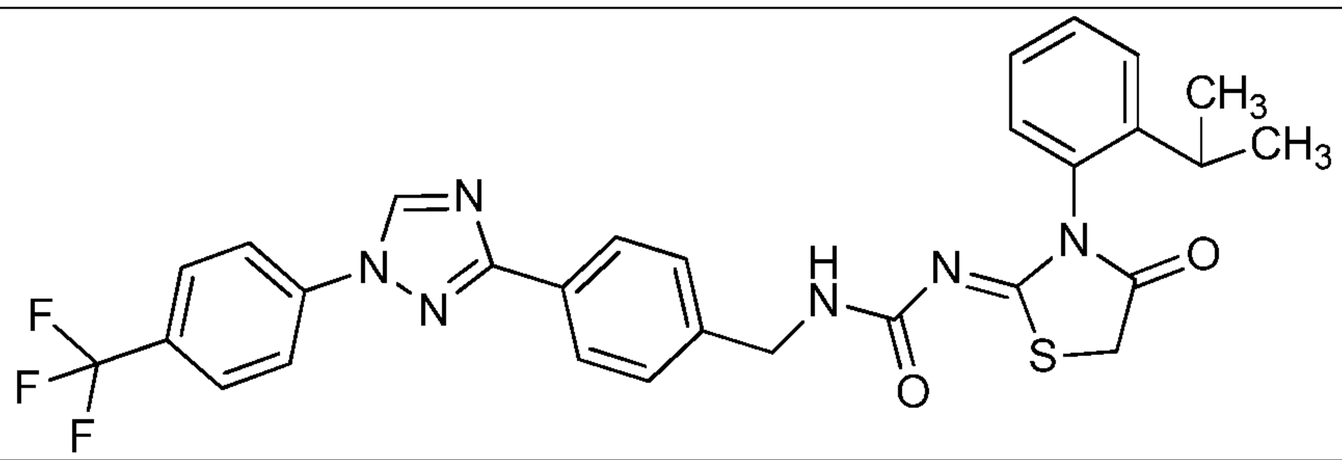
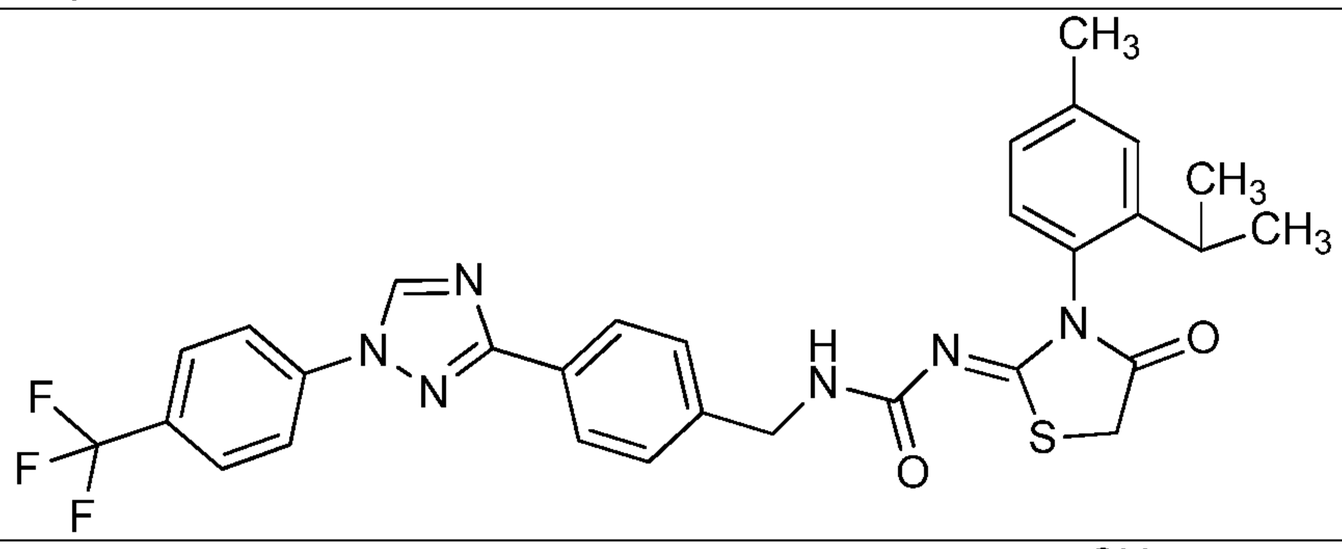
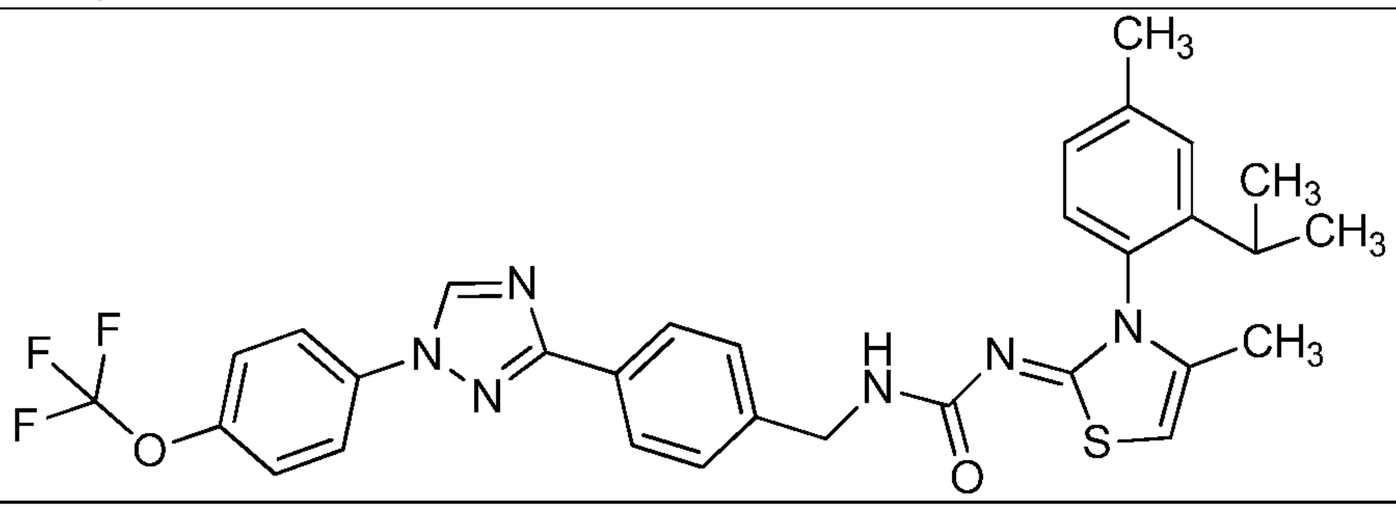
F19	
F20	
F21	
F22	
F23	
F24	

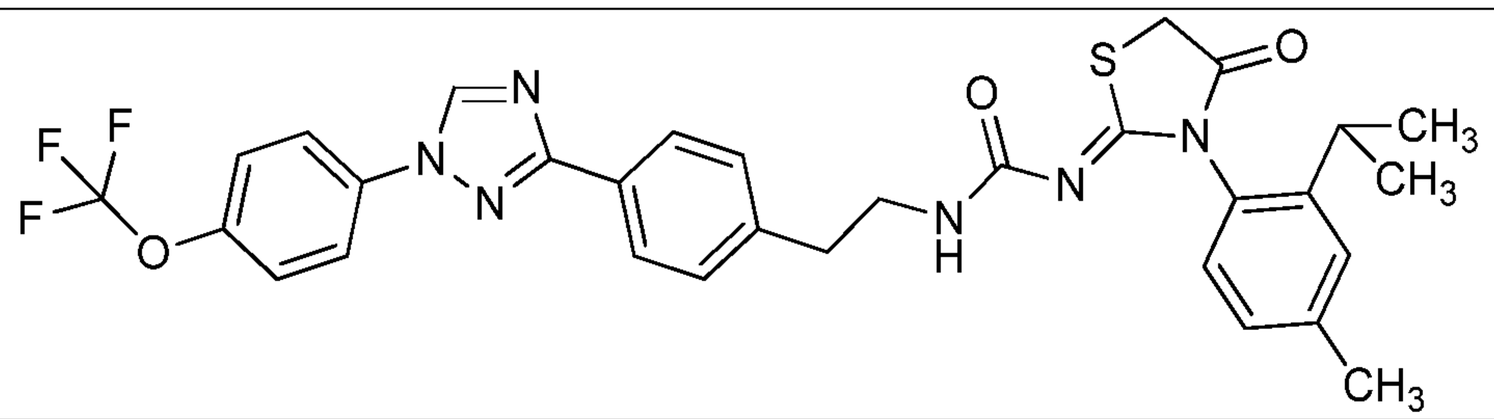
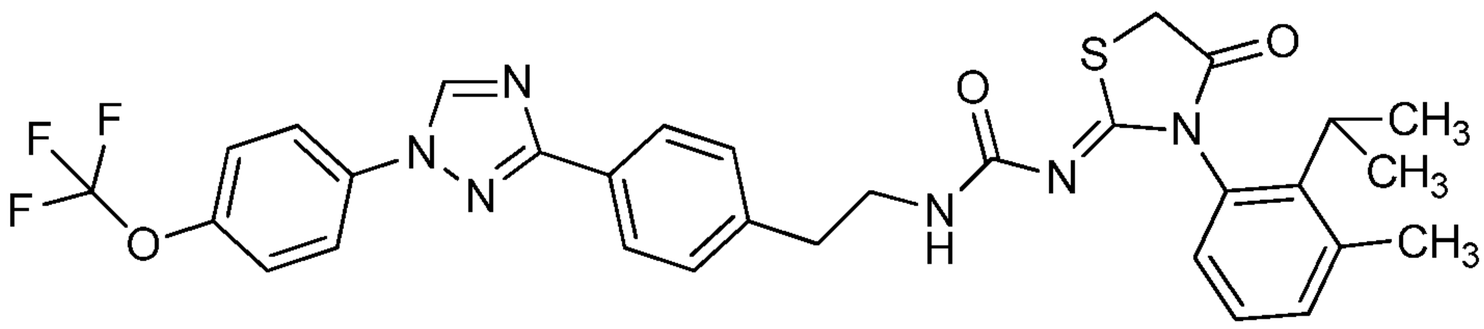
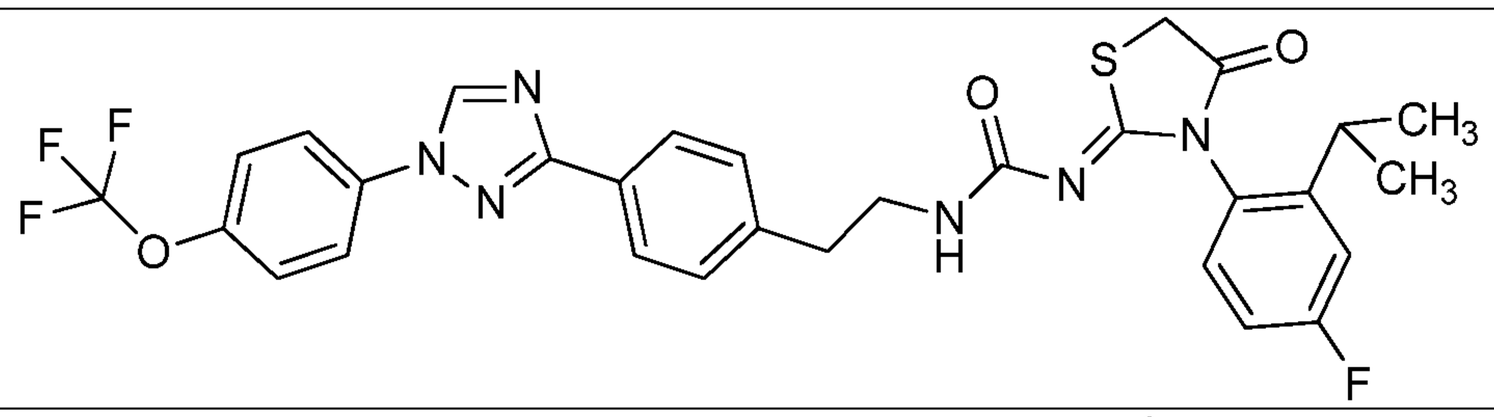
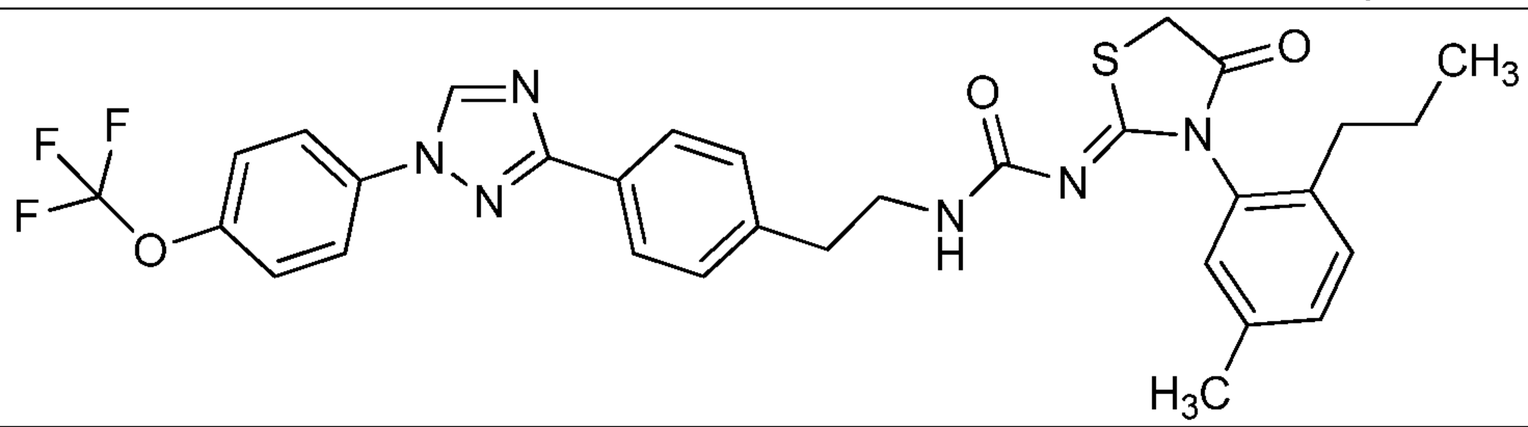
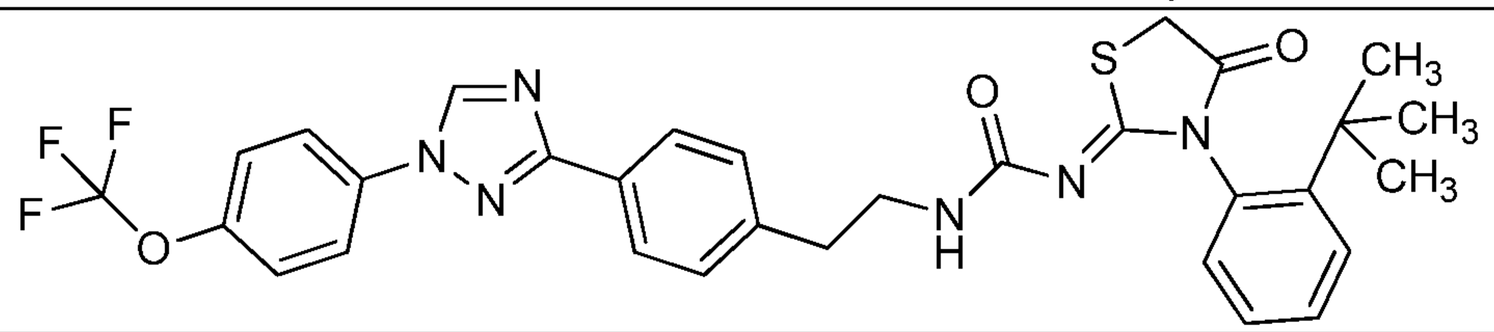
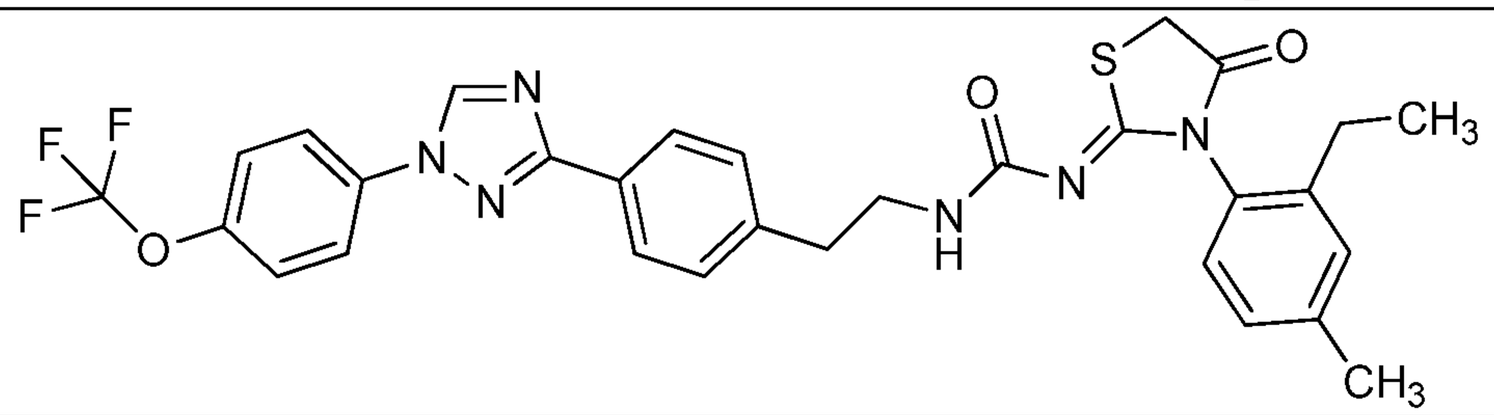
F25	
F26	
F27	
F28	
F29	
F30	

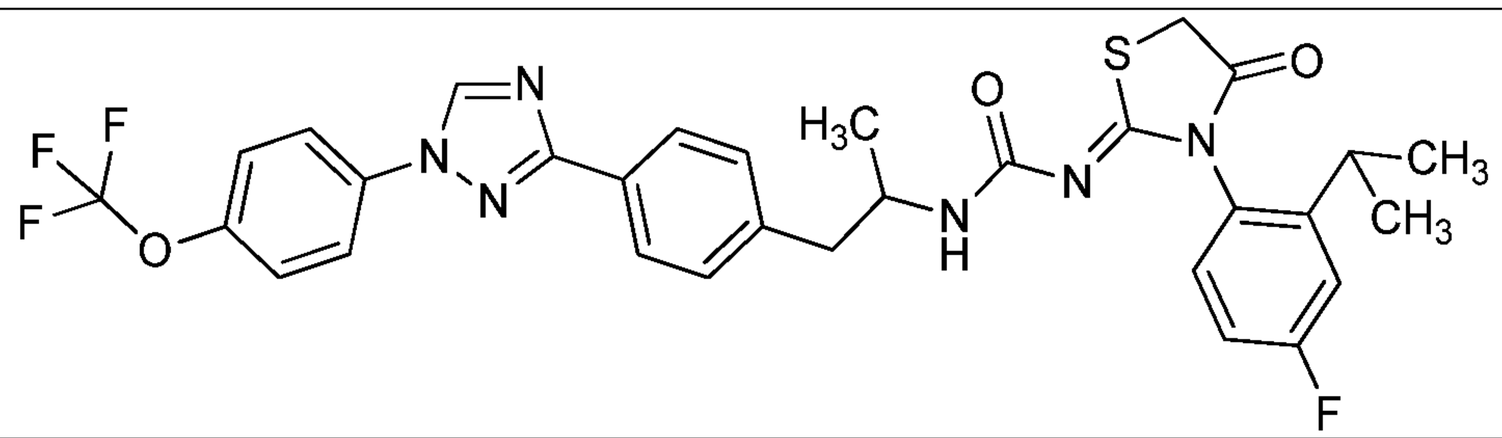
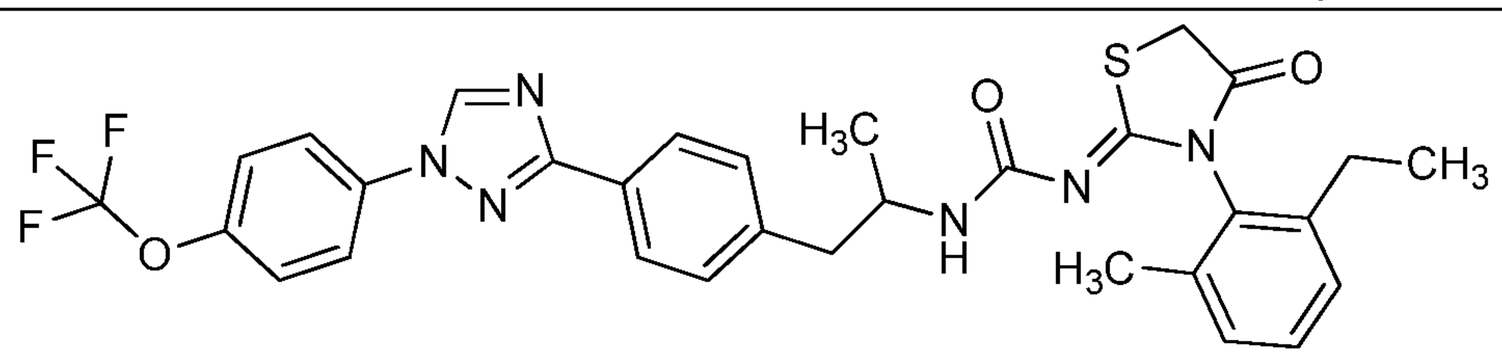
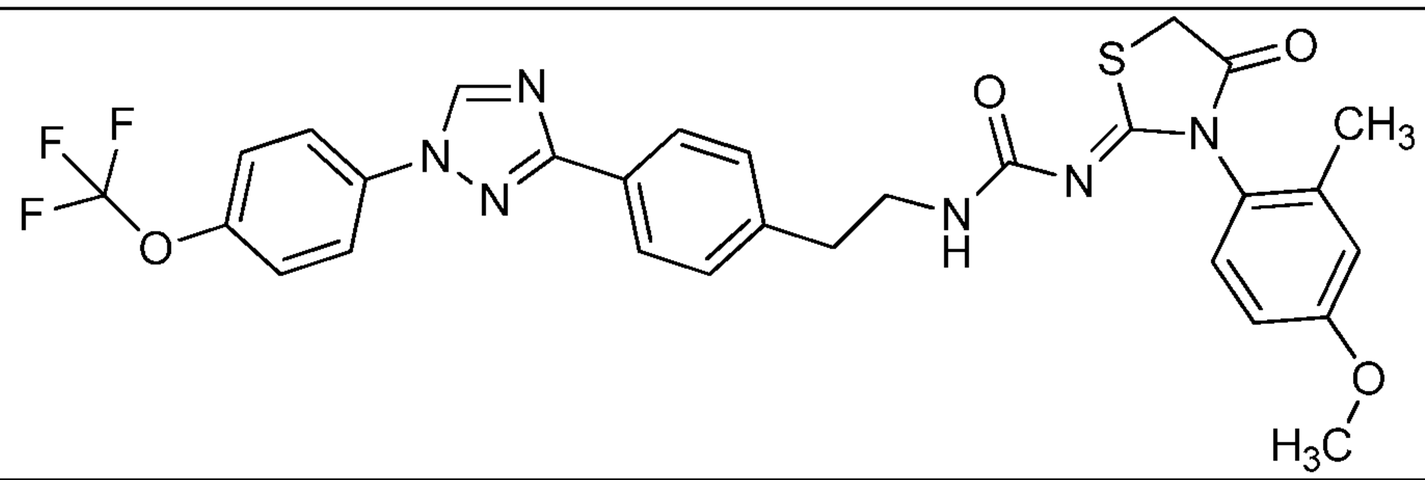
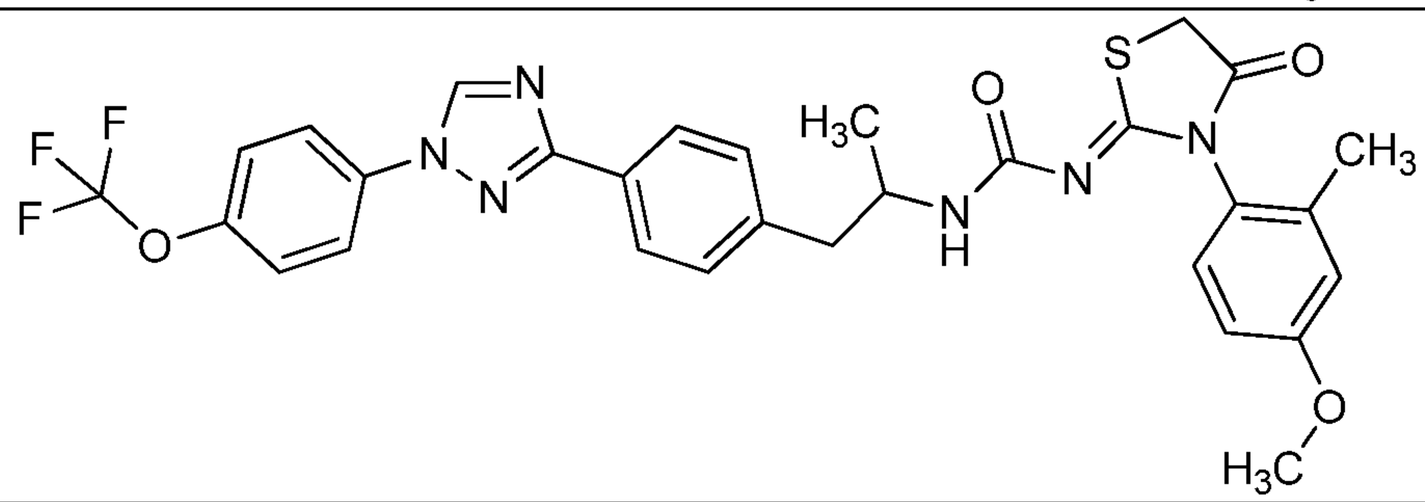
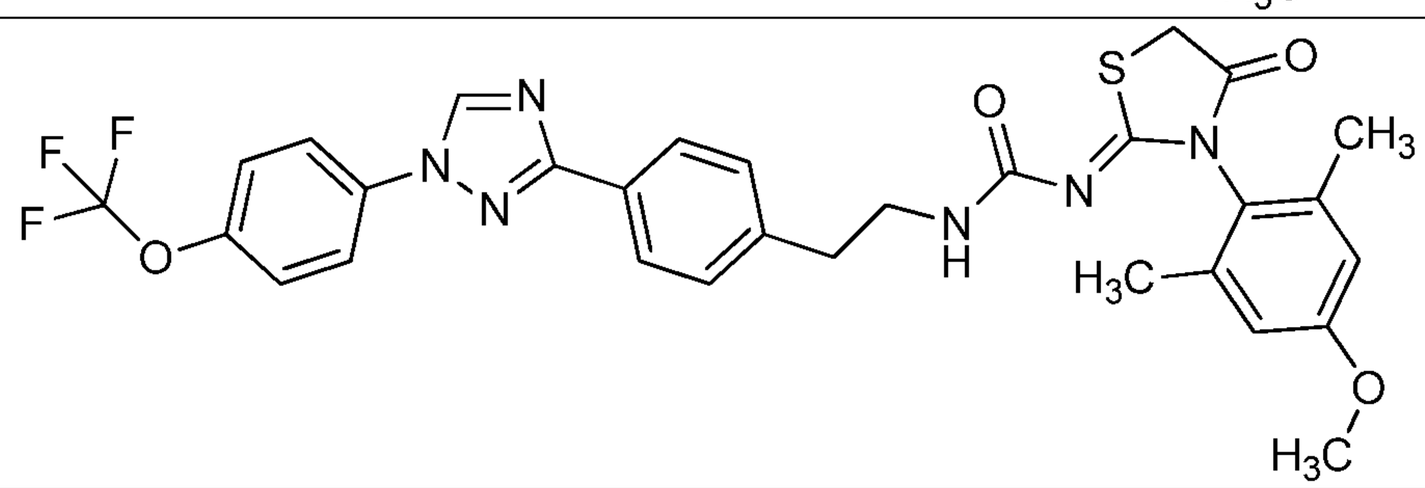
F31	
F32	
F33	
F34	
F35	

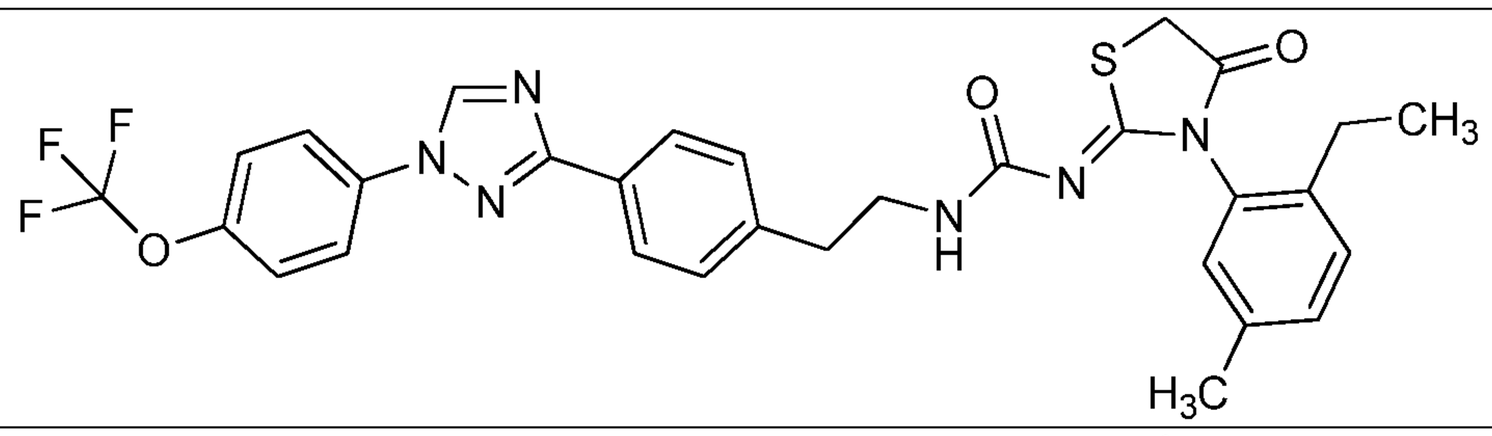
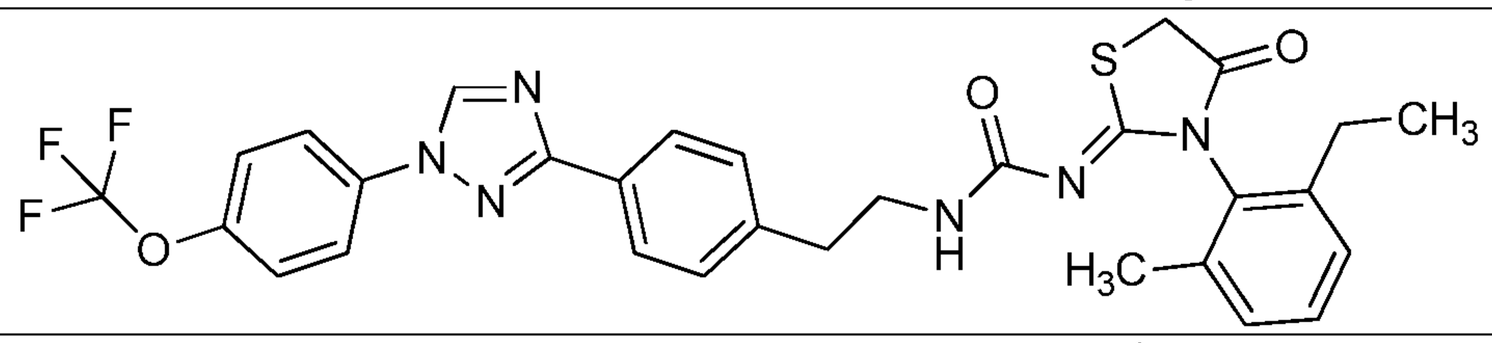
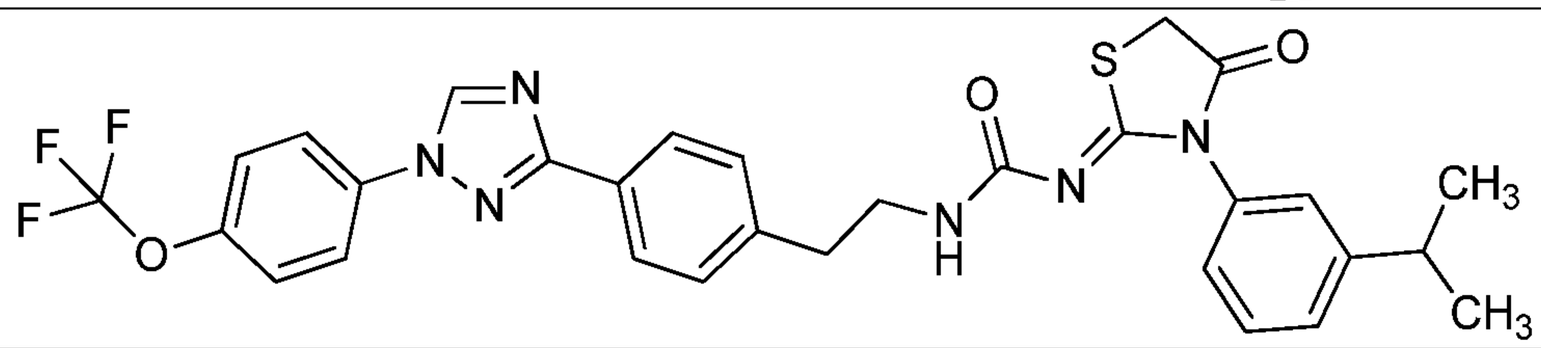
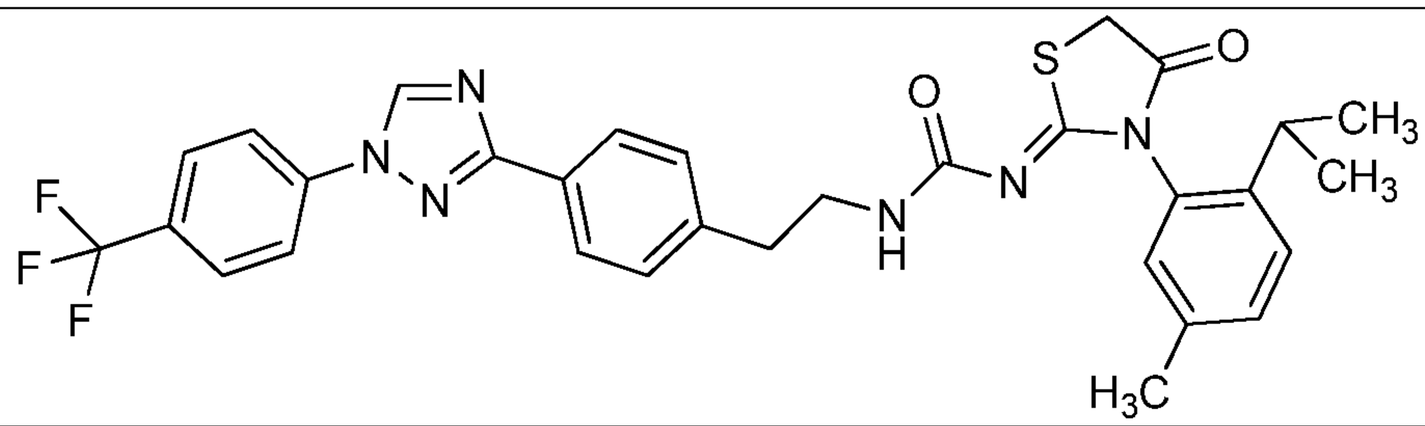
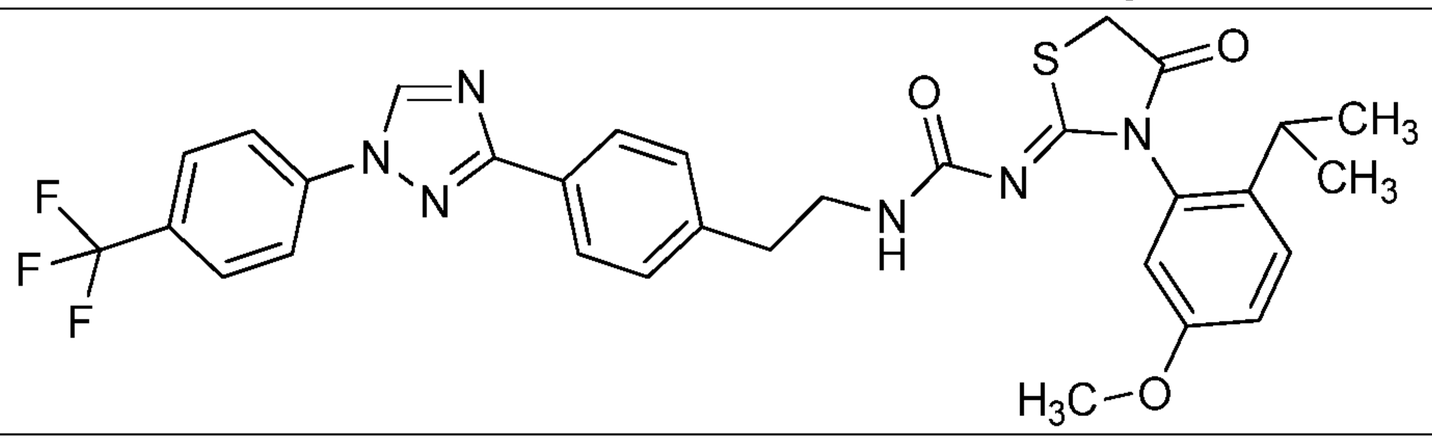
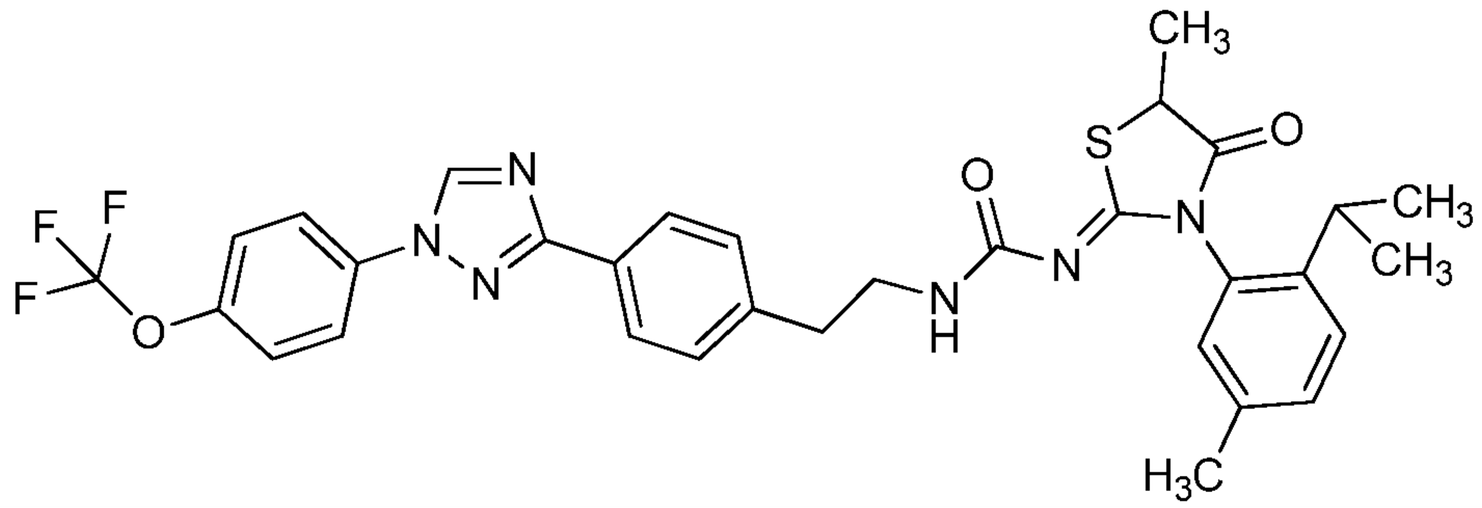
No.	Structure

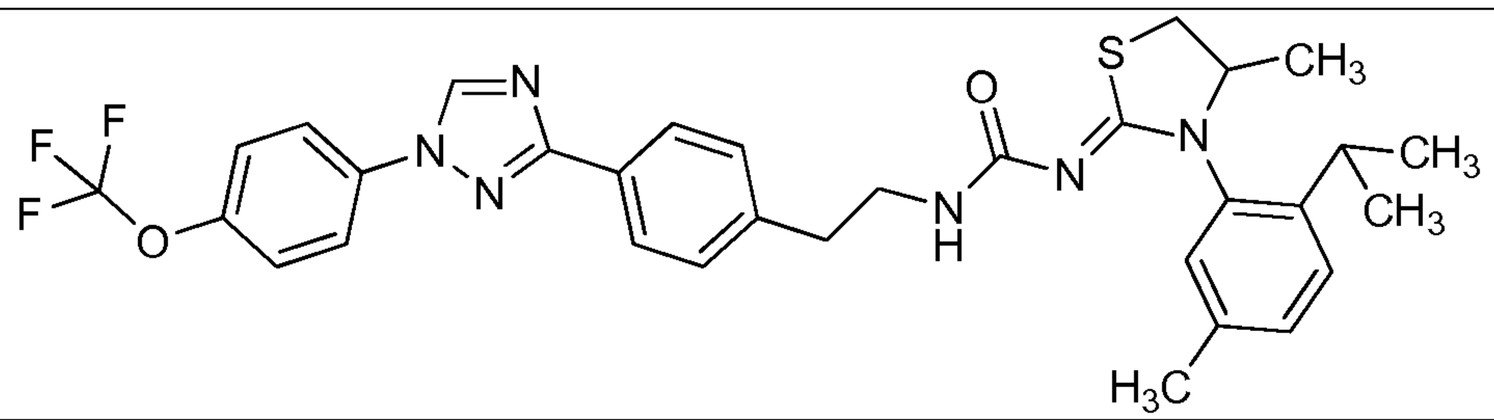
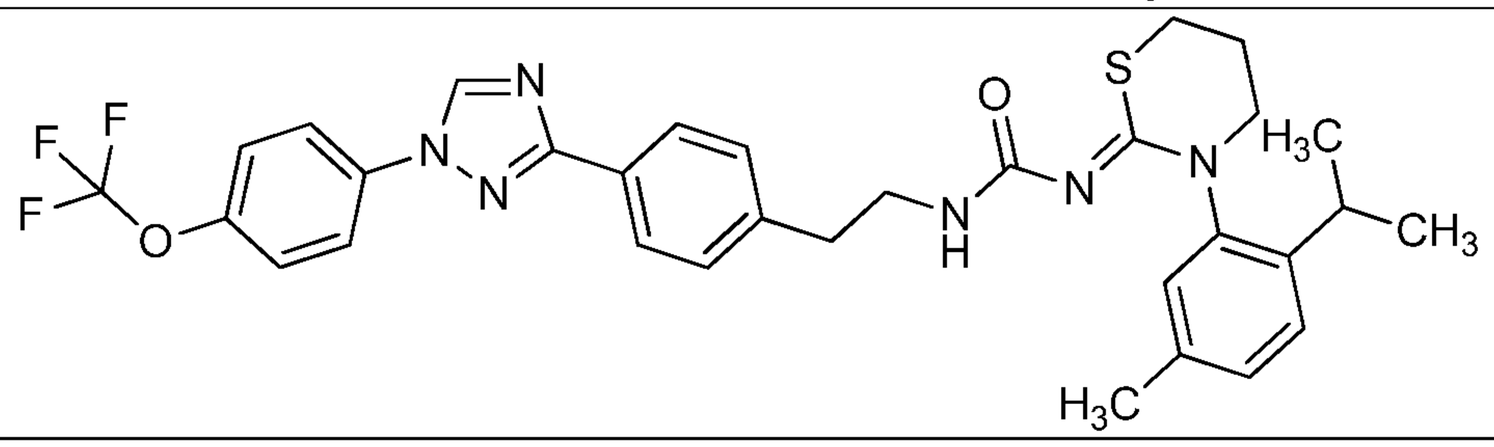
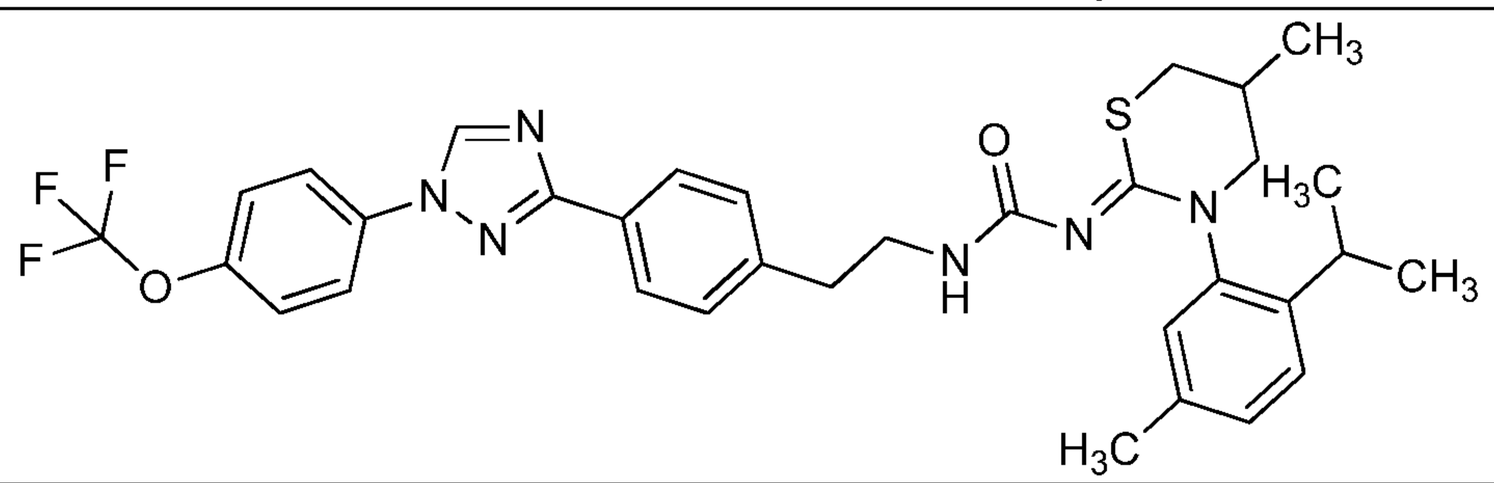
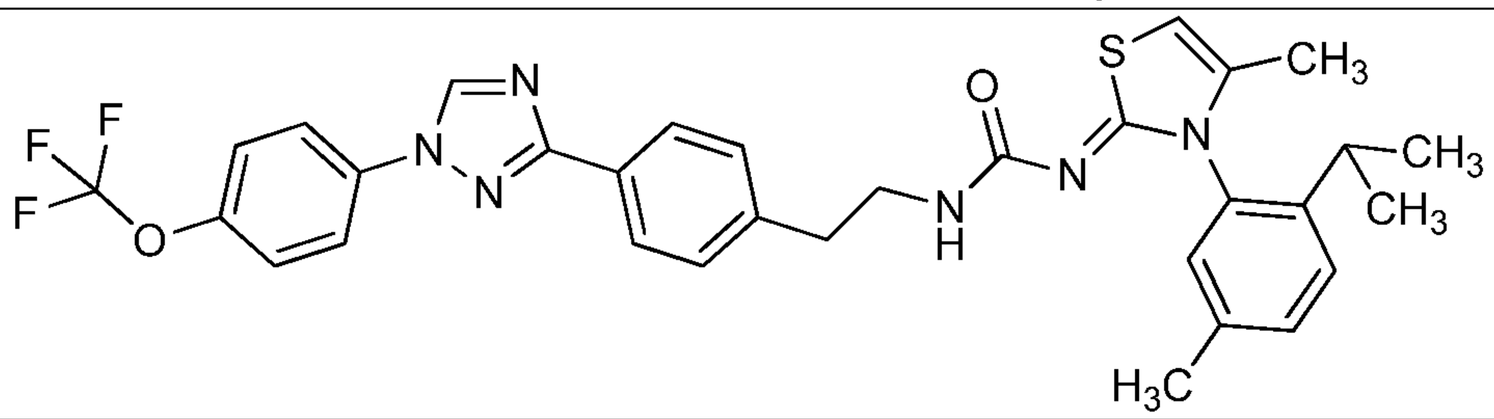
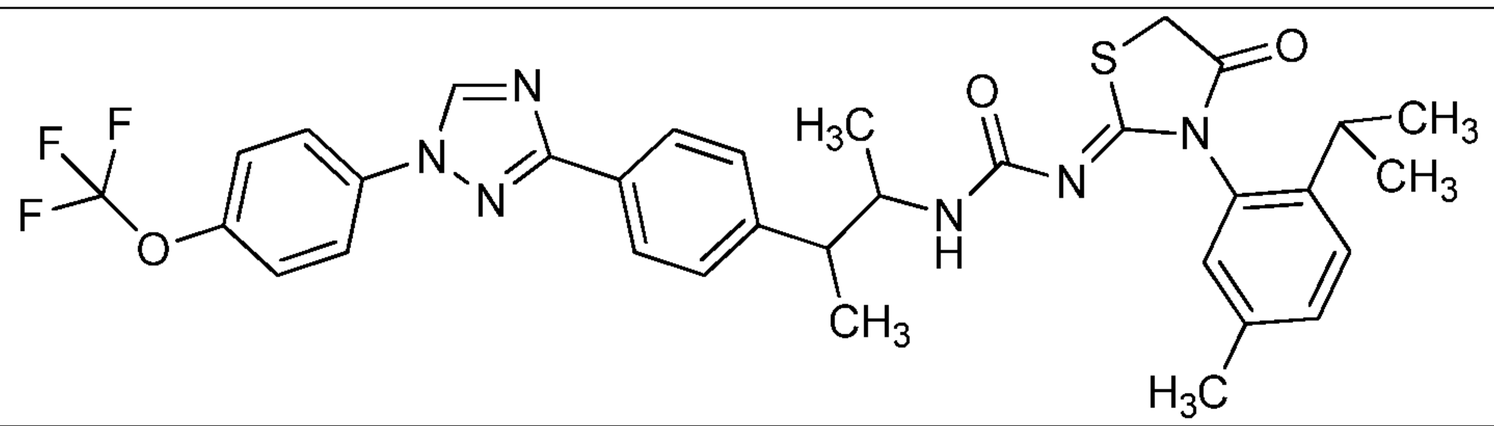
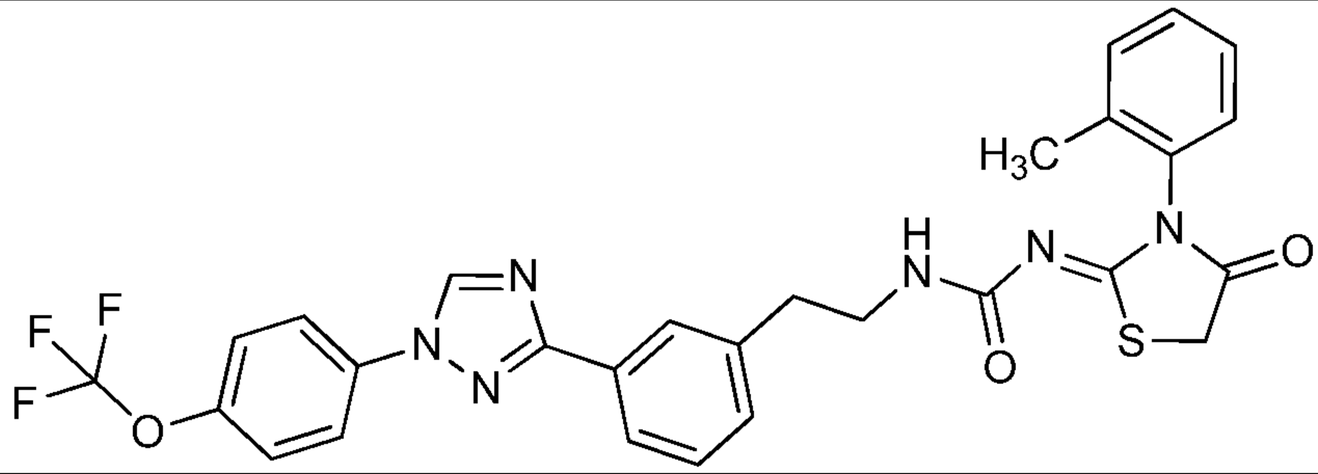
P1	
P2, P532	
P3, P1172	
P5	
P6	

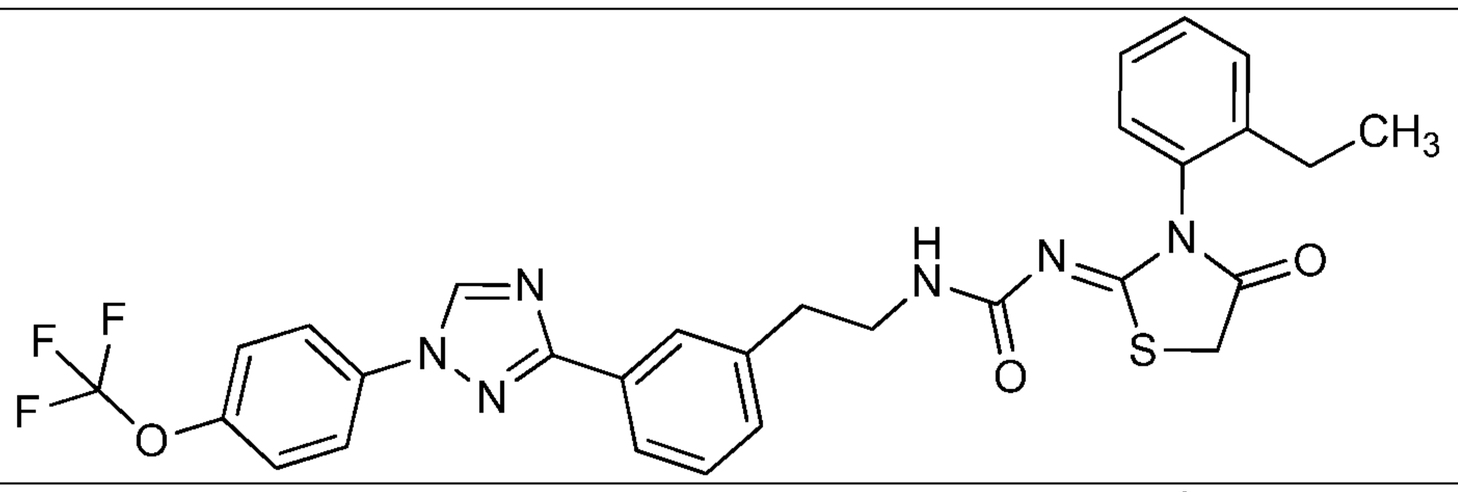
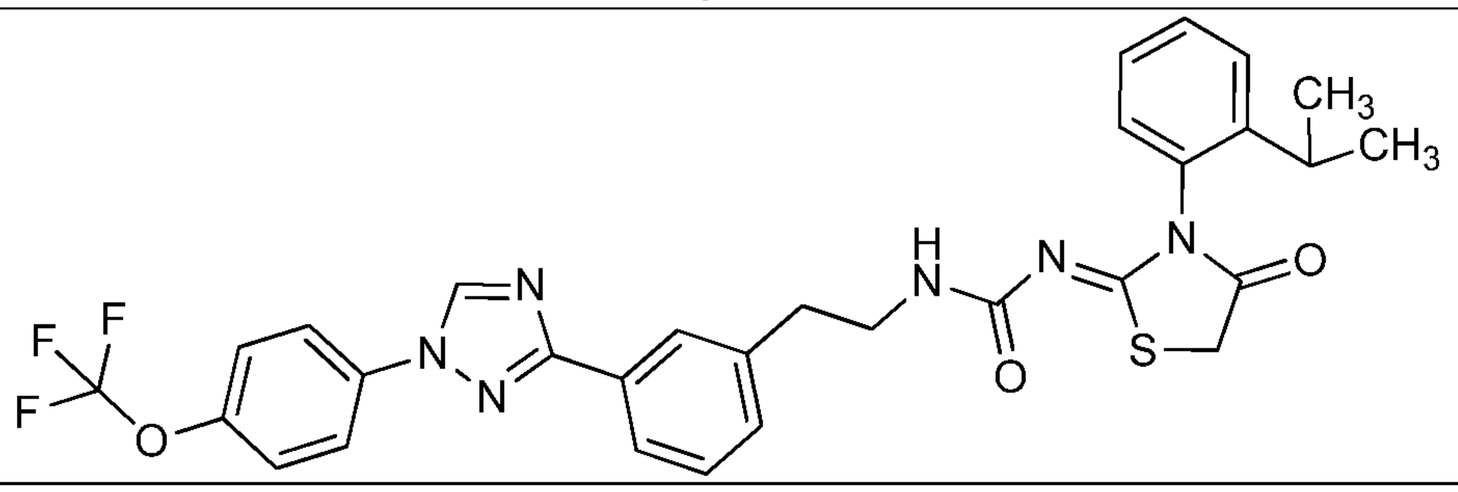
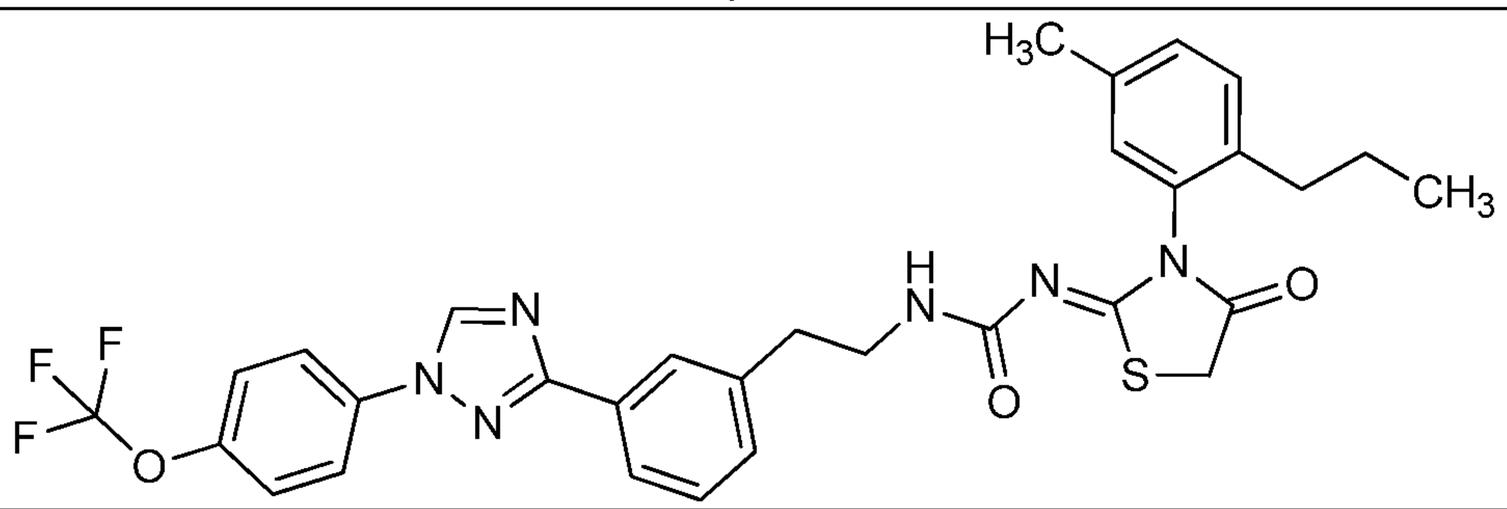
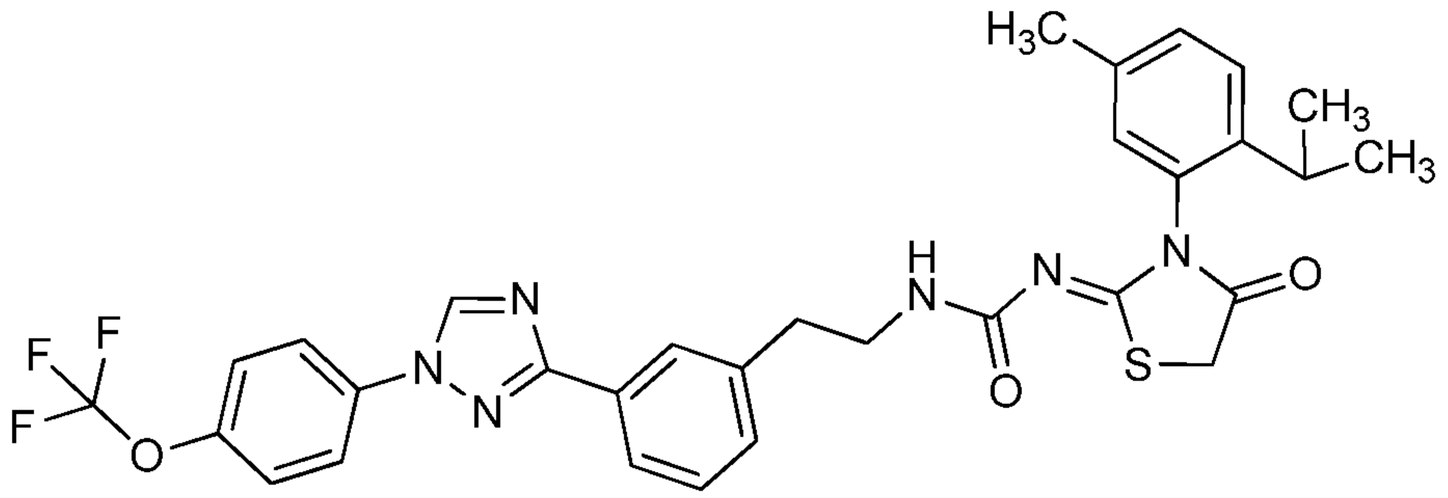
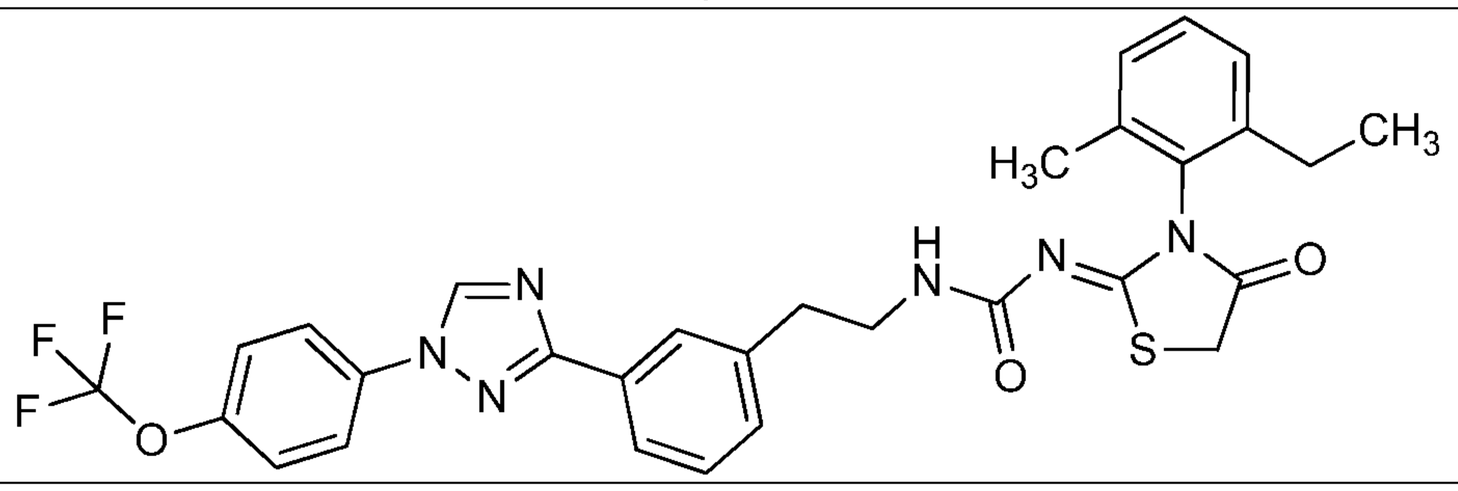
P7	
P8, P852	
P14	
P15	
P20	

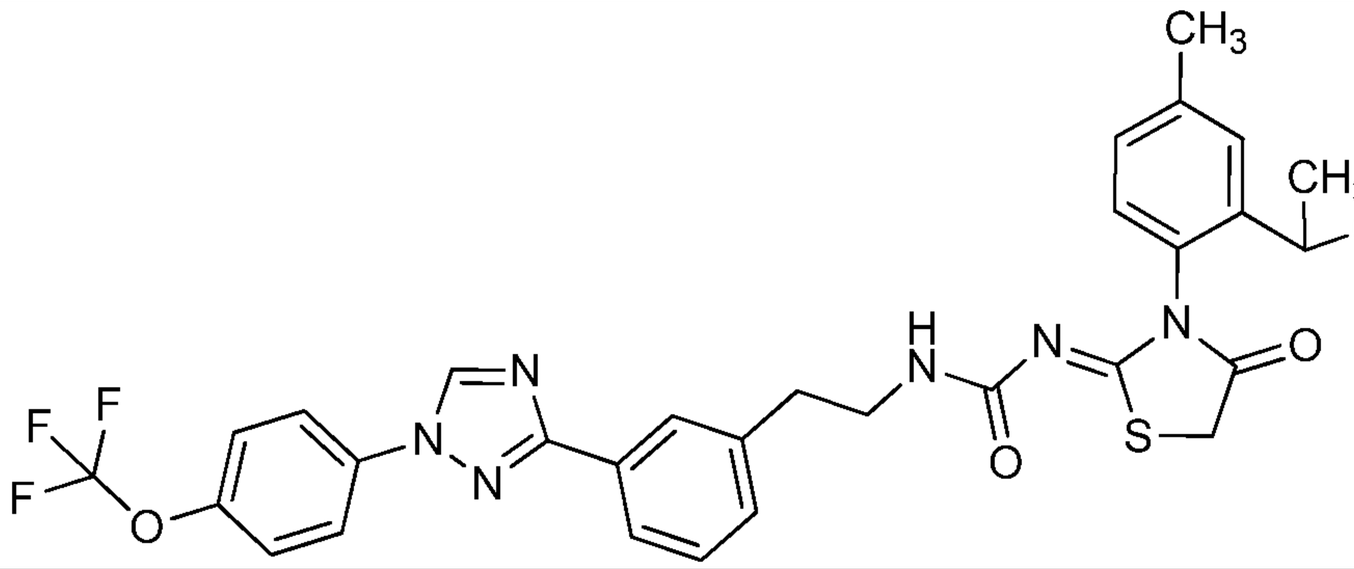
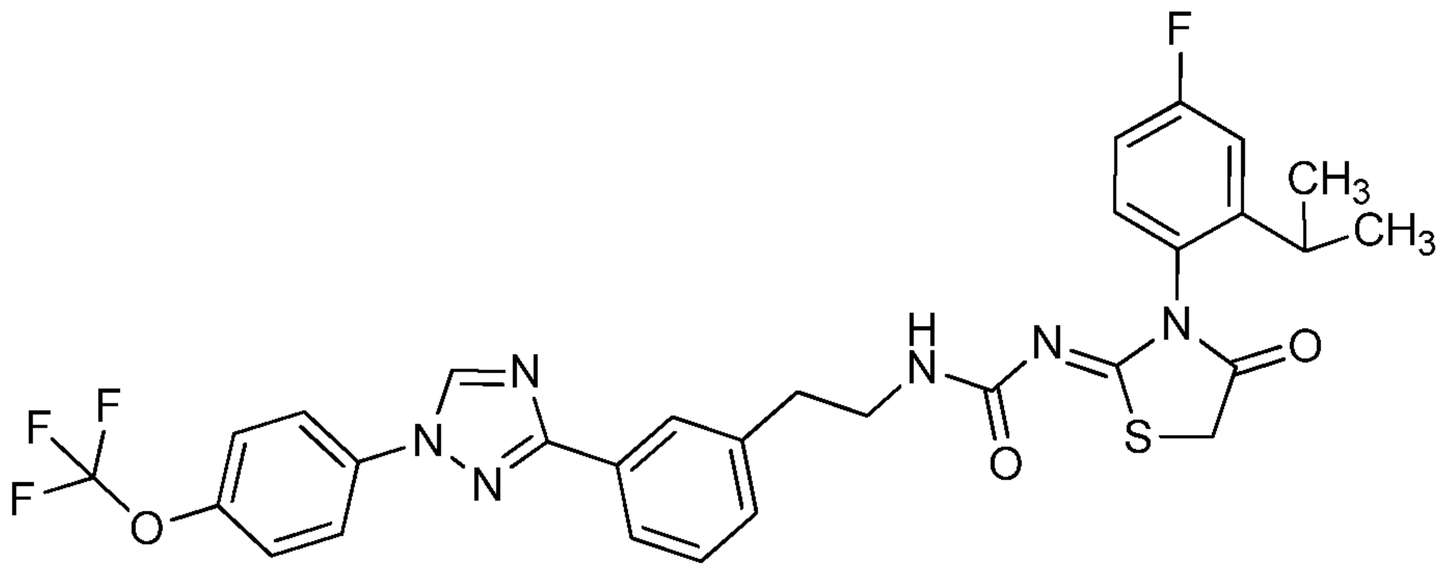
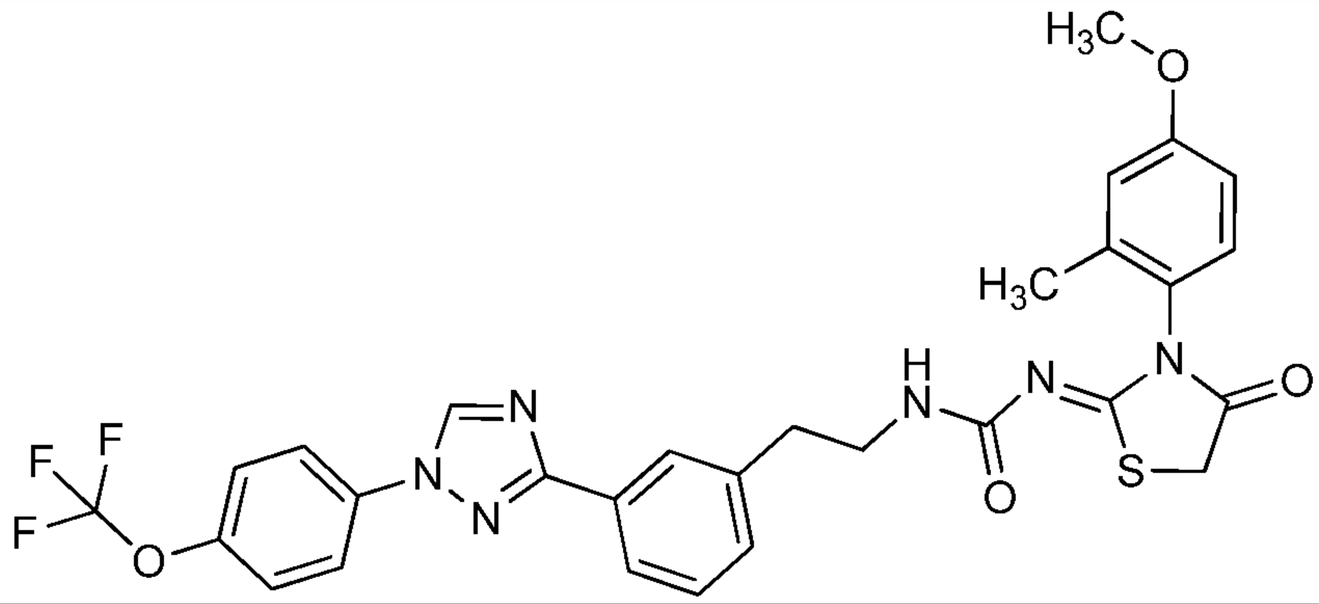
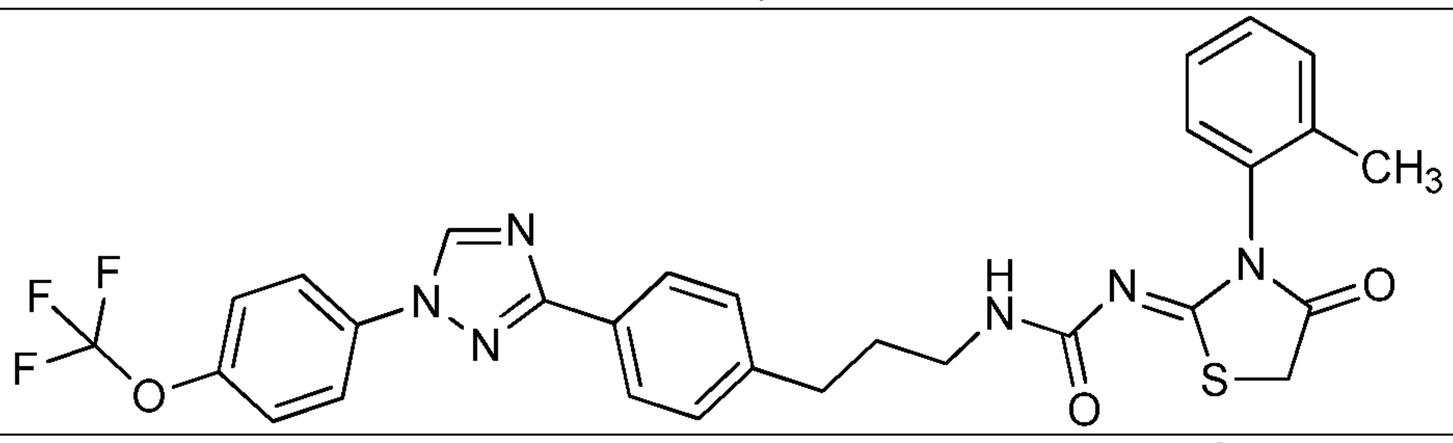
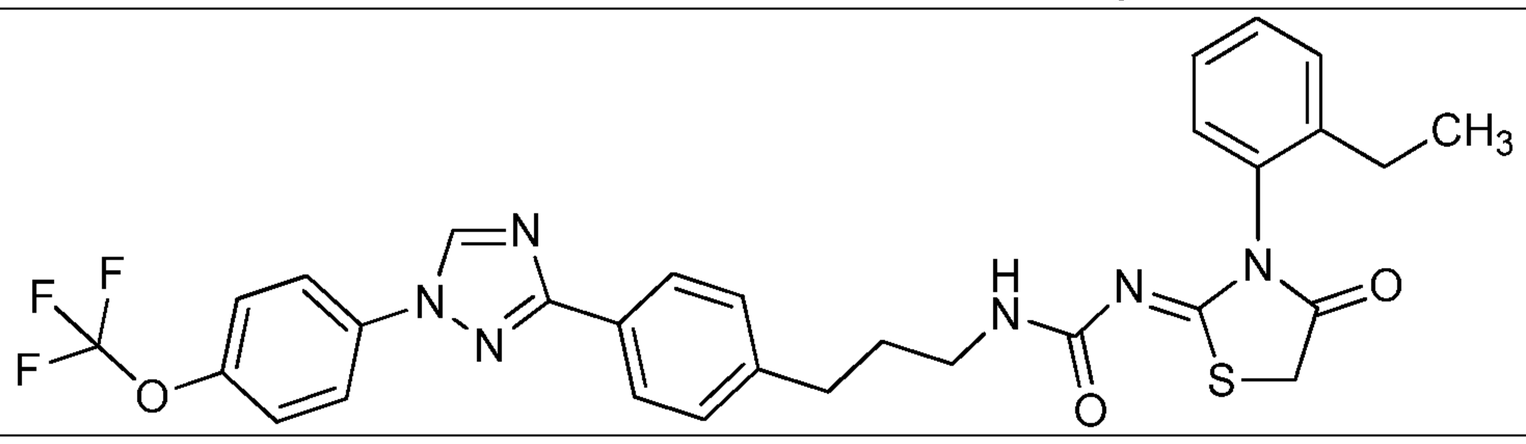
P26	
P27	
P28	
P29	
P30	
P31	

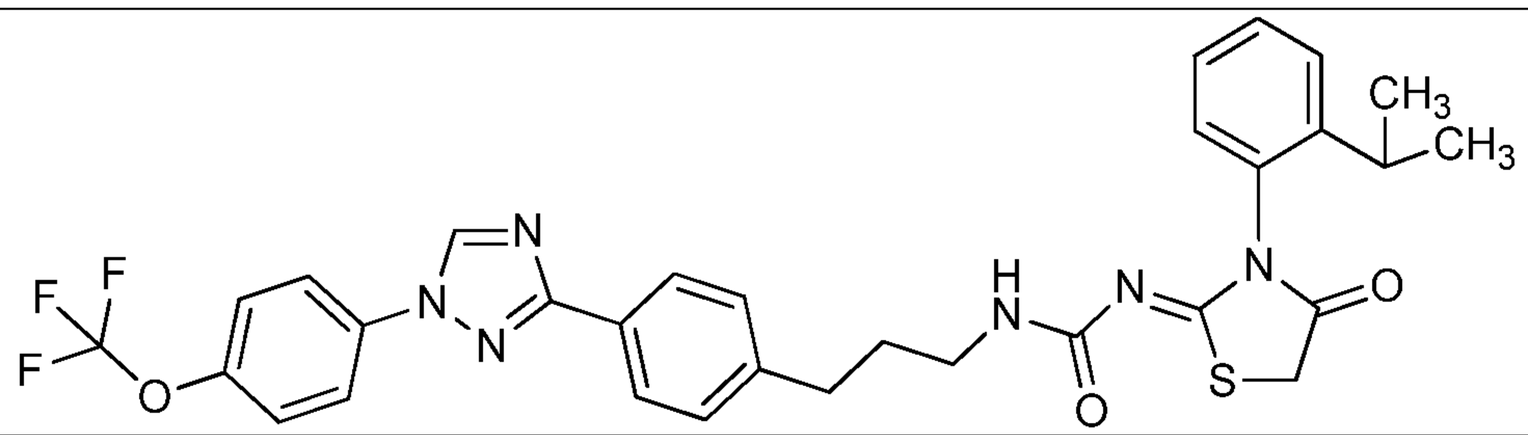
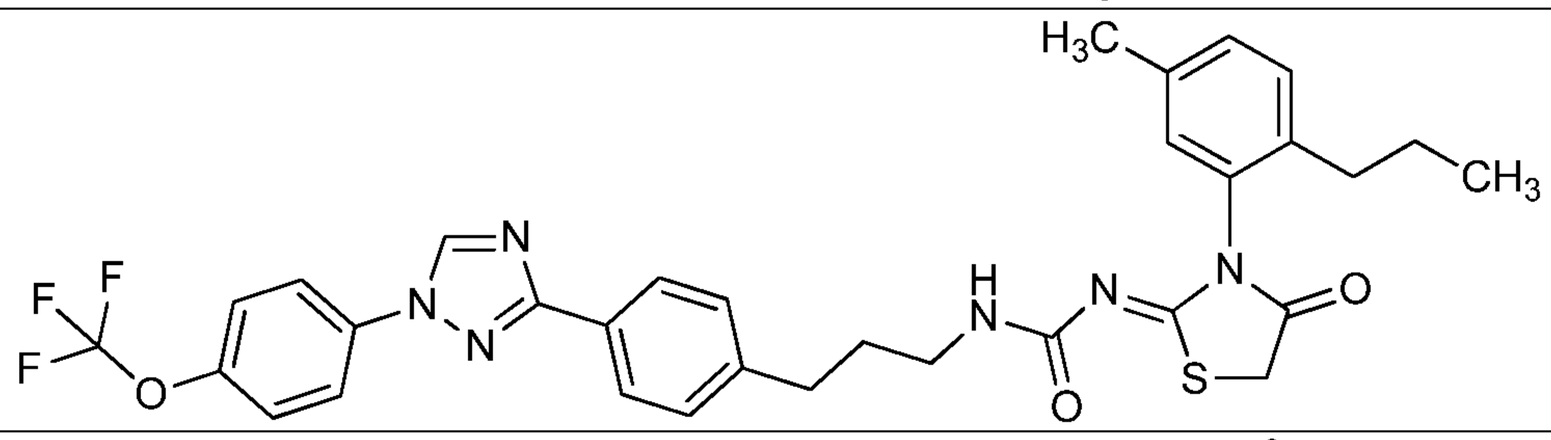
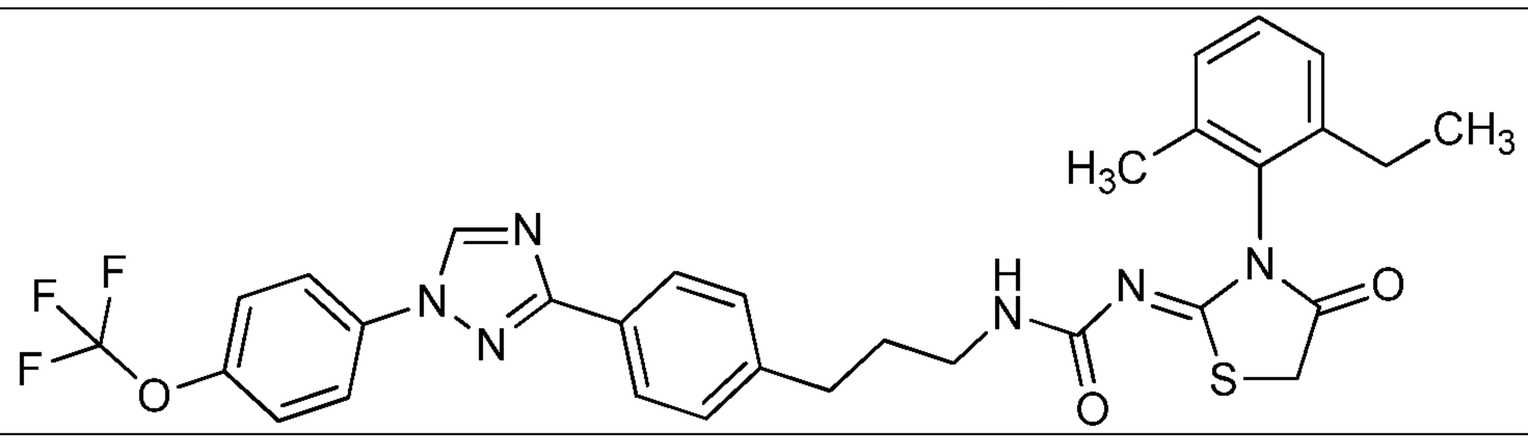
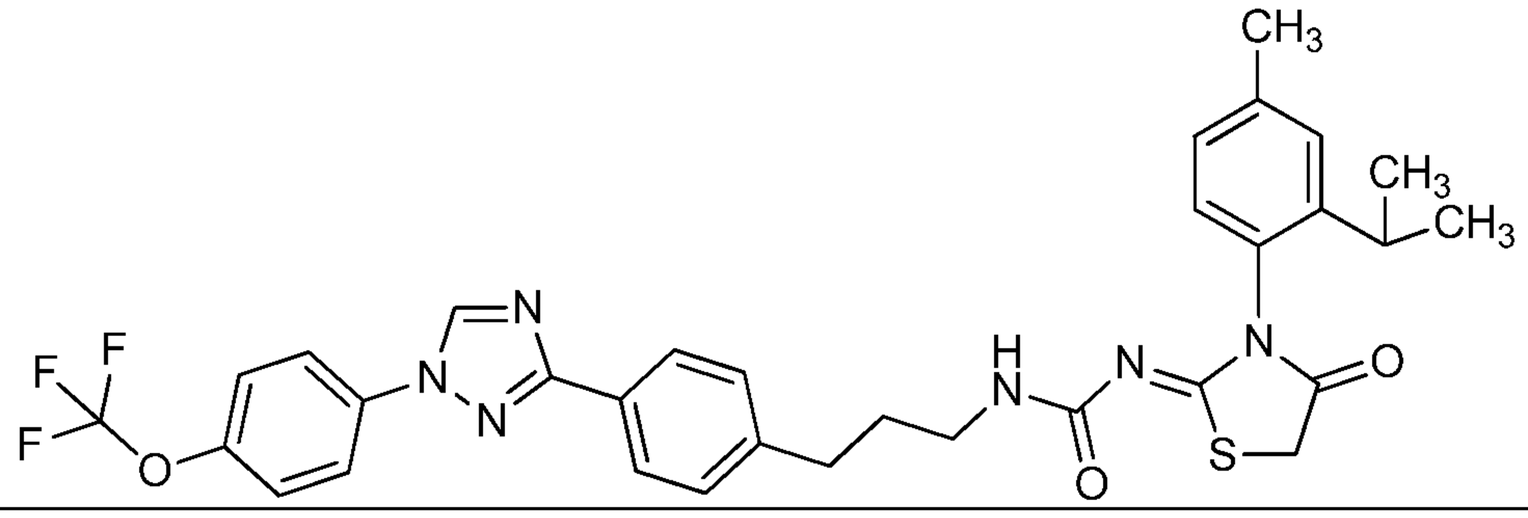
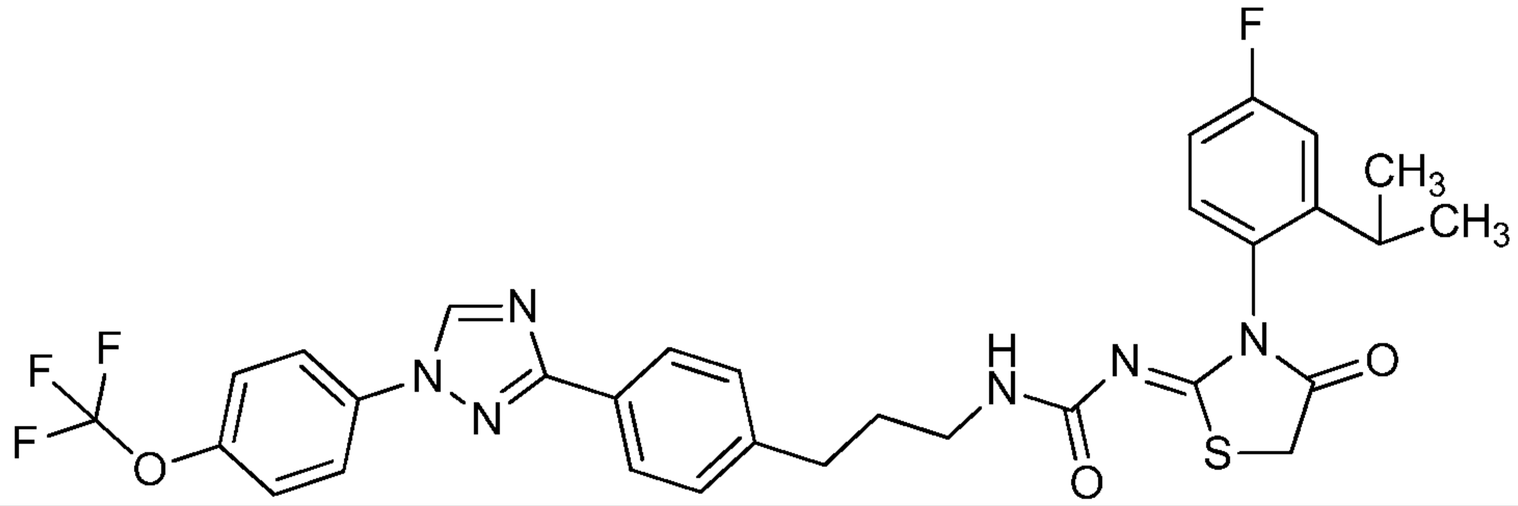
P33	
P42	
P44	
P45	
P47	

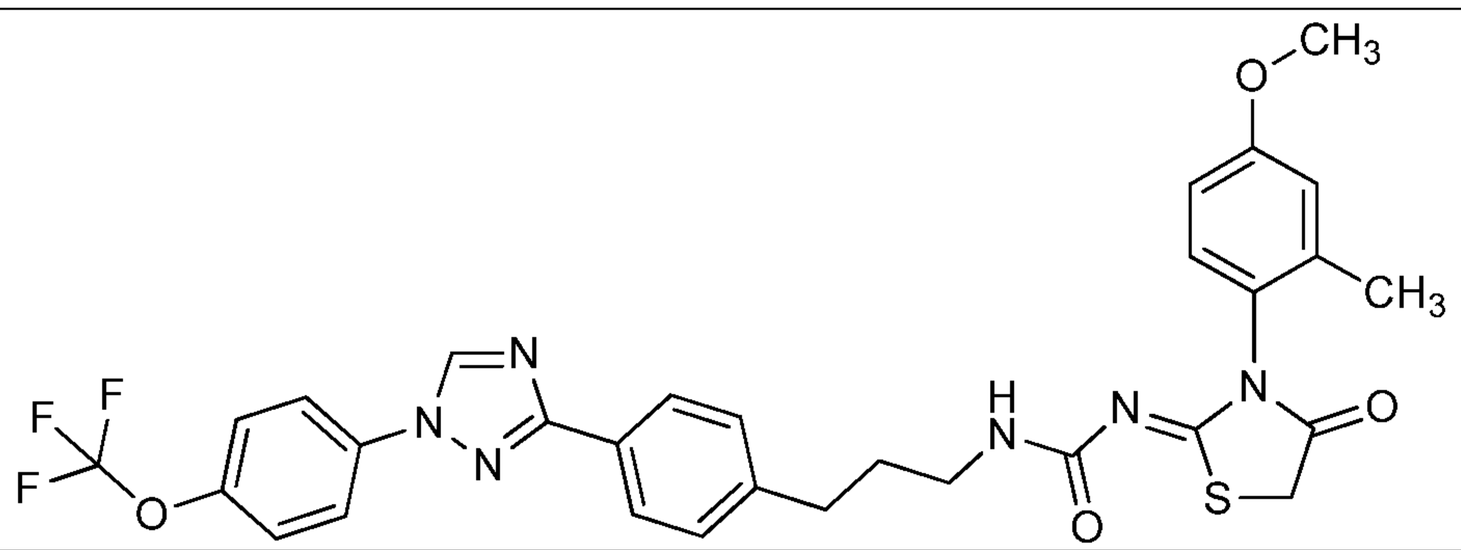
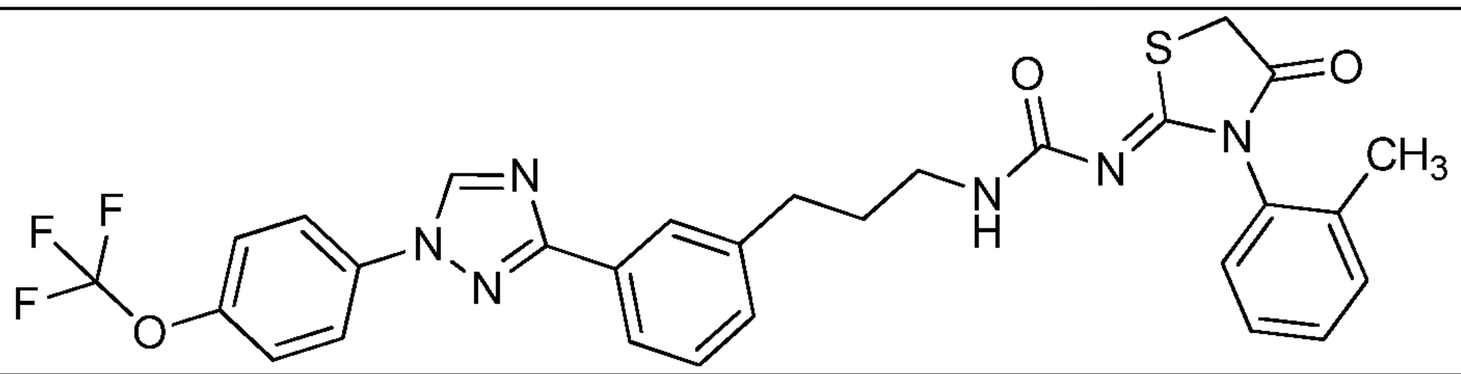
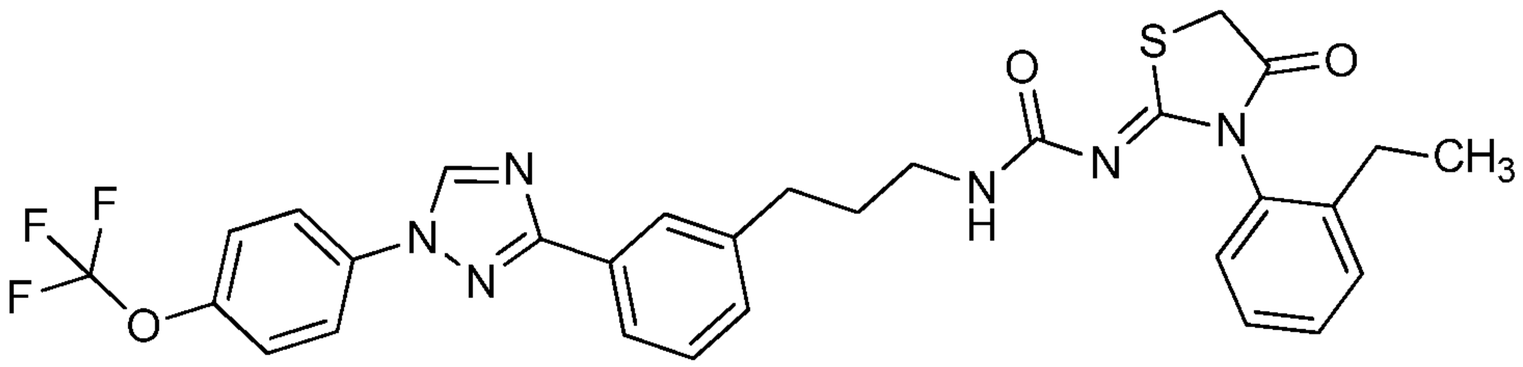
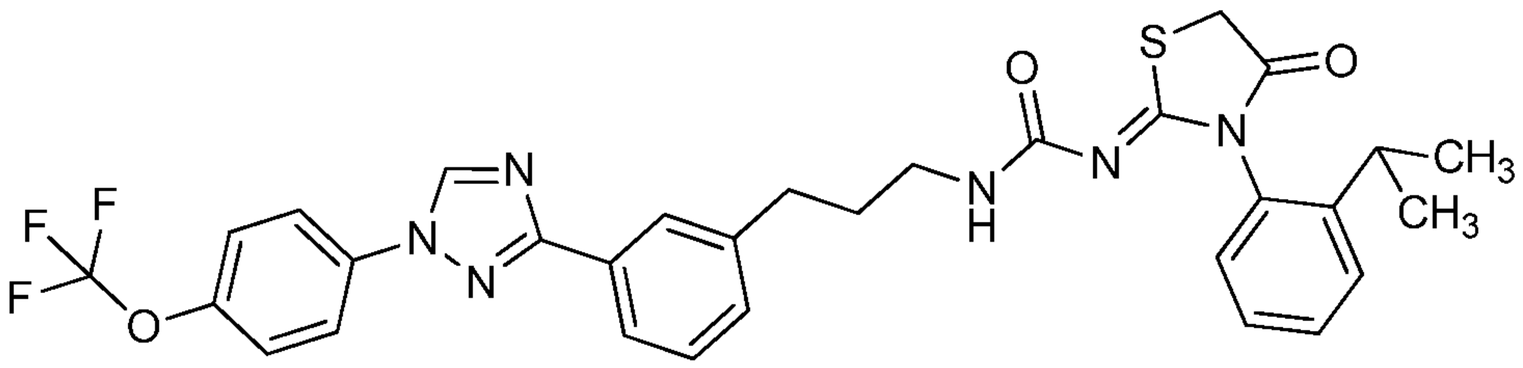
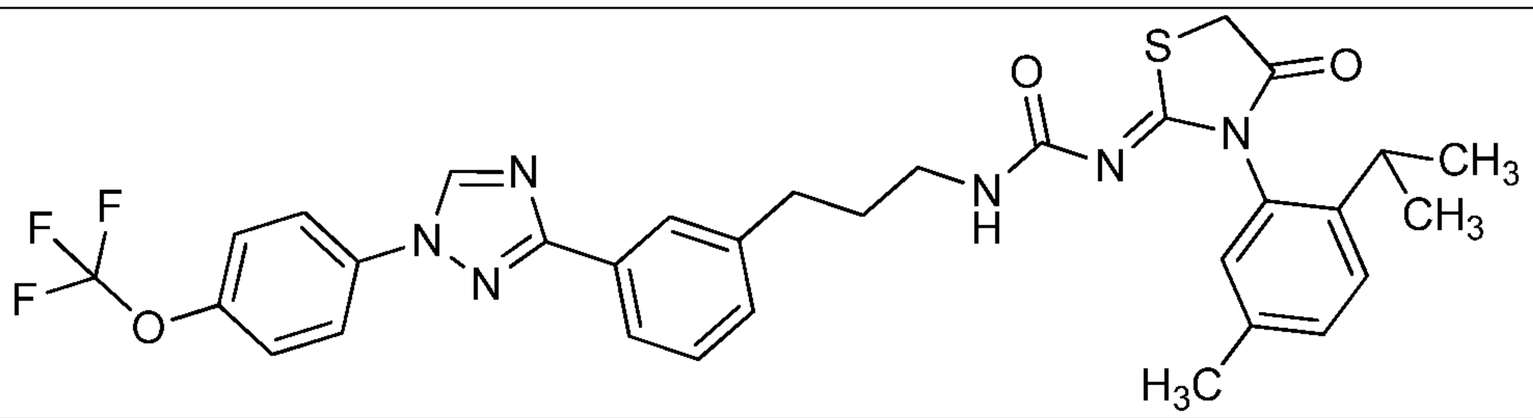
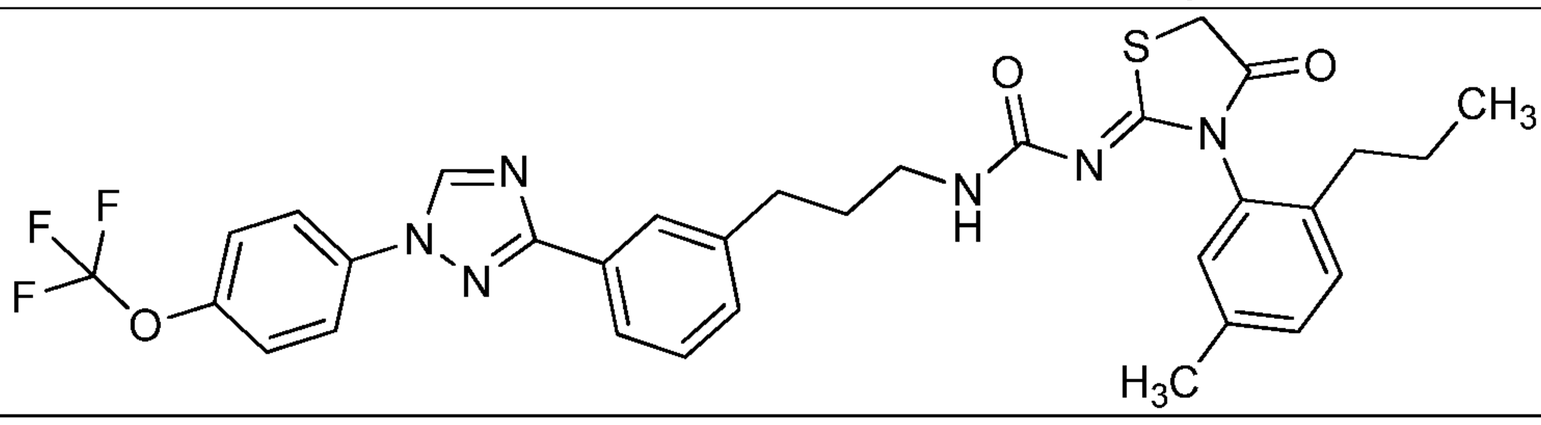
P49	
P50	
P51	
P52	
P53	
P57	

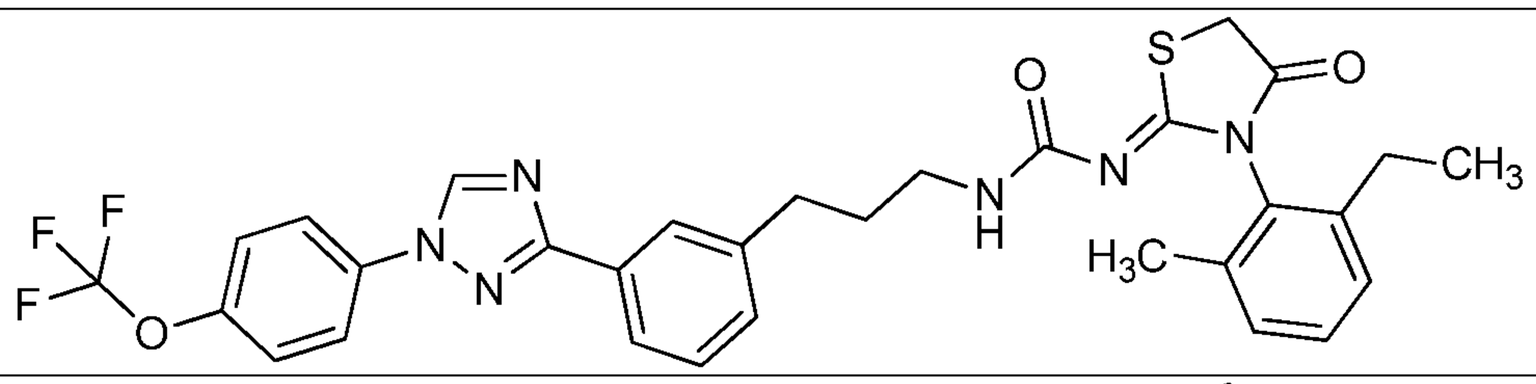
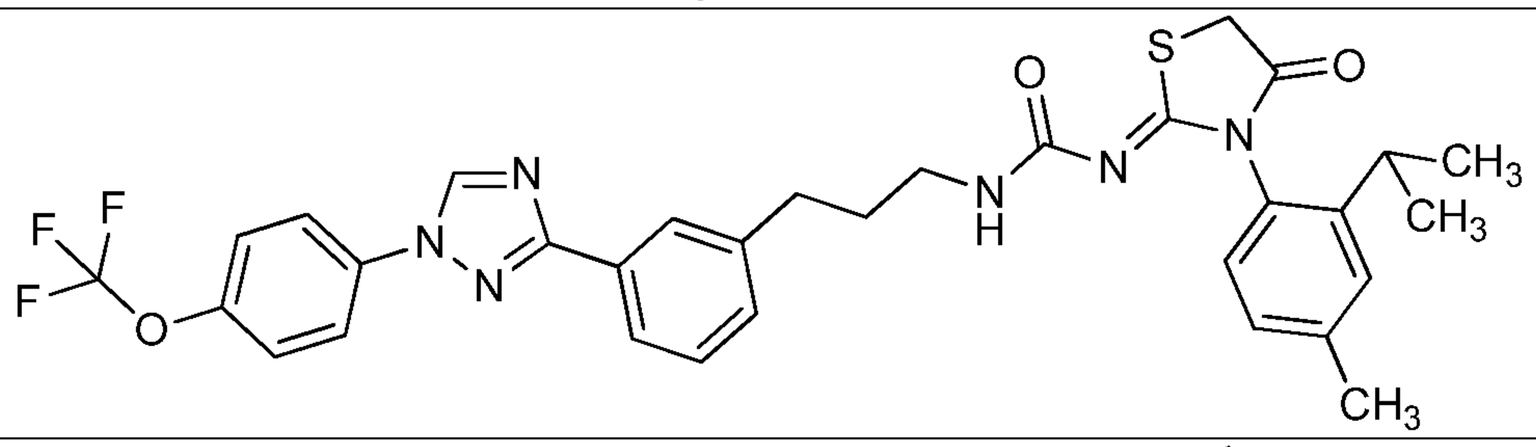
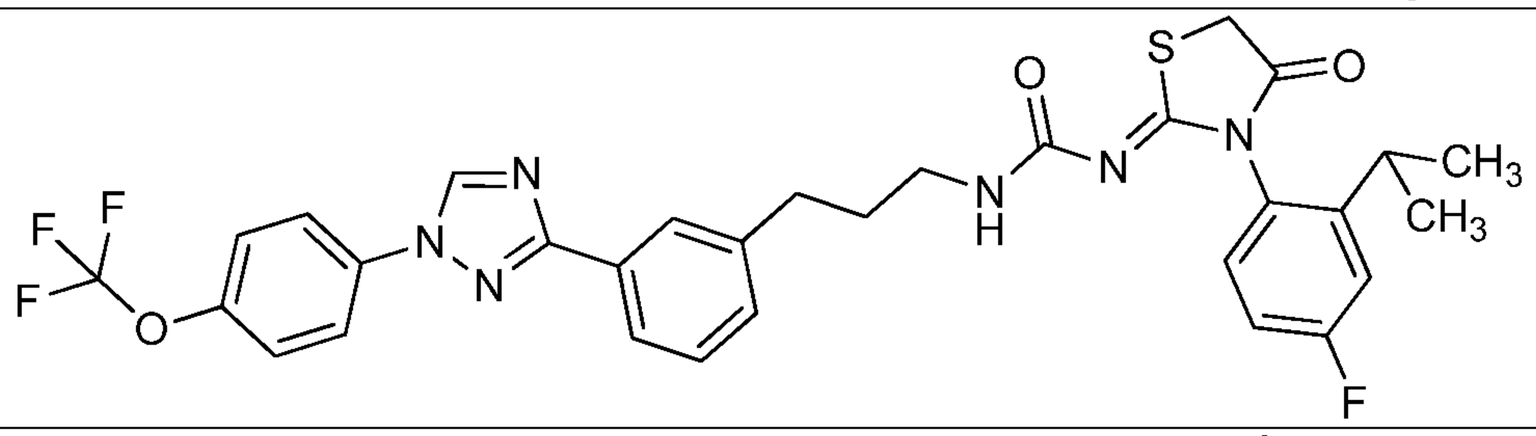
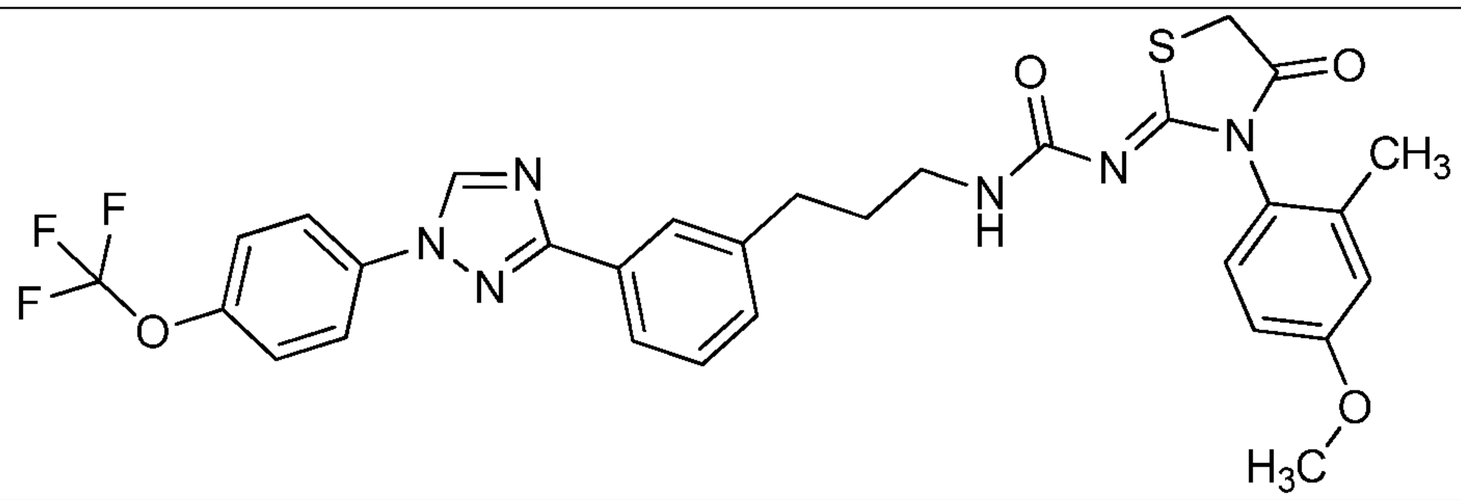
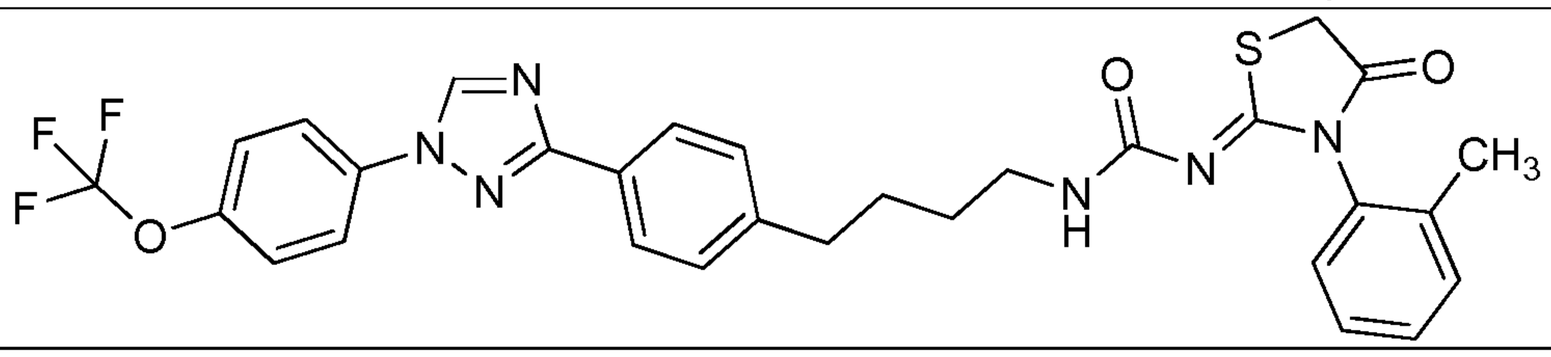
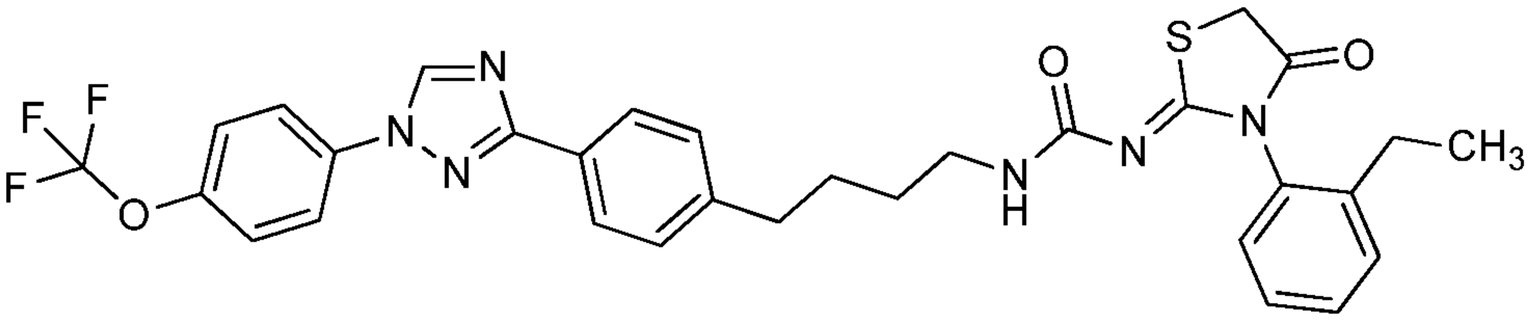
P58	
P59	
P64	
P65	
P66, P353	
P74	

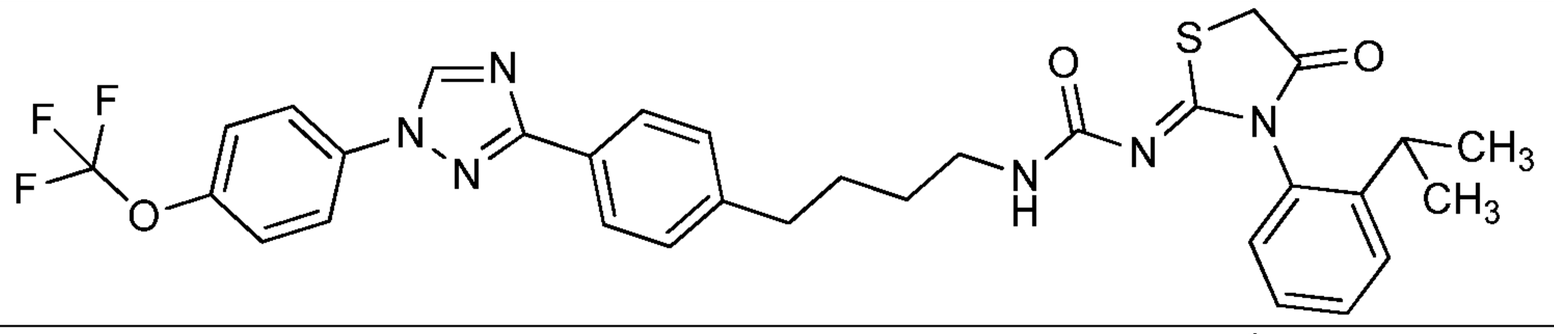
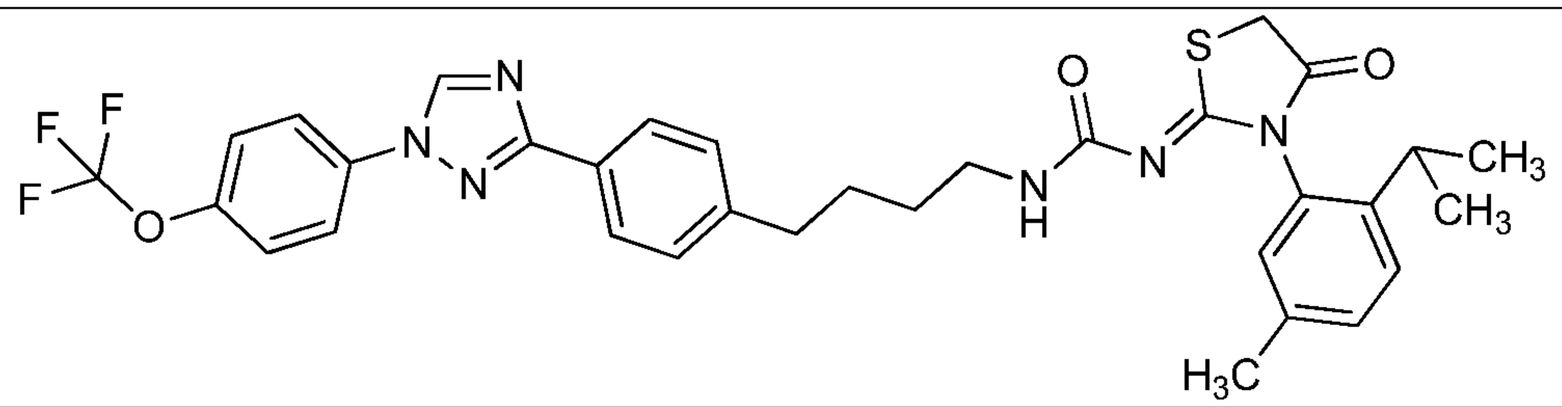
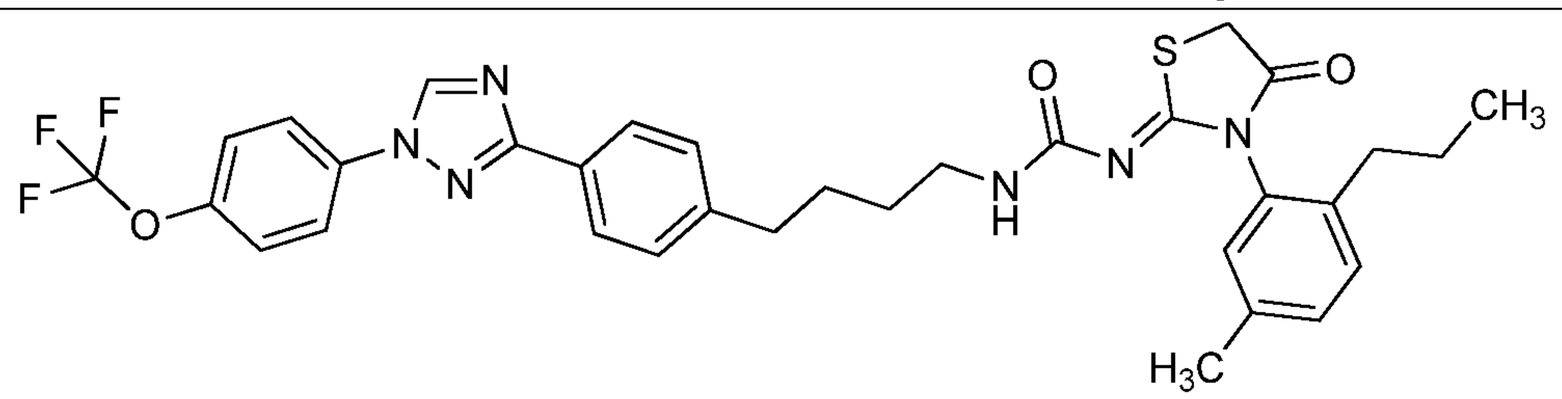
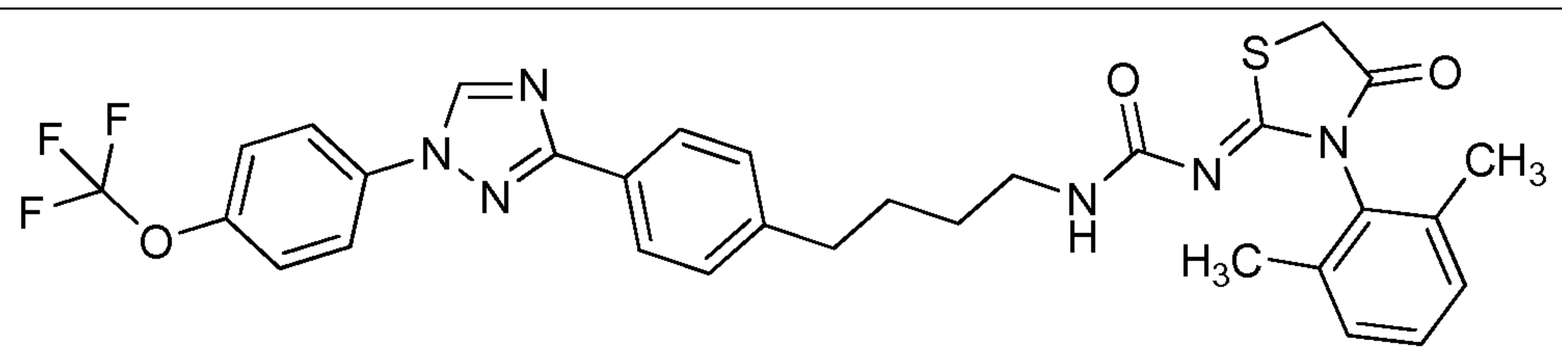
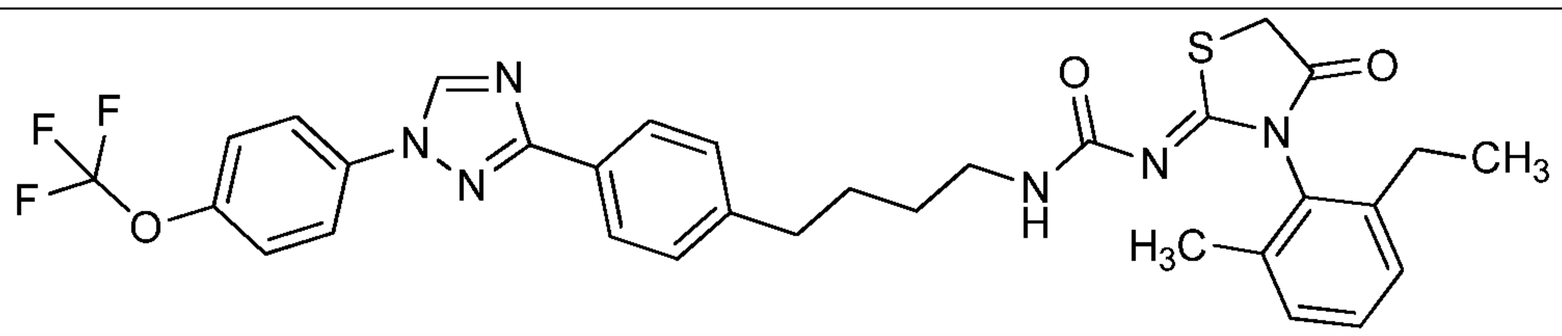
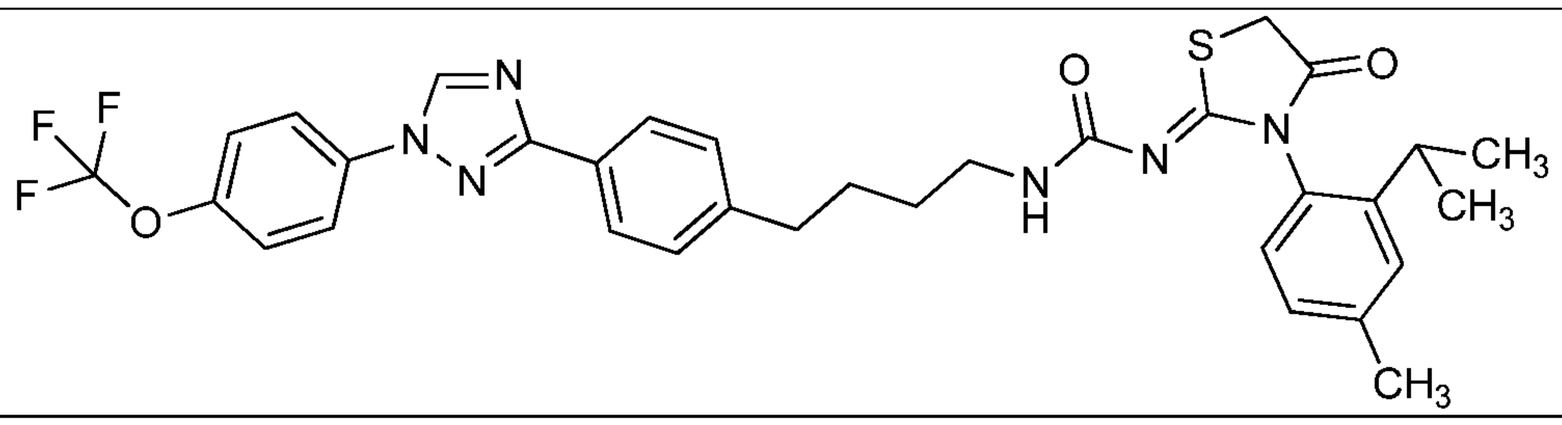
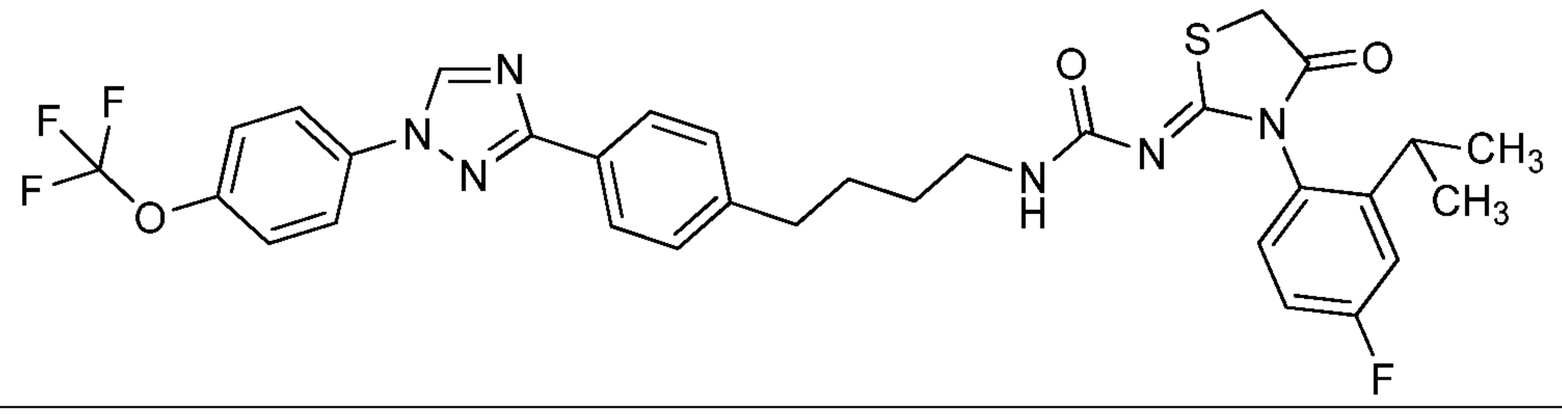
P75	
P76	
P80	
P81	
P83	

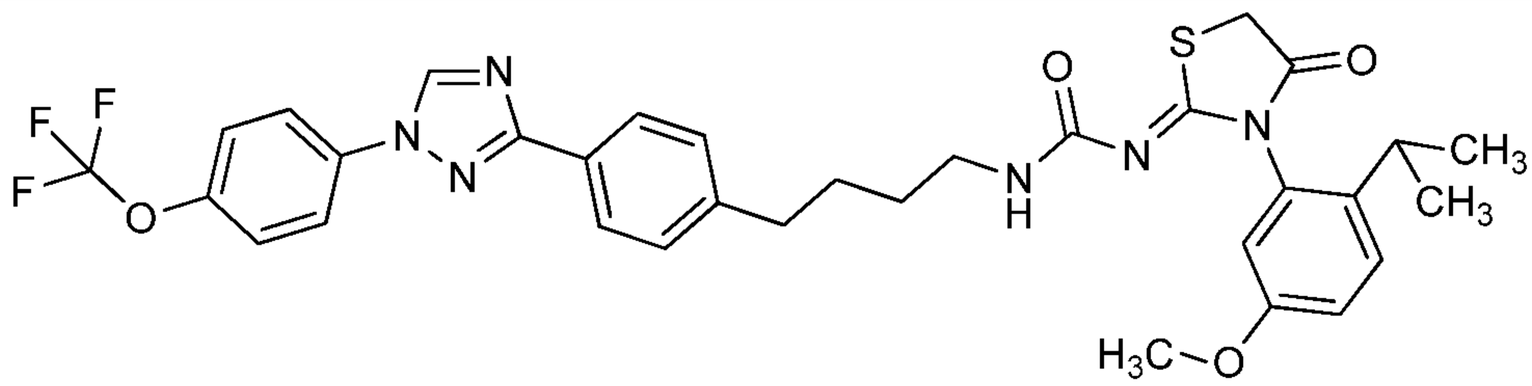
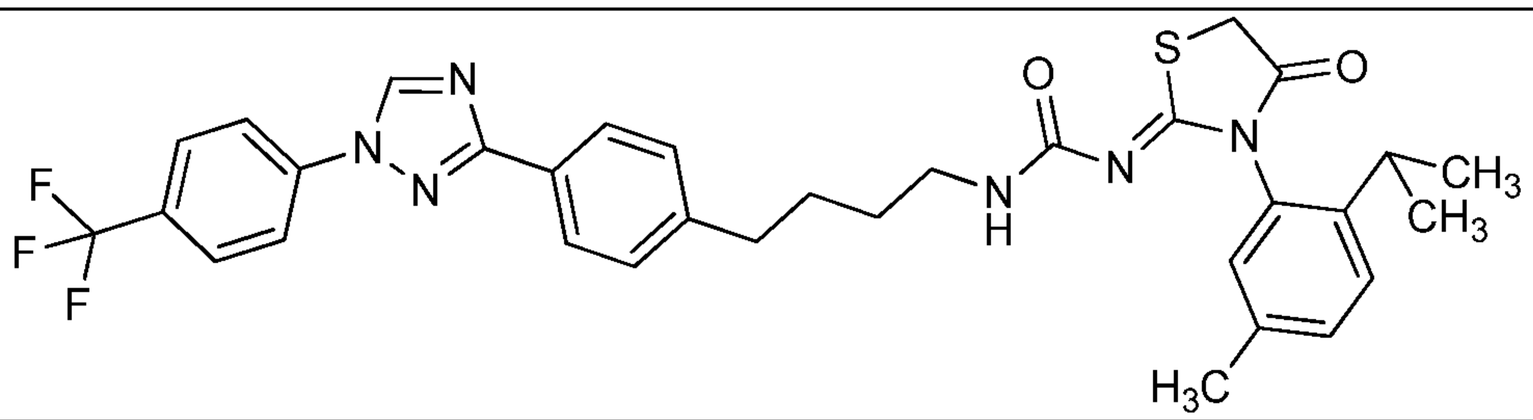
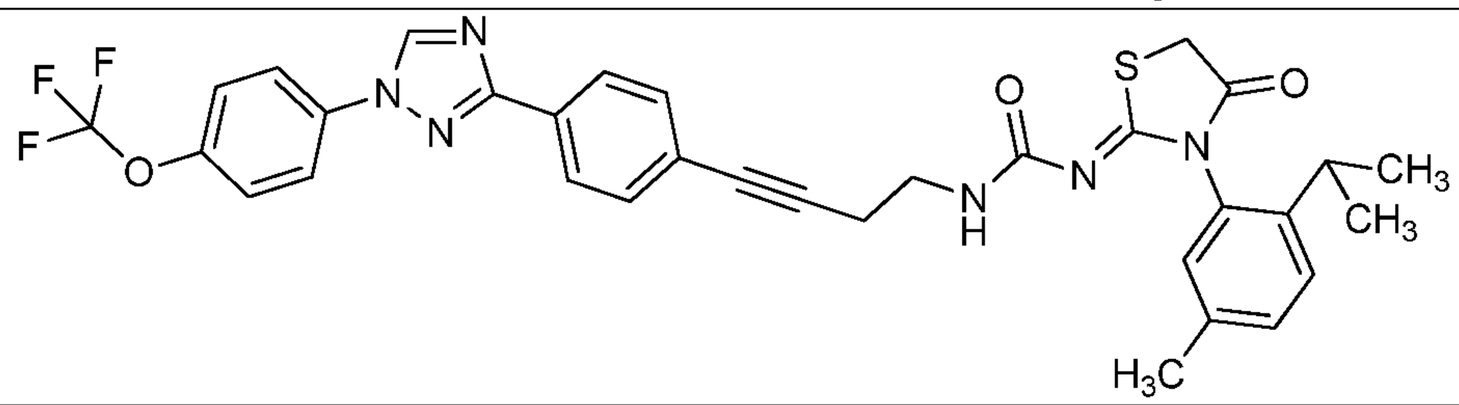
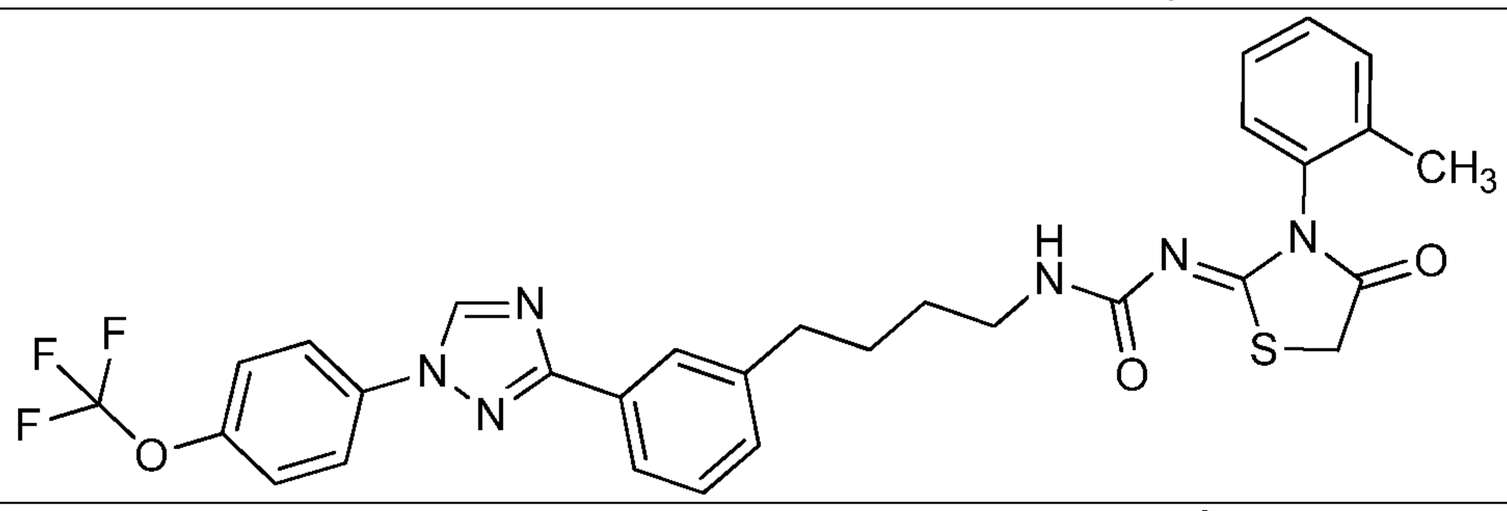
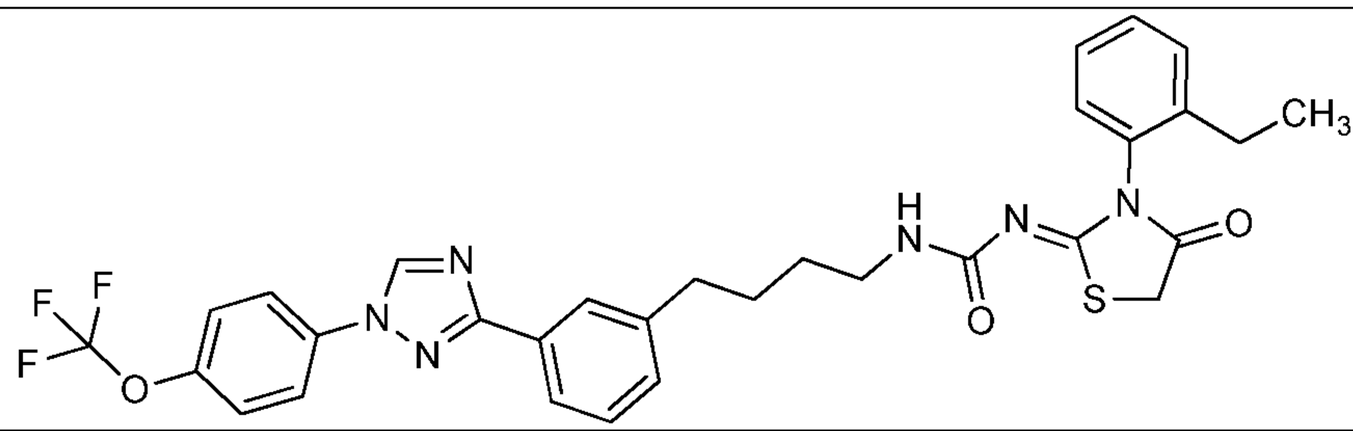
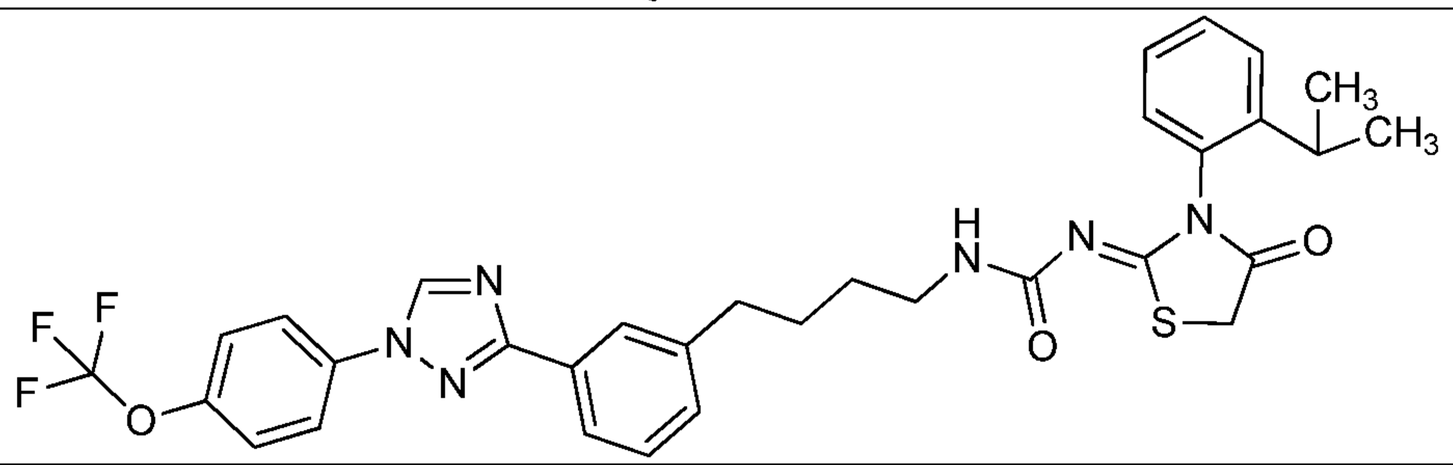
P84	
P85	
P87	
P92	
P93, P510	

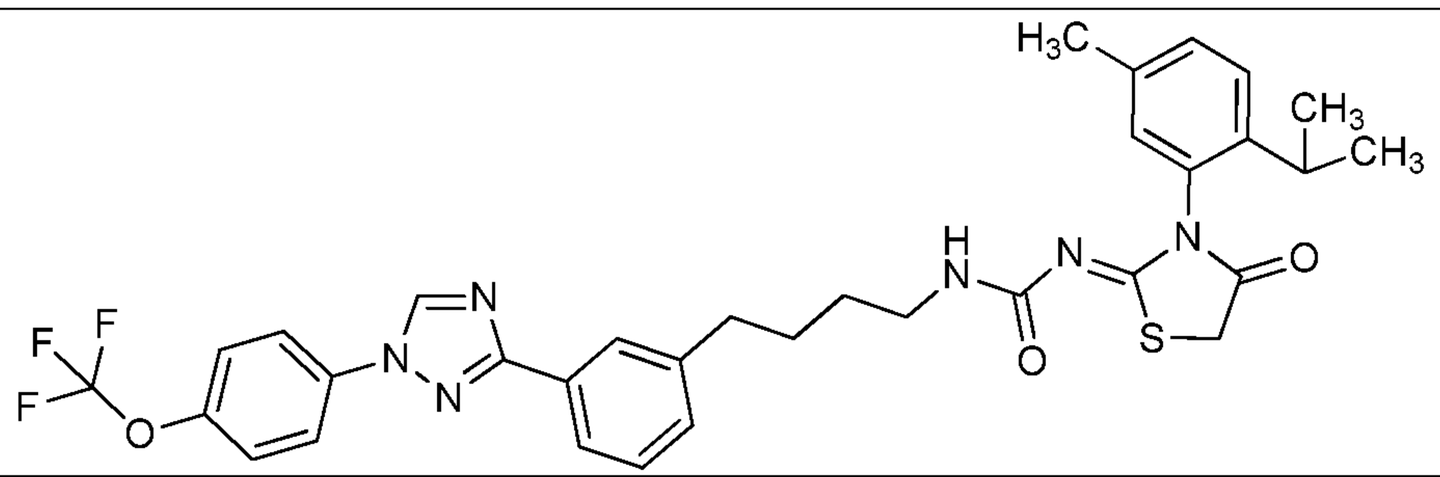
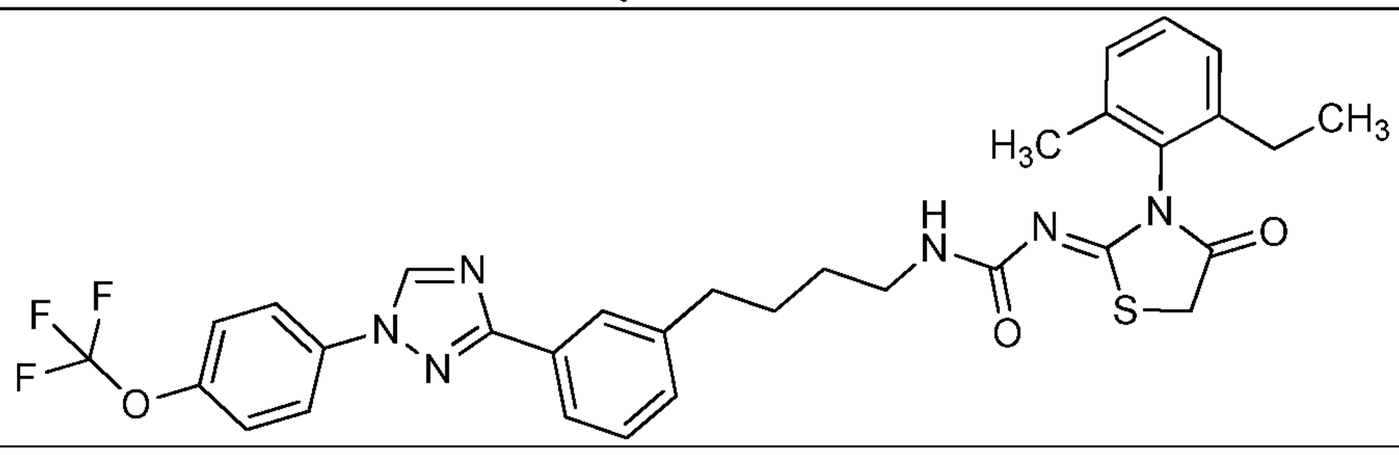
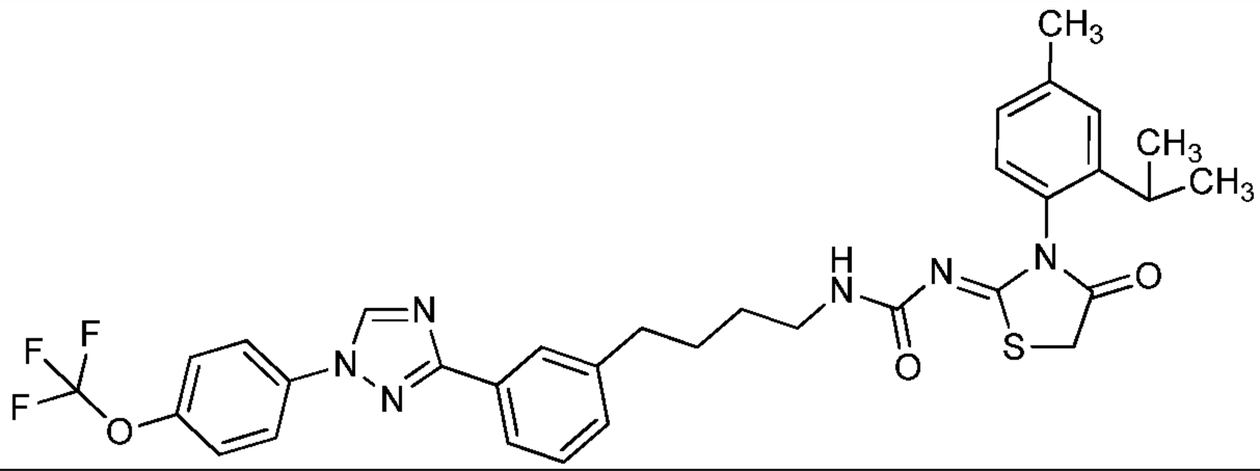
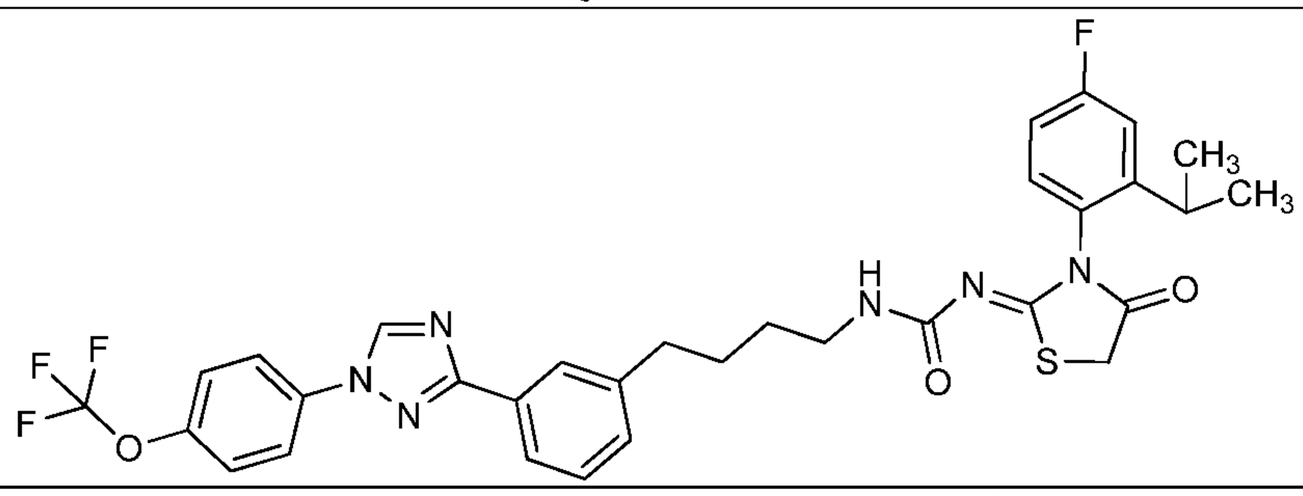
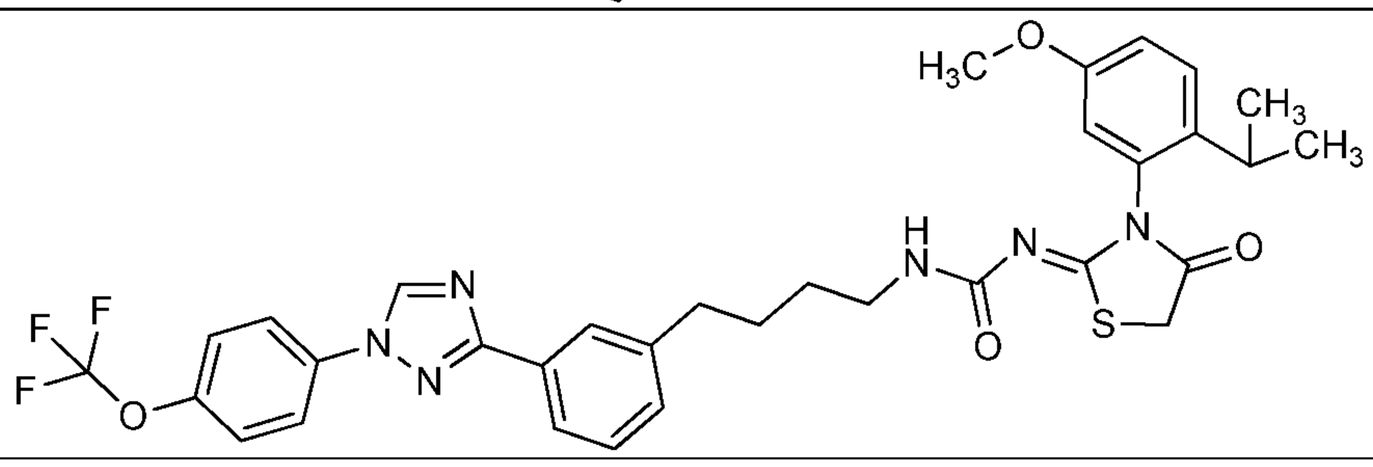
P94, P197	
P99, P830	
P101	
P102	
P103, P1150	

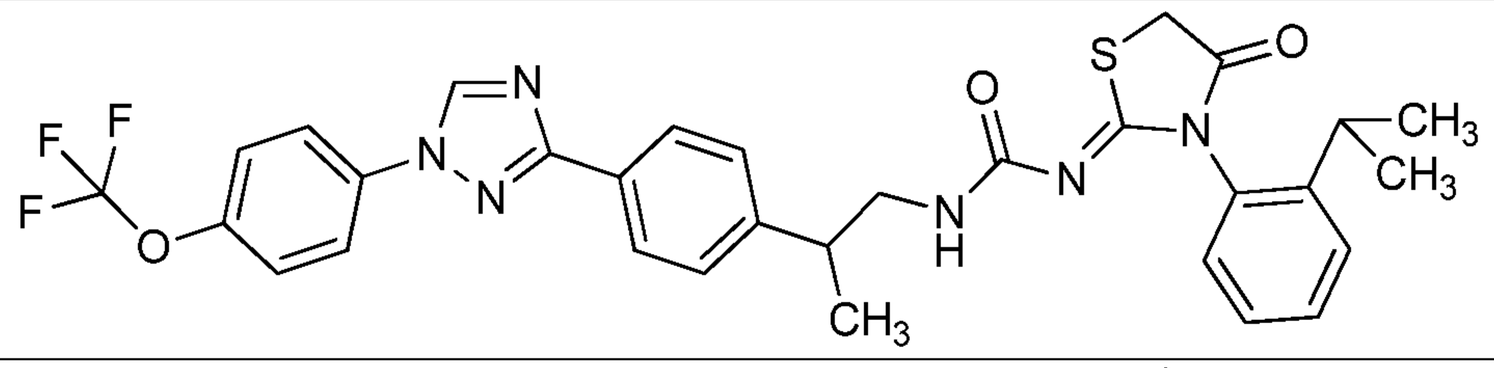
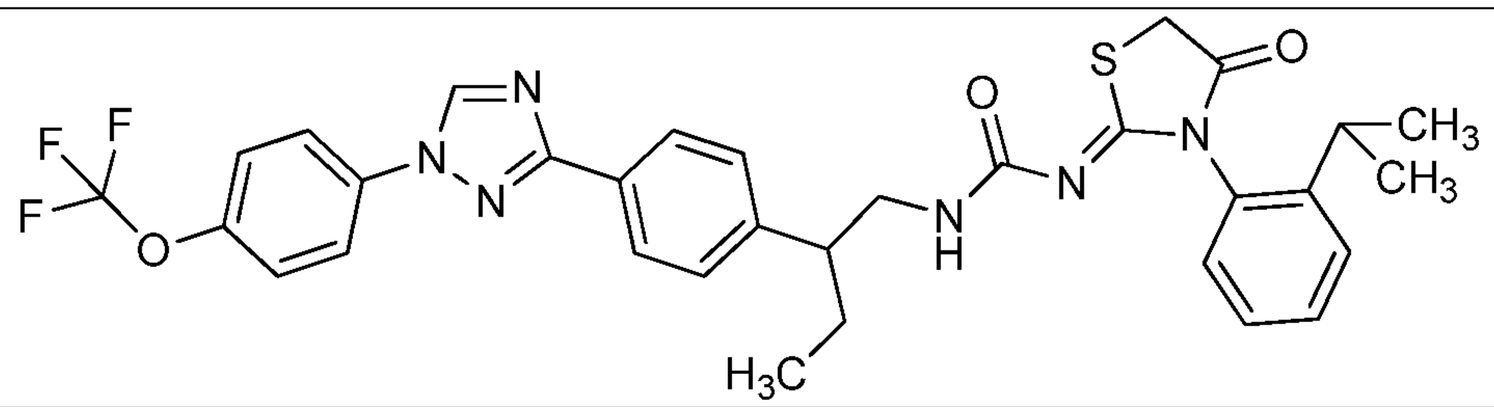
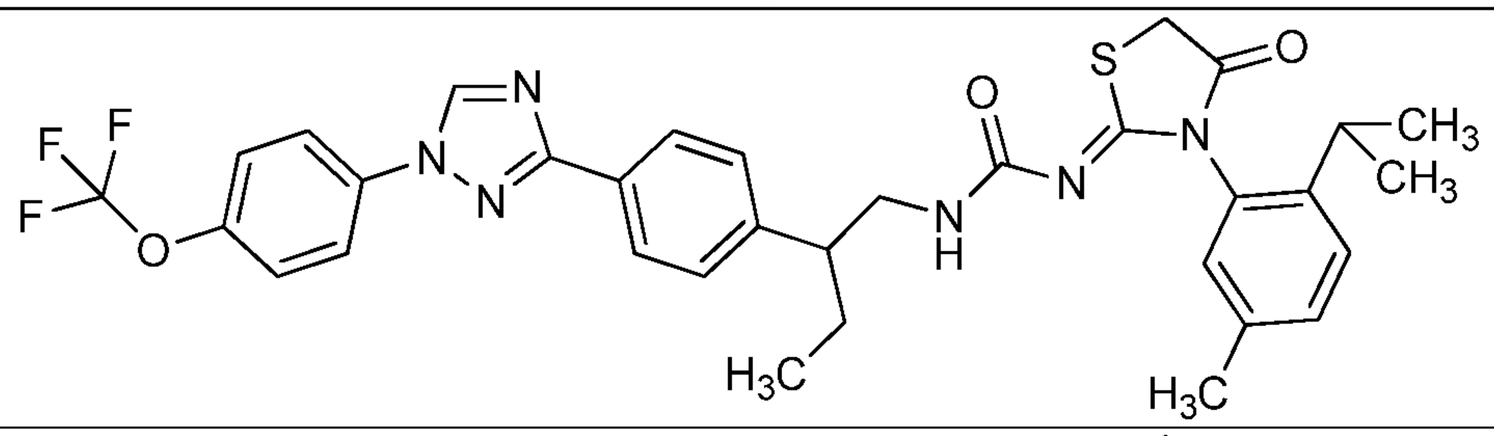
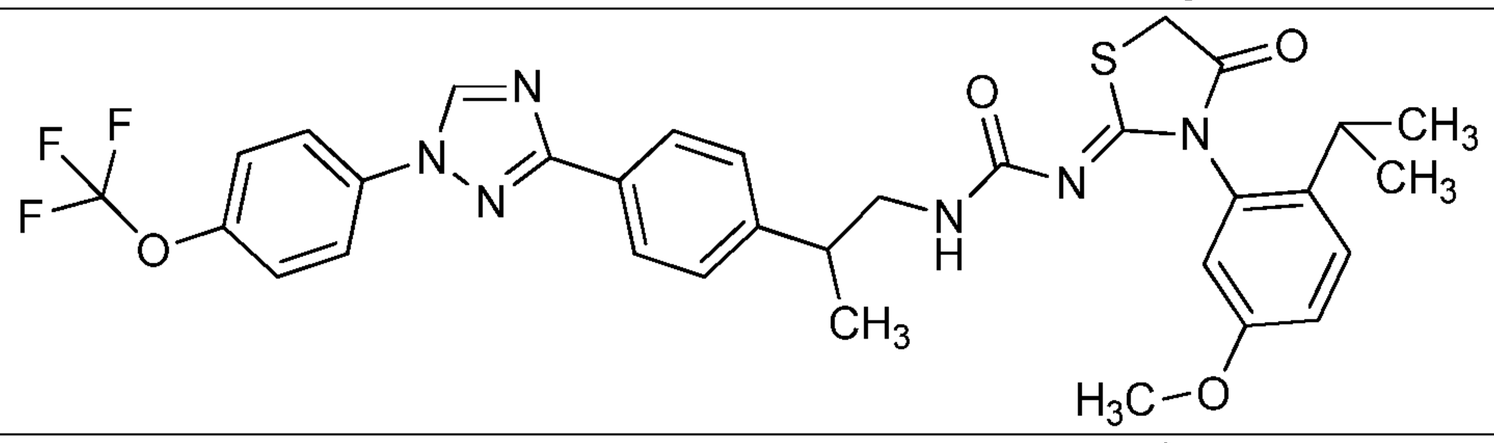
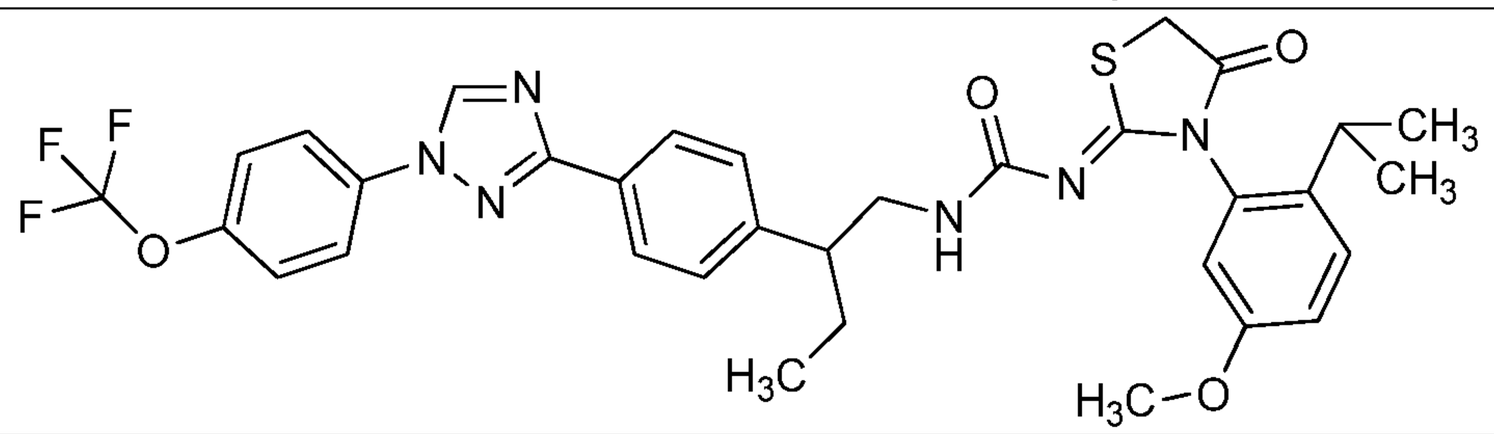
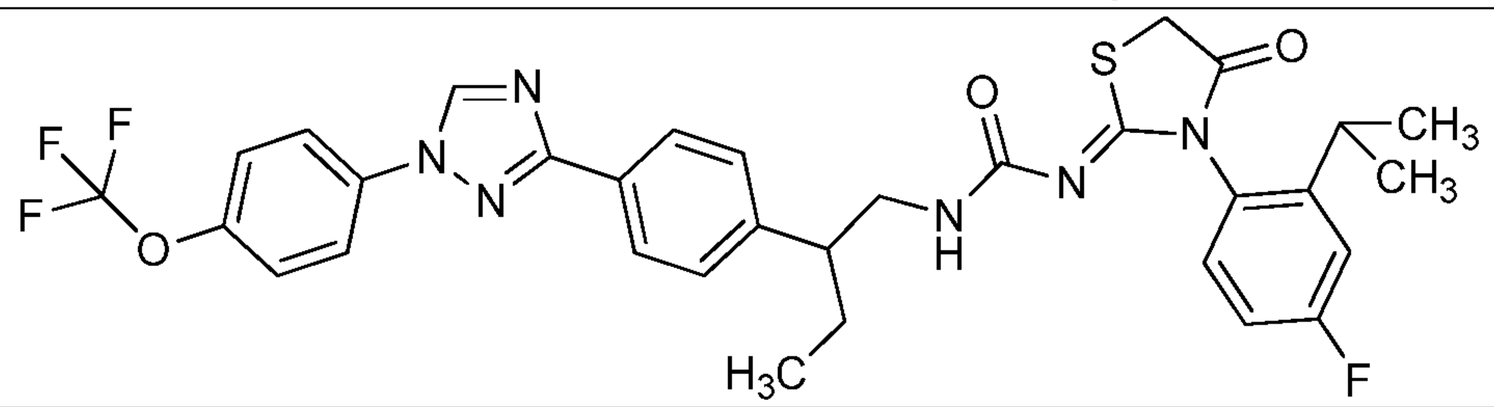
P105	
P118	
P119	
P120	
P124	
P125	

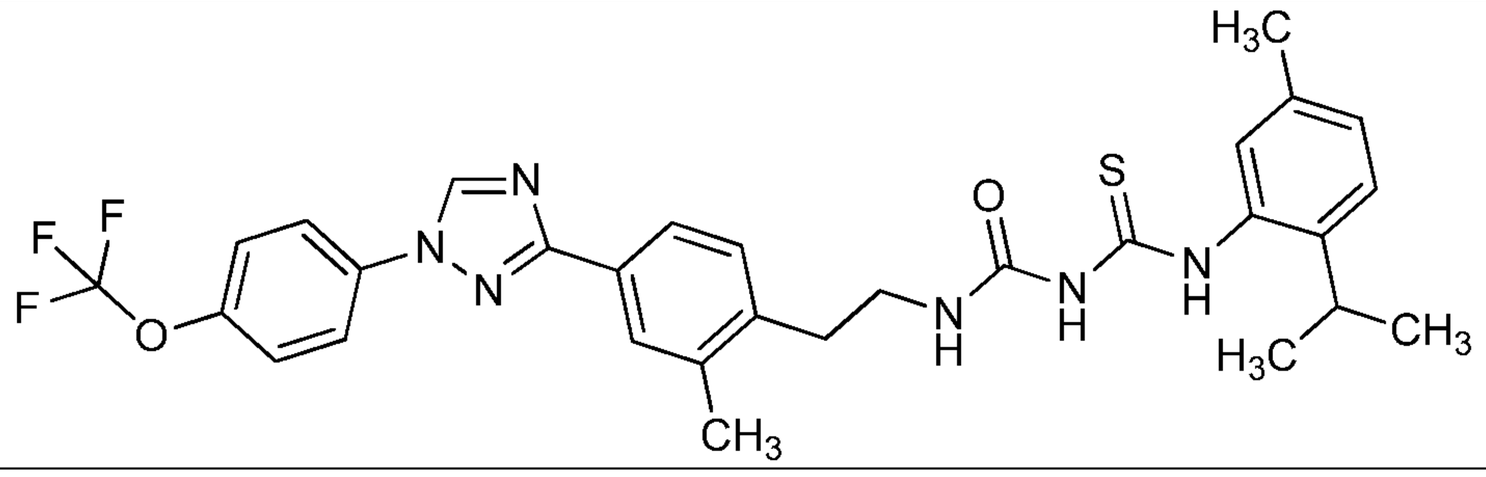
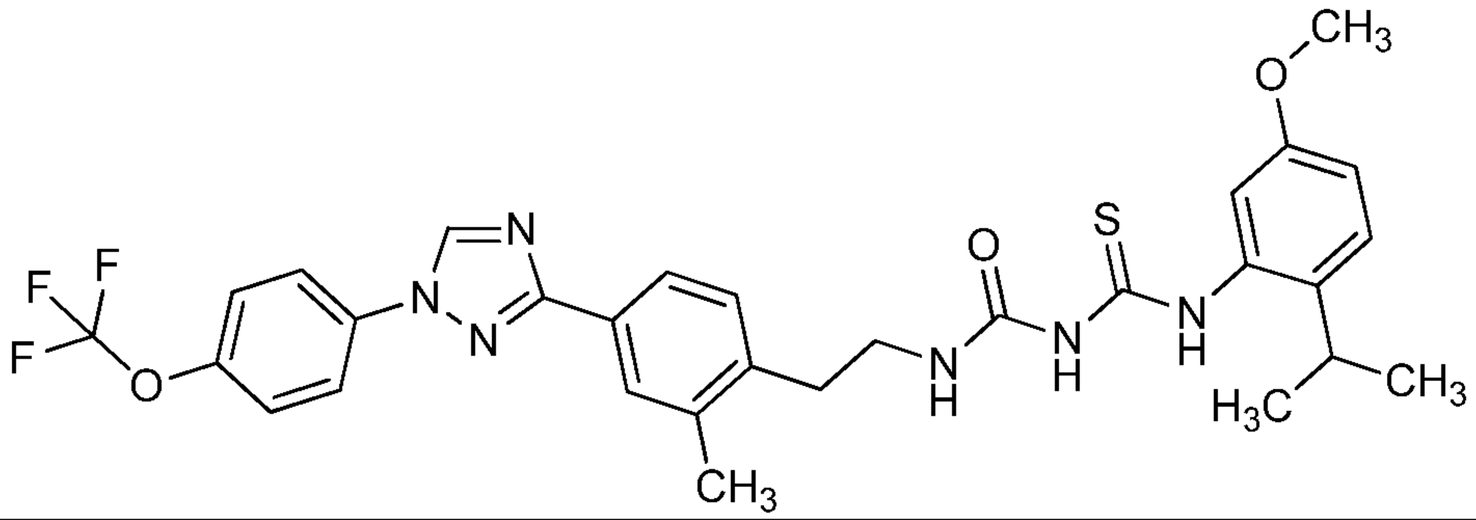
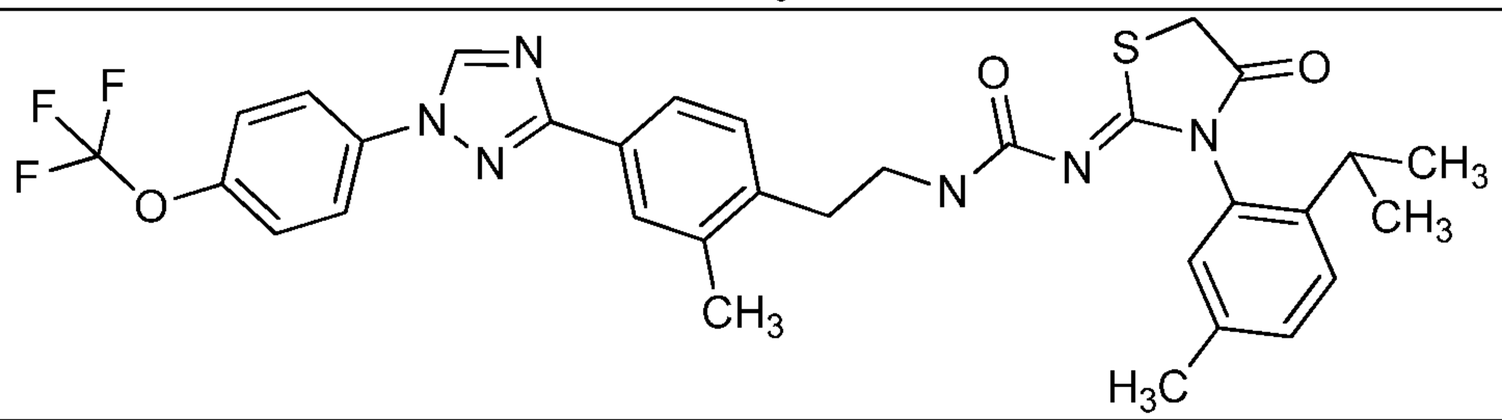
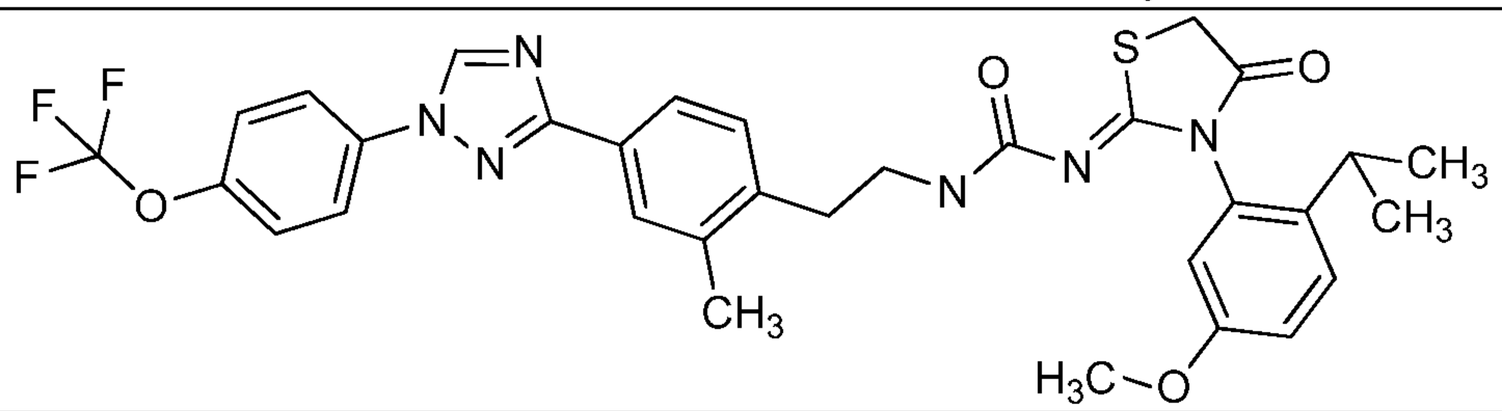
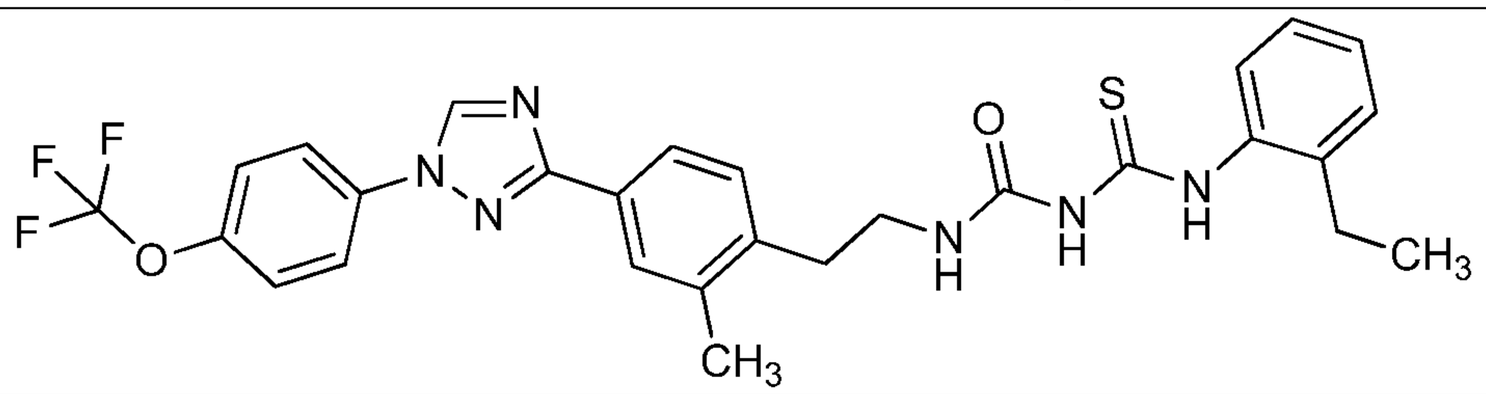
P127	
P128	
P129	
P131	
P144	
P145, P522	

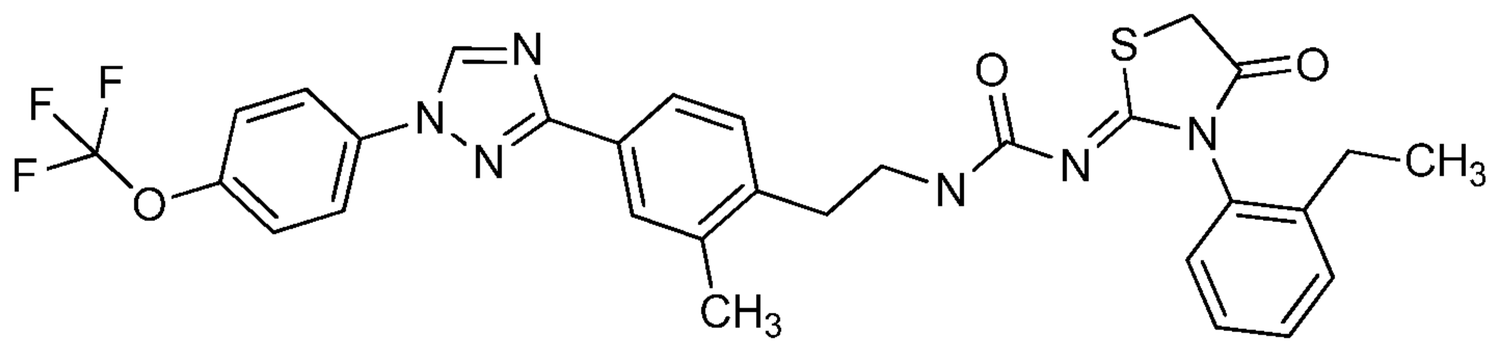
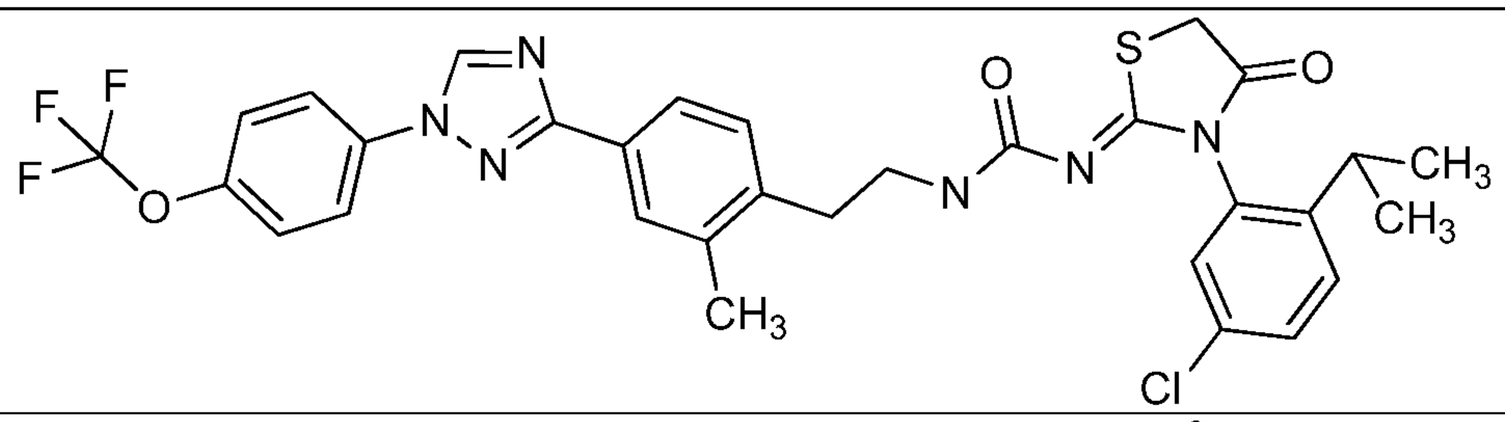
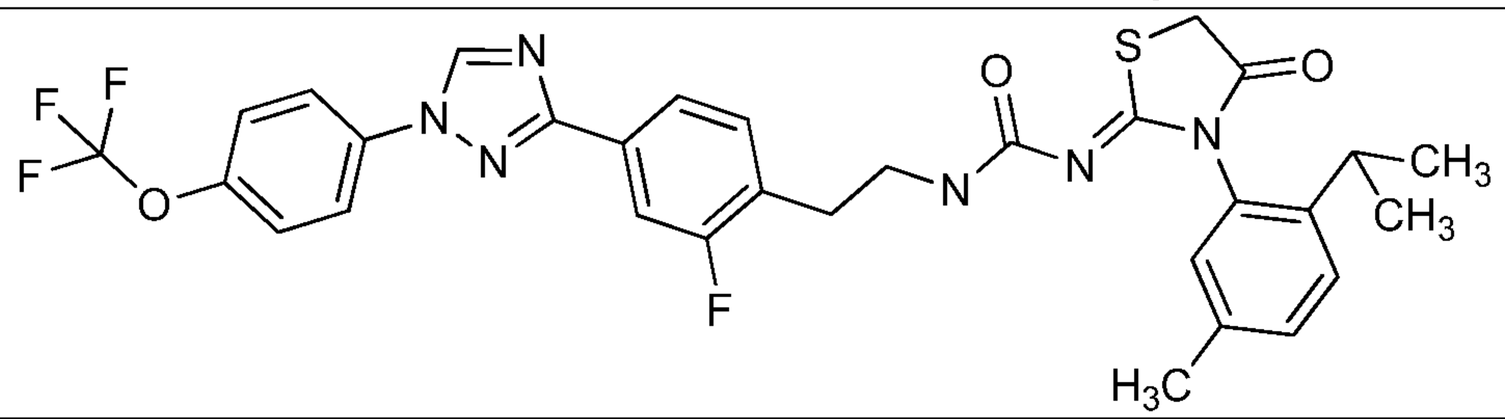
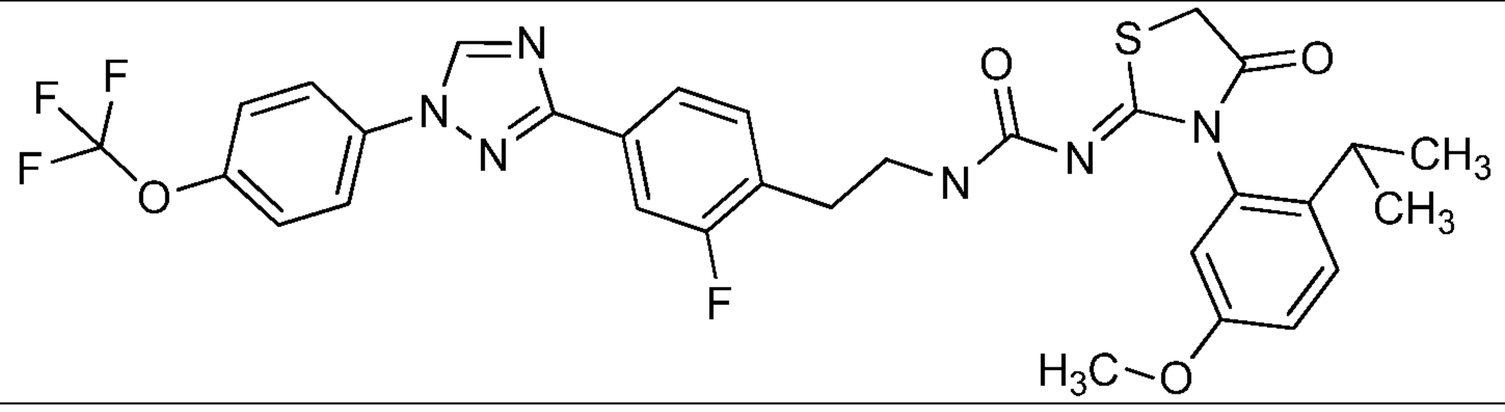
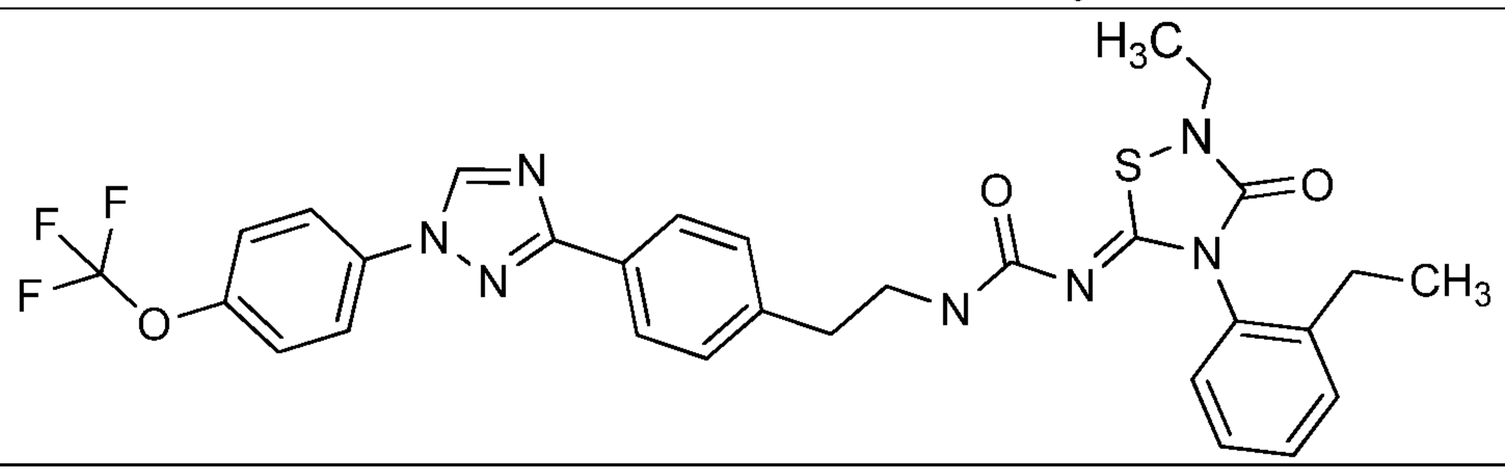
P146, P208	
P150, P363	
P151, P842	
P152, P1481	
P153	
P154	
P155, P1162	

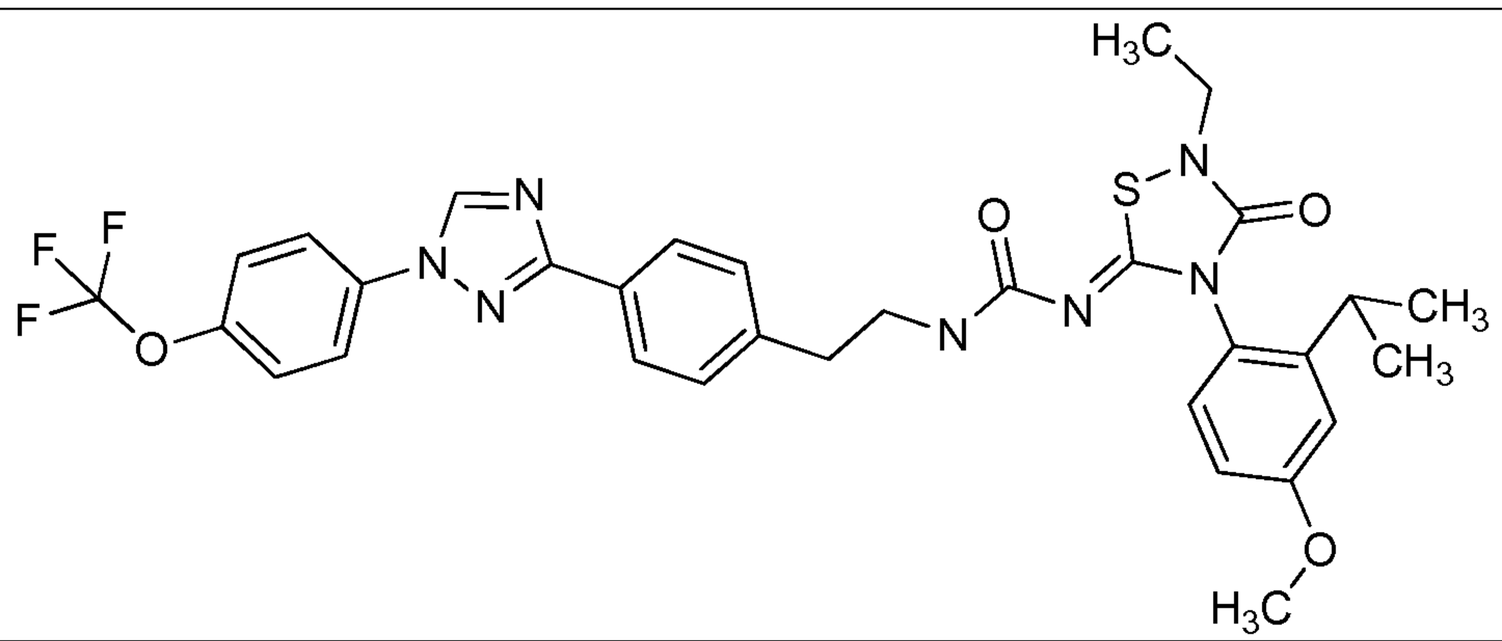
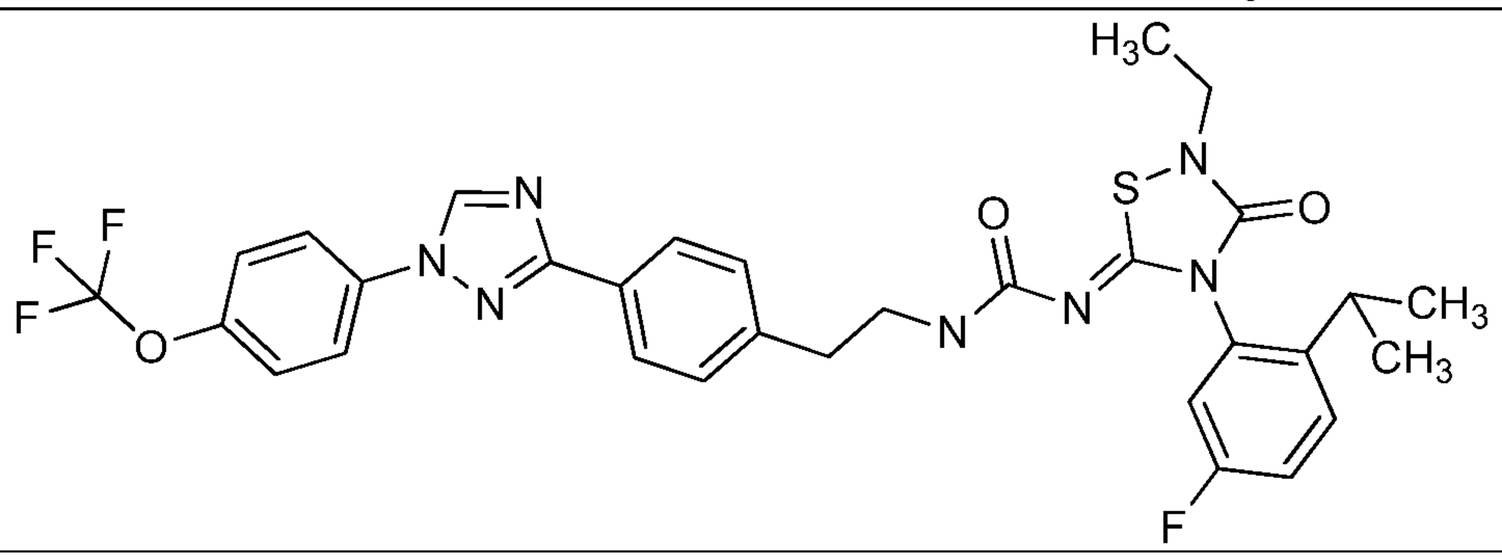
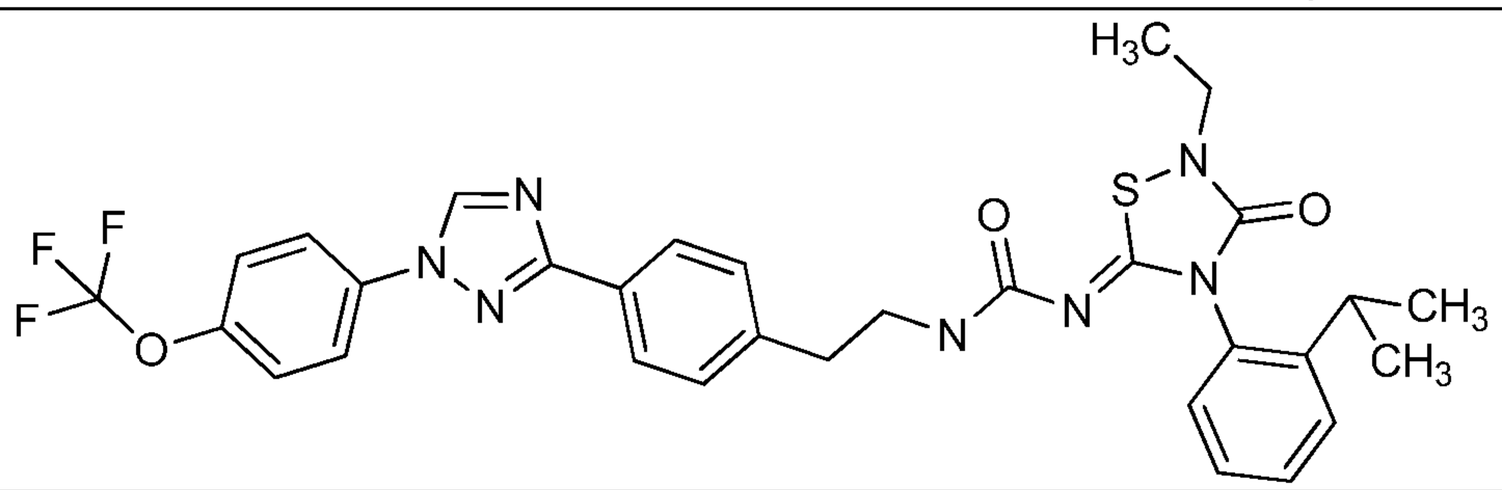
P156, P682	
P159	
P160	
P170	
P171	
P172	

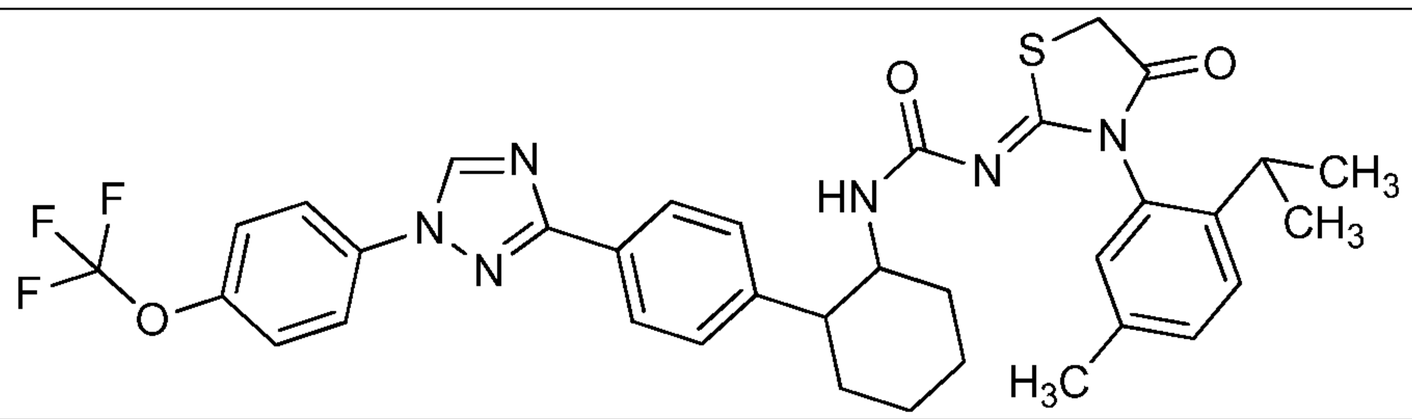
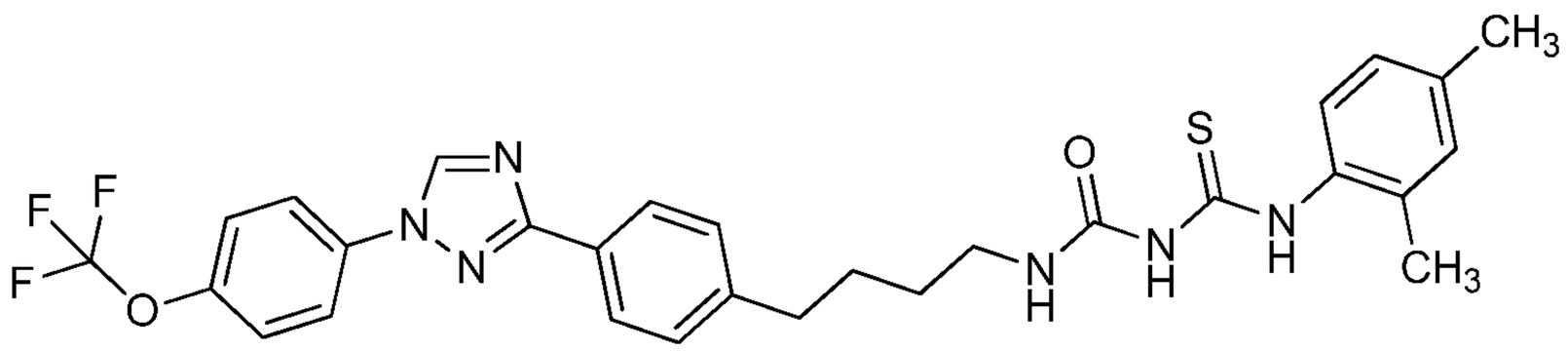
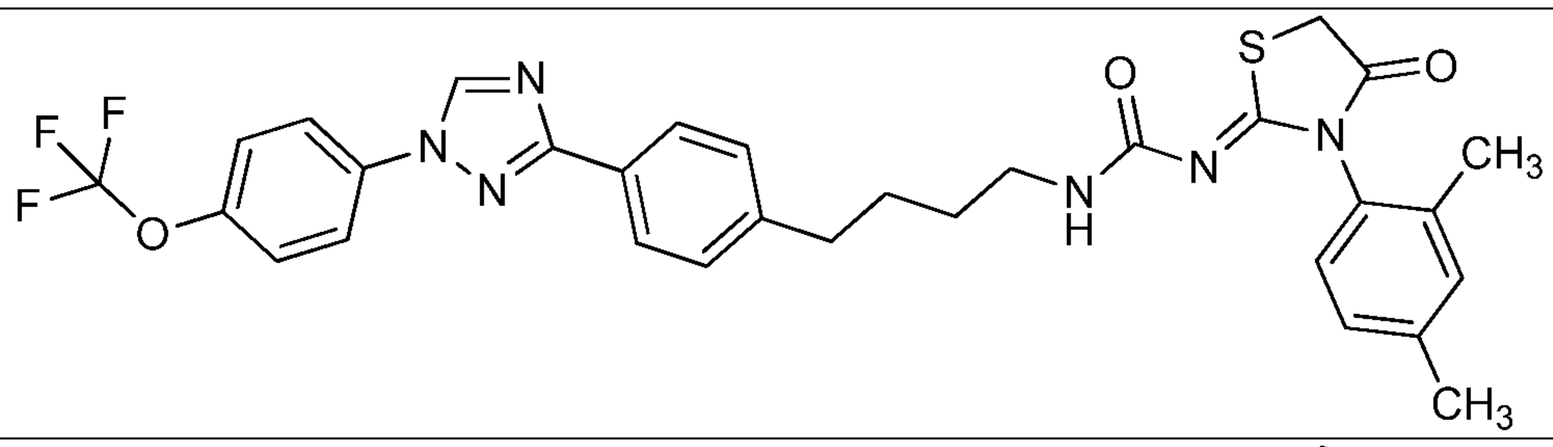
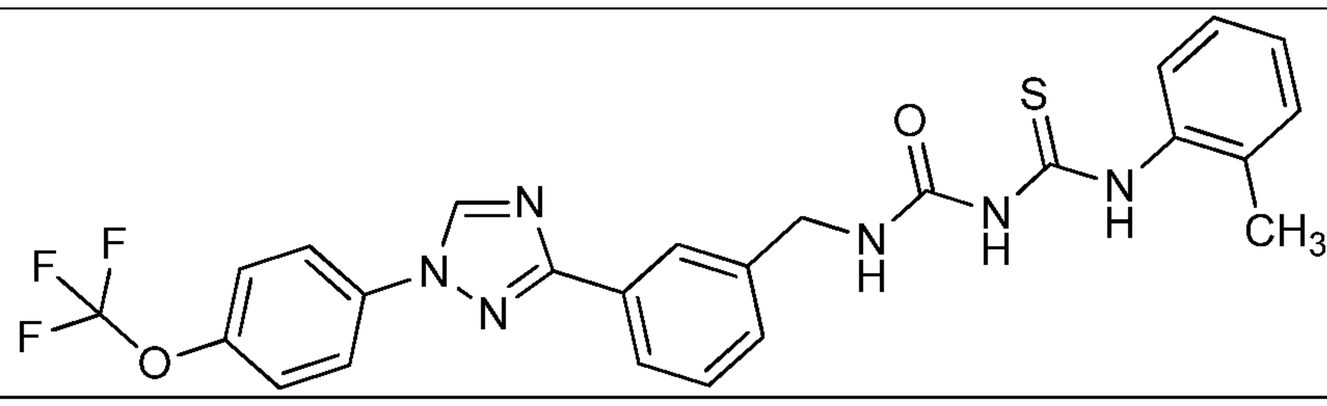
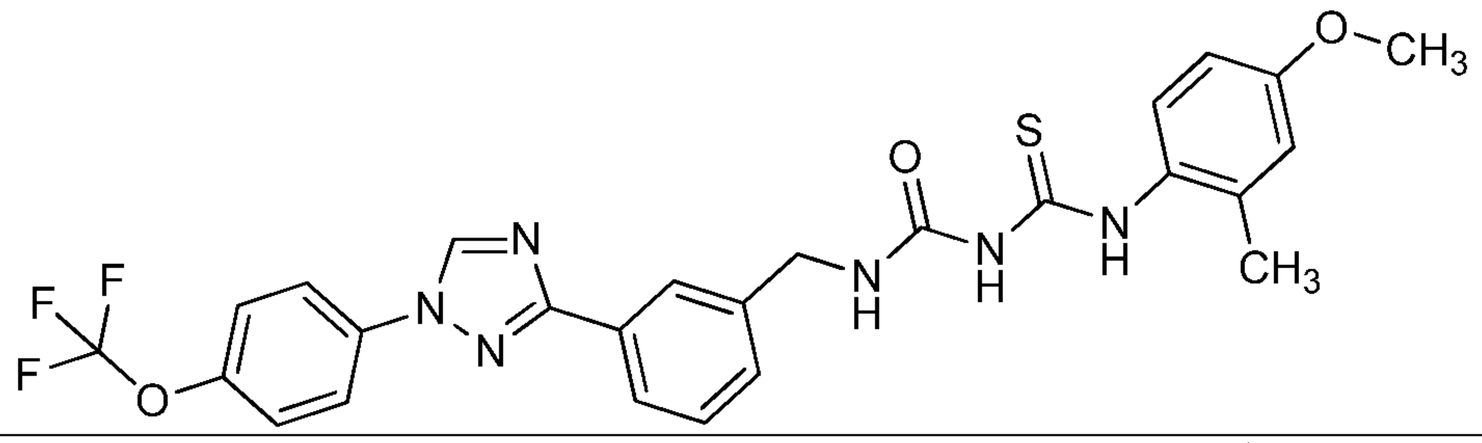
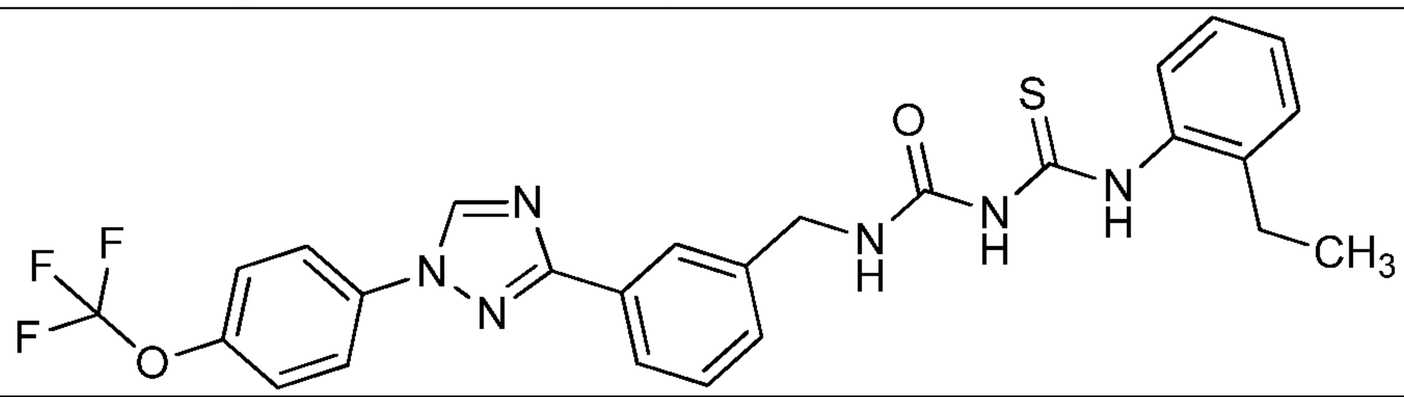
P176	
P179	
P180	
P181	
P182	

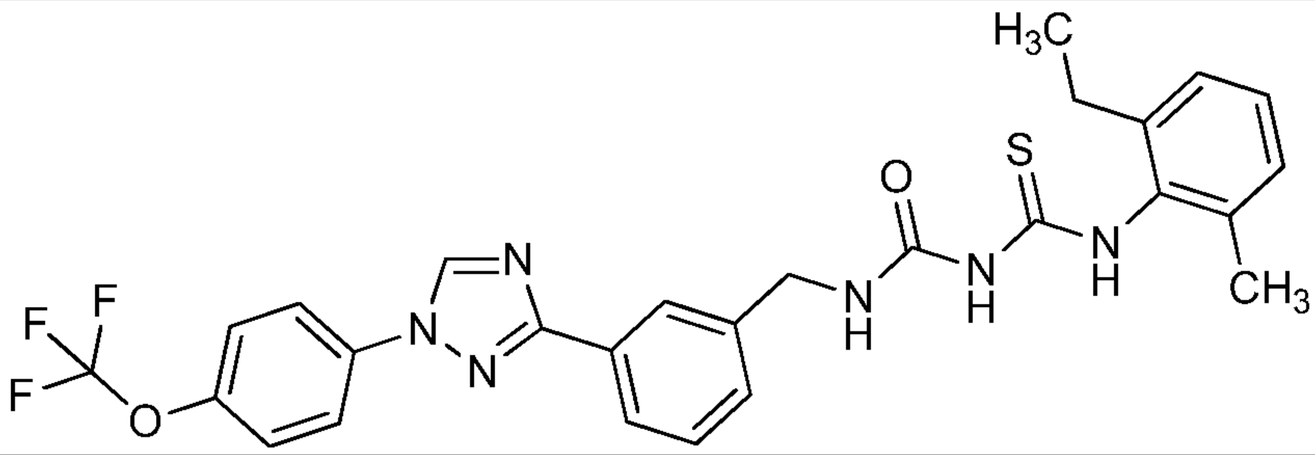
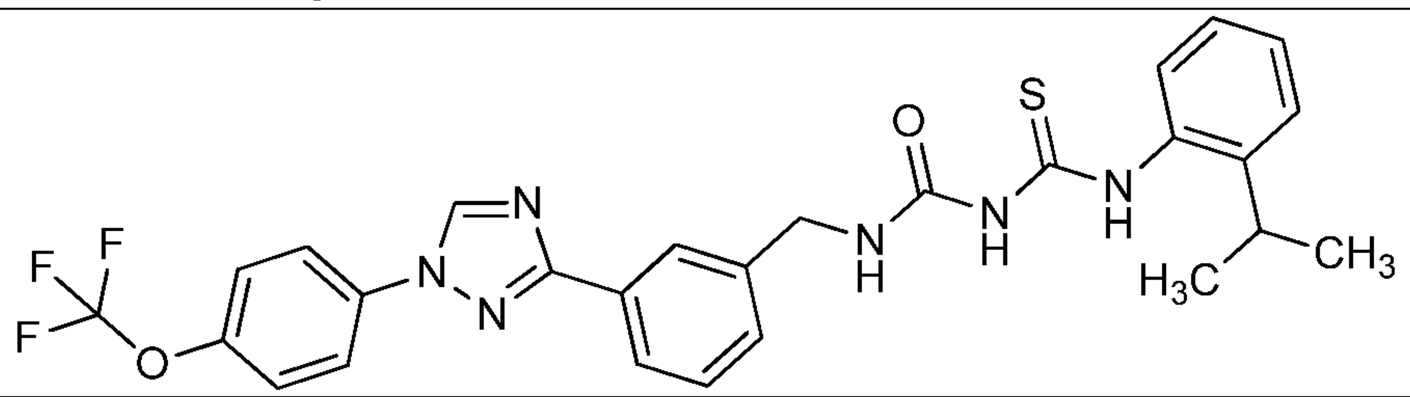
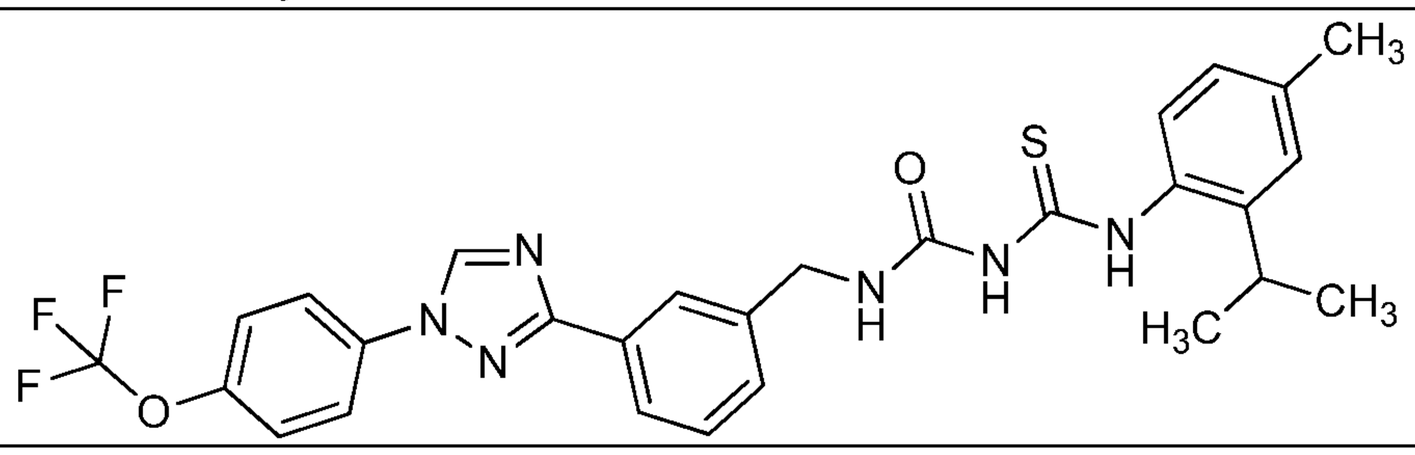
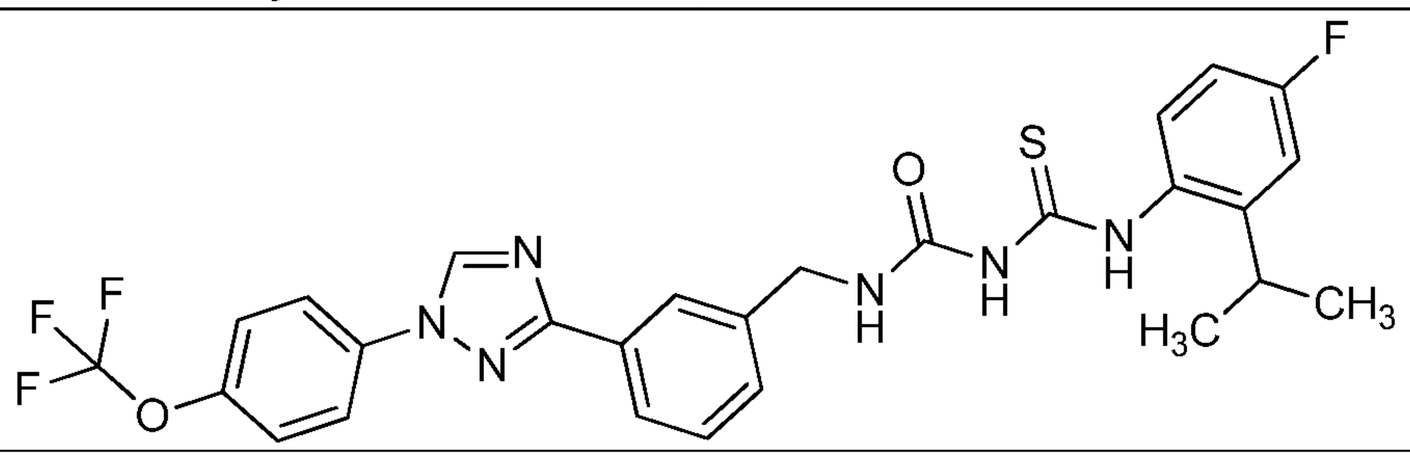
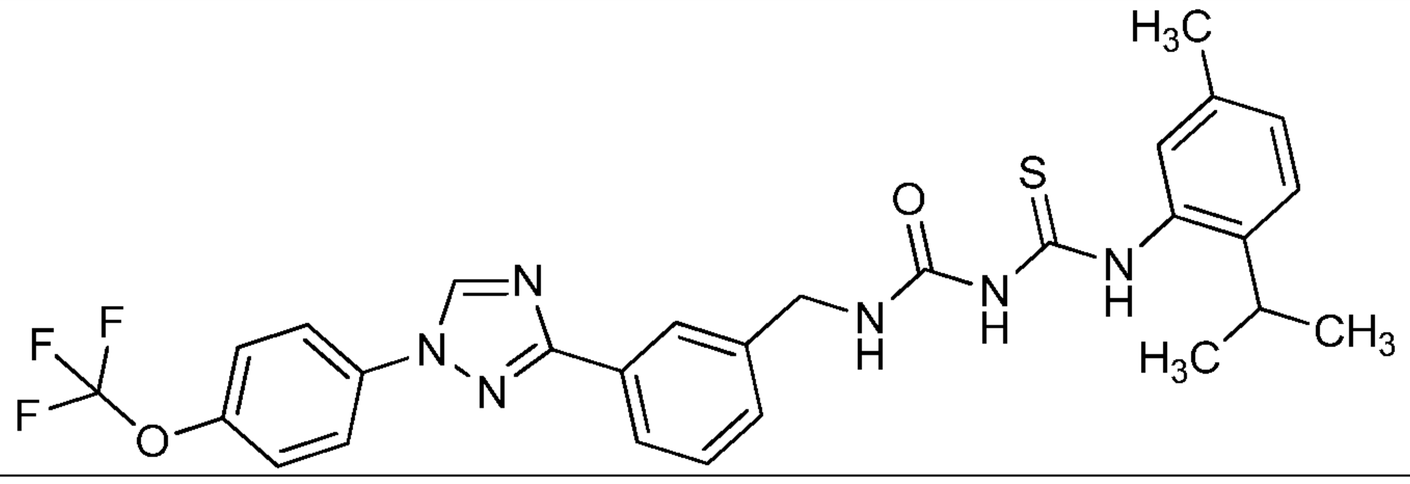
P205	
P209	
P364	
P679	
P683	
P1163	

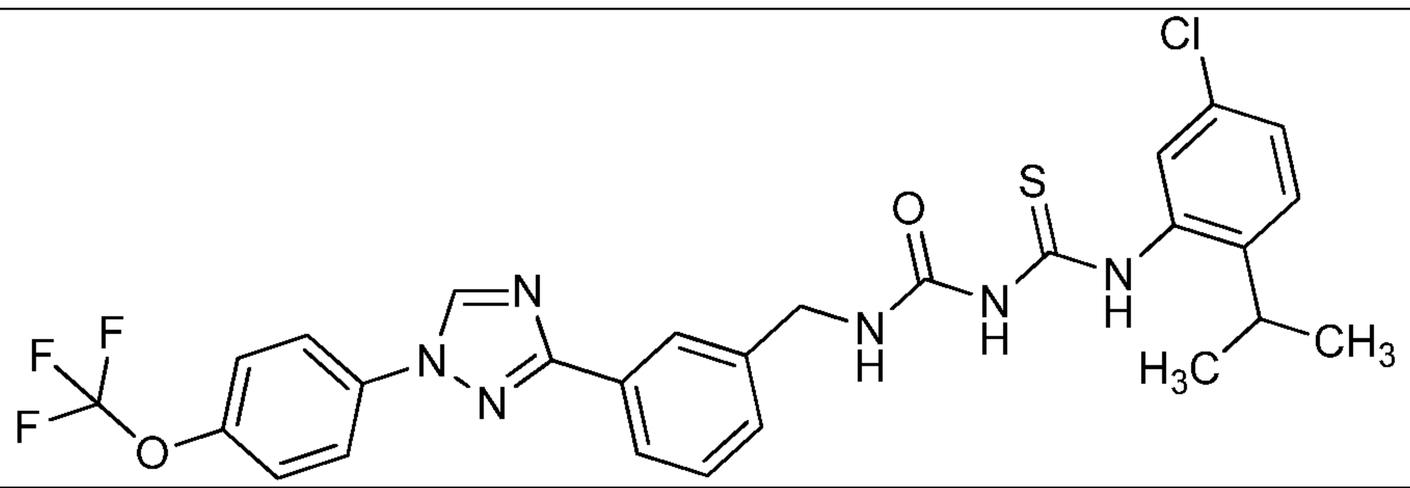
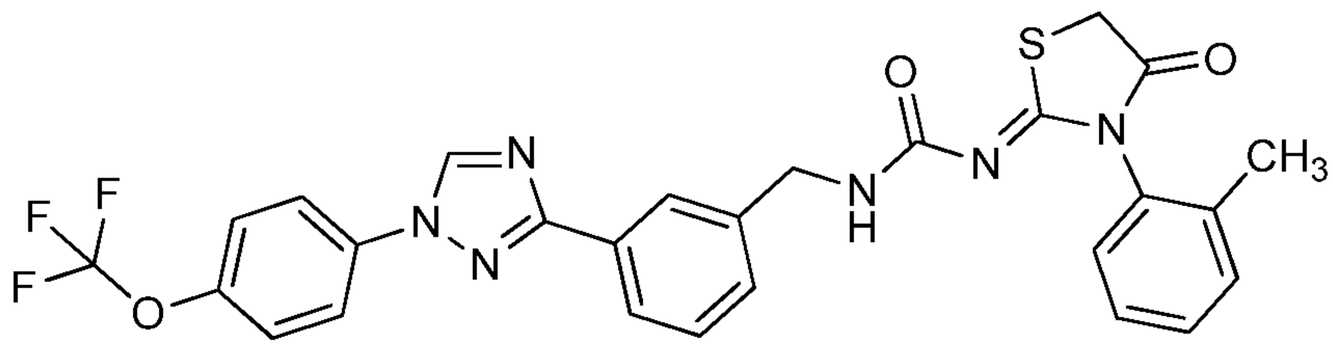
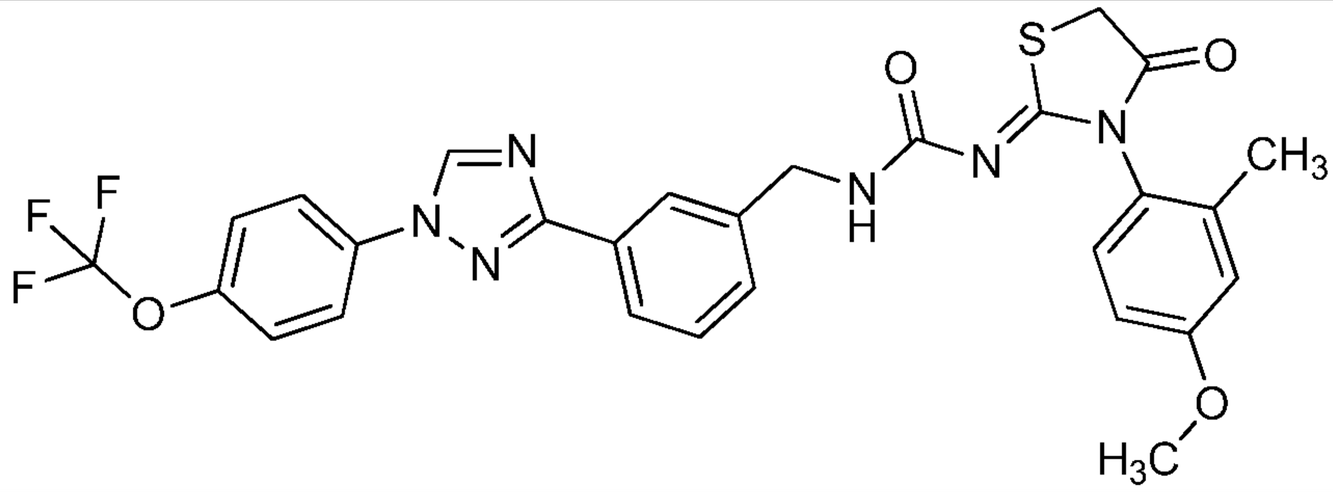
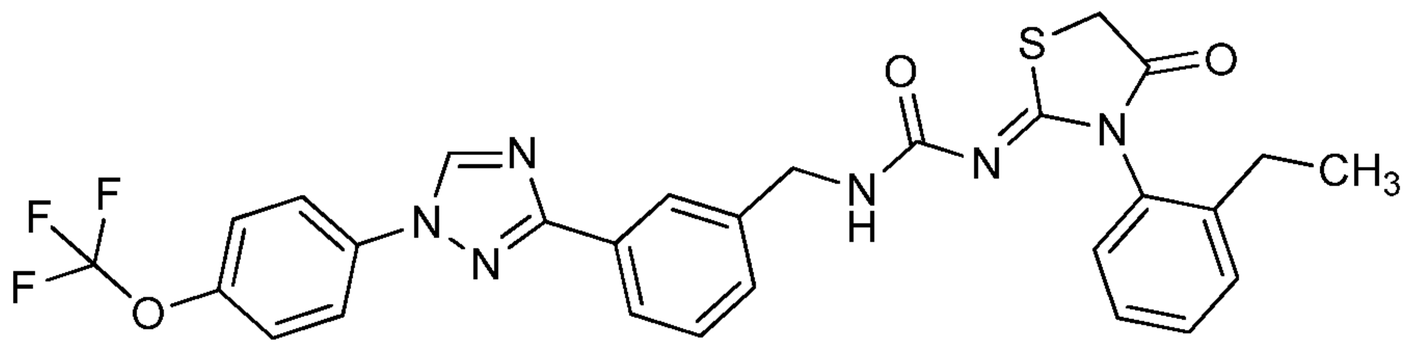
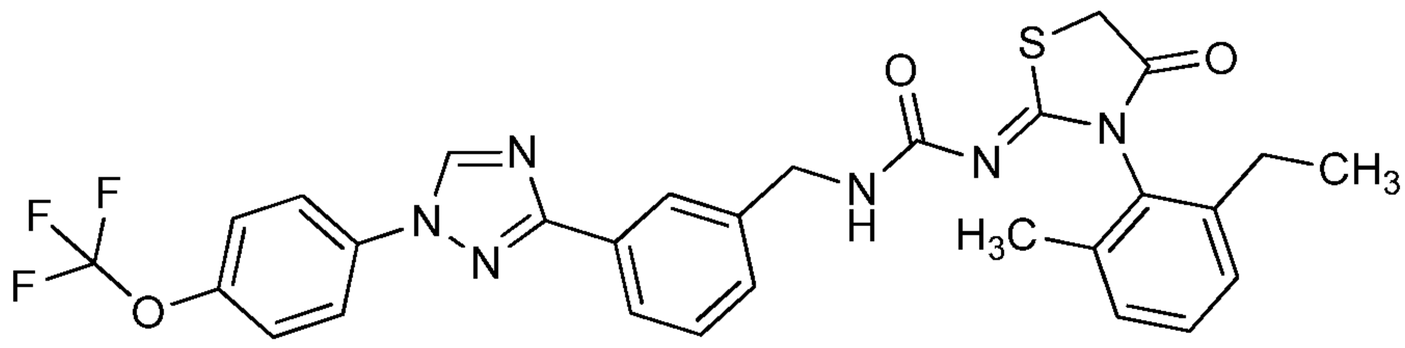
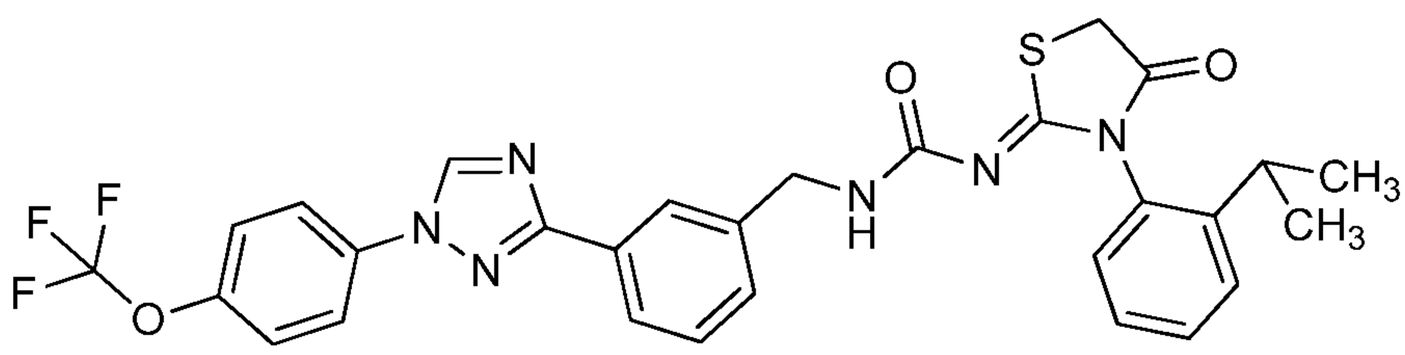
No.	Structure
FB1	
FB2	
FB3	
FB4	
FB5	

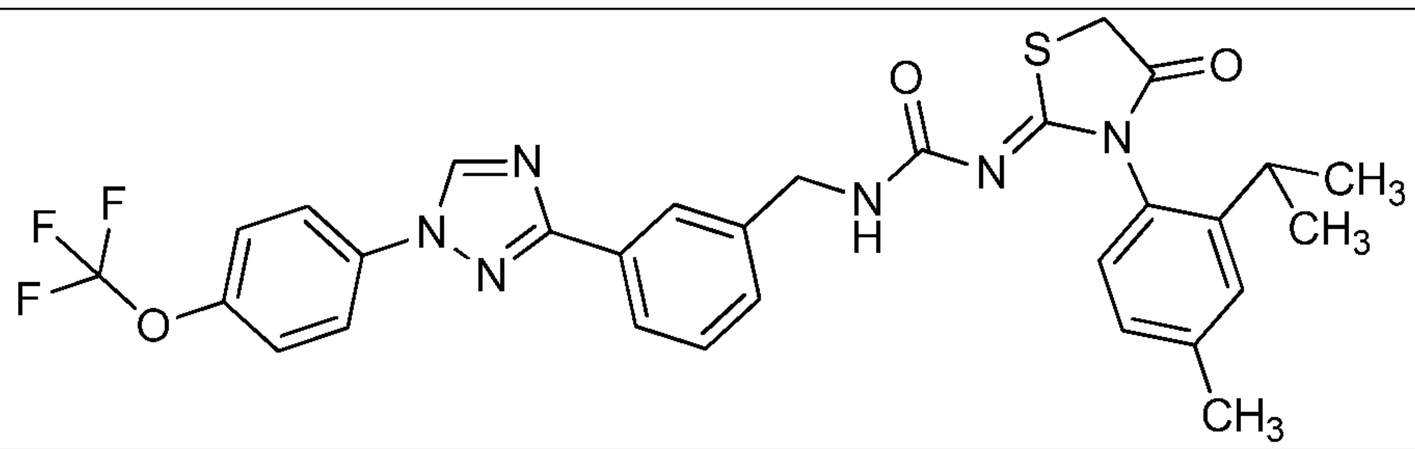
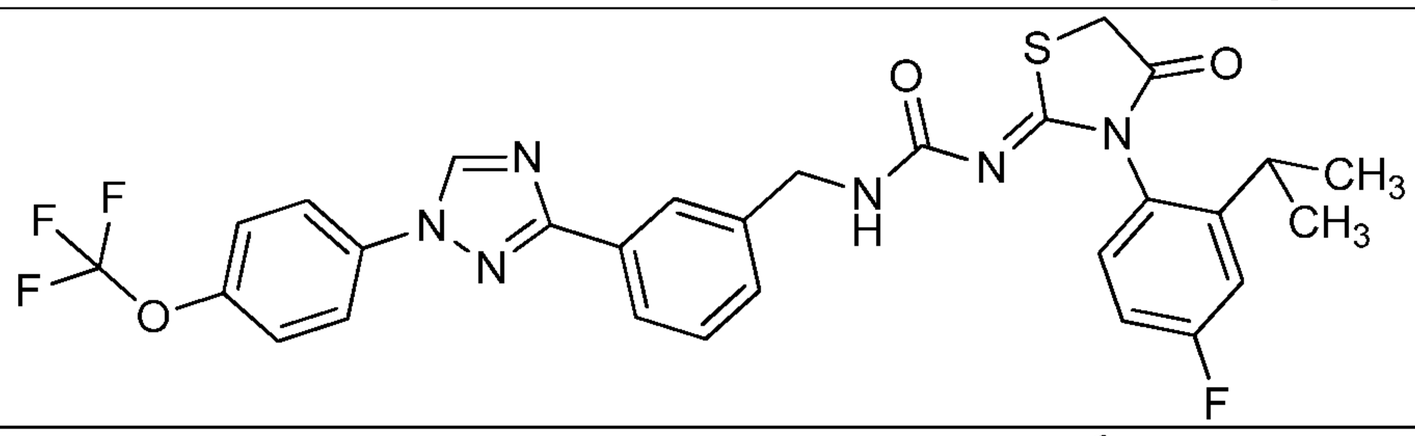
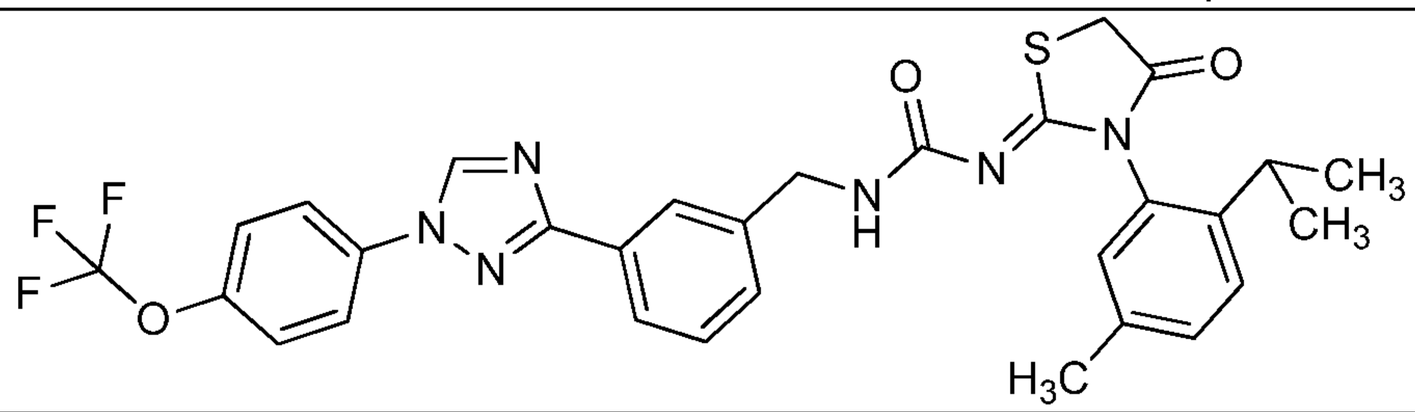
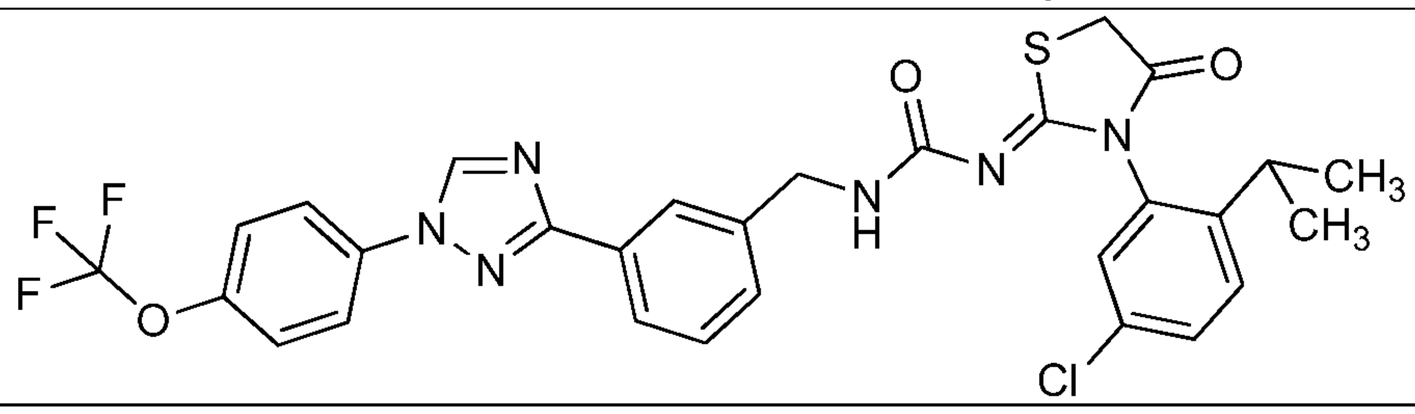
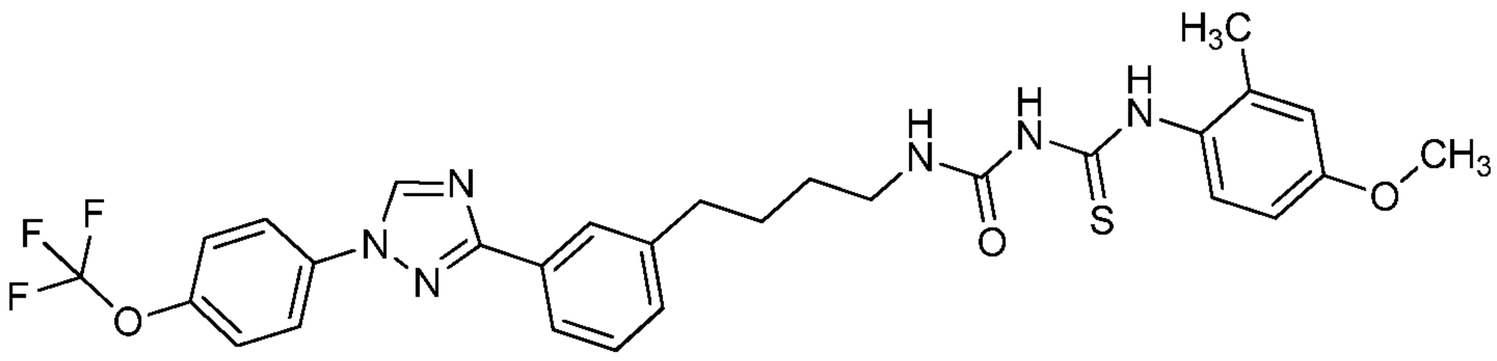
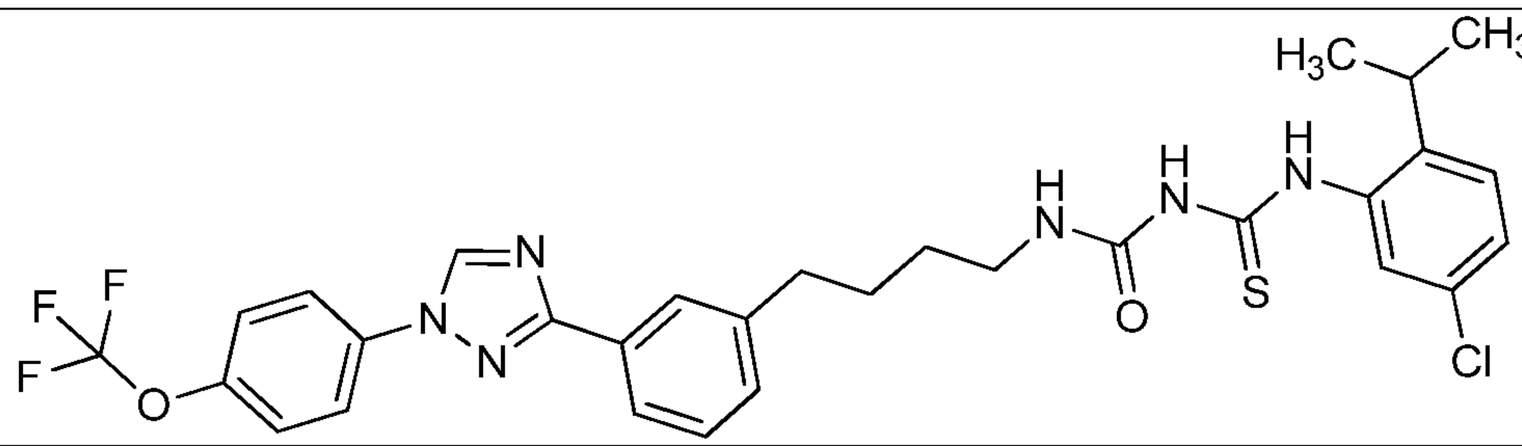
FB6	
FB7	
FB8	
FB9	
FB10	

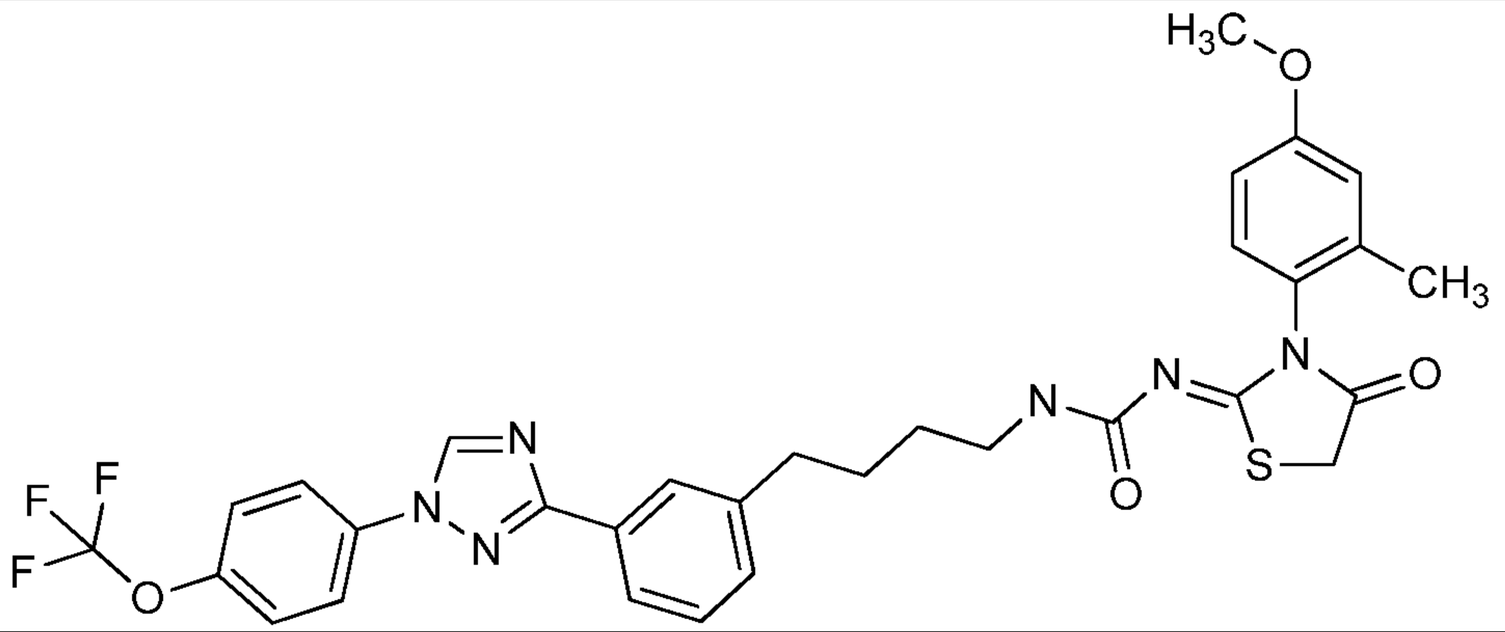
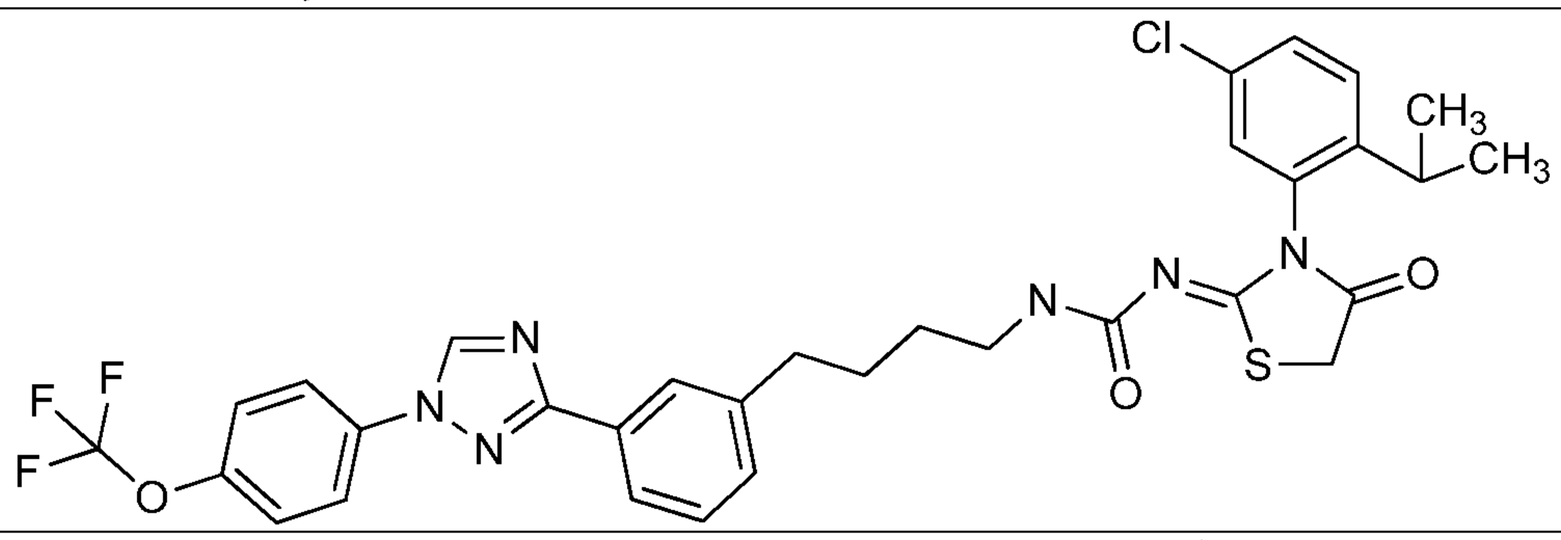
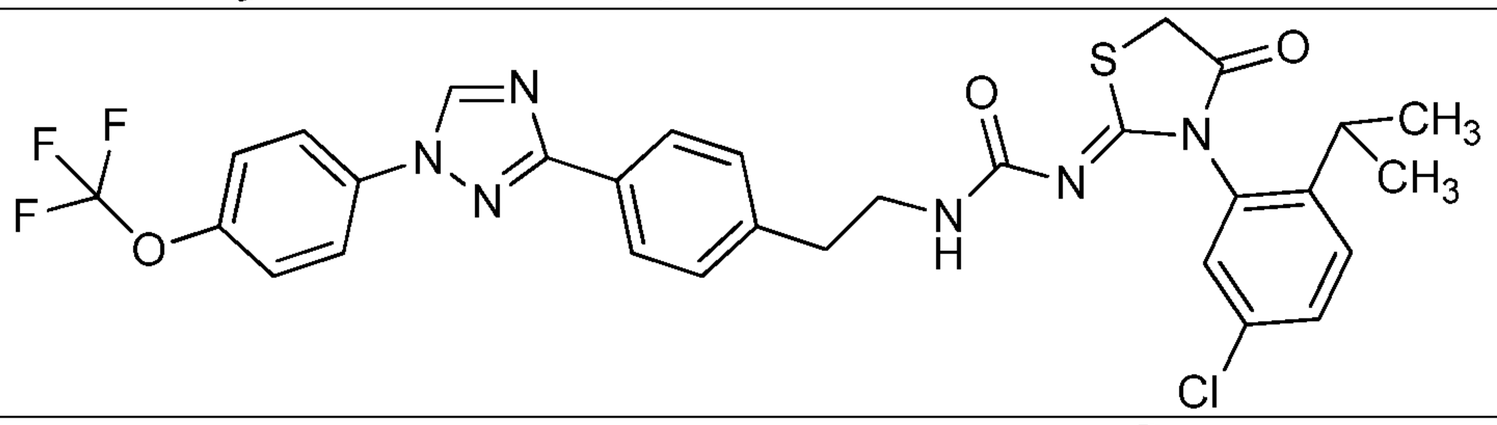
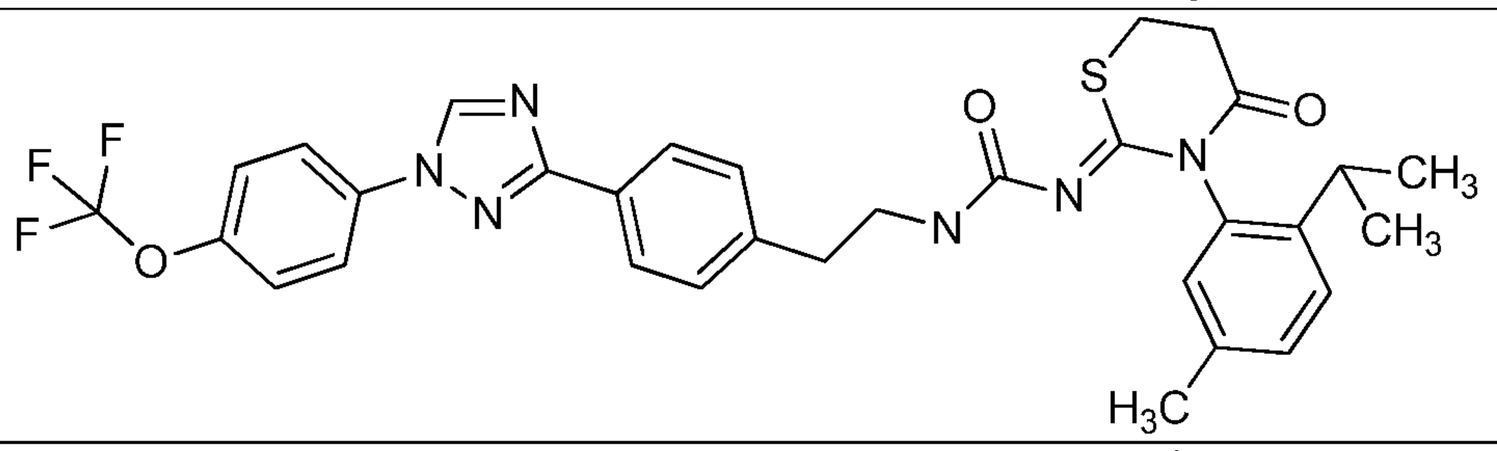
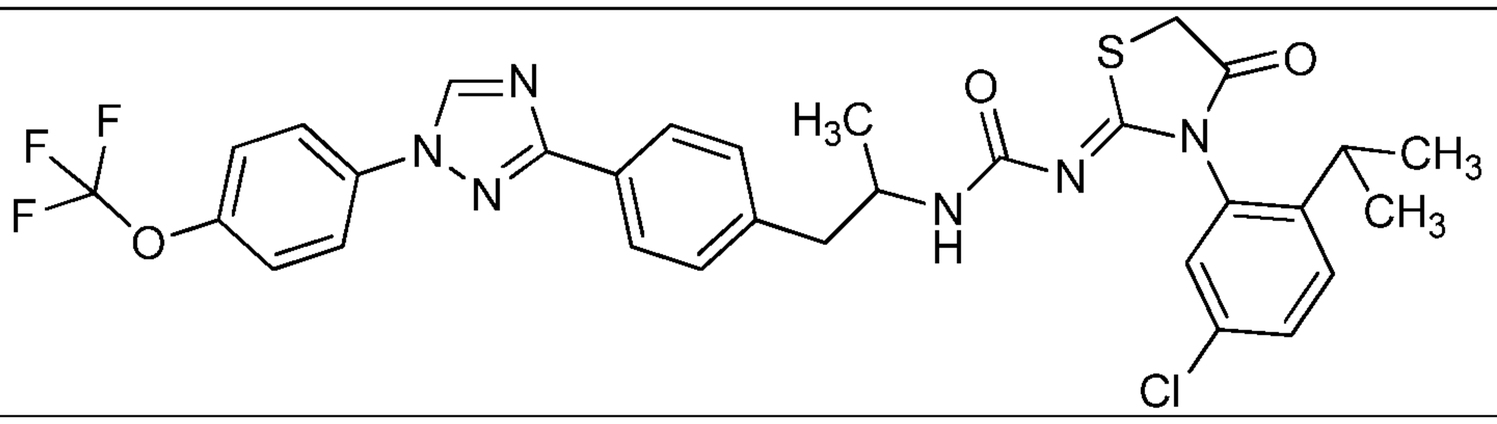
FB11	
FB12	
FB13	
FB14	

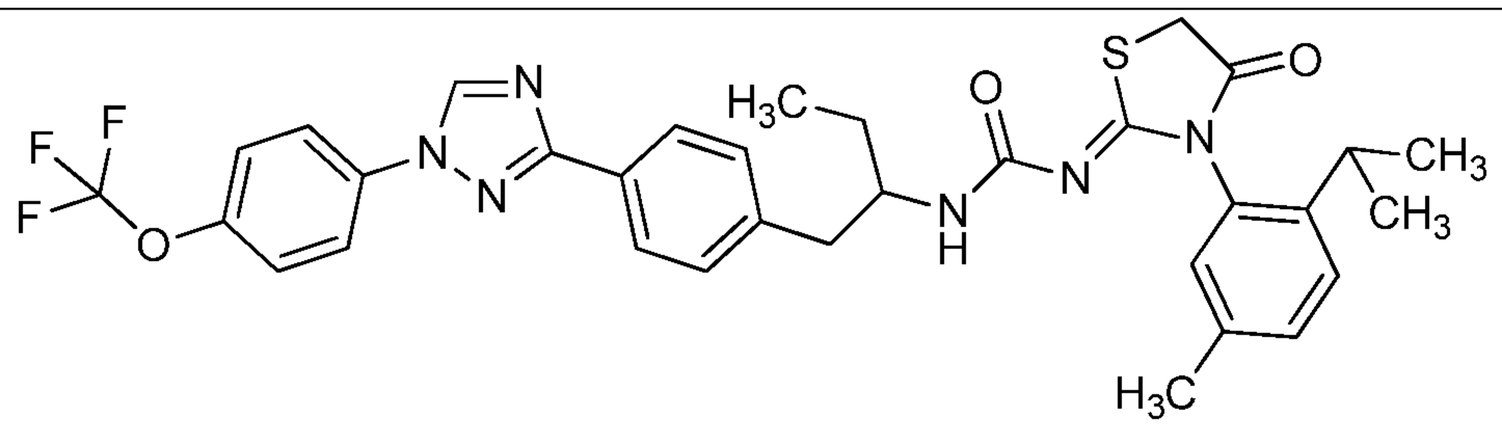
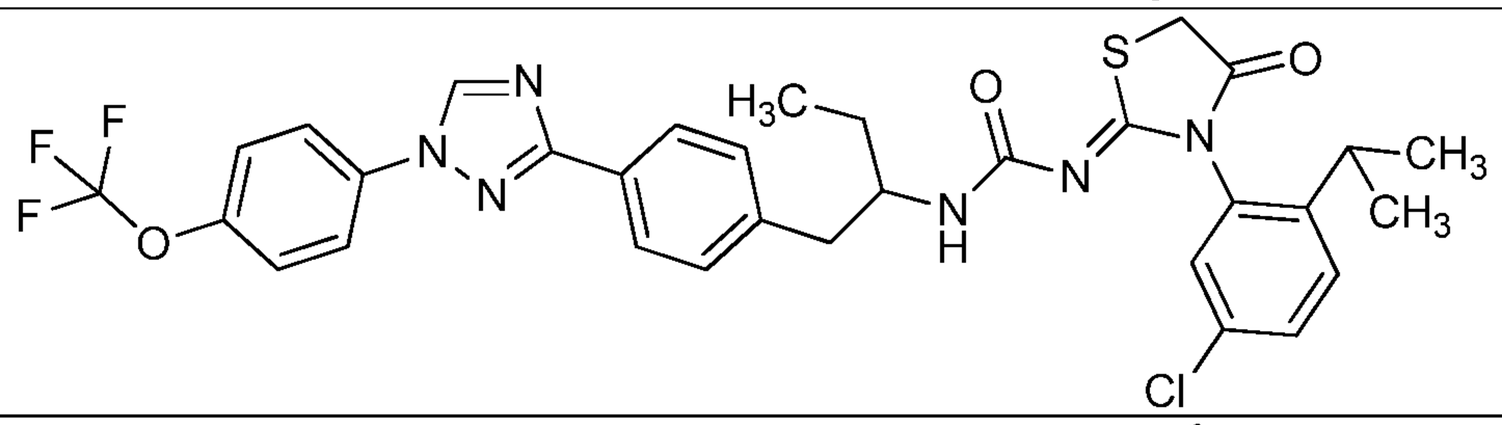
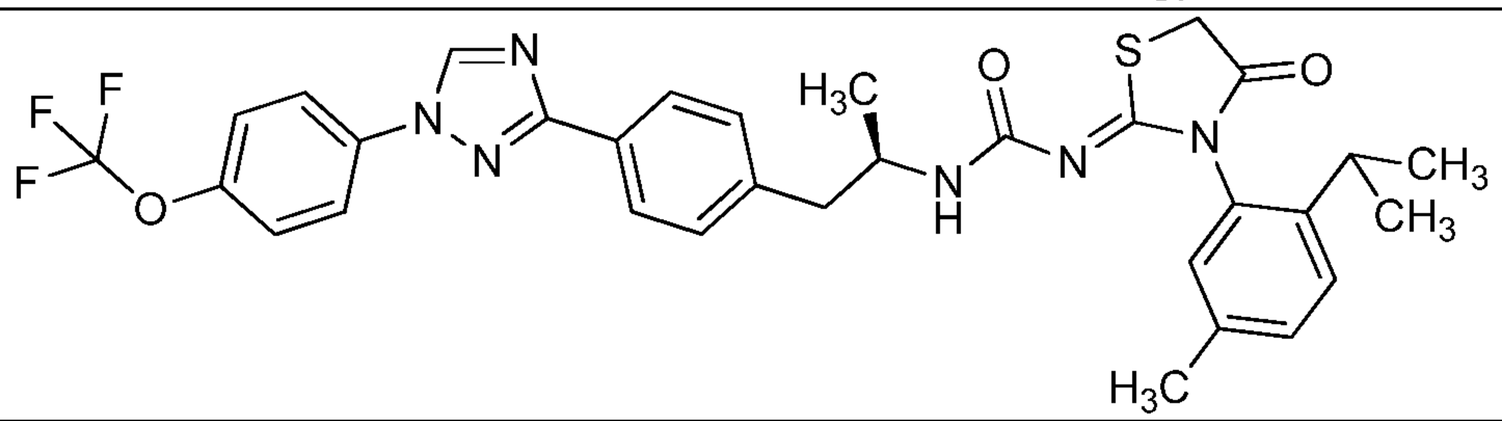
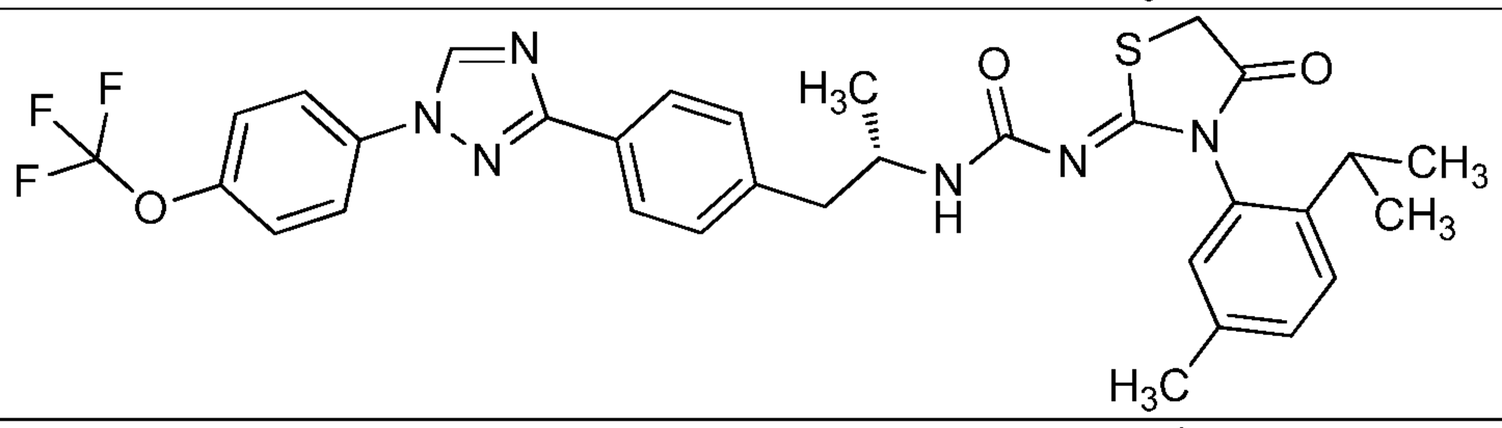
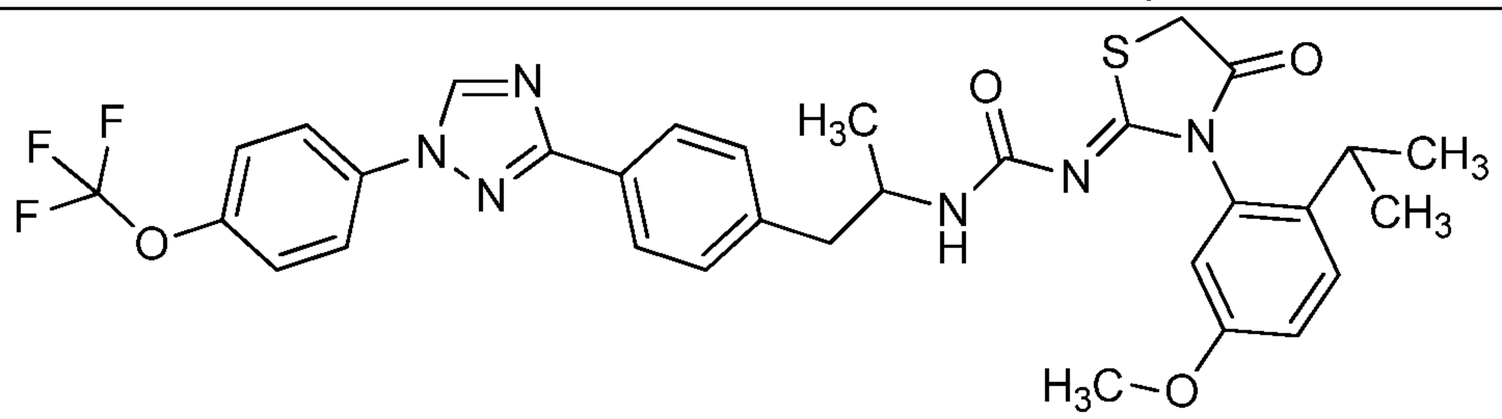
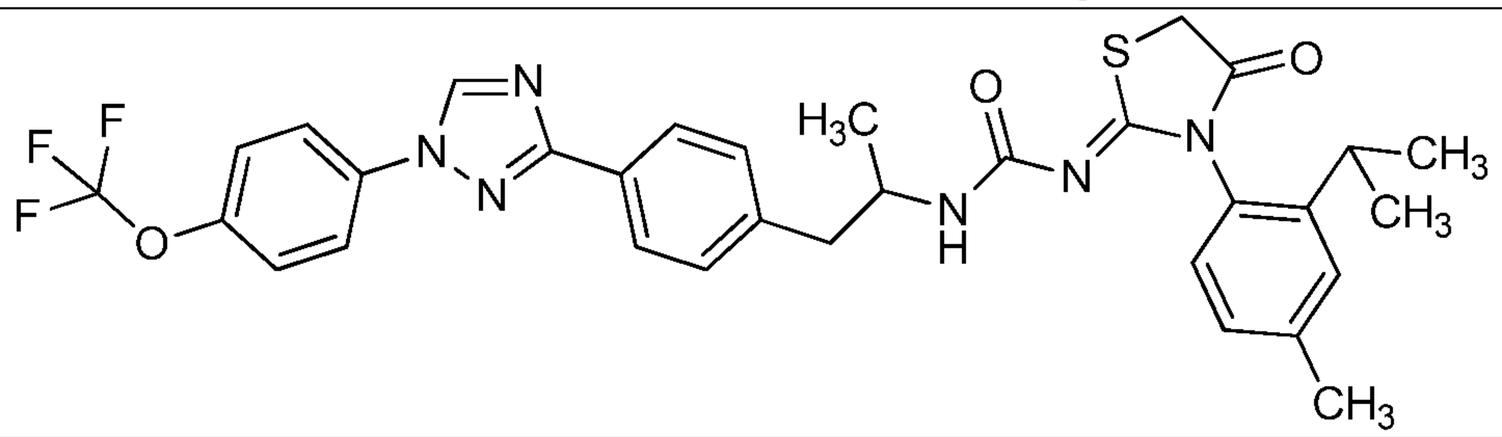
FB15	
FB16	
FB17	
FB18	
FB19	
FB20	

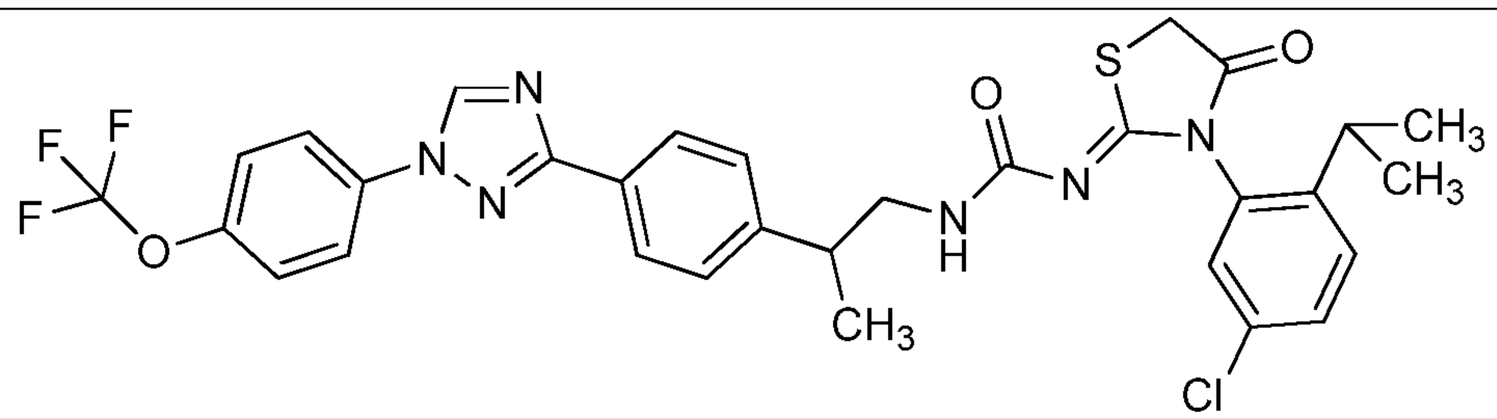
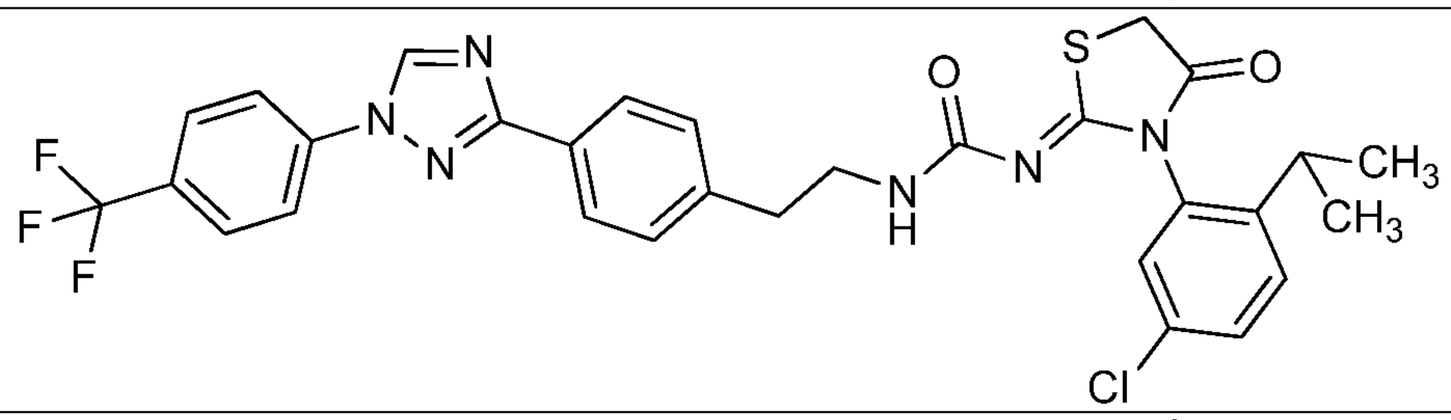
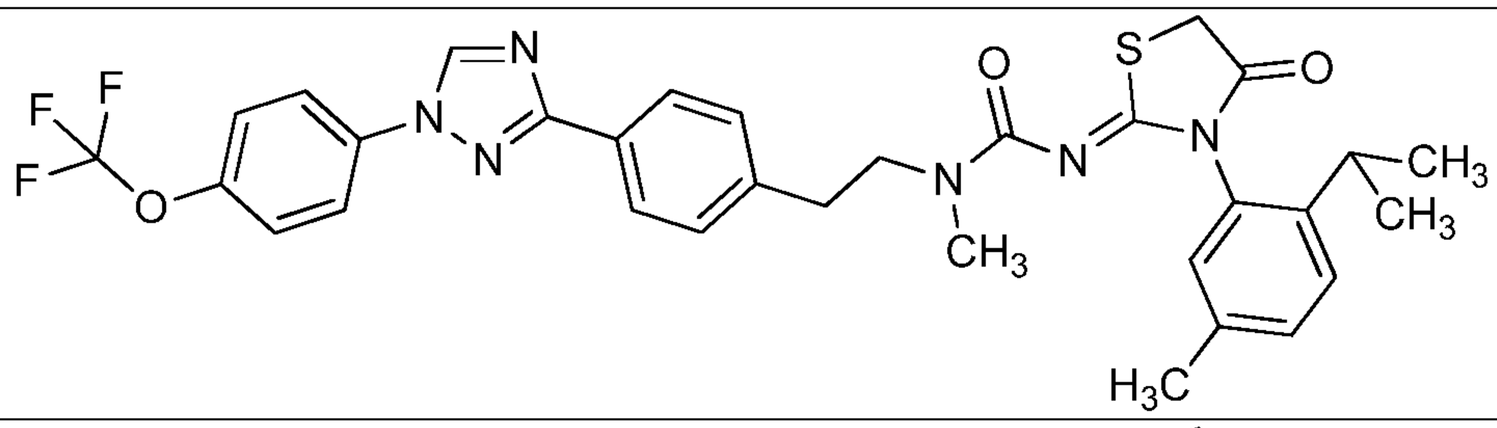
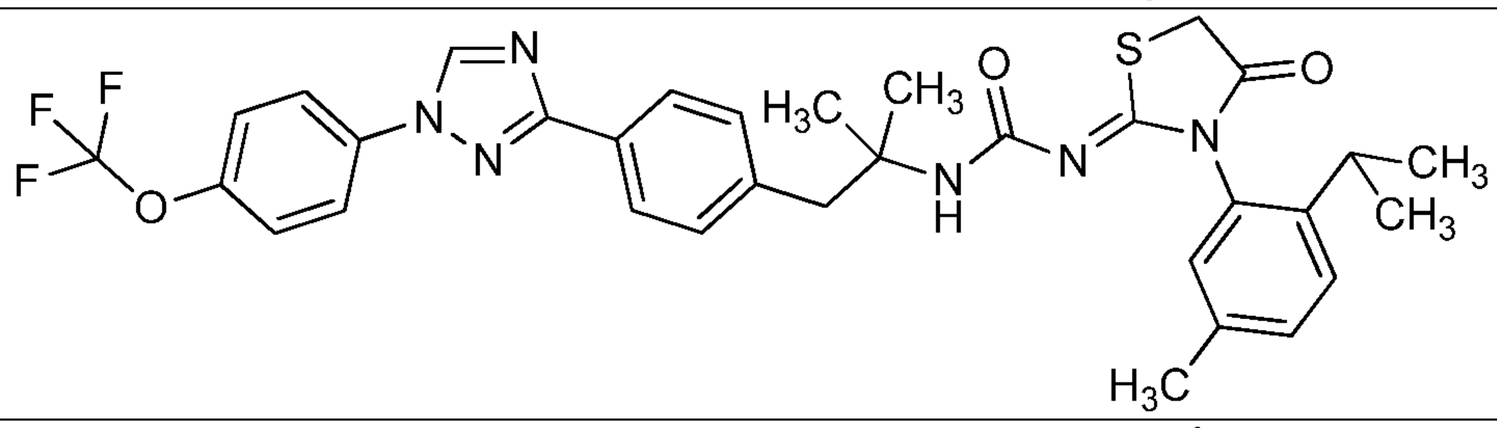
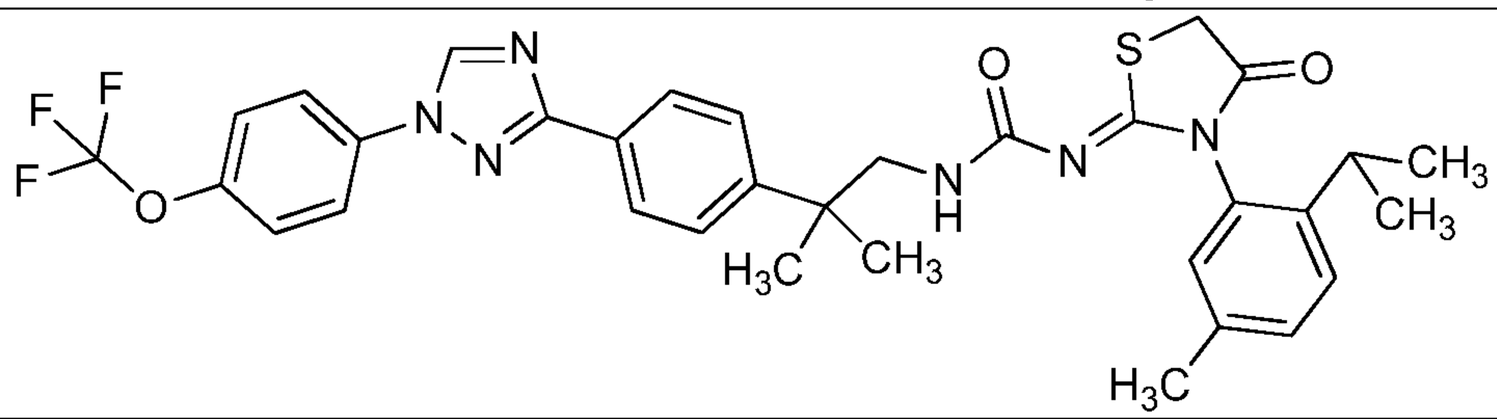
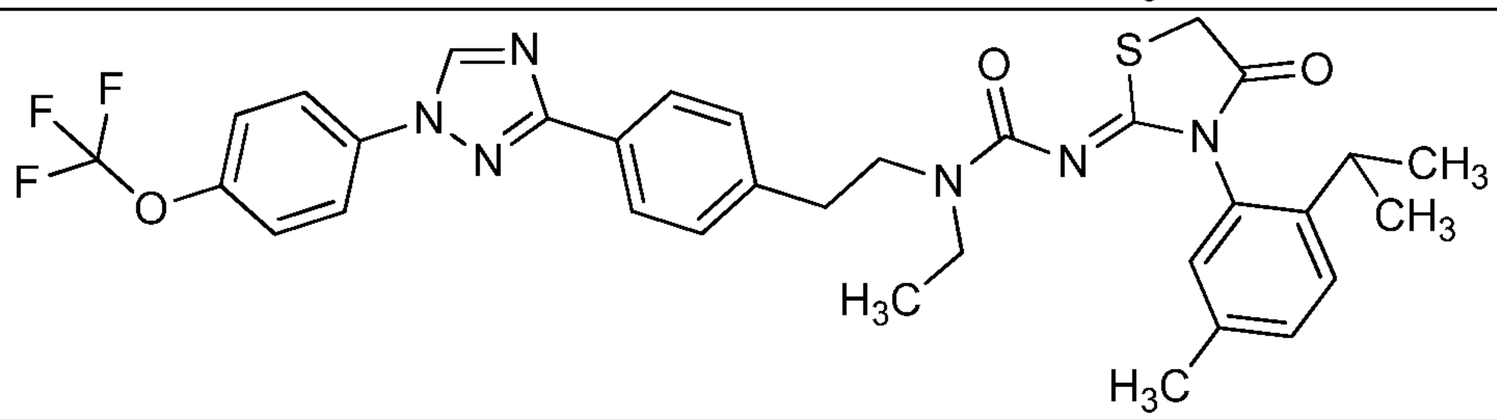
FB21	
FB22	
FB23	
FB24	
FB25	

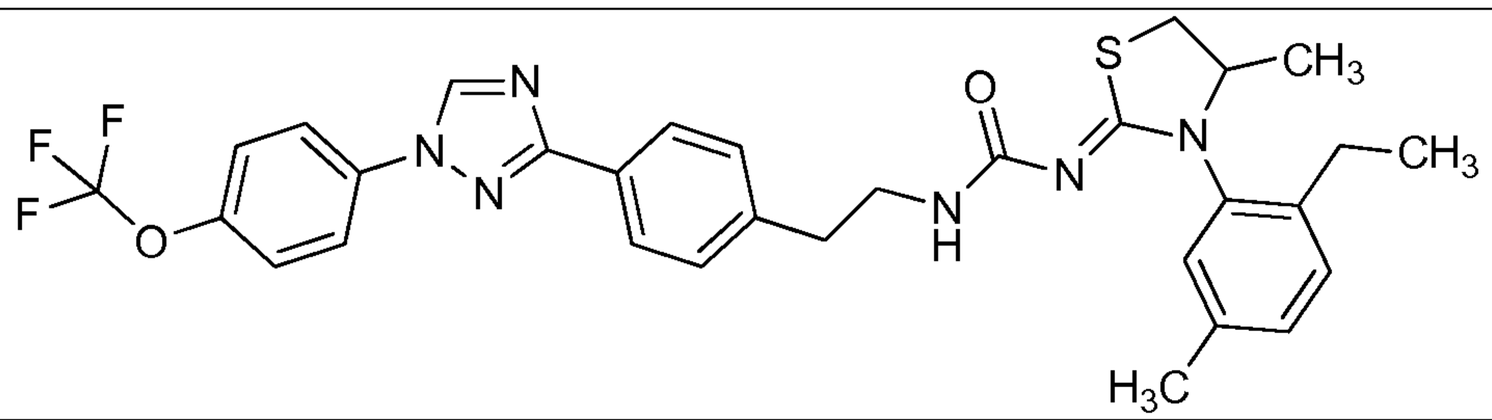
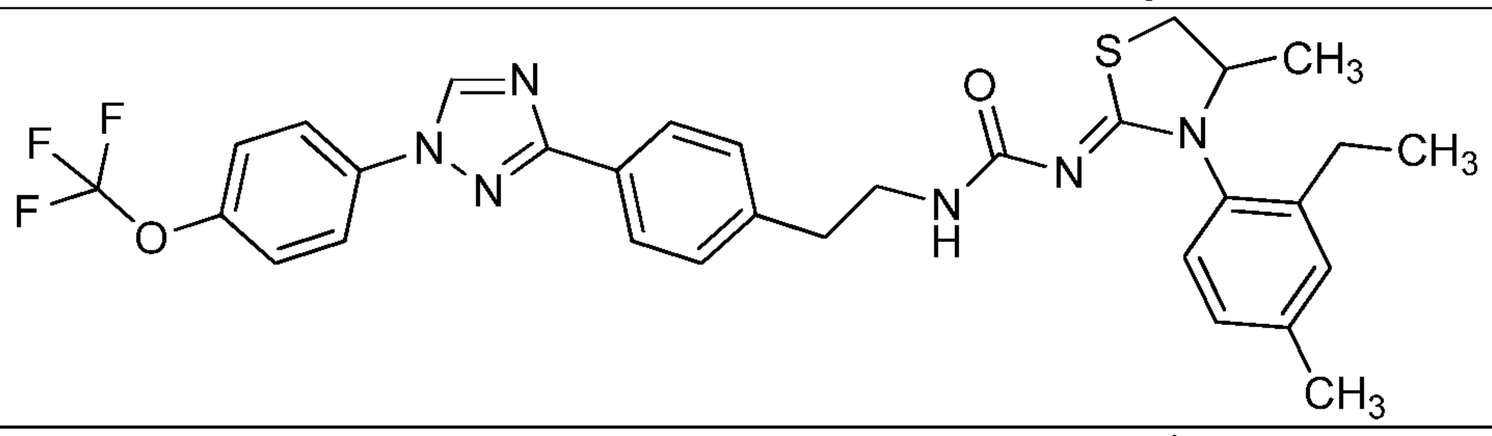
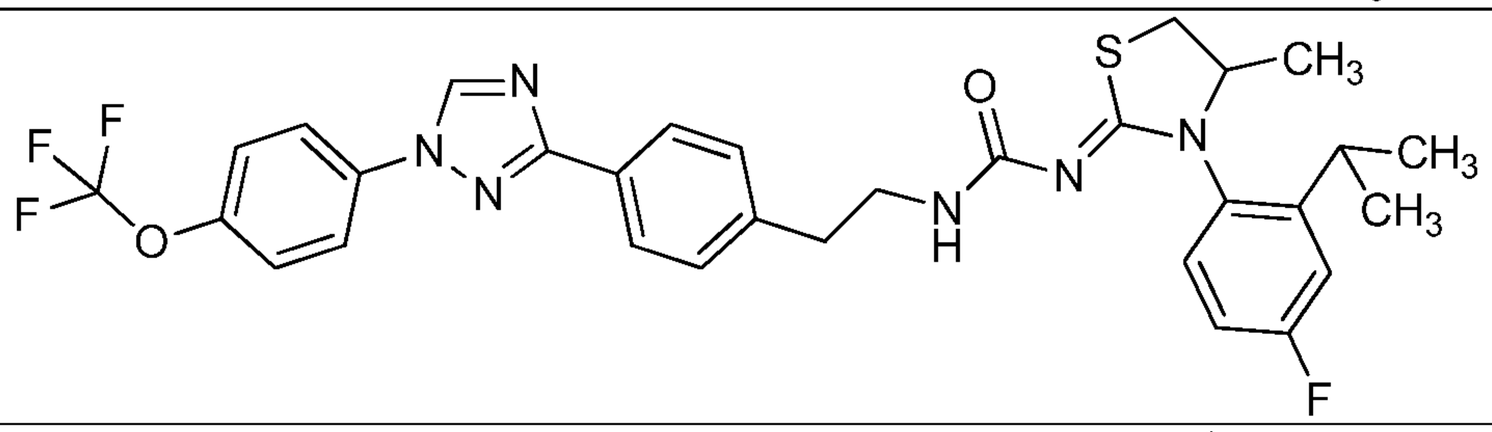
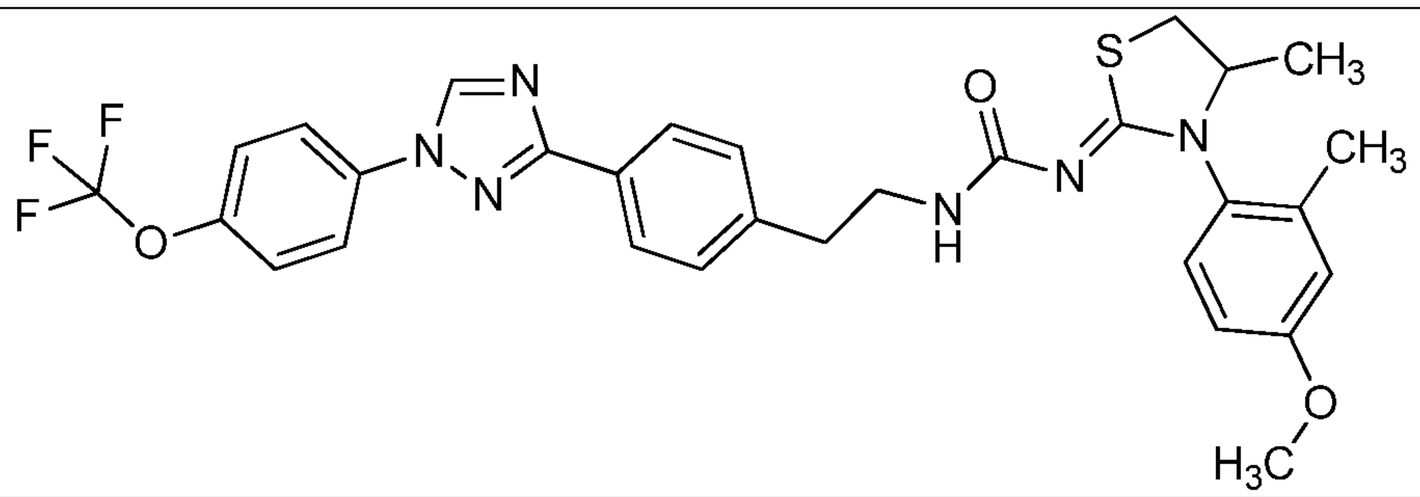
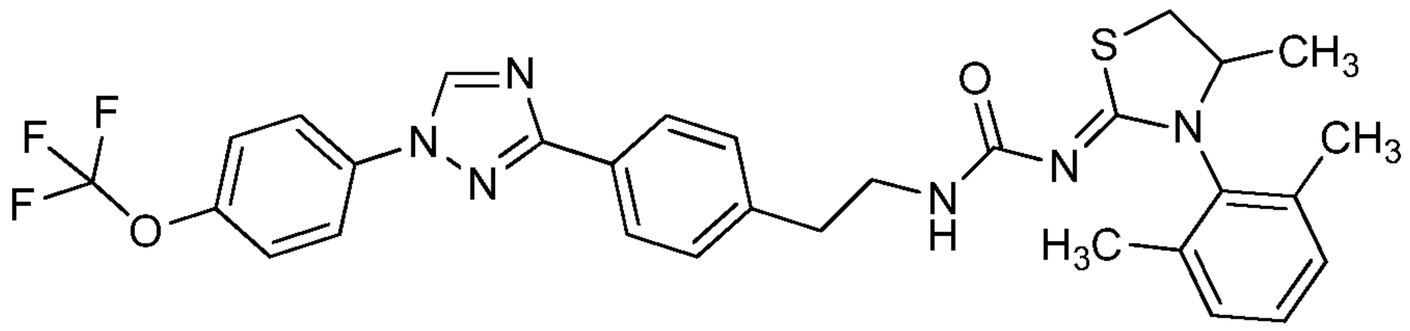
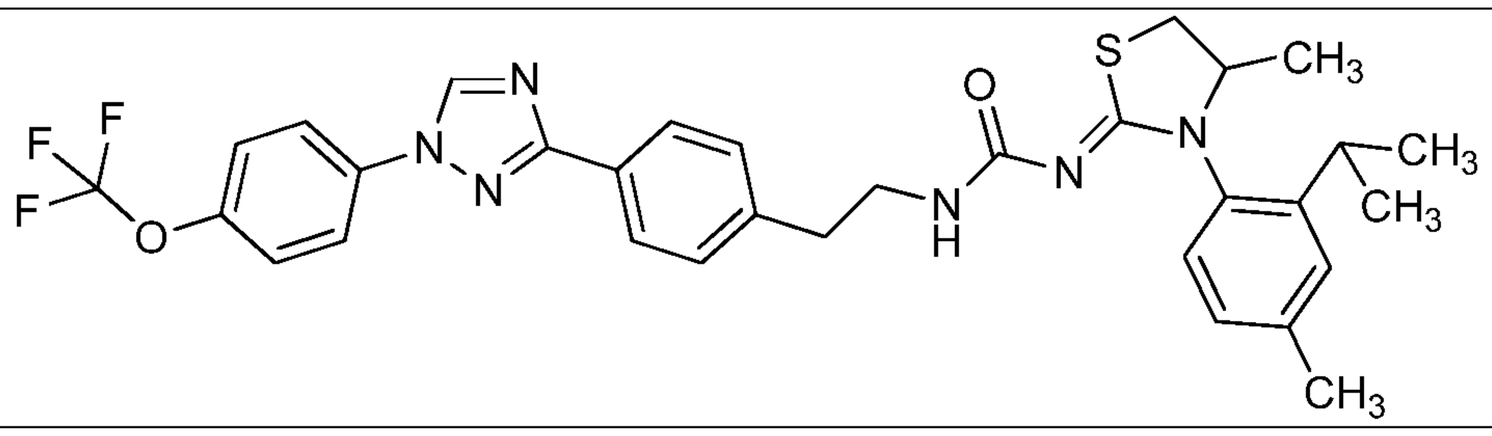
FB26	
FB27	
FB28	
FB29	
FB30	
FB31	

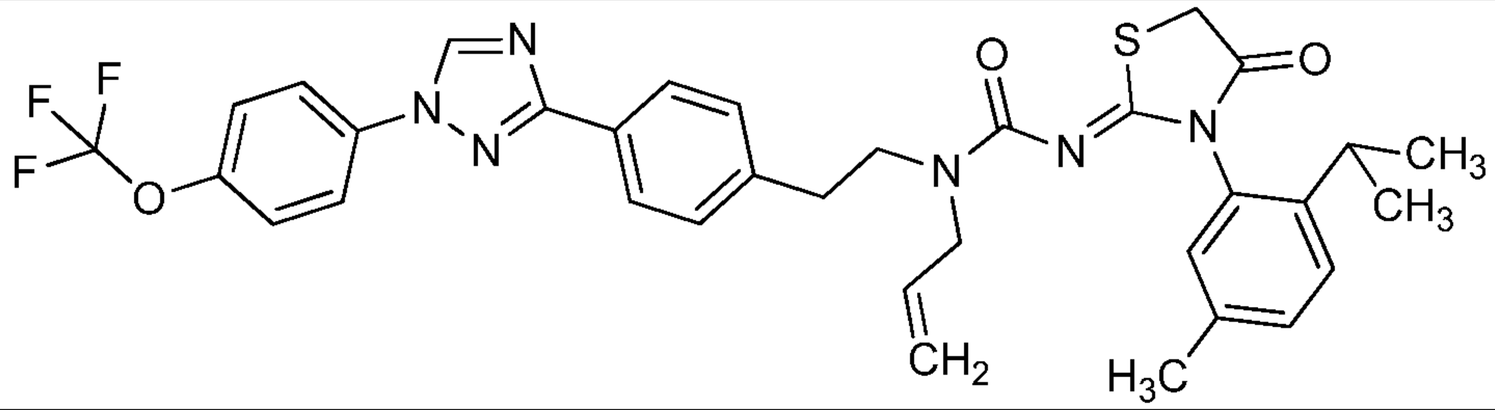
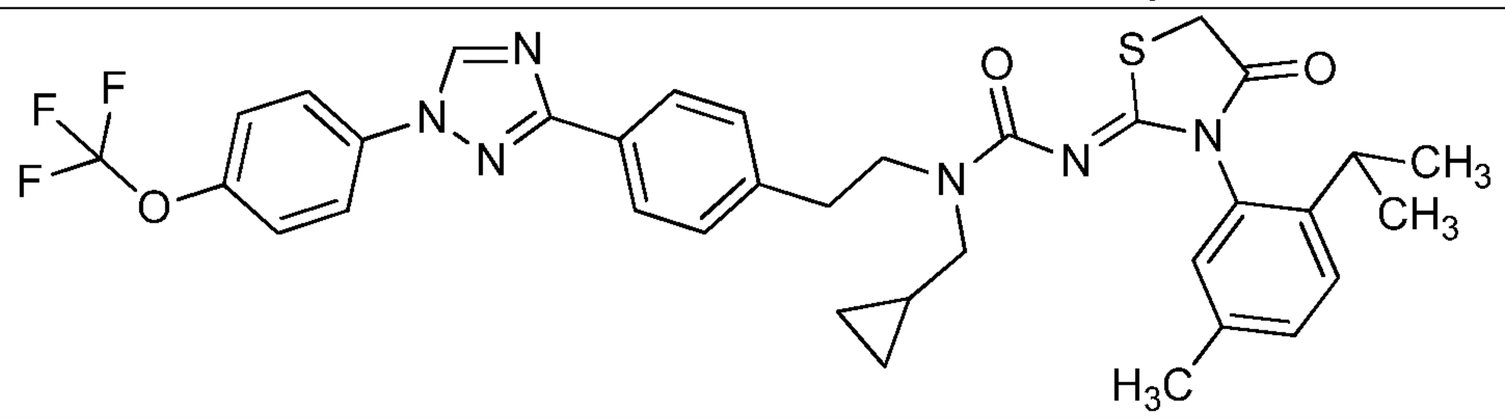
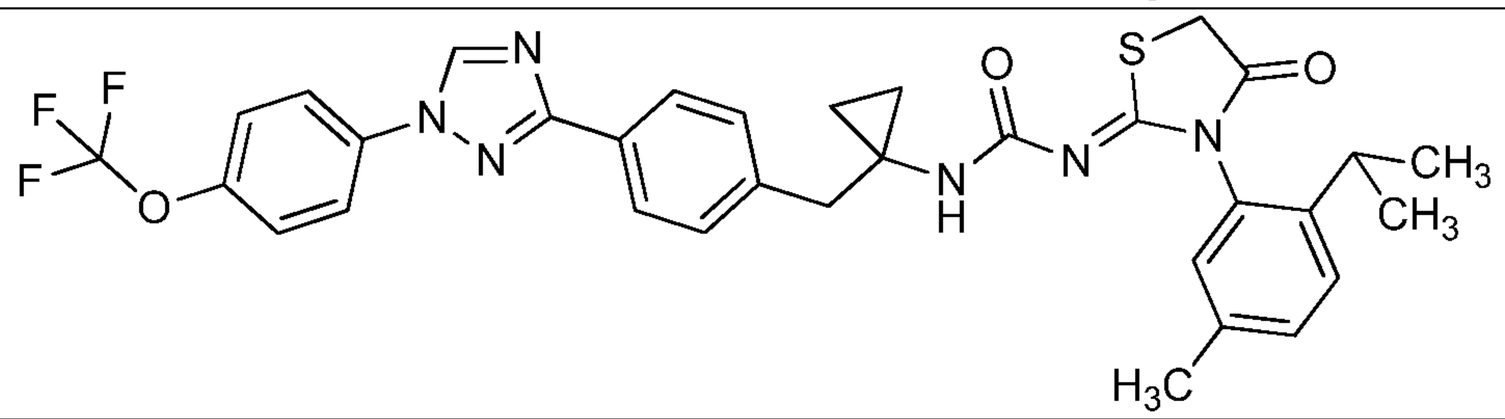
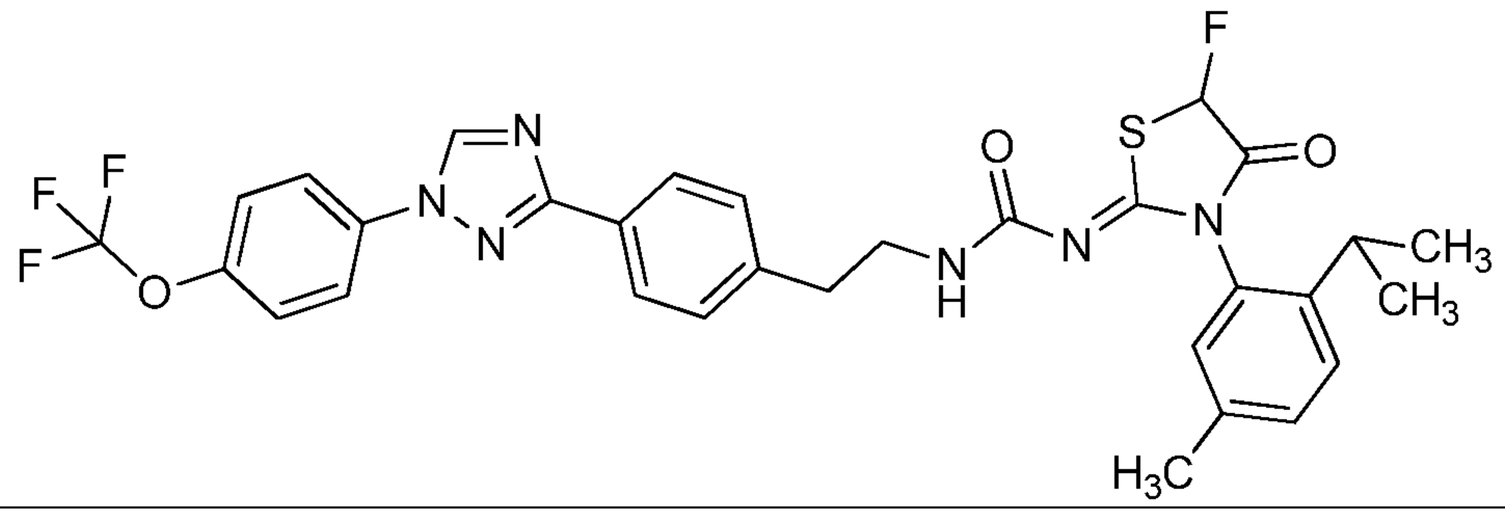
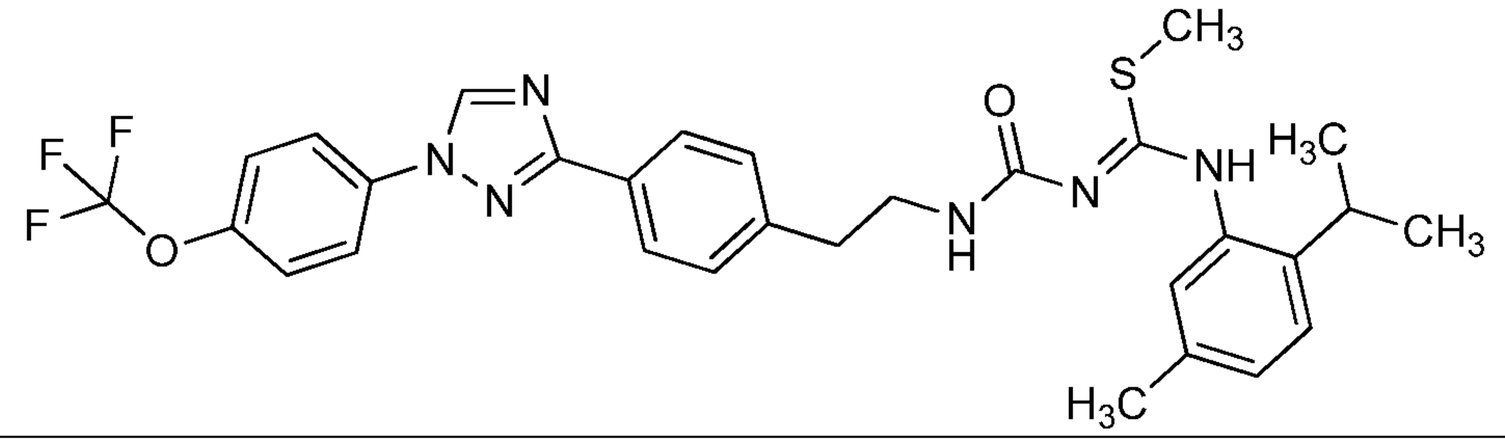
FB32	
FB33	
FB34	
FB35	
FB36	
FB37	

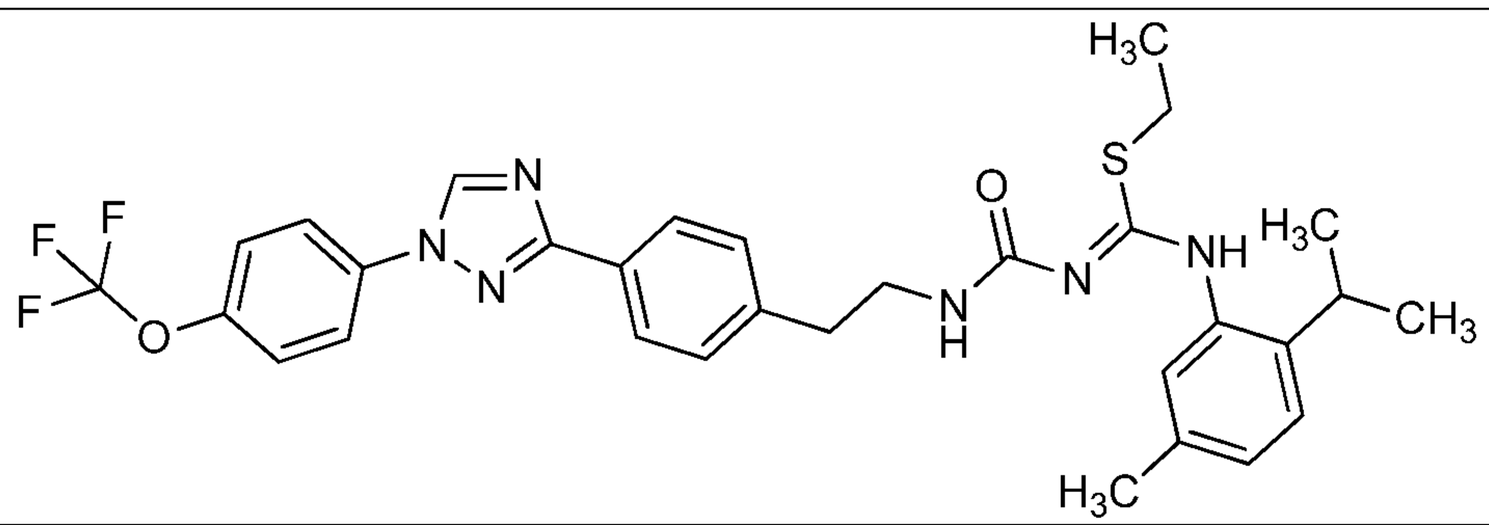
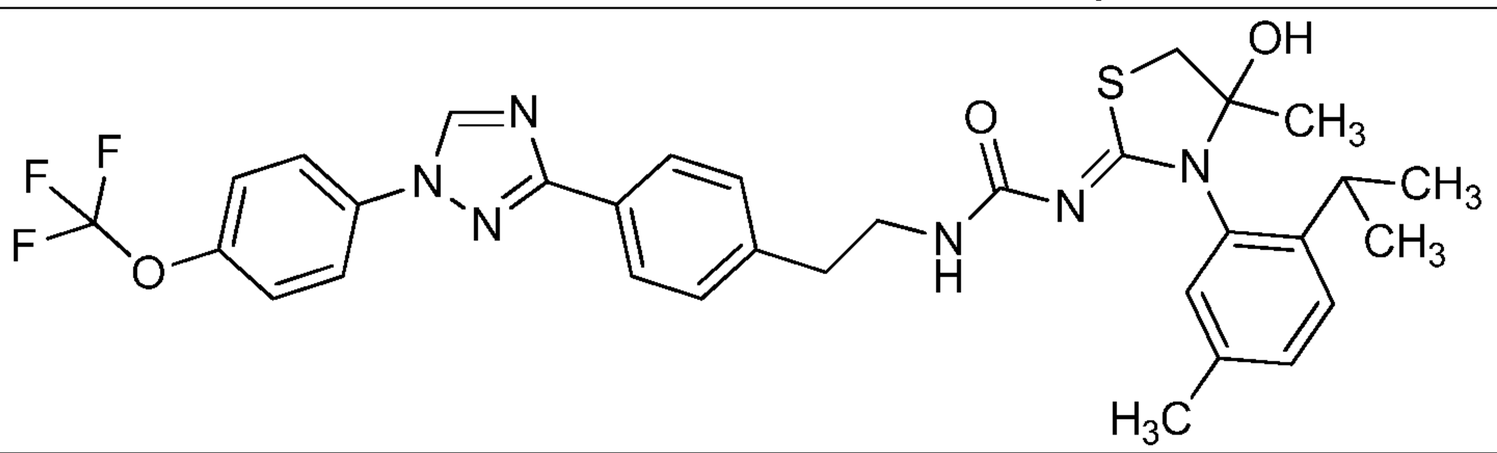
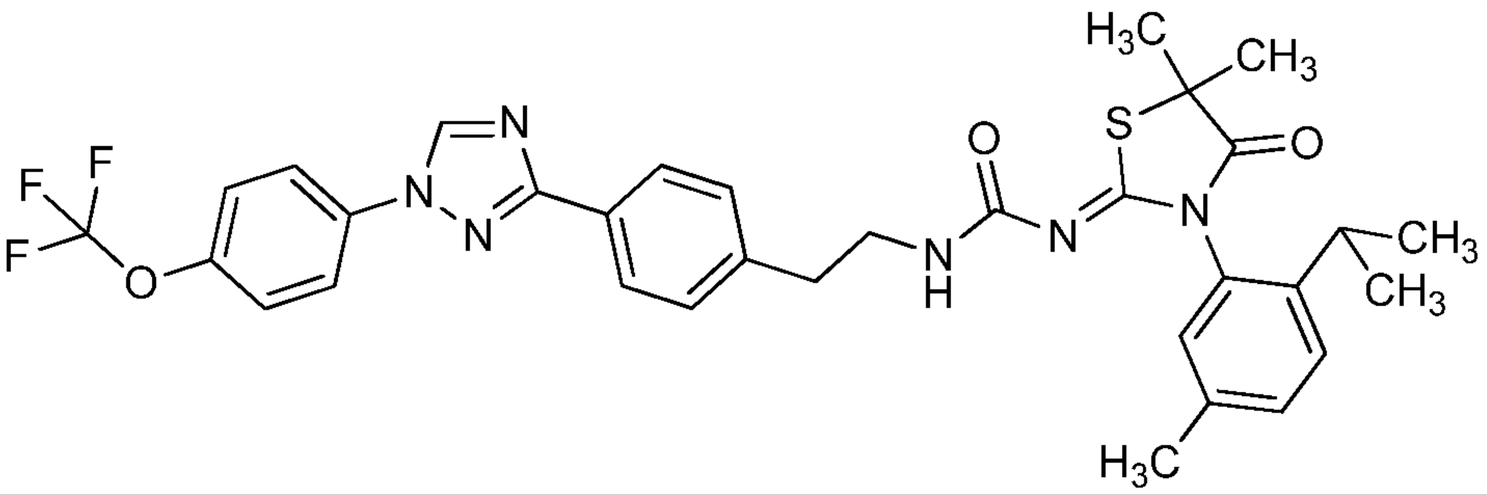
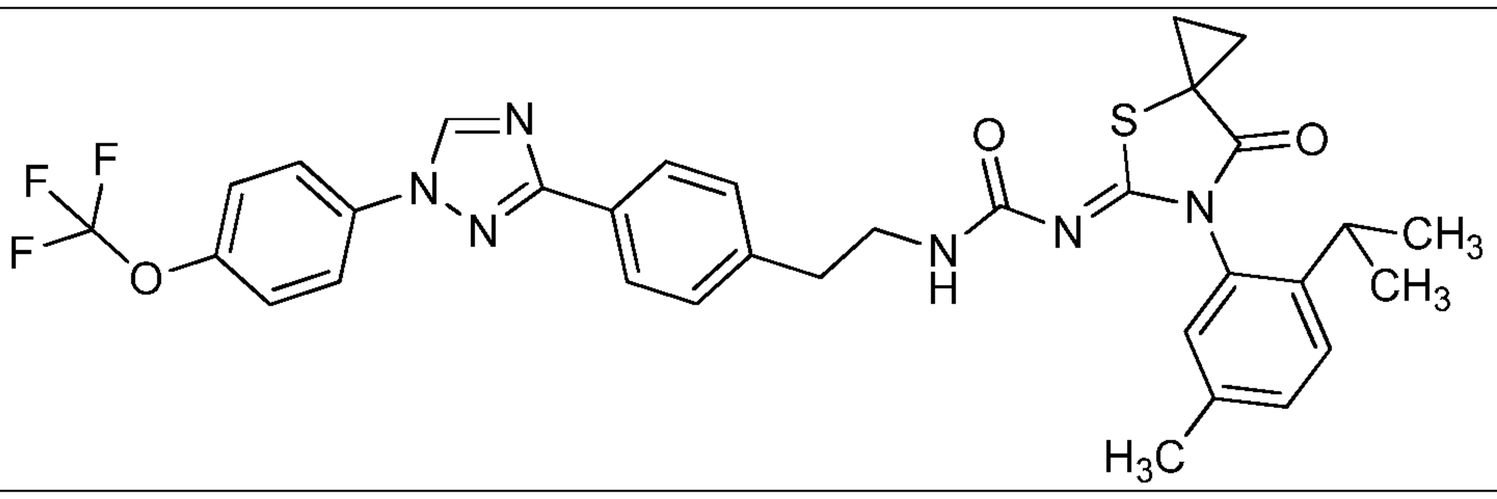
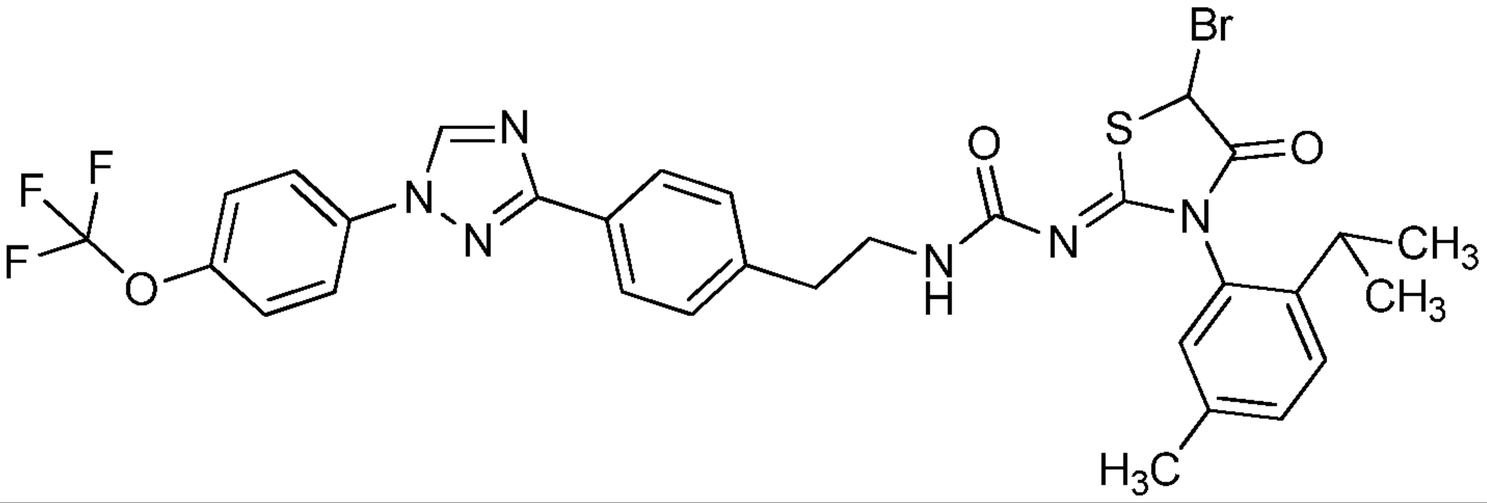
FB38	
FB39	
FB40	
FB41	
FB42	

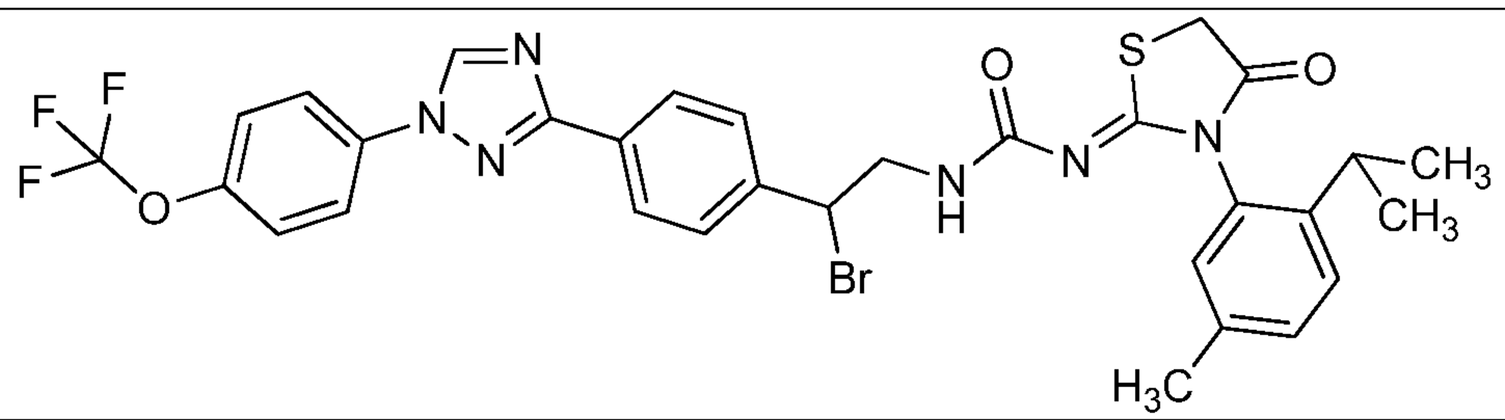
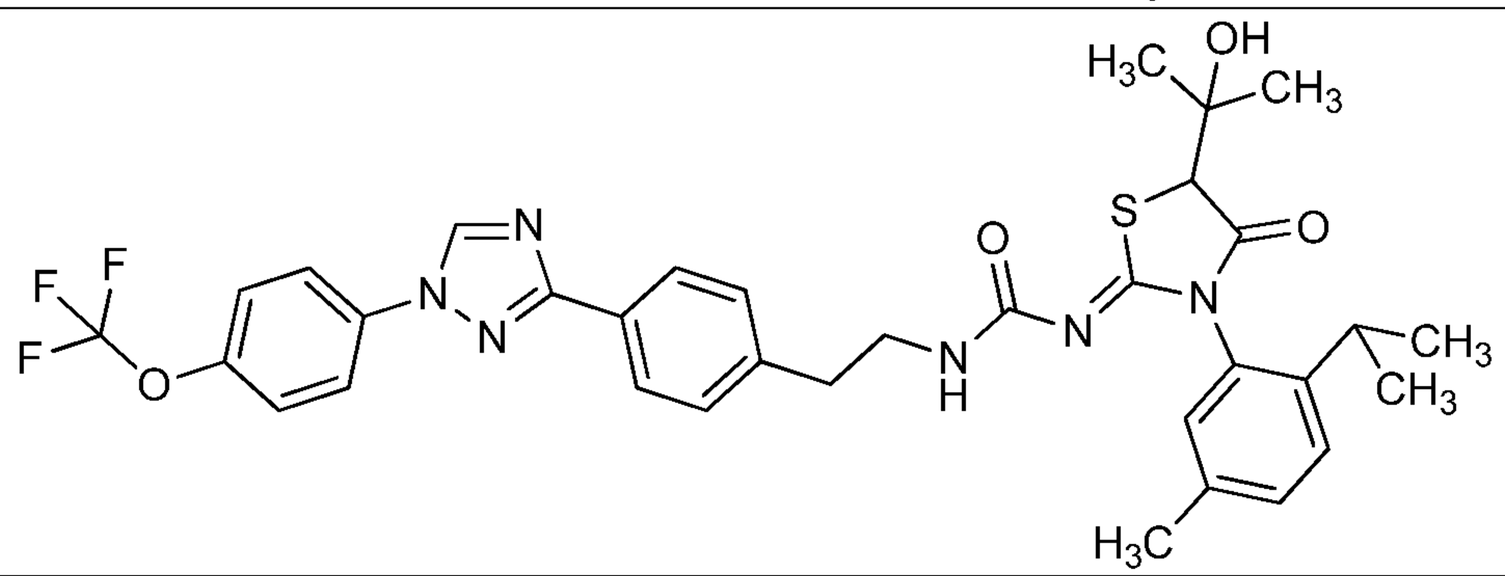
FB43	
FB44	
FB45	
FB46	
FB47	
FB48	

FB49	
FB50	
FB51	
FB52	
FB53	
FB54	

FB55	
FB56	
FB57	
FB58	
FB59	
FB60	

FB61	
FB62	
FB63	
FB64	
FB65	

FB66	
FB67	
FB68	
FB69	
FB70	

FB71	
FB72	

.

14. A composition comprising a molecule according to any of the proceeding claims and:

(a) one or more compounds having a mode of action selected from Acetylcholinesterase (AChE) inhibitors; GABA-gated chloride channel antagonists; Sodium channel modulators; Nicotinic acetylcholine (nAChR) agonists; Nicotinic acetylcholine receptor (nAChR) allosteric activators; Chloride channel activators; Juvenile hormone mimics; Miscellaneous non-specific (multi-site) inhibitors; Selective homopteran feeding blockers; Mite growth inhibitors; Microbial disruptors of insect midgut membranes; Inhibitors of mitochondrial ATP synthase; Uncouplers of oxidative phosphorylation via disruption of the proton gradient; Nicotinic acetylcholine receptor (nAChR) channel blockers; Inhibitors of chitin biosynthesis, type 0; Inhibitors of chitin biosynthesis, type 1; Moulting disruptor, Dipteran; Ecdysone receptor agonists; Octopamine receptor agonists; Mitochondrial complex III electron transport inhibitors; Mitochondrial complex I electron transport inhibitors; Voltage-dependent sodium channel blockers; Inhibitors of acetyl CoA carboxylase; Mitochondrial complex IV electron transport inhibitors; Mitochondrial complex II electron transport inhibitors; and Ryanodine receptor modulators; and/or

(b) one or more compounds having acaricidal, algicidal, avicidal, bactericidal, fungicidal, herbicidal, insecticidal, molluscicidal, nematicidal, rodenticidal, and/or virucidal properties; and/or

(c) one or more compounds that are antifeedants, bird repellents, chemosterilants, herbicide safeners, insect attractants, insect repellents, mammal repellents, mating disrupters, plant activators, plant growth regulators, and/or synergists; and/or

(d) one or more of the following compounds – (3-ethoxypropyl)mercury bromide, 1,2-dichloropropane, 1,3-dichloropropene, 1-methylcyclopropene, 1-naphthol, 2-(octylthio)ethanol, 2,3,5-tri-iodobenzoic acid, 2,3,6-TBA, 2,3,6-TBA-dimethylammonium, 2,3,6-TBA-lithium, 2,3,6-TBA-potassium, 2,3,6-TBA-sodium, 2,4,5-T, 2,4,5-T-2-butoxypropyl, 2,4,5-T-2-ethylhexyl, 2,4,5-T-3-butoxypropyl, 2,4,5-TB, 2,4,5-T-butometyl, 2,4,5-T-butotyl, 2,4,5-T-butyl, 2,4,5-T-isobutyl, 2,4,5-T-isoctyl, 2,4,5-T-isopropyl, 2,4,5-T-methyl, 2,4,5-T-pentyl, 2,4,5-T-sodium, 2,4,5-T-triethylammonium, 2,4,5-T-trolamine, 2,4-D, 2,4-D-2-butoxypropyl, 2,4-D-2-ethylhexyl, 2,4-D-3-butoxypropyl, 2,4-D-ammonium, 2,4-DB, 2,4-DB-butyl, 2,4-DB-dimethylammonium, 2,4-DB-isoctyl, 2,4-DB-potassium, 2,4-DB-sodium, 2,4-D-butotyl, 2,4-D-butyl, 2,4-D-diethylammonium, 2,4-D-dimethylammonium, 2,4-D-diolamine, 2,4-D-dodecylammonium, 2,4-DEB, 2,4-DEP, 2,4-D-ethyl, 2,4-D-heptylammonium, 2,4-D-isobutyl, 2,4-D-isoctyl, 2,4-D-isopropyl, 2,4-D-isopropylammonium, 2,4-D-lithium, 2,4-D-meptyl, 2,4-D-methyl, 2,4-D-octyl, 2,4-D-pentyl, 2,4-D-potassium, 2,4-D-propyl, 2,4-D-sodium, 2,4-D-tefuryl, 2,4-D-tetradecylammonium, 2,4-D-triethylammonium, 2,4-D-tris(2-hydroxypropyl)ammonium, 2,4-D-trolamine, 2iP, 2-methoxyethylmercury chloride, 2-phenylphenol, 3,4-DA, 3,4-DB, 3,4-DP, 4-aminopyridine, 4-CPA, 4-CPA-diolamine, 4-CPA-potassium, 4-CPA-sodium, 4-CPB, 4-CPP, 4-hydroxyphenethyl alcohol, 8-hydroxyquinoline sulfate, 8-phenylmercurioxyquinoline, abamectin, abscisic acid, ACC, acephate, acequinocyl, acetamiprid, acethion, acetochlor, acetophos, acetoprole, acibenzolar, acibenzolar-S-methyl, acifluorfen, acifluorfen-methyl, acifluorfen-sodium, aclonifen, acrep, acrinathrin, acrolein, acrylonitrile, acypetacs, acypetacs-copper, acypetacs-zinc, afidopyropen, alachlor, alanycarb, albendazole,

aldicarb, aldimorph, aldoxycarb, aldrin, allethrin, allicin, allidochlor, allosamidin, alloxydim, alloxydim-sodium, allyl alcohol, allyxycarb, alorac, *alpha*-cypermethrin, *alpha*-endosulfan, ametoctradin, ametridione, ametryn, amibuzin, amicarbazone, amicarthiazol, amidithion, amidoflumet, amidosulfuron, aminocarb, aminocyclopyrachlor, aminocyclopyrachlor-methyl, aminocyclopyrachlor-potassium, aminopyralid, aminopyralid-potassium, aminopyralid-tris(2-hydroxypropyl)ammonium, amiprofos-methyl, amiprophos, amisulbrom, amiton, amiton oxalate, amitraz, amitrole, ammonium sulfamate, ammonium α-naphthaleneacetate, amobam, ampropylfos, anabasine, anabasine sulfate, ancymidol, anilazine, anilofos, anisuron, anthraquinone, antu, apholate, aramite, arsenous oxide, asomate, aspirin, asulam, asulam-potassium, asulam-sodium, athidathion, atraton, atrazine, aureofungin, aviglycine, aviglycine hydrochloride, azaconazole, azadirachtin, azafenidin, azamethiphos, azimsulfuron, azinphos-ethyl, azinphos-methyl, aziprotryne, azithiram, azobenzene, azocyclotin, azothoate, azoxystrobin, bachmedesh, barban, barium hexafluorosilicate, barium polysulfide, barthrin, BCPC, beflubutamid, benalaxyl, benalaxyl-M, benazolin, benazolin-dimethylammonium, benazolin-ethyl, benazolin-potassium, bencarbazone, benclothiaz, bendiocarb, benfluralin, benfuracarb, benfuresate, benodanil, benomyl, benoxacor, benoxafos, benquinox, bensulfuron, bensulfuron-methyl, bensulide, bensultap, bentaluron, bentazone, bentazone-sodium, benthiavalicarb, benthiavalicarb-isopropyl, benthiazole, bentranil, benzadox, benzadox-ammonium, benzalkonium chloride, benzamacril, benzamacril-isobutyl, benzamorf, benzfendizone, benzipram, benzobicyclon, benzofenap, benzofluor, benzohydroxamic acid, benzovindiflupyr, benzoximate, benzoylprop, benzoylprop-ethyl, benzthiazuron, benzyl benzoate, benzyladenine, berberine, berberine chloride, *beta*-cyfluthrin, *beta*-cypermethrin, bethoxazin, bicyclopyrone, bifenazate, bifenox, bifenthrin, bifujunzhi, bilanafos, bilanafos-sodium, binapacryl, bingqingxiao, bioallethrin, bioethanomethrin, biopermethrin, bioresmethrin, biphenyl, bisazir, bismerthiazol, bispyribac, bispyribac-sodium, bistrifluron, bitertanol, bithionol, bixafen, blasticidin-S, borax, Bordeaux mixture, boric acid, boscalid, brassinolide, brassinolide-ethyl, brevicomin, brodifacoum, brofenvalerate, brofluthrinate, bromacil,

bromacil-lithium, bromacil-sodium, bromadiolone, bromethalin, bromethrin, bromfenvinfos, bromoacetamide, bromobonil, bromobutide, bromocyclen, bromo-DDT, bromofenoxim, bromophos, bromophos-ethyl, bromopropylate, bromothalonil, bromoxynil, bromoxynil butyrate, bromoxynil heptanoate, bromoxynil octanoate, bromoxynil-potassium, brompyrazon, bromuconazole, bronopol, bucarpolate, bufencarb, buminafos, bupirimate, buprofezin, Burgundy mixture, busulfan, butacarb, butachlor, butafenacil, butamifos, butathiofos, butenachlor, butethrin, buthidazole, buthiobate, buthiuron, butocarboxim, butonate, butopyronoxyl, butoxycarboxim, butralin, butroxydim, buturon, butylamine, butylate, cacodylic acid, cadusafos, cafenstrole, calcium arsenate, calcium chlorate, calcium cyanamide, calcium polysulfide, calvinphos, cambendichlor, camphechlor, camphor, captafol, captan, carbamorph, carbanolate, carbaryl, carbasulam, carbendazim, carbendazim benzenesulfonate, carbendazim sulfite, carbetamide, carbofuran, carbon disulfide, carbon tetrachloride, carbophenothion, carbosulfan, carboxazole, carboxide, carboxin, carfentrazone, carfentrazone-ethyl, carpropamid, cartap, cartap hydrochloride, carvacrol, carvone, CDEA, cellocidin, CEPC, ceralure, Cheshunt mixture, chinomethionat, chitosan, chlobenthiazone, chlomethoxyfen, chloralose, chloramben, chloramben-ammonium, chloramben-diolamine, chloramben-methyl, chloramben-methylammonium, chloramben-sodium, chloramine phosphorus, chloramphenicol, chloraniformethan, chloranil, chloranocryl, chlorantraniliprole, chlorazifop, chlorazifop-propargyl, chlorazine, chlorbenside, chlorbenzuron, chlorbicyclen, chlorbromuron, chlorbufam, chlordane, chlordecone, chlordimeform, chlordimeform hydrochloride, chlorempenthrin, chlorethoxyfos, chloreturon, chlorfenac, chlorfenac-ammonium, chlorfenac-sodium, chlorfenapyr, chlorfenazole, chlorfenethol, chlorfenprop, chlorfenson, chlorfensulphide, chlorfenvinphos, chlorfluazuron, chlorflurazole, chlorfluren, chlorfluren-methyl, chlorflurenol, chlorflurenol-methyl, chloridazon, chlorimuron, chlorimuron-ethyl, chlormephos, chlormequat, chlormequat chloride, chlornidine, chlornitrofen, chlorobenzilate, chlorodinitronaphthalenes, chloroform, chloromebuform, chloromethiuron, chloroneb, chlorophacinone, chlorophacinone-sodium, chloropicrin, chloropon, chloropropylate, chlorothalonil, chlorotoluron, chloroxuron, chloroxynil, chlorphonium, chlorphonium

chloride, chlorphoxim, chlorprazophos, chlorprocarb, chlorpropham, chlorpyrifos, chlorpyrifos-methyl, chlorquinox, chlorsulfuron, chlorthal, chlorthal-dimethyl, chlorthal-monomethyl, chlorthiamid, chlorthiophos, chlozolinate, choline chloride, chromafenozide, cinerin I, cinerin II, cinerins, cinidon-ethyl, cinmethylin, cinosulfuron, ciobutide, cisanilide, cismethrin, clacyfos, clethodim, climbazole, cliodinate, clodinafop, clodinafop-propargyl, cloethocarb, clofencet, clofencet-potassium, clofentezine, clofibric acid, clofop, clofop-isobutyl, clomazone, clomeprop, cloprop, cloproxydim, clopyralid, clopyralid-methyl, clopyralid-olamine, clopyralid-potassium, clopyralid-tris(2-hydroxypropyl)ammonium, cloquintocet, cloquintocet-mexyl, cloransulam, cloransulam-methyl, closantel, clothianidin, clotrimazole, cloxyfonac, cloxyfonac-sodium, CMA, codlelure, colophonate, copper acetate, copper acetoarsenite, copper arsenate, copper carbonate, basic, copper hydroxide, copper naphthenate, copper oleate, copper oxychloride, copper silicate, copper sulfate, copper zinc chromate, coumachlor, coumafuryl, coumaphos, coumatetralyl, coumithoate, coumoxystrobin, coumoxystrobin, CPMC, CPMF, CPPC, credazine, cresol, crimidine, crotamiton, crotoxyphos, crufomate, cryolite, cue-lure, cufraneb, cumyluron, cuprobam, cuprous oxide, curcumenol, cyanamide, cyanatryn, cyanazine, cyanofenphos, cyanophos, cyanthoate, cyantraniliprole, cyazofamid, cybutryne, cyclafuramid, cyclanilide, cyclethrin, cycloate, cycloheximide, cycloprate, cycloprothrin, cyclopyrimorate, cyclosulfamuron, cycloxydim, cycluron, cyenopyrafen, cyflufenamid, cyflumetofen, cyfluthrin, cyhalofop, cyhalofop-butyl, cyhalothrin, cyhexatin, cymiazole, cymiazole hydrochloride, cymoxanil, cyometrinil, cypendazole, cypermethrin, cyperquat, cyperquat chloride, cyphenothrin, cyprazine, cyprazole, cyproconazole, cyprodinil, cyprofuram, cypromid, cyprosulfamide, cyromazine, cythioate, daimuron, dalapon, dalapon-calcium, dalapon-magnesium, dalapon-sodium, daminozide, dayoutong, dazomet, dazomet-sodium, DBCP, *d*-camphor, DCIP, DCPTA, DDT, debacarb, decafentin, decarbofuran, dehydroacetic acid, delachlor, deltamethrin, demephion, demephion-O, demephion-S, demeton, demeton-methyl, demeton-O, demeton-O-methyl, demeton-S, demeton-S-methyl, demeton-S-methylsulphon, desmedipham, desmetryn, *d*-fanshiluquebingjuzhi, diafenthiuron, dialifos, di-allate, diamidafos, diatomaceous earth, diazinon, dibutyl

phthalate, dibutyl succinate, dicamba, dicamba-diglycolamine, dicamba-dimethylammonium, dicamba-diolamine, dicamba-isopropylammonium, dicamba-methyl, dicamba-olamine, dicamba-potassium, dicamba-sodium, dicamba-trolamine, dicapthon, dichlobenil, dichlofenthion, dichlofluanid, dichlone, dichloralurea, dichlorbenzuron, dichlorflurenol, dichlorflurenol-methyl, dichlormate, dichlormid, dichlorophen, dichlorprop, dichlorprop-2-ethylhexyl, dichlorprop-butotyl, dichlorprop-dimethylammonium, dichlorprop-ethylammonium, dichlorprop-isoctyl, dichlorprop-methyl, dichlorprop-P, dichlorprop-P-2-ethylhexyl, dichlorprop-P-dimethylammonium, dichlorprop-potassium, dichlorprop-P-potassium, dichlorprop-P-sodium, dichlorprop-sodium, dichlorvos, dichlozoline, diclobutrazol, diclocymet, diclofop, diclofop-methyl, diclomezine, diclomezine-sodium, dicloran, diclosulam, dicofol, dicoumarol, dicresyl, dicrotophos, dicyclanil, dicyclonon, dieldrin, dienochlor, diethamquat, diethamquat dichloride, diethatyl, diethatyl-ethyl, diethofencarb, dietholate, diethyl pyrocarbonate, diethyltoluamide, difenacoum, difenoconazole, difenopenten, difenopenten-ethyl, difenoxuron, difenzoquat, difenzoquat metilsulfate, difethialone, diflovidazin, diflubenzuron, diflufenican, diflufenzopyr, diflufenzopyr-sodium, diflumetorim, dikegulac, dikegulac-sodium, dilor, dimatif, dimefluthrin, dimefox, dimefuron, dimepiperate, dimetachlone, dimetan, dimethacarb, dimethachlor, dimethametryn, dimethenamid, dimethenamid-P, dimethipin, dimethirimol, dimethoate, dimethomorph, dimethrin, dimethyl carbate, dimethyl phthalate, dimethylvinphos, dimetilan, dimexano, dimidazon, dimoxystrobin, dinex, dinex-diclexine, dingjunezuo, diniconazole, diniconazole-M, dinitramine, dinobuton, dinocap, dinocap-4, dinocap-6, dinocton, dinofenate, dinopenton, dinoprop, dinosam, dinoseb, dinoseb acetate, dinoseb-ammonium, dinoseb-diolamine, dinoseb-sodium, dinoseb-trolamine, dinosulfon, dinotefuran, dinoterb, dinoterb acetate, dinoterbon, diofenolan, dioxabenzofos, dioxacarb, dioxathion, diphacinone, diphacinone-sodium, diphenamid, diphenyl sulfone, diphenylamine, dipropalin, dipropetryn, dipyrithione, diquat, diquat dibromide, disparlure, disul, disulfiram, disulfoton, disul-sodium, ditalimfos, dithianon, dithicrofos, dithioether, dithiopyr, diuron, d-limonene, DMPA, DNOC, DNOC-ammonium, DNOC-potassium, DNOC-sodium, dodemorph, dodemorph acetate, dodemorph benzoate, dodicin, dodicin hydrochloride, dodicin-

sodium, dodine, dofenapyn, dominicalure, doramectin, drazoxolon, DSMA, dufulin, EBEP, EBP, ecdysterone, edifenphos, eglinazine, eglinazine-ethyl, emamectin, emamectin benzoate, EMPC, empenthrin, endosulfan, endothal, endothal-diammonium, endothal-dipotassium, endothal-disodium, endothion, endrin, enestroburin, enoxastrobin, EPN, epocholeone, epofenonane, epoxiconazole, eprinomectin, epronaz, EPTC, erbon, ergocalciferol, erlujixiancaoan, esdépalléthrine, esfenvalerate, esprocarb, etacelasil, etaconazole, etaphos, etem, ethaboxam, ethachlor, ethalfluralin, ethametsulfuron, ethametsulfuron-methyl, ethaprochlor, ethephon, ethidimuron, ethiofencarb, ethiolate, ethion, ethiozin, ethiprole, ethirimol, ethoate-methyl, ethofumesate, ethohexadiol, ethoprophos, ethoxyfen, ethoxyfen-ethyl, ethoxyquin, ethoxysulfuron, ethychlozate, ethyl formate, ethyl α-naphthaleneacetate, ethyl-DDD, ethylene, ethylene dibromide, ethylene dichloride, ethylene oxide, ethylicin, ethylmercury 2,3-dihydroxypropyl mercaptide, ethylmercury acetate, ethylmercury bromide, ethylmercury chloride, ethylmercury phosphate, etinofen, etnipromid, etobenzanid, etofenprox, etoxazole, etridiazole, etrimfos, eugenol, EXD, famoxadone, famphur, fenamidone, fenaminosulf, fenaminstrobin, fenamiphos, fenapanil, fenarimol, fenasulam, fenazaflor, fenazaquin, fenbuconazole, fenbutatin oxide, fenchlorazole, fenchlorazole-ethyl, fenchlorphos, fenclorim, fenethacarb, fenfluthrin, fenfuram, fenhexamid, fenitropan, fenitrothion, fenjuntong, fenobucarb, fenoprop, fenoprop-3-butoxypropyl, fenoprop-butometyl, fenoprop-butotyl, fenoprop-butyl, fenoprop-isoctyl, fenoprop-methyl, fenoprop-potassium, fenothiocarb, fenoxacrim, fenoxanil, fenoxaprop, fenoxaprop-ethyl, fenoxaprop-P, fenoxaprop-P-ethyl, fenoxasulfone, fenoxycarb, fenpiclonil, fenpirithrin, fenpropathrin, fenpropidin, fenpropimorph, fenpyrazamine, fenpyroximate, fenridazon, fenridazon-potassium, fenridazon-propyl, fenson, fensulfothion, fenteracol, fenthiaprop, fenthiaprop-ethyl, fenthion, fenthion-ethyl, fentin, fentin acetate, fentin chloride, fentin hydroxide, fentrazamide, fentrifanil, fenuron, fenuron TCA, fenvalerate, ferbam, ferimzone, ferrous sulfate, fipronil, flamprop, flamprop-isopropyl, flamprop-M, flamprop-methyl, flamprop-M-isopropyl, flamprop-M-methyl, flazasulfuron, flocoumafen, flometoquin, flonicamid, florasulam, fluacrypyrim, fluazifop, fluazifop-butyl, fluazifop-methyl, fluazifop-P, fluazifop-P-butyl, fluazinam,

fluazolate, fluazuron, flubendiamide, flubenzimine, flucarbazone, flucarbazone-sodium, flucetosulfuron, fluchloralin, flucofuron, flucycloxuron, flucythrinate, fludioxonil, fluenetil, fluensulfone, flufenacet, flufenerim, flufenican, flufenoxuron, flufenoxystrobin, flufenprox, flufenpyr, flufenpyr-ethyl, flufiprole, flumethrin, flumetover, flumetralin, flumetsulam, flumezin, flumiclorac, flumiclorac-pentyl, flumioxazin, flumipropyn, flumorph, fluometuron, fluopicolide, fluopyram, fluorbenside, fluoridamid, fluoroacetamide, fluorodifen, fluoroglycofen, fluoroglycofen-ethyl, fluoroimide, fluoromidine, fluoronitrofen, fluothiuron, fluotrimazole, fluoxastrobin, flupoxam, flupropacil, flupropadine, flupropanate, flupropanate-sodium, flupyradifurone, flupyrsulfuron, flupyrsulfuron-methyl, flupyrsulfuron-methyl-sodium, fluquinconazole, flurazole, flurenol, flurenol-butyl, flurenol-methyl, fluridone, flurochloridone, fluroxypyr, fluroxypyr-butometyl, fluroxypyr-meptyl, flurprimidol, flursulamid, flurtamone, flusilazole, flusulfamide, fluthiacet, fluthiacet-methyl, flutianil, flutolanil, flutriafol, fluvalinate, fluxapyroxad, fluxofenim, folpet, fomesafen, fomesafen-sodium, fonofos, foramsulfuron, forchlorfenuron, formaldehyde, formetanate, formetanate hydrochloride, formothion, formparanate, formparanate hydrochloride, fosamine, fosamine-ammonium, fosetyl, fosetyl-aluminium, fosmethilan, fospirate, fosthiazate, fosthietan, frontalin, fuberidazole, fucaojing, fucaomi, funaihecaoling, fuphenthiourea, furalane, furalaxyl, furamethrin, furametpyr, furathiocarb, furcarbanil, furconazole, furconazole-cis, furethrin, furfural, furilazole, furmecyclox, furophanate, furyloxyfen, *gamma*-cyhalothrin, *gamma*-HCH, genit, gibberellic acid, gibberellins, gliftor, glufosinate, glufosinate-ammonium, glufosinate-P, glufosinate-P-ammonium, glufosinate-P-sodium, glyodin, glyoxime, glyphosate, glyphosate-diammonium, glyphosate-dimethylammonium, glyphosate-isopropylammonium, glyphosate-monoammonium, glyphosate-potassium, glyphosate-sesquisodium, glyphosate-trimesium, glyphosine, gossyplure, grandlure, griseofulvin, guazatine, guazatine acetates, halacrinate, halauxifen, halauxifen-methyl, halfenprox, halofenozide, halosafen, halosulfuron, halosulfuron-methyl, haloxydine, haloxyfop, haloxyfop-etotyl, haloxyfop-methyl, haloxyfop-P, haloxyfop-P-etotyl, haloxyfop-P-methyl, haloxyfop-sodium, HCH, hemel, hempa, HEOD, heptachlor, heptafluthrin, heptenophos, heptopargil,

herbimycin, heterophos, hexachloroacetone, hexachlorobenzene, hexachlorobutadiene, hexachlorophene, hexaconazole, hexaflumuron, hexaflurate, hexalure, hexamide, hexazinone, hexylthiofos, hexythiazox, HHDN, holosulf, huancaiwo, huangcaoling, huanjunzuo, hydramethylnon, hydrargaphen, hydrated lime, hydrogen cyanide, hydroprene, hymexazol, hyquincarb, IAA, IBA, icaridin, imazalil, imazalil nitrate, imazalil sulfate, imazamethabenz, imazamethabenz-methyl, imazamox, imazamox-ammonium, imazapic, imazapic-ammonium, imazapyr, imazapyr-isopropylammonium, imazaquin, imazaquin-ammonium, imazaquin-methyl, imazaquin-sodium, imazethapyr, imazethapyr-ammonium, imazosulfuron, imibenconazole, imicyafos, imidacloprid, imidaclothiz, iminoctadine, iminoctadine triacetate, iminoctadine trialbesilate, imiprothrin, inabenfide, indanofan, indaziflam, indoxacarb, inezin, iodobonil, iodocarb, iodomethane, iodosulfuron, iodosulfuron-methyl, iodosulfuron-methyl-sodium, iofensulfuron, iofensulfuron-sodium, ioxynil, ioxynil octanoate, ioxynil-lithium, ioxynil-sodium, ipazine, ipconazole, ipfencarbazone, iprobenfos, iprodione, iprovalicarb, iprymidam, ipsdienol, ipsenol, IPSP, isamidofos, isazofos, isobenzan, isocarbamid, isocarbophos, isocil, isodrin, isofenphos, isofenphos-methyl, isofetamid, isolan, isomethiozin, isonoruron, isopolinate, isoprocarb, isopropalin, isoprothiolane, isoproturon, isopyrazam, isopyrimol, isothioate, isotianil, isouron, isovaledione, isoxaben, isoxachlortole, isoxadifen, isoxadifen-ethyl, isoxaflutole, isoxapyrifop, isoxathion, ivermectin, izopamfos, japonilure, japothrins, jasmolin I, jasmolin II, jasmonic acid, jiahuangchongzong, jiajizengxiaolin, jiaxiangjunzhi, jiecaowan, jiecaoxi, jodfenphos, juvenile hormone I, juvenile hormone II, juvenile hormone III, kadethrin, karbutilate, karetazan, karetazan-potassium, kasugamycin, kasugamycin hydrochloride, kejunlin, kelevan, ketospiradox, ketospiradox-potassium, kinetin, kinoprene, kresoxim-methyl, kuicaoxi, lactofen, lambda-cyhalothrin, latilure, lead arsenate, lenacil, lepimectin, leptophos, lindane, lineatin, linuron, lirimfos, litlure, looplure, lufenuron, lvdingjunzhi, lvxiancaolin, lythidathion, MAA, malathion, maleic hydrazide, malonoben, maltodextrin, MAMA, mancopper, mancozeb, mandipropamid, maneb, matrine, mazidox, MCPA, MCPA-2-ethylhexyl, MCPA-butotyl, MCPA-butyl, MCPA-dimethylammonium, MCPA-diolamine, MCPA-ethyl, MCPA-isobutyl, MCPA-isoctyl,

MCPA-isopropyl, MCPA-methyl, MCPA-olamine, MCPA-potassium, MCPA-sodium, MCPA-thioethyl, MCPA-trolamine, MCPB, MCPB-ethyl, MCPB-methyl, MCPB-sodium, mebenil, mecarbam, mecarbinzid, mecarphon, mecoprop, mecoprop-2-ethylhexyl, mecoprop-dimethylammonium, mecoprop-diolamine, mecoprop-ethadyl, mecoprop-isoctyl, mecoprop-methyl, mecoprop-P, mecoprop-P-2-ethylhexyl, mecoprop-P-dimethylammonium, mecoprop-P-isobutyl, mecoprop-potassium, mecoprop-P-potassium, mecoprop-sodium, mecoprop-trolamine, medimeform, medinoterb, medinoterb acetate, medlure, mefenacet, mefenpyr, mefenpyr-diethyl, mefluidide, mefluidide-diolamine, mefluidide-potassium, megatomoic acid, menazon, mepanipyrim, meperfluthrin, mephenate, mephosfolan, mepiquat, mepiquat chloride, mepiquat pentaborate, mepronil, meptyldinocap, mercuric chloride, mercuric oxide, mercurous chloride, merphos, mesoprazine, mesosulfuron, mesosulfuron-methyl, mesotrione, mesulfen, mesulfenfos, metaflumizone, metalaxyl, metalaxyl-M, metaldehyde, metam, metam-ammonium, metamifop, metamitron, metam-potassium, metam-sodium, metazachlor, metazosulfuron, metazoxolon, metconazole, metepa, metflurazon, methabenzthiazuron, methacrifos, methalpropalin, methamidophos, methasulfocarb, methazole, methfuroxam, methidathion, methiobencarb, methiocarb, methiopyrisulfuron, methiotepa, methiozolin, methiuron, methocrotophos, methometon, methomyl, methoprene, methoprotryne, methoquin-butyl, methothrin, methoxychlor, methoxyfenozide, methoxyphenone, methyl apholate, methyl bromide, methyl eugenol, methyl iodide, methyl isothiocyanate, methylacetophos, methylchloroform, methyldymron, methylene chloride, methylmercury benzoate, methylmercury dicyandiamide, methylmercury pentachlorophenoxide, methylneodecanamide, metiram, metobenzuron, metobromuron, metofluthrin, metolachlor, metolcarb, metominostrobin, metosulam, metoxadiazone, metoxuron, metrafenone, metribuzin, metsulfovax, metsulfuron, metsulfuron-methyl, mevinphos, mexacarbate, mieshuan, milbemectin, milbemycin oxime, milneb, mipafox, mirex, MNAF, moguchun, molinate, molosultap, monalide, monisouron, monochloroacetic acid, monocrotophos, monolinuron, monosulfuron, monosulfuron-ester, monuron, monuron TCA, morfamquat, morfamquat dichloride, moroxydine, moroxydine

hydrochloride, morphothion, morzid, moxidectin, MSMA, muscalure, myclobutanil, myclozolin, N-(ethylmercury)-p-toluenesulphonanilide, nabam, naftalofos, naled, naphthalene, naphthaleneacetamide, naphthalic anhydride, naphthoxyacetic acids, naproanilide, napropamide, naptalam, naptalam-sodium, natamycin, neburon, niclosamide, niclosamide-olamine, nicosulfuron, nicotine, nifluridide, nipyraclofen, nitenpyram, nithiazine, nitralin, nitrapyrin, nitrilacarb, nitrofen, nitrofluorfen, nitrostyrene, nitrothal-isopropyl, norbormide, norflurazon, nornicotine, noruron, novaluron, noviflumuron, nuarimol, OCH, octachlorodipropyl ether, octhilinone, ofurace, omethoate, orbencarb, orfralure, ortho-dichlorobenzene, orthosulfamuron, oryctalure, orysastrobin, oryzalin, osthol, ostramone, oxabetrinil, oxadiargyl, oxadiazon, oxadixyl, oxamate, oxamyl, oxapyrazon, oxapyrazon-dimolamine, oxapyrazon-sodium, oxasulfuron, oxathiapiprolin, oxaziclomefone, oxine-copper, oxolinic acid, oxpoconazole, oxpoconazole fumarate, oxycarboxin, oxydemeton-methyl, oxydeprofos, oxydisulfoton, oxyfluorfen, oxymatrine, oxytetracycline, oxytetracycline hydrochloride, paclobutrazol, paichongding, para-dichlorobenzene, parafluron, paraquat, paraquat dichloride, paraquat dimetilsulfate, parathion, parathion-methyl, parinol, pebulate, pefurazoate, pelargonic acid, penconazole, pencycuron, pendimethalin, penflufen, penfluron, penoxsulam, pentachlorophenol, pentachlorophenyl laurate, pentanochlor, penthiopyrad, pentmethrin, pentoxazone, perfluidone, permethrin, pethoxamid, phenamacril, phenazine oxide, phenisopham, phenkapton, phenmedipham, phenmedipham-ethyl, phenobenzuron, phenothrin, phenproxide, phenthoate, phenylmercuriurea, phenylmercury acetate, phenylmercury chloride, phenylmercury derivative of pyrocatechol, phenylmercury nitrate, phenylmercury salicylate, phorate, phosacetim, phosalone, phosdiphen, phosfolan, phosfolan-methyl, phosglycin, phosmet, phosnichlor, phosphamidon, phosphine, phosphocarb, phosphorus, phostin, phoxim, phoxim-methyl, phthalide, picloram, picloram-2-ethylhexyl, picloram-isoctyl, picloram-methyl, picloram-olamine, picloram-potassium, picloram-triethylammonium, picloram-tris(2-hydroxypropyl)ammonium, picolinafen, picoxystrobin, pindone, pindone-sodium, pinoxaden, piperalin, piperonyl butoxide, piperonyl cyclonene, piperophos, piproctanyl, piproctanyl bromide, piprotal, pirimetaphos, pirimicarb, pirimioxyphos,

pirimiphos-ethyl, pirimiphos-methyl, plifenate, polycarbamate, polyoxins, polyoxorim, polyoxorim-zinc, polythialan, potassium arsenite, potassium azide, potassium cyanate, potassium gibberellate, potassium naphthenate, potassium polysulfide, potassium thiocyanate, potassium α-naphthaleneacetate, *pp'*-DDT, prallethrin, precocene I, precocene II, precocene III, pretilachlor, primidophos, primisulfuron, primisulfuron-methyl, probenazole, prochloraz, prochloraz-manganese, proclonol, procyazine, procymidone, prodiamine, profenofos, profluazol, profluralin, profluthrin, profoxydim, proglinazine, proglinazine-ethyl, prohexadione, prohexadione-calcium, prohydrojasmon, promacyl, promecarb, prometon, prometryn, promurit, propachlor, propamidine, propamidine dihydrochloride, propamocarb, propamocarb hydrochloride, propanil, propaphos, propaquizafop, propargite, proparthrin, propazine, propetamphos, propham, propiconazole, propineb, propisochlor, propoxur, propoxycarbazone, propoxycarbazone-sodium, propyl isome, propyrisulfuron, propyzamide, proquinazid, prosuler, prosulfalin, prosulfocarb, prosulfuron, prothidathion, prothiocarb, prothiocarb hydrochloride, prothioconazole, prothiofos, prothoate, protrifenbute, proxan, proxan-sodium, prynachlor, pydanon, pyflubumide, pymetrozine, pyracarbolid, pyraclofos, pyraclonil, pyraclostrobin, pyraflufen, pyraflufen-ethyl, pyrafluprole, pyramat, pyrametostrobin, pyraoxystrobin, pyrasulfotole, pyrazolynate, pyrazophos, pyrazosulfuron, pyrazosulfuron-ethyl, pyrazothion, pyrazoxyfen, pyresmethrin, pyrethrin I, pyrethrin II, pyrethrins, pyribambenz-isopropyl, pyribambenz-propyl, pyribencarb, pyribenzoxim, pyributicarb, pyriclor, pyridaben, pyridafol, pyridalyl, pyridaphenthion, pyridate, pyridinitril, pyrifenox, pyrifluquinazon, pyriftalid, pyrimethanil, pyrimidifen, pyriminobac, pyriminobac-methyl, pyriminostrobin, pyrimisulfan, pyrimitate, pyrinuron, pyriofenone, pyriprole, pyripropanol, pyriproxyfen, pyrisoxazole, pyrithiobac, pyrithiobac-sodium, pyrolan, pyroquilon, pyroxasulfone, pyroxsulam, pyroxychlor, pyroxyfur, quassia, quinacetol, quinacetol sulfate, quinalphos, quinalphos-methyl, quinazamid, quinclorac, quinconazole, quinmerac, quinoclamine, quinonamid, quinothion, quinoxyfen, quintiofos, quintozene, quizalofop, quizalofop-ethyl, quizalofop-P, quizalofop-P-ethyl, quizalofop-P-tefuryl, quwenzhi, quyingding, rabenzazole, rafoxanide, rebemide, rescalure, resmethrin, rhodethanil, rhodojaponin-

III, ribavirin, rimsulfuron, rotenone, ryania, saflufenacil, saijunmao, saisentong, salicylanilide, sanguinarine, santonin, schradan, scilliroside, sebuthylazine, secbumeton, sedaxane, selamectin, semiamitraz, semiamitraz chloride, sesamex, sesamolin, sethoxydim, shuangjiaancaolin, siduron, siglure, silafluofen, silatrane, silica gel, silthiofam, simazine, simeconazole, simeton, simetryn, sintofen, SMA, S-metolachlor, sodium arsenite, sodium azide, sodium chlorate, sodium fluoride, sodium fluoroacetate, sodium hexafluorosilicate, sodium naphthenate, sodium orthophenylphenoxide, sodium pentachlorophenoxide, sodium polysulfide, sodium thiocyanate, sodium α-naphthaleneacetate, sophamide, spinetoram, spinosad, spirodiclofen, spiromesifen, spirotetramat, spiroxamine, streptomycin, streptomycin sesquisulfate, strychnine, sulcatol, sulcofuron, sulcofuron-sodium, sulcotrione, sulfallate, sulfentrazone, sulfiram, sulfluramid, sulfometuron, sulfometuron-methyl, sulfosulfuron, sulfotep, sulfoxaflor, sulfoxide, sulfoxime, sulfur, sulfuric acid, sulfuryl fluoride, sulglycapin, sulprofos, sultropen, swep, *tau*-fluvalinate, tavron, tazimcarb, TCA, TCA-ammonium, TCA-calcium, TCA-ethadyl, TCA-magnesium, TCA-sodium, TDE, tebuconazole, tebufenozide, tebufenpyrad, tebufloquin, tebupirimfos, tebutam, tebuthiuron, tecloftalam, tecnazene, tecoram, teflubenzuron, tefluthrin, tefuryltrione, tembotrione, temephos, tepa, TEPP, tepraloxydim, terallethrin, terbacil, terbucarb, terbuchlor, terbufos, terbumeton, terbuthylazine, terbutryn, tetcyclacis, tetrachloroethane, tetrachlorvinphos, tetraconazole, tetradifon, tetrafluron, tetramethrin, tetramethylfluthrin, tetramine, tetranactin, tetrasul, thallium sulfate, thenylchlor, theta-cypermethrin, thiabendazole, thiacloprid, thiadifluor, thiamethoxam, thiapronil, thiazafluron, thiazopyr, thicrofos, thicyofen, thidiazimin, thidiazuron, thiencarbazone, thiencarbazone-methyl, thifensulfuron, thifensulfuron-methyl, thifluzamide, thiobencarb, thiocarboxime, thiochlorfenphim, thiocyclam, thiocyclam hydrochloride, thiocyclam oxalate, thiodiazole-copper, thiodicarb, thiofanox, thiofluoximate, thiohempa, thiomersal, thiometon, thionazin, thiophanate, thiophanate-methyl, thioquinox, thiosemicarbazide, thiosultap, thiosultap-diammonium, thiosultap-disodium, thiosultap-monosodium, thiotepa, thiram, thuringiensin, tiadinil, tiaojiean, tiocarbazil, tioclorim, tioxymid, tirpate, tolclofos-methyl, tolfenpyrad, tolprocarb, tolylfluanid, tolylmercury acetate, topramezone,

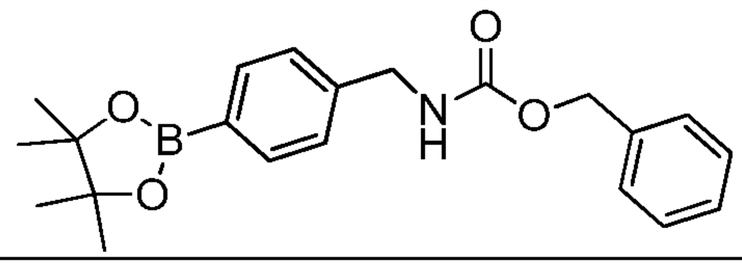
tralkoxydim, tralocythrin, tralomethrin, tralopyril, transfluthrin, transpermethrin, tretamine, triacontanol, triadimefon, triadimenol, triafamone, tri-allate, triamiphos, triapenthenol, triarathene, triarimol, triasulfuron, triazamate, triazbutil, triaziflam, triazophos, triazoxide, tribenuron, tribenuron-methyl, tribufos, tributyltin oxide, tricamba, trichlamide, trichlorfon, trichlormetaphos-3, trichloronat, triclopyr, triclopyr-butotyl, triclopyr-ethyl, triclopyricarb, triclopyr-triethylammonium, tricyclazole, tridemorph, tridiphane, trietazine, trifenmorph, trifenofos, trifloxystrobin, trifloxysulfuron, trifloxysulfuron-sodium, triflumizole, triflumuron, trifluralin, triflusulfuron, triflusulfuron-methyl, trifop, trifop-methyl, trifopsime, triforine, trihydroxytriazine, trimedlure, trimethacarb, trimeturon, trinexapac, trinexapac-ethyl, triprene, tripropindan, triptolide, tritac, triticonazole, tritosulfuron, trunc-call, uniconazole, uniconazole-P, urbacide, uredepa, valerate, validamycin, valifenalate, valone, vamidothion, vangard, vaniliprole, vernolate, vinclozolin, warfarin, warfarin-potassium, warfarin-sodium, xiaochongliulin, xinjunan, xiwojunan, XMC, xylachlor, xylenols, xylylcarb, yishijing, zarilamid, zeatin, zengxiaoan, zeta-cypermethrin, zinc naphthenate, zinc phosphide, zinc thiazole, zineb, ziram, zolaprofos, zoxamide, zuomihuanglong, α-chlorohydrin, α-ecdysone, α-multistriatin, and α-naphthaleneacetic acid; and/or

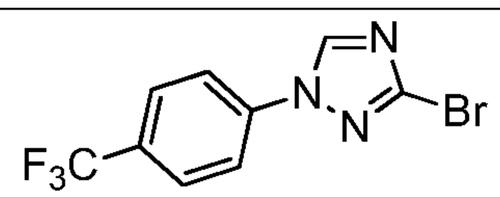
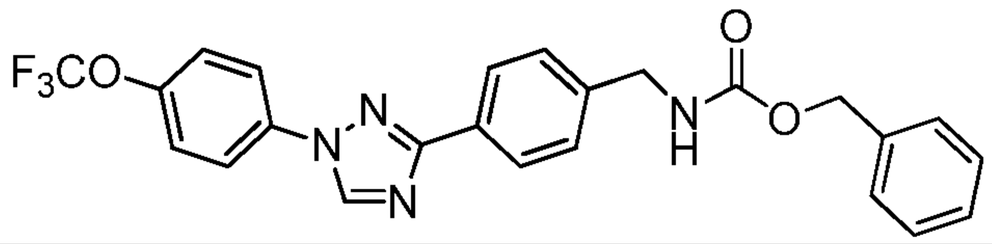
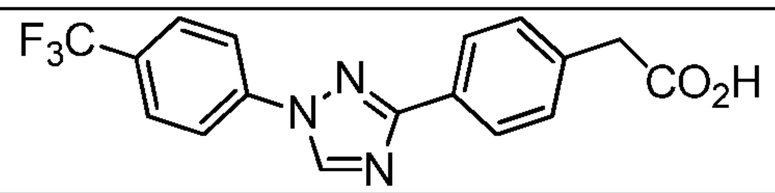
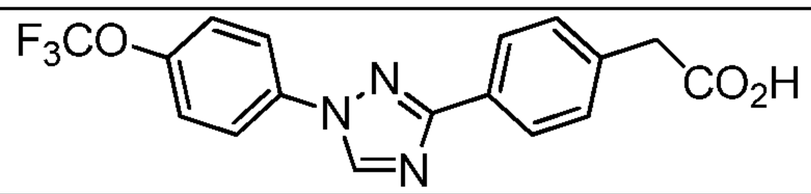
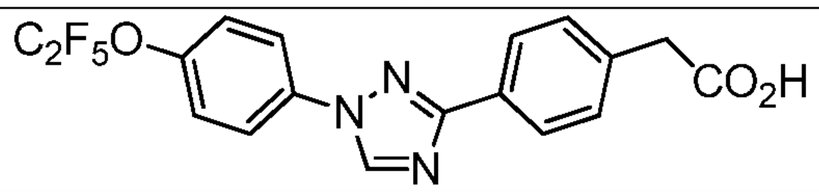
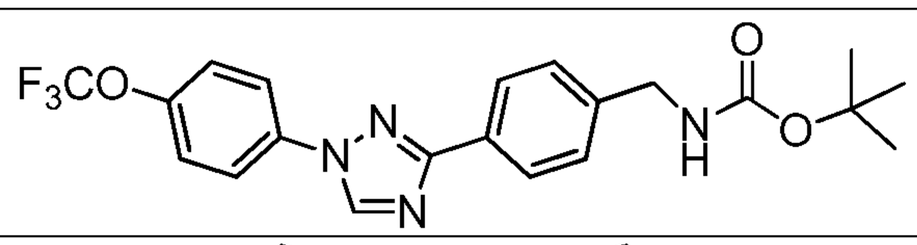
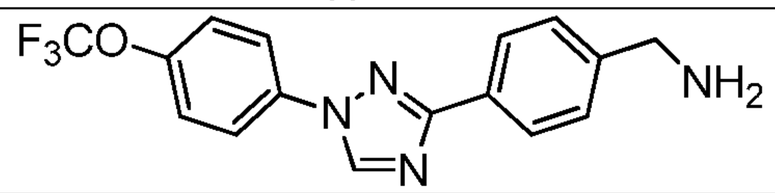
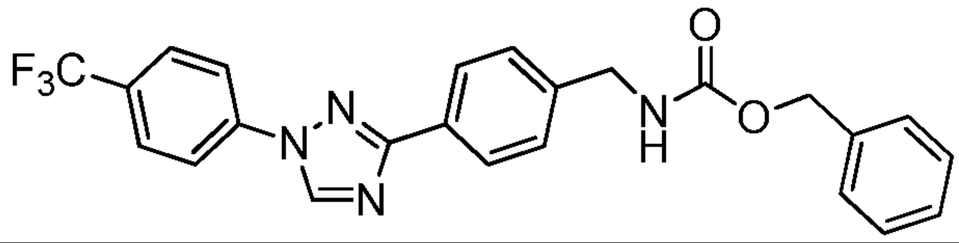
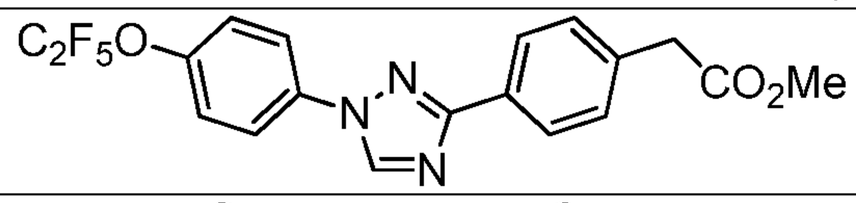
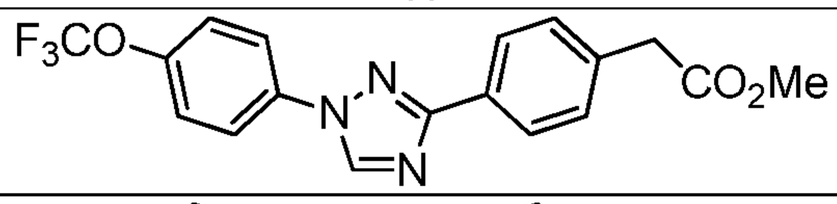
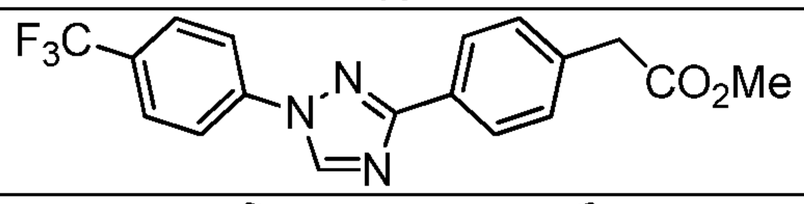
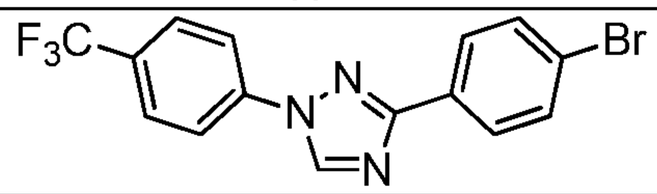
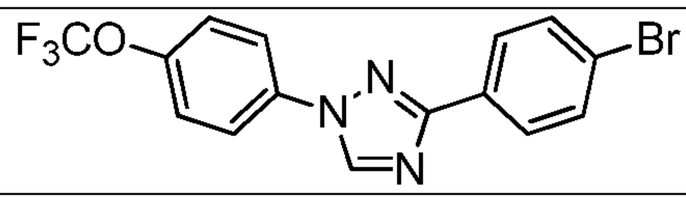
(e) one or more biopesticides.

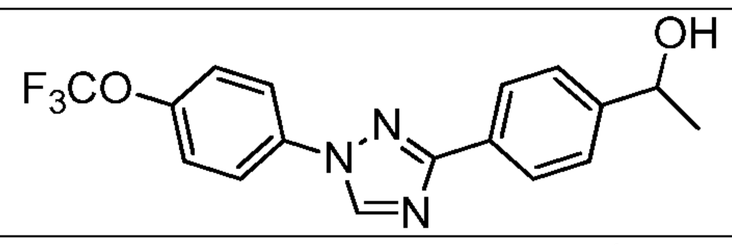
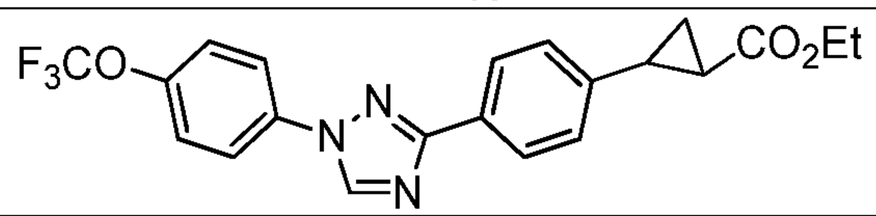
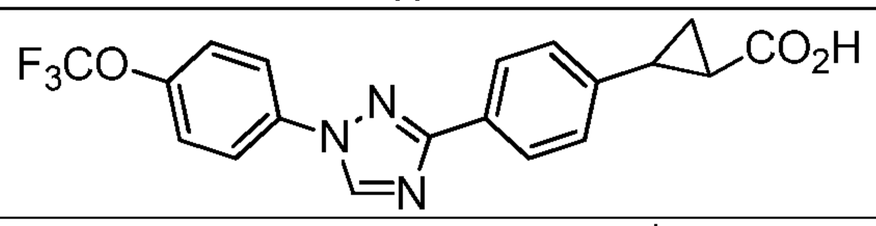
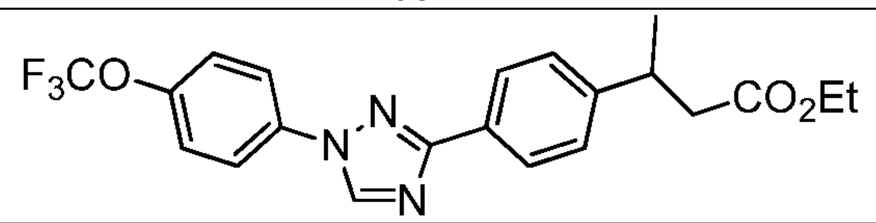
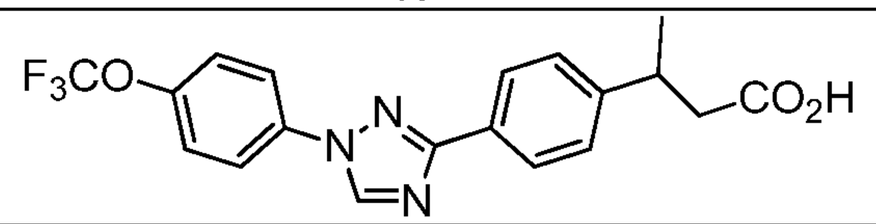
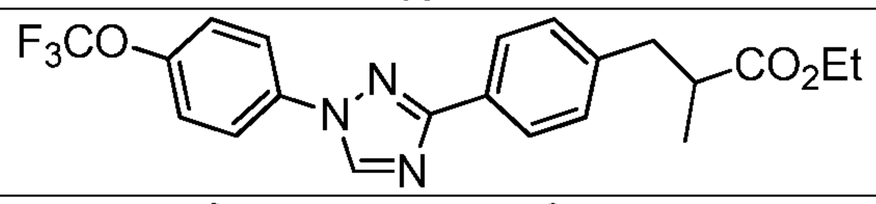
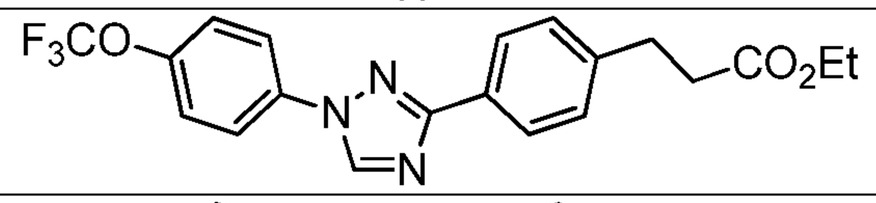
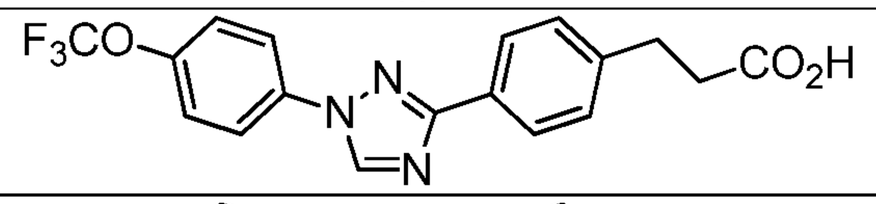
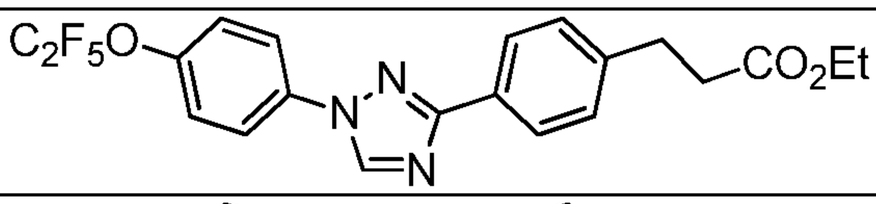
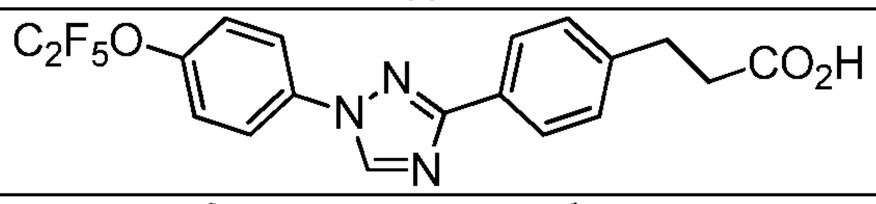
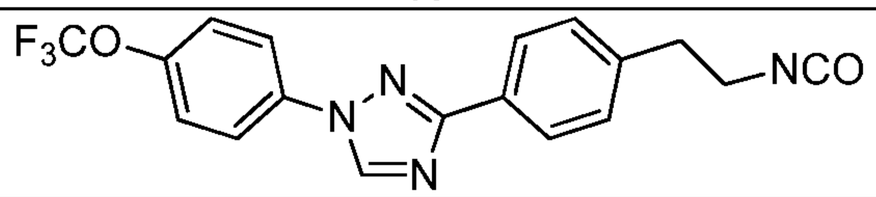
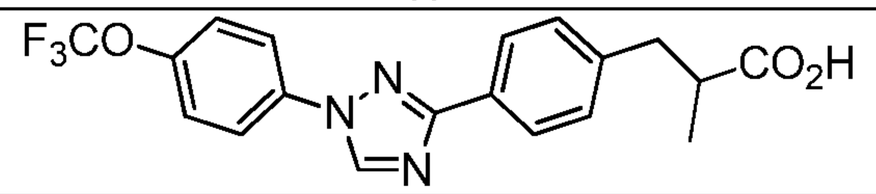
15. A composition comprising a seed and a molecule acccording to any of claims 1-13.

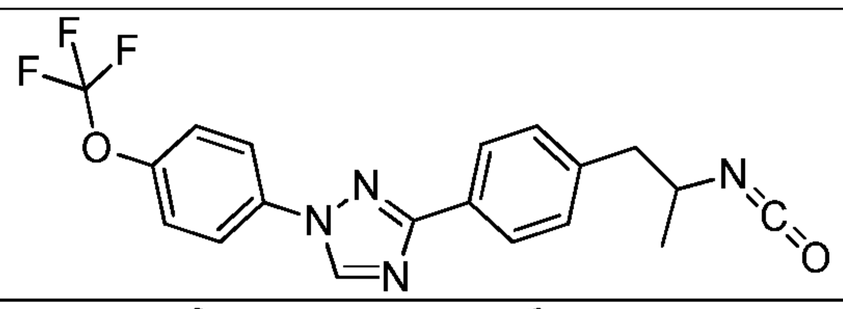
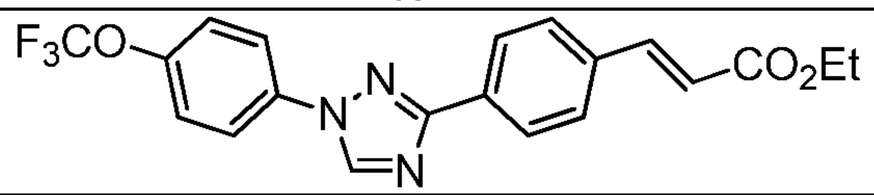
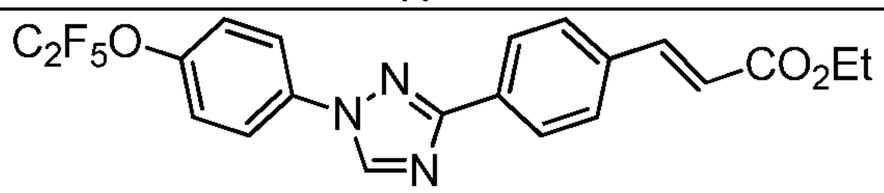
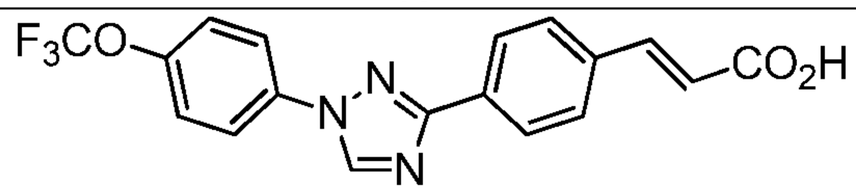
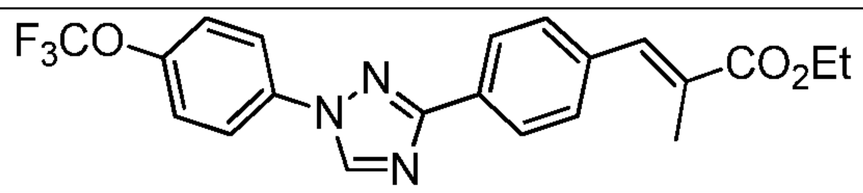
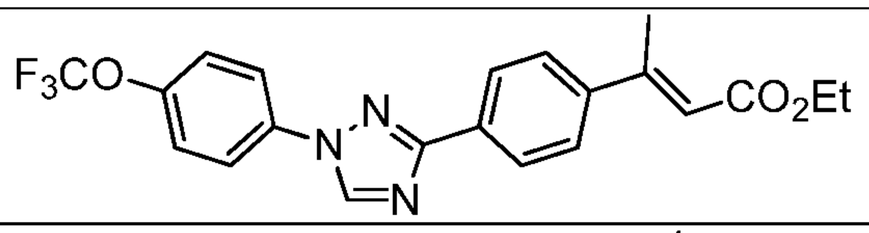
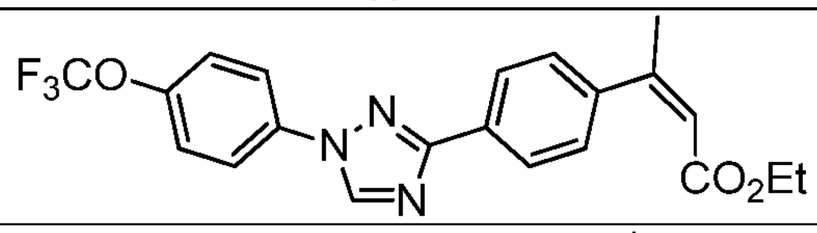
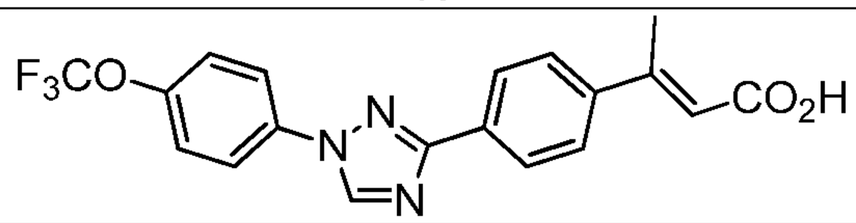
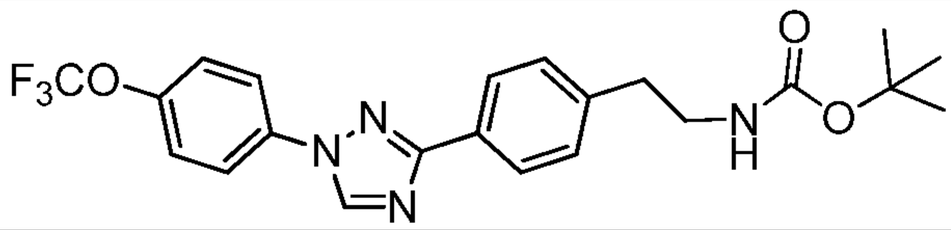
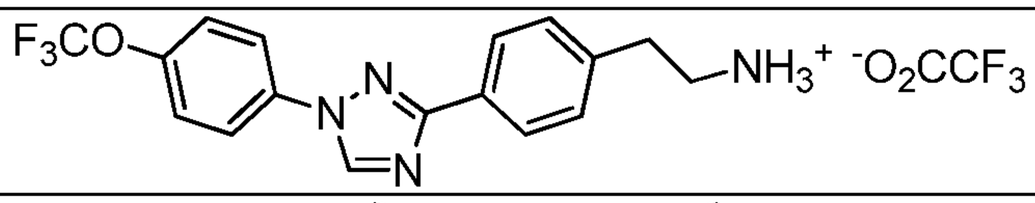
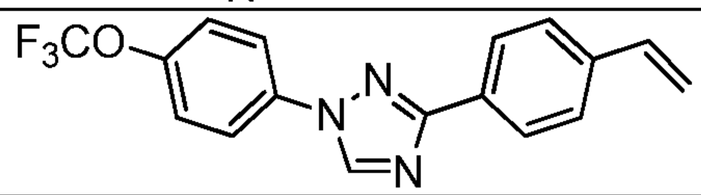
16. A process comprising: applying a molecule according to any of claims 1-13 to a locus to control a pest in an amount sufficient to control such pest.

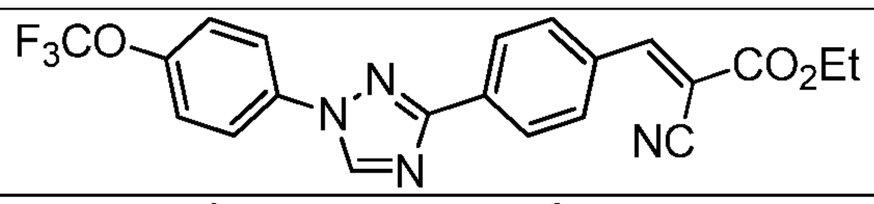
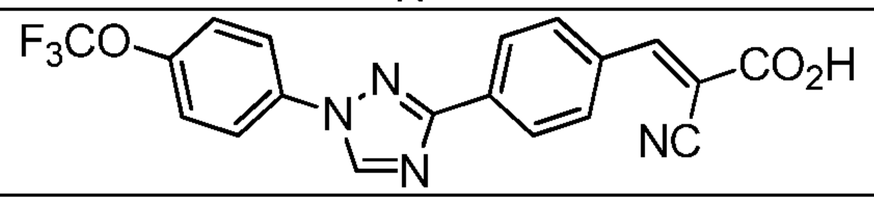
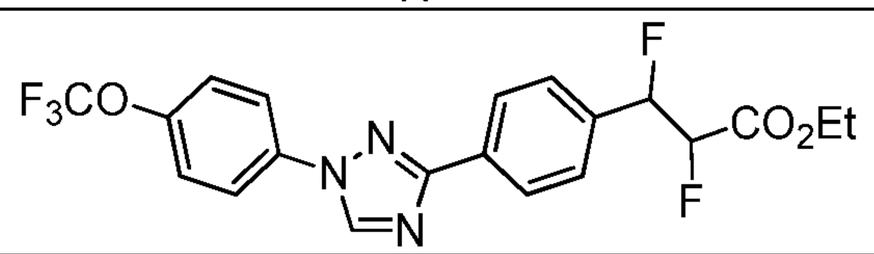
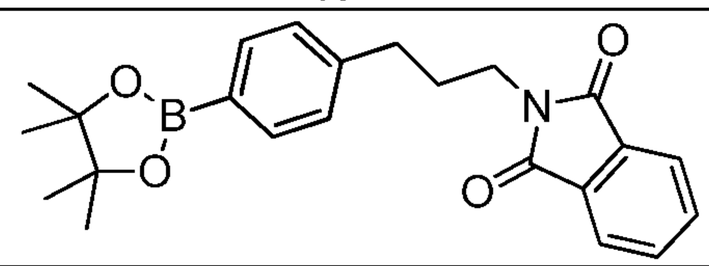
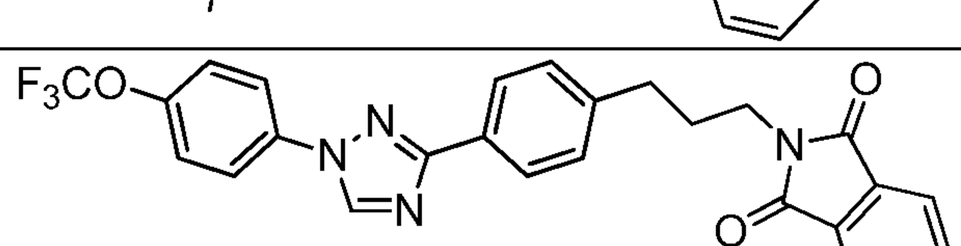
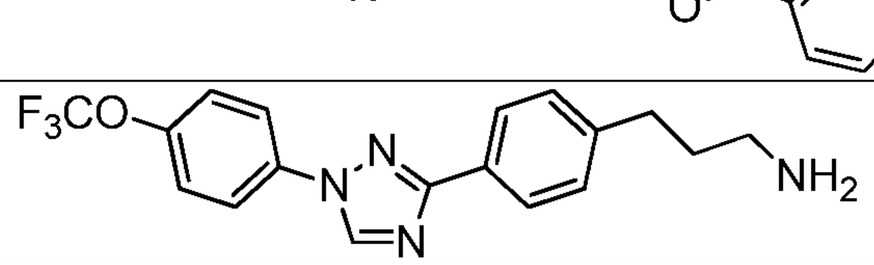
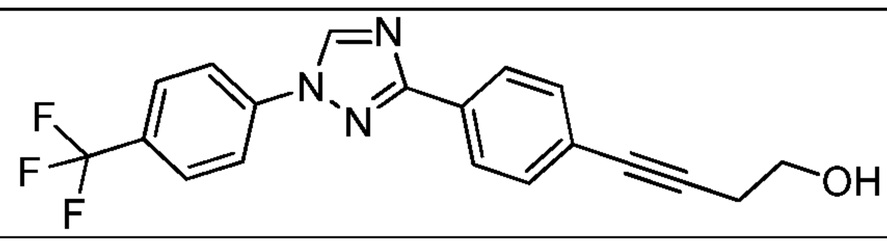
17. A intermediate having the following formula

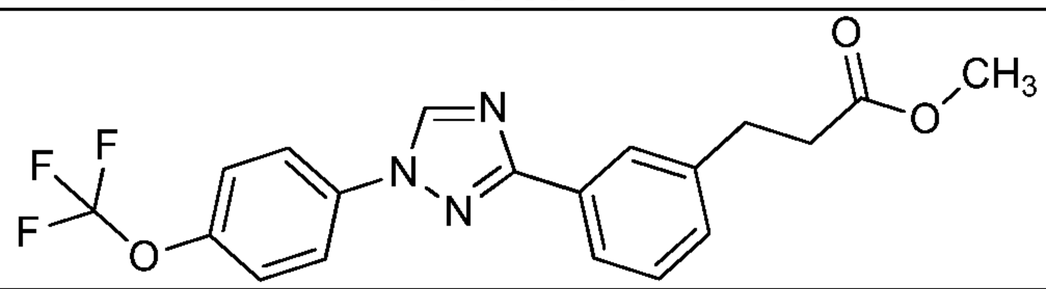
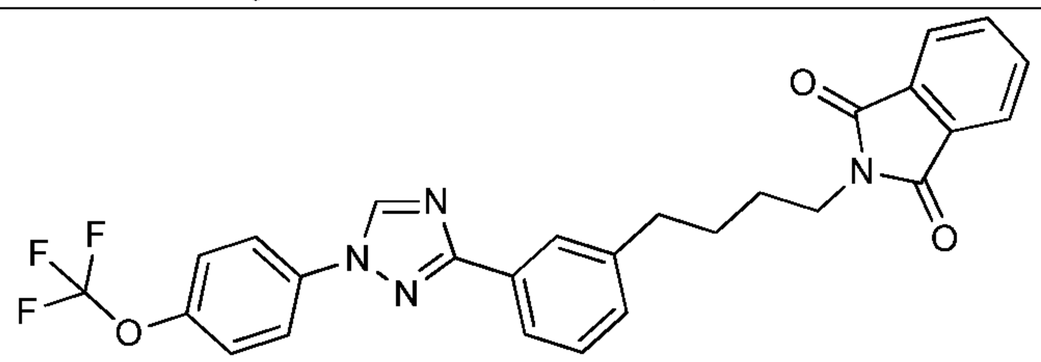
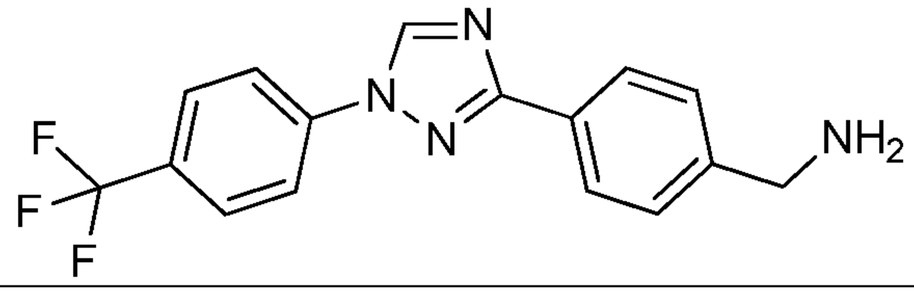
No.	Structure
C13	

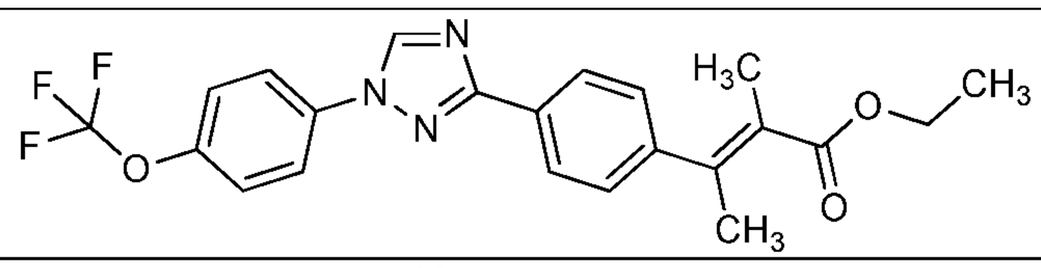
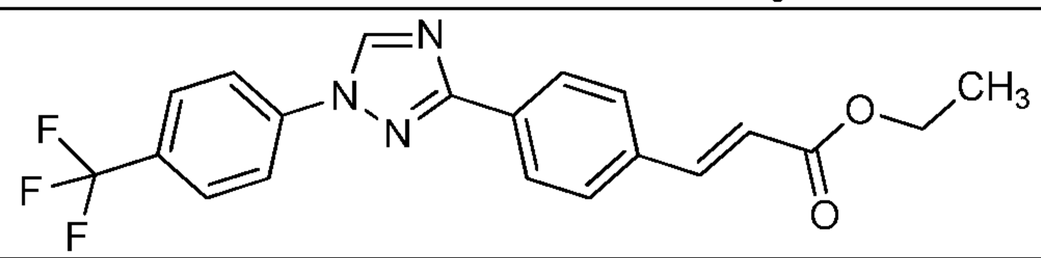
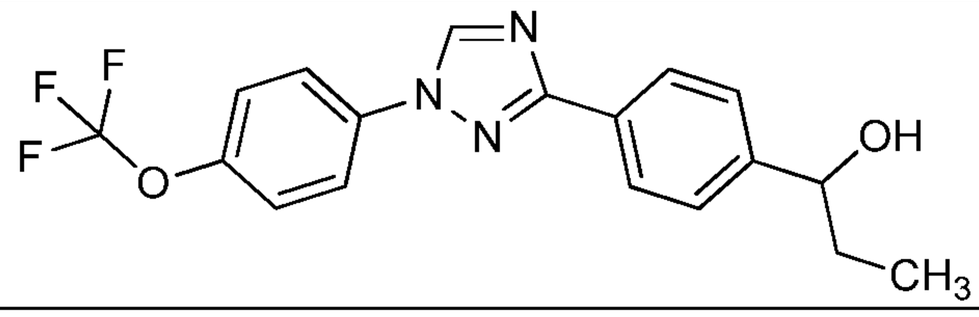
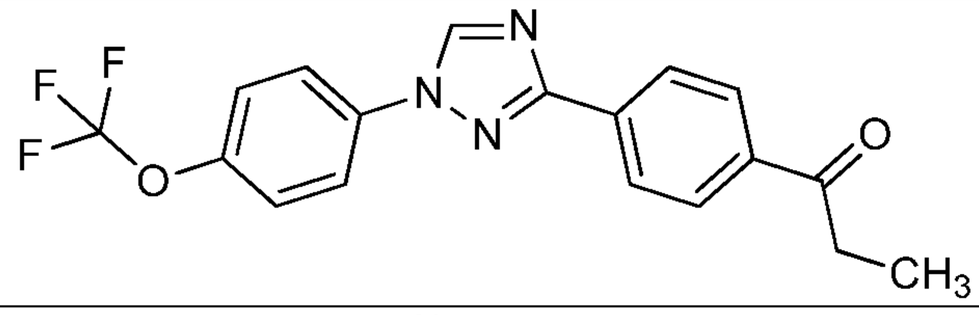
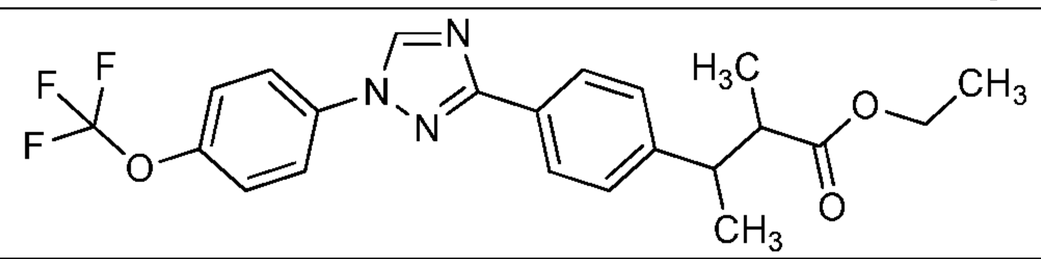
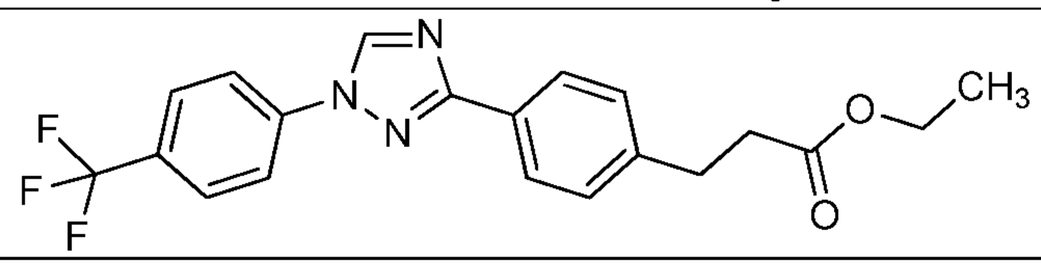
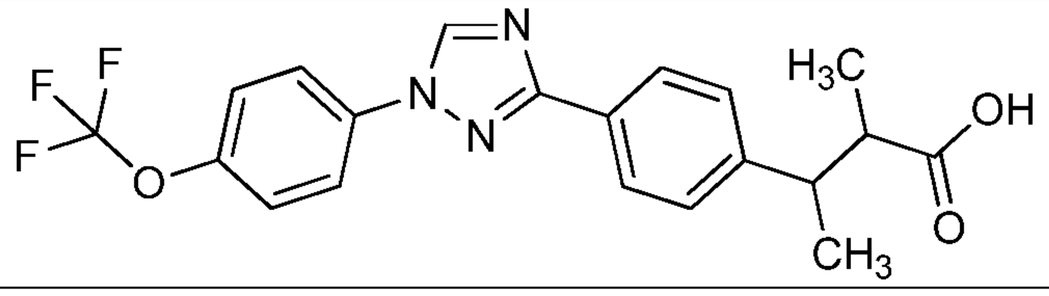
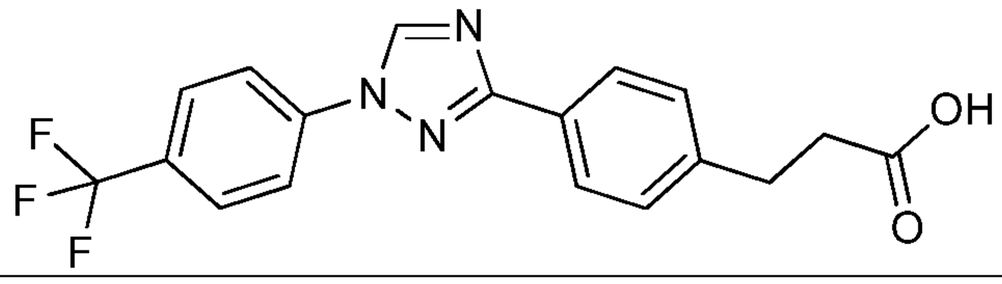
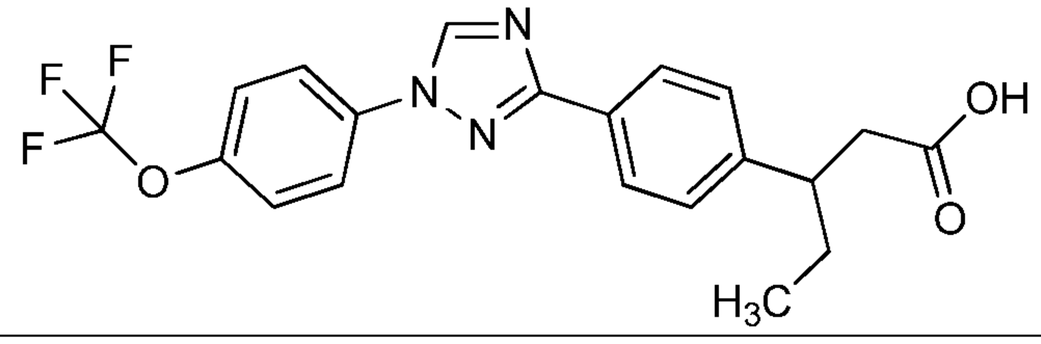
C1b	
C14	
C8	
C6	
C7	
C15a	
C16	
C15	
C4	
C3	
C5	
C53	
C52	

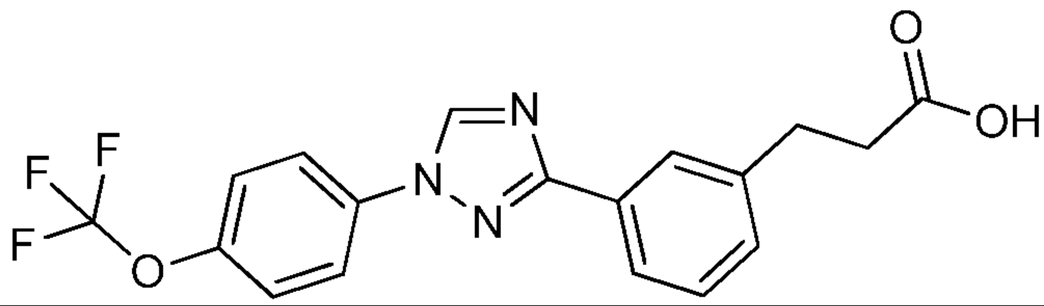
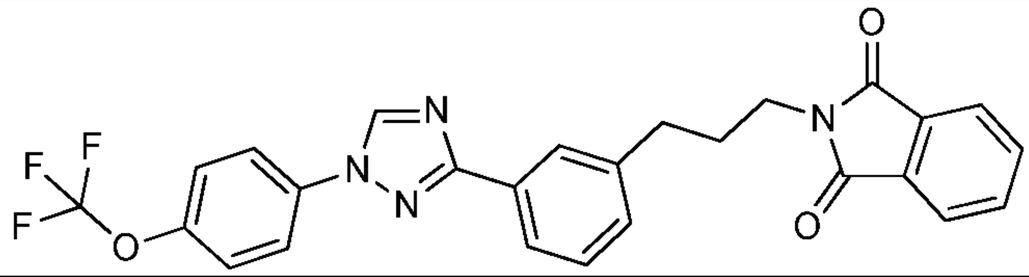
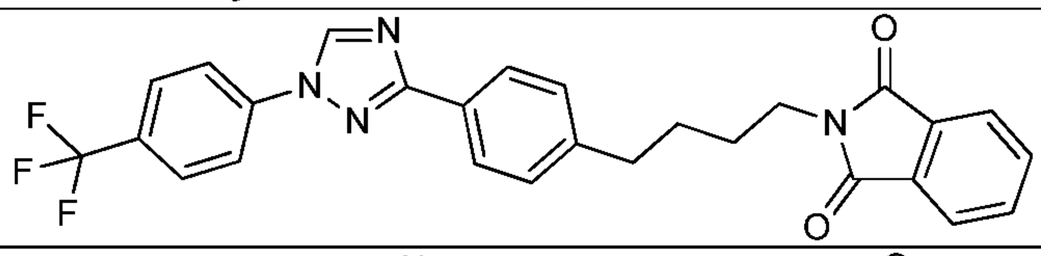
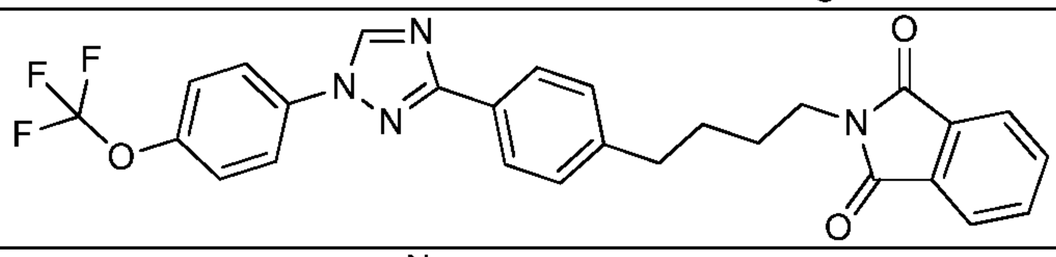
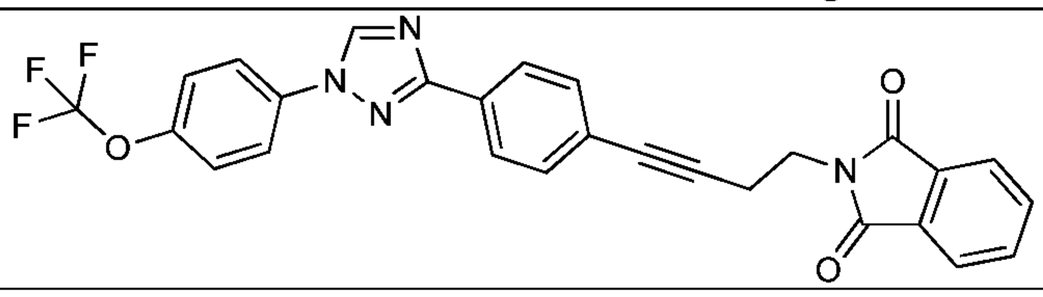
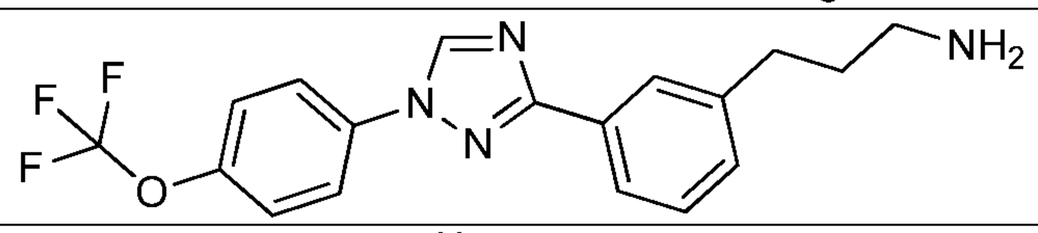
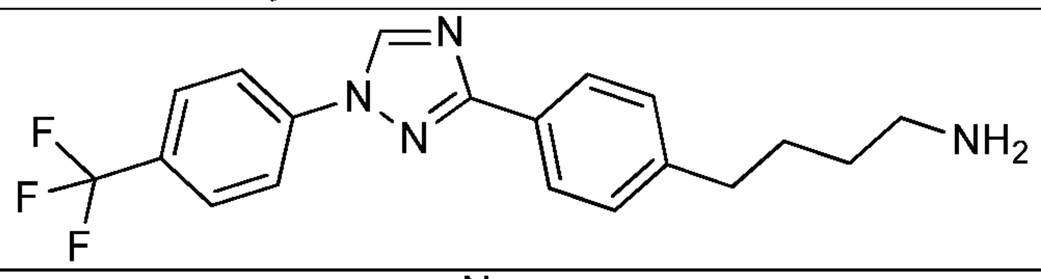
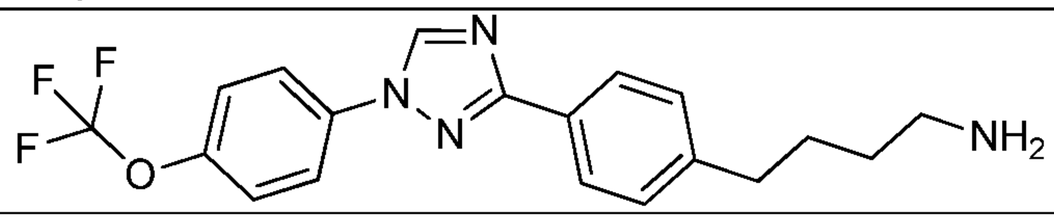
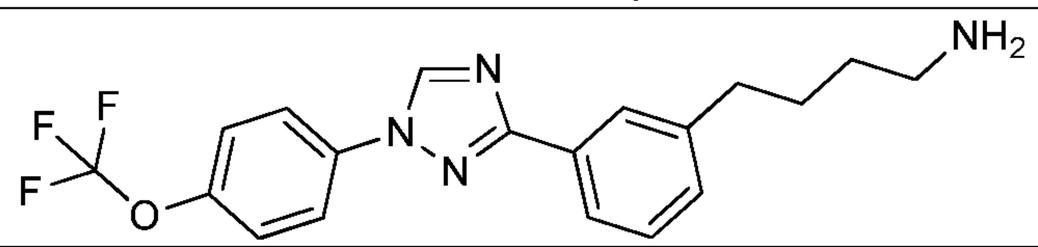
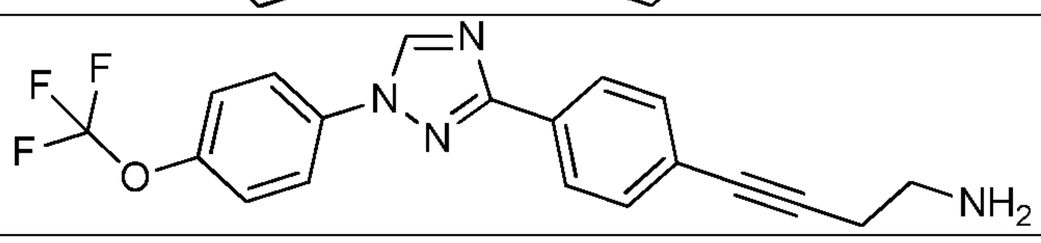
C24	
C19	
C20	
C40	
C41	
C37	
C30	
C32	
C31	
C33	
C34a	
C38	

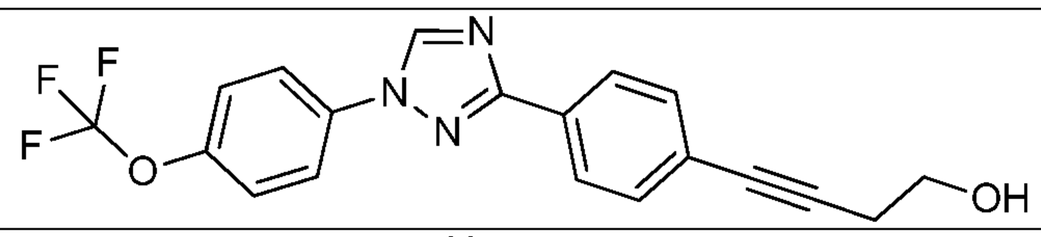
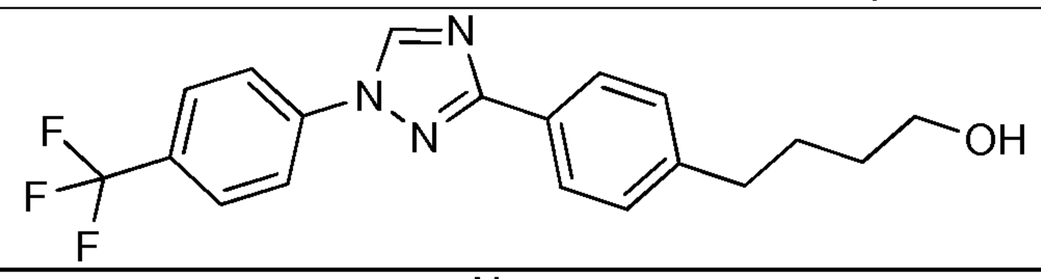
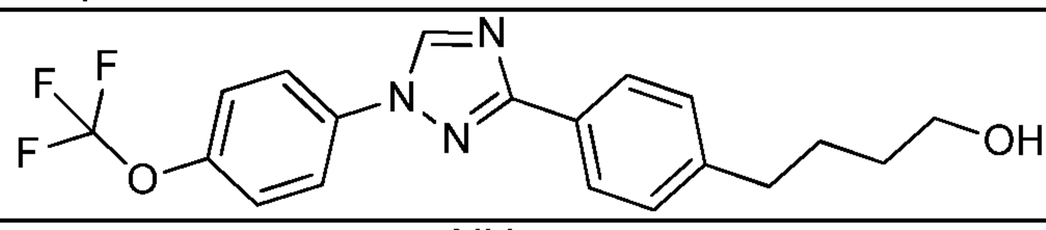
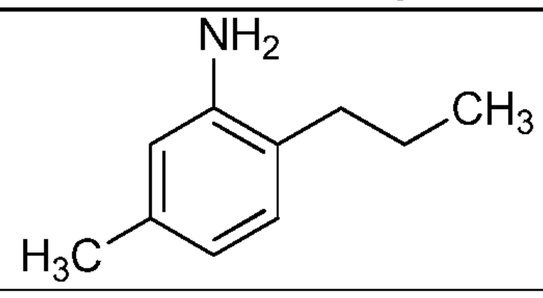
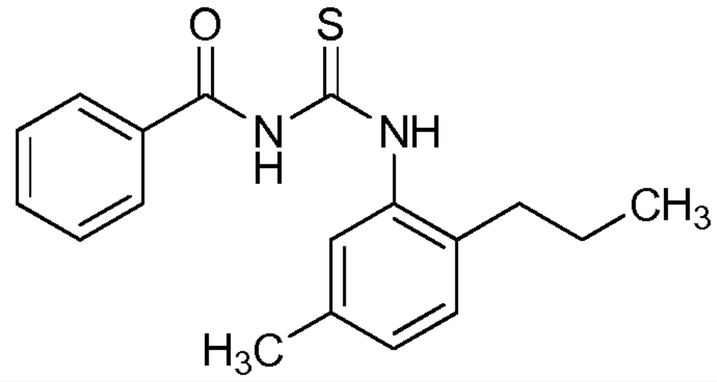
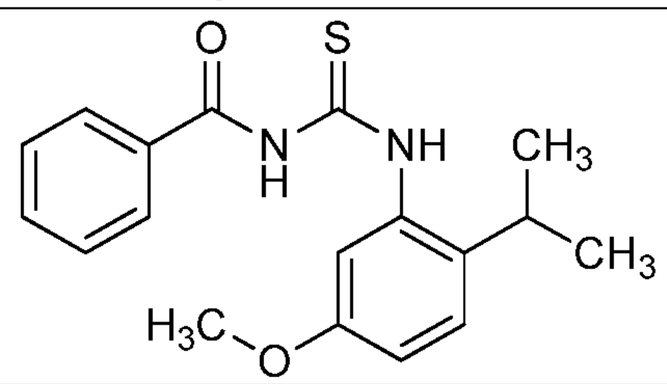
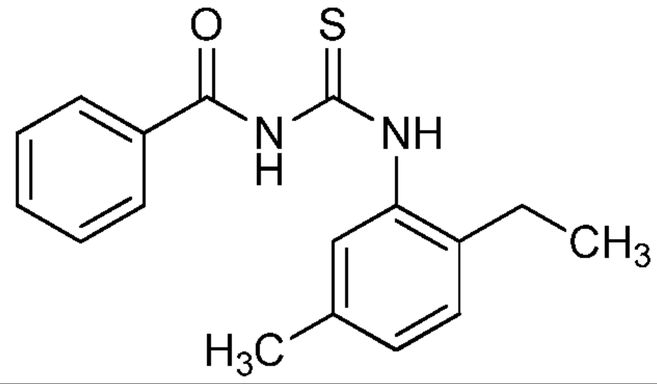
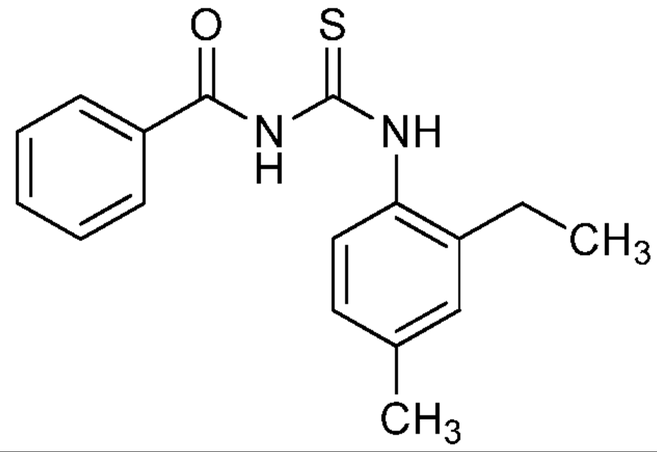
C39	
C17	
C18	
C22	
C36	
C26	
C27	
C28	
C50	
C55	
C43	
C44	

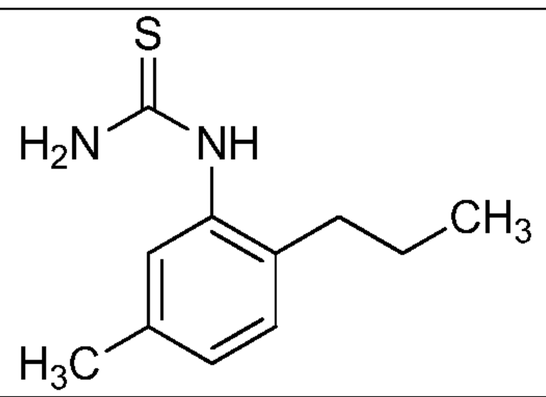
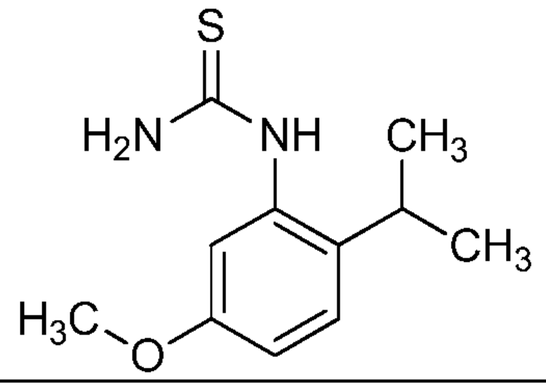
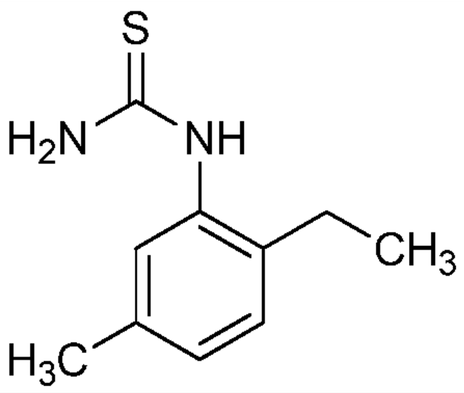
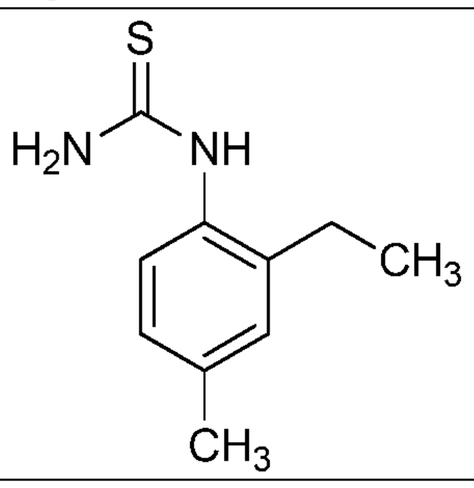
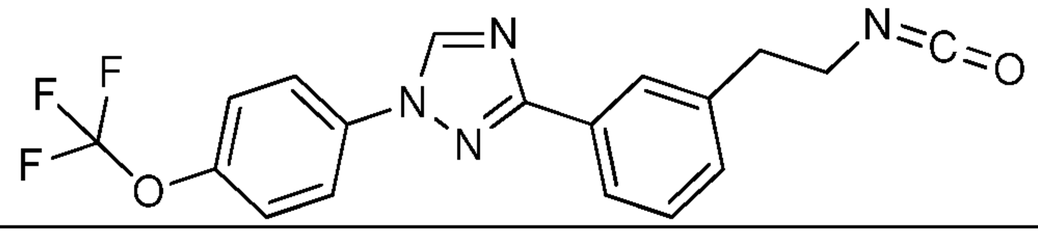
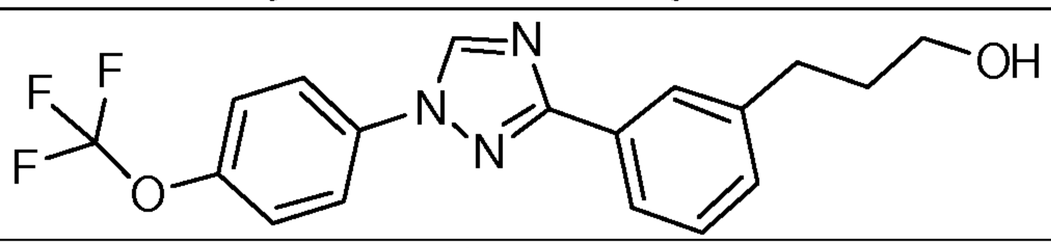
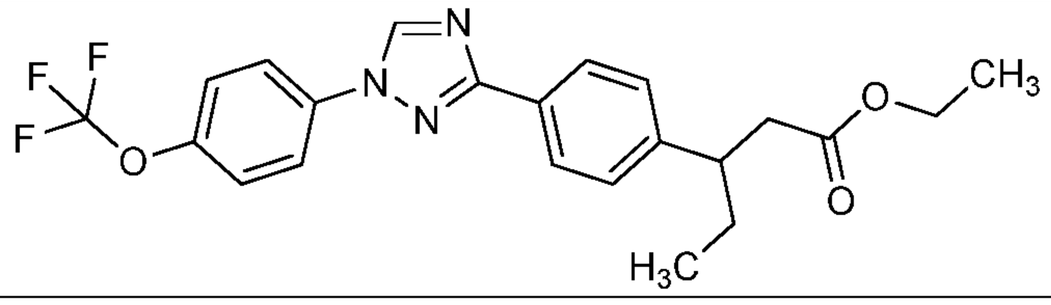
C46	
C47	
C45	
C58	
C59	
C60	
C61	

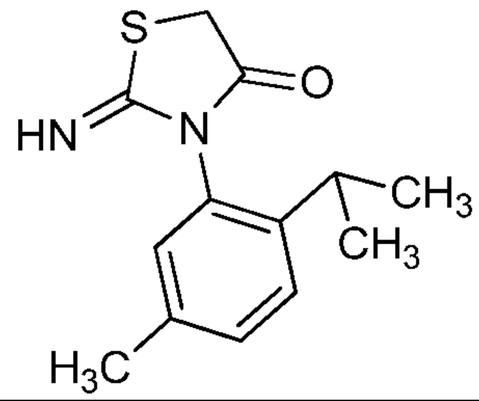
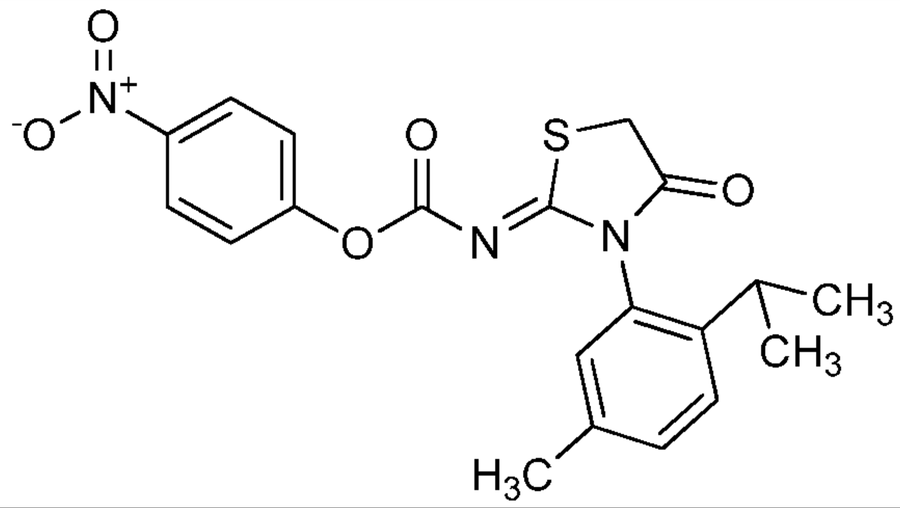
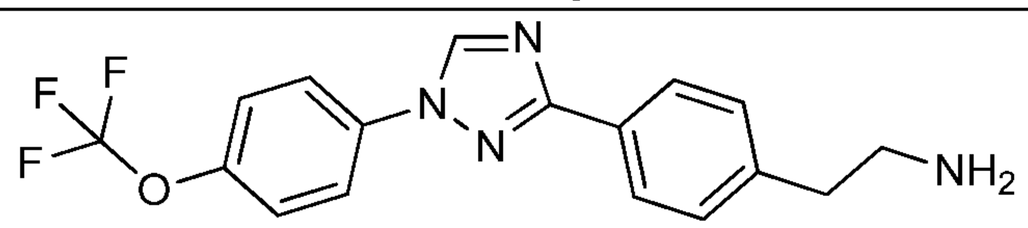
No.	Structure
CA1	
CA2	
CA3	

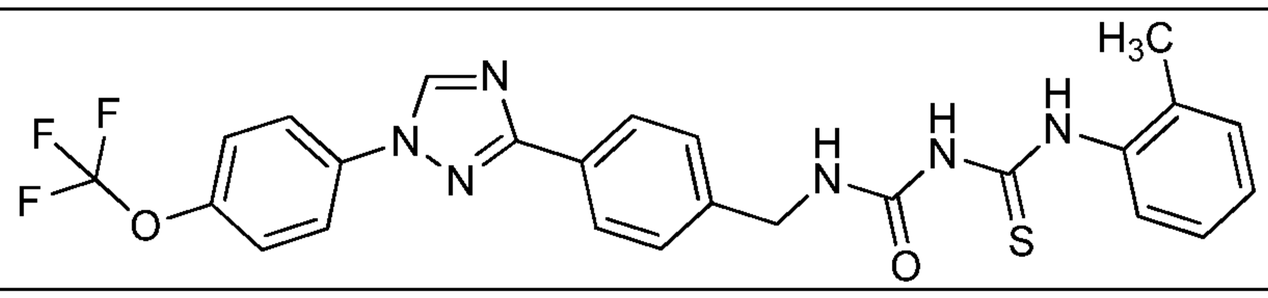
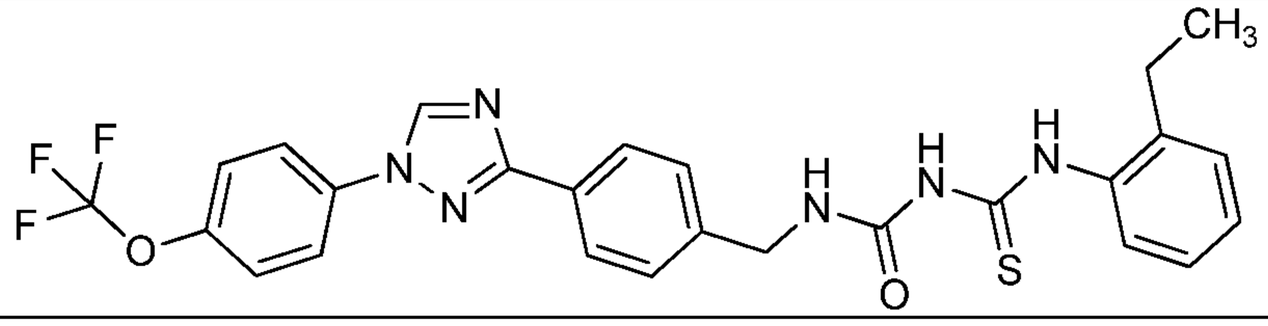
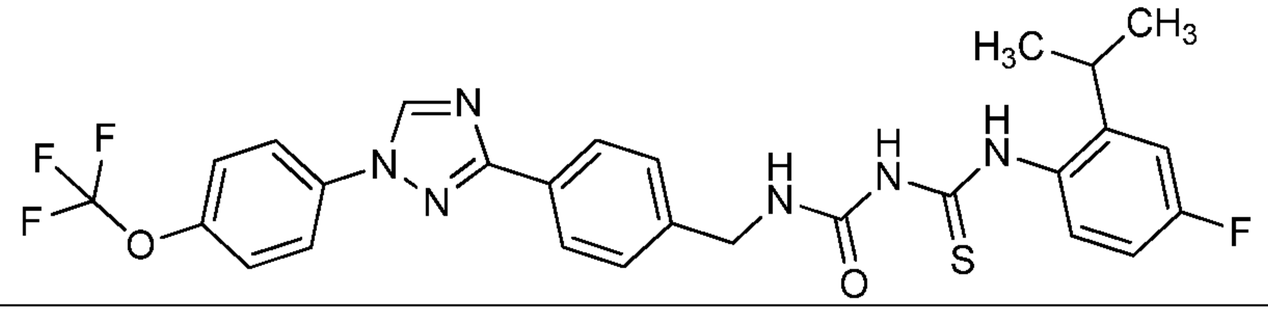
CA4	
CA5	
CA6	
CA7	
CA8	
CA9	
CA10	
CA11	
CA12	

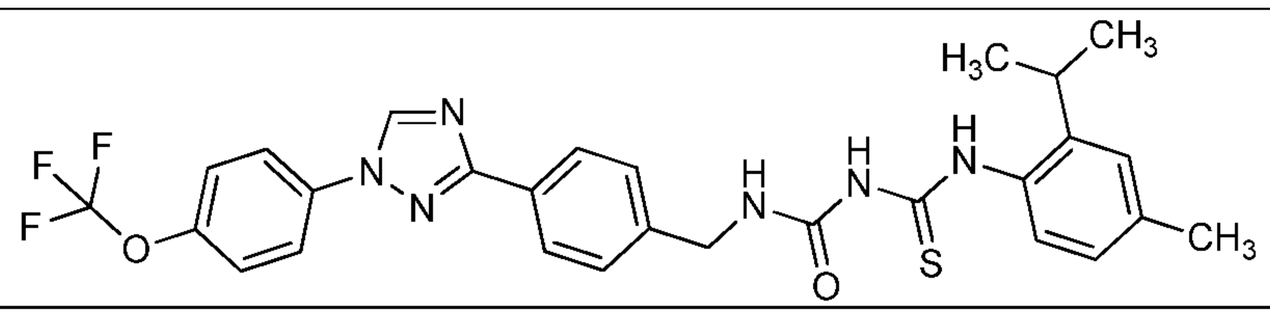
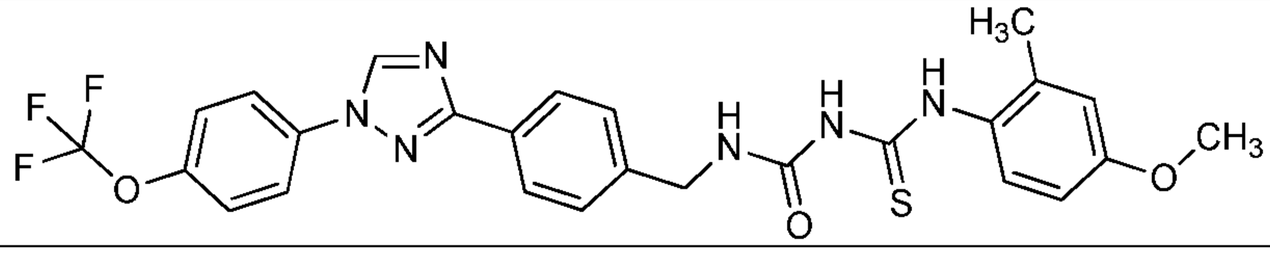
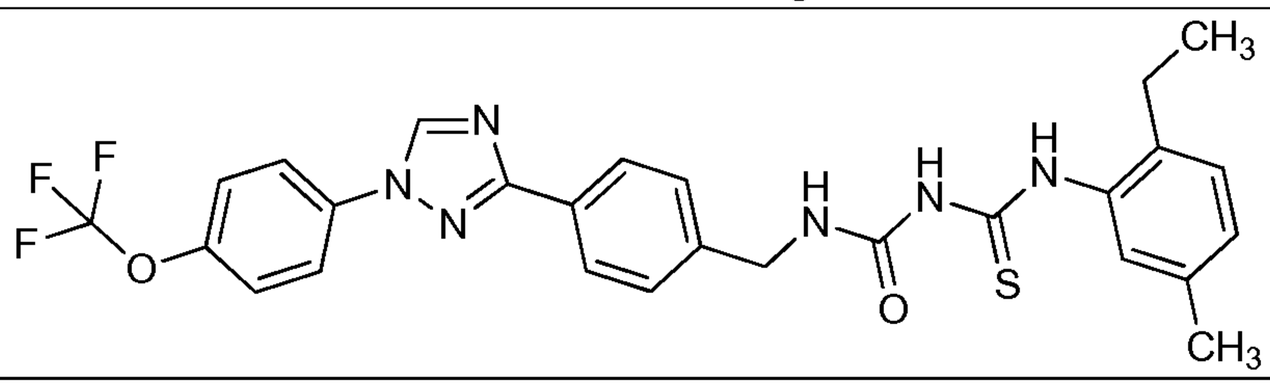
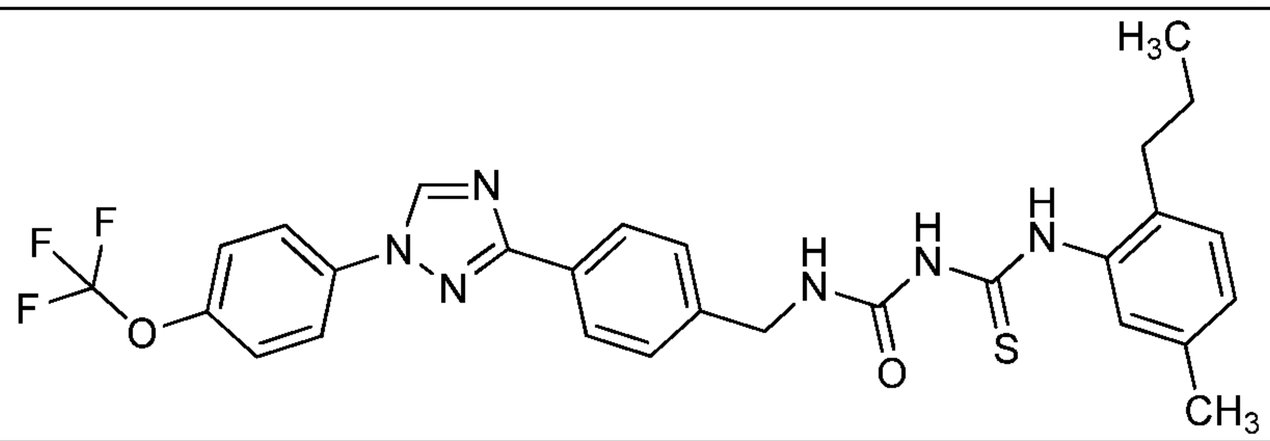
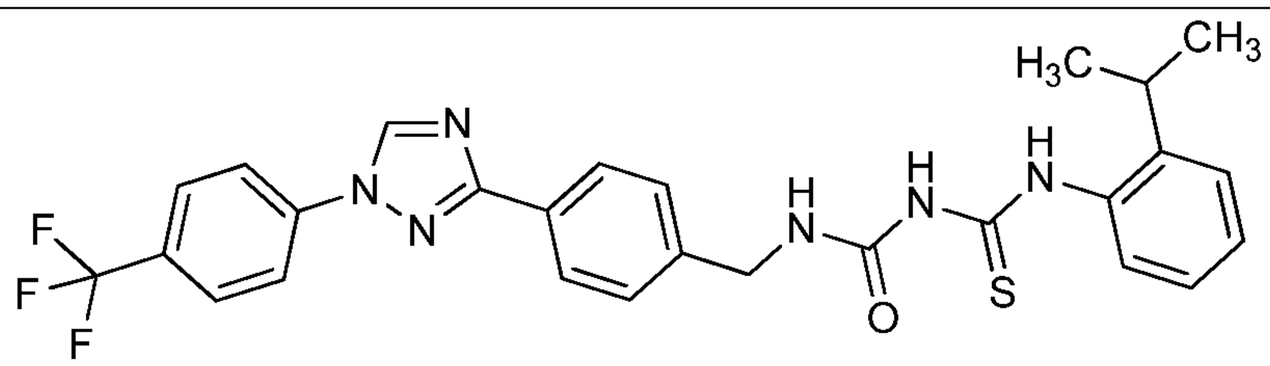
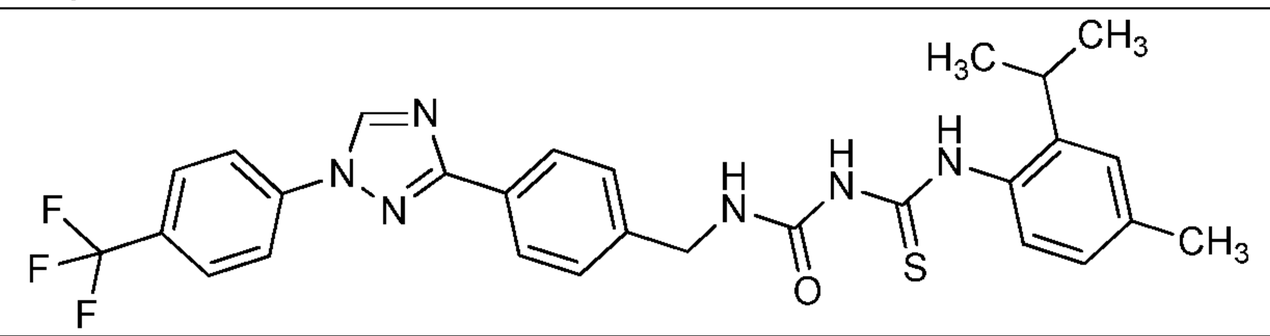
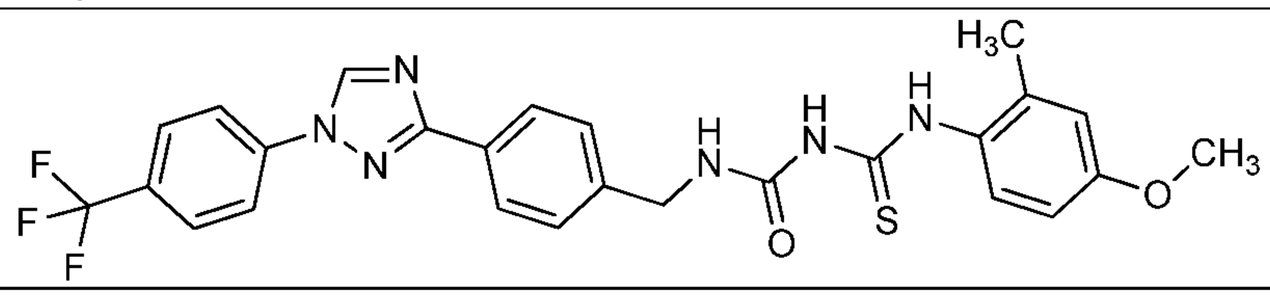
CA13	
CA14	
CA15	
CA16	
CA17	
CA18	
CA19	
CA20	
CA21	
CA22	

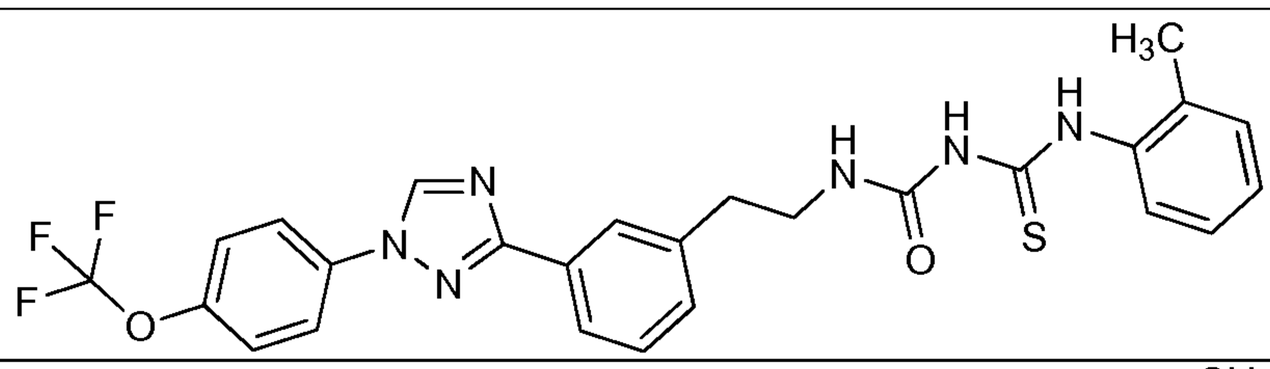
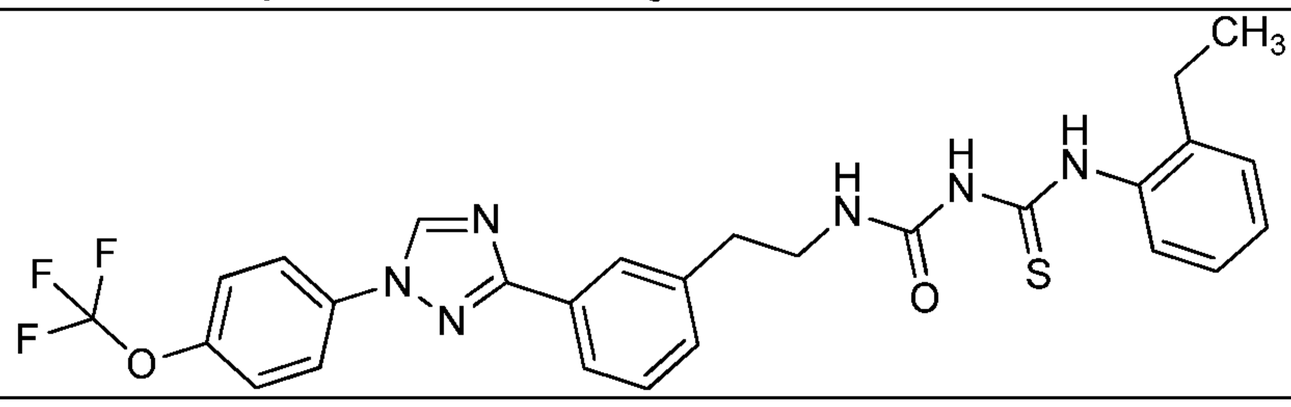
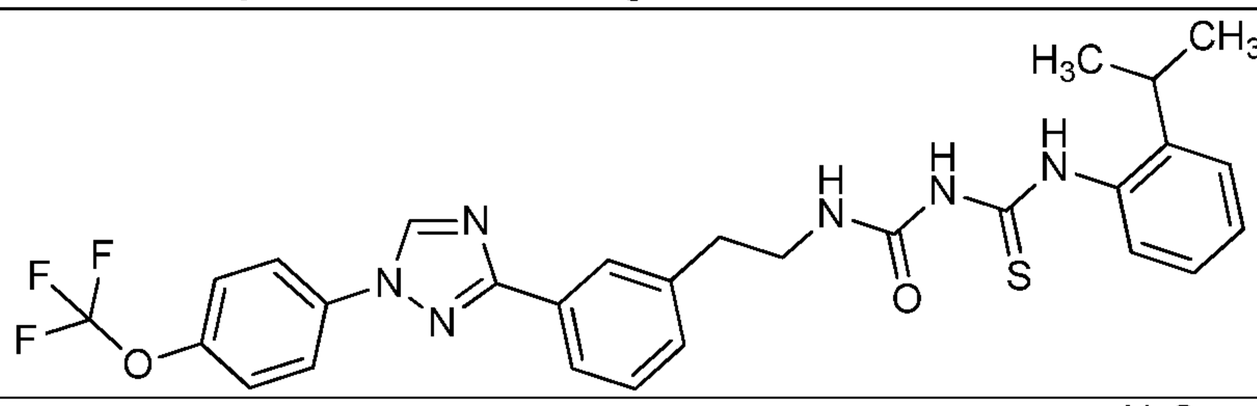
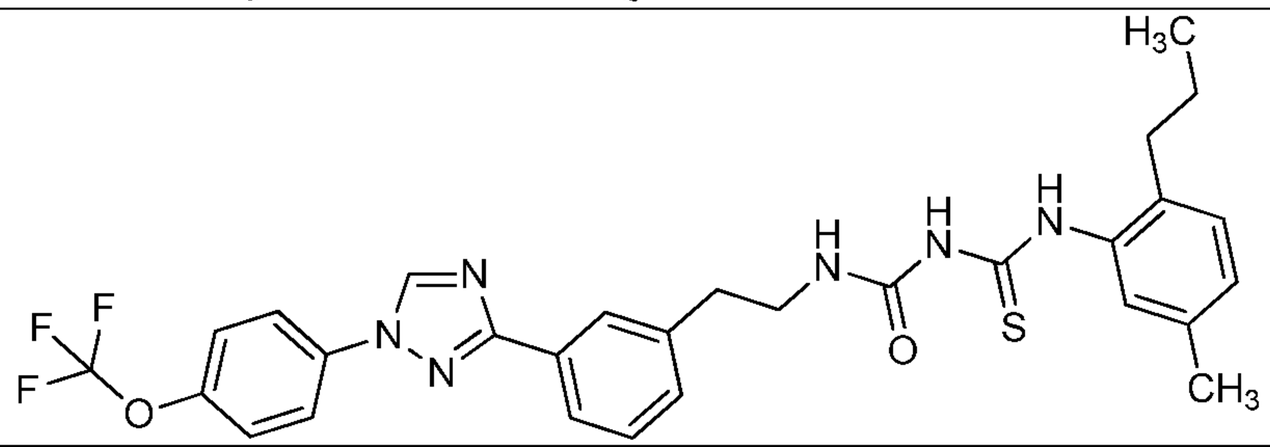
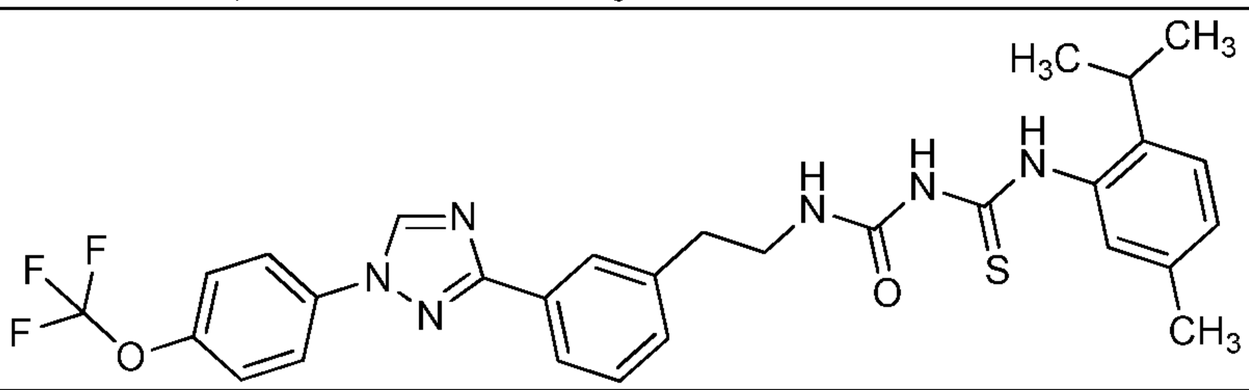
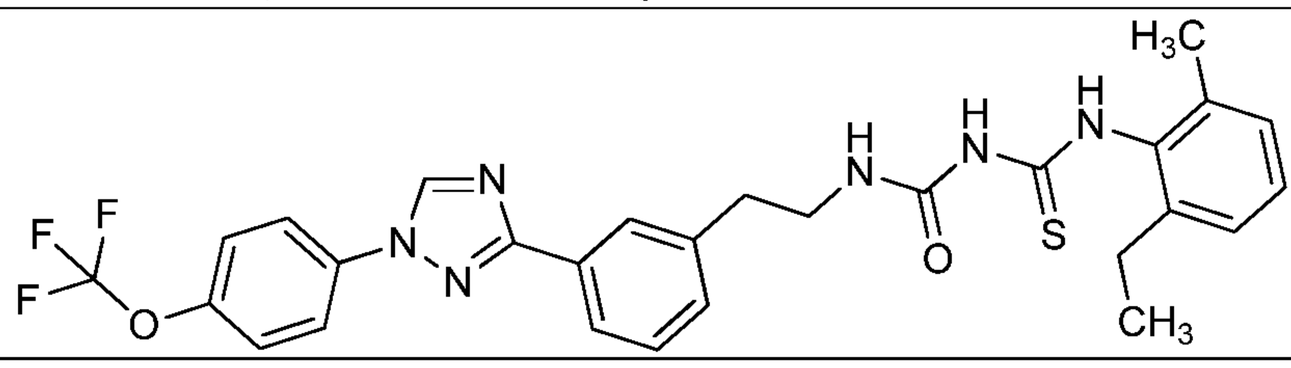
CA23	
CA24	
CA25	
CA26	
CA33	
CA35	
CA36	
CA37	

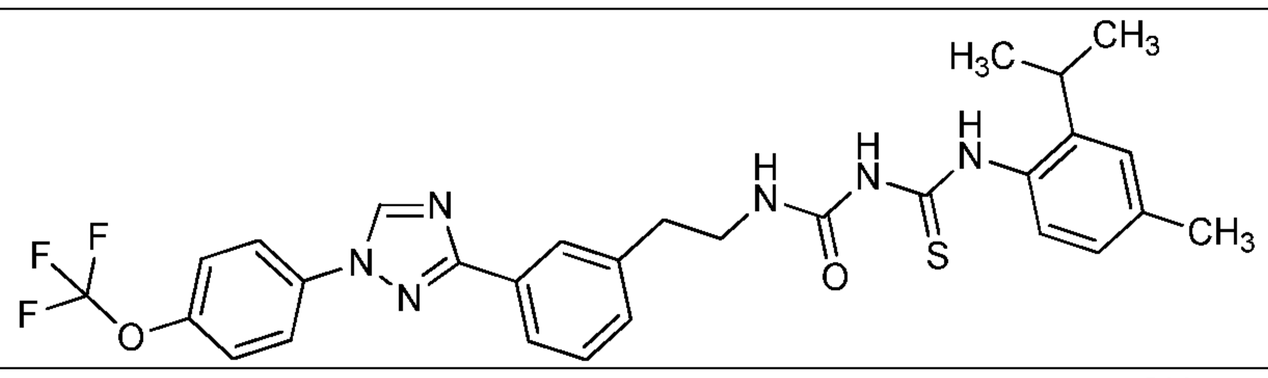
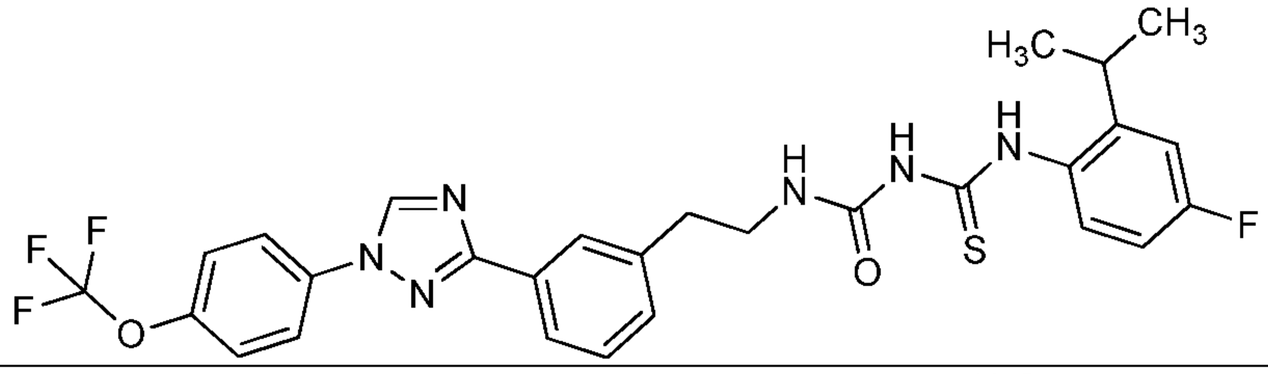
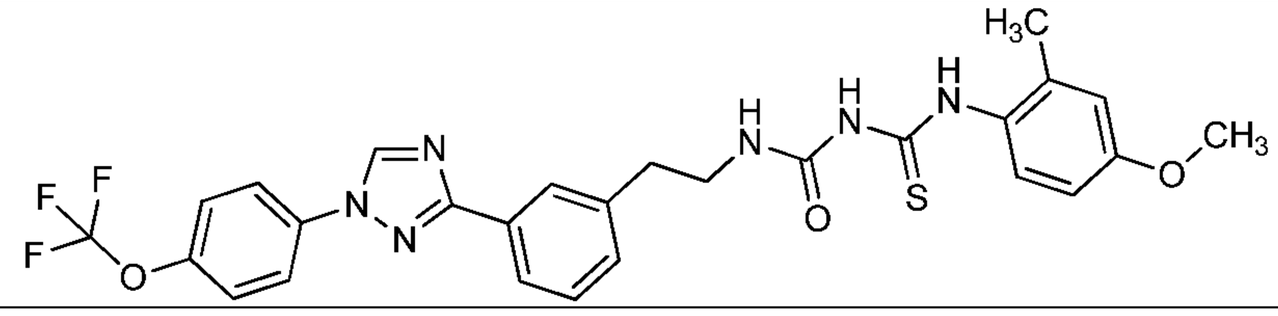
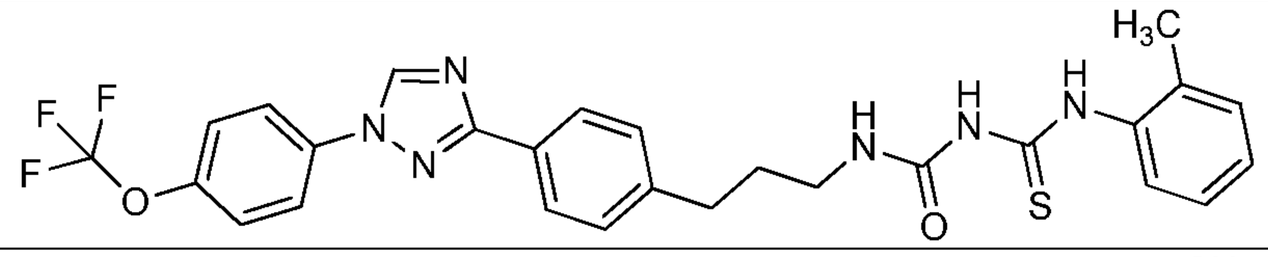
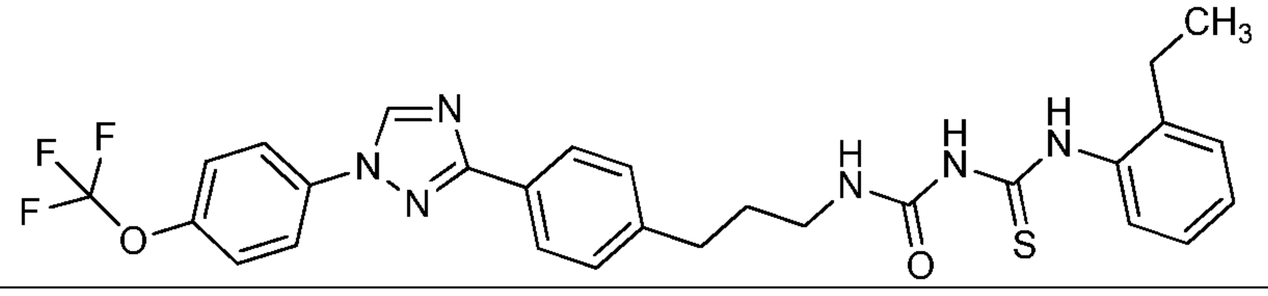
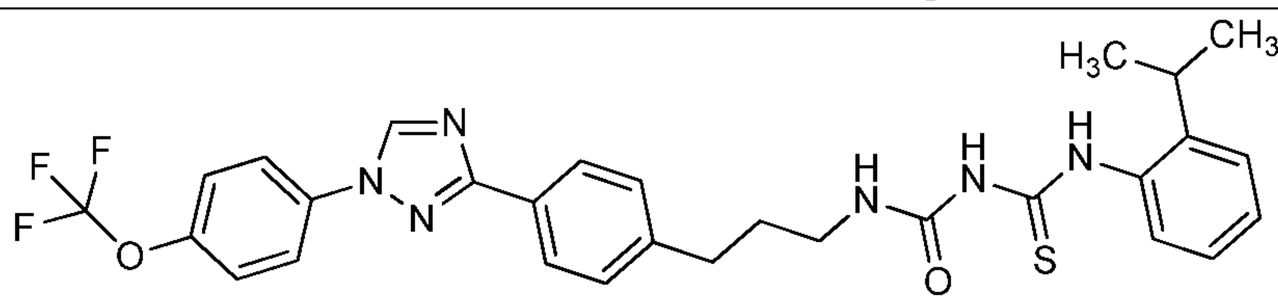
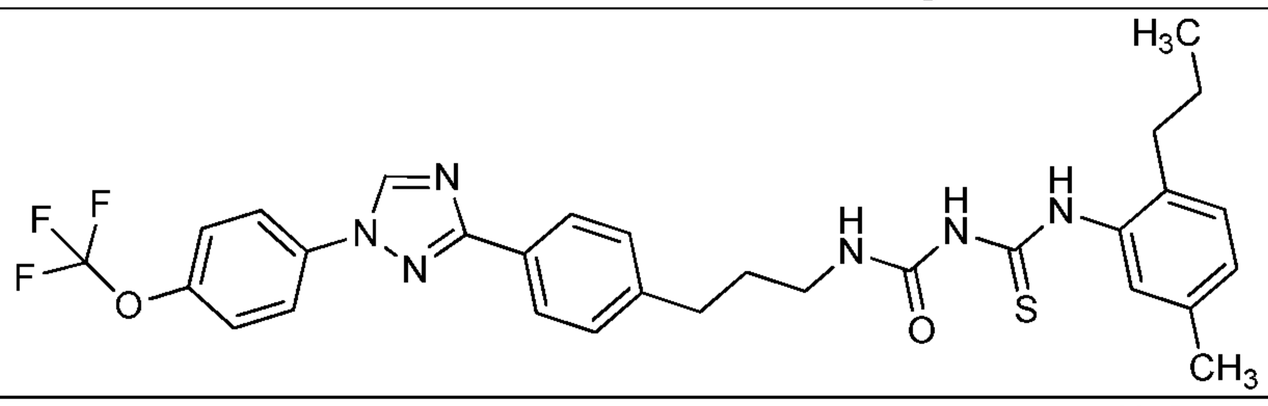
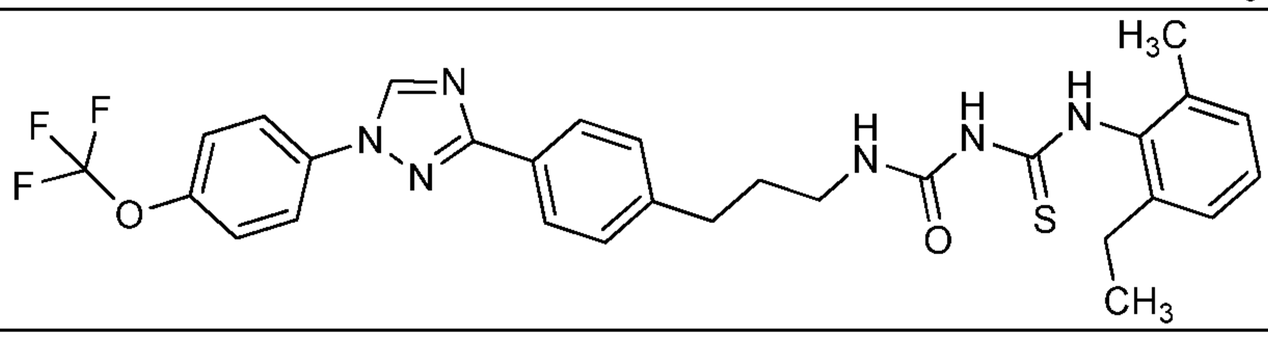
CA38	
CA40	
CA41	
CA42	
CA44	
CA45	
CA48	

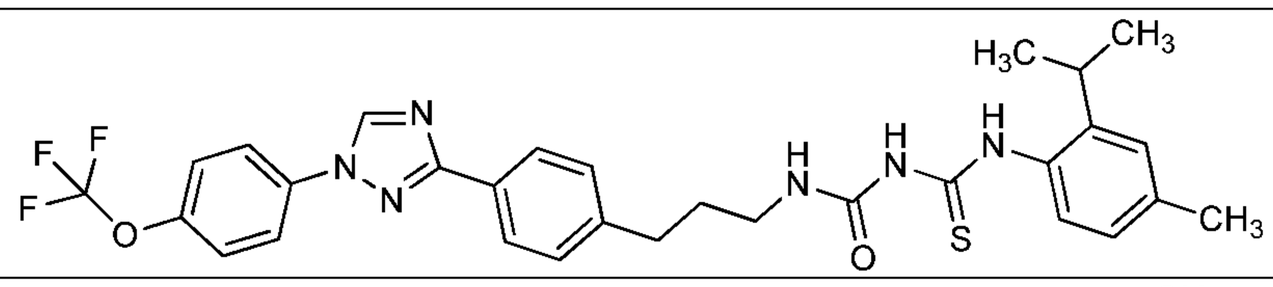
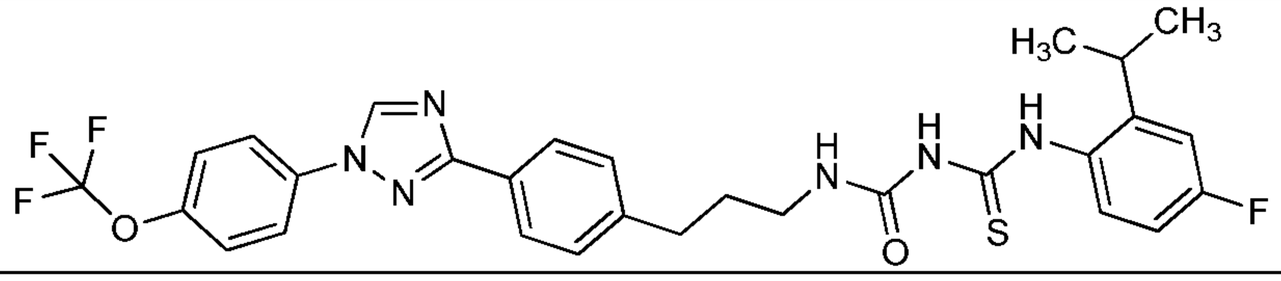
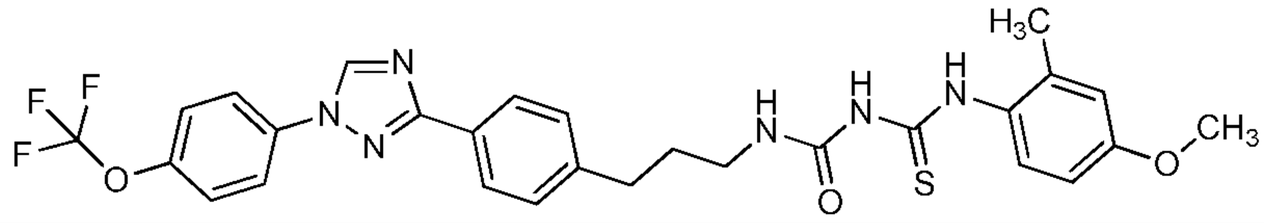
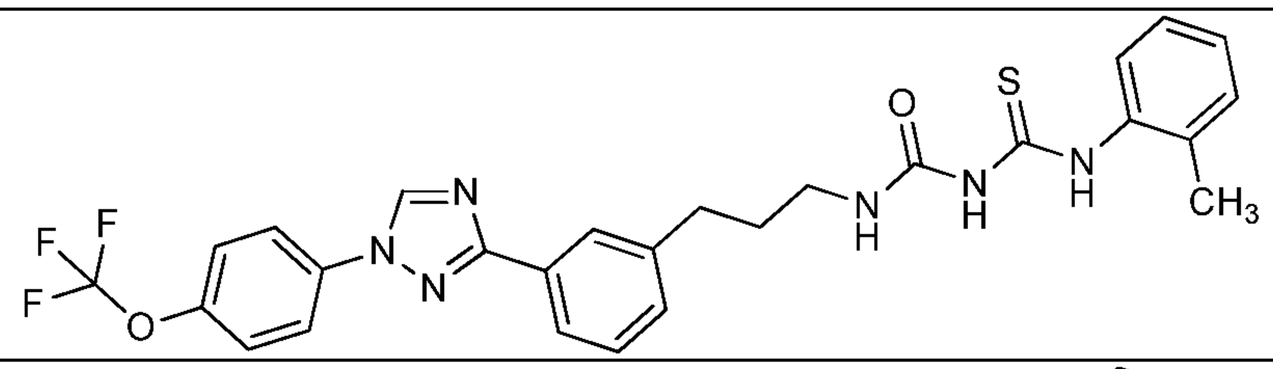
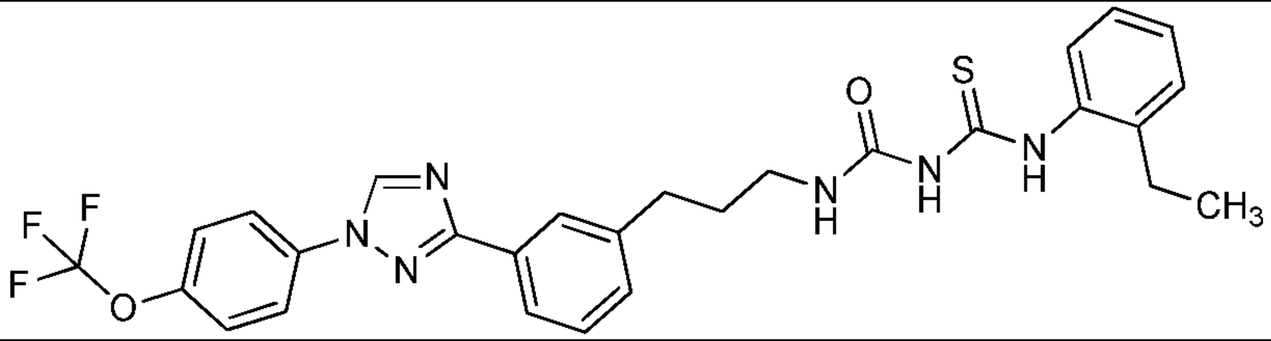
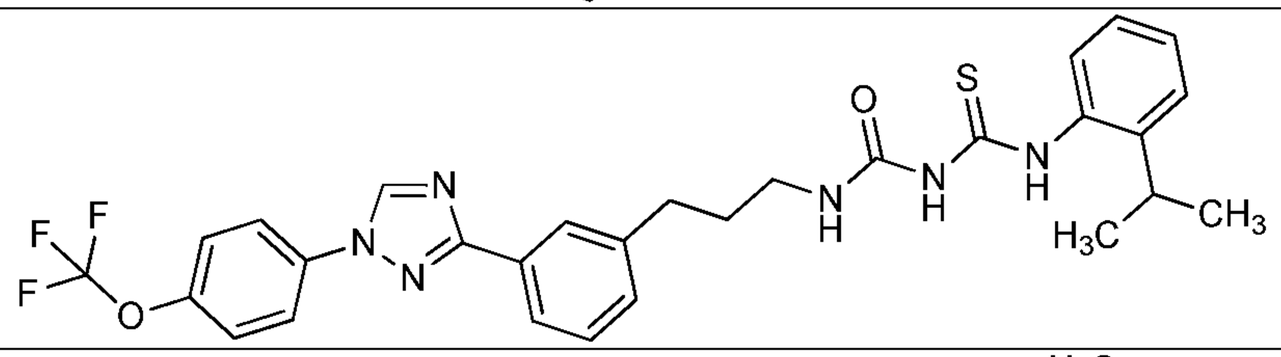
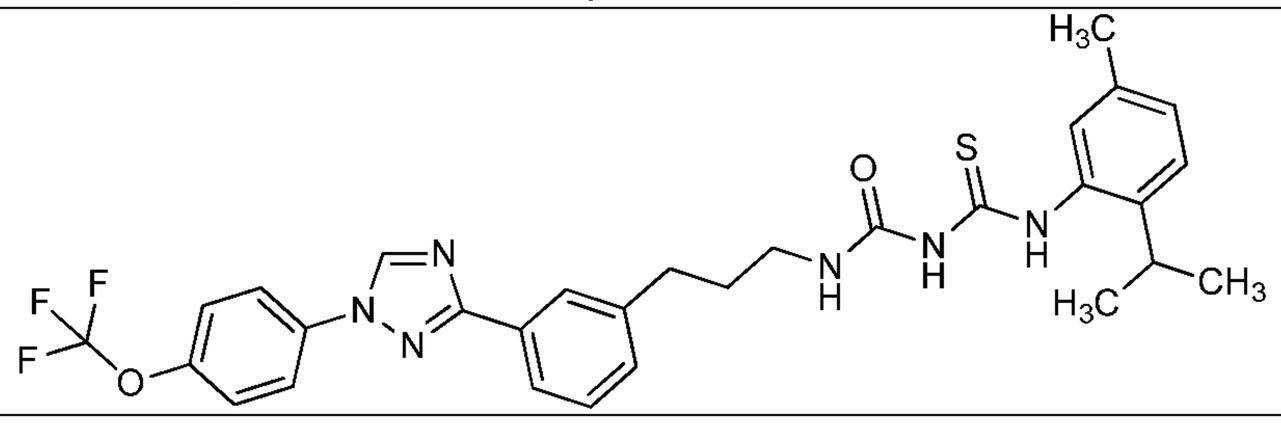
CA49	
CA50	
CA51	

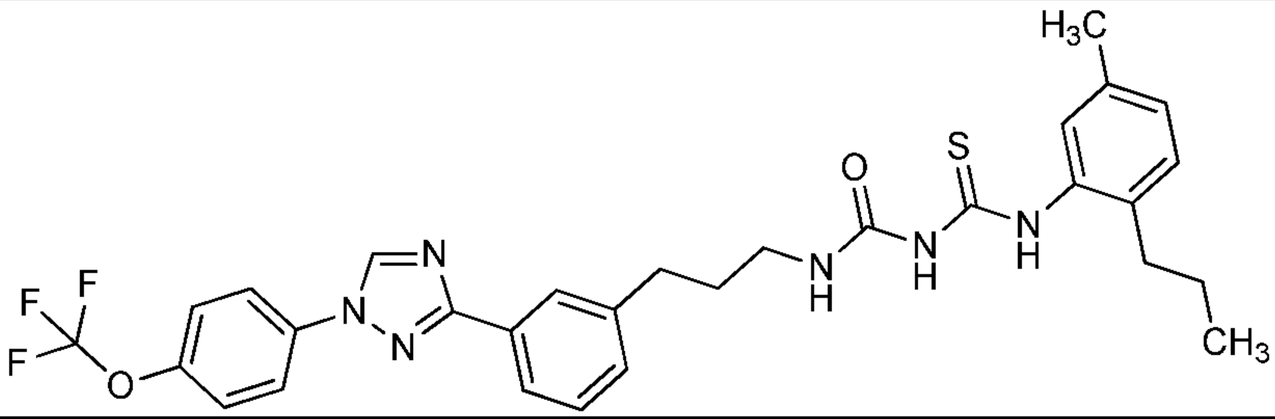
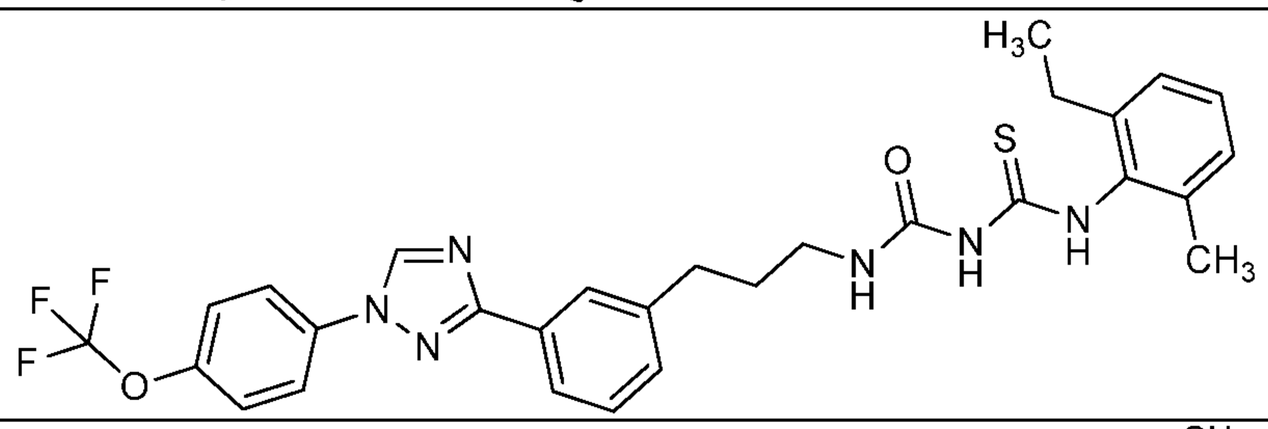
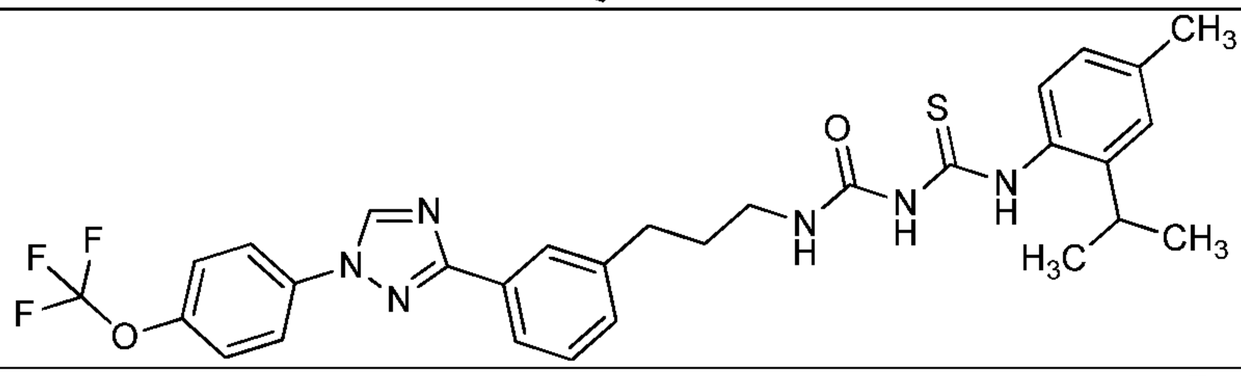
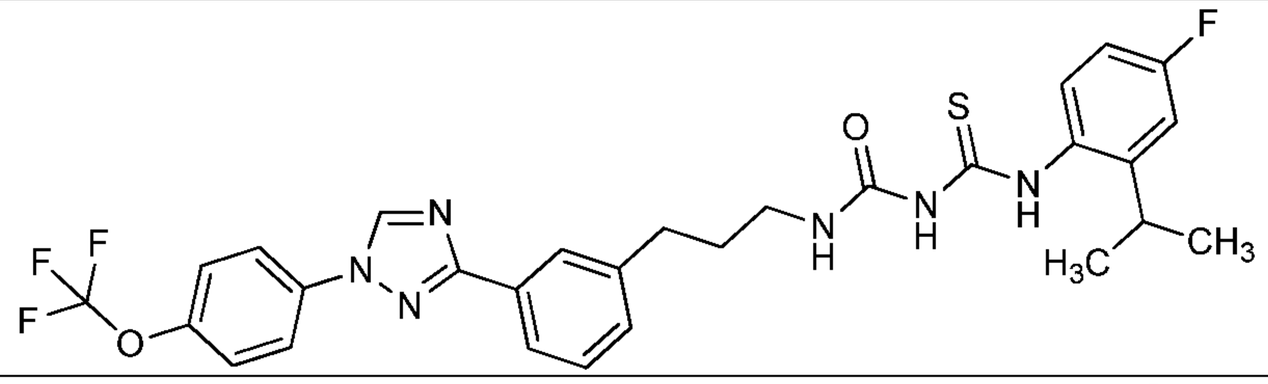
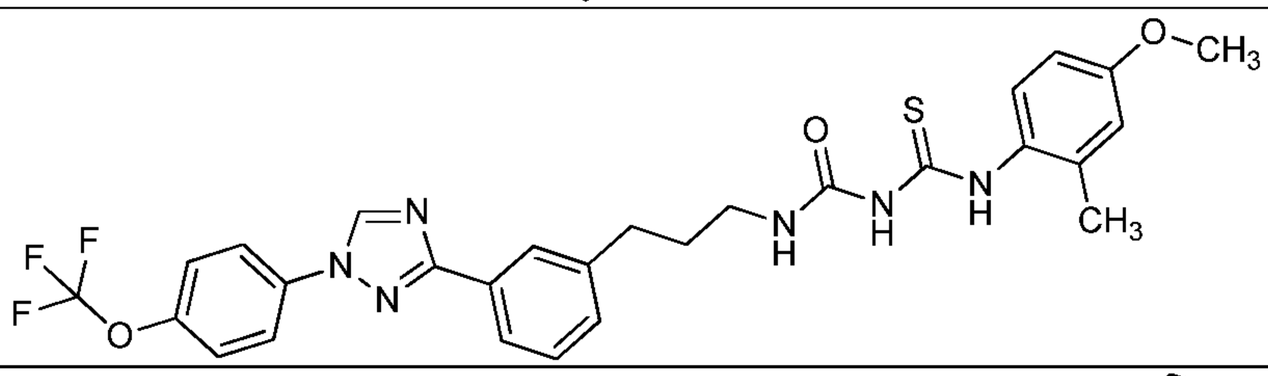
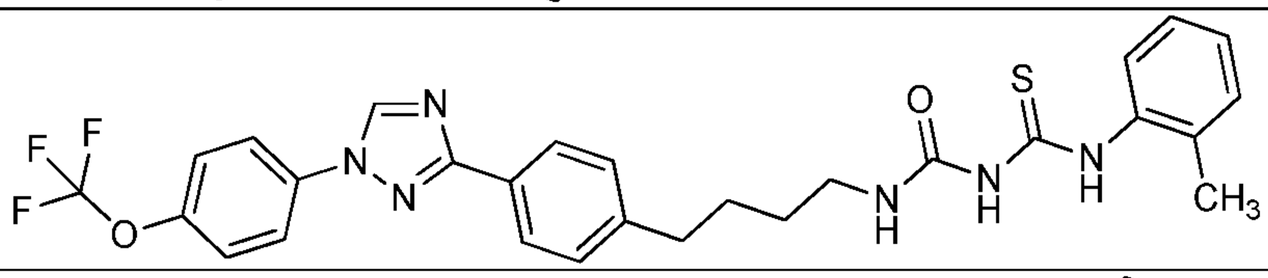
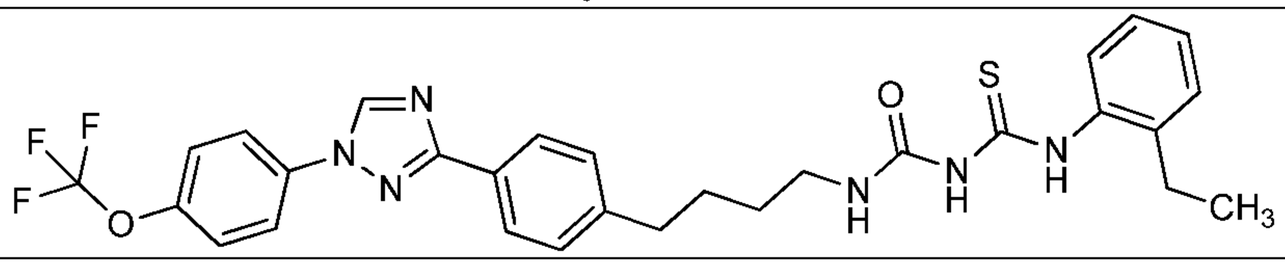
No.	Structure
PC1	
PC2	
PC3	

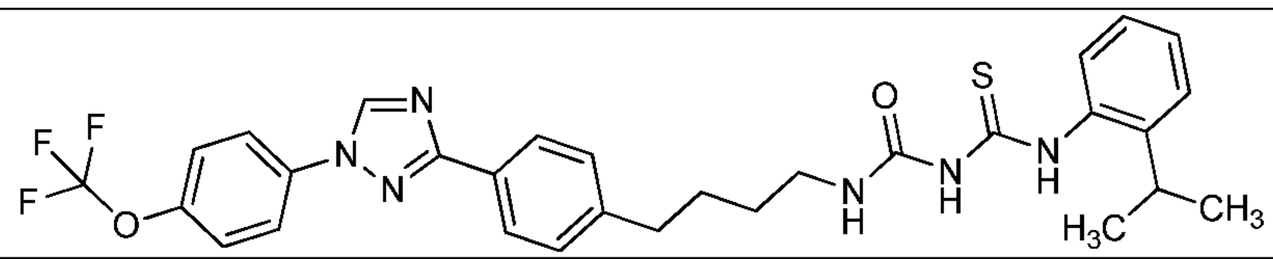
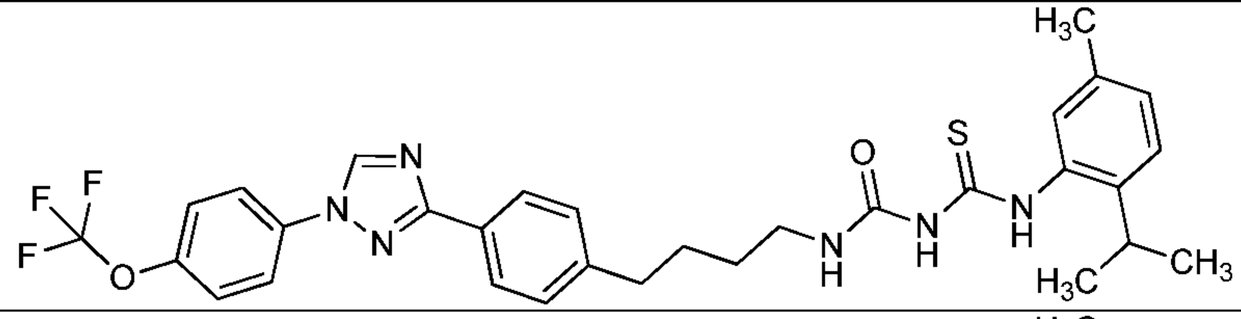
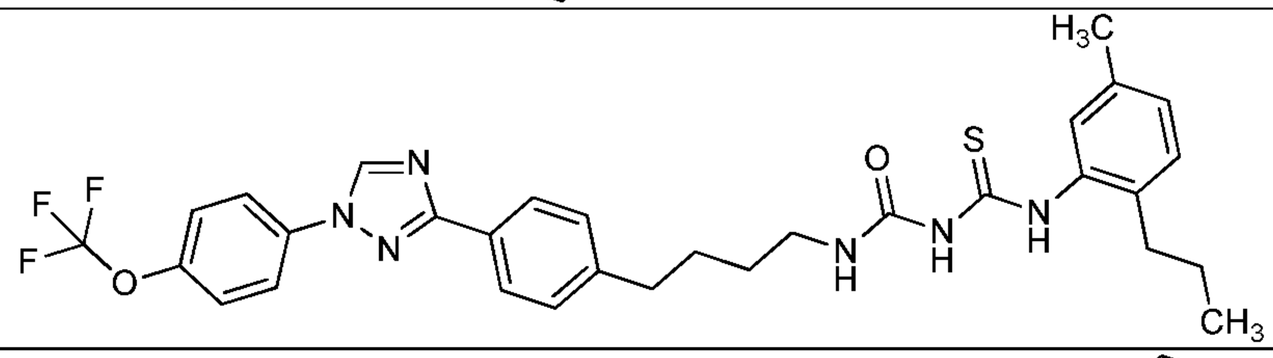
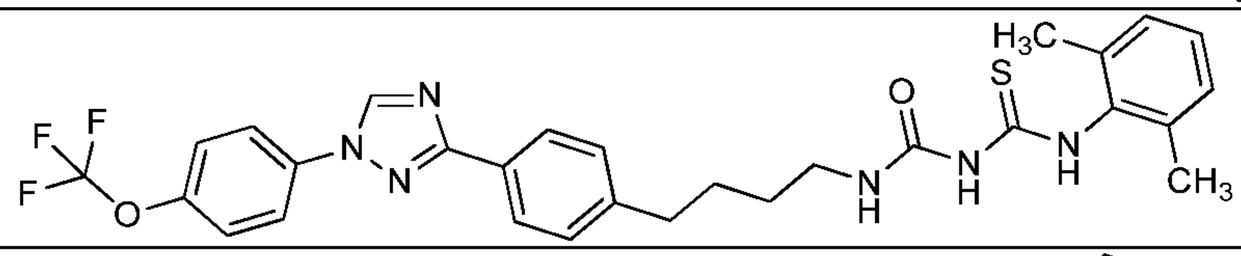
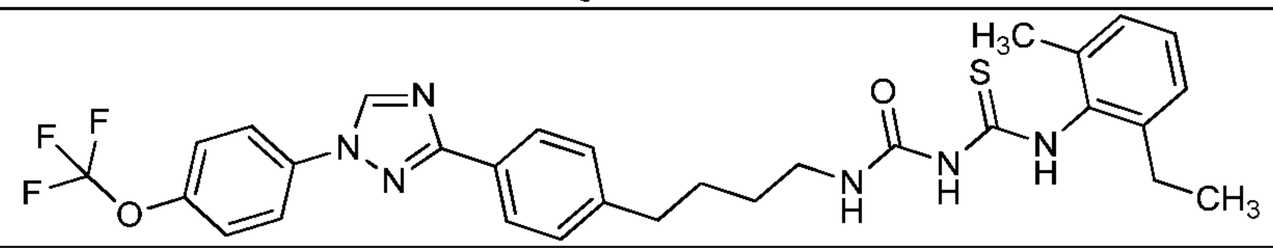
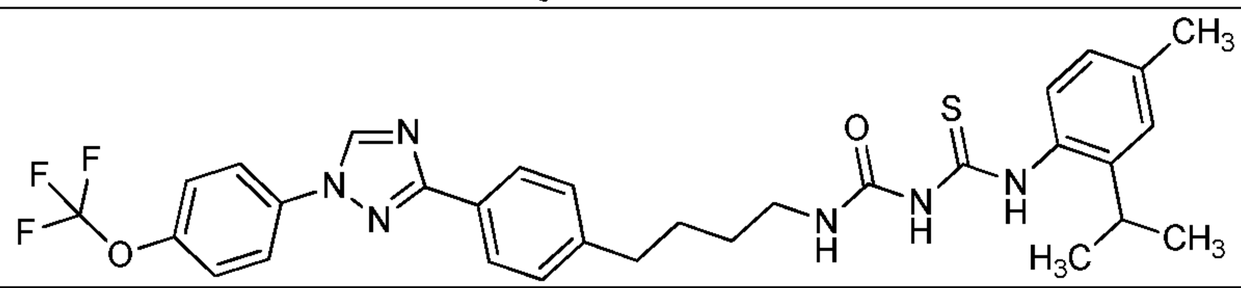
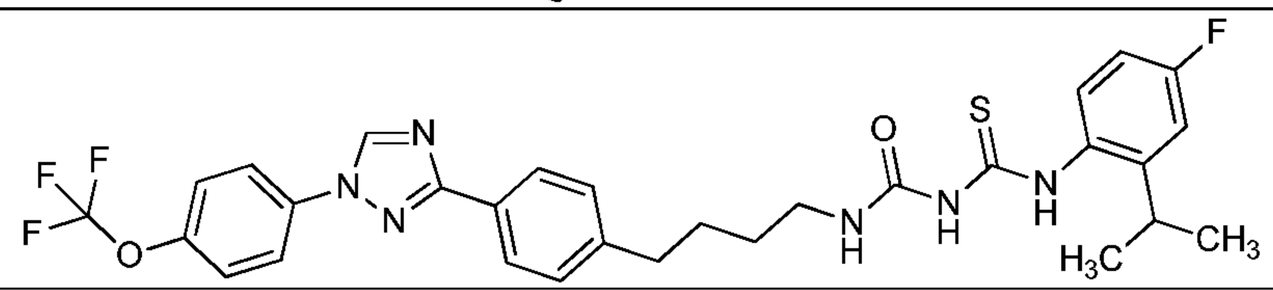
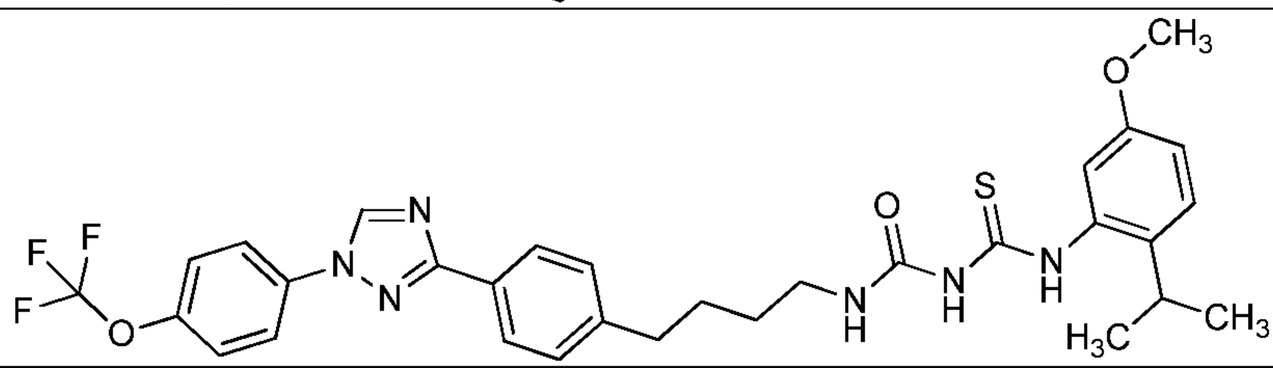
PC5	
PC6	
PC7	
PC8	
PC14	
PC15	
PC16	

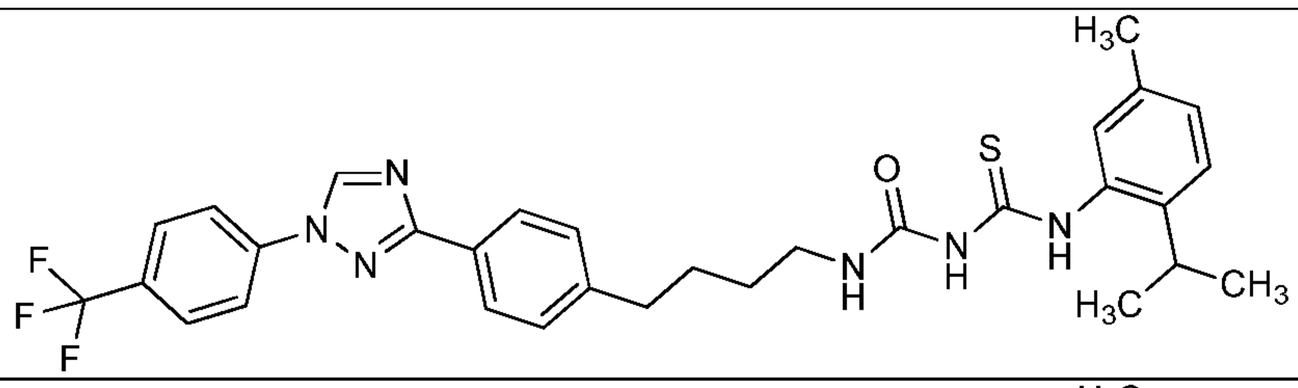
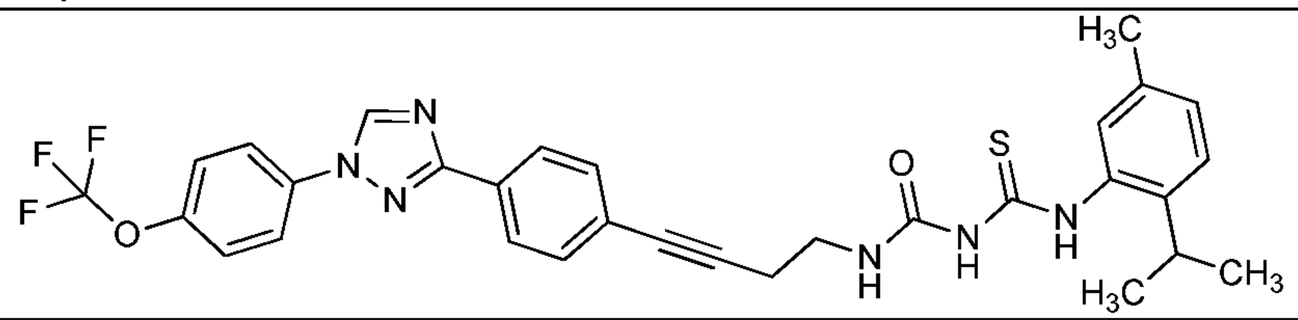
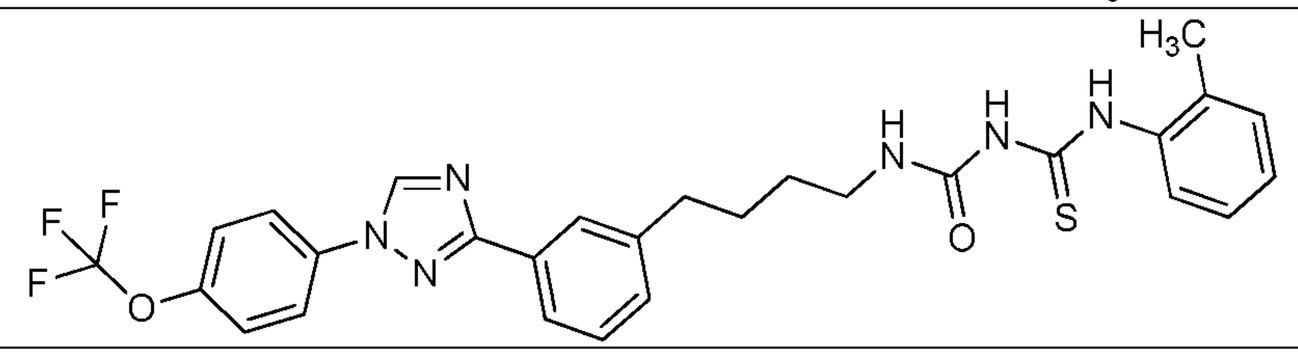
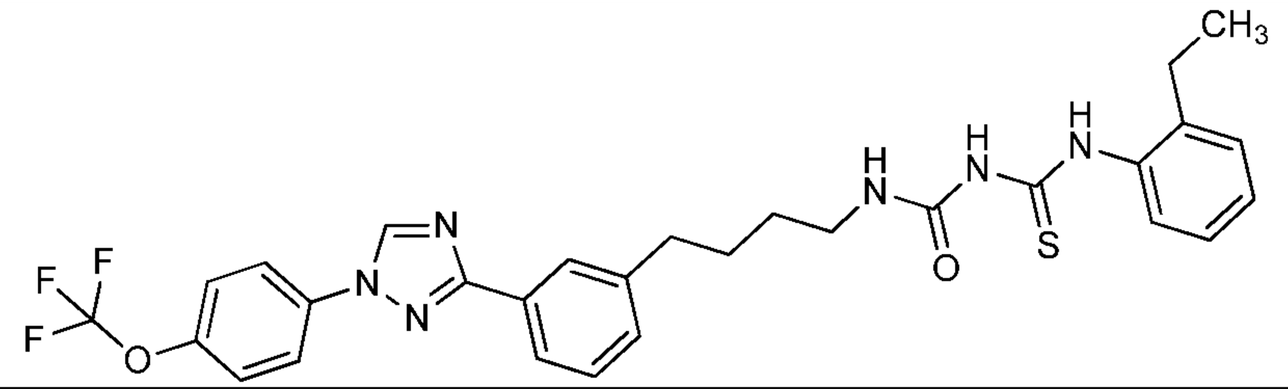
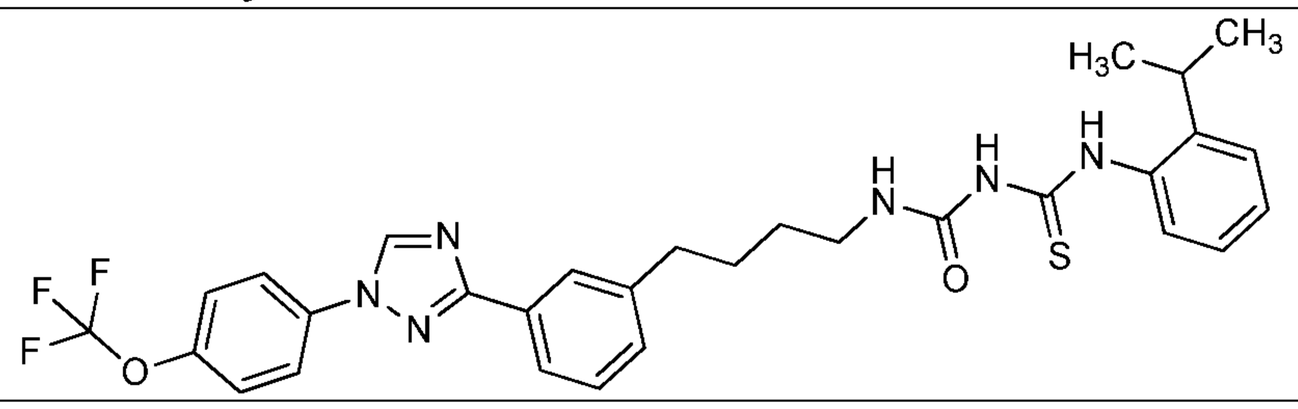
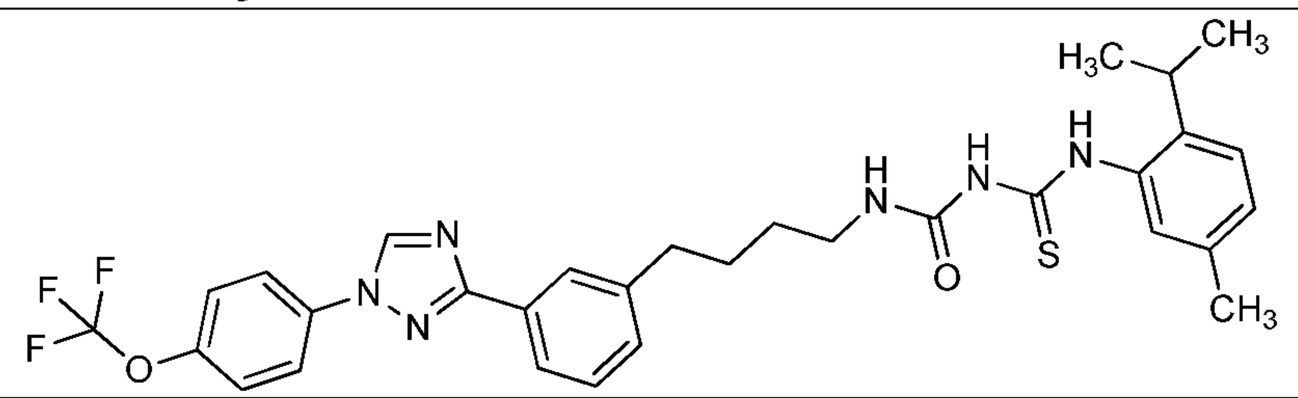
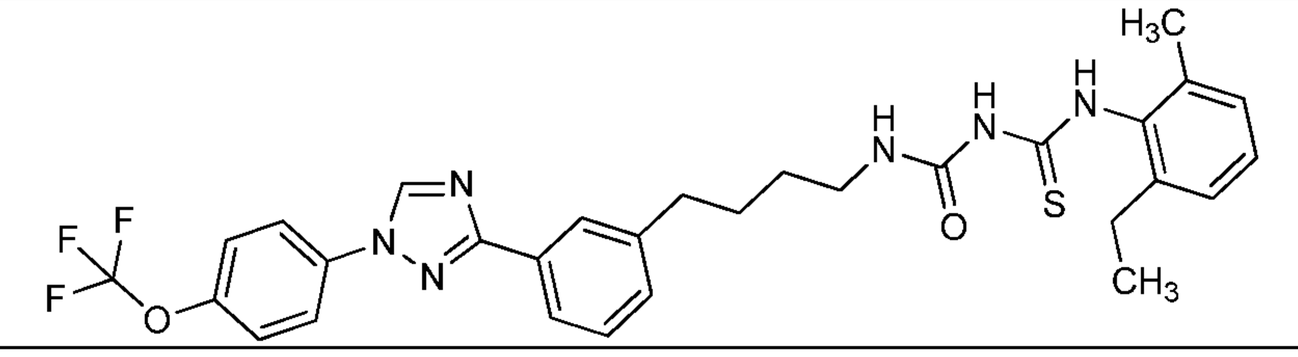
PC74	
PC75	
PC76	
PC80	
PC81	
PC83	

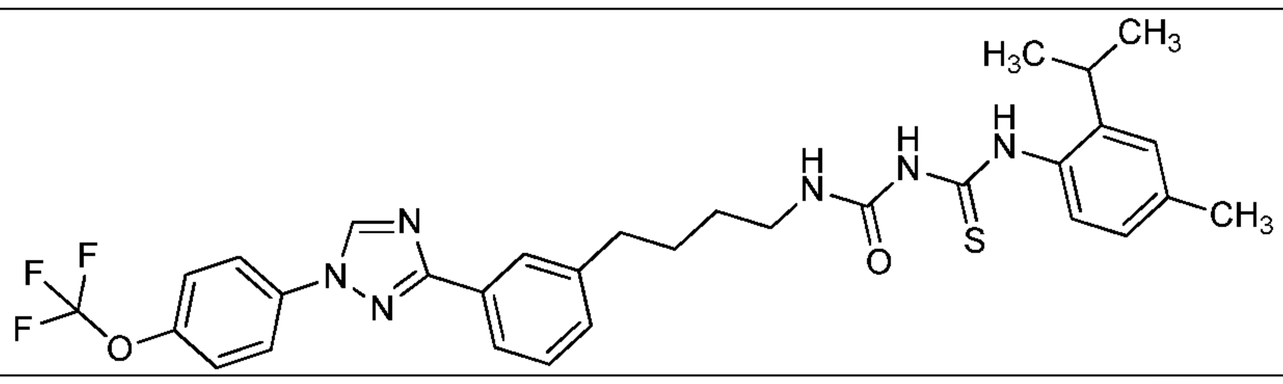
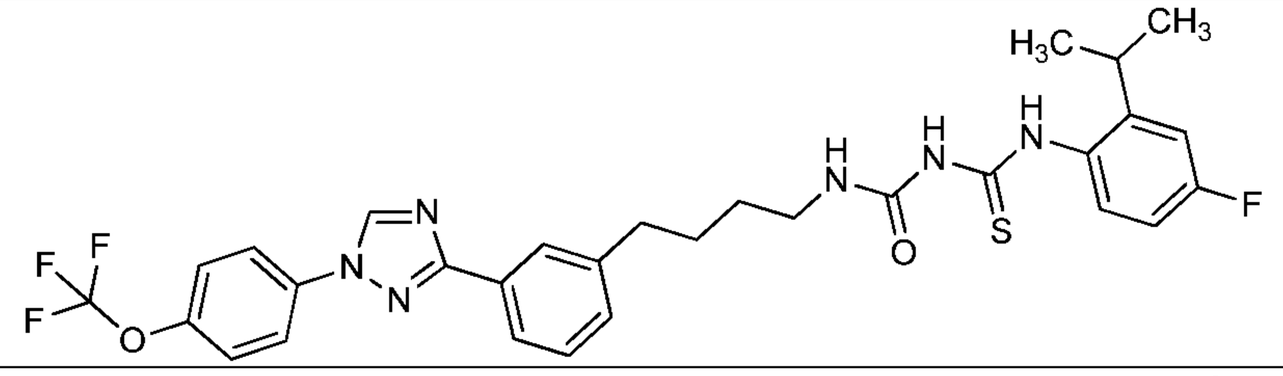
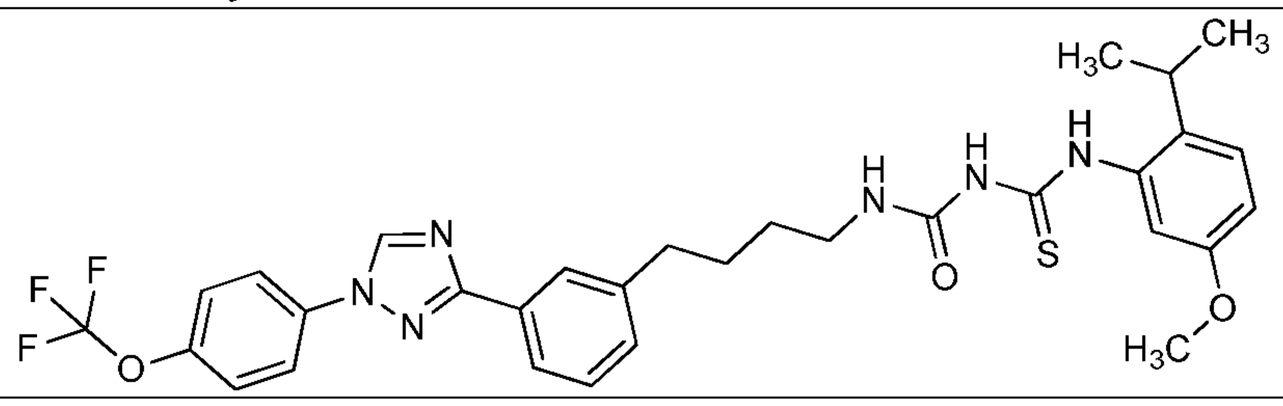
PC84	
PC85	
PC87	
PC92	
PC93	
PC94	
PC99	
PC101	

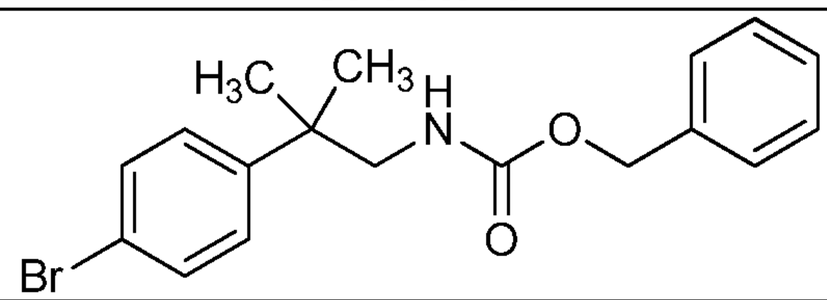
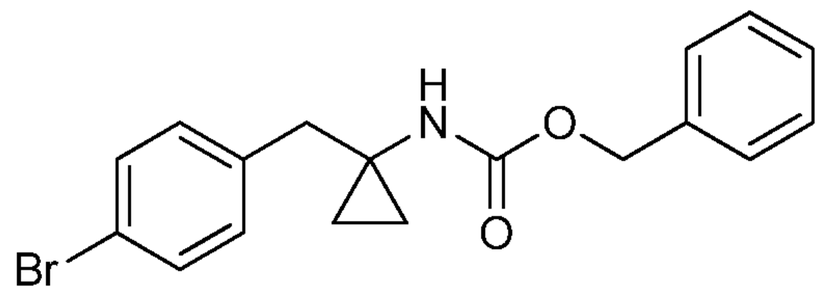
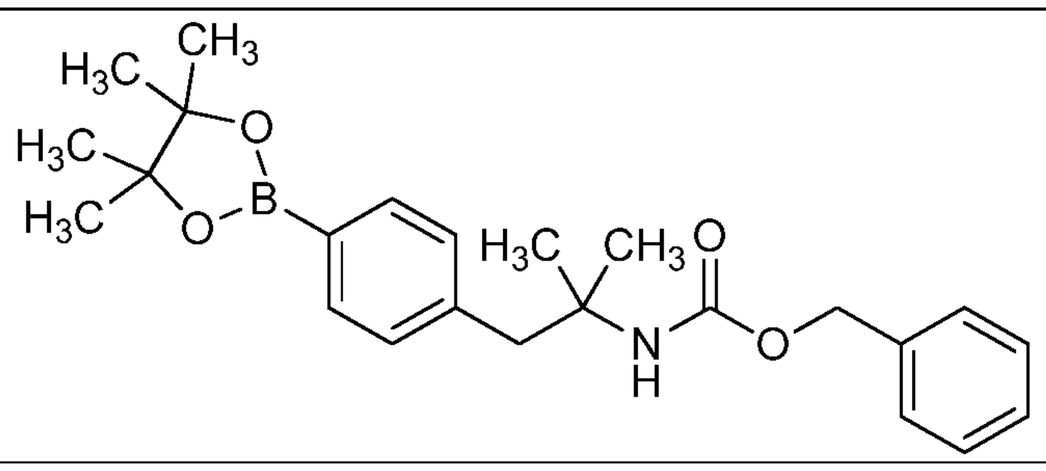
PC102	
PC103	
PC105	
PC118	
PC119	
PC120	
PC124	

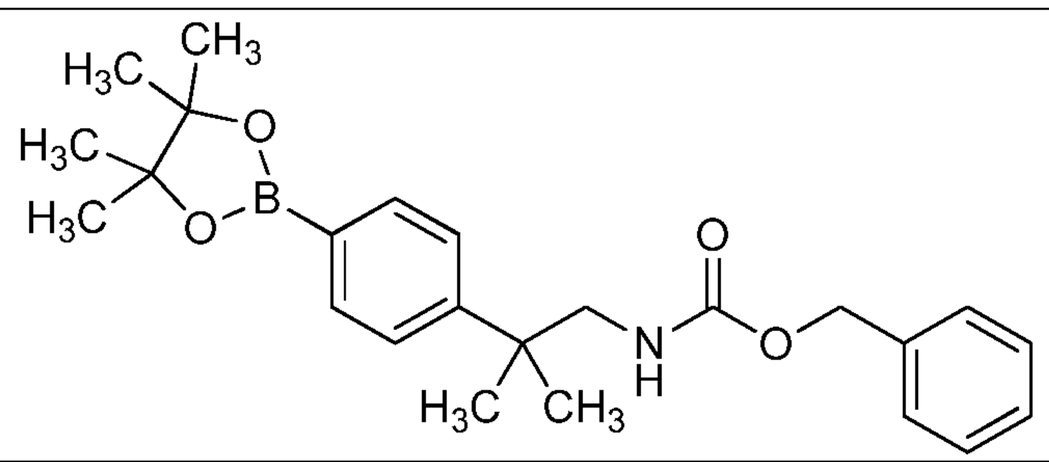
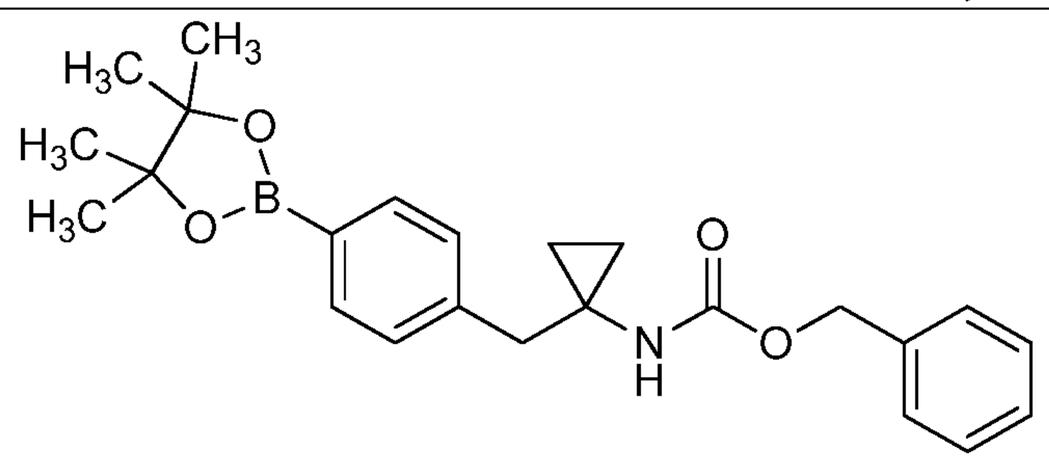
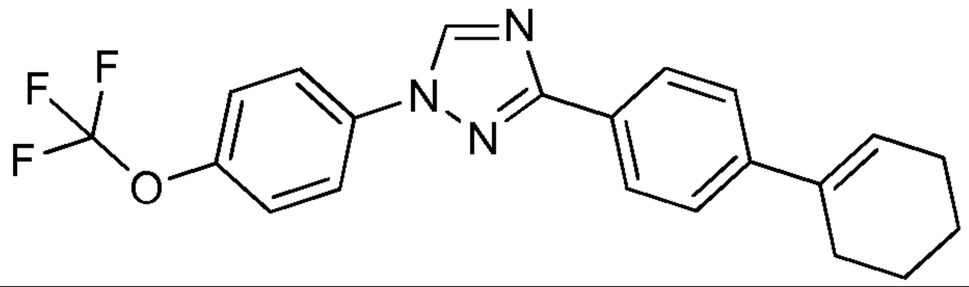
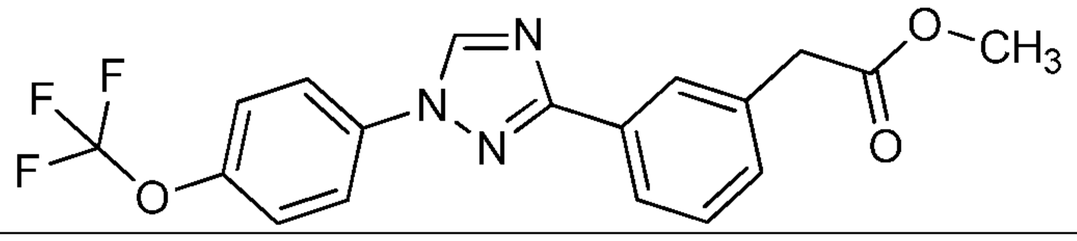
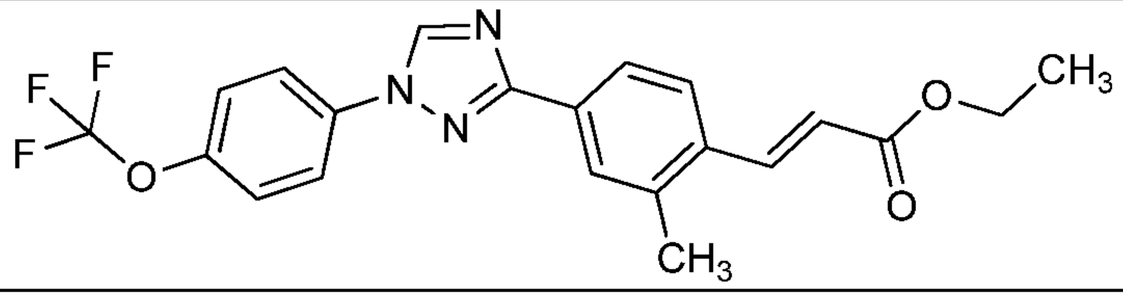
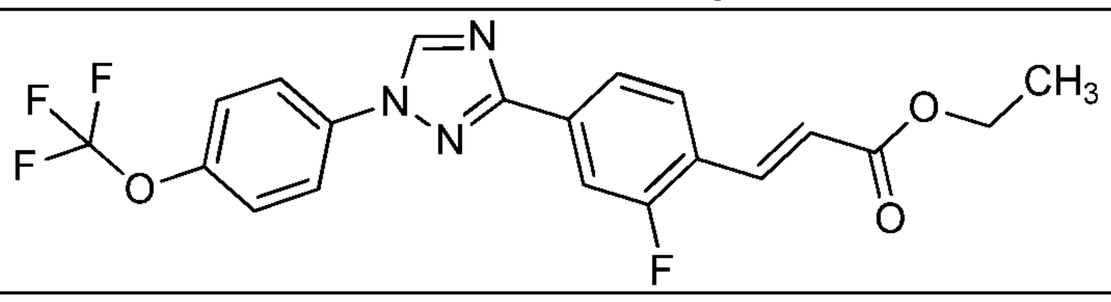
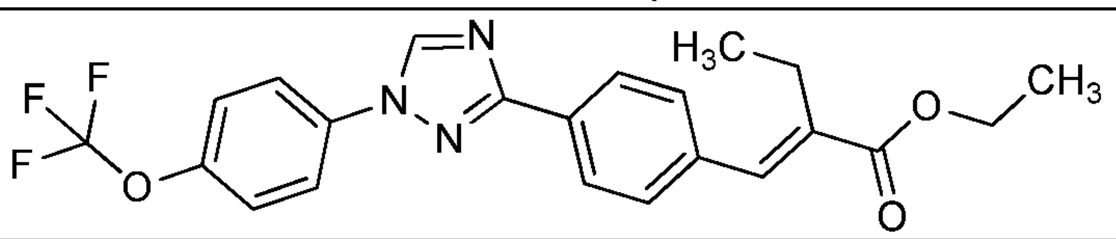
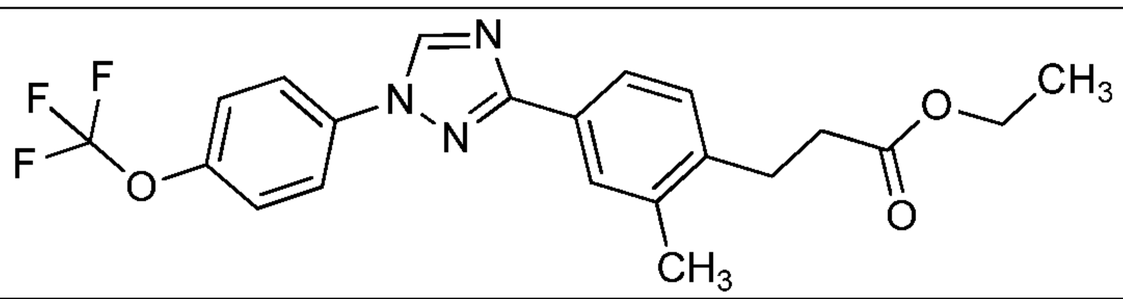
PC125	
PC127	
PC128	
PC129	
PC131	
PC144	
PC145	

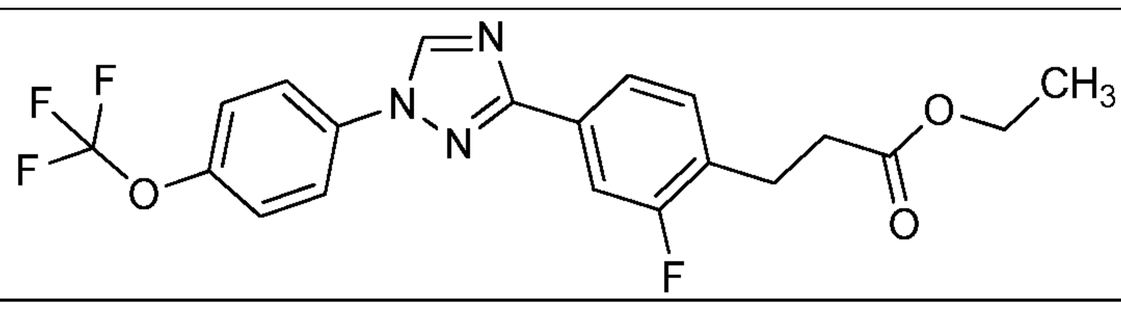
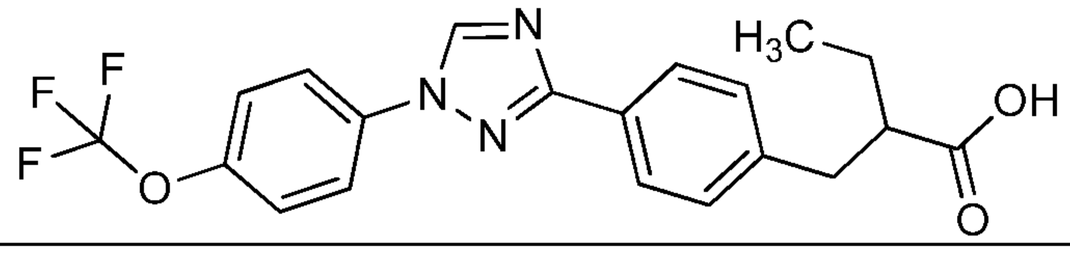
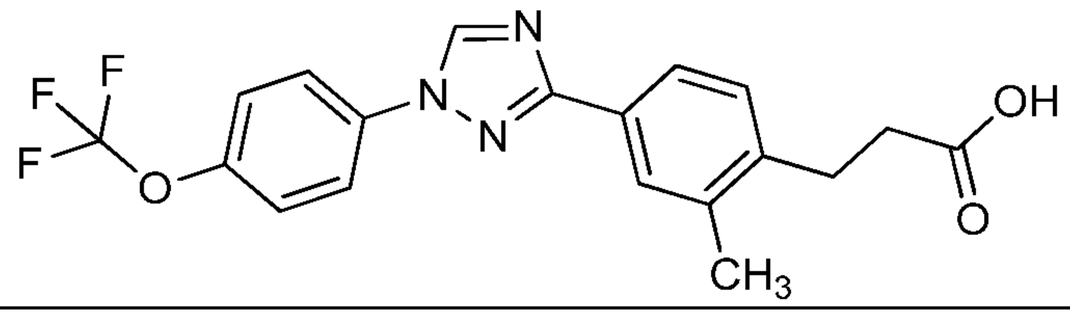
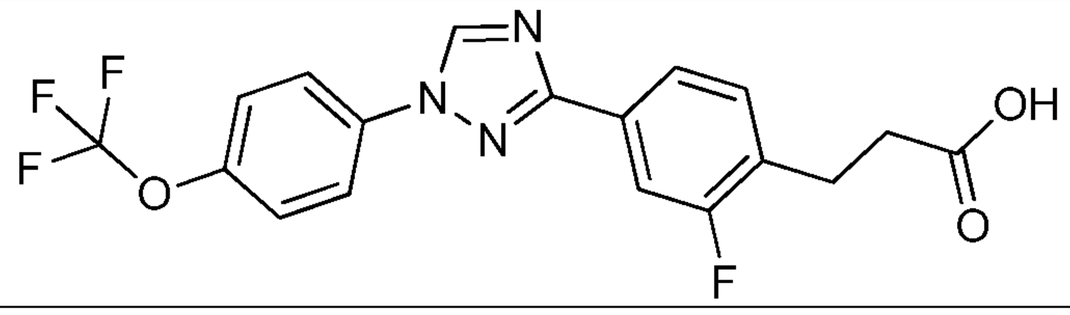
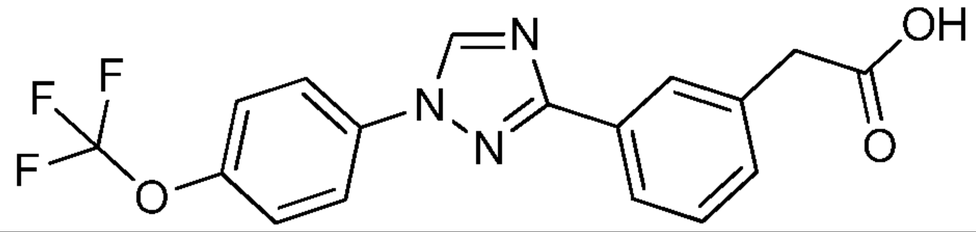
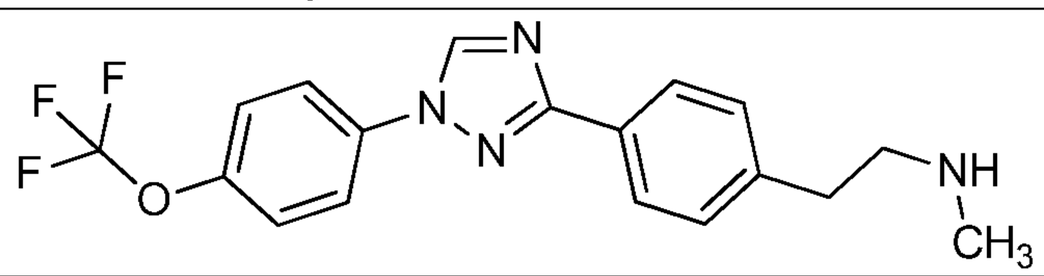
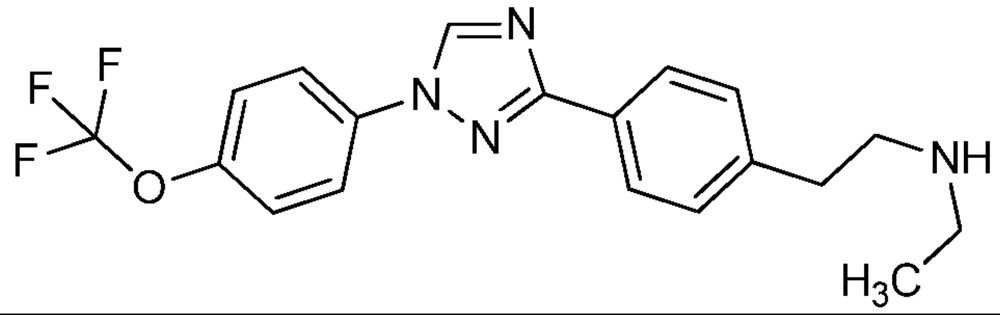
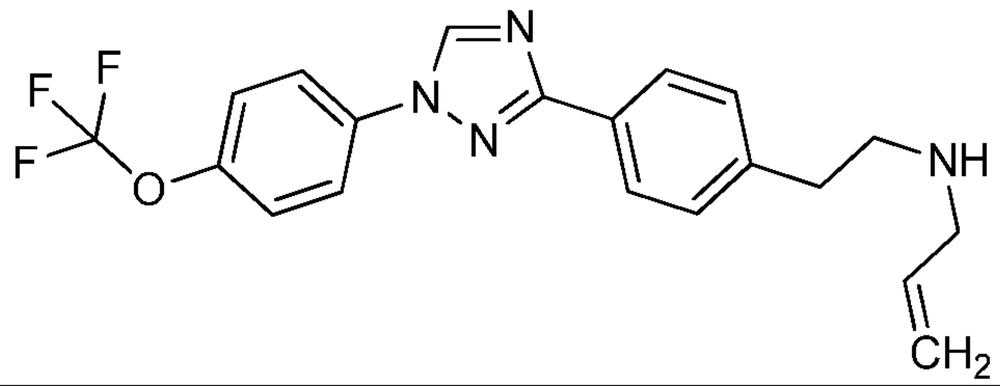
PC146	
PC150	
PC151	
PC152	
PC153	
PC154	
PC155	
PC156	

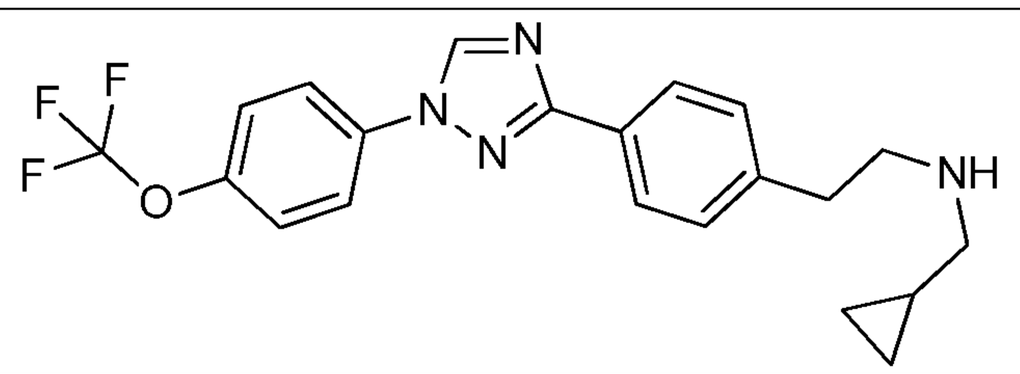
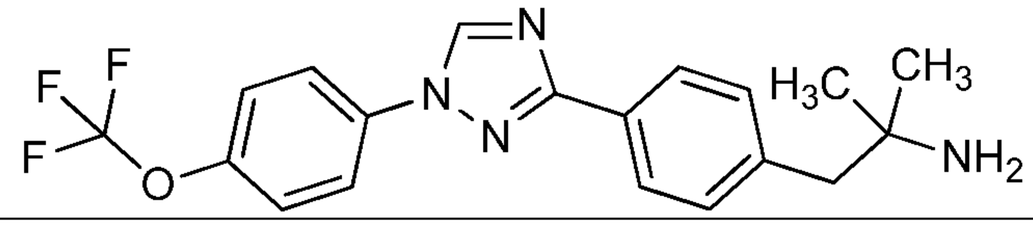
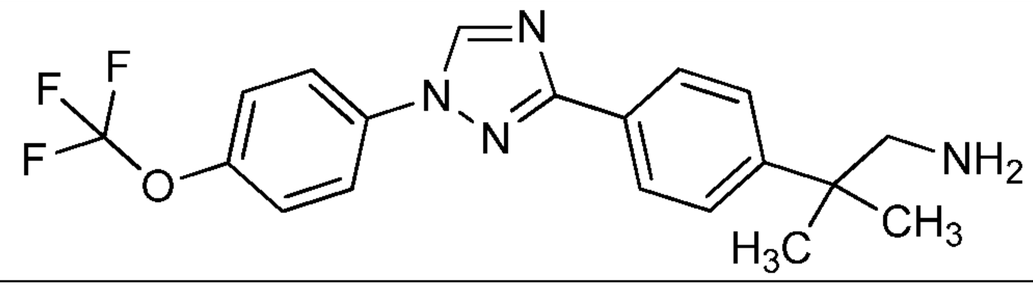
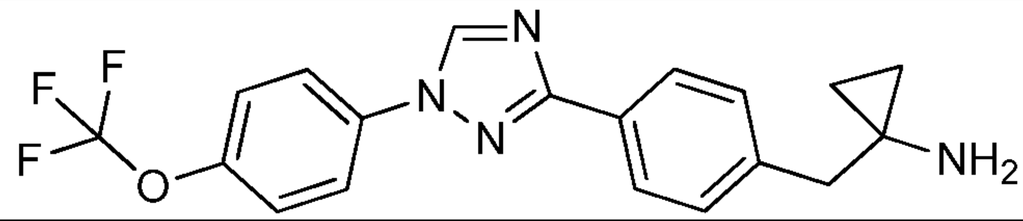
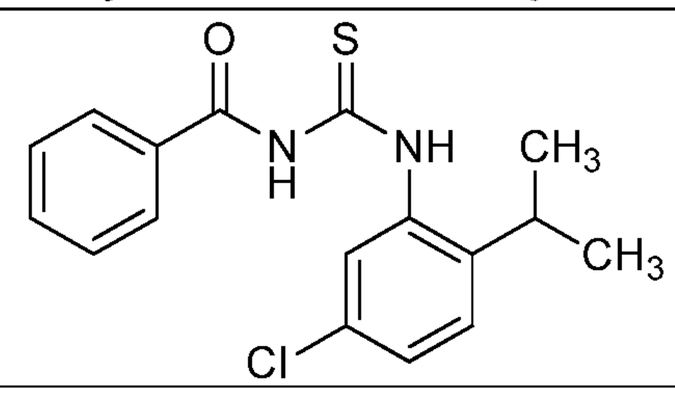
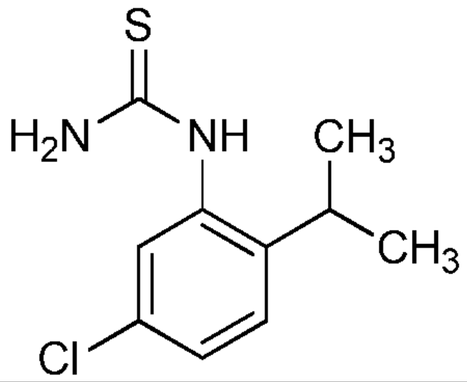
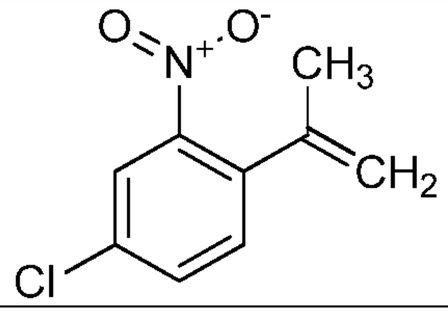
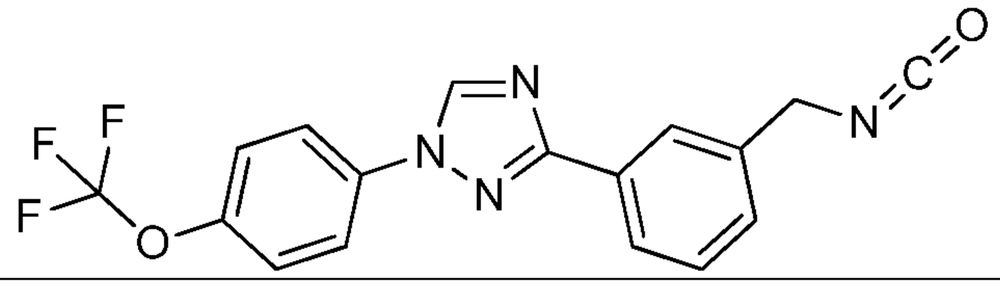
PC159	
PC160	
PC170	
PC171	
PC172	
PC176	
PC179	

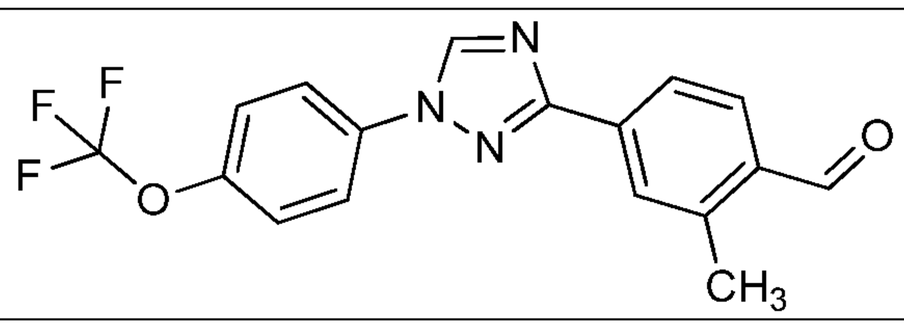
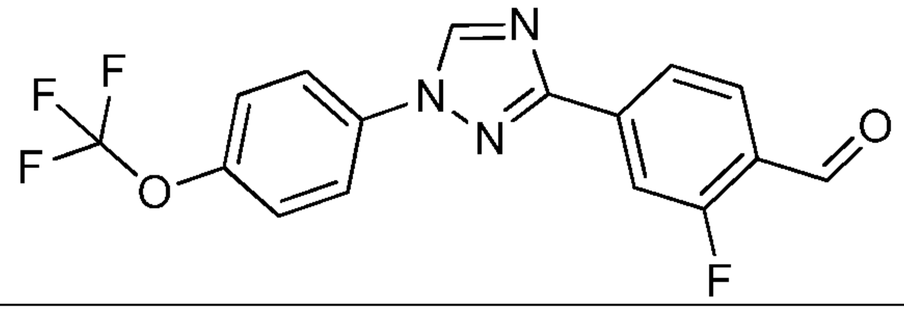
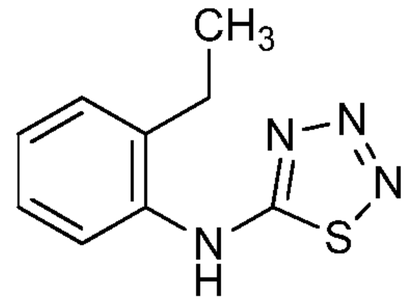
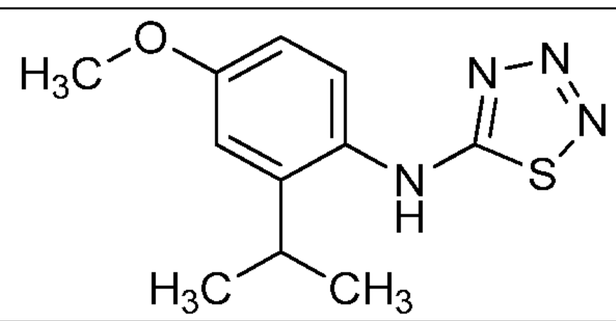
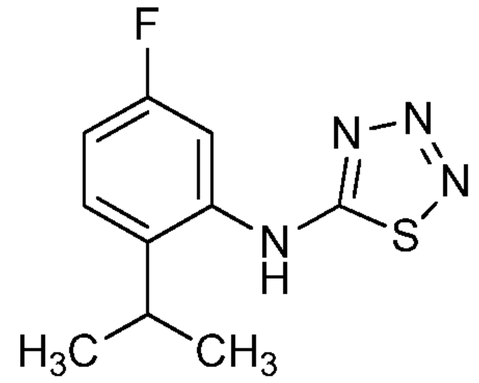
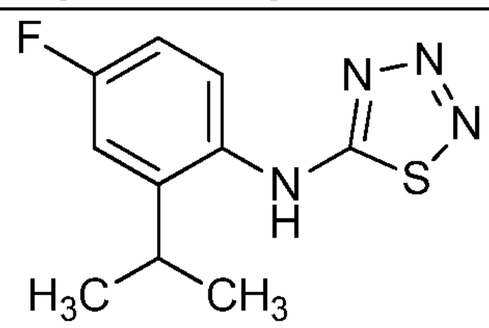
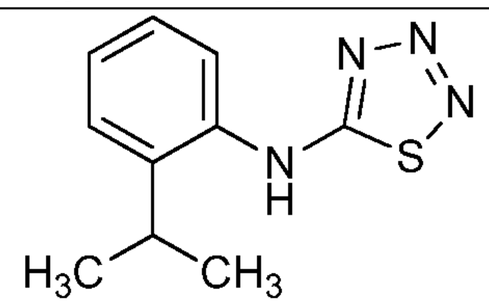
PC180	
PC181	
PC182	

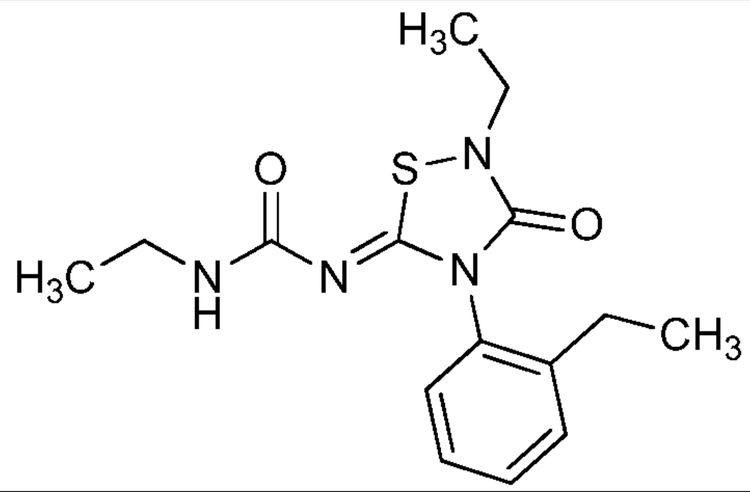
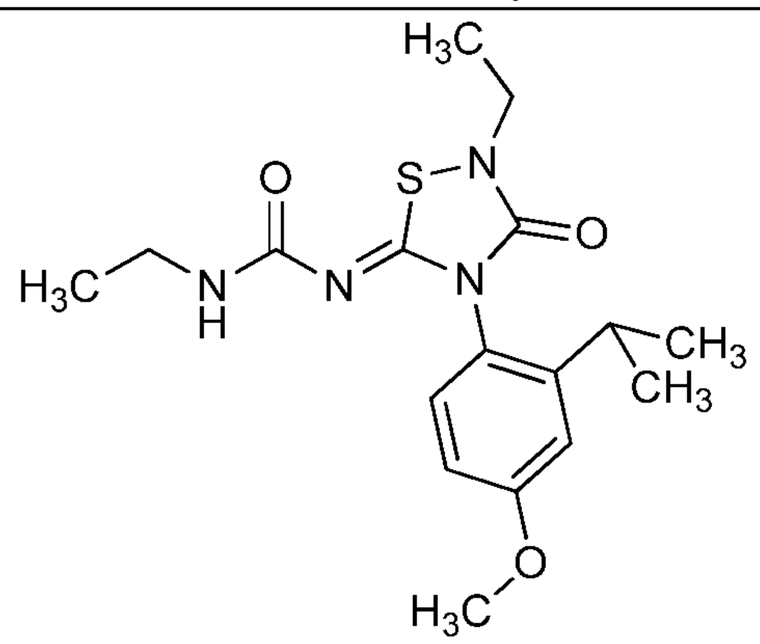
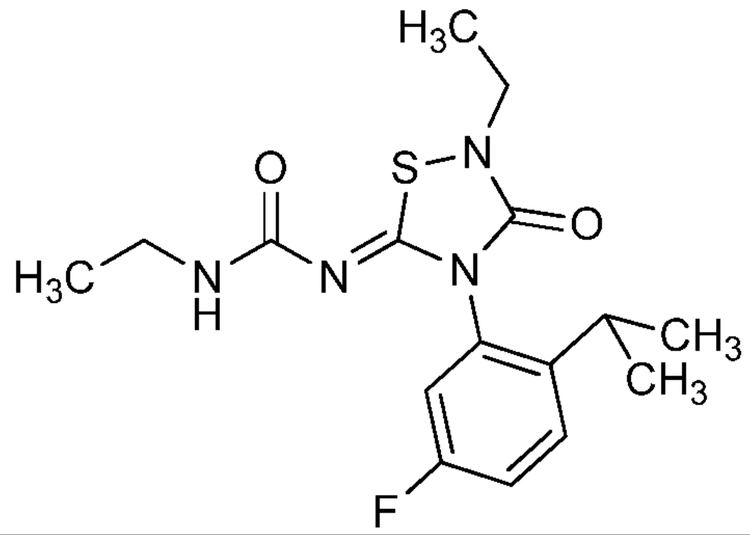
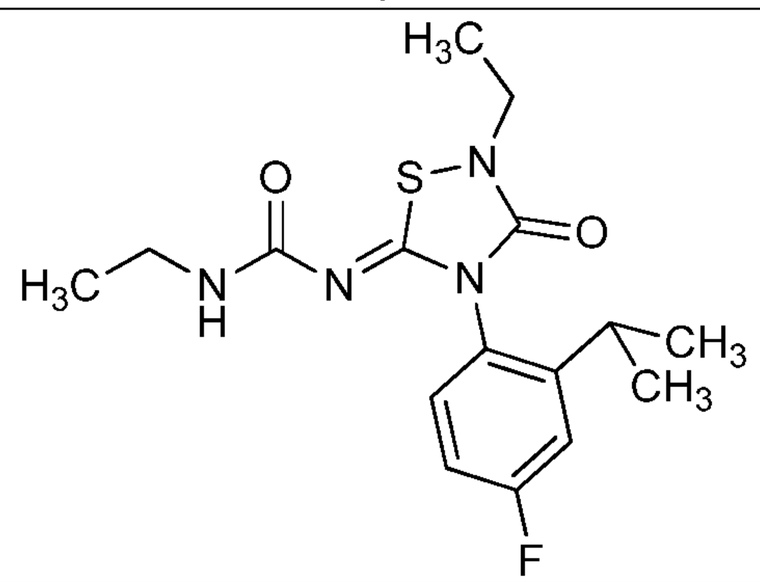
No.	Structure
CB2	
CB3	
CB7	

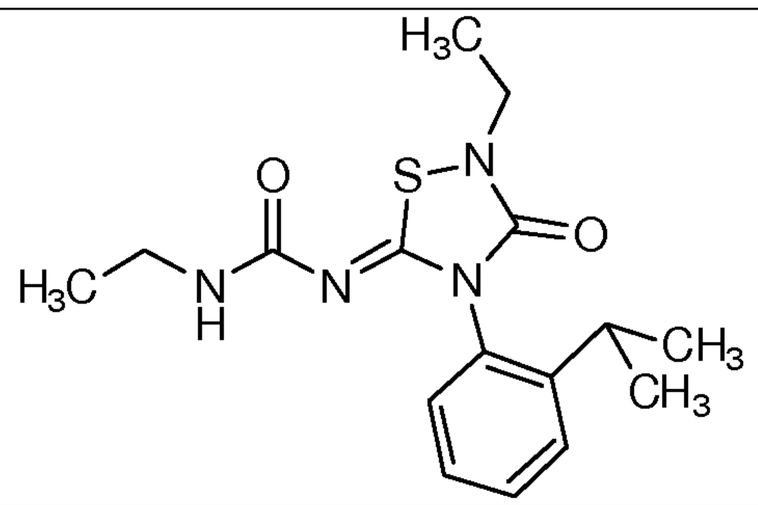
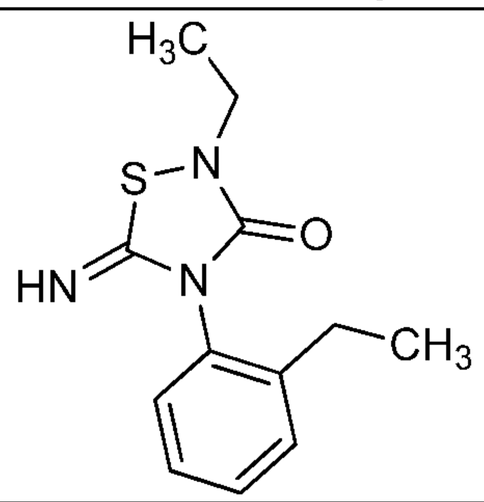
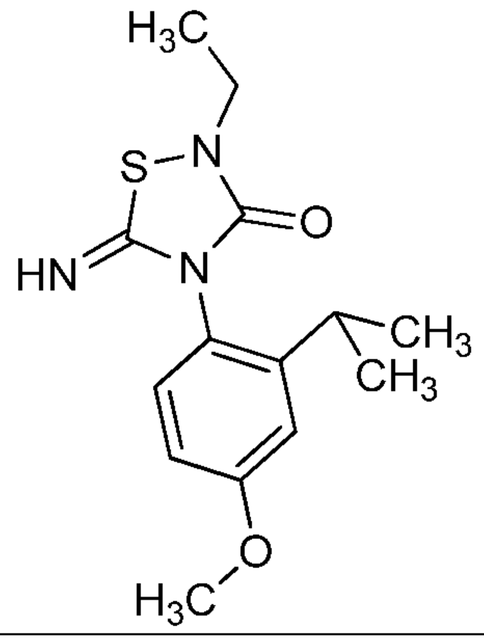
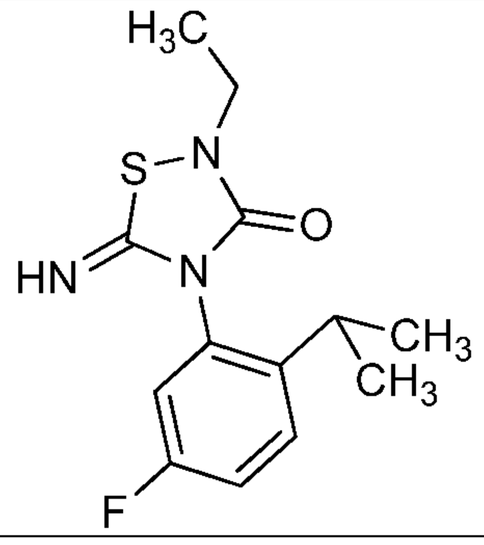
CB8	
CB9	
CB10	
CB11	
CB12	
CB13	
CB14	
CB15	

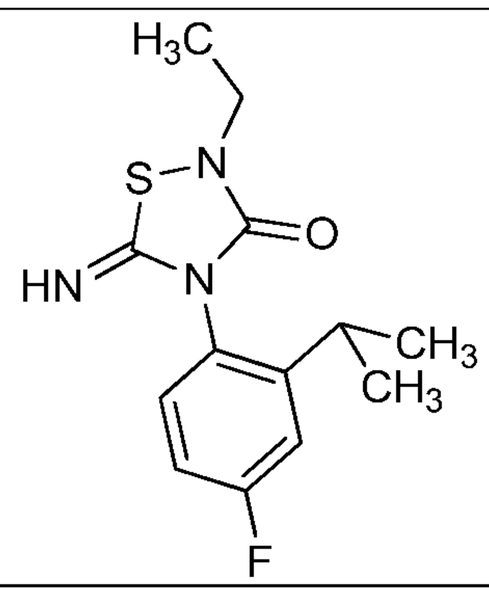
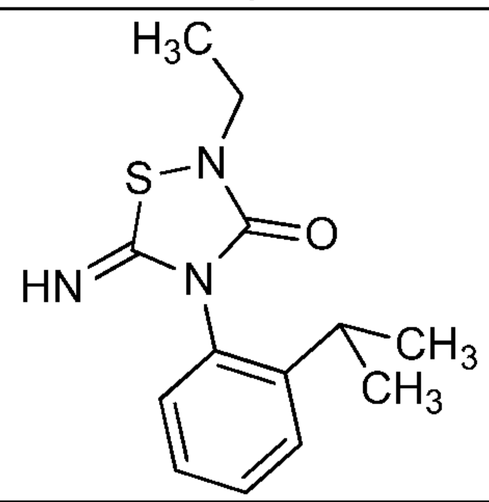
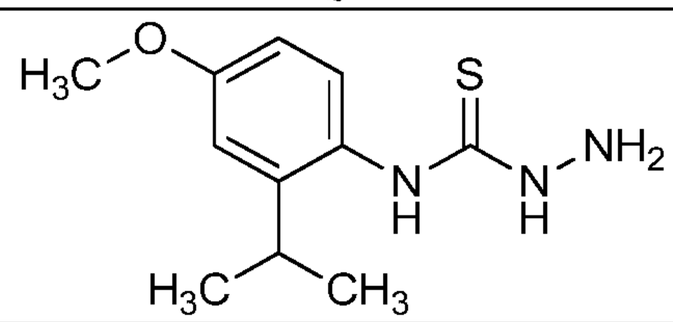
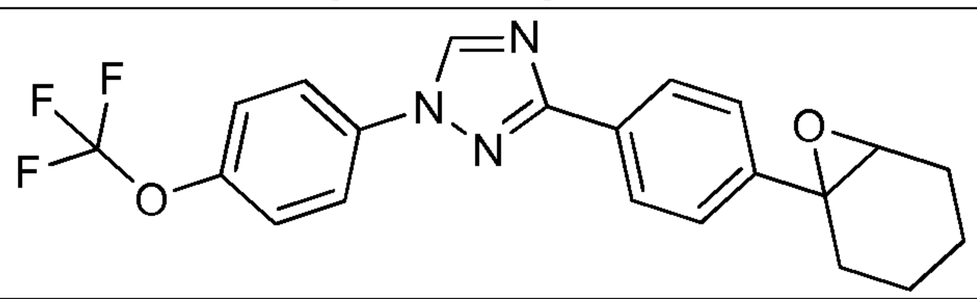
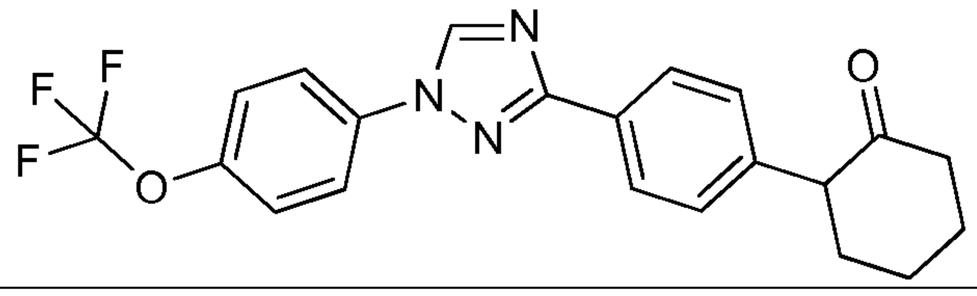
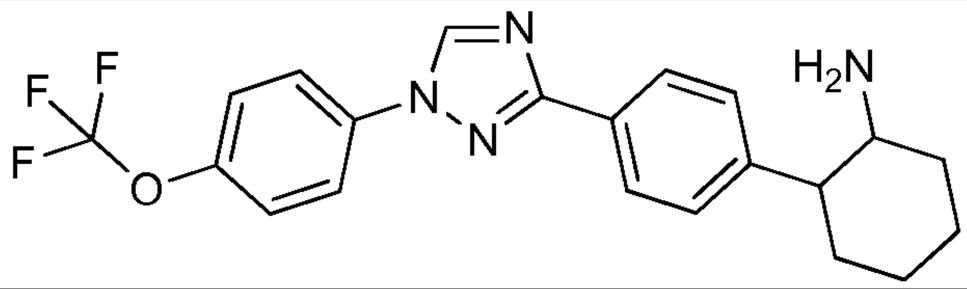
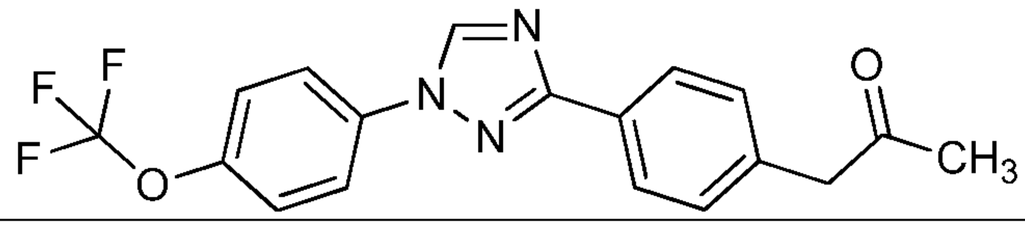
CB16	
CB17	
CB18	
CB19	
CB23	
CB24	
CB25	
CB26	

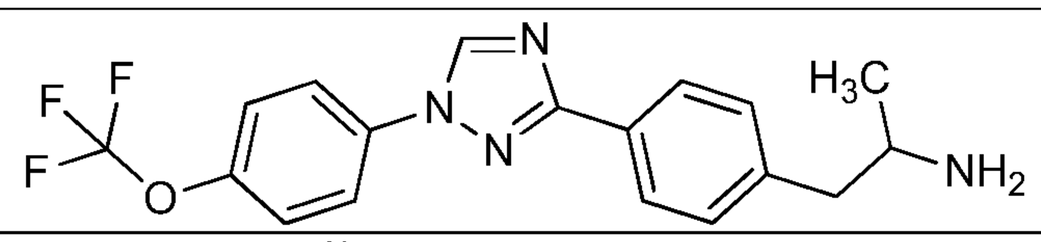
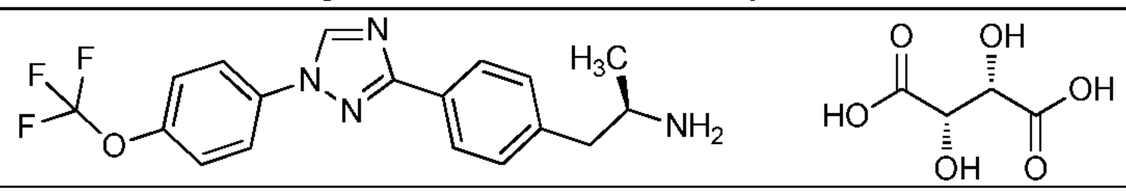
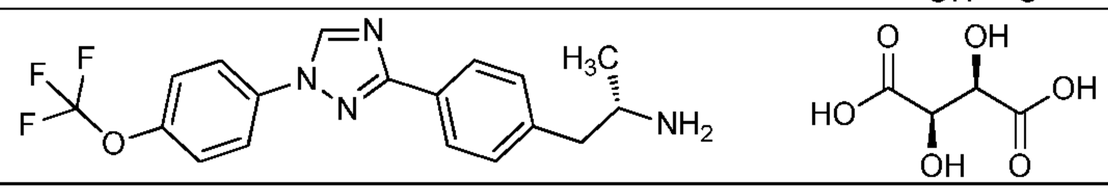
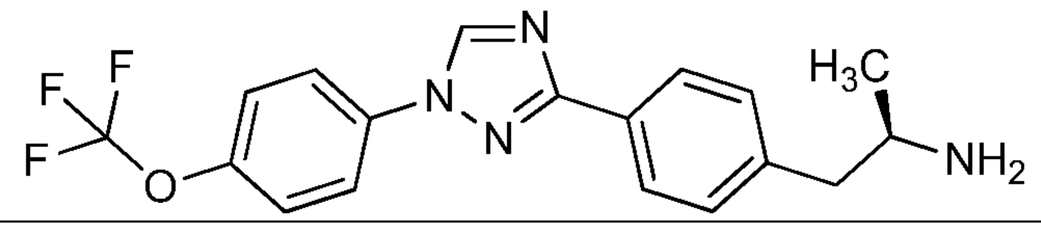
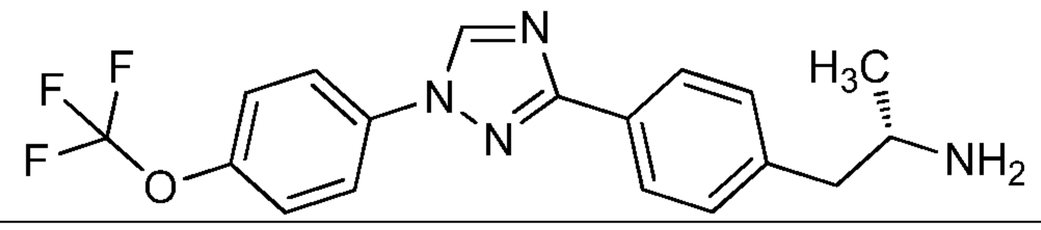
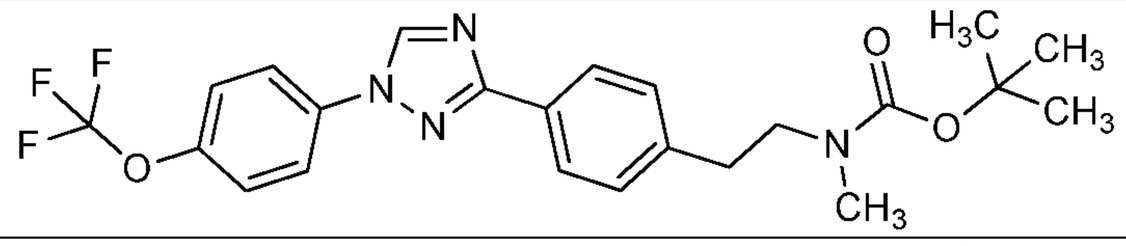
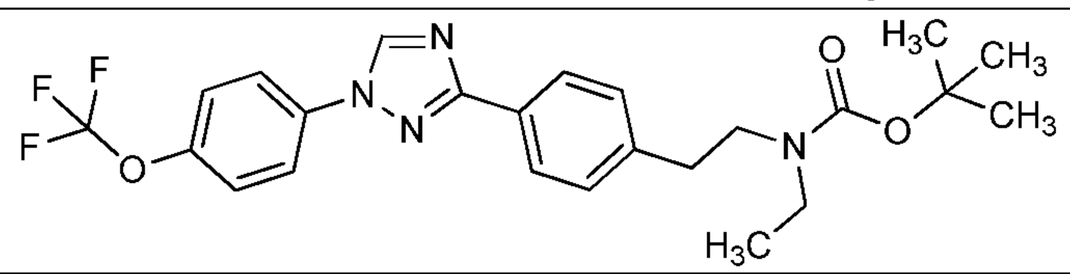
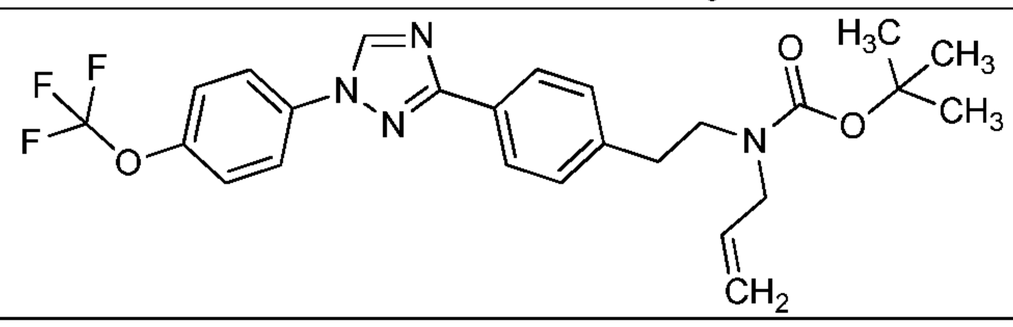
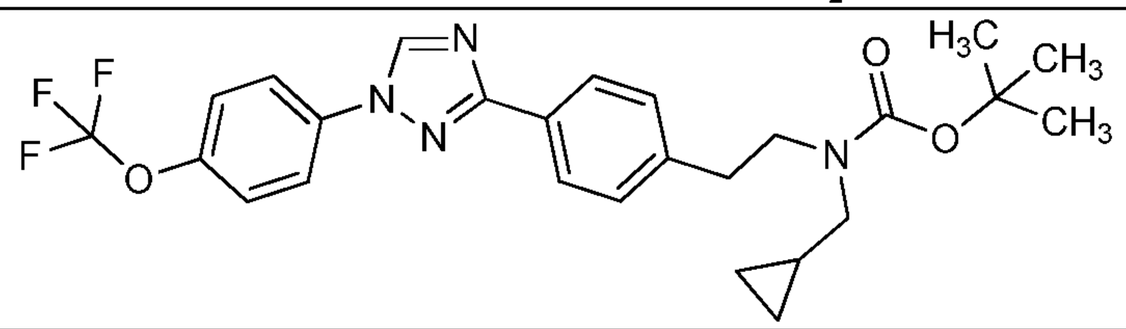
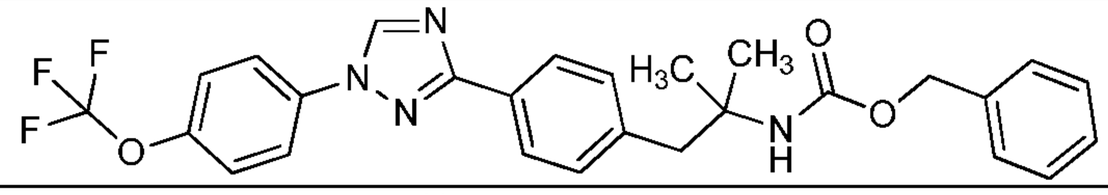
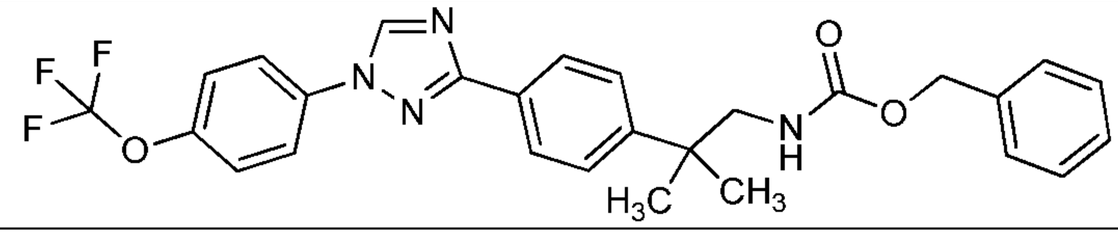
CB27	
CB28	
CB29	
CB30	
CB31	
CB32	
CB33	
CB34	

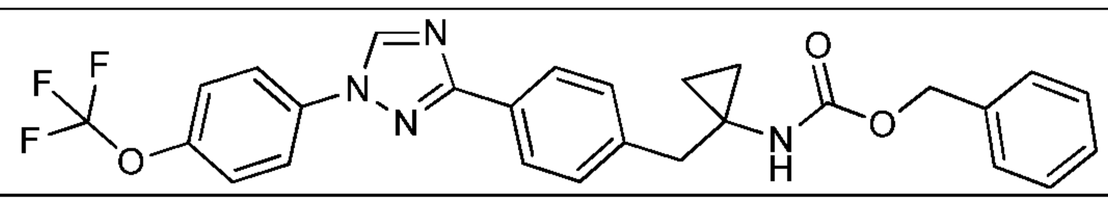
CB35	
CB36	
CB37	
CB38	
CB39	
CB40	
CB41	

CB42	
CB43	
CB44	
CB45	

CB46	
CB47	
CB48	
CB49	

CB50	
CB51	
CB53	
CB54	
CB55	
CB56	
CB57	

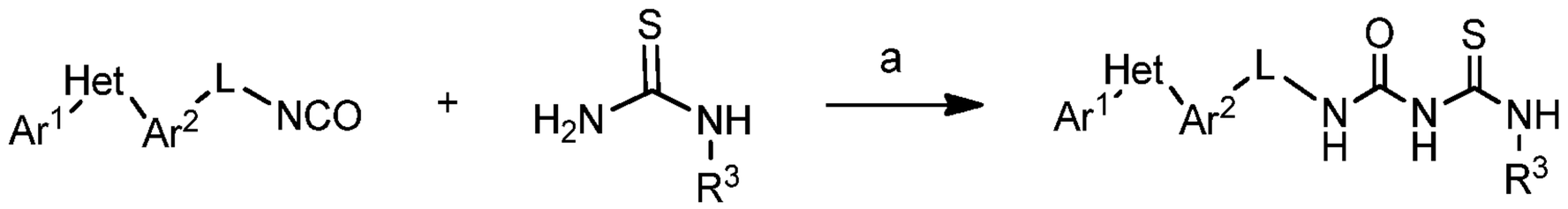
CB58	
CB59	
CB60	
CB61	
CB62	
CB63	
CB64	
CB65	
CB66	
CB67	
CB68	

CB69	

.

18. A process comprising reacting an isocyanate, Ar^1-Het-Ar^2-L-NCO (1-2), with an *N*-aryl thiourea (2-1) to produce a thiobiuret (2-2, Scheme 2)

Scheme 2



1-2 2-1 2-2

wherein Ar^1, Het, Ar^2, L, and R^3 are as defined in claim 1 .

19. A process comprising reacting a Thiobiuret (2-2) as in Scheme 3 with

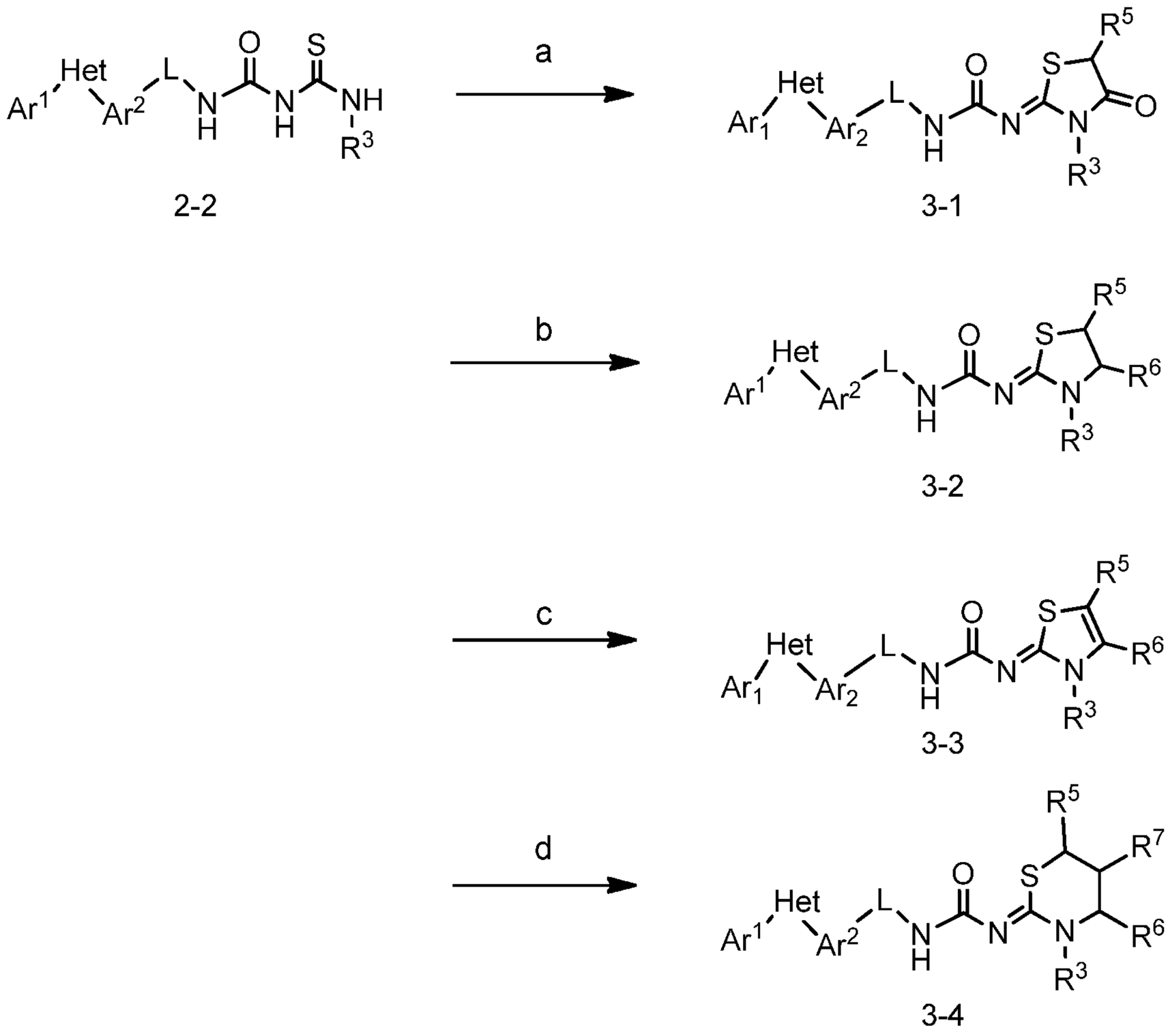
(a) an α-halo ester to form 2-imino 1,3-thiazolin-4-ones (3-1, step a);

(b) vicinal dihalides to form 2-imino-1,3-thiazolines (3-2, step b);

(c) α-halo ketones to form 2-imino-1,3-thiazoles (3-3, step c); or

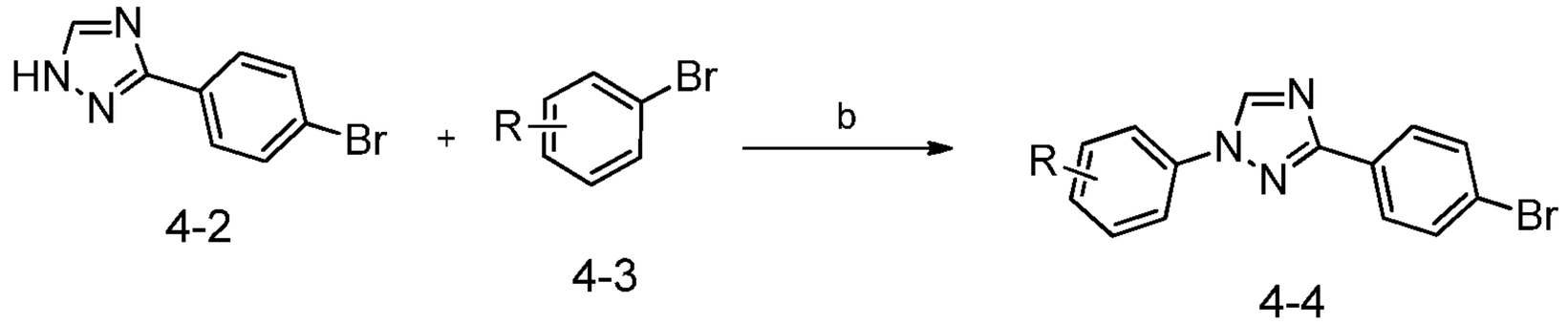
(d) 1,3-dihalopropane to form 2-imino-1,3-thiazinanes (3-4, step d);

Scheme 3



wherein Ar^1, Het, Ar^2, L, R^3, R^5, R^6, and R^7 are as defined in claim 1.

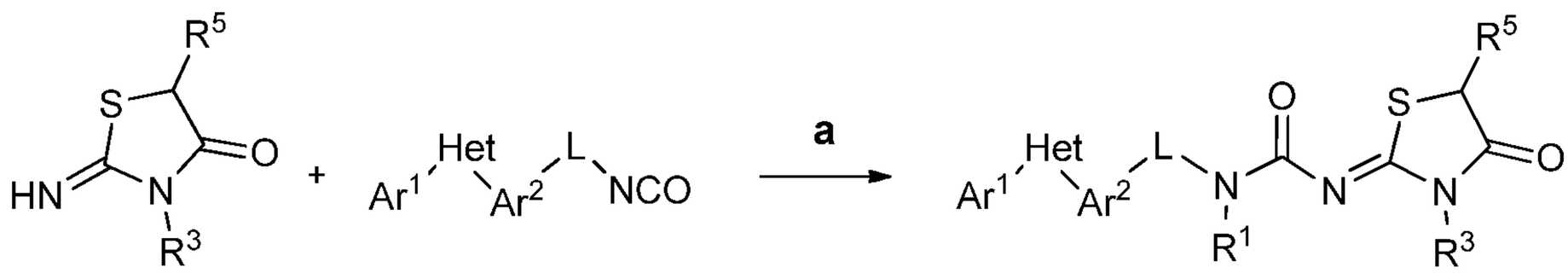
20. A process comprising reacting 3-(4-Bromophenyl)-1,2,4-triazole (4-2) with an aryl halide (4.3) (R is C_1-C_6 haloalkoxy) to form 1-aryl-3-(4-bromophenyl) triazole



4-2 4-3 4-4

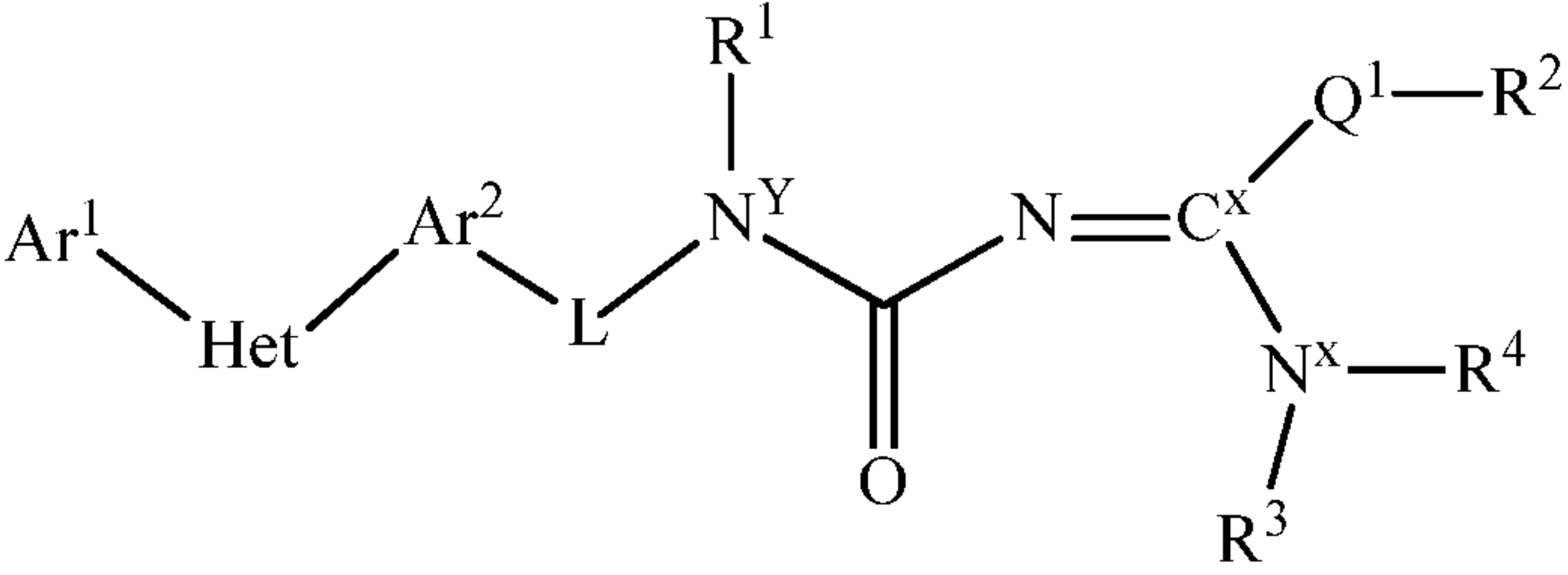
21. A process comprising reacting (*Z*)-1-(3-(2-isopropyl-5-methylphenyl)-4-oxothiazolidin-2-ylidene)-3-(4-(1-(4-(trifluoromethoxy)phenyl)-1*H*-1,2,4-triazol-3-yl)phenethyl)urea with and acid to form a salt.

22. A process comprising reacting 2-iminolthiazolidin-4-one (3-1a) with an isocyanate (1-2) to produce thiobiuret (3-1')



3-1a **1-2** **3-1'**

wherein Ar^1, Het, Ar^2, L, R^3, and R^5 are as defined in claim 1.


R1
Q1
R2
Ar1
Ar2
NY
N
Cx
Het
L
O
Nx
R4
R3