Innovation, Sciences et Développement économique Canada
Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 3041650 A1 2018/05/03

(21) 3 041 650

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

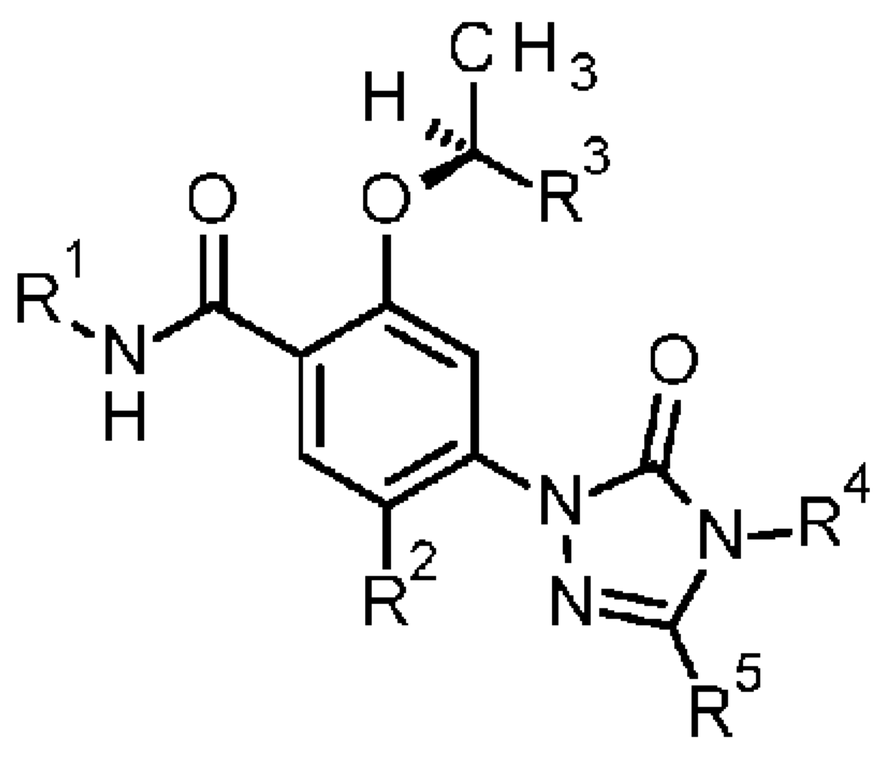
(86) Date de dépôt PCT/PCT Filing Date: 2017/10/25
(87) Date publication PCT/PCT Publication Date: 2018/05/03
(85) Entrée phase nationale/National Entry: 2019/04/24
(86) N° demande PCT/PCT Application No.: EP 2017/077301
(87) N° publication PCT/PCT Publication No.: 2018/077944
(30) Priorité/Priority: 2016/10/27 (CN PCT/CN2016/103642)

(51) Cl.Int./Int.Cl. *C07D 471/04* (2006.01), *A61K 31/4196* (2006.01), *C07D 487/04* (2006.01), *C07D 498/04* (2006.01), *C07D 513/04* (2006.01), *C12N 15/70* (2006.01)

(71) Demandeurs/Applicants:
BAYER AKTIENGESELLSCHAFT, DE;
BAYER PHARMA AKTIENGESELLSCHAFT, DE;
...

(72) Inventeurs/Inventors:
GRADL, STEFAN NIKOLAUS, DE;
NGUYEN, DUY, DE;
EIS, KNUT, DE;
GUENTHER, JUDITH, DE; ...

(54) Titre : 1,2,4-TRIAZOLONES 4,5-ANNELEES
(54) Title: 4,5-ANNULATED 1,2,4-TRIAZOLONES



(I)

(57) Abrégé/Abstract:
The present invention provides triazolone compounds compounds of general formula (I) : in which R^1, R^2, R^3, R^4 and R^5 are as defined herein, methods of preparing said compounds, intermediate compounds useful for preparing said compounds, pharmaceutical compositions and combinations comprising said compounds and the use of said compounds for manufacturing pharmaceutical compositions for the treatment or prophylaxis of diseases, in particular of hyperproliferative disorders, as a sole agent or in combination with other active ingredients.

CA 3041650 A1 2018/05/03

(21) 3 041 650

(13) A1

(71) Demandeurs(suite)/Applicants(continued): THE BROAD INSTITUTE, INC., US;
PRESIDENT AND FELLOWS OF HARVARD COLLEGE, US; THE GENERAL HOSPITAL CORPORATION, US

(72) Inventeurs(suite)/Inventors(continued): STELLFELD, TIMO, DE; JANZER, ANDREAS, DE; CHRISTIAN, SVEN, DE; MUELLER, THOMAS, DE; EL SHEIKH, SHERIF, DE; ZHOU, HAN JIE, CN; ZHAO, CHANGJIA, CN; SYKES, DAVID B, US; FERRARA, STEVEN JAMES, US; LIU, KERY, CN; HERBERT, SIMON ANTHONY, DE; MERZ, CLAUDIA, DE; NIEHUES, MICHAEL, DE; NISING, CARL FRIEDRICH, DE; SCHAFER, MARTINA, DE; ZIMMERMANN, KATJA, DE; KNAEBLEIN, JORG, DE; THEDE, KAI, DE; FAUPEL, THOMAS, DE

(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
03 May 2018 (03.05.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/077944 A3

(51) International Patent Classification:
C07D 471/04 (2006.01) *C07D 498/04* (2006.01)
A61K 31/4196 (2006.01) *C07D 513/04* (2006.01)
C07D 487/04 (2006.01) *C12N 15/70* (2006.01)

(21) International Application Number:
PCT/EP2017/077301

(22) International Filing Date:
25 October 2017 (25.10.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/CN2016/103642
27 October 2016 (27.10.2016) CN

(71) Applicants: **BAYER AKTIENGESELLSCHAFT** [DE/DE]; Kaiser-Wilhelm-Allee 1, 51373 Leverkusen (DE). **BAYER PHARMA AKTIENGESELLSCHAFT** [DE/DE]; Müllerstr. 178, 13353 Berlin (DE). **THE BROAD INSTITUTE, INC.** [US/US]; 415 Main Street Cambridge, Massachusetts, 02142 (US). **PRESIDENT AND FELLOWS OF HARVARD COLLEGE** [US/US]; 17, Quincy Street Cambridge, Massachusetts, 02138 (US). **THE GENERAL HOSPITAL CORPORATION** [US/US]; 55 Fruit Street Boston, Massachusetts, 02114 (US).

(72) Inventors: **GRADL, Stefan, Nikolaus**; Rudolf-Ditzen-Weg 18/20, 13156 Berlin (DE). **NGUYEN, Duy**; Heinrich-Heine-Straße 27, 10179 Berlin (DE). **EIS, Knut**; Fichtenweg 1, 13587 Berlin (DE). **GUENTHER, Judith**; Parkstr. 60, 13187 Berlin (DE). **STELLFELD, Timo**; Johannisberger Str. 67, 14197 Berlin (DE). **JANZER, Andreas**; Schliemannstraße 17, 10437 Berlin (DE). **CHRISTIAN, Sven**; Scharnhorststrasse 16, 10115 Berlin (DE). **MUELLER, Thomas**; Parkstrasse 24, 40764 Langenfeld (DE). **EL SHEIKH, Sherif**; Quellenstr. 74, 45481 Mülheim/Ruhr (DE). **ZHOU, Han, Jie**; 830 Argus CT, Foster City, 94404 (CN). **ZHAO, Changjia**; 14th Street, Room 202, Unit 2, Huilongsen Park, No 99, Kechuang, 14th Street Beijing Economic-Technological Development Area, Beijing, 101111 (CN). **SYKES, David B**; 83 Plymouth Street, Cambridge, 02141 (US). **FERRARA, Steven, James**; 27 Whitney Avenue, Cambridge, 02139 (US). **LIU, Kery**; Unit 2-502, Building No. 14, Long Teng Yuan II, Hui Long Guan Town, Chang Ping District, Beijing, 102208 (CN). **HERBERT, Simon, Anthony**; Chausseestraße 88D, 10115 Berlin (DE). **MERZ, Claudia**; Wunsiedeler Weg 37, 12247 Berlin (DE). **NIEHUES, Michael**; Albestraße 19, 12159 Berlin (DE). **NISING, Carl, Friedrich**; Sybelstraße 35, 10629 Berlin (DE). **SCHÄFER, Martina**; Gurnemanzpfad 77, 13465 Berlin (DE). **ZIMMERMANN, Katja**; Bockumer Str. 370, 40489 Düsseldorf (DE). **KNAEBLEIN, Jörg**; Wasgenstr. 61, 14129 Berlin (DE). **THEDE, Kai**; Stargarder Straße 62, 10437 Berlin (DE). **FAUPEL, Thomas**; Willmanndamm 7, 10827 Berlin (DE).

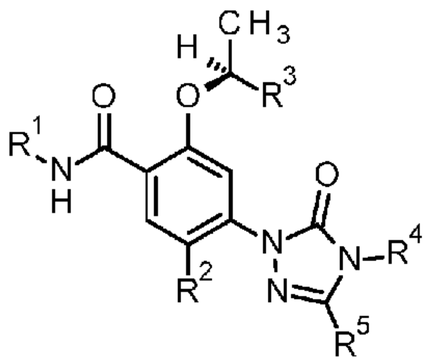
(74) Agent: **BIP PATENTS**; Alfred-Nobel-Str. 10, 40789 Monheim am Rhein NRW (DE).

(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, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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

WO 2018/077944 A3

(54) Title: 4,5-ANNULATED 1,2,4-TRIAZOLONES



(I)

(57) Abstract: The present invention provides triazolone compounds compounds of general formula (I) : in which R^1, R^2, R^3, R^4 and R^5 are as defined herein, methods of preparing said compounds, intermediate compounds useful for preparing said compounds, pharmaceutical compositions and combinations comprising said compounds and the use of said compounds for manufacturing pharmaceutical compositions for the treatment or prophylaxis of diseases, in particular of hyperproliferative disorders, as a sole agent or in combination with other active ingredients.

[Continued on next page]

WO 2018/077944 A3

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))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:

14 June 2018 (14.06.2018)

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	449

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	449

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

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

4,5-ANNULATED 1,2,4-TRIAZOLONES

The present invention provides 4,5-a-annulated 1,2,4-triazolone compounds of general formula (I) as described and defined herein, methods of preparing said compounds, intermediate compounds useful for preparing said compounds, pharmaceutical compositions and combinations comprising said compounds, and the use of said compounds for manufacturing pharmaceutical compositions for the treatment or prophylaxis of diseases, in particular of hyperproliferative and/or inflammatory disorders, as a sole agent or in combination with other active ingredients.

BACKGROUND

The present invention provides 4,5-annulated 1,2,4-triazolone compounds of general formula (I) which inhibit Dihydroorotate Dehydrogenase (DHODH).

Acute myeloid leukemia (AML) is the most common acute leukemia in humans with a 5 year survival of only about 30%. AML is a malignancy of the myeloid line of blood cells. The incidence rates and chances of cure are highly age dependent. The chemotherapy standard of care for AML has not changed significantly over the last decades highlighting the need for novel therapies. A major hallmark of AML is differentiation arrest of the leukemic cells at early stages of cellular differentiation. The potential of leukemic differentiation therapy can be seen with the success of ATRA or arsenic trioxide inducing differentiation in acute promyelocytic leukemia (APL). Around 10% of AML belong to the APL subtype where leukemic cells are harbouring a chromosomal translocation resulting in fusions of oncoproteins involving the retinoic acid receptor. While treatment with ATRA or arsenic trioxide leads to a dramatic increase of patient survival, with overall survival rates of over 70%, unfortunately a comparable differentiation therapy for the non-APL AMLs is lacking (Management of acute promyelocytic leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet, Sanz M.A. et al, Blood 2009, 113(9), 1875-1891). Therefore new therapies inducing differentiation of AML cells are of high interest and medical need.

<u>Dihydroorotate Dehydrogenase (DHODH)</u>

DHODH is located in the mitochondria and the enzyme responsible for the 4th and rate limiting step in de novo pyrimidine synthesis converting dihydroorotate to orotate (Dihydroorotat-ubiquinone oxidoreductase links mitochondria in the biosynthesis of pyrimidine nucleotides, Löffler M. et al, Molecular and Cellular Biochemistry 1997, 174, 125-129).

As pyrimdine production is essential for DNA and RNA synthesis DHODH is highly important for cellular proliferation. The enzyme is considered an attractive drug target for cancer, immunological, parasitic and viral diseases and DHODH small molecule inhibitors like Leflunomide/Teriflunomide and Brequinar have been approved for clinical use in Rheumatoid

Arthritis and Multiple Sclerosis. Additionally, preclinical studies indicate that DHODH inhibitors may be useful for the treatment of haematological cancer indications, for the treatment of solid tumors (e.g., neuroblastoma, melanoma, colon, breast and lung tumors), for the treatment of parasitic diseases (e.g., malaria), and for viral disease therapy.

US 6444613 B1 relates to the field of defoliants, in particular thidiazuron-comprising mixtures, and their use in crops of cotton. These mixtures comprise among others 2,4,5-trisubstituted 1,2,4-triazolone compounds as herbicides, which inhibit the enzyme protoporphyrinogen-(IX) oxidase (PPO inhibitors).

WO199802422 describes substituted aromatic carbonyl compounds, among others 2,4,5-trisubstituted 1,2,4-triazolone compounds, as herbicides.

From CN106543139 some triazolone compounds are known as agrochemicals.

US 2016/0251341 A1 describes triazole compounds as serine protease inhibitors useful for the inhibition of thrombin and/or kallikrein.

WO 2013/186692 A1 describes triazolone compounds as mPGES-1 inhibitors, useful in the treatment of pain and/or inflammation from a variety of diseases or conditions, such as asthma, osteoarthritis, rheumatoid arthritis, acute or chronic pain and neurodegenerative diseases.

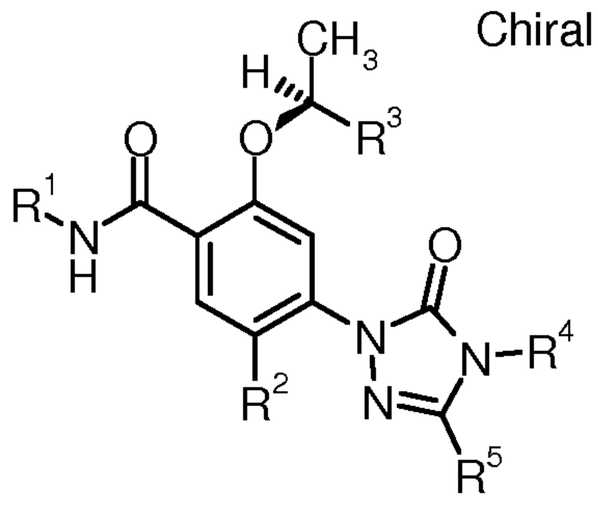
WO2010/077686 A1 describes sirtuin-modulating compounds, e.g. isoindolinone and related compounds, and methods of use thereof. The sirtuin-modulating compounds may be used for increasing the lifespan of a cell, and treating and/or preventing a wide variety of diseases and disorders including, for example, diseases or disorders related to aging or stress, diabetes, obesity, neurodegenerative diseases, cardiovascular disease, blood clotting disorders, inflammation, cancer, and/or flushing as well as diseases or disorders that would benefit from increased mitochondrial activity.

DESCRIPTION of the INVENTION

It has now been found, and this partially constitutes the basis of the present invention, that the compounds of the present invention (e.g., 4,5-annulated 1,2,4-triazolone compounds of general formula (I)) have surprising and advantageous properties.

In particular, the compounds of the present invention have surprisingly been found to effectively inhibit DHODH and may therefore be used for the treatment or prophylaxis of disease including hyperproliferative and/or inflammatory disorders, such as cancer, for example.

In accordance with one aspect, the present invention provides compounds of general formula (I):



(I),

in which

R^1 represents a group selected from

a C_1-C_8-alkyl group, which is optionally substituted with a group selected from

C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times with one or more substituents independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_8-haloalkyl group,

a C_3-C_8-cycloalkyl group, whch is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenyl group and a -$N(R^7)(R^8)$ group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group,

a -(C_1-C_6-alkyl)-C(=O)$N(R^7)(R^8)$ group,

a 4- to 7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a-C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -$S(=O)_2$(C_1-C_6-alkyl) group and a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8)

and

a monocyclic or bicyclic heteroaryl group which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a halogen atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group,

a C_3-C_8-cycloalkyl group,

a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group,

a C_2-C_6-alkenyl group,

a C_2-C_6-alkinyl group,

a C_4-C_8-cycloalkenyl group,

a (C_1-C_6-alkyl)-N(R^7)R^8 group,

a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group,

a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,

a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group, wherein

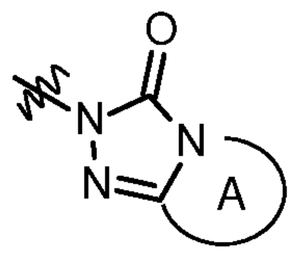
said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group and , wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,

and

a phenyl group,

which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

R^4 and R^5 jointly form a 5- to 6-membered, optionally unsaturated, heterocyclic ring A of partial formula (i)



(i)

whereby ring A in addition to the two mandatory atoms, the nitrogen atom and the carbon atom bridging the two rings, bears additional 3 to 6 members selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -S(=O)(=NR^{14})-, -N=, -N(R^7)-, -C(=O)-, -CH=, -CR^{11}=, -C(R^{12})$_2$-, -C(H)(R^{13})-,

R^6 represents a hydrogen atom or a group selected from

a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-hydroxyalkyl group, a haloalkyl group, a aryl group, a (C_1-C_6-alkyl)-aryl group, and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_6-alkyl, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), and -C(=O)OR^6-,

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

R^{15} represents a group selected from

a C_1-C_6-alkyl group and a benzyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

DEFINITIONS

The term “substituted” means that one or more hydrogen atoms on the designated atom or group are replaced with a selection from the indicated group, provided that the designated atom's normal valency under the existing circumstances is not exceeded. Combinations of substituents and/or variables are permissible.

The term “optionally substituted” means that the number of substituents can be equal to or different from zero. Unless otherwise indicated, it is possible that optionally substituted groups are substituted with as many optional substituents as can be accommodated by replacing a hydrogen atom with a non-hydrogen substituent on any available carbon or nitrogen atom. Commonly, it is possible for the number of optional substituents, when present, to be 1, 2, 3, 4 or 5, in particular 1, 2 or 3.

As used herein, the term “one or more”, *e.g.* in the definition of the substituents of the compounds of general formula (I) of the present invention, means “1, 2, 3, 4 or 5, particularly 1, 2, 3 or 4, more particularly 1, 2 or 3, even more particularly 1 or 2”.

As used herein, an oxo substituent represents an oxygen atom, which is bound to a carbon atom or to a sulfur atom via a double bond.

The term “ring substituent” means a substituent attached to an aromatic or nonaromatic ring which replaces an available hydrogen atom on the ring.

Should a composite substituent be composed of more than one parts, *e.g.* (C_1-C_3-alkoxy)-(C_1-C_6-alkyl)-, it is possible for the position of a given part to be at any suitable position of said composite substituent, *i.e.* the C_1-C_3-alkoxy part can be attached to any carbon atom of the C_1-C_6-alkyl part of said (C_1-C_3-alkoxy)-(C_1-C_6alkyl)- group. A hyphen at the beginning or at the end of such a composite substituent indicates the point of attachment of said composite substituent to the rest of the molecule. Should a ring, comprising carbon atoms and optionally one or more heteroatoms, such as nitrogen, oxygen or sulfur atoms for example, be substituted with a substituent, it is possible for said substituent to be bound at any suitable position of said ring, be it bound to a suitable carbon atom and/or to a suitable heteroatom.

The term “comprising” when used in the specification includes “consisting of”.

If within the present text any item is referred to as “as mentioned herein”, it means that it may be mentioned anywhere in the present text.

The terms as mentioned in the present text have the following meanings:

The term “halogen atom” means a fluorine, chlorine, bromine or iodine atom, particularly a fluorine, chlorine or bromine atom.

The term “C_1-C_8-alkyl” means a linear or branched, saturated, monovalent hydrocarbon group having 1, 2, 3, 4, 5 or 6 carbon atoms, *e.g.* a methyl, ethyl, propyl, isopropyl, butyl, *sec*-butyl, isobutyl, *tert*-butyl, pentyl, isopentyl, 2-methylbutyl, 1-methylbutyl, 1-ethylpropyl, 1,2-dimethylpropyl, *neo*-pentyl, 1,1-dimethylpropyl, hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1-ethylbutyl, 2-ethylbutyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 2,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, heptyl or octyl group, or an isomer thereof. Particularly, said group has 1, 2, 3, 4, 5 or 6 carbon atoms (“C_1-C_6-alkyl”), *e.g.* a methyl, ethyl, propyl, isopropyl, butyl, *sec*-butyl, isobutyl, *tert*-butyl, pentyl, isopentyl, 2-methylbutyl, 1-methylbutyl, 1-ethylpropyl, 1,2-dimethylpropyl, *neo*-pentyl, 1,1-dimethylpropyl, hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1-ethylbutyl, 2-ethylbutyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 2,3-dimethylbutyl, 1,2-dimethylbutyl or 1,3-dimethylbutyl group. Particularly, said group has 1, 2, 3 or 4 carbon atoms (“C_1-C_4-alkyl”), *e.g.* a methyl, ethyl, propyl, isopropyl, butyl, sec-butyl isobutyl, or *tert*-butyl group, more particularly 1, 2 or 3 carbon atoms (“C_1-C_3-alkyl”), *e.g.* a methyl, ethyl, *n*-propyl or isopropyl group.

The term “C_1-C_6-hydroxyalkyl” means a linear or branched, saturated, monovalent hydrocarbon group in which the term “C_1-C_6-alkyl” is defined *supra*, and in which 1 or 2 hydrogen atoms are replaced with a hydroxy group, *e.g.* a hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 1,2-dihydroxyethyl, 3-hydroxypropyl, 2-hydroxypropyl, 1-hydroxypropyl, 1-hydroxypropan-2-yl, 2-hydroxypropan-2-yl, 2,3-dihydroxypropyl, 1,3-dihydroxypropan-2-yl, 3-hydroxy-2-methylpropyl, 2-hydroxy-2-methyl-propyl, 1-hydroxy-2-methyl-propyl group. Particularly, said group has 1, 2 or 3 carbon atoms (“C_1-C_3-hydroxyalkyl”), *e.g.* a hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 1,2-dihydroxyethyl, 3-hydroxypropyl, 2-hydroxypropyl, 1-hydroxypropyl, 1-hydroxypropan-2-yl, 2-hydroxypropan-2-yl, 2,3-dihydroxypropyl or 1,3-dihydroxypropan-2-yl group.

The term “C_1-C_6-alkylsulfanyl” means a linear or branched, saturated, monovalent group of formula (C_1-C_6-alkyl)-S-, in which the term “C_1-C_6-alkyl” is as defined *supra*, *e.g.* a methylsulfanyl, ethylsulfanyl, propylsulfanyl, isopropylsulfanyl, butylsulfanyl, *sec*-butylsulfanyl, isobutylsulfanyl, *tert*-butylsulfanyl, pentylsulfanyl, isopentylsulfanyl, hexylsulfanyl group.

The term “C_2-C_8-haloalkyl” means a linear or branched, saturated, monovalent hydrocarbon group in which the term “C_2-C_8-alkyl” is as defined *supra*, and in which one or more of the

hydrogen atoms are replaced, identically or differently, with a halogen atom. Particularly, said halogen atom is a fluorine atom. Said C_2-C_8-haloalkyl group is, for example, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 3,3,3-trifluoropropyl or 1,3-difluoropropan-2-yl. Particularly, said group has 2, 3, 4 5 or 6 carbon atoms ("C_2-C_6-haloalkyl").

The term "C_1-C_6-haloalkyl" means a linear or branched, saturated, monovalent hydrocarbon group in which the term "C_1-C_6-alkyl" is as defined *supra*, and in which one or more of the hydrogen atoms are replaced, identically or differently, with a halogen atom. Particularly, said halogen atom is a fluorine atom. Said C_1-C_6-haloalkyl group is, for example, fluoromethyl, difluoromethyl, trifluoromethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 3,3,3-trifluoropropyl or 1,3-difluoropropan-2-yl. Particularly, said group has 1, 2, 3 or 4 carbon atoms ("C_1-C_4-haloalkyl"), more particularly 1, 2 or 3 carbon atoms ("C_1-C_3-haloalkyl"), *e.g.* fluoromethyl, difluoromethyl, trifluoromethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 3,3,3-trifluoropropyl or 1,3-difluoropropan-2-yl.

The term "C_1-C_6-alkoxy" means a linear or branched, saturated, monovalent group of formula (C_1-C_6-alkyl)-O-, in which the term "C_1-C_6-alkyl" is as defined *supra*, *e.g.* a methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, *sec*-butoxy, isobutoxy, *tert*-butoxy, pentyloxy, isopentyloxy or *n*-hexyloxy group, or an isomer thereof. Particularly, said group has 1, 2 or 3 carbon atoms ("C_1-C_3-alkoxy"), *e.g.* a methoxy, ethoxy, *n*-propoxy or isopropoxy group.

The term "C_1-C_6-haloalkoxy" means a linear or branched, saturated, monovalent C_1-C_6-alkoxy group, as defined *supra*, in which one or more of the hydrogen atoms is replaced, identically or differently, with a halogen atom. Particularly, said halogen atom is a fluorine atom. Said C_1-C_6-haloalkoxy group is, for example, fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy or pentafluoroethoxy. Particularly, said group has 1, 2 or 3 carbon atoms ("C_1-C_3-haloalkoxy"), *e.g.* a fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy or pentafluoroethoxy group.

The term "C_2-C_6-alkenyl" means a linear or branched, monovalent hydrocarbon group, which contains one double bond, and which has 2, 3, 4, 5 or 6 carbon atoms, particularly 2 or 3 carbon atoms ("C_2-C_3-alkenyl"), it being understood that in the case in which said alkenyl group contains more than one double bond, then it is possible for said double bonds to be isolated from, or conjugated with, each other. Said alkenyl group is, for example, an ethenyl (or "vinyl"), prop-2-en-1-yl (or "allyl"), prop-1-en-1-yl, but-3-enyl, but-2-enyl, but-1-enyl, pent-4-enyl, pent-3-enyl, pent-2-enyl, pent-1-enyl, hex-5-enyl, hex-4-enyl, hex-3-enyl, hex-2-enyl, hex-1-enyl, prop-1-en-2-yl (or "isopropenyl"), 2-methylprop-2-enyl, 1-methylprop-2-enyl, 2-methylprop-1-enyl, 1-methylprop-1-enyl, 3-methylbut-3-enyl, 2-methylbut-3-enyl, 1-methylbut-3-enyl, 3-methylbut-2-enyl, 2-methylbut-2-enyl, 1-methylbut-2-enyl,

3-methylbut-1-enyl, 2-methylbut-1-enyl, 1-methylbut-1-enyl, 1,1-dimethylprop-2-enyl, 1-ethylprop-1-enyl, 1-propylvinyl, 1-isopropylvinyl, 4-methylpent-4-enyl, 3-methylpent-4-enyl, 2-methylpent-4-enyl, 1-methylpent-4-enyl, 4-methylpent-3-enyl, 3-methylpent-3-enyl, 2-methylpent-3-enyl, 1-methylpent-3-enyl, 4-methylpent-2-enyl, 3-methylpent-2-enyl, 2-methylpent-2-enyl, 1-methylpent-2-enyl, 4-methylpent-1-enyl, 3-methylpent-1-enyl, 2-methylpent-1-enyl, 1-methylpent-1-enyl, 3-ethylbut-3-enyl, 2-ethylbut-3-enyl, 1-ethylbut-3-enyl, 3-ethylbut-2-enyl, 2-ethylbut-2-enyl, 1-ethylbut-2-enyl, 3-ethylbut-1-enyl, 2-ethylbut-1-enyl, 1-ethylbut-1-enyl, 2-propylprop-2-enyl, 1-propylprop-2-enyl, 2-isopropylprop-2-enyl, 1-isopropylprop-2-enyl, 2-propylprop-1-enyl, 1-propylprop-1-enyl, 2-isopropylprop-1-enyl, 1-isopropylprop-1-enyl, 3,3-dimethylprop-1-enyl, or 1-(1,1-dimethylethyl)ethenyl group. Particularly, said group is allyl.

The term "C_2-C_6-alkynyl" means a linear or branched, monovalent hydrocarbon group which contains one triple bond, and which contains 2, 3, 4, 5 or 6 carbon atoms, particularly 2 or 3 carbon atoms ("C_2-C_3-alkynyl"). Said C_2-C_6-alkynyl group is, for example, ethynyl, prop-1-ynyl, prop-2-ynyl (or "propargyl"), but-1-ynyl, but-2-ynyl, but-3-ynyl, pent-1-ynyl, pent-2-ynyl, pent-3-ynyl, pent-4-ynyl, hex-1-ynyl, hex-2-ynyl, hex-3-ynyl, hex-4-ynyl, hex-5-ynyl, 1-methylprop-2-ynyl, 2-methylbut-3-ynyl, 1-methylbut-3-ynyl, 1-methylbut-2-ynyl, 3-methylbut-1-ynyl, 1-ethylprop-2-ynyl, 3-methylpent-4-ynyl, 2-methylpent-4-ynyl, 1-methylpent-4-ynyl, 2-methylpent-3-ynyl, 1-methylpent-3-ynyl, 4-methylpent-2-ynyl, 1-methylpent-2-ynyl, 4-methylpent-1-ynyl, 3-methylpent-1-ynyl, 2-ethylbut-3-ynyl, 1-ethylbut-3-ynyl, 1-ethylbut-2-ynyl, 1-propylprop-2-ynyl, 1-isopropylprop-2-ynyl, 2,2-dimethylbut-3-ynyl, 1,1-dimethylbut-3-ynyl, 1,1-dimethylbut-2-ynyl or 3,3-dimethylbut-1-ynyl group.

The term "C_3-C_8-cycloalkyl" means a saturated, monovalent, mono- or bicyclic hydrocarbon ring which contains 3, 4, 5, 6, 7 or 8 carbon atoms ("C_3-C_8-cycloalkyl"). Said C_3-C_8-cycloalkyl group is for example, a monocyclic hydrocarbon ring, *e.g.* a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl group, or a bicyclic hydrocarbon ring, *e.g.* a bicyclo[4.2.0]octyl or octahydropentalenyl. Particularly, said group contains 3, 4, 5 or 6 carbon atoms ("C_3-C_6-cycloalkyl"), *e.g.* a cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl group. Particularly, said group contains 4, 5, 6, 7 or 8 carbon atoms ("C_4-C_8-cycloalkyl")., *e.g.* a cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl group.

The term "C_4-C_8-cycloalkenyl" means a monovalent, mono- or bicyclic hydrocarbon ring which contains 4, 5, 6, 7 or 8 carbon atoms and one double bond. Particularly, said ring contains 4, 5 or 6 carbon atoms ("C_4-C_6-cycloalkenyl"). Said C_4-C_8-cycloalkenyl group is for example, a monocyclic hydrocarbon ring, *e.g.* a cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl or cyclooctenyl group, or a bicyclic hydrocarbon ring, *e.g.* a bicyclo[2.2.1]hept-2-enyl or bicyclo[2.2.2]oct-2-enyl.

The term "C_3-C_8-cycloalkoxy" means a saturated, monovalent, mono- or bicyclic group of formula (C_3-C_8-cycloalkyl)-O-, which contains 3, 4, 5, 6, 7 or 8 carbon atoms, in which the term "C_3-C_8-cycloalkyl" is defined *supra*, *e.g.* a cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy or cyclooctyloxy group. Particularly, said group has 3, 4, 5 or 6 carbon atoms ("C_3-C_6-cycloalkoxy"), *e.g.* a cyclopropyloxy, cyclobutyloxy, cyclopentyloxy or cyclohexyloxy group.

The terms "4- to 7-membered heterocycloalkyl" and "4- to 6-membered heterocycloalkyl" mean a monocyclic, saturated heterocycle with 4, 5, 6 or 7 or, respectively, 4, 5 or 6 ring atoms in total, which contains one or two identical or different ring heteroatoms from the series N, O and S.

Said heterocycloalkyl group, without being limited thereto, can be a 4-membered ring, such as azetidinyl, oxetanyl or thietanyl, for example; or a 5-membered ring, such as tetrahydrofuranyl, 1,3-dioxolanyl, thiolanyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, 1,1-dioxidothiolanyl, dioxidotetrahydrothiopyranyl, 1,2-oxazolidinyl, 1,3-oxazolidinyl or 1,3-thiazolidinyl, for example; or a 6-membered ring, such as tetrahydropyranyl, tetrahydrothiopyranyl, piperidinyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl, 1,3-dioxanyl, 1,4-dioxanyl or 1,2-oxazinanyl, for example, or a 7-membered ring, such as azepanyl, 1,4-diazepanyl or 1,4-oxazepanyl, for example.

The terms "4- to 7-membered nitrogen containing heterocycloalkyl" and "4- to 6-membered nitrogen containing heterocycloalkyl" mean a monocyclic, saturated heterocycle with 4, 5, 6 or 7 or, respectively, 4, 5 or 6 ring atoms in total, containing one ring nitrogen atom and optionally one further ring heteroatom from the series: N, O, S. atom.

Said nitrogen containing heterocycloalkyl group, without being limited thereto, can be a 4-membered ring, such as azetidinyl for example; or a 5-membered ring, such as pyrrolidinyl, imidazolidinyl, pyrazolidinyl, 1,2-oxazolidinyl, 1,3-oxazolidinyl or 1,3-thiazolidinyl, for example; or a 6-membered ring, such as piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl or 1,2-oxazinanyl, for example, or a 7-membered ring, such as azepanyl, 1,4-diazepanyl or 1,4-oxazepanyl, for example.

The term "5- to 7-membered heterocycloalkenyl" means a monocyclic, unsaturated, non-aromatic heterocycle with 5, 6 or 7 ring atoms in total, which contains one or two double bonds and one or two identical or different ring heteroatoms from the series: N, O, S.

Said heterocycloalkenyl group is, for example, 4H-pyranyl, 2H-pyranyl, 2,5-dihydro-1H-pyrrolyl, [1,3]dioxolyl, 4H-[1,3,4]thiadiazinyl, 2,5-dihydrofuranyl, 2,3-dihydrofuranyl, 2,5-dihydrothiophenyl, 2,3-dihydrothiophenyl, 4,5-dihydrooxazolyl or 4H-[1,4]thiazinyl.

The term "4-7-membered, optionally unsaturated, heterocyclic group" includes the terms "4- to 7-membered heterocycloalkyl" and "5- to 7-membered heterocycloalkenyl".

The term “aryl” includes aromatic ring systems being mono- or bicyclic, especially phenyl and naphthyl.

The term “phenyl groups of which two vicinal substituents may form together a 5- or 6-membered, optionally aromatic or non-aromatic ring, and optionally containing a C(=O) group” and sepecially includes naphthalinyl, indanyl and tetralinyl.

The term “heteroaryl” means a monovalent, monocyclic or bicyclic aromatic ring having 5, 6, 8, 9 or 10 ring atoms (a “5- to 10-membered heteroaryl” group), particularly 5, 6, 9 or 10 ring atoms, which contains at least one ring heteroatom and optionally one, two or three further ring heteroatoms from the series: N, O and/or S, and which is bound via a ring carbon atom or optionally via a ring nitrogen atom (if allowed by valency).

Said heteroaryl group can be a 5-membered heteroaryl group, such as, for example, thienyl, furanyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl or tetrazolyl; or a 6-membered heteroaryl group, such as, for example, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl or triazinyl; or a 9-membered heteroaryl group, such as, for example, benzofuranyl, benzothienyl, benzoxazolyl, benzisoxazolyl, benzimidazolyl, benzothiazolyl, benzotriazolyl, indazolyl, indolyl, isoindolyl, indolizinyl or purinyl; or a 10-membered heteroaryl group, such as, for example, quinolinyl, quinazolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinoxalinyl or pteridinyl.

In general, and unless otherwise mentioned, the heteroaryl or heteroarylene groups include all possible isomeric forms thereof, *e.g.*: tautomers and positional isomers with respect to the point of linkage to the rest of the molecule. Thus, for some illustrative non-restricting examples, the term pyridinyl includes pyridin-2-yl, pyridin-3-yl and pyridin-4-yl; or the term thienyl includes thien-2-yl and thien-3-yl.

The term “C_1-C_6”, as used in the present text, *e.g.* in the context of the definition of “C_1-C_6-alkyl”, “C_1-C_6-haloalkyl”, “C_1-C_6-hydroxyalkyl”, “C_1-C_6-alkoxy” or “C_1-C_6-haloalkoxy” means an alkyl group having a finite number of carbon atoms of 1 to 6, *i.e.* 1, 2, 3, 4, 5 or 6 carbon atoms.

Further, as used herein, the term “C_3-C_8”, as used in the present text, *e.g.* in the context of the definition of “C_3-C_8-cycloalkyl”, means a cycloalkyl group having a finite number of carbon atoms of 3 to 8, *i.e.* 3, 4, 5, 6, 7 or 8 carbon atoms.

When a range of values is given, said range encompasses each value and sub-range within said range.

For example:

"C_1-C_8" encompasses C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_1-C_8, C_1-C_7, C_1-C_6, C_1-C_5, C_1-C_4, C_1-C_3, C_1-C_2, C_2-C_8, C_2-C_7, C_2-C_6, C_2-C_5, C_2-C_4, C_2-C_3, C_3-C_8, C_3-C_7, C_3-C_6, C_3-C_5, C_3-C_4, C_4-C_8, C_4-C_7, C_4-C_6, C_4-C_5, C_5-C_8, C_5-C_7, C_5-C_6, C_6-C_8, C_6-C_7 and C_7-C_8;

"C_1-C_6" encompasses C_1, C_2, C_3, C_4, C_5, C_6, C_1-C_6, C_1-C_5, C_1-C_4, C_1-C_3, C_1-C_2, C_2-C_6, C_2-C_5, C_2-C_4, C_2-C_3, C_3-C_6, C_3-C_5, C_3-C_4, C_4-C_6, C_4-C_5, and C_5-C_6;

"C_1-C_4" encompasses C_1, C_2, C_3, C_4, C_1-C_4, C_1-C_3, C_1-C_2, C_2-C_4, C_2-C_3 and C_3-C_4;

"C_1-C_3" encompasses C_1, C_2, C_3, C_1-C_3, C_1-C_2 and C_2-C_3;

"C_2-C_6" encompasses C_2, C_3, C_4, C_5, C_6, C_2-C_6, C_2-C_5, C_2-C_4, C_2-C_3, C_3-C_6, C_3-C_5, C_3-C_4, C_4-C_6, C_4-C_5, and C_5-C_6;

"C_3-C_8" encompasses C_3, C_4, C_5, C_6, C_7, C_8, C_3-C_8, C_3-C_7, C_3-C_6, C_3-C_5, C_3-C_4, C_4-C_8, C_4-C_7, C_4-C_6, C_4-C_5, C_5-C_8, C_5-C_7, C_5-C_6, C_6-C_8, C_6-C_7 and C_7-C_8;

"C_3-C_6" encompasses C_3, C_4, C_5, C_6, C_3-C_6, C_3-C_5, C_3-C_4, C_4-C_6, C_4-C_5, and C_5-C_6;

"C_4-C_8" encompasses C_4, C_5, C_6, C_7, C_8, C_4-C_8, C_4-C_7, C_4-C_6, C_4-C_5, C_5-C_8, C_5-C_7, C_5-C_6, C_6-C_8, C_6-C_7 and C_7-C_8;

"C_4-C_7" encompasses C_4, C_5, C_6, C_7, C_4-C_7, C_4-C_6, C_4-C_5, C_5-C_7, C_5-C_6 and C_6-C_7;

"C_4-C_6" encompasses C_4, C_5, C_6, C_4-C_6, C_4-C_5 and C_5-C_6;

"C_5-C_{10}" encompasses C_5, C_6, C_7, C_8, C_9, C_{10}, C_5-C_{10}, C_5-C_9, C_5-C_8, C_5-C_7, C_5-C_6, C_6-C_{10}, C_6-C_9, C_6-C_8, C_6-C_7, C_7-C_{10}, C_7-C_9, C_7-C_8, C_8-C_{10}, C_8-C_9 and C_9-C_{10};

"C_6-C_{10}" encompasses C_6, C_7, C_8, C_9, C_{10}, C_6-C_{10}, C_6-C_9, C_6-C_8, C_6-C_7, C_7-C_{10}, C_7-C_9, C_7-C_8, C_8-C_{10}, C_8-C_9 and C_9-C_{10}.

As used herein, the term “leaving group” means an atom or a group of atoms that is displaced in a chemical reaction as stable species taking with it the bonding electrons. In particular, such a leaving group is selected from the group comprising: halide, in particular fluoride, chloride, bromide or iodide, (methylsulfonyl)oxy, [(trifluoromethyl)sulfonyl]oxy, [(nonafluorobutyl)-sulfonyl]oxy, (phenylsulfonyl)oxy, [(4-methylphenyl)sulfonyl]oxy, [(4-bromophenyl)sulfonyl]oxy, [(4-nitrophenyl)sulfonyl]oxy, [(2-nitrophenyl)sulfonyl]oxy, [(4-isopropylphenyl)sulfonyl]oxy, [(2,4,6-triisopropylphenyl)sulfonyl]oxy, [(2,4,6-trimethylphenyl)sulfonyl]oxy, [(4-*tert*-butyl-phenyl)sulfonyl]oxy and [(4-methoxyphenyl)sulfonyl]oxy.

The term “substituent” refers to a group “substituted” on, e.g., an alkyl, haloalkyl, cycloalkyl, heterocyclyl, heterocycloalkenyl, cycloalkenyl, aryl, or heteroaryl group at any atom of that group, replacing one or more hydrogen atoms therein. In one aspect, the substituent(s) on a group are independently any one single, or any combination of two or more of the permissible atoms or groups of atoms delineated for that substituent. In another aspect, a substituent may

itself be substituted with any one of the above substituents. Further, as used herein, the phrase "optionally substituted" means unsubstituted (e.g., substituted with an H) or substituted.

It will be understood that the description of compounds herein is limited by principles of chemical bonding known to those skilled in the art. Accordingly, where a group may be substituted by one or more of a number of substituents, such substitutions are selected so as to comply with principles of chemical bonding with regard to valencies, etc., and to give compounds which are not inherently unstable. For example, any carbon atom will be bonded to two, three, or four other atoms, consistent with the four valence electrons of carbon.

By "subject" is meant a mammal, including, but not limited to, a human or non-human mammal, such as a bovine, equine, canine, ovine, rodent, or feline

It is possible for the compounds of general formula (I) to exist as isotopic variants. The invention therefore includes one or more isotopic variant(s) of the compounds of general formula (I), particularly deuterium-containing compounds of general formula (I).

The term "isotopic variant" of a compound or a reagent is defined as a compound exhibiting an unnatural proportion of one or more of the isotopes that constitute such a compound.

The expression "unnatural proportion" in relation to an isotope means a proportion of such isotope which is higher than its natural abundance. The natural abundances of isotopes to be applied in this context are described in "Isotopic Compositions of the Elements 1997", Pure Appl. Chem., 70(1), 217-235, 1998.

Examples of such isotopes include stable and radioactive isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, chlorine, bromine and iodine, such as ^{2}H (deuterium), ^{3}H (tritium), ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{17}O, ^{18}O, ^{32}P, ^{33}P, ^{33}S, ^{34}S, ^{35}S, ^{36}S, ^{18}F, ^{36}Cl, ^{82}Br, ^{123}I, ^{124}I, ^{125}I, ^{129}I and ^{131}I, respectively.

With respect to the treatment and/or prophylaxis of the disorders specified herein the isotopic variant(s) of the compounds of general formula (I) preferably contain deuterium ("deuterium-containing compounds of general formula (I)"). Isotopic variants of the compounds of general formula (I) in which one or more radioactive isotopes, such as ^{3}H or ^{14}C, are incorporated are useful e.g. in drug and/or substrate tissue distribution studies. These isotopes are particularly preferred for the ease of their incorporation and detectability. Positron emitting isotopes such as ^{18}F or ^{11}C may be incorporated into a compound of general formula (I). These isotopic variants of the compounds of general formula (I) are useful for in vivo imaging applications. Deuterium-containing and ^{13}C-containing compounds of general formula (I) can be used in mass spectrometry analyses in the context of preclinical or clinical studies.

Isotopic variants of the compounds of general formula (I) can generally be prepared by methods known to a person skilled in the art, such as those described in the schemes and/or examples herein, by substituting a reagent for an isotopic variant of said reagent, preferably for

a deuterium-containing reagent. Depending on the desired sites of deuteration, in some cases deuterium from D_2O can be incorporated either directly into the compounds or into reagents that are useful for synthesizing such compounds. Deuterium gas is also a useful reagent for incorporating deuterium into molecules. Catalytic deuteration of olefinic bonds and acetylenic bonds is a rapid route for incorporation of deuterium. Metal catalysts (i.e. Pd, Pt, and Rh) in the presence of deuterium gas can be used to directly exchange deuterium for hydrogen in functional groups containing hydrocarbons. A variety of deuterated reagents and synthetic building blocks are commercially available from companies such as for example C/D/N Isotopes, Quebec, Canada; Cambridge Isotope Laboratories Inc., Andover, MA, USA; and CombiPhos Catalysts, Inc., Princeton, NJ, USA.

The term “deuterium-containing compound of general formula (I)” is defined as a compound of general formula (I), in which one or more hydrogen atom(s) is/are replaced by one or more deuterium atom(s) and in which the abundance of deuterium at each deuterated position of the compound of general formula (I) is higher than the natural abundance of deuterium, which is about 0.015%. Particularly, in a deuterium-containing compound of general formula (I) the abundance of deuterium at each deuterated position of the compound of general formula (I) is higher than 10%, 20%, 30%, 40%, 50%, 60%, 70% or 80%, preferably higher than 90%, 95%, 96% or 97%, even more preferably higher than 98% or 99% at said position(s). It is understood that the abundance of deuterium at each deuterated position is independent of the abundance of deuterium at other deuterated position(s).

The selective incorporation of one or more deuterium atom(s) into a compound of general formula (I) may alter the physicochemical properties (such as for example acidity [C. L. Perrin, et al., J. Am. Chem. Soc., 2007, 129, 4490], basicity [C. L. Perrin et al., J. Am. Chem. Soc., 2005, 127, 9641], lipophilicity [B. Testa et al., Int. J. Pharm., 1984, 19(3), 271]) and/or the metabolic profile of the molecule and may result in changes in the ratio of parent compound to metabolites or in the amounts of metabolites formed. Such changes may result in certain therapeutic advantages and hence may be preferred in some circumstances. Reduced rates of metabolism and metabolic switching, where the ratio of metabolites is changed, have been reported (A. E. Mutlib et al., Toxicol. Appl. Pharmacol., 2000, 169, 102). These changes in the exposure to parent drug and metabolites can have important consequences with respect to the pharmacodynamics, tolerability and efficacy of a deuterium-containing compound of general formula (I). In some cases deuterium substitution reduces or eliminates the formation of an undesired or toxic metabolite and enhances the formation of a desired metabolite (e.g. Nevirapine: A. M. Sharma et al., Chem. Res. Toxicol., 2013, 26, 410; Efavirenz: A. E. Mutlib et al., Toxicol. Appl. Pharmacol., 2000, 169, 102). In other cases the major effect of deuteration is to reduce the rate of systemic clearance. As a result, the biological half-life of the compound is increased. The potential clinical benefits would include the ability to maintain similar systemic

exposure with decreased peak levels and increased trough levels. This could result in lower side effects and enhanced efficacy, depending on the particular compound's pharmacokinetic/ pharmacodynamic relationship. ML-337 (C. J. Wenthur et al., J. Med. Chem., 2013, 56, 5208) and Odanacatib (K. Kassahun et al., WO2012/112363) are examples for this deuterium effect. Still other cases have been reported in which reduced rates of metabolism result in an increase in exposure of the drug without changing the rate of systemic clearance (e.g. Rofecoxib: F. Schneider et al., Arzneim. Forsch. / Drug. Res., 2006, 56, 295; Telaprevir: F. Maltais et al., J. Med. Chem., 2009, 52, 7993). Deuterated drugs showing this effect may have reduced dosing requirements (e.g. lower number of doses or lower dosage to achieve the desired effect) and/or may produce lower metabolite loads.

A compound of general formula (I) may have multiple potential sites of attack for metabolism. To optimize the above-described effects on physicochemical properties and metabolic profile, deuterium-containing compounds of general formula (I) having a certain pattern of one or more deuterium-hydrogen exchange(s) can be selected. Particularly, the deuterium atom(s) of deuterium-containing compound(s) of general formula (I) is/are attached to a carbon atom and/or is/are located at those positions of the compound of general formula (I), which are sites of attack for metabolizing enzymes such as e.g. cytochrome P_{450}.

In another embodiment the present invention concerns a deuterium-containing compound of general formula (I) having 1, 2, 3 or 4 deuterium atoms, particularly with 1, 2 or 3 deuterium atoms.

Where the plural form of the word compounds, salts, polymorphs, hydrates, solvates and the like, is used herein, this is taken to mean also a single compound, salt, polymorph, isomer, hydrate, solvate or the like. The terms “a” or “an,” as used in herein means one or more.

By "stable compound' or "stable structure" is meant a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

The compounds of the present invention optionally contain one or more asymmetric centres, depending upon the location and nature of the various substituents desired. It is possible that one or more asymmetric carbon atoms are present in the (R) or (S) configuration, which can result in racemic mixtures in the case of a single asymmetric centre, and in diastereomeric mixtures in the case of multiple asymmetric centres. In certain instances, it is possible that asymmetry also be present due to restricted rotation about a given bond, for example, the central bond adjoining two substituted aromatic rings of the specified compounds.

Preferred isomers are those which produce the more desirable biological activity. These separated, pure or partially purified isomers or racemic mixtures of the compounds of this

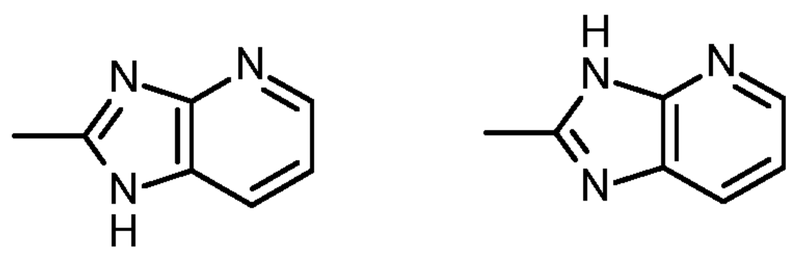
invention are also included within the scope of the present invention. The purification and the separation of such materials can be accomplished by standard techniques known in the art.

The optical isomers can be obtained by resolution of the racemic mixtures according to conventional processes, for example, by the formation of diastereoisomeric salts using an optically active acid or base or formation of covalent diastereomers. Examples of appropriate acids are tartaric, diacetyltartaric, ditoluoyltartaric and camphorsulfonic acid. Mixtures of diastereoisomers can be separated into their individual diastereomers on the basis of their physical and/or chemical differences by methods known in the art, for example, by chromatography or fractional crystallisation. The optically active bases or acids are then liberated from the separated diastereomeric salts. A different process for separation of optical isomers involves the use of chiral chromatography (*e.g.*, HPLC columns using a chiral phase), with or without conventional derivatisation, optimally chosen to maximise the separation of the enantiomers. Suitable HPLC columns using a chiral phase are commercially available, such as those manufactured by Daicel, *e.g.*, Chiracel OD and Chiracel OJ, for example, among many others, which are all routinely selectable. Enzymatic separations, with or without derivatisation, are also useful. The optically active compounds of the present invention can likewise be obtained by chiral syntheses utilizing optically active starting materials.

In order to distinguish different types of isomers from each other reference is made to IUPAC Rules Section E (Pure Appl Chem 45, 11-30, 1976).

Isolation of a single stereoisomer, *e.g.* a single enantiomer or a single diastereomer, of a compound of the present invention is achieved by any suitable state of the art method, such as chromatography, especially chiral chromatography, for example.

Further, it is possible for the compounds of the present invention to exist as tautomers. For example, any compound of the present invention which contains an imidazopyridine moiety as a heteroaryl group for example can exist as a 1H tautomer, or a 3H tautomer, or even a mixture in any amount of the two tautomers, namely :



1H tautomer 3H tautomer

The present invention includes all possible tautomers of the compounds of the present invention as single tautomers, or as any mixture of said tautomers, in any ratio.

Further, the compounds of the present invention can exist as N-oxides, which are defined in that at least one nitrogen of the compounds of the present invention is oxidised. The present invention includes all such possible N-oxides.

The present invention also provides useful forms of the compounds of the present invention, such as metabolites, hydrates, solvates, prodrugs, salts, in particular pharmaceutically acceptable salts, and/or co-precipitates.

The compounds of the present invention can exist as a hydrate, or as a solvate, wherein the compounds of the present invention contain polar solvents, in particular water, methanol or ethanol for example, as structural element of the crystal lattice of the compounds. It is possible for the amount of polar solvents, in particular water, to exist in a stoichiometric or non-stoichiometric ratio. In the case of stoichiometric solvates, *e.g.* a hydrate, hemi-, (semi-), mono-, sesqui-, di-, tri-, tetra-, penta- *etc*. solvates or hydrates, respectively, are possible. The present invention includes all such hydrates or solvates.

Further, it is possible for the compounds of the present invention to exist in free form, *e.g.* as a free base, or as a free acid, or as a zwitterion, or to exist in the form of a salt. Said salt may be any salt, either an organic or inorganic addition salt, particularly any pharmaceutically acceptable organic or inorganic addition salt, which is customarily used in pharmacy, or which is used, for example, for isolating or purifying the compounds of the present invention.

The term “pharmaceutically acceptable salt" refers to an inorganic or organic acid addition salt of a compound of the present invention. For example, see S. M. Berge, *et al*. “Pharmaceutical Salts,” J. Pharm. Sci. 1977, 66, 1-19.

A suitable pharmaceutically acceptable salt of the compounds of the present invention may be, for example, an acid-addition salt of a compound of the present invention bearing a nitrogen atom, in a chain or in a ring, for example, which is sufficiently basic, such as an acid-addition salt with an inorganic acid, or “mineral acid”, such as hydrochloric, hydrobromic, hydroiodic, sulfuric, sulfamic, bisulfuric, phosphoric, or nitric acid, for example, or with an organic acid, such as formic, acetic, acetoacetic, pyruvic, trifluoroacetic, propionic, butyric, hexanoic, heptanoic, undecanoic, lauric, benzoic, salicylic, 2-(4-hydroxybenzoyl)-benzoic, camphoric, cinnamic, cyclopentanepropionic, digluconic, 3-hydroxy-2-naphthoic, nicotinic, pamoic, pectinic, 3-phenylpropionic, pivalic, 2-hydroxyethanesulfonic, itaconic, trifluoromethanesulfonic, dodecylsulfuric, ethanesulfonic, benzenesulfonic, para-toluenesulfonic, methanesulfonic, 2-naphthalenesulfonic, naphthalinedisulfonic, camphorsulfonic acid, citric, tartaric, stearic, lactic, oxalic, malonic, succinic, malic, adipic, alginic, maleic, fumaric, D-gluconic, mandelic, ascorbic, glucoheptanoic, glycerophosphoric, aspartic, sulfosalicylic, or thiocyanic acid, for example.

Further, another suitably pharmaceutically acceptable salt of a compound of the present invention which is sufficiently acidic, is an alkali metal salt, for example a sodium or potassium salt, an alkaline earth metal salt, for example a calcium, magnesium or strontium salt, or an aluminium or a zinc salt, or an ammonium salt derived from ammonia or from an organic primary, secondary or tertiary amine having 1 to 20 carbon atoms, such as ethylamine,

diethylamine, triethylamine, ethyldiisopropylamine, monoethanolamine, diethanolamine, triethanolamine, dicyclohexylamine, dimethylaminoethanol, diethylaminoethanol, tris(hydroxymethyl)aminomethane, procaine, dibenzylamine, *N*-methylmorpholine, arginine, lysine, 1,2-ethylenediamine, *N*-methylpiperidine, *N*-methyl-glucamine, *N,N*-dimethyl-glucamine, *N*-ethyl-glucamine, 1,6-hexanediamine, glucosamine, sarcosine, serinol, 2-amino-1,3-propanediol, 3-amino-1,2-propanediol, 4-amino-1,2,3-butanetriol, or a salt with a quarternary ammonium ion having 1 to 20 carbon atoms, such as tetramethylammonium, tetraethylammonium, tetra(*n*-propyl)ammonium, tetra(*n*-butyl)ammonium, *N*-benzyl-*N,N,N*-trimethylammonium, choline or benzalkonium.

Those skilled in the art will further recognise that it is possible for acid addition salts of the claimed compounds to be prepared by reaction of the compounds with the appropriate inorganic or organic acid via any of a number of known methods. Alternatively, alkali and alkaline earth metal salts of acidic compounds of the present invention are prepared by reacting the compounds of the present invention with the appropriate base via a variety of known methods.

The present invention includes all possible salts of the compounds of the present invention as single salts, or as any mixture of said salts, in any ratio.

The present invention includes diastereomers, racemates, tautomers, N-oxides, hydrates, solvates, and salts of the compounds of the present invention, and mixtures of same.

In the present text, in particular in the Experimental Section, for the synthesis of intermediates and of examples of the present invention, when a compound is mentioned as a salt form with the corresponding base or acid, the exact stoichiometric composition of said salt form, as obtained by the respective preparation and/or purification process, is, in most cases, unknown.

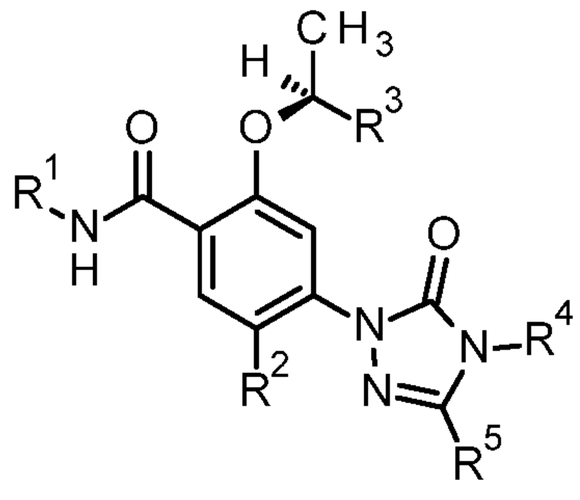
Unless specified otherwise, suffixes to chemical names or structural formulae relating to salts, such as "hydrochloride", "trifluoroacetate", "sodium salt", or "x HCl", "x CF_3COOH", "x Na^+", for example, mean a salt form, the stoichiometry of which salt form not being specified.

This applies analogously to cases in which synthesis intermediates or example compounds or salts thereof have been obtained, by the preparation and/or purification processes described, as solvates, such as hydrates, with (if defined) unknown stoichiometric composition.

Furthermore, the present invention includes all possible crystalline forms, or polymorphs, of the compounds of the present invention, either as single polymorph, or as a mixture of more than one polymorph, in any ratio.

Moreover, the present invention also includes prodrugs of the compounds according to the invention. The term “prodrugs” here designates compounds which themselves can be biologically active or inactive, but are converted (for example metabolically or hydrolytically) into compounds according to the invention during their residence time in the body.

In accordance with certain embodiments, the present invention provides compounds of general formula (I),



(I),

in which

R^1 represents a group selected from

a C_1-C_8-alkyl group, which is optionally substituted with a group selected from

C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a C_2-C_8-haloalkyl group,

a C_3-C_8-cycloalkyl group,which is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from hydroxy, phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,

a 4- to 7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8)

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

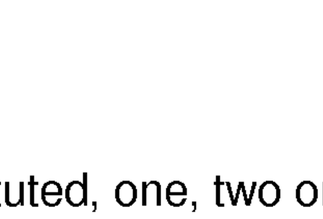
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-

haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a halogen atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group,
a C_3-C_8-cycloalkyl group,
a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group,
a C_2-C_6-alkenyl group,
a C_2-C_6-alkinyl group
a C_4-C_8-cycloalkenyl group,
a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group, wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group and in which said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
a phenyl group,
which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

R^4 and R^5 jointly form a 5- to 6-membered, optionally unsaturated, heterocyclic ring A of partial formula (i)



(i)

whereby ring A in addition to the two mandatory atoms, the nitrogen atom and the carbon atom bridging the two rings, bears additional 3 to 6 members selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N=, -N(R^7)-, -C(=O)-, -CH=, -CR^{11}=, -C(R^{12})$_2$-, -CHR^{13}-,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-hydroxyalkyl group, a haloalkyl group, a aryl group, a (C_1-C_6-alkyl)-aryl group, and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_6-alkyl, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), and -C(=O)OR^6-,

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^9 and R^{10} together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

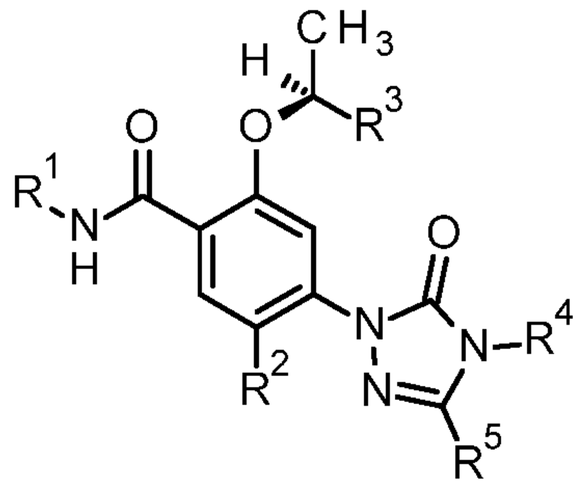
R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

and tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides of said compounds.

In accordance with certain embodiments, the present invention provides compounds of general formula (I),



(I),

in which

R^1 represents a group selected from
a C_1-C_8-alkyl group, a C_2-C_8-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_2-C_6-cyanoalkyl group, a C_2-C_6-hydroxyalkyl group, a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)-group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group, a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group, a 4- to 7-membered, optionally unsaturated, heterocyclic group, a phenyl group, and a monocyclic or bicyclic heteroaryl group,
wherein said C_1-C_8-alkyl group is optionally substituted with a group selected from
C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said C_3-C_8-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
hydroxy, phenyl and -N(R^7)(R^8),

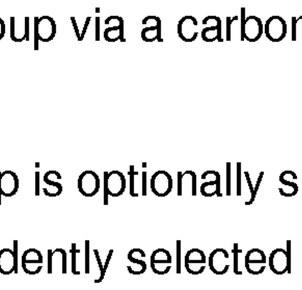
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said 4-7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,
or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(O)$_2$, -N(O)$_2$, and -N(R^7)(R^8)
and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(O)$_2$, -N(O)$_2$, and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a halogen atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group and
a phenyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(O)$_2$, -N(O)$_2$, and -N(R^7)(R^8),

R^4 and R^5 jointly form a 5- to 6-membered, optionally unsaturated, heterocyclic ring A of partial formula (i)



(i)

whereby ring A in addition to the two mandatory atoms, the nitrogen atom and the carbon atom bridging the two rings, bears additional 3 to 6 members selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N=, -N(R^7)-, -C(=O)-, -CH=, -CR^{11}=, -C(R^{12})$_2$-, -CHR^{13}-,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-hydroxyalkyl group, a haloalkyl group, a aryl group, a (C_1-C_6-alkyl)-aryl group, and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_6-alkyl, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), and -C(=O)OR^6-,

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-

C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

and tautomers, N-oxides, or salts thereof, and salts of tautomers or N-oxides of said compound.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_8-alkyl group, which is optionally substituted with a group selected from
C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a C_2-C_8-haloalkyl group,
a C_3-C_8-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenyl group anda -N(R^7)(R^8) group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,
a C_2-C_6-cyanoalkyl group,
a C_2-C_6-hydroxyalkyl group,
a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,
a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,
a 4- to 7-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group, a -C(=O)(C_3-

C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and
a oxo (=O) group,
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a 5- to 7-membered heterocycloalkenyl group, which is connected to the rest of the molecule via a carbon atom of said 5- to 7-membered heterocycloalkenyl group and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group,a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and a oxo (=O) group,
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,
an indanyl group, a tetralinyl group wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom, a C_1-C_6-alkyl group, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group,a hydroxy group and a -N(R^7)(R^8) group,
and
a monocyclic or bicyclic heteroaryl group, which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_6-alky groupl, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-

alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group, a hydroxy group and a -N(R^7)(R^8) group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group,
a C_3-C_8-cycloalkyl group,
a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group,
a C_2-C_6-alkenyl group,
a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group,
a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group,
a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group, and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
a phenyl group, which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $-N(R^7)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)(=NR^{14})-$ and $-S(=O)_2-$,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from

a C_1-C_6-alkyl group, a C_2-C_6-hydroxyalkyl group and a $-(C_2$-C_6-alkyl$)$-$N(R^9)(R^{10})$ group,

or

R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from C_1-C_3-alkyl, $-S(=O)_2(C_1$-C_3-alkyl$)$ and $-C(=O)O(C_1$-C_4-alkyl$)$,

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

or

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

R^{15} represents a group selected from
a C_1-C_6-alkyl group and a benzyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_8-alkyl group, a C_2-C_8-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_2-C_6-cyanoalkyl group, a C_2-C_6-hydroxyalkyl group, a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)-group, a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group, a -(C_1-C_6-alkyl)-C(=O)$N(R^7)(R^8)$ group, a 4- to 7-membered heterocycloalkyl group, a 5- to 7-membered heterocycloalkenyl group, a phenyl group, an indanyl group, a tetralinyl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_1-C_8-alkyl group is optionally substituted with a group selected from
C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said C_3-C_8-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
hydroxy, phenyl and $-N(R^7)(R^8)$,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said 4- to 7-membered heterocycloalkyl group and 5- to 7-membered heterocycloalkenyl group, which are connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group and of said 5- to 7-membered heterocycloalkenyl group, and which are optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,
and
wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),
and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a fluorine atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group and
a phenyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,
or
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$-N(R^7)-$, $-O-$, $-S-$, $-S(=O)-$ and $-S(=O)_2-$,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-hydroxyalkyl group and a -(C_2-C_6-alkyl)-$N(R^9)(R^{10})$ group,

or

R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, $-S(=O)_2(C_1$-C_3-alkyl) and $-C(=O)O(C_1$-C_4-alkyl),

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

or

R^9 and R^{10} together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or a tautomer, an N-oxide, or a salt thereof, and a salt of a tautomer or an N-oxide.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_6-alkyl group, which is optionally substituted with a group selected from
C_3-C_6-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,
a C_2-C_6-haloalkyl group,
a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenylgroup and a -N(R^7)(R^8) group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group,a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,
a C_2-C_6-cyanoalkyl group,
a C_2-C_6-hydroxyalkyl group,
a (C_2-C_3-hydroxyalkyl)-O-(C_2-C_6-alky)- group,
a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group,a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a 5- to 6-membered heterocycloalkenyl group, which is connected to the rest of the molecule via a carbon atom of said 5- to 6-membered heterocycloalkenyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group,a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and oxo (=O) group, and

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group,which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_3-C_6-cycloalkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -(C_1-C_3-alkyl)-C(=O)OR^6, -(C_1-C_3-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

an indanyl group, a tetralinyl group which are optionally substituted one or two times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group, a C_3-C_6-cycloalkoxy group, a cyano group, ahydroxy group and a -N(R^7)(R^8) group,

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_3-C_6-cycloalky groupl, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group, a C_3-C_6-cycloalkoxy group, a cyano group, a hydroxy group and a -N(R^7)(R^8) group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl, a C_2-C_6-alkinyl group,

a C_4-C_6-cycloalkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,

a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group, a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,

a -(C_1-C_6-alkyl)-(4- to 6-membered nitrogen containing heterocycloalkyl) group and

a phenyl group,

wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,

and

wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,

and

wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH(R^{13})-X^1-X^2-X^3-#,

*-CH=CH-CH(R^{13})-X^3-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from -N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from

a C_1-C_3-alkyl group, a C_2-C_3-hydroxyalkyl group and a -(C_2-C_3-alkyl)-N(R^9)(R^{10}),

or

R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from

C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

or

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group, a $-C(=O)OR^6$ group and a $-C(=O)N(R^7)(R^8)$ group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a $-C(=O)(C_1$-C_3-haloalkyl) group,

R^{15} represents a group selected from
a C_1-C_4-alkyl group and a benzyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-haloalkyl group, a C_3-C_6-cycloalkyl group, a C_2-C_6-cyanoalkyl group, a C_2-C_6-hydroxyalkyl group, a (C_2-C_3-hydroxyalkyl)-O-(C_2-C_6-alky)-group, a $-(C_2$-C_6-alkyl)-$N(R^7)(R^8)$ group, a $-(C_1$-C_6-alkyl)-$C(=O)N(R^7)(R^8)$ group, a 4- to 6-membered heterocycloalkyl group, a 5-6-membered heterocycloalkenyl group, a phenyl group, an indanyl group, a tetralinyl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_1-C_6-alkyl group is optionally substituted with a group selected from
C_3-C_6-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and

wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
hydroxy, phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said 4- to 6-membered heterocycloalkyl group and said 5- to 6-membered heterocyclocalkenyl group, which are connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group and said heterocycloalkenyl group, are optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_3-C_6-cycloalkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -(C_1-C_3-alkyl)-C(=O)OR^6, -(C_1-C_3-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,
and
wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),
and
wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a fluorine atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl, a C_2-C_6-alkinyl group,
a C_4-C_6-cycloalkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-(4- to 6-membered nitrogen containing heterocycloalkyl) group and
a phenyl group,
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from -N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from

a C_1-C_3-alkyl group, a C_2-C_3-hydroxyalkyl group and a -(C_2-C_3-alkyl)-N(R^9)(R^{10}),

or

R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

or

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a group selected from a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and –a N(R^7)(R^8) group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
a C_2-C_6-hydroxyalkyl group,
a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and a oxo (=O) group,
a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a cyano group, a hydroxy group, a -C(=O)OR^6 group, a -C(=O)N(R^7)(R^8)group, a -N(R^7)(R^8) group, a -(C_1-C_3-alkyl)-N(R^7)(R^8) group, a -S(=O)$_2$N(R^7)(R^8) group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from $-CH_2-N(R^7)-CH_2-$ and $-O-CH_2-C(=O)-NH-$,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-alkoxy group, a hydroxy group and a-$N(R^7)(R^8)$ group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, (C_1-C_6-alkyl)-$N(R^7)R^8$ group,

a -(C_1-C_6-alkyl)-$N(H)C(=O)OR^{15}$ group and a phenyl group,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-#,

*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

*-$N=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

and

*-$CH=C(R^{11})$-$N=C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O-, -S- and -S(=O)(=NR^{14})-,
X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents a hydrogen atom,

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group and a -C(=O)OR^6 group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)CF_3 group,

R^{15} represents a C_1-C_4-alkyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
phenyl and -N(R^7)(R^8),
wherein said phenyl substitituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
and
wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,
and
wherein said indanyl group is optionally substituted with a hydroxy group,
and
wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, (C_1-C_6-alkyl)-$N(R^7)R^8$ and
a phenyl group,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,
*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,
and
*-CH=$C(R^{11})$-N=$C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
or
one of X^1, X^2, X^3 and X^4 represents a group selected from
-$N(R^7)$-, -O- and -S-,
X^1, X^2, X^3 and X^4 represents a $C(R^{12})_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or
a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represent a hydrogen atom,

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group and a -C(=O)OR^6 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from cyclopropyl and cyclohexyl, and which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and a -N(R^7)(R^8) group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
a C_2-C_6-hydroxyalkyl group,
a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is selected from azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alky group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and a oxo (=O) group,
a phenyl group, which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alky groupl, a C_1-C_3-haloalkyl group,a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a hydroxy group, a cyano group, a -C(=O)OR^6 group, a -C(=O)N(R^7)(R^8) group, a -N(R^7)(R^8) group, a -(C_1-C_3-alkyl)-N(R^7)(R^8) group,a -S(=O)$_2$N(R^7)(R^8) group and a SF_5 group,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,
an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is selected from imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl, and

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,

a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} and a phenyl group,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH(R^{13})-X^1-X^2-X^3-#,

*-CH=CH-CH(R^{13})-X^3-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O-, -S- and -S(=O)(=NH)-,

and one of X^1, X^2, X^3 and X^4 represents a $C(R^{12})_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence,a hydrogen atom or
a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents a hydrogen atom,

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group and a $-C(=O)OR^6$ group,

R^{15} represents a C_1-C_4-alkyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a $-(C_2$-C_6-alkyl$)$-$N(R^7)(R^8)$ group,
a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and
a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is selected from cyclopropyl and cyclohexyl,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
phenyl and $-N(R^7)(R^8)$,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

and

wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is selected from

azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,

which 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

and

wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

and

wherein said indanyl group is optionally substituted with a hydroxy group,

and

wherein said monocyclic or bicyclic heteroaryl group is selected from

imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl,

which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a fluorine atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group and
a phenyl group,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,
*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,
and
*-CH=$C(R^{11})$-N=$C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
or
one of X^1, X^2, X^3 and X^4 represents a group selected from
-$N(R^7)$-, -O- and -S-,
and one of X^1, X^2, X^3 and X^4 represents a $C(R^{12})_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence,a hydrogen atom or
a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represent a hydrogen atom,

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from a hydroxy group and a $-C(=O)OR^6$ group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from a cyclopropyl group and a cyclohexyl group,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom, a phenyl group and a dimethylamino group,
wherein said phenyl substituent is optionally substituted with a fluorine atom
a 2-hydroxy-2-methylpropyl group,
a 2-(dimethylamino)ethyl group,
a 4- to 6-membered heterocycloalkyl group, which is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl, and
which is optionally substituted one or two times, each substituent independently selected from a group selected from a methyl group, an ethyl group, a pyrazinyl group, a *tert*-butoxycarbonyl group, a acetyl group, a 1-cyclopropanecarbonyl group, amethylsulfonyl group and a oxo (=O) group,
a phenyl group, which, is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, an ethyl group, a difluoromethyl group, a trifluoromethyl group, a hydroxymethyl group, a methoxy group, a hydroxy group, a cyano group,a $-C(=O)OH$ group,a $-C(=O)OCH_3$ group, a $-C(=O)OC(CH_3)$, group, a $-C(=O)NH_2$ group, a-$C(=O)N(CH_3)_2$ group, an amino group, a methylamino group, an aminomethyl group,a $-S(=O)_2NH_2$ group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH-CH_2-NH-CH_2- and -O-CH_2-C(=O)-NH-,

a 2-hydroxyindan-1-yl group and

a monocyclic or bicyclic heteroaryl group,

which is selected from

imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl, pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl, and

which is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, a methoxy group, a hydroxy group and a morpholin-4-yl group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

propyl, cyclohexyl, trifluoromethyl, 1-hydroxyethyl, allyl, aminomethyl, (dimethylamino)methyl, (tert-butoxycarbonylamino)methyl, 2-(dimethylamino)ethyl, pyrrolidin-1-yl-methyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-CH(OH)-$(CH_2)_3$-#,

*-CH_2-CH(OH)-$(CH_2)_2$-#,

*-$(CH_2)_2$-CH(OH)-CH_2-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-CH=CH-CH(OH)-CH_2-#,

*-CH_2-C$(CH_3)_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#,

*-$(CH_2)_3$-S(=O)(=NH)-,#
*-$(CH_2)_5$-#,
*-$(CH_2)_3$-O-CH_2-#,
*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#
*-CH=CH-CH=CH-#,
*-N=CH-CH=CH-#,
and
*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

In accordance with certain embodiments, the present invention provides compounds of general formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a 2-hydroxy-2-methylpropyl group,
a 2-(dimethylamino)ethyl group, a 4- to 6-membered heterocycloalkyl group,
a phenyl group, a 2-hydroxyindan-1-yl group and
a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is selected from cyclopropyl and cyclohexyl,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom or a group selected from
phenyl and dimethylamino,
wherein said phenyl substituent is optionally substituted with a fluorine atom,
and
wherein said 4- to 6-membered heterocycloalkyl group is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl,
which 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from

methyl, ethyl, pyrazinyl, *tert*-butoxycarbonyl, acetyl, 1-cyclopropanecarbonyl, methylsulfonyl and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, hydroxymethyl, methoxy, cyano, $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)OC(CH_3)_3$, $-C(=O)NH_2$, $-C(=O)N(CH_3)_2$, amino, methylamino, aminomethyl, $-S(=O)_2NH_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
$-CH-CH_2-NH-CH_2-$ and $-O-CH_2-C(=O)-NH-$,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from
imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl, pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, methoxy, hydroxy and morpholin-4-yl,

R^2 represents a hydrogen atom or a fluorine atom,

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl, 1-hydroxyethyl, allyl, (dimethylamino)methyl, 2-(dimethylamino)ethyl, pyrrolidin-1-yl-methyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
$*-(CH_2)_2-S-\#$,
$*-(CH_2)_4-\#$,
$*-CH_2-C(H)(C(=O)OH)-(CH_2)_2-\#$,
$*-CH_2-CF_2-(CH_2)_2-\#$,
$*-(CH_2)_3-C(H)(C(=O)OH)-\#$,
$*-(CH_2)_3-C(H)(OH)-\#$,

*-CH_2-$C(CH_3)_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#

*-$(CH_2)_5$-#,

*-$(CH_2)_3$-O-CH_2-#,

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

*-CH=CH-CH=CH-#,

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with further embodiments, the present invention provides the compounds of general formula (I), *supra*, which are exemplified in the experimental section.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_1-C_8-alkyl group, which is optionally substituted with a group selected from

C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times with one or more substituents independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_8-haloalkyl group,

a C_3-C_8-cycloalkyl group, whch is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenyl group and a -$N(R^7)(R^8)$ group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen

atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,

a 4- to 7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a-C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8)

and

a monocyclic or bicyclic heteroaryl group which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_8-alkyl group, which is optionally substituted with a group selected from a C_3-C_8-cycloalkyl group, a phenyl group and a monocyclic- or bicyclic heteroaryl group, wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a C_2-C_8-haloalkyl group,
a C_3-C_8-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from a hydroxy group, a phenyl group and a -N(R^7)(R^8) group, wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a C_2-C_6-cyanoalkyl group,
a C_2-C_6-hydroxyalkyl group,
a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,
a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,
a 4- to 7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group,which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8)

and

a monocyclic or bicyclic heteroaryl group, which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides of said compound.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_8-alkyl group, a C_2-C_8-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_2-C_6-cyanoalkyl group, a C_2-C_6-hydroxyalkyl group, a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)-group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group, a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group, a 4- to 7-membered, optionally unsaturated, heterocyclic group, a phenyl group, and a monocyclic or bicyclic heteroaryl group,
wherein said C_1-C_8-alkyl group is optionally substituted with a group selected fromsaid
C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said C_3-C_8-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
hydroxy, phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said 4-7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and

wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,
or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(O)$_2$, -N(O)$_2$, and -N(R^7)(R^8)
and
wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(O)$_2$, -N(O)$_2$, and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with further embodiments, the present invention provides compounds of general formula (I), in which

R^1 represents a phenyl group which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -

$S(=O)_2N(R^7)(R^8)$, $-S(=O)_2(C_1\text{-}C_3\text{-alkyl})$, $-S(=O)(=NR^{11})(C_1\text{-}C_3\text{-alkyl})$, $-P(=O)(C_1\text{-}C_3\text{-alkyl})_2$ and SF_5,

or in which two substituents of said phenyl groups, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

$-CH_2\text{-}N(R^7)\text{-}CH_2\text{-}$, $-CH_2\text{-}O\text{-}CH_2\text{-}$, $-O\text{-}CH_2\text{-}C(=O)\text{-}NH\text{-}$ and $-NH\text{-}C(=O)\text{-}NH\text{-}$,

In accordance with further embodiments, the present invention provides compounds of general formula (I), in which

R^1 represents a phenyl group, which is optionally substituted, one or two times, each substituent independently selected from a fluorine atom, a chlorine atom and a methyl group.

In accordance with further embodiments, the present invention provides compounds of general formula (I), in which

R^1 represents a C_4-C_8-cycloalkyl group or a $-(C_3\text{-}C_8\text{-cycloalkyl})\text{-}N(R^7)(R^8)$ group which are optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from hydroxy, phenyl and $-N(R^7)(R^8)$,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy.

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with further embodiments, the present invention provides compounds of general formula (I), in which

R^1 represents a 4- to 7-membered heterocycloalkyl group or a 5- to 7-membered heterocycloalkenyl group, wherein said 4- to 7-membered heterocycloalkyl group and 5- to 7-membered heterocycloalkenyl group are optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl,

$-C(=O)O(C_1\text{-}C_4\text{-alkyl})$, $-C(=O)(C_1\text{-}C_6\text{-alkyl})$, $-C(=O)(C_3\text{-}C_6\text{-cycloalkyl})$, $-S(=O)_2(C_1\text{-}C_6\text{-alkyl})$ and oxo (=O),

and wherein said 4- to 7-membered heterocycloalkyl group and 5- to 7-membered heterocycloalkenyl group are connected to the rest of the molecule via a carbon atom of the said heterocycloalkyl- or heterocyclalkenyl group and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with further embodiments, the present invention provides compounds of general formula (I), in which R^1 represents a indanyl group, a tetralinyl group and a monocyclic - or bicyclic heteroaryl group

wherein said indanyl or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8).

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_1-C_8-alkyl group, which is optionally substituted with a group selected from

C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a C_2-C_8-haloalkyl group,

a C_3-C_8-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenyl group anda -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,

a 4- to 7-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group, a -C(=O)(C_3-

C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and
a oxo (=O) group,
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a 5- to 7-membered heterocycloalkenyl group, which is connected to the rest of the molecule via a carbon atom of said 5- to 7-membered heterocycloalkenyl group and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group,a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and a oxo (=O) group,
wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,
an indanyl group, a tetralinyl group wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom, a C_1-C_6-alkyl group, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group,a hydroxy group and a -N(R^7)(R^8) group,
and
a monocyclic or bicyclic heteroaryl group, which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_6-alky groupl, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-

alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group, a hydroxy group and a -N(R^7)(R^8) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_1-C_8-alkyl group, a C_2-C_8-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_2-C_6-cyanoalkyl group, a C_2-C_6-hydroxyalkyl group, a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)-group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group, a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group, a 4- to 7-membered heterocycloalkyl group, a 5- to 7-membered heterocycloalkenyl group, a phenyl group, an indanyl group, a tetralinyl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_1-C_8-alkyl group is optionally substituted with a group selected from
C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said C_3-C_8-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
hydroxy, phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,
and
wherein said 4- to 7-membered heterocycloalkyl group and said 5- to 7-membered heterocycloalkenyl group, which are connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group and
said 5- to 7-membered heterocycloalkenyl group, are optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

and

wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_8-cycloalkyl group, which is optionally substituted, one or two times, each

substituent independently selected from a halogen atom, a hydroxy group, a phenyl group anda -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a 4- to 7-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and

a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a 5- to 7-membered heterocycloalkenyl group, which is connected to the rest of the molecule via a carbon atom of said 5- to 7-membered heterocycloalkenyl group and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group,a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

an indanyl group, a tetralinyl group wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom, a C_1-C_6-alkyl group, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group,a hydroxy group and a -N(R^7)(R^8) group,

and

a monocyclic or bicyclic heteroaryl group, which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_6-alky groupl, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group, a hydroxy group and a -N(R^7)(R^8) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_8-cycloalkyl group, a 4- to 7-membered heterocycloalkyl group,

a 5- to 7-membered heterocycloalkenyl group, a phenyl group, an indanyl group, a tetralinyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_3-C_8-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from

hydroxy, phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said 4- to 7-membered heterocycloalkyl group and said 5- to 7-membered heterocycloalkenyl group, which are connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group and

5- to 7-membered heterocycloalkenyl group, are optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_6-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_6-alkyl) and oxo (=O),

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)$N(R^7)(R^8)$, -$N(R^7)(R^8)$, -(C_1-C_6-alkyl)-$N(R^7)(R^8)$, -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)$N(R^7)(R^8)$, -$S(=O)_2N(R^7)(R^8)$, -$S(=O)_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-$N(R^7)$-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

and

wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -$N(R^7)(R^8)$,

and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, hydroxy and -$N(R^7)(R^8)$,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_1-C_6-alkyl group, a C_2-C_6-haloalkyl group, a C_3-C_6-cycloalkyl group, a C_2-C_6-cyanoalkyl group, a C_2-C_6-hydroxyalkyl group, a (C_2-C_3-hydroxyalkyl)-O-(C_2-C_6-alky)-group, a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group, a -(C_1-C_6-alkyl)-C(=O)$N(R^7)(R^8)$ group, a 4- to

6-membered heterocycloalkyl group, a 5 to 6-membered heterocycloalkenyl group, a phenyl group, an indanyl group, a tetralinyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_1-C_6-alkyl group is optionally substituted with a group selected from

C_3-C_6-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from

hydroxy, phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said 4- to 6-membered heterocycloalkyl group and said heterocycloalkenyl group, which are connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group and said hjeterocycloalkenyl group, are optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_3-C_6-cycloalkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6,

-C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -(C_1-C_3-alkyl)-C(=O)OR^6, -(C_1-C_3-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

and

wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, a 4- to 6-membered heterocycloalkyl group, a heterocycloalkenyl group, a phenyl group, an indanyl group, a tetralinyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from

hydroxy, phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said 4- to 6-membered heterocycloalkyl group and said heterocycloalkenyl group, which are connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group and of said heterocycloalkenyl group, are optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and

wherein said phenyl group is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_3-C_6-cycloalkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -(C_1-C_3-alkyl)-C(=O)OR^6, -(C_1-C_3-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

and

wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, cyano, hydroxy and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and –a $N(R^7)(R^8)$ group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a C_2-C_6-hydroxyalkyl group,

a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group,

a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroary groupl, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -$S(=O)_2$(C_1-C_3-alkyl) group and a oxo (=O) group,

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a cyano group, a hydroxy group, a -C(=O)OR^6 group, a -C(=O)$N(R^7)(R^8)$group, a -$N(R^7)(R^8)$ group, a -(C_1-C_3-alkyl)-$N(R^7)(R^8)$ group, a -$S(=O)_2N(R^7)(R^8)$ group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-alkoxy group, a hydroxy group and a-$N(R^7)(R^8)$ group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group, a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
and
wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,
and
wherein said indanyl group is optionally substituted with a hydroxy group,
and
wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and –a $N(R^7)(R^8)$ group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroary groupl, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and a oxo (=O) group,

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a cyano group, a hydroxy group, a -C(=O)OR^6 group, a -C(=O)N(R^7)(R^8)group, a -N(R^7)(R^8) group, a -(C_1-C_3-alkyl)-N(R^7)(R^8) group, a -S(=O)$_2$N(R^7)(R^8) group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-alkoxy group, a hydroxy group and a-N(R^7)(R^8) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
and
wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,
and
wherein said indanyl group is optionally substituted with a hydroxy group,
and
wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, which is selected from cyclopropyl and cyclohexyl, and which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and a -N(R^7)(R^8) group, wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a C_2-C_6-hydroxyalkyl group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is selected from azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alky groupl, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and a oxo (=O) group,

a phenyl group, which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alky groupl, a C_1-C_3-haloalkyl group,a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a hydroxy group, a cyano group, a -C(=O)OR^6 group, a -C(=O)N(R^7)(R^8) group, a -N(R^7)(R^8) group, a -(C_1-C_3-alkyl)-N(R^7)(R^8) group,a -S(=O)$_2$N(R^7)(R^8) group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is selected from imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl, and

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and
a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is selected from cyclopropyl and cyclohexyl,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
and
wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is selected from
azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,
which 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
$-CH_2-N(R^7)-CH_2-$ and $-O-CH_2-C(=O)-NH-$,
and
wherein said indanyl group is optionally substituted with a hydroxy group,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and $-N(R^7)(R^8)$,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from cyclopropyl and cyclohexyl, and which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and a $-N(R^7)(R^8)$ group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is selected from azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alky groupl, a 5- to 6-membered heteroaryl group, a $-C(=O)O(C_1$-C_4-alkyl) group, a $-C(=O)(C_1$-C_3-alkyl) group, a $-C(=O)(C_3$-C_6-cycloalkyl) group, a $-S(=O)_2(C_1$-C_3-alkyl) group and a oxo (=O) group,
a phenyl group, which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alky groupl, a C_1-C_3-haloalkyl group,a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a hydroxy group, a cyano group, a $-C(=O)OR^6$ group, a $-C(=O)N(R^7)(R^8)$ group, a

-N(R^7)(R^8) group, a -(C_1-C_3-alkyl)-N(R^7)(R^8) group,a -S(=O)$_2$N(R^7)(R^8) group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is selected from imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl, and

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_3-C_6-cycloalkyl group is selected from cyclopropyl and cyclohexyl,

which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from

phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

and

wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is selected from

azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,

which 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,
and
wherein said indanyl group is optionally substituted with a hydroxy group,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from a cyclopropyl group and a cyclohexyl group,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom, a phenyl group and a dimethylamino group,

wherein said phenyl substituent is optionally substituted with a fluorine atom

a 2-hydroxy-2-methylpropyl group,

a 2-(dimethylamino)ethyl group,

a 4- to 6-membered heterocycloalkyl group, which is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl, and

which is optionally substituted one or two times, each substituent independently selected from a group selected from a methyl group, an ethyl group, a pyrazinyl group, a *tert*-butoxycarbonyl group, a acetyl group, a 1-cyclopropanecarbonyl group, amethylsulfonyl group and a oxo (=O) group,

a phenyl group, which, is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, an ethyl group, a difluoromethyl group, a trifluoromethyl group, a hydroxymethyl group, a methoxy group, a hydroxy group, a cyano group,a -C(=O)OH group,a $-C(=O)OCH_3$ group, a $-C(=O)OC(CH_3)$, group, a $-C(=O)NH_2$ group, a-$C(=O)N(CH_3)_2$ group, an amino group, a methylamino group, an aminomethyl group,a $-S(=O)_2NH_2$ group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH-CH_2-NH-CH_2- and -O-CH_2-C(=O)-NH-,

a 2-hydroxyindan-1-yl group and

a monocyclic or bicyclic heteroaryl group,

which is selected from

imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl, pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl, and

which is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, a methoxy group, a hydroxy group and a morpholin-4-yl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a 2-hydroxy-2-methylpropyl group,
a 2-(dimethylamino)ethyl group, a 4- to 6-membered heterocycloalkyl group,
a phenyl group, a 2-hydroxyindan-1-yl group and
a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is selected from cyclopropyl and cyclohexyl,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom or a group selected from
phenyl and dimethylamino,
wherein said phenyl substituent is optionally substituted with a fluorine atom,
and
wherein said 4- to 6-membered heterocycloalkyl group is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl,
which 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from methyl, ethyl, pyrazinyl, *tert*-butoxycarbonyl, acetyl, 1-cyclopropanecarbonyl, methylsulfonyl and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, hydroxymethyl, methoxy, cyano, -C(=O)OH, $-C(=O)OCH_3$, $-C(=O)OC(CH_3)_3$, $-C(=O)NH_2$, $-C(=O)N(CH_3)_2$, amino, methylamino, aminomethyl, $-S(=O)_2NH_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
$-CH-CH_2-NH-CH_2-$ and $-O-CH_2-C(=O)-NH-$,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl,

pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, methoxy, hydroxy and morpholin-4-yl,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from a cyclopropyl group and a cyclohexyl group,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom, a phenyl group and a dimethylamino group,
wherein said phenyl substituent is optionally substituted with a fluorine atom
a 4- to 6-membered heterocycloalkyl group, which is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl, and
which is optionally substituted one or two times, each substituent independently selected from a group selected from a methyl group, an ethyl group, a pyrazinyl group, a *tert*-butoxycarbonyl group, a acetyl group, a 1-cyclopropanecarbonyl group, amethylsulfonyl group and a oxo (=O) group,
a phenyl group, which, is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, an ethyl group, a difluoromethyl group, a trifluoromethyl group, a hydroxymethyl group, a methoxy group, a hydroxy group, a cyano group,a -C(=O)OH group,a $-C(=O)OCH_3$ group, a $-C(=O)OC(CH_3)$, group, a $-C(=O)NH_2$ group, a-$C(=O)N(CH_3)_2$ group, an amino group, a methylamino group, an aminomethyl group,a $-S(=O)_2NH_2$ group and a SF_5 group,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH-CH_2-NH-CH_2- and -O-CH_2-C(=O)-NH-,
a 2-hydroxyindan-1-yl group and
a monocyclic or bicyclic heteroaryl group,

which is selected from
imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl, pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl, and
which is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, a methoxy group, a hydroxy group and a morpholin-4-yl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a 4- to 6-membered heterocycloalkyl group, a phenyl group, a 2-hydroxyindan-1-yl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is selected from cyclopropyl and cyclohexyl,
which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom or a group selected from
phenyl and dimethylamino,
wherein said phenyl substituent is optionally substituted with a fluorine atom,
and
wherein said 4- to 6-membered heterocycloalkyl group is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl,
which 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from methyl, ethyl, pyrazinyl, *tert*-butoxycarbonyl, acetyl, 1-cyclopropanecarbonyl, methylsulfonyl and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, hydroxymethyl, methoxy, cyano,

-C(=O)OH, -C(=O)OCH_3, -C(=O)$OC(CH_3)_3$, -C(=O)NH_2, -C(=O)$N(CH_3)_2$, amino, methylamino, aminomethyl, -$S(=O)_2NH_2$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH-CH_2-NH-CH_2- and -O-CH_2-C(=O)-NH-,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl, pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, methoxy, hydroxy and morpholin-4-yl,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents a hydrogen atom or a halogen atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compound.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents a hydrogen atom or a fluorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents a fluorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents chlorine atom or a fluorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents chlorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^2 represents a hydrogen atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
a C_1-C_6-alkyl group,
a C_3-C_8-cycloalkyl group,
a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group,
a C_2-C_6-alkenyl group,
a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group,
a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,
a -(C_1-C_6-alkyl)-$N(H)C(=O)R^6$ group,
a -(C_1-C_6-alkyl)-$N(H)C(=O)OR^{15}$ group,

a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group, which is connected to the alkyl group via a carbon atom of the heterocycloalkyl group and which is optionally substituted with a C_1-C_3-alkyl group,

and

a phenyl group,

which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from

a C_1-C_6-alkyl group,

a C_3-C_8-cycloalkyl group,

a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group,

a C_2-C_6-alkenyl group,

a C_2-C_6-alkinyl group,

a C_4-C_8-cycloalkenyl group,

a (C_1-C_6-alkyl)-N(R^7)R^8 group,

a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group and wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group, and

a phenyl group,

whichis optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group and
a phenyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -$S(O)_2$, -$N(O)_2$, and -$N(R^7)(R^8)$,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,
a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group, a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group and
a phenyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,

and

wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-alkinyl group,

a C_4-C_8-cycloalkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,

a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group and

a phenyl group,

wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,

and

wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,

and

wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl, a C_2-C_6-alkinyl group,

a C_4-C_6-cycloalkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,

a -(C_1-C_6-alkyl)-$N(H)C(=O)R^6$ group, a -(C_1-C_6-alkyl)-$N(H)C(=O)OR^{15}$ group,

a -(C_1-C_6-alkyl)-(4- to 6-membered nitrogen containing heterocycloalkyl) group

wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
a phenyl group, which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl, a C_2-C_6-alkinyl group,
a C_4-C_6-cycloalkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,
a -(C_1-C_6-alkyl)-(4- to 6-membered nitrogen containing heterocycloalkyl) group and
a phenyl group,
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group and a phenyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, (C_1-C_6-alkyl)-N(R^7)R^8 and
a phenyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl, 1-hydroxyethyl, allyl, (dimethylamino)methyl,
2-(dimethylamino)ethyl, pyrrolidin-1-yl-methyl and phenyl,

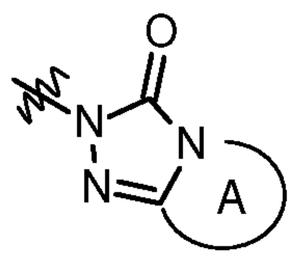
and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl, 1-hydroxyethyl, allyl, aminomethyl,
(dimethylamino)methyl, (tert-butoxycarbonylamino)methyl, 2-(dimethylamino)ethyl,
pyrrolidin-1-yl-methyl and phenyl,

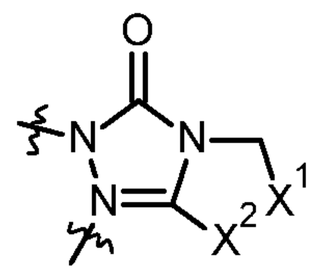
or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which R^4 and R^5 jointly form a 5- to 6-membered, optionally unsaturated, heterocyclic ring A of partial formula (i)

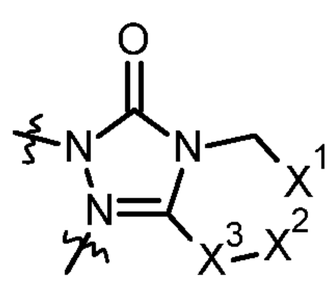


(i)

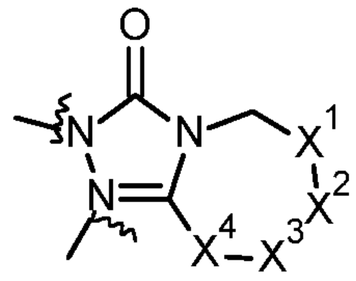
In which partial formula (i) includes but is not limited thereto e.g.



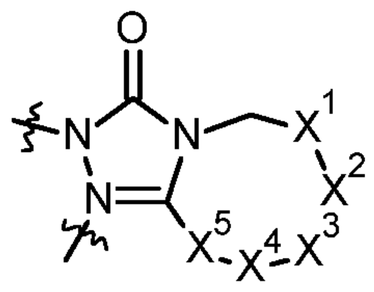
(ii)



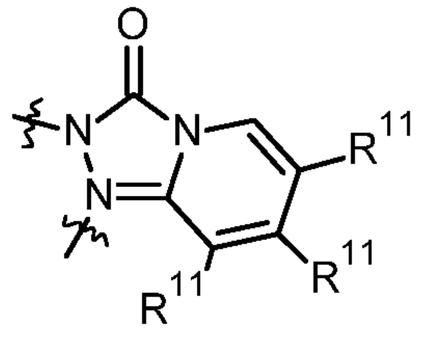
(iii)



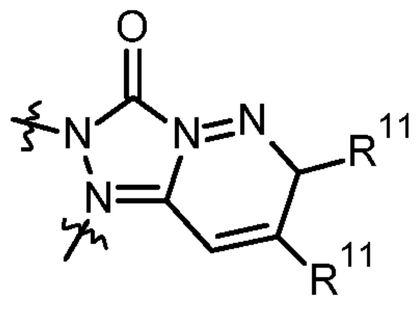
(iv)



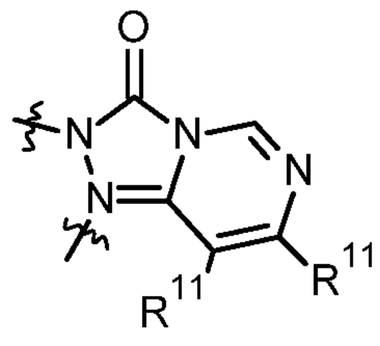
(v)



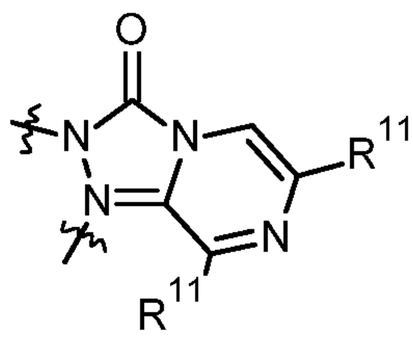
(vi)



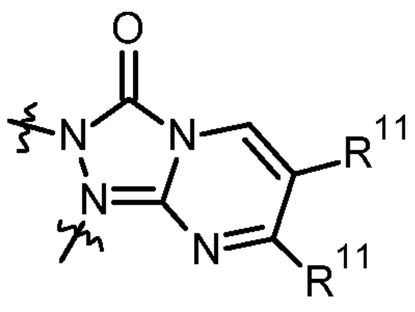
(vii)



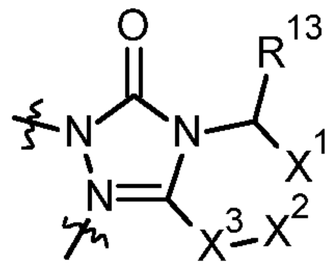
(viii)



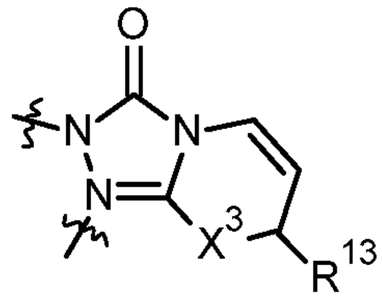
(ix)



(x)



(xi)



(xii)

in which X^1, X^2, X^3, X^4 and X^5 represents a group independently selected from -N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$- and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

more specifically a group selected from

a hydrogen atom, a halogen atom or a group selected from a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

more specifically in which groups (ii) to (x)

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$-N(R^7)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)(=NR^{14})-$ and $-S(=O)_2-$,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

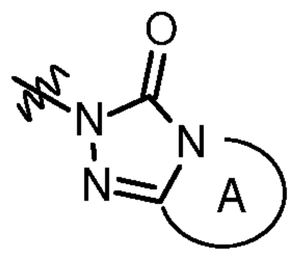
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group, and

R^{11} represents independently from each occurrence a hydrogen atom, a halogen atom or a group selected from a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

even more specifically those ring systems as disclosed in the examples

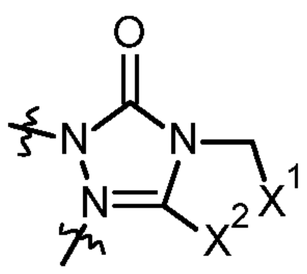
or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compouds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which R^4 and R^5 jointly form a 5- to 6-membered, optionally unsaturated, heterocyclic ring A of partial formula (i)

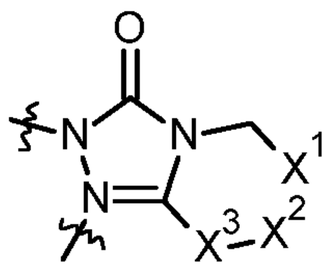


(i)

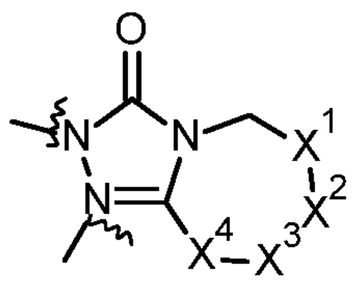
In which partial formula (i) includes but is not limited thereto e.g.



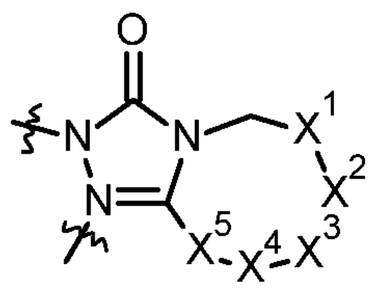
(ii)



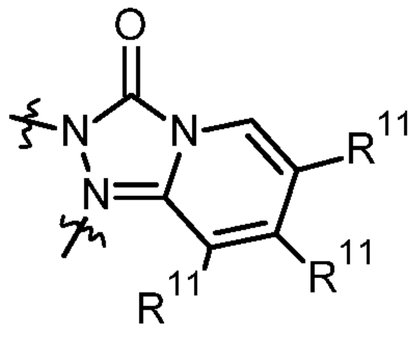
(iii)



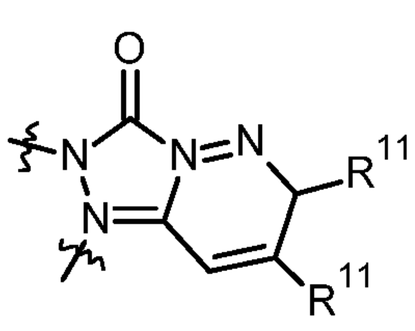
(iv)



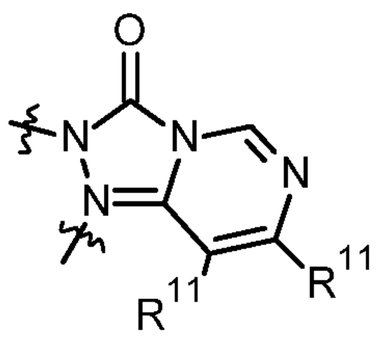
(v)



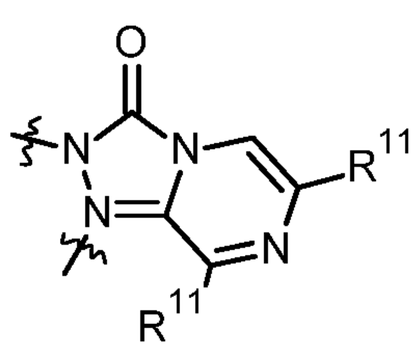
(vi)



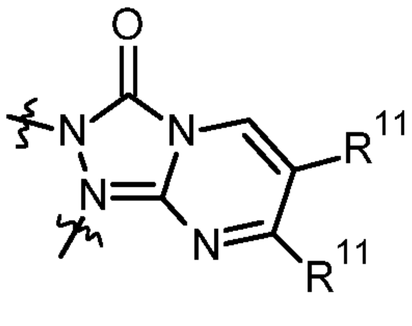
(vii)



(viii)



(ix)



(x)

in which X^1, X^2, X^3, X^4 and X^5 represents a group independently selected from -N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$- and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

more specifically a group selected from

a hydrogen atom, a halogen atom or a group selected from a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

more specifically in which groups (ii) to (x)

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group, and

R^{11} represents independently from each occurrence a hydrogen atom, a halogen atom or a group selected from a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

even more specifically those ring systems as disclosed in the examples

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-#,

*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-CH=N-$C(R^{11})$=$C(R^{11})$-#,

*-CH=$C(R^{11})$-N=$C(R^{11})$-#,

and

*-CH=$C(R^{11})$-$C(R^{11})$=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-$N(R^7)$-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -$S(=O)_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-#,

*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

*-$N=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

*-$CH=N$-$C(R^{11})=C(R^{11})$-#,

*-$CH=C(R^{11})$-$N=C(R^{11})$-#,

and

*-$CH=C(R^{11})$-$C(R^{11})=N$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-#,

*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

*-$N=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

*-$CH=N$-$C(R^{11})=C(R^{11})$-#,

*-$CH=C(R^{11})$-$N=C(R^{11})$-#,

and

*-$CH=C(R^{11})$-$C(R^{11})=N$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$-N(R^7)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)(=NR^{14})-$ and $-S(=O)_2-$,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from -N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
and
*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
or

one of X^1, X^2, X^3 and X^4 represents a group selected from
-N(R^7)-, -O-, -S- and -S(=O)(=NR^{14})-,
X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-+,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
and
*-CH=C(R^{11})-N=C(R^{11})-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O-, -S- and -S(=O)(=NR^{14})-,

X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O- and -S-,

and one of X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O- and -S-,

and one of X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-CH(OH)-$(CH_2)_3$-#,

*-CH_2-CH(OH)-$(CH_2)_2$-#,

*-$(CH_2)_2$-CH(OH)-CH_2-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-CH=CH-CH(OH)-CH_2-#,

*-CH_2-C(CH_3)$_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#,

*-$(CH_2)_3$-S(=O)(=NH)-,#

*-$(CH_2)_5$-#,

*-$(CH_2)_3$-O-CH_2-#,

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

*-CH=CH-CH=CH-#,

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-CH_2-C$(CH_3)_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#

*-$(CH_2)_5$-#,

*-$(CH_2)_3$-O-CH_2-#,

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

*-CH=CH-CH=CH-#,

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH(R^{13})-X^1-X^2-X^3-#,

*-CH=CH-CH(R^{13})-X^3-,

and

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

and

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,
*-$CH(R^{13})$-X^1-X^2-X^3-#,
*-CH=CH-$CH(R^{13})$-X^3-,
and
*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
and
*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-CH(OH)-$(CH_2)_3$-#,

*-CH_2-CH(OH)-$(CH_2)_2$-#,

*-$(CH_2)_2$-CH(OH)-CH_2-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-CH=CH-CH(OH)-CH_2-#,

*-$(CH_2)_5$-#,

and

*-CH=CH-CH=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

and

*-CH(R^{13})-X^1-X^2-X^3-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

and

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH=CH-$CH(R^{13})$-X^3-,

and

*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

X^3 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-# group,

in which group "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH(R^{13})-X^1-X^2-X^3-#,

*-CH=CH-CH(R^{13})-X^3-,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

and

*-CH(R^{13})-X^1-X^2-X^3-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

and

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from -$N(R^7)$-, -O-, -S-, -S(=O)- and -$S(=O)_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH=CH-$CH(R^{13})$-X^3-,

*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-CH=N-$C(R^{11})$=$C(R^{11})$-#,

*-CH=$C(R^{11})$-N=$C(R^{11})$-#,

and

*-CH=$C(R^{11})$-$C(R^{11})$=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

X^3 represents a group selected from

-$N(R^7)$-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -$S(=O)_2$-,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-,
and
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-$(CH_2)_5$-#,

and

*-CH=CH-CH=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-$(CH_2)_3$-C(H)(OH)-#,

and

*-$(CH_2)_5$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-CH_2-C(CH_3)$_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#,

*-$(CH_2)_3$-S(=O)(=NH)-,#

*-$(CH_2)_3$-O-CH_2-#,

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-CH_2-$C(CH_3)_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#

*-$(CH_2)_3$-O-CH_2-#,

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-CH_2-$C(CH_3)_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#,

*-$(CH_2)_3$-S(=O)(=NH)-,#

*-$(CH_2)_3$-O-CH_2-#,

and

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_2$-S-#,

*-CH_2-$C(CH_3)_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#,

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S-#

*-$(CH_2)_3$-O-CH_2-#,

and

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-,

*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-CH=N-$C(R^{11})$=$C(R^{11})$-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from -N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

and

R^{14} represents a hydrogen atom or a group selected from

a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

or

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from -N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH(R^{13})-X^1-X^2-X^3-#,

*-CH=CH-CH(R^{13})-X^3-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

and

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
-N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-

C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

and

R^{14} represents a hydrogen atom or a group selected from

a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-$N(R^7)$-, -O-, -S-, -S(=O)- and -$S(=O)_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,
and
R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,
and
R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
and
*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
or
one of X^1, X^2, X^3 and X^4 represents a group selected from
-N(R^7)-, -O-, -S- and -S(=O)(=NR^{14})-,
X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from
a hydroxy group and a -C(=O)OR^6 group,

and

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)CF_3 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
and
*-CH=C(R^{11})-N=C(R^{11})-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group and a -C(=O)OR^6 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH(R^{13})-X^1-X^2-X^3-#,

*-CH=CH-CH(R^{13})-X^3-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O-, -S- and -S(=O)(=NR^{14})-,

X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group and a -C(=O)OR^6 group,

and

R^{14} represents a hydrogen atom or a group selected from

a cyano group and a -C(=O)CF_3 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

or

one of X^1, X^2, X^3 and X^4 represents a group selected from

-N(R^7)-, -O- and -S-,

and one of X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group and a -C(=O)OR^6 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group and a -C(=O)OR^6 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

and

*-CH=C(R^{11})-N=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from -N(R^7)-, -O- and -S-,

and one of X^1, X^2, X^3 and X^4 represents a C(R^{12})$_2$ group,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-(CH_2)$_2$-S-#,

*-(CH_2)$_4$-#,

*-CH_2-C(H)(C(=O)OH)-(CH_2)$_2$-#,

*-CH_2-CF_2-(CH_2)$_2$-#,

*-(CH_2)$_3$-C(H)(C(=O)OH)-#,

*-(CH_2)$_3$-C(H)(OH)-#,

*-CH_2-C(CH_3)$_2$-CH_2-O-#,

*-(CH_2)$_2$-O-CH_2-#,

*-(CH_2)$_3$-O-#,

*-(CH_2)$_3$-N(CH_3)-#,

*-(CH_2)$_3$-S-#

*-(CH_2)$_5$-#,

*-(CH_2)$_3$-O-CH_2-#,

*-(CH_2)$_2$-N(H)-(CH_2)$_2$-#

*-CH=CH-CH=CH-#,

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-,

and

*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
and
*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-,

and

*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

and

*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3 and X^4 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

and

R^{11} represents a hydrogen atom,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from a hydroxy group and a $-C(=O)OR^6$ group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

and

*-$CH(R^{13})$-X^1-X^2-X^3-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from $C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
and
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH=CH-CH(R^{13})-X^3-#,

and

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

X^3 represents a group selected from

$C(R^{12})_2$ and CH(R^{13}),

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a

*-CH=C(R^{11})-C(R^{11})=C(R^{11})-# group,

in which group "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-#,

*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-CH=N-$C(R^{11})$=$C(R^{11})$-#,

*-CH=$C(R^{11})$-N=$C(R^{11})$-#,

and

*-CH=$C(R^{11})$-$C(R^{11})$=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-$N(R^7)$-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -$S(=O)_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,
and
R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
-N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,
and
R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,
and
R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

and

*-$CH(R^{13})$-X^1-X^2-X^3-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-$N(R^7)$-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

$C(R^{12})_2$ and $CH(R^{13})$,

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)$N(R^7)(R^8)$ group,

and

R^{14} represents a hydrogen atom or a group selected from

a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

and

*-CH_2-X^1-X^2-X^3-X^4-X^5-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)- and -S(=O)$_2$-,

and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from

C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

and

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH=CH-CH(R^{13})-X^3-#,

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

X^3 represents a group selected from

-N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and

R^{13} represents a group selected from

a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

and

R^{14} represents a hydrogen atom or a group selected from

a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-(CH$_2$)$_2$-S-#,

*-CH$_2$-C(CH$_3$)$_2$-CH$_2$-O-#,

*-(CH$_2$)$_2$-O-CH$_2$-#,

*-(CH$_2$)$_3$-O-#,

*-(CH$_2$)$_3$-N(CH$_3$)-#,

*-(CH$_2$)$_3$-S-#,

*-(CH$_2$)$_3$-S(=O)(=NH)-,#

*-(CH$_2$)$_5$-#,

*-(CH$_2$)$_3$-O-CH$_2$-#,

*-(CH$_2$)$_2$-N(H)-(CH$_2$)$_2$-#

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_4$-#,

*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,

*-CH_2-CF_2-$(CH_2)_2$-#,

*-$(CH_2)_3$-C(H)(C(=O)OH)-#,

*-CH(OH)-$(CH_2)_3$-#,

*-CH_2-CH(OH)-$(CH_2)_2$-#,

*-$(CH_2)_2$-CH(OH)-CH_2-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-CH=CH-CH(OH)-CH_2-#,

*-$(CH_2)_5$-#, and

*-CH=CH-CH=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-C(CH_3)$_2$-CH_2-O-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_3$-O-#, and

*-$(CH_2)_3$-O-CH_2-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_3$-N(CH_3)-#,

*-$(CH_2)_3$-S(=O)(=NH)-,#

*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#

*-N=CH-CH=CH-#,

and

*-CH=CH-N=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,

*-CH=N-C(R^{11})=C(R^{11})-#,

*-CH=C(R^{11})-N=C(R^{11})-#,

and

*-CH=C(R^{11})-C(R^{11})=N-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups

and

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^6 represents a hydrogen atom or a group selected from

a C_1-C_6-alkyl group and a benzyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^6 represents a hydrogen atom or a group selected from

a C_1-C_4-alkyl group and a benzyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-hydroxyalkyl group and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-hydroxyalkyl group and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_3-alkyl group, a C_2-C_3-hydroxyalkyl group and a -(C_2-C_3-alkyl)-N(R^9)(R^{10}),
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_3-alkyl group, a C_2-C_3-hydroxyalkyl group and a -(C_2-C_3-alkyl)-N(R^9)(R^{10}),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or
a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

or

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,

or

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 6-membered heterocycloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from

a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{11} represents a hydrogen atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{13} represents a group selected from
a hydroxy group and a -C(=O)OR^6 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)CF_3 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{14} represents a hydrogen atom,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{14} represents a group selected from a cyano group and a $-C(=O)CF_3$ group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{15} represents a group selected from a C_1-C_6-alkyl group and a benzyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{15} represents a group selected from a C_1-C_4-alkyl group and a benzyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^{15} represents a C_1-C_4-alkyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and a $-N(R^7)(R^8)$ group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
a C_2-C_6-hydroxyalkyl group,
a $-(C_2$-C_6-alkyl)$-N(R^7)(R^8)$ group,
a 4- to 6-membered heterocycloalkyl group, wherein said 4- to 6-membered heterocycloalkyl group is connected to the rest of the molecule via a carbon

atom of said 4- to 6-membered heterocycloalkyl group,and said 4- to 6-membered heterocycloalkyl group is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),and

and

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and a -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a C_2-C_6-hydroxyalkyl group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

a phenyl group,which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),and

and

R^2 represents a hydrogen atom or a fluorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from a phenyl group and a -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a C_2-C_6-hydroxyalkyl group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

a phenyl group, whichis optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),and

and

R^2 represents a chlorine atom or a fluorine atom,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group, a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from

phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

and

wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

and

wherein said phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

and

wherein said indanyl group is optionally substituted with a hydroxy group,

and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),and

R^2 represents a hydrogen atom or a fluorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from a phenyl group anda -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a C_2-C_6-hydroxyalkyl group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

a phenyl group which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),and

and

R^2 represents a fluorine atom,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,
wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from
phenyl and -N(R^7)(R^8),
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
and
wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from
C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),
and
wherein said phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,
and
wherein said indanyl group is optionally substituted with a hydroxy group,
and
wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8), and

R^2 represents a fluorine atom,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from a phenylgroup and a -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

a C_2-C_6-hydroxyalkyl group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl),

-C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8),and

and

R^3 represents a C_1-C_6-haloalkyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a C_3-C_6-cycloalkyl group, a C_2-C_6-hydroxyalkyl group, a -(C_2-C_6-alkyl)-N(R^7)(R^8) group, a 4- to 6-membered heterocycloalkyl group, a phenyl group, an indanyl group and a monocyclic or bicyclic heteroaryl group,

wherein said C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a halogen atom or a group selected from

phenyl and -N(R^7)(R^8),

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,

and

wherein said 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, is optionally substituted one or two times, each substituent independently selected from a group selected from

C_1-C_3-alkyl, 5- to 6-membered heteroaryl, -C(=O)O(C_1-C_4-alkyl), -C(=O)(C_1-C_3-alkyl), -C(=O)(C_3-C_6-cycloalkyl), -S(=O)$_2$(C_1-C_3-alkyl) and oxo (=O),

and

wherein said phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8) and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

and

wherein said indanyl group is optionally substituted with a hydroxy group, and

wherein said monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -N(R^7)(R^8), and

R^3 represents a C_1-C_6-haloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, hydroxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2- and -O-CH_2-C(=O)-NH-,

and

R^3 represents a C_1-C_6-haloalkyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group,

which is phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-

haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -$N(O)_2$, and -$N(R^7)(R^8)$, or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,
and

R^3 represents a C_1-C_6-haloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group,

which is phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -$S(O)_2$, -$N(O)_2$, and -$N(R^7)(R^8)$,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,
and

R^3 represents a C_1-C_6-haloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)$N(R^7)(R^8)$, -$N(R^7)(R^8)$, -(C_1-C_3-alkyl)-$N(R^7)(R^8)$, -$S(=O)_2N(R^7)(R^8)$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,
and

R^3 represents a C_1-C_6-haloalkyl group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group,

which is phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)$N(R^7)(R^8)$, -$N(R^7)(R^8)$, -(C_1-C_3-alkyl)-$N(R^7)(R^8)$, -$S(=O)_2N(R^7)(R^8)$ and SF_5,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from
-CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,
and

R^3 represents a C_1-C_6-haloalkyl group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)$N(R^7)(R^8)$, -$N(R^7)(R^8)$, -(C_1-C_3-alkyl)-$N(R^7)(R^8)$, -$S(=O)_2N(R^7)(R^8)$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,

and

R^3 represents a CF_3 group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group,

which is phenyl group is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, cyano, -C(=O)OR^6, -C(=O)$N(R^7)(R^8)$, -$N(R^7)(R^8)$, -(C_1-C_3-alkyl)-$N(R^7)(R^8)$, -$S(=O)_2N(R^7)(R^8)$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

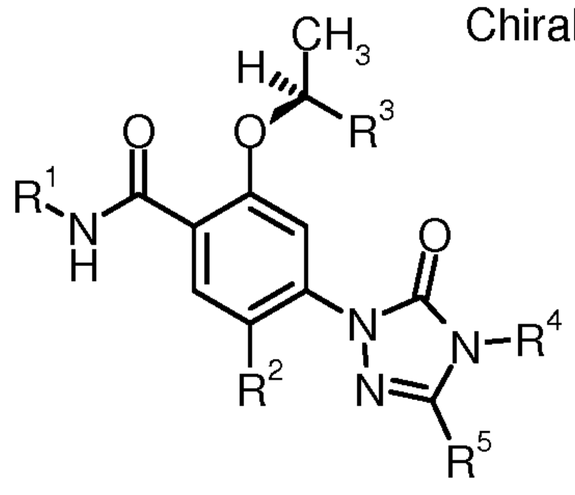
-CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,

and

R^3 represents a CF_3 group,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with further embodiments, the present invention provides compounds of general formula (I),



(I),

in which

R^1 represents a group selected from

a 4,4-difluorocyclohexyl group, a 1-(methylsulfonyl)piperidin-4-yl group, a phenyl group and a monocyclic or bicyclic heteroaryl group,

wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy, hydroxy, cyano, -C(=O)OC(CH$_3$)$_3$, amino and -S(=O)$_2$NH$_2$,

and

wherein said monocyclic or bicyclic heteroaryl group is selected from 1,2-oxazol-4-yl, pyrazol-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrimidin-4-yl, pyrimidin-5-yl and indazol-5-yl,

and which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a chlorine atom, a methyl group and a methoxy group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

propyl, cyclohexyl, trifluoromethyl, (dimethylamino)methyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-(CH$_2$)$_4$-#,

*-(CH$_2$)$_3$-C(H)(OH)-#,

*-(CH$_2$)$_2$-O-CH$_2$-#,

*-(CH$_2$)$_5$-#,

*-(CH$_2$)$_3$-O-CH$_2$-#,

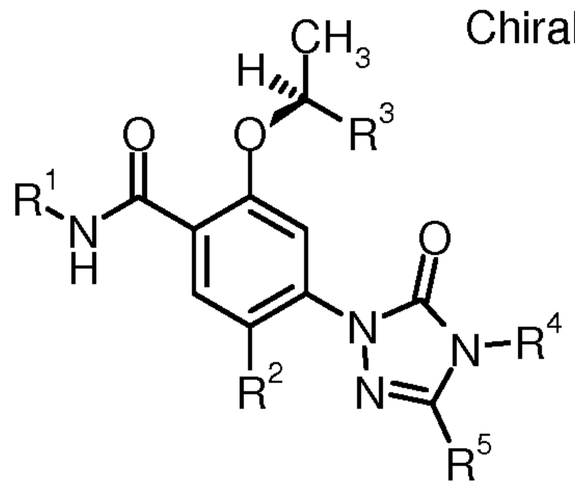
and

*-CH=CH-CH=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In accordance with further embodiments, the present invention provides compounds of general formula (I),



(I),

in which

R^1 represents a group selected from
a 4,4-difluorocyclohexyl group, a 1-(methylsulfonyl)piperidin-4-yl group, a phenyl group and a monocyclic or bicyclic heteroaryl group,
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy, cyano, $-C(=O)OC(CH_3)_3$, amino and $-S(=O)_2NH_2$,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from
1,2-oxazol-4-yl, pyrazol-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrimidin-4-yl, pyrimidin-5-yl and indazol-5-yl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a chlorine atom or a group selected from
methyl and methoxy,

R^2 represents a hydrogen atom or a fluorine atom,

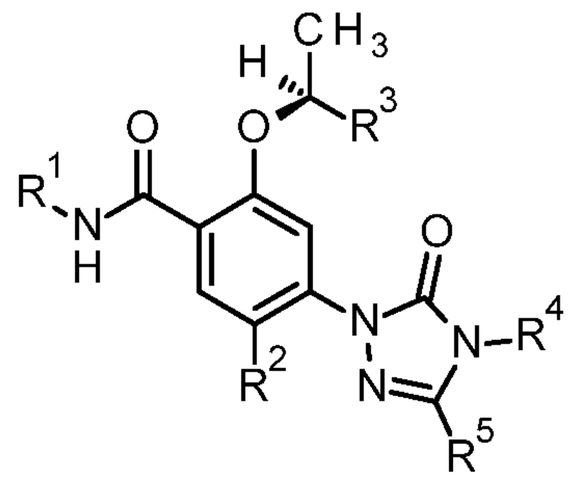
R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl, (dimethylamino)methyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-$(CH_2)_4$-#,
*-$(CH_2)_3$-C(H)(OH)-#,
*-$(CH_2)_2$-O-CH_2-#,
*-$(CH_2)_5$-#,
*-$(CH_2)_3$-O-CH_2-#,
and
*-CH=CH-CH=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In accordance with further embodiments, the present invention provides compounds of general formula (I),



(I),

in which

R^1 represents a group selected from
a phenyl group and a monocyclic heteroaryl group,
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom a methyl group, an ethyl group, a difluoromethyl group, a trifluoromethyl group, a methoxy group, a hydroxy group and an amino group,
and
wherein said monocyclic heteroaryl group is selected from
pyridin-2-yl, pyridin-3-yl and pyridazin-3-yl,

which monocyclic heteroaryl group is optionally substituted one or two times, each substituent independently selected from a chlorine atom or a group selected from a methyl group and a methoxy group,

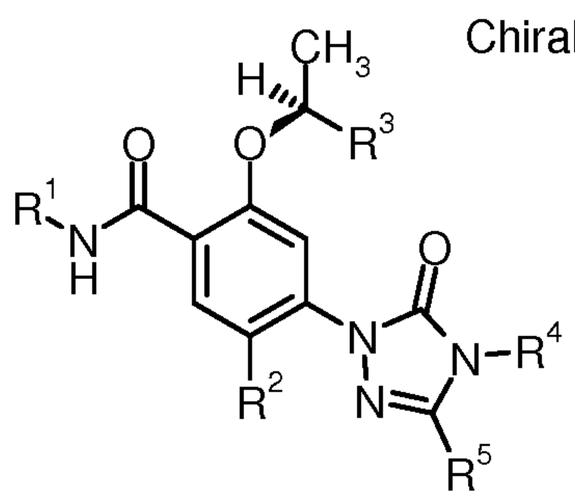
R^2 represents a fluorine atom,

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-$(CH_2)_4$-#,
*-$(CH_2)_2$-O-CH_2-#,
*-$(CH_2)_5$-#,
and
*-$(CH_2)_3$-O-CH_2-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said comppounds.

In accordance with further embodiments, the present invention provides compounds of general formula (I),



(I),

in which

R^1 represents a group selected from
a phenyl group and a monocyclic heteroaryl group,
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom

or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy and amino,
and
wherein said monocyclic heteroaryl group is selected from
pyridin-2-yl, pyridin-3-yl and pyridazin-3-yl,
which monocyclic heteroaryl group is optionally substituted one or two times,
each substituent independently selected from a chlorine atom or a group
selected from
methyl and methoxy,

R^2 represents a fluorine atom,

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-$(CH_2)_4$-#,
*-$(CH_2)_2$-O-CH_2-#,
*-$(CH_2)_5$-#,
and
*-$(CH_2)_3$-O-CH_2-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a 4,4-difluorocyclohexyl group, a 1-(methylsulfonyl)piperidin-4-yl group, a phenyl group and a monocyclic or bicyclic heteroaryl group,
wherein said phenyl group is optionally substituted, one, two or three times,
each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy, hydroxy, cyano, -C(=O)OC$(CH_3)_3$, amino and -S(=O)$_2NH_2$,
and

wherein said monocyclic or bicyclic heteroaryl group is selected from 1,2-oxazol-4-yl, pyrazol-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrimidin-4-yl, pyrimidin-5-yl and indazol-5-yl,
and which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a chlorine atom, a methyl group and a methoxy group,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a 4,4-difluorocyclohexyl group, a 1-(methylsulfonyl)piperidin-4-yl group, a phenyl group and a monocyclic or bicyclic heteroaryl group,
wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy, cyano, $-C(=O)OC(CH_3)_3$, amino and $-S(=O)_2NH_2$,
and
wherein said monocyclic or bicyclic heteroaryl group is selected from 1,2-oxazol-4-yl, pyrazol-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrimidin-4-yl, pyrimidin-5-yl and indazol-5-yl,
which monocyclic or bicyclic heteroaryl group is optionally substituted one, two or three times, each substituent independently selected from a chlorine atom or a group selected from
methyl and methoxy,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl, (dimethylamino)methyl and phenyl,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-$(CH_2)_4$-#,

*-$(CH_2)_3$-C(H)(OH)-#,

*-$(CH_2)_2$-O-CH_2-#,

*-$(CH_2)_5$-#,

*-$(CH_2)_3$-O-CH_2-#,

and

*-CH=CH-CH=CH-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from

a phenyl group and a monocyclic heteroaryl group,

wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom or a chlorine atom or a group selected from

methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy, hydroxy and amino,

and

wherein said monocyclic heteroaryl group is selected from

pyridin-2-yl, pyridin-3-yl and pyridazin-3-yl,

which monocyclic heteroaryl group is optionally substituted one or two times, each substituent independently selected from a chlorine atom or a group selected from

methyl and methoxy,

or tautomers, N-oxides, or salts thereof, or salts of tautomers or N-oxides of said compounds.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^1 represents a group selected from
a phenyl group and a monocyclic heteroaryl group,
wherein said phenyl group is optionally substituted, one, two or three times,
each substituent independently selected from a fluorine atom or a chlorine atom
or a group selected from
methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy and amino,
and
wherein said monocyclic heteroaryl group is selected from
pyridin-2-yl, pyridin-3-yl and pyridazin-3-yl,
which monocyclic heteroaryl group is optionally substituted one or two times,
each substituent independently selected from a chlorine atom or a group
selected from
methyl and methoxy,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl and phenyl,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, in which:

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-$(CH_2)_4$-#,
*-$(CH_2)_2$-O-CH_2-#,
*-$(CH_2)_5$-#,
and
*-$(CH_2)_3$-O-CH_2-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, which are selected from the group consisting of:

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[3-(trifluoromethyl)phenyl]benzamide,
N-(1-acetylpiperidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(3-chloropyridin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(5-methylpyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(5-chloropyrimidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,

N-(3-chloropyridin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[1-(pyrazin-2-yl)piperidin-4-yl]benzamide,
N-[1-(cyclopropylcarbonyl)piperidin-4-yl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(1-methyl-2-oxopiperidin-(4R,S)-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide, mixture of diastereomers,
5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-aminophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-[2-(methylamino)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-amino-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(4-amino-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[3-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-chloro-4-(pentafluoro-lambda6-sulfanyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(oxetan-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)benzamide,
N-(2-chloro-3-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-[2-methyl-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-3,5-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(3,5-dimethyl-1,2-oxazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methyl-1,2-oxazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methyl-1H-imidazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(dimethylamino)ethyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[4-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-cyclopropyl-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
tert-butyl 3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}azetidine-1-carboxylate,
N-(azetidin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(4,4-difluorocyclohexyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(1-ethylazetidin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[4-(dimethylamino)cyclohexyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-ethylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-N-(2,4,6-trimethylpyridin-3-yl)benzamide,
N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-phenyl-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,4,6-trifluorophenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[2-(trifluoromethyl)phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-methylpyridin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-3-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(1-methyl-1H-pyrazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(tetrahydro-2H-pyran-4-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-methylpyridin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(1,3-dimethyl-1H-pyrazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(1,4-dimethyl-1H-pyrazol-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-hydroxy-2-methylpropyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-(hydroxymethyl)-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-[3-(hydroxymethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-8-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-6-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}-4-methylbenzoic acid,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-5-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylquinolin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-7-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(3-sulfamoyl-phenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(7H-pyrrolo[2,3-d]-pyrimidin-4-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylquinolin-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methyl-1,3-benzothiazol-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methyl-1H-indazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,3-dimethoxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(1H-indazol-7-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[1-(4-fluorophenyl)cyclopropyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-3-hydroxy-1H-indazol-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[(1S,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(3-carbamoyl-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

2-[(1S)-1-cyclohexylethoxy]-N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(4,4-difluorocyclohexyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methoxy-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxy-2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-[3-(dimethylcarbamoyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[6-(morpholin-4-yl)pyridazin-3-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methoxypyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methoxypyrimidin-5-yl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(4,6-dimethoxypyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxypyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methoxypyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxypyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(5,6-dimethylpyrimidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyrimidin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,

2-[(1S)-1-cyclohexylethoxy]-N-(2,4-dimethylpyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methylpyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-fluoropyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[3-(morpholin-4-yl)pyrazin-2-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(4,6-dimethylpyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(3-amino-2-methylphenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-[4-amino-2-(trifluoromethyl)phenyl]-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methyl-4-sulfamoylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-[2-(aminomethyl)-6-methylphenyl]-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
methyl 2-({2-[(1R)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoate,
2-[(1R)-1-cyclohexylethoxy]-N-(2,3-dihydro-1H-isoindol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(5-amino-3-methylpyridin-2-yl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-({2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoic acid,
tert-butyl 4-({2-[(1S)-1-cyclohexylethoxy]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoate,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[3-(trifluoromethyl)phenyl]benzamide,

2-[(1S)-1-cyclohexylethoxy]-N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,4,6-trifluorophenyl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[2-(trifluoromethyl)phenyl]benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyridin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(2,4-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-[2-(dimethylamino)ethyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-fluoro-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(1-methyl-1H-pyrazol-5-yl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(tetrahydro-2H-pyran-4-yl)benzamide,
N-(2-cyano-4-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-5-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyridin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide
N-(2-chloro-6-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-3-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(1,3-dimethyl-1H-pyrazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(1-methylpiperidin-4-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(1,4-dimethyl-1H-pyrazol-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-hydroxy-2-methylpropyl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-(hydroxymethyl)-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methyl-1,2-oxazol-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-4-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-3,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-N-(2,4,6-trifluoro-phenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(4,5-difluoro-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamid,e
5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide
N-(4-chloro-2-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[3-(trifluoro-methyl)phenyl]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenyl-ethoxy]benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenyl-ethoxy]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenyl-ethoxy]-N-[3-(trifluoromethyl)phenyl]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(4-chloro-2-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamid,e
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(8-methyl-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyrimidin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro[1,3]thiazolo[2,3-c][1,2,4]triazol-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7,8,9-tetrahydro-3H-[1,2,4]triazolo[4,3-a]azepin-2(5H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyrazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]thiazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-4-(6,6-dimethyl-3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-2(3H)-yl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
4-(6,6-difluoro-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-b]pyridazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
2-(4-[(2,6-difluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-(R,S)-carboxylic acid, mixture of diastereomers,
2-(4-[(2-chloro-6-fluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-(R,S)-carboxylic acid, mixture of diastereomers,
2-(4-[(2-chloro-6-fluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-6-(R,S)-carboxylic acid, mixture of diastereomers,
N-(2,6-difluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-

2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-2-{[(2R,3R)-3-hydroxybutan-2-yl]oxy}-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2R)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
rac-2-{[4-(dimethylamino)butan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzamide,
rac-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7,8,9-tetrahydro-3H-[1,2,4]triazolo[4,3-d][1,4]-diazepin-2(5H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide, and
N-(2,6-difluorophenyl)-5-fluoro-4-[(8R,S)-8-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3-a]pyridin-2(3H)-yl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide, mixture of diastereomers,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

In further embodiments, the present invention provides compounds of formula (I), *supra*, which are selected from the group consisting of:

5-chloro-N-(2,6-difluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(2-chloro-6-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-[1-(4-fluorophenyl)cyclopropyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-[2-(difluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide
5-chloro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluoro-4-hydroxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluoro-3-hydroxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(8-imino-3,8-dioxo-5,6,7,8-tetrahydro-8λ^6-[1,2,4]triazolo-[3,4-b][1,3]thiazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(7-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(6-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(6-hydroxy-3-oxo-5,6-dihydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(8-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
rac-tert-butyl [2-{2-[(2-chloro-6-fluorophenyl)carbamoyl]-4-fluoro-5-(3-oxo-5,6,7,8-tetrahydro-

[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)phenoxy}propyl]carbamate, and rac-2-{[1-aminopropan-2-yl]oxy}-N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide, salt with hydrochloric acid,

and tautomers, N-oxides, and salts thereof, and salts of tautomers or N-oxides.

The present invention provides any sub-combination within any embodiment or aspect of the present invention of compounds of general formula (I), *supra*.

The present invention provides any sub-combination within any embodiment or aspect of the present invention of intermediate compounds of general formulae (IV), (VI), (VIII), (IX), (X), (XV), (XVIII), (XIX), (X) and (XXI).

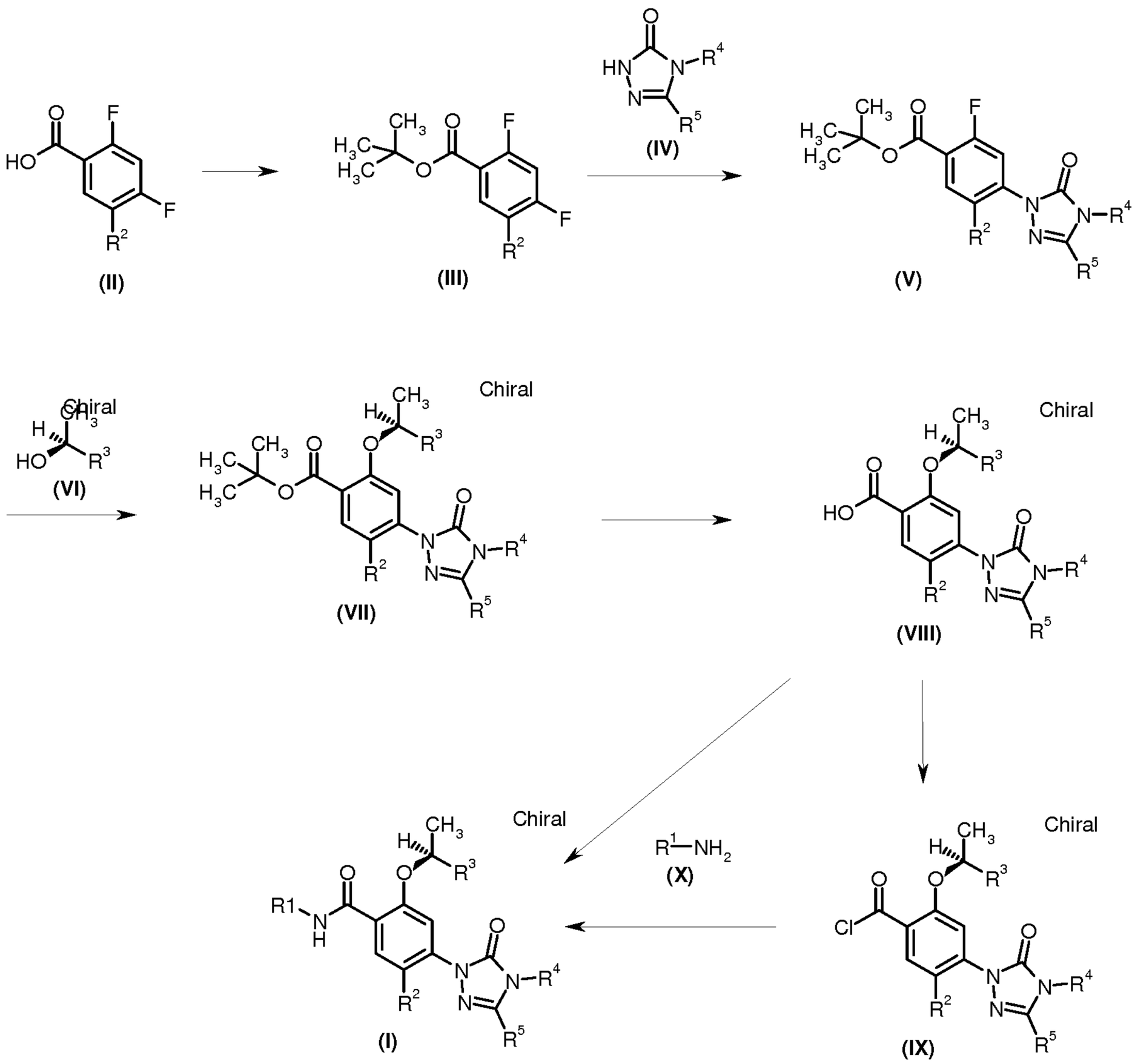
The present invention provides the compounds of general formula (I) which are disclosed in the Example Section of this text, *infra*.

The compounds according to the invention of general formula (I) can be prepared according to the following schemes 1, 2, 3, 4 and 5. The schemes and procedures described below illustrate synthetic routes to the compounds of general formula (I) of the invention and are not intended to be limiting. It is clear to the person skilled in the art that the order of transformations as exemplified in schemes 1, 2, 3, 4 and 5 can be modified in various ways. The order of transformations exemplified in these schemes is therefore not intended to be limiting. In addition, interconversion of any of the substituents, R^1, R^2, R^3, R^4 or R^5 can be achieved before and/or after the exemplified transformations. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wuts in *Protective Groups in Organic Synthesis*, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Synthetic Routes

Five routes for the preparation of compounds of general formula (I) are described in schemes 1, 2, 3, 4 and 5.

Synthetic Route 1



Scheme 1: Route for the preparation of compounds of general formula (I) in which R^1, R^2, R^3, R^4 and R^5 have the meaning as given for general formula (I), *supra*.

Compounds of general formulae (II), (IV), (VI) and (X) are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art. Specific examples are described in the Experimental Section.

(II) -> (III):

tert-Butyl benzoates of general formula (III) can be prepared from benzoic acid derivatives of general formula (II) according to procedures available from the public domain, as understandable to the person skilled in the art.

In connection with the method of the invention, the use of di-*tert*-butyl-dicarbonate in *tert*-butanol was preferable.

Alternatively, the *tert*-butyl benzoates of general formula (III) can be prepared from benzoic acid derivatives of general formula (II) by *in situ* formation of the the corresponding acid chlorides and subsequent reaction with *tert*-butanol.

In situ formation of acid chlorides from benzoic acids of general formular (II) can be accomplished, for example by using oxalyl chloride or thionyl chloride, both reagents used in the presence of catalytic amount of *N,N*-dimethylformamide.

(III) + (IV) -> (V):

The formation of *tert*-butyl benzoates of general formula (V) can be accomplished by the reaction of triazolinones of general formula (IV) with *tert*-butyl benzoates of general formula (III) in the presence of a base. In connection with the method of the invention, the use of 1,8-diazabicyclo[5.4.0]undec-7-ene as organic base in acetonitrile at 80℃ was preferrable.

(V) + (VI) -> (VII) -> (VIII):

The formation of benzoic acids of general formula (VIII) can be accomplished by reaction of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) in the presence of a base, and subsequent saponification of the resulting ester of general formula (VII).

Bases that can be employed for the reaction of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are for example sodium hydride, sodium *tert*-butanolate, potassium *tert*-butanolate, or cesium carbonate. In connection with the method of the invention, potassium hexamethyldisilazide solution in tetrahydrofuran was preferrably used as organic base.

Solvents that can be used for the reactions of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are for example tetrahydrofuran, dimethyl sulfoxide and *N,N*-dimethylformamide. In connection with the method according to the invention tertahydrofuran was preferrably used as solvent.

Reaction temperatures for the reactions of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are for example ranging from room temperature to 130℃. Cooling of the reaction mixture is optionally necessary on adding the reactants or bases. In connection with the method of the invention, cooling the reaction to -10℃ prior addition of potassium hexamethyldisilazide solution in tetrahydrofuran and subsequent running the reaction at room temperature was preferable.

Suitable reaction times for the reaction of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are ranging from 1h several days.

The reaction of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) can also result in transesterification, such as the *tert*-butoxide moiety of the *tert*-butyl

benzoates of general formula (V) can be replaced by the alkoxide $R^3CH(CH_3)O$ moiety of the alcohols of general formula (VI). In order to obtain the benzoic acids of general formula (VIII), subsequent ester hydrolysis is required.

Ester hydrolysis can be achieved by various methods which are well known to the person skilled in the art, for example by treatment of the esters with lithium hydroxide, sodium hydroxide or potassium hydroxide, in sovents, such as, for example water, 1,4-dioxane, ethanol or tetrahydrofuran or mixtures thereof. The reactions can be carried out at temperatures ranging from room temperature to the boiling point of the respective solvent or solvent mixture.

In connection with the method of the invention, use of lithium hydroxide in water/dioxane was preferrable.

(VIII) -> (IX), (VIII)/((IX) + (X) -> (I):

The compounds of general formula (I) can be prepared by the reaction of the benzoic acids of general formula (VIII) with amines of general formula (X) either by

- *in situ* formation of the the corresponding acid chlorides of general formula (IX) and subsequent reaction with amines of general formula (X),

or by

- amide coupling of the benzoic acids of general formula (VIII) with amines of general formula (X).

In situ formation of acid chlorides of general formula (IX) from benzoic acids of general formular (VIII) can be accomplished, for example by using oxalyl chloride or thionyl chloride, both reagents used in the presence of catalytic amount of *N,N*-dimethylformamide. In connection with the method according to the invention, oxalyl chloride is preferably used in the presence of *N,N*-dimethylformamide.

Suitable solvents for the *in situ* formation of acid chlorides of general formula (IX) from benzoic acids of general formula (VIII) include aprotic nonpolar solvents such as for example dichloromethane or toluene. In connection with the method according to the invention, dichloromethane is preferably used as sovent.

Suitable reaction temperatures for the *in situ* formation of acid chlorides of general formula (IX) from benzoic acids of general formula (VIII) mostly reflect the boiling point of the solvents used in the reaction. In connection with the method according to the invention, adding of oxalyl chloride was carried out at 0℃ and the reaction mixtur e was subsequently allowed to warm up to room temperature.

Subsequent reactions of the *in situ* formed acid chlorides of general formula (IX) with amines of general formula (X) can be carried out in the presence of an organic base. Suitable organic

bases are for example triethylamine, pyridine or *N*-ethyl-*N,N*-diisopropylamine. In connection with the method according to the invention, triethylamine was preferably used as organic base.

Suitable solvents for the reaction of acid chlorides of general formula (IX) with amines of general formula (X) include aprotic polar solvents such as for example acetonitrile, *N,N*-dimethylformamide or aprotic nonpolar solvents such as dichloromethane. In connection with the method according to the invention dichoromethane was used as solvent.

Suitable coupling reagents for the reaction of benzoic acids of general formula (VIII) with amines of general formula (X) are for example *O*-(7-aza-1*H*-benzotriazol-1-yl)-*N,N,N´,N´*-tetramethyluronium hexafluorophosphate (HATU), dicyclohexylcarbodiimide or a combination of 1*H*-benzotria-1-ol and 1-ethyl-3-[3-(diemthylaminopropyl]carbodiimide hydrochloride.

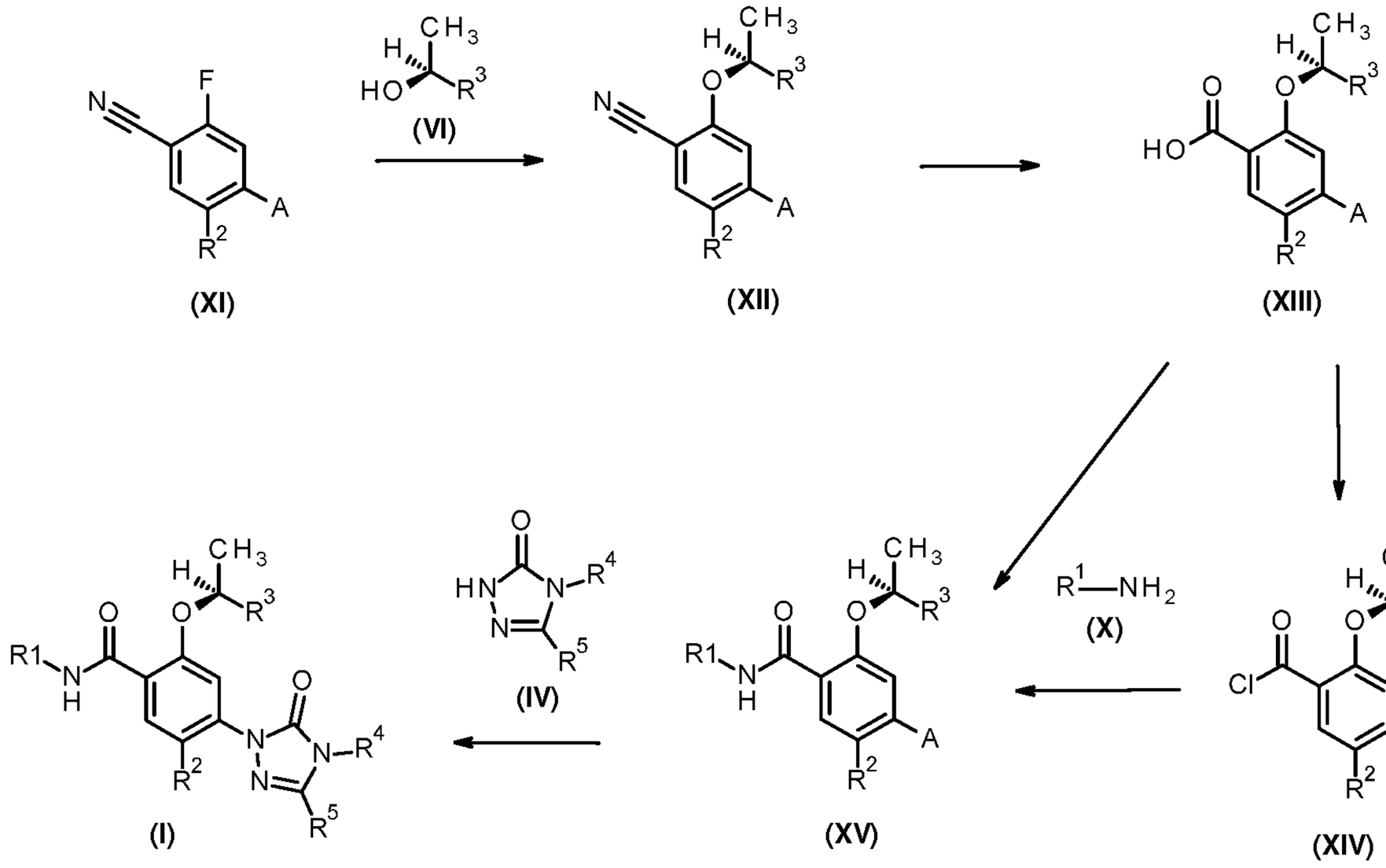
Suitable organic bases for the amide coupling of benzoic acids of general formula (VIII) with amines of general formula (X) are for example 4-(dimethylamino)pyridine, *N*-ethyl-*N,N*-diisopropylamine or triethylamine.

Suitable solvents for the for the amide coupling of benzoic acids of general formula (VIII) with amines of general formula (X) are for example *N,N*-dimethylformamide, dichoromethane or tetrahydrofuran.

For coupling of the amide bond, other methods which are well known to the person skilled in the art are also suitable, such as a condensation between amine and acid using propanephosphonic acid anhydride (T3P) as coupling reagent.

In connection with the invention, formation of the compounds according to the invention of general formula (I) were preferrably accomplished by *in situ* formation of acid chlorides of general formula (IX) from benzoic acids of general formula (VIII) and subsequent reaction with amines of general formula (X).

Synthetic Route 2



Scheme 2: Route for the preparation of compounds of general formula (I) in which R^1, R^2, R^3, R^4 and R^5 have the meaning as given for general formula (I), *supra*, and A represents a chlorine, bromine or iodine atom.

Compounds of general formulae (XI), (IV), (VI) and (X) are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art. Specific examples are described in the Experimental Section.

(XI) + (VI) -> (XII):

Nitriles of general formula (XII) can be prepared from nitriles of general formula (XI) and with alcohols of general formula (VI) according to procedures available from the public domain, as understandable to the person skilled in the art.

In connection with the method of the invention, the use of sodium hydride in DMF was preferable.

Alternatively, for alcohols of sufficiently high acidity the use of potassium carbonate was preferable.

(XII) -> (XIII):

The formation of benzoates of general formula (XIII) can be accomplished by hydrolysis of nitriles of general formula XII using strong acids or bases.

In connection with the method of the invention, the use of sodium hydroxide in ethanol at 90℃ was preferrable.

(XIII) -> (XIV) + (X) -> (XV):

The compounds of general formula (XV) can be prepared by the reaction of the benzoic acids of general formula (XIII) with amines of general formula (X) either by

- *in situ* formation of the the corresponding acid chlorides of general formula (XIV) and subsequent reaction with amines of general formula (X),

or by

- amide coupling of the benzoic acids of general formula (XV) with amines of general formula (X).

In situ formation of acid chlorides of general formula (XIV) from benzoic acids of general formular (XIII) can be accomplished, for example by using oxalyl chloride or thionyl chloride, both reagents used in the presence of catalytic amount of *N,N*-dimethylformamide. In connection with the method according to the invention, oxalyl chloride is preferably used in the presence of *N,N*-dimethylformamide.

Suitable solvents for the *in situ* formation of acid chlorides of general formula (XIV) from benzoic acids of general formula (XIII) include aprotic nonpolar solvents such as for example dichloromethane or toluene. In connection with the method according to the invention, dichloromethane is preferably used as sovent.

Suitable reaction temperatures for the *in situ* formation of acid chlorides of general formula (XIV) from benzoic acids of general formula (XIII) mostly reflect the boiling point of the solvents used in the reaction. In connection with the method according to the invention, adding of oxalyl chloride was carried out at 0℃ and the reaction mixtur e was subsequently allowed to warm up to room temperature.

Subsequent reactions of the *in situ* formed acid chlorides of general formula (XIV) with amines of general formula (X) can be carried out in the presence of an organic base. Suitable organic bases are for example triethylamine, pyridine or *N*-ethyl-*N,N*-diisopropylamine. In connection with the method according to the invention, triethylamine was preferably used as organic base.

Suitable solvents for the reaction of acid chlorides of general formula (XIV) with amines of general formula (X) include aprotic polar solvents such as for example acetonitrile, *N,N*-dimethylformamide or aprotic nonpolar solvents such as dichloromethane. In conection with the method according to the invention dichoromethane was used as solvent.

Suitable coupling reagents for the reaction of benzoic acids of general formula (XIII) with amines of general formula (X) are for example *O*-(7-aza-1*H*-benzotriazol-1-yl)-*N,N,N´,N´*-tetramethyluronium hexafluorophosphate (HATU), dicyclohexylcarbodiimide or a combination of 1*H*-benzotria-1-ol and 1-ethyl-3-[3-(diemthylaminopropyl]carbodiimide hydrochloride.

Suitable organic bases for the amide coupling of benzoic acids of general formula (XIII) with amines of general formula (X) are for example 4-(dimethylamino)pyridine, *N*-ethyl-*N,N*-diisopropylamine or triethylamine.

Suitable solvents for the for the amide coupling of benzoic acids of general formula (XIII) with amines of general formula (X) are for example *N,N*-dimethylformamide, dichoromethane or tetrahydrofuran.

For coupling of the amide bond, other methods which are well known to the person skilled in the art are also suitable, such as a condensation between amine and acid using propanephosphonic acid anhydride (T3P) as coupling reagent.

In connection with the invention, formation of the compounds according to the invention of general formula (XV) were preferrably accomplished by *in situ* formation of acid chlorides of general formula (XIV) from benzoic acids of general formula (XIII) and subsequent reaction with amines of general formula (X).

(XV) + (IV) -> (I):

Compounds according to the invention of general formula (I) can be prepared from halides of general formula (XV) and from triazolones of general formula (IV) using transition metals as catalysts.

Intermediates of general formula (XV) can be reacted with a suitable triazolone of general formula (IV), such as, for example 3-ethyl-4-methyl-1H-1,2,4-triazol-5(4H)-one, in the presence of a suitable base, such as, for example cesium carbonate, and a suitable palladium catalyst, such as for example (1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one–palladium, in the presence of a suitable ligand, such as for example (9,9-dimethyl-9*H*-xanthene-4,5-diyl)bis(diphenyl-phosphine), in a suitable solvent system, such as, for example, dioxane, in a temperature range from room temperature to the boiling point of the respective solvent, preferably the reaction is carried out at 100℃ to furnish compounds of general formula (I). Alternatively the following palladium catalysts can be used:

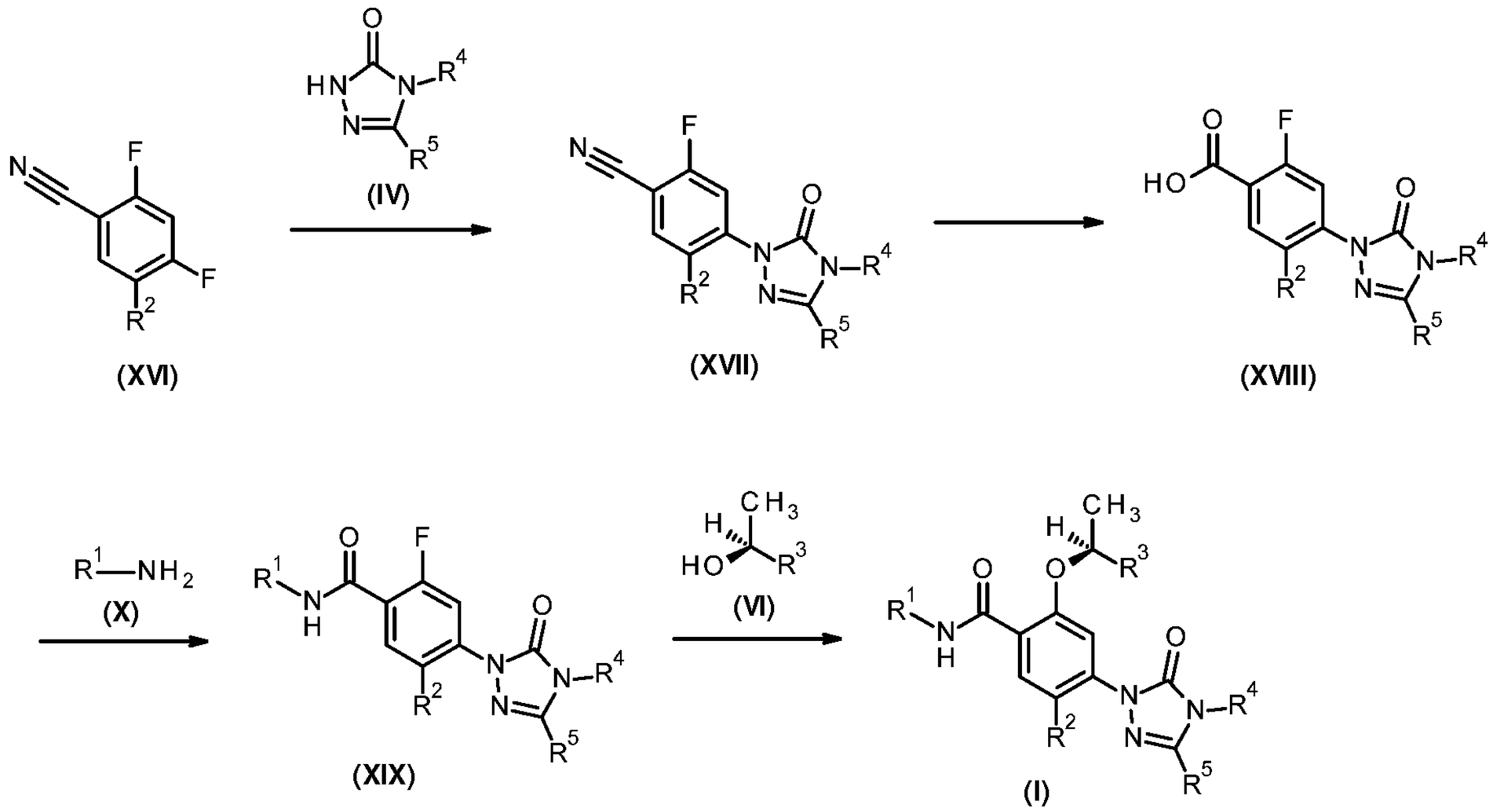
allylpalladium chloride dimer, dichlorobis(benzonitrile)palladium (II), palladium (II) acetate, palladium (II) chloride, tetrakis(triphenylphosphine)palladium (0), tris(dibenzylideneacetone)dipalladium (0), chloro(2'-amino-1,1'-biphenyl-2-yl)palladium(II) dimer, (2'-amino-1,1'-biphenyl-2-yl)methanesulfonatopalladium(II) dimer, trans-di(μ-acetato)bis[o-(di-o-tolylphosphino)benzyl]dipalladium(II) [cataCXium® C], allylchloro[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene]palladium(II), allylchloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]palladium(II), chloro[(1,3-dimesitylimidazol-[1,3-bis(2,4,6-trimethylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene](chloro){2-[(dimethylamino)methyl]phenyl}palladium, chloro[(1,2,3-N)-3-phenyl-2-propenyl][1,3-bis(2,6-di-iso-propylphenyl)imidazol-2-ylidene]palladium(II), [2-(acetylamino)phenyl]{1,3-bis[2,6-

di(propan-2-yl)phenyl]-1,3-dihydro-2H-imidazol-2-ylidene}chloropalladium, {1,3-bis[2,6-di(propan-2-yl)phenyl]-1,3-dihydro-2H-imidazol-2-ylidene}(chloro){2-[(dimethylamino)methyl]phenyl} palladium, {1,3-bis[2,6-di(propan-2-yl)phenyl]-2,3-dihydro-1H-imidazol-2-yl}(dichloro)(3-chloropyridine-kappaN)palladium, [1,3-bis(2,6-diisopropylphenyl) imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride, [2-(acetylamino)-4-methoxyphenyl]{1,3-bis[2,6-di(propan-2-yl)phenyl]-1,3-dihydro-2H-imidazol-2-ylidene}chloropalladium, {1,3-bis[2,6-di(propan-2-yl)phenyl]-1,3-dihydro-2H-imidazol-2-ylidene}(chloro){2-[(dimethylamino)methyl]-3,5-dimethoxyphenyl}palladium, dichloro[1,3-bis(2,6-di-3-pentylphenyl)imidazol-2-ylidene](3-chloropyridyl) palladium(II), dichloro(di-µ-chloro)bis[1,3-bis(2,6-di-iso-propylphenyl) imidazol-2-ylidene]dipalladium(II), 2-(2'-di-tert-butylphosphine)biphenylpalladium(II) acetate, chloro[dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)-lambda5-phosphanyl][2-(phenyl-kappaC2)ethanaminato-kappaN]palladium, [2-(2-aminoethyl)phenyl](chloro)palladium - di-tert-butyl[2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane, {dicyclohexyl[2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane}{2-[2-(methylazanidyl-kappaN)ethyl]phenyl-kappaC1}palladium, chloro(2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl)(2'-amino-1,1'-biphenyl-2-yl) palladium(II), [2',6'-bis(propan-2-yloxy)biphenyl-2-yl](dicyclohexyl)phosphane - [2-(2-aminoethyl)phenyl](chloro)palladium, [2-(2-aminoethyl)phenyl](chloro){dicyclohexyl[2',4',6'-tri(propan-2-yl)biphenyl-2-yl]-lambda5-phosphanylidene}palladium, 2'-(dicyclohexylphosphanyl)-N,N,N',N'-tetramethylbiphenyl-2,6-diamine - (2'-aminobiphenyl-2-yl)(chloro)palladium, chloro(2-dicyclohexylphosphino-2',4',6'-tri-iso-propyl-1,1'-biphenyl)[2-(2-aminoethyl)phenyl]palladium(II), (2'-aminobiphenyl-2-yl)(methane-sulfonato-kappaO)palladium - [2',6'-bis(propan-2-yloxy)biphenyl-2-yl](dicyclohexyl) phosphane, (2'-aminobiphenyl-2-yl)(methanesulfonato-kappaO)palladium - dicyclohexyl[2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane, (2'-aminobiphenyl-2-yl)palladium(1+) methanesulfonate - dicyclohexyl[2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane, dicyclohexyl[3,6-dimethoxy-2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane - (2'-aminobiphenyl-2-yl)(chloro)palladium, (2'-aminobiphenyl-2-yl)(methanesulfonato-kappaO)palladium - di-tert-butyl[3,6-dimethoxy-2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane, (2'-aminobiphenyl-2-yl)(methanesulfonato-kappaO)palladium -

dicyclohexyl[3,6-dimethoxy-2',4',6'-tri(propan-2-yl)biphenyl-2-yl]phosphane or the following ligands:

racemic-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, rac-BINAP, 1,1'-bis(diphenylphosphino)ferrocene, bis(2-diphenylphosphinophenyl)ether, di-*tert*-butylmethylphosphonium tetrafluoroborate, 2-(di-*tert*-butylphosphino)biphenyl, tri-*tert*-butylphosphonium tetrafluoroborate, tri-2-furylphosphine, tris(2,4-di-*tert*-butylphenyl)phosphite, tri-*o*-tolylphosphine, (9,9-dimethyl-9*H*-xanthene-4,5-diyl)bis(diphenylphosphine), dicyclohexyl(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphine, di-tert-butyl (2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphine, di-tert-butyl(2',4',6'-triiso propylbiphenyl-2-yl)phosphine, dicyclohexyl(2',4',6'-triisopropylbiphenyl-2-yl) phosphine, di-tert-butyl(2',4',6'-triisopropyl-3-methoxy-6-methylbiphenyl-2-yl)phos-phine, di-tert-butyl(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl) phosphine, adamantan-1-yl(adamantan-2-yl)(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl) phosphine, dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine, dicyclohexyl(2',6'-diisopropoxybiphenyl-2-yl)phosphine, 2'-(dicyclohexylphosphino)-N,N-dimethyl-biphenyl-2-amine, 2'-(di-tert-butylphosphino)-N,N-dimethylbiphenyl-2-amine, 2'-(di-phenylphosphino)-N,N,N',N'-tetramethylbiphenyl-2,6-diamine, di-tert-butyl(2',4',6'-tricyclohexyl-3,6-dimethoxybiphenyl-2-yl)phosphine, bis[3,5-bis(trifluoromethyl)phe-nyl] (2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphine, biphenyl-2-yl(di-tert-butyl)phosphine, dicyclohexyl(2'-methylbiphenyl-2-yl)phosphine, biphenyl-2-yl (dicyclohexyl)phosphine, 2'-(dicyclohexylphosphino)-N,N-dimethylbiphenyl-2-amine, 2'-(dicyclohexylphosphino)-N,N,N',N'-tetramethylbiphenyl-2,6-diamine, sodium 2'-(dicyclohexylphosphino)-2,6-diisopropylbiphenyl-4-sulfonate, sodium 2'-(dicyclohexylphosphino)-2,6-dimethoxybiphenyl-3-sulfonate, 1,1'-binaphthalen-2-yl(di-tert-butyl)phosphine, 1,3-bis(2,4,6-trimethylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene, 1,3-bis[2,6-di(propan-2-yl)phenyl]-1,3-dihydro-2H-imidazol-2-ylidene.

Synthetic Route 3



Scheme 3: Route for the preparation of compounds of general formula (I) in which R^1, R^2, R^3, R^4 and R^5 have the meaning as given for general formula (I), *supra*.

Compounds of general formulae (XVI), (IV), (VI) and (X) are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art. Specific examples are described in the Experimental Section.

Nitriles of general formula (XVII) can be prepared from nitriles of general formula (XVI) and triazolinones of general formula (IV) in the presence of a base. In connection with the method of the invention, the use of potassium carbonate as base in acetonitrile at 80℃ was preferrable.

The formation of benzoates of general formula (XVIII) can be accomplished by hydrolysis of nitriles of general formula XVII using strong acids or bases. In connection with the method of the invention, the use of sodium hydroxide in ethanol at 85 ℃ was preferrable.

The compounds of general formula (XIX) can be prepared by the reaction of the benzoic acids of general formula (XVIII) with amines of general formula (X) by amide coupling.

Suitable coupling reagents for the reaction of benzoic acids of general formula (XVIII) with amines of general formula (X) are for example *O*-(7-aza-1*H*-benzotriazol-1-yl)-*N,N,N´,N´*-tetramethyluronium hexafluorophosphate (HATU), dicyclohexylcarbodiimide or a combination of 1*H*-benzotria-1-ol and 1-ethyl-3-[3-(diemthylaminopropyl]carbodiimide hydrochloride.

Suitable organic bases for the amide coupling of benzoic acids of general formula (XVIII) with amines of general formula (X) are for example 4-(dimethylamino)pyridine, *N*-ethyl-*N,N*-diisopropylamine, *N*-methylpyrollidine, or triethylamine.

Suitable solvents for the for the amide coupling of benzoic acids of general formula (XVIII) with amines of general formula (X) are for example *N,N*-dimethylformamide, dichoromethane or tetrahydrofuran.

For coupling of the amide bond, other methods which are well known to the person skilled in the art are also suitable, such as a condensation between amine and acid using propanephosphonic acid anhydride (T3P) as coupling reagent, or transformation of benzoic acids of general formula (XVIII) into their respective acid chlorides and subsequent reaction with amines of general formula (X) as described above.

In connection with the invention, formation of the compounds of general formula (XIX) were preferrably accomplished by HATU mediated amide coupling of benzoic acids of general formula (XVIII) and amines of general formula (X).

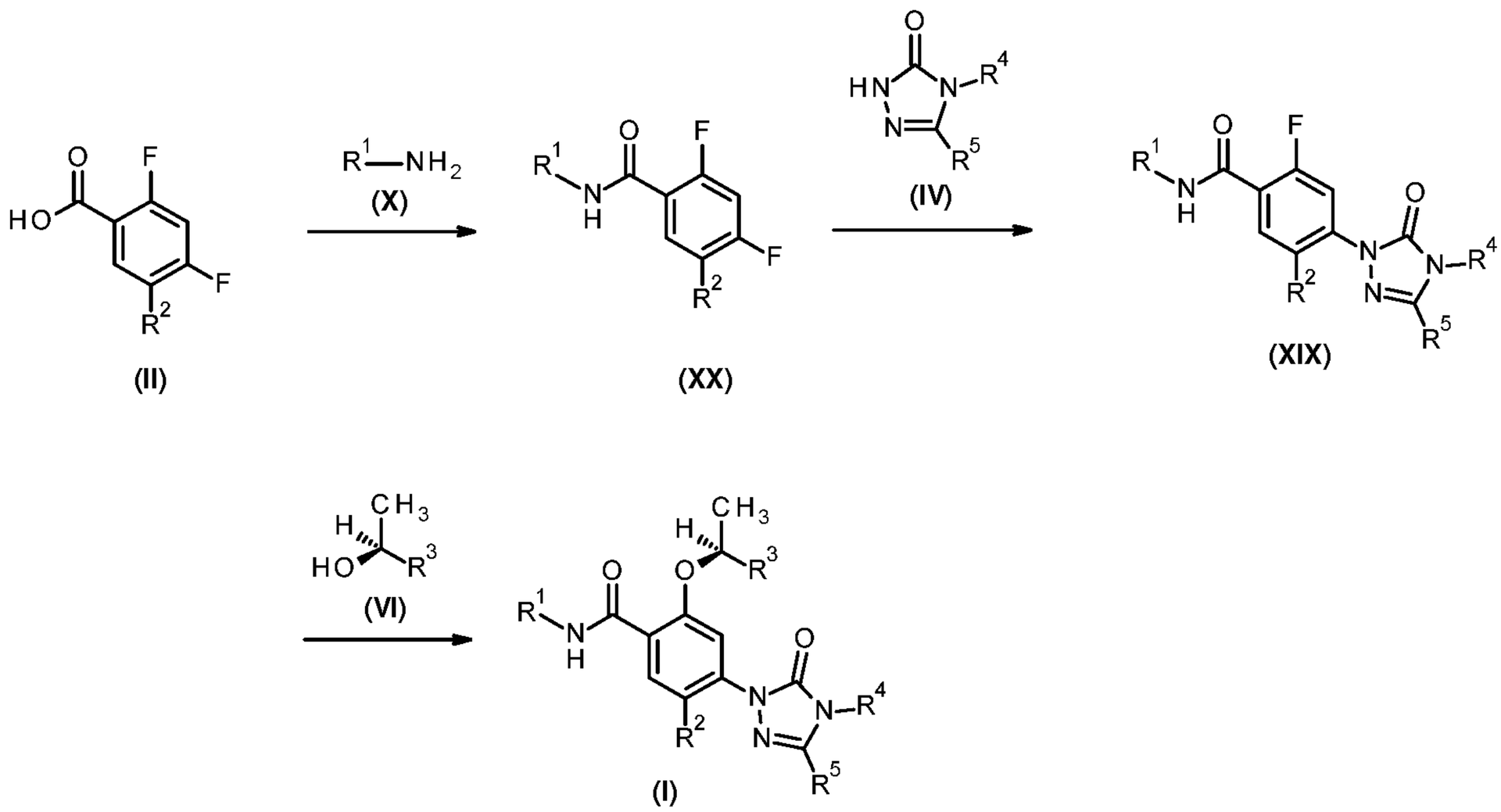
The formation of compounds of of general formula (I) can be accomplished by reaction of amides of general formula (XIX) and alcohols of general formula (VI) in the presence of a base. Bases that can be employed for the reaction of amides of general formula (XIX) with alcohols of general formula (VI) are for example sodium hydride, sodium *tert*-butanolate, potassium *tert*-butanolate, or cesium carbonate. In connection with the method of the invention, sodium hydride was preferrably used as organic base.

Solvents that can be used for the reactions of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are for example tetrahydrofuran, dimethyl sulfoxide and *N,N*-dimethylformamide. In connection with the method according to the invention *N,N*-dimethylformamide was preferrably used as solvent.

Reaction temperatures for the reactions of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are for example ranging from room temperature to 80℃. In connection with the method of the invention, the reaction of alcohols of general formula (VI) with sodium hydride was preferably performed at room temperature for 1h before addition of amides of formula (XIX) and subsequent heating of the reaction mixture to 80℃.

Suitable reaction times for the reaction of *tert*-butyl benzoates of general formula (V) with alcohols of general formula (VI) are ranging from 3h to several days.

Synthetic Route 4



Scheme 4: Route for the preparation of compounds of general formula (I) in which R^1, R^2, R^3, R^4 and R^5 have the meaning as given for general formula (I), *supra*.

Compounds of general formulae (II), (IV), (VI) and (X) are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art. Specific examples are described in the Experimental Section.

Amides of general formula (XX) can be prepared by the reaction of the benzoic acids of general formula (II) with amines of general formula (X) by amide coupling.

Suitable coupling reagents for the reaction of benzoic acids of general formula (II) with amines of general formula (X) are for example *O*-(7-aza-1*H*-benzotriazol-1-yl)-*N,N,N´,N´*-tetramethyluronium hexafluorophosphate (HATU), dicyclohexylcarbodiimide or a combination of 1*H*-benzotria-1-ol and 1-ethyl-3-[3-(diemthylaminopropyl]carbodiimide hydrochloride.

Suitable organic bases for the amide coupling of benzoic acids of general formula (II) with amines of general formula (X) are for example 4-(dimethylamino)pyridine, *N*-ethyl-*N,N*-diisopropylamine, *N*-methylpyrollidine, or triethylamine.

Suitable solvents for the for the amide coupling of benzoic acids of general formula (II) with amines of general formula (X) are for example *N,N*-dimethylformamide, dichoromethane or tetrahydrofuran.

For coupling of the amide bond, other methods which are well known to the person skilled in the art are also suitable, such as a condensation between amine and acid using propanephosphonic acid anhydride (T3P) as coupling reagent, or transformation of benzoic

acids of general formula (II) into their respective acid chlorides and subsequent reaction with amines of general formula (X) as described above.

In connection with the invention, formation of the compounds of general formula (XX) were preferrably accomplished by HATU mediated amide coupling of benzoic acids of general formula (II) and amines of general formula (X).

Alternatively, amides of general formula (XX) can be prepared from benzoic acid derivatives of general formula (II) by *in situ* formation of the the corresponding acid chlorides and subsequent reaction with amines of general formula (X).

In situ formation of acid chlorides from benzoic acids of general formular (II) can be accomplished, for example by using oxalyl chloride or thionyl chloride, both reagents used in the presence of catalytic amount of *N,N*-dimethylformamide.

(XX) + (IV) -> (XIX):

The formation of compounds of general formula (XIX) can be accomplished by the reaction of triazolinones of general formula (IV) with amides of general formula (XX) in the presence of a base, such as potassium carbonate. In connection with the method of the invention, the use of 1,8-diazabicyclo[5.4.0]undec-7-ene as organic base in acetonitrile at 80℃ was preferrable.

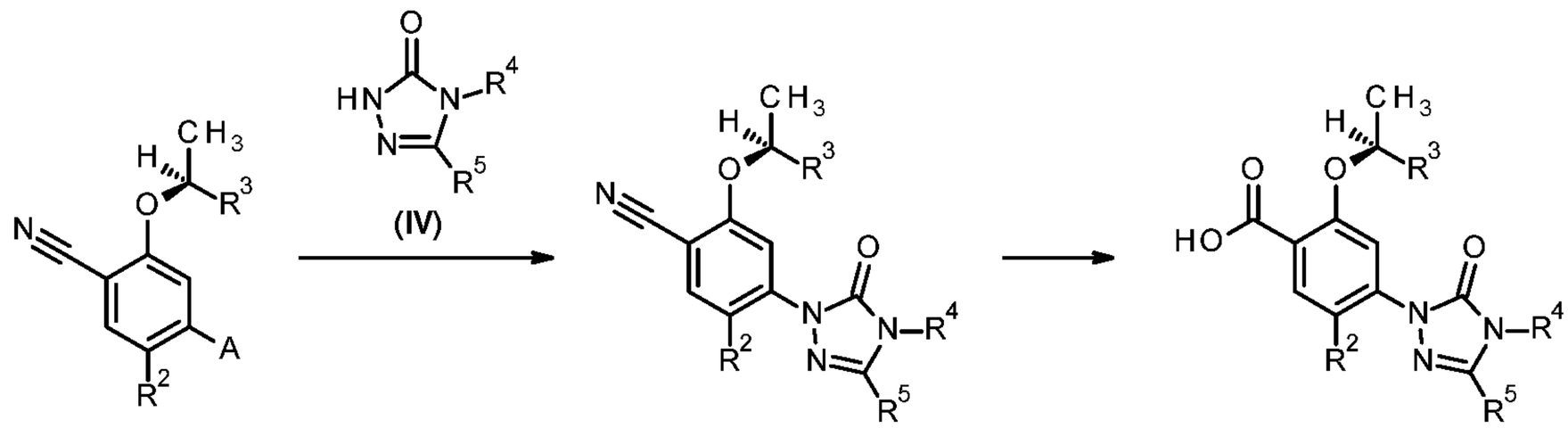
The formation of compounds of general formula (I) can be accomplished by reaction of amides of general formula (XIX) and alcohols of general formula (VI) in the presence of a base. Bases that can be employed for the reaction of amides of general formula (XIX) with alcohols of general formula (VI) are for example sodium hydride, sodium *tert*-butanolate, potassium *tert*-butanolate, or cesium carbonate. In connection with the method of the invention, sodium hydride was preferrably used as organic base.

Solvents that can be used for the reactions of amides of general formula (XIX) with alcohols of general formula (VI) are for example tetrahydrofuran, dimethyl sulfoxide and *N,N*-dimethylformamide. In connection with the method according to the invention *N,N*-dimethylformamide was preferrably used as solvent.

Reaction temperatures for the reactions of amides of general formula (XIX) with alcohols of general formula (VI) are for example ranging from room temperature to 140℃. In connection with the method of the invention, the reaction of alcohols of general formula (VI) with sodium hydride was preferably performed at room temperature for 1h before addition of amides of formula (XIX) and subsequent heating of the reaction mixture to 80℃.

Suitable reaction times for the reaction of amides of general formula (XIX) with alcohols of general formula (VI) are ranging from 3h to several days.

Synthetic Route 5



Scheme 5: Alternative route for the preparation of compounds of general formula (VIII) in which R^2, R^3, R^4 and R^5 have the meaning as given for general formula (I), *supra*, and A represents a chlorine, bromine or iodine atom.

An alternative synthesis of compounds of formula (VIII) is described in scheme 5.

Compounds of general formula (XXI) can be prepared from halides of general formula (XII) and from triazolones of general formula (IV) using transition metals as catalysts.

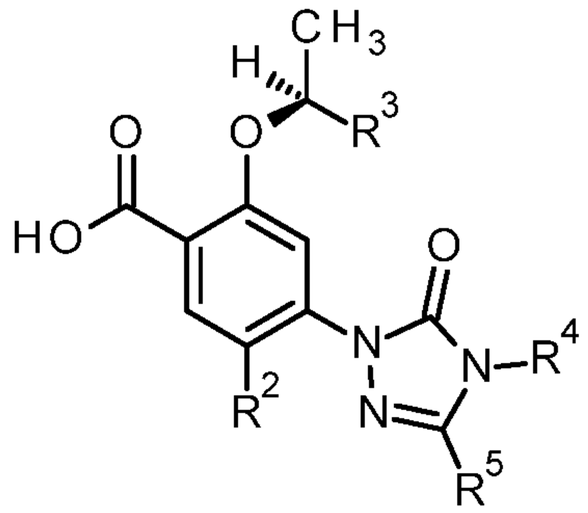
The formation of benzoates of general formula (VIII) can be accomplished by hydrolysis of nitriles of general formula XXI using strong acids or bases. In connection with the method of the invention, the use of sulphuric acid, acetic acid and water at 120 °C was preferrable.

The synthesis of ompounds of general formula (XII) and the synthesis of compounds of general formula (I) from compounds of general formula (VIII) is described above.

The order of transformations exemplified in these schemes is therefore not intended to be limiting. In addition, interconversion of any of the substituents, R^1, R^2, R^3, R^4 or R^5 can be achieved before and/or after the exemplified transformations. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wuts in *Protective Groups in Organic Synthesis*, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

The resulting compounds of general formula (I) are optionally converted with corresponding (i) solvents and/or (ii) bases or acids to their solvates, salts and/or solvates of the salts, in which R^1, R^2, R^3, R^4 and R^5 have the meaning as given for general formula (I), *supra*.

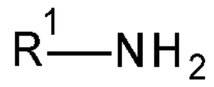
In accordance with another aspect, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (VIII) :



(VIII),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

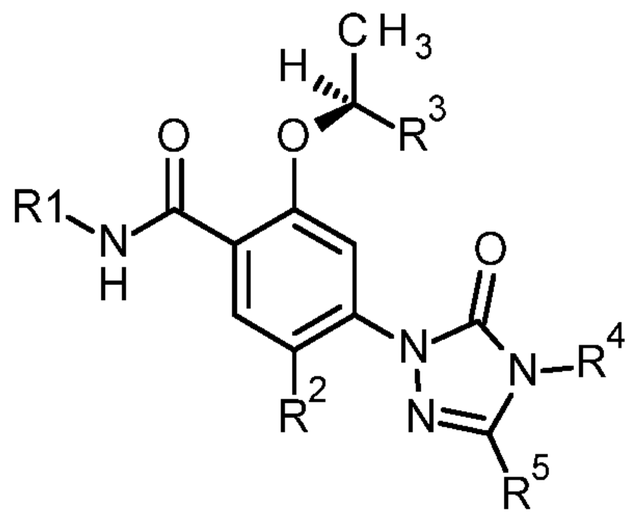
to react with a compound of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) as defined *supra*,

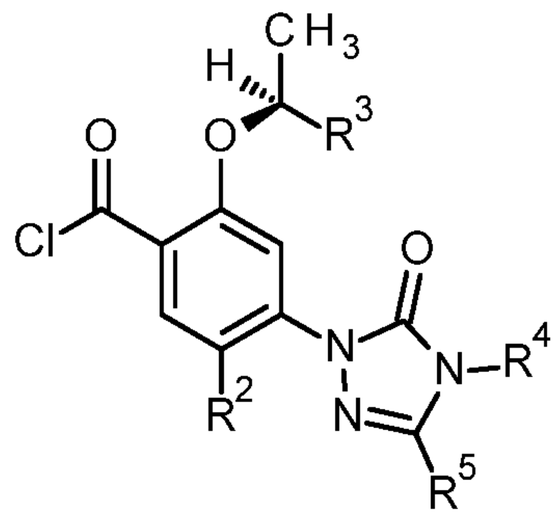
thereby giving a compound of general formula (I) :



(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*.

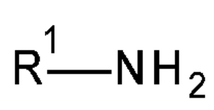
In accordance with certain embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (IX) :



(IX),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

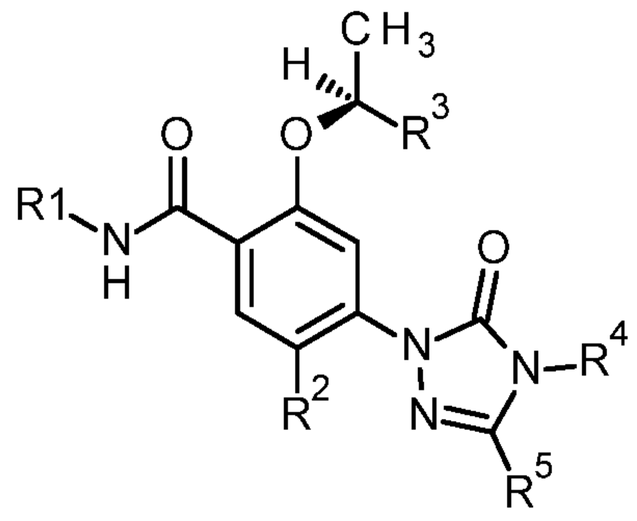
to react with a compound of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) as defined *supra*,

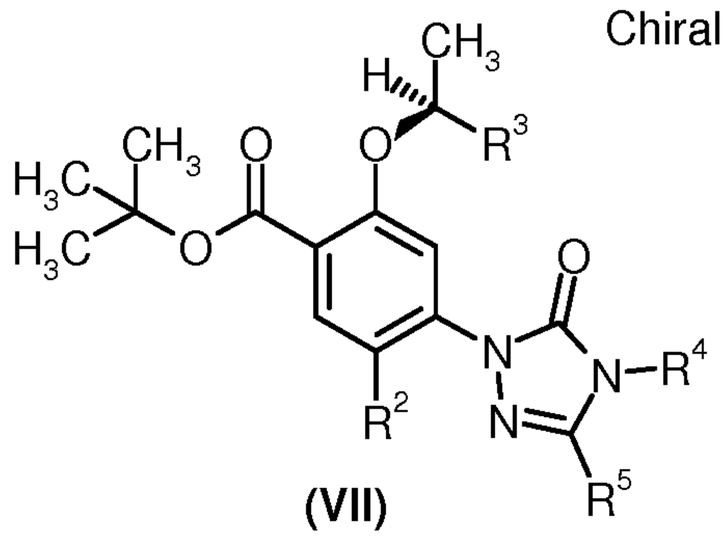
thereby giving a compound of general formula (I) :



(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*.

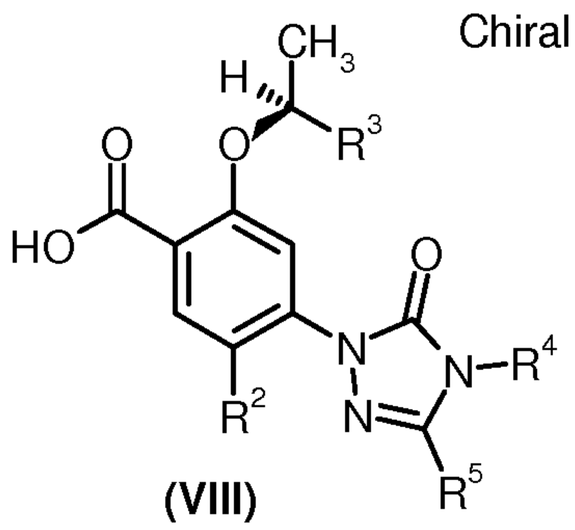
In accordance with certain embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (VII)



(VII)

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

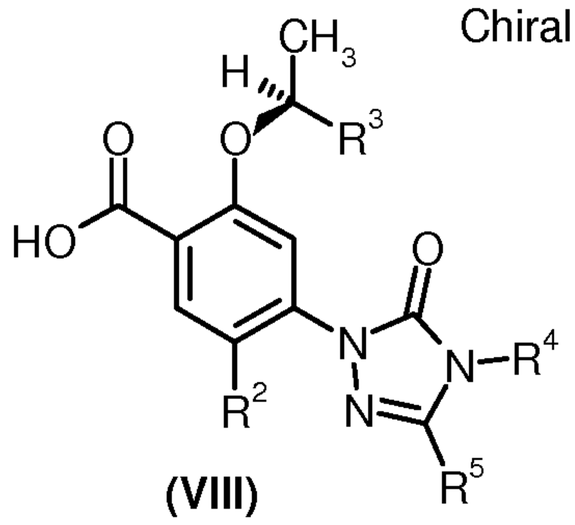
to be saponified resulting in a compound of general formula (VIII)



(VIII)

.

In accordance with certain embodiments, the present invention provides the intermediate compound of general formula (VIII)

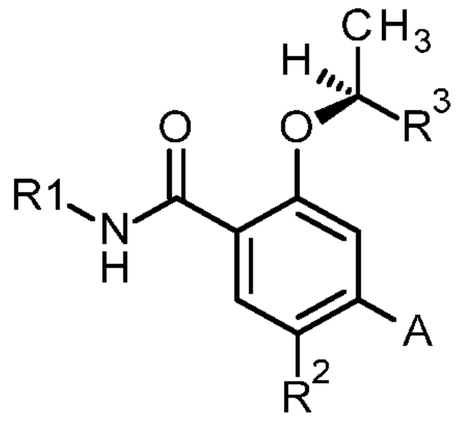


(VIII)

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

In accordance with certain embodiments, the present invention provides the use of the intermeidate compound (VIII) in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra* for the production of a compound of general formula (I).

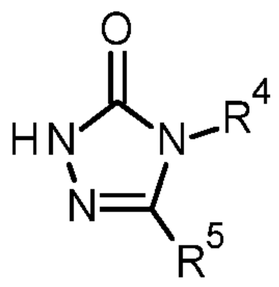
In accordance with further embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (XV) :



(XV),

in which R^1, R^2 and R^3 are as defined for the compound of general formula (I) as defined *supra*, and A represents a chlorine, bromine or iodine atom,

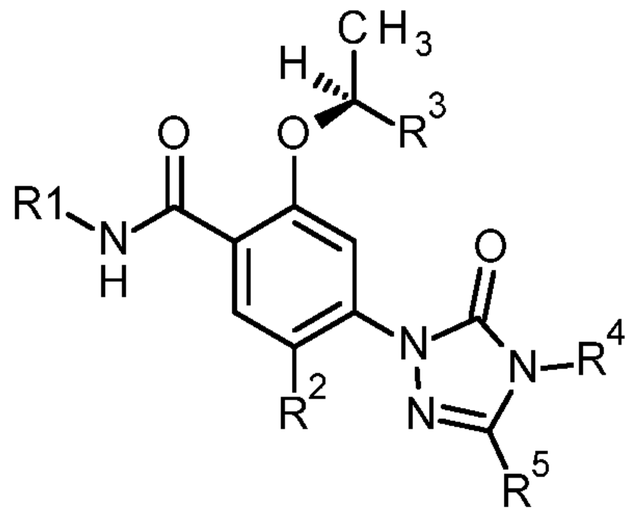
to react with a compound of general formula (IV) :



(IV),

in which R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

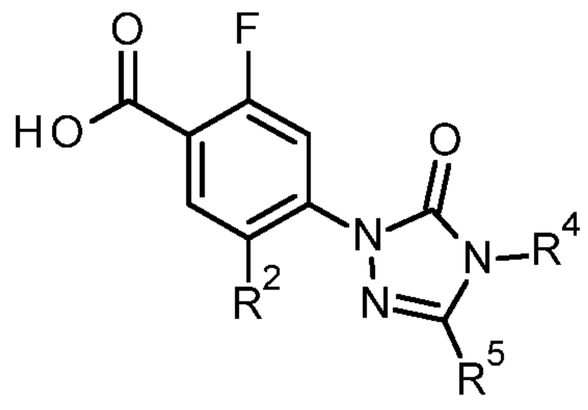
thereby giving a compound of general formula (I) :



(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*.

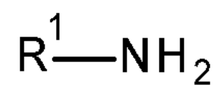
In accordance with other embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (XVIII) :



(XVIII),

in which R^2, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

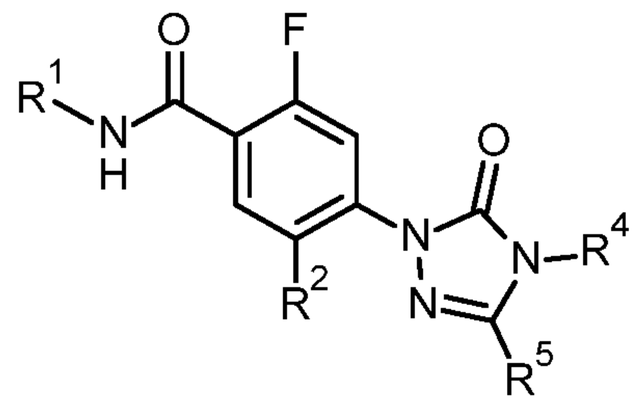
to react with a compound of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) as defined *supra*,

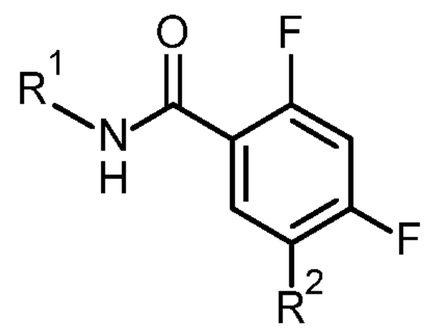
thereby giving a compound of general formula (XIX) :



(XIX),

in which R^1, R^2, R^4 and R^5 are as defined *supra*.

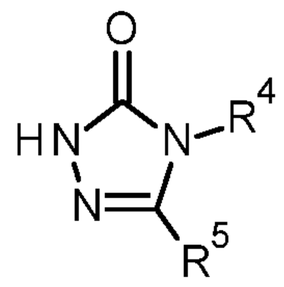
In accordance with other embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (XX) :



(XX),

in which R^1 and R^2 are as defined for the compound of general formula (I) as defined *supra*,

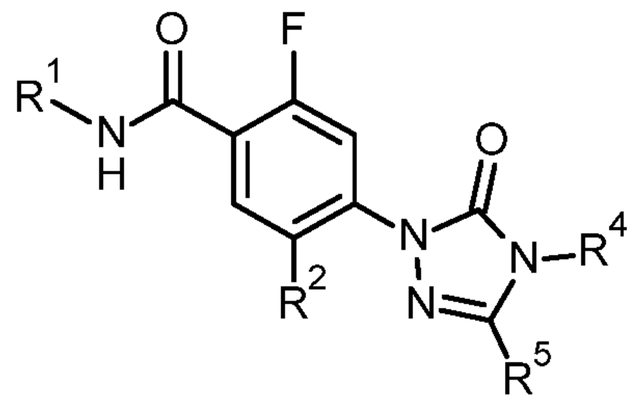
to react with a compound of general formula (IV) :



(IV),

in which R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

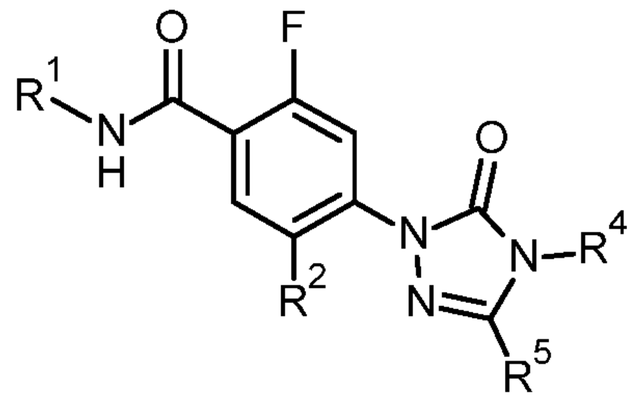
thereby giving a compound of general formula (XIX) :



(XIX),

in which R^1, R^2, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*.

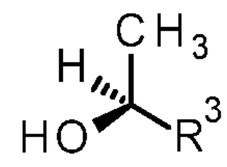
In accordance with further embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (XIX) :



(XIX),

in which R^1, R^2, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

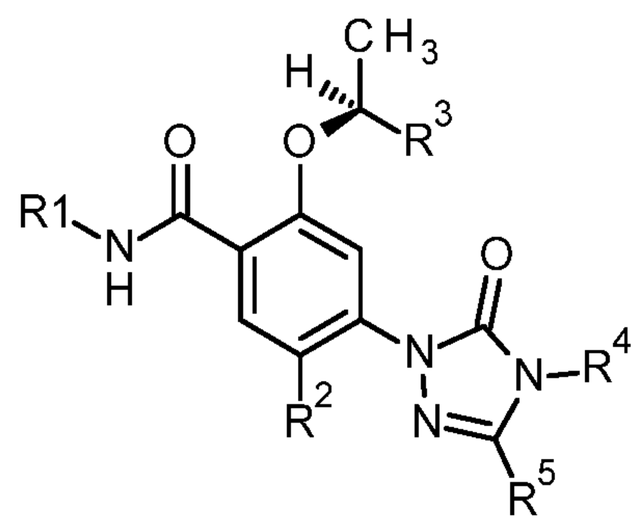
to react with a compound of general formula (VI) :



(VI),

in which R^3 is as defined for the compound of general formula (I) as defined *supra*,

thereby giving a compound of general formula (I) :

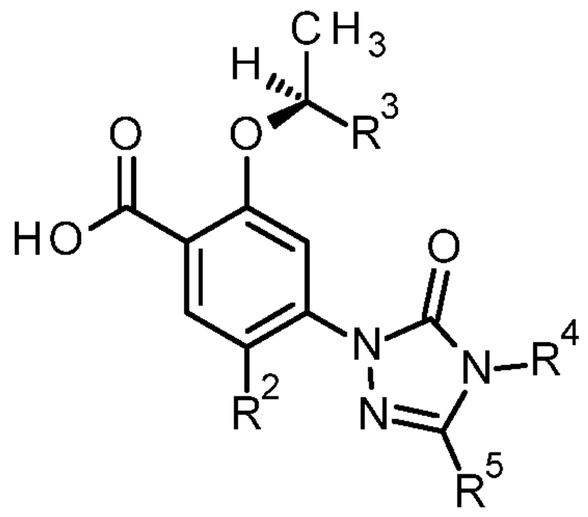


(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*.

In accordance with another aspect, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*,

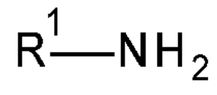
said methods comprise the step of allowing an intermediate compound of general formula (VIII) :



(VIII),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

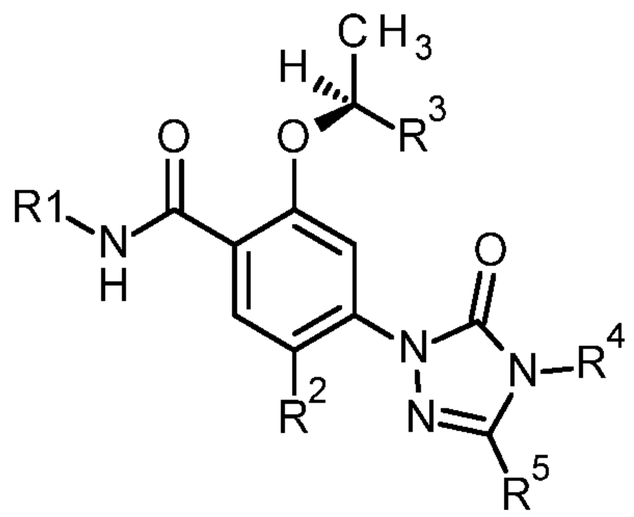
to react with a compound of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) as defined *supra*,

thereby giving a compound of general formula (I) :

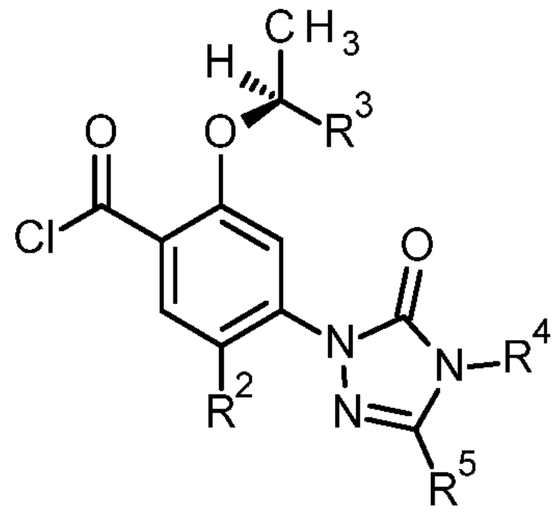


(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*,

then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

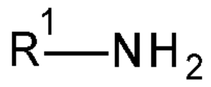
In accordance with certain embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (IX) :



(IX),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

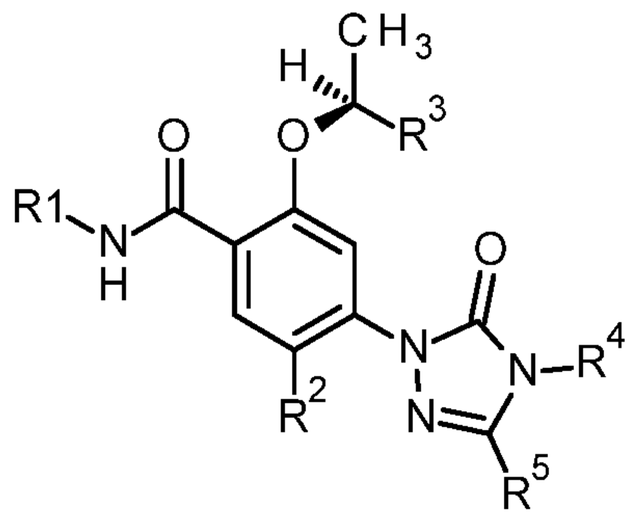
to react with a compound of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) as defined *supra*,

thereby giving a compound of general formula (I) :

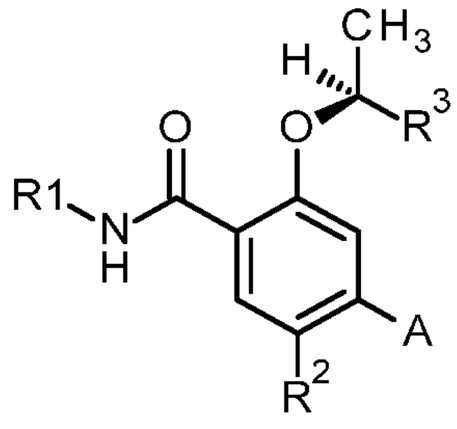


(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*,

then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

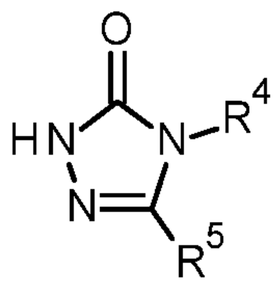
In accordance with further embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (XV) :



(XV),

in which R^1, R^2 and R^3 are as defined for the compound of general formula (I) as defined *supra*, and A represents a chlorine, bromine or iodine atom,

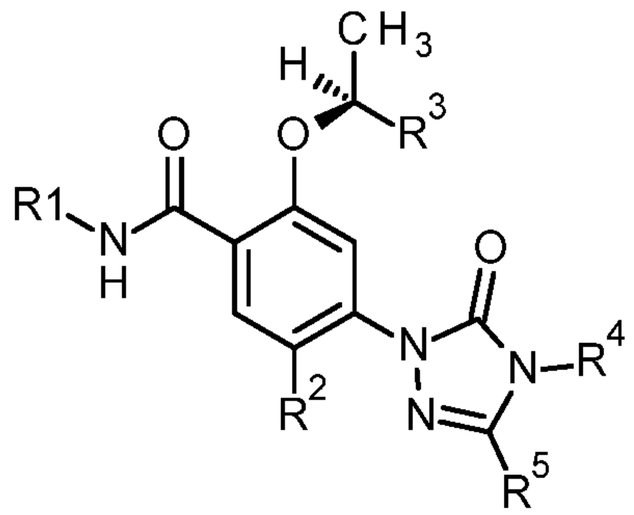
to react with a compound of general formula (IV) :



(IV),

in which R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

thereby giving a compound of general formula (I) :

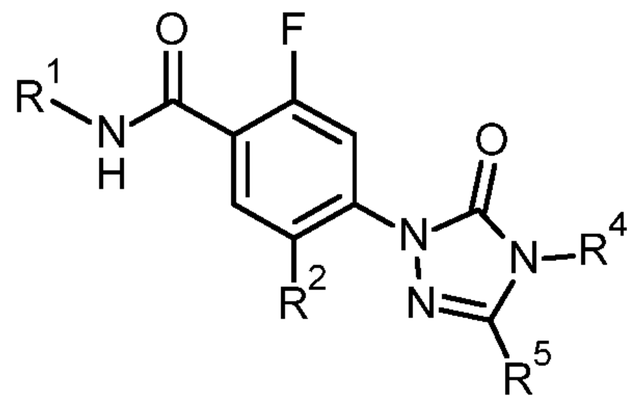


(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*,

then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

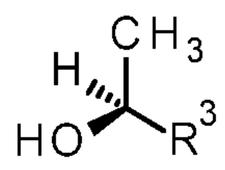
In accordance with other embodiments, the present invention provides methods of preparing compounds of general formula (I) as defined *supra*, said methods comprising the step of allowing an intermediate compound of general formula (XIX) :



(XIX),

in which R^1, R^2, R^4 and R^5 are as defined for the compound of general formula (I) as defined *supra*,

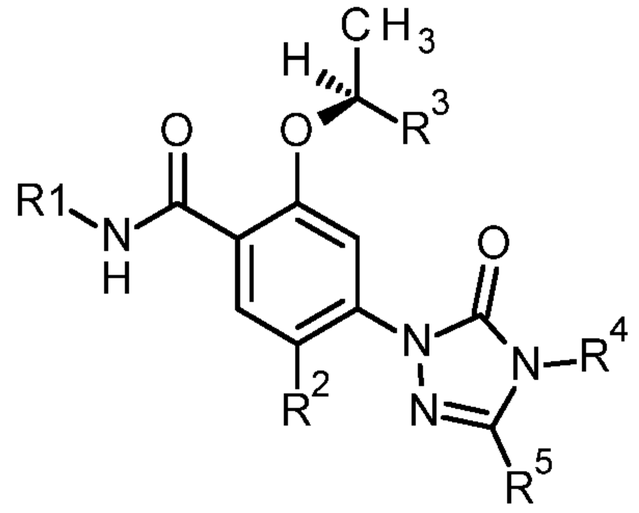
to react with a compound of general formula (VI) :



(VI),

in which R^3 is as defined for the compound of general formula (I) as defined *supra*,

thereby giving a compound of general formula (I) :



(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined *supra*,

then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

The present invention provides methods of preparing compounds of the present invention of general formula (I), said methods comprising the steps as described in the Experimental Section herein.

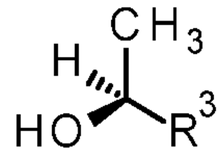
In accordance with a further aspect, the present invention provides intermediate compounds which are useful for the preparation of the compounds of general formula (I), *supra*.

Particularly, the invention provides the intermediate compounds of general formula (IV) :

(IV),

in which R^4 and R^5 are as defined for the compound of general formula (I) *supra*.

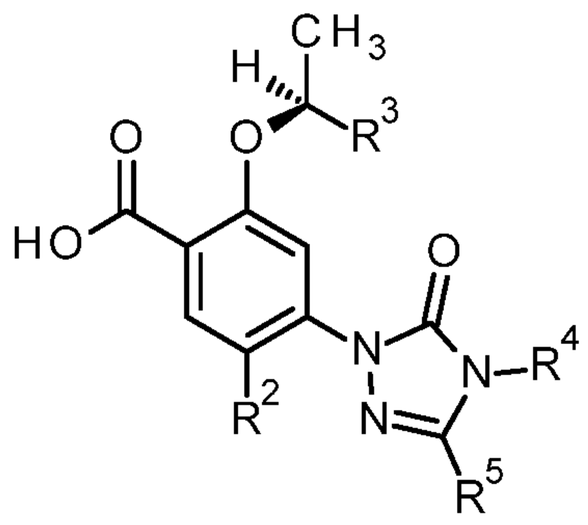
Furthermore, the invention provides the intermediate compounds of general formula (VI) :



(VI),

in which R^3 is as defined for the compound of general formula (I) *supra*.

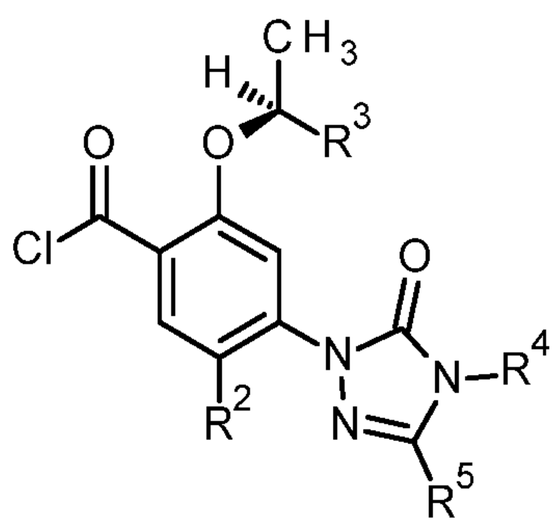
Particularly, the invention provides the intermediate compounds of general formula (VIII) :



(VIII),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) *supra*.

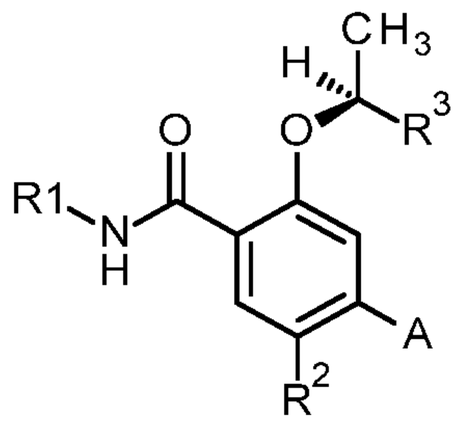
Particularly, the inventions provides the intermediate compounds of general formula (IX) :



(IX),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) *supra*.

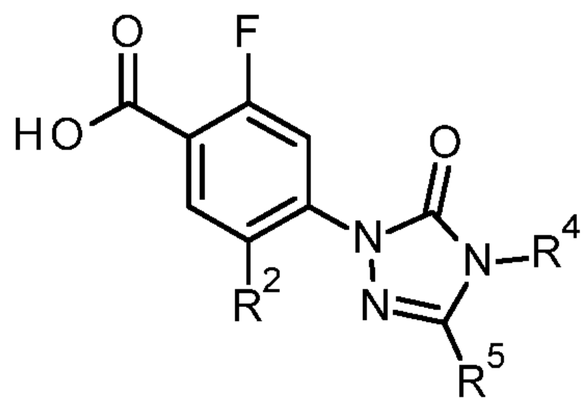
Particularly, the inventions provides the intermediate compounds of general formula (XV) :



(XV),

in which R^1, R^2 and R^3 are as defined for the compound of general formula (I) *supra*, and A represents a chlorine, bromine or iodine atom.

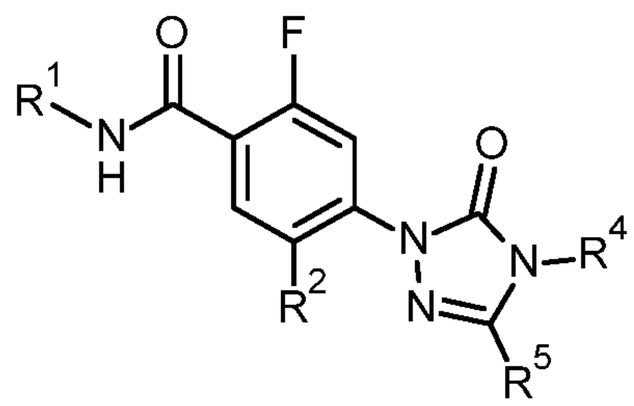
Particularly, the inventions provides the intermediate compounds of general formula (XVIII) :



(XVIII),

in which R^2, R^4 and R^5 are as defined for the compound of general formula (I) *supra*.

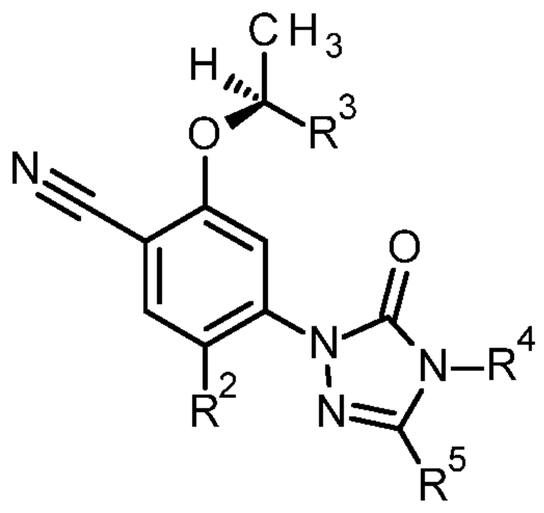
Particularly, the invention provides the intermediate compounds of general formula (XIX) :



(XIX),

in which R^1, R^2, R^4 and R^5 are as defined for the compound of general formula (I) *supra*.

Particularly, the invention provides the intermediate compounds of general formula (XXI) :

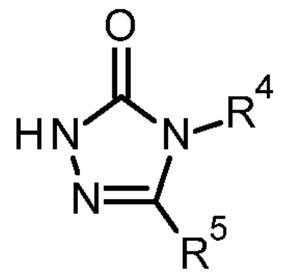


(XXI),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) *supra*.

In accordance with another aspect, the present invention provides the use of said intermediate compounds for the preparation of a compound of general formula (I) as defined *supra*.

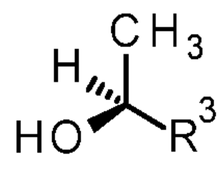
Particularly, the invention provides the use of intermediate compounds of general formula (IV) :



(IV),

in which R^4 and R^5 are as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

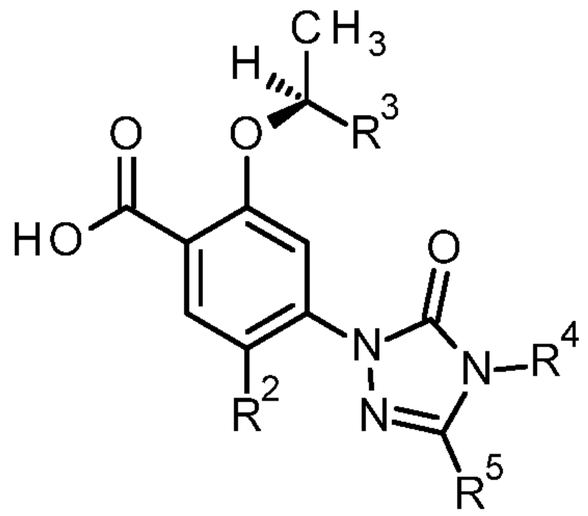
Particularly, the invention provides the use of intermediate compounds of general formula (VI) :



(VI),

in which R^3 is as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

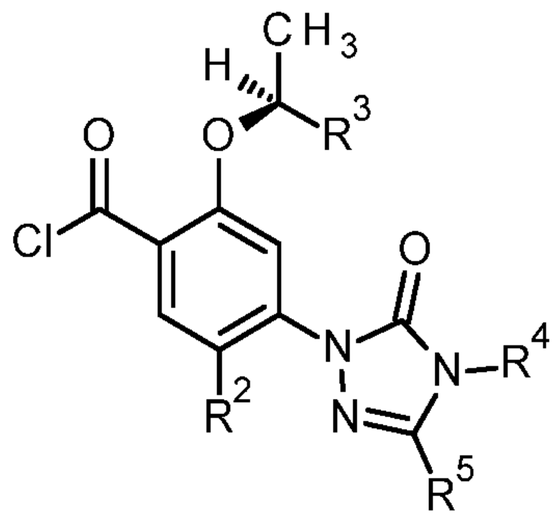
Particularly, the invention provides the use of intermediate compounds of general formula (VIII) :



(VIII),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

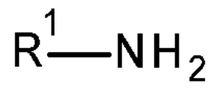
Particularly, the invention provides the use of intermediate compounds of general formula (IX) :



(IX),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

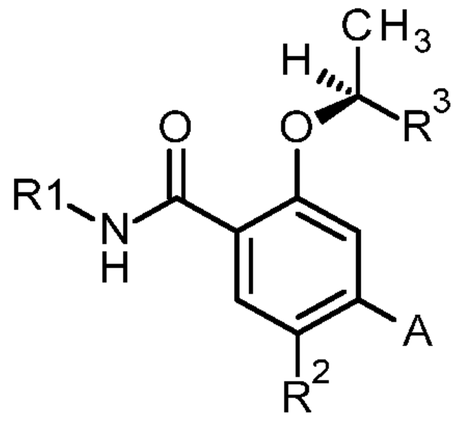
Particularly, the invention provides the use of intermediate compounds of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) as defined *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

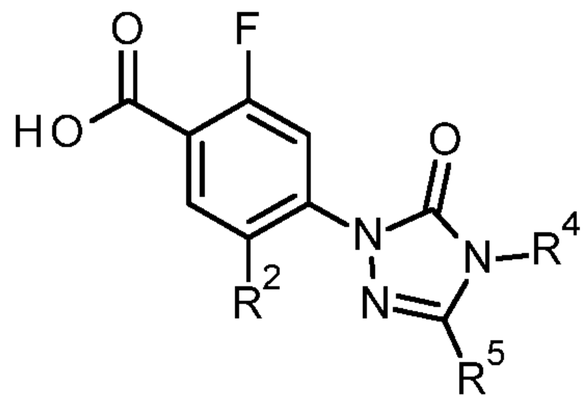
Particularly, the invention provides the use of intermediate compounds of general formula (XV) :



(XV),

in which R^1, R^2 and R^3 are as defined for the compound of general formula (I) *supra*, and A represents a chlorine, bromine or iodine atom, for the preparation of a compound of general formula (I) as defined *supra*.

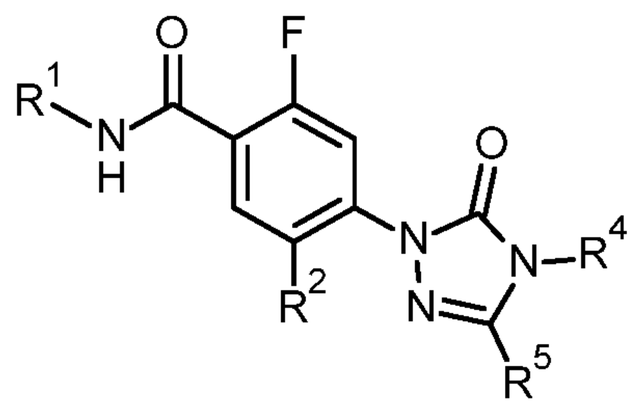
Particularly, the invention provides the use of intermediate compounds of general formula (XVIII) :



(XVIII),

in which R^2, R^4 and R^5 are as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

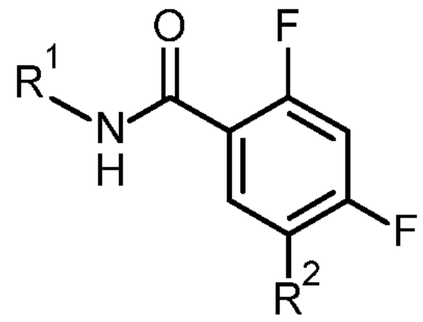
Particularly, the invention provides the use of intermediate compounds of general formula (XIX) :



(XIX),

in which R^1, R^2, R^4 and R^5 are as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

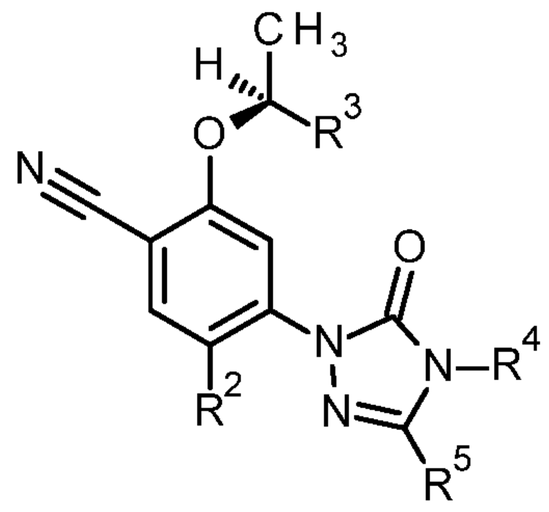
Particularly, the invention provides the use of intermediate compounds of general formula (XX) :



(XX),

in which R^1 and R^2 are as defined for the compound of general formula (I) as defined *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

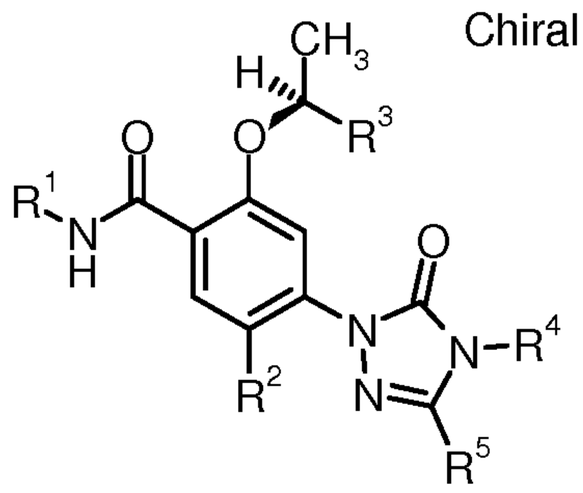
Particularly, the invention provides the use of intermediate compounds of general formula (XXI) :



(XXI),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) *supra*, for the preparation of a compound of general formula (I) as defined *supra*.

In one embodiment the present invention provides methods of preparing compounds of the present invention of general formula (I),



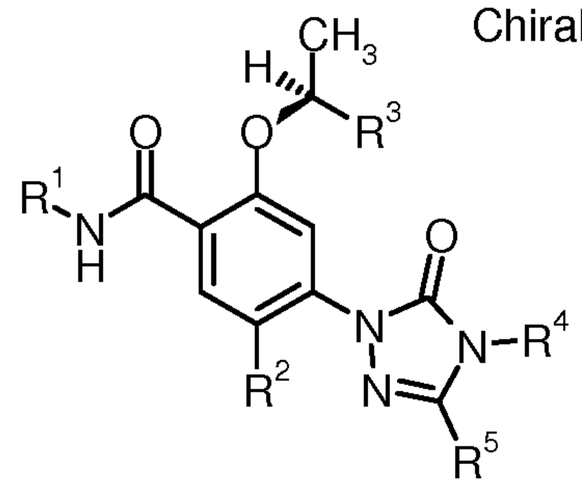
(I),

in which

R^1, R^2, R^3 are as defined in anyone of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form together with the nitrogen atom and the carbon atom to which they are attached a 5 to 7 membered saturated or partially unsaturated heterocyclic ring that is substituted once with a hydroxy group,

said methods comprising the step of reacting a compound of general formula (Ia)



(Ia),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

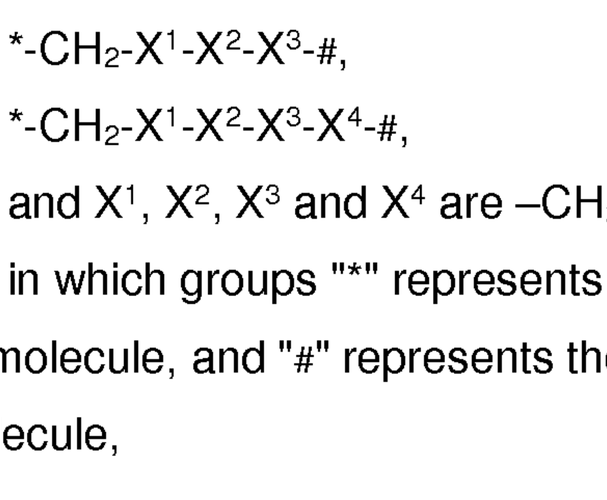
*-CH_2-X^1-X^2-X^3-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

with a suitable microorganism, under suitable conditions and in a suitable medium.

In one embodiment the present invention provides methods of preparing compounds of the present invention of general formula (I),



(I),

in which

R^1, R^2, R^3 are as defined in anyone of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group

*-CH(OH)-X^1-X^2-#,

*-CH_2-CH(OH)-X^2-#,

*-CH(OH)-X^1-X^2-X^3-#,

*-CH_2-CH(OH)-X^2-X^3-#,

*-CH_2-X^1-CH(OH)-X^3-#,

*-CH=CH-CH(OH)-X^3-#,

*-CH(OH)-X^1-X^2-X^3-X^4-#,

*-CH_2-CH(OH)-X^2-X^3-X^4-#,

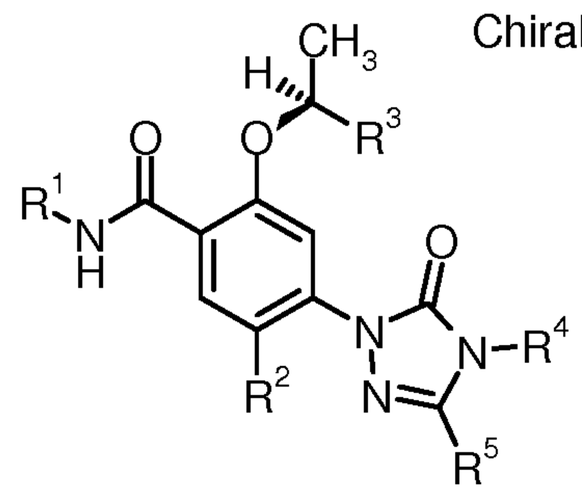
*-CH_2-X^1-CH(OH)-X^3-X^4-#,

*-CH_2-X^1-X^2-CH(OH)-X^4-#,

and X^1, X^2, X^3 and X^4 are $-CH_2-$.

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule.

said methods comprising the step of reacting a compound of general formula (Ia)



(Ia),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

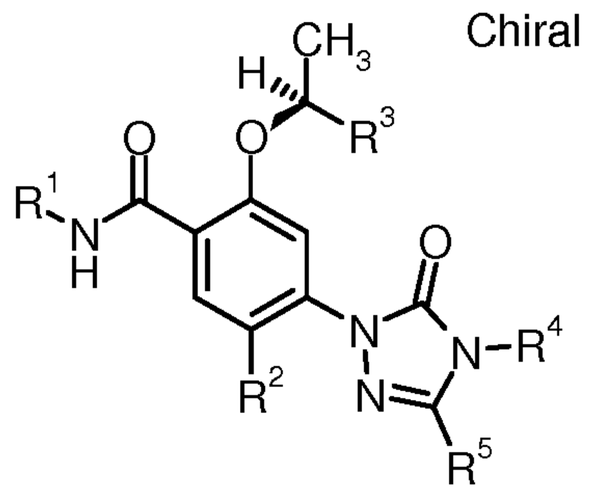
*-CH_2-X^1-X^2-X^3-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

with a suitable microorganism, under suitable conditions and in a suitable medium.

In one embodiment the present invention provides methods of preparing compounds of the present invention of general formula (I),



(I),

in which

R^1, R^2, R^3 are as defined in anyone of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group

*-CH(OH)-X^1-X^2-#,

*-CH_2-CH(OH)-X^2-#,

*-CH(OH)-X^1-X^2-X^3-#,

*-CH_2-CH(OH)-X^2-X^3-#,

*-CH_2-X^1-CH(OH)-X^3-#,

*-CH=CH-CH(OH)-X^3-#,

*-CH(OH)-X^1-X^2-X^3-X^4-#,

*-CH_2-CH(OH)-X^2-X^3-X^4-#,

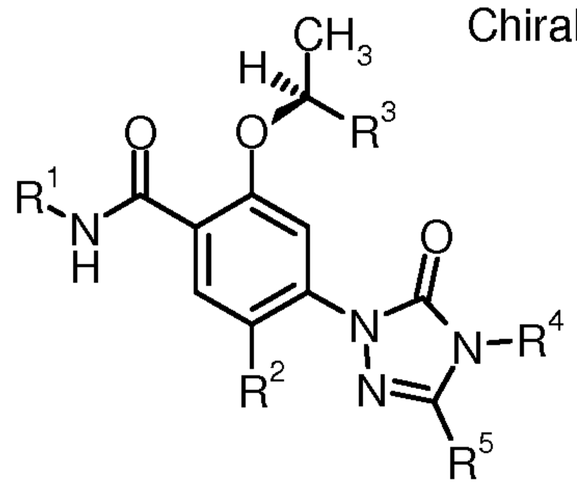
*-CH_2-X^1-CH(OH)-X^3-X^4-#,

*-CH_2-X^1-X^2-CH(OH)-X^4-#,

and X^1, X^2, X^3 and X^4 are $–CH_2-$.

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule.

said methods comprising the step of reacting a compound of general formula (Ia)



(Ia),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

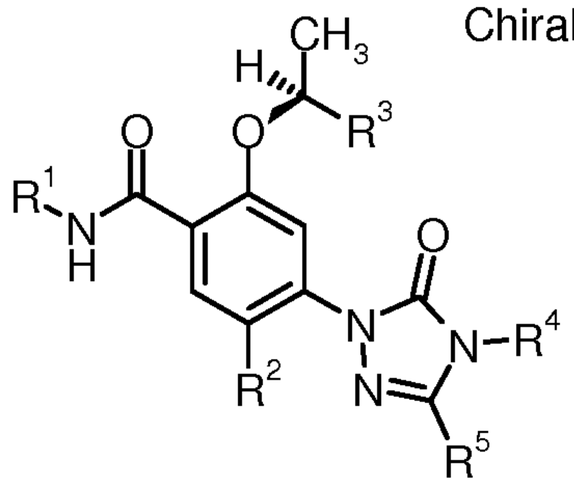
*-CH_2-X^1-X^2-X^3-X^4-#,

and X^1, X^2, X^3 and X^4 are $–CH_2-$

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

with a modified E. Coli or a fungus under suitable conditions and in a suitable medium.

In one embodiment the present invention provides methods of preparing compounds of the present invention of general formula (I), as defined in any one of claims 1-6, said methods comprising the step of reacting a compound of general formula (Ia)



(Ia)

wherein

R^1, R^2 and R^3 are as defined in any embodiment or aspect supra and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

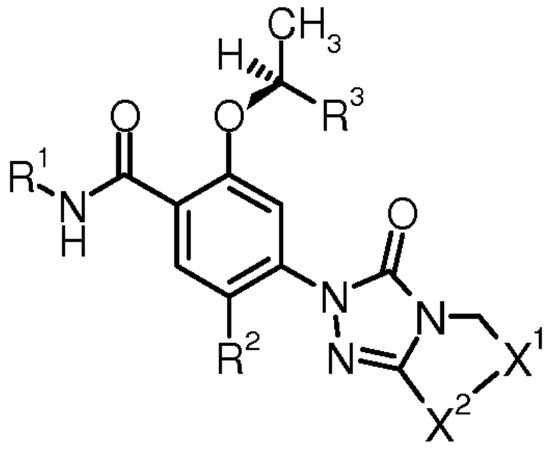
*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

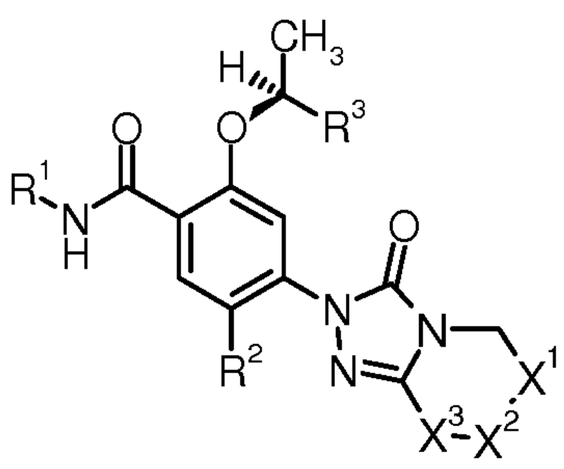
and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

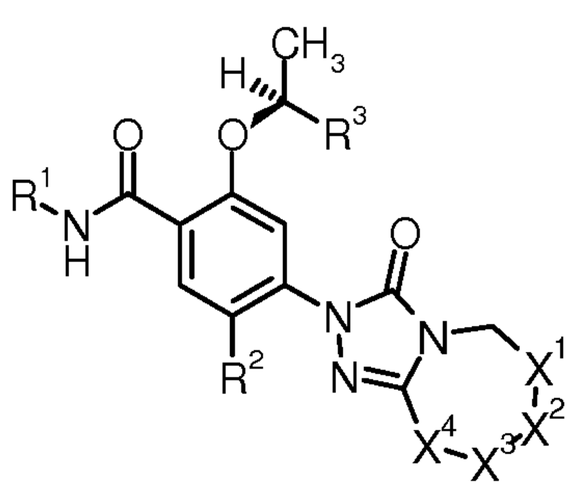
resulting in the following subgroups of compounds of general formula (Ia):



(Ia-1)



(Ia-2)



(Ia-3)

preferably a compound of formula (Ia-2),

with a microorganism such as a e.g. a modified E. Coli hosting a suitable plasmid, such as a nucleic acid sequence of Seq.ID.No.1 or Seq.ID.No.2, or a fungus

and subsequently harvesting the culture and isolating the reaction product after a suitable reaction time

to obtain a compound of formula (Ib)

wherein

R^1, R^2 and R^3 are as defined in any embodiment or aspect supra and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH(OH)-X^1-X^2-#,

*-CH_2-CH(OH)-X^2-#,

*-CH(OH)-X^1-X^2-X^3-#,

*-CH_2-CH(OH)-X^2-X^3-#,

*-CH_2-X^1-CH(OH)-X^3-#,

*-CH=CH-CH(OH)-X^3-#,

*-CH(OH)-X^1-X^2-X^3-X^4-#,

*-CH_2-CH(OH)-X^2-X^3-X^4-#,

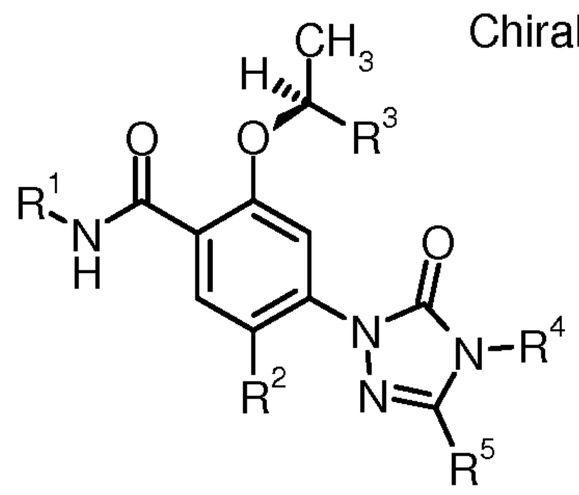
*-CH_2-X^1-CH(OH)-X^3-X^4-#,

*-CH_2-X^1-X^2-CH(OH)-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2- .

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule.

In one embodiment the present invention provides methods of preparing compounds of the present invention of general formula (I), as defined in any one of claims 1-6, said methods comprising the step of reacting a compound of general formula (Ia)



(Ia)

wherein

R^1, R^2 and R^3 are as defined in any aspect or embodiment defined *supra* and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in a suitable medium with a microorganism, such as a modified E. Coli e.g. hosting certain modified plasmids, particularly those having the Seq ID No. 1 or Seq. ID No. 2, or a fungus such as e.g. nigrospora sphaerica (ATCC 12772, CBS 98469) and

subsequently harvesting the culture and isolating the reaction product after a suitable reaction time to produce a compound of formula (Ib) wherein

R^1, R^2 and R^3 are as defined in any aspect or embodiment *supra* and
R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH(OH)-X^1-X^2-X^3-#,

*-CH_2-CH(OH)-X^2-X^3-#,

*-CH_2-X^1-CH(OH)-X^3-#,

*-CH=CH-CH(OH)-X^3-#.

In one embodiment the process as described above further comprises subsequently harvesting the culture and isolating the reaction product after a suitable reaction time.

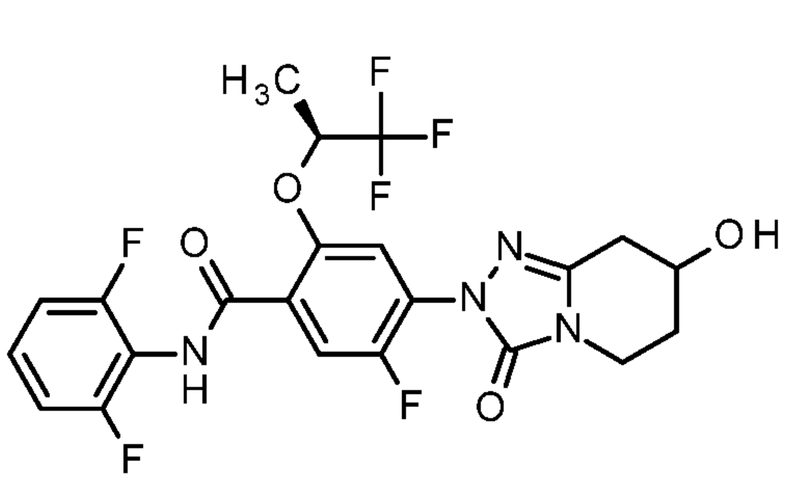
In another embodiment the present invention provides methods of preparing a compound of formula (I), wherein the suitable medium is a suitable nutrition solution comprising a buffer and an aqueous sugar solution.

In another embodiment the present invention provides methods of preparing a compound of formula (I), wherein the suitable medium is a suitable nutrition solution comprising a buffer such as an aqueous phosphatebuffer solution e.g. a potassiumdihydrogen-phosphate/potassiumhydrogenphosphate buffer, a sodiumdihydrogenphosphate/sodium-hydrogenphosphate buffer, particularly a potassiumdihydrogenphosphate/potassium-hydrogenphosphate buffer and an aqueous sugar solution such as e.g. an aqueous glucose solution optionally further comprising an aqueous solution of a complexing agent such as e.g. ethylendiamintetraacetate.

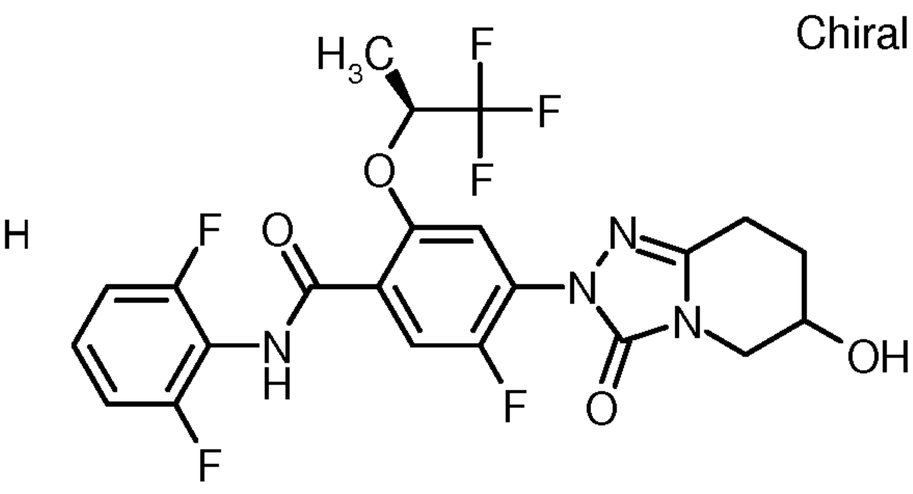
In another embodiment the present invention provides methods of preparing a compound of formula (I), as disclosed *supra* and optionally further comprising aeration of the culture thus providing aerobic reaction conditions.

In another embodiment the present invention provides methods of preparing a compound of formula (I), as disclosed *supra* and further comprising the steps of harvesting the culture after a suitable reaction time such as e.g. 3-6h, particularly 3-4h and isolating the product.

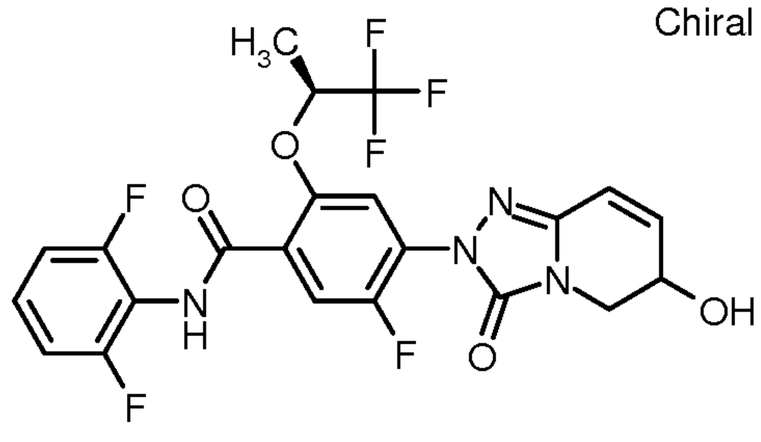
In another embodiment the present invention provides methods of preparing a compound of formula (I), which are example compounds 293-296



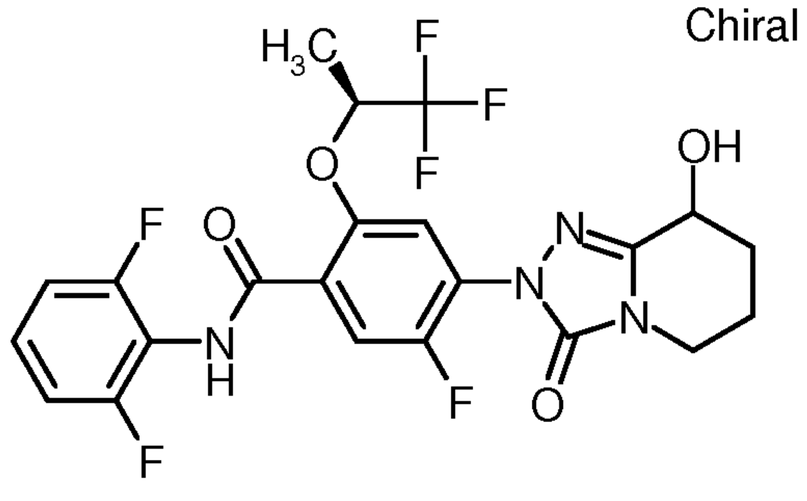
293



294

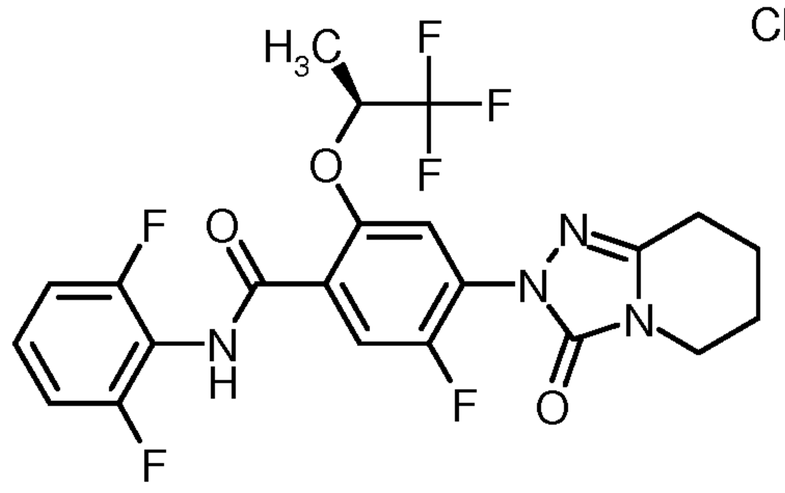


295 and



296

reacting a compound of formula (Ic)



Chiral

(Ic)

named N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide

with *E. coli DH5α LPSd pACYC_pel_POR_pETDuet_Δ3_CYP2C19* in a medium comprising a suitable buffer such as e.g. potassiumdihydrogenphosphate/potassiumhydrogenphosphate and an aqueous sugar solution such as e.g. glucose solution at a temparature range of 20-30℃, particularly 25°-30℃, the ranges including t he lower and upper limit temperature, more particularly 27℃ under aerobic conditions and subs equently harvesting the culture and isolating the reaction product after a suitable reaction time, such as 3-6h, particularly 3-4h.

In a further embodiment the present invention provides methods of preparing a compound of formula (I), which are example compounds 293-296 under the conditions as described in example 293.

A further embodiment of the invention is the compound of formula (I) obtained by the method disclosed *supra*.

A further aspect of the invention is the nucleic acid sequence of Seq..ID. No.1., plasmid 1 of example 293.

Yet another aspect of the invention is the nucleic acid sequence of Seq ID. No.2, plasmid 2 of example 293.

A further aspect is the use of a plasmid of Seq.ID. No. 1 and/or Seq..ID. No.2 for the production of a mircoorganism suitable for a hydroxylation reaction, preferably the hydroxylation of a compound of formula (I), more preferably a compound of formula (Ia), even more preferably a compound of formula (Ia-2).

A further aspect is the use of nucleic acid sequence Seq. ID No. 1 or nucleic acid sequence Seq. ID No. 2

for the preparation of a microorganism suitable for the production of a compound of formula (I) according to claim 1

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form together with the nitrogen atom and the carbon atom to which they are attached a 5 to 7 membered saturated or partially unsaturated heterocyclic ring that is substituted once with a hydroxy group,

more particularly, for the production of a compound of formula (I) according to claim 1 in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH(OH)-X^1-X^2-#,
*-CH_2-CH(OH)-X^2-#,
*-CH(OH)-X^1-X^2-X^3-#,
*-CH_2-CH(OH)-X^2-X^3-#,
*-CH_2-X^1-CH(OH)-X^3-#,
*-CH=CH-CH(OH)-X^3-#,
*-CH(OH)-X^1-X^2-X^3-X^4-#,
*-CH_2-CH(OH)-X^2-X^3-X^4-#,
*-CH_2-X^1-CH(OH)-X^3-X^4-#,
*-CH_2-X^1-X^2-CH(OH)-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule.

A further aspect is the use of a plasmid of Seq. ID. No. 1 and/or Seq.ID.no. 2 for the production of a mircoorganism suitable for the production of a compound of formula (I).

A further aspect is the use of a plasmid of Seq. ID. No. 1 and/or Seq.ID.no. 2 for the production of a mircoorganism suitable for the production of a compound of formula (I), more particularly a hydroxylated compound of formula (I), even more particularly a hydroxylated compound of formula (I) in which

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH(OH)-X^1-X^2-#,
*-CH_2-CH(OH)-X^2-#,
*-CH(OH)-X^1-X^2-X^3-#,
*-CH_2-CH(OH)-X^2-X^3-#,
*-CH_2-X^1-CH(OH)-X^3-#,

*-CH=CH-CH(OH)-X^3-#,

*-CH(OH)-X^1-X^2-X^3-X^4-#,

*-CH_2-CH(OH)-X^2-X^3-X^4-#,

*-CH_2-X^1-CH(OH)-X^3-X^4-#,

*-CH_2-X^1-X^2-CH(OH)-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule.

Another aspcet of the invention is a compound of formula (I), particularly a compound of formula (Ib) more particularly the compounds of examples 293-296, according to claim 1 obtained by a method according to claims 21-22.

The present invention provides the use of the intermediate compounds of general formula (IV), (VI), (VIII), (IX), (X), (XV), (XVIII), (XIX) and (XXI) which are disclosed in the Example Section of this text, *infra*.

The present invention provides the intermediate compounds which are disclosed in the Example Section of this text, *infra*.

The present invention provides the intermediate compounds of general formula (IV), (VI), (VIII), (IX), (X), (XV), (XVIII), (XIX) and (XXI) which are disclosed in the Example Section of this text, *infra*.

The present invention provides any sub-combination within any embodiment or aspect of the present invention of intermediate compounds of general formula (IV), (VI), (VIII), (IX), (X), (XV), (XVIII), (XIX) and (XXI), *supra*.

The compounds of general formula (I) of the present invention can be converted to any salt, preferably pharmaceutically acceptable salts, as described herein, by any method which is known to the person skilled in the art. Similarly, any salt of a compound of general formula (I) of the present invention can be converted into the free compound, by any method which is known to the person skilled in the art.

Compounds of general formula (I) of the present invention demonstrate a valuable pharmacological spectrum of action, which could not have been predicted. Compounds of the present invention have surprisingly been found to effectively inhibit DHODH and it is possible therefore that said compounds be used for the treatment or prophylaxis of diseases, preferably hyperproliferative and/or inflammatory disorders in humans and animals.

Compounds of the present invention can be utilized to inhibit the activity of DHODH. This method comprises administering to a mammal in need thereof, including a human, an effective amount of a compound of general formula (I) of the present invention, or a pharmaceutically

acceptable salt, polymorph, metabolite, hydrate, solvate or ester thereof, for the treatment of hyperproliferative and/or inflammatory disorders.

Another aspect of the invention is a method of inhibiting proliferation of a cell, comprising contacting the cell with a compound of formula (I).

Hyperproliferative disorders include, but are not limited to, for example : psoriasis, keloids, and other hyperplasias affecting the skin, benign prostate hyperplasia (BPH), solid tumours, such as cancers of the breast, respiratory tract, brain, reproductive organs, digestive tract, urinary tract, eye, liver, skin, head and neck, thyroid, parathyroid and their distant metastases. Those disorders also include sarcomas, and haematological malignancies including but not limiting to leukemias, lymphomas, multiple myeolomas.

Examples of breast cancers include, but are not limited to, invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma *in situ*, and lobular carcinoma *in situ*.

Examples of cancers of the respiratory tract include, but are not limited to, small-cell and non-small-cell lung carcinoma, as well as bronchial adenoma and pleuropulmonary blastoma.

Examples of brain cancers include, but are not limited to, brain stem and hypophtalmic glioma, cerebellar and cerebral astrocytoma, medulloblastoma, ependymoma, as well as neuroectodermal and pineal tumour.

Tumours of the male reproductive organs include, but are not limited to, prostate and testicular cancer.

Tumours of the female reproductive organs include, but are not limited to, endometrial, cervical, ovarian, vaginal, and vulvar cancer, as well as sarcoma of the uterus.

Tumours of the digestive tract include, but are not limited to, anal, colon, colorectal, oesophageal, gallbladder, gastric, pancreatic, rectal, small-intestine, and salivary gland cancers.

Tumours of the urinary tract include, but are not limited to, bladder, penile, kidney, renal pelvis, ureter, urethral and human papillary renal cancers.

Eye cancers include, but are not limited to, intraocular melanoma and retinoblastoma.

Examples of liver cancers include, but are not limited to, hepatocellular carcinoma (liver cell carcinomas with or without fibrolamellar variant), cholangiocarcinoma (intrahepatic bile duct carcinoma), and mixed hepatocellular cholangiocarcinoma.

Skin cancers include, but are not limited to, squamous cell carcinoma, Kaposi's sarcoma, malignant melanoma, Merkel cell skin cancer, and non-melanoma skin cancer.

Head-and-neck cancers include, but are not limited to, laryngeal, hypopharyngeal, nasopharyngeal, oropharyngeal cancer, lip and oral cavity cancer and squamous cell.

Lymphomas include, but are not limited to, AIDS-related lymphoma, chronic lymphocytic lymphoma (CLL), non-Hodgkin's lymphoma (NHL), T-non-Hodgkin lymphoma (T-NHL), subtypes of NHL such as Diffuse Large Cell Lymphoma (DLBCL), activated B-cell DLBCL, germinal center B-cell lymphoma DLBCL, double-hit lymphoma and double-expressor lymphoma; anaplastic large cell lymphoma, B-cell lymphoma, cutaneous T-cell lymphoma, Burkitt's lymphoma, follicular lymphoma, hairy cell lymphoma, Hodgkin's disease, mantle cell lymphoma (MCL), lymphoma of the central nervous system, small lymphocytic lymphoma and chronic lymphocytic lymphoma and Sezary syndrome.

Sarcomas include, but are not limited to, sarcoma of the soft tissue, gliosarcoma, osteosarcoma, malignant fibrous histiocytoma, lymphosarcoma, and rhabdomyosarcoma.

Leukemias include, but are not limited to acute lymphoblastic leukemia, acute myeloid leukemia, (acute) T-cell leukemia, acute lymphoblastic leukemia, acute lymphocytic leukemia (ALL) , acute monocytic leukemia (AML), acute promyelocytic leukemia, bisphenotypic B myelomonocytic leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, chronic myeloid leukemia, chronic myelomonocytic leukemia (CMML), large granular lymphocytic leukemia, plasma cell leukemia, and also myelodysplastic syndrome (MDS), which can develop into an acute myeloid leukemia.

Inhibition of DHODH can also lead to differentiation of tumor initiating cells in hematological and solid cancers, especially leukemias.

The present invention also provides methods of treating angiogenic disorders including diseases associated with excessive and/or abnormal angiogenesis.

Inappropriate and ectopic expression of angiogenesis can be deleterious to an organism. A number of pathological conditions are associated with the growth of extraneous blood vessels. These include, for example, diabetic retinopathy, ischemic retinal-vein occlusion, and retinopathy of prematurity [Aiello *et al.*, New Engl. J. Med., **1994**, 331, 1480 ; Peer *et al.,* Lab. Invest., **1995**, 72, 638], age-related macular degeneration (AMD) [Lopez *et al.*, Invest. Opthalmol. Vis. Sci., **1996**, 37, 855], neovascular glaucoma, psoriasis, retrolental fibroplasias, angiofibroma, inflammation, rheumatoid arthritis (RA), restenosis, in-stent restenosis, vascular graft restenosis, *etc*. In addition, the increased blood supply associated with cancerous and neoplastic tissue, encourages growth, leading to rapid tumour enlargement and metastasis. Moreover, the growth of new blood and lymph vessels in a tumour provides an escape route for renegade cells, encouraging metastasis and the consequence spread of the cancer. Thus, compounds of general formula (I) of the present invention can be utilized to treat and/or prevent any of the aforementioned angiogenesis disorders, for example by inhibiting and/or reducing blood vessel formation; by inhibiting, blocking, reducing, decreasing, *etc.* endothelial cell proliferation, or other types involved in angiogenesis, as well as causing cell death or apoptosis of such cell types.

Another aspect of the invention is a method for controlling cancer in humans and animals by administering an effective amount of at least one compound of general formula (I) of the present invention, or a pharmaceutically acceptable salt, polymorph, metabolite, hydrate, solvate or ester thereof, or of a medicament, comprising at least one compound of general formula (I) of the present invention.

Another aspect of the invention is a method for controlling cancer (*e.g.*, through treatment prophylaxis, etc.) in a subject (*e.g.*, human, rat, etc.) by administering an effective amount of at least one compound of general formula (I), or a pharmaceutically acceptable salt, polymorph, metabolite, hydrate, solvate or ester thereof to the subject. In some embodiments, the subject may be administered a medicament, comprising at least one compound of general formula (I) and one or more pharmaceutically acceptable carriers, excipients, and/or diluents.. In some embodimetns, the method of treatment and/or prophylaxis of a hyperproliferative disorder in a subject may comprise administering to the subject an effective amount of a compound of general formula (I). The hyperproliferative disorder may be, for example, cancer (*e.g.*but not limited to lung cancer, acute myeloid leukemia, lymphoma, glioblastoma, prostate cancer, etc.).

A method of inhibiting dihydroorotate dehydrogenase activity in a cancer cell is also provided, wherein the method comprises contacting a cancer cell with a compound of general formula (I). The cancer cell may be *in vitro* or *in vivo*.

Another aspect of the invention is a method of treating lymphoma in a subject, the method comprising administering to the subject an effective amount of a compound of general formula (I).

A yet other aspect of the invention is a method of treating leukemia in a subject, the method comprising administering to the subject an effective amount of a compound of general formula (I).

In another aspect, the present invention provides the use of a compound of general formula (I) of the present invention, or a pharmaceutically acceptable salt, polymorph, metabolite, hydrate, solvate or ester thereof, for the preparation of a medicament for the treatment or prophylaxis of a disease.

In another aspect, the present invention provides methods of treating cancer, which cancer is selected from a solid tumor such as e.g. lung cancer, glioblastoma, and prostate cancer, leukemia such as e.g. acute myeloid leukemia and lymphoma.

In another aspect, the present invention provides methods of treating cancer, which cancer is selected from lung cancer, leukemia, lymphoma, glioblastoma, and prostate cancer.

In another aspect, the present invention provides methods of treating cancer, which cancer is selected from lung cancer, acute myeloid leukemia, lymphoma, glioblastoma, and prostate cancer.

In another aspect, the present invention provides the use of a compound of general formula (I) of the present invention, or a pharmaceutically acceptable salt, polymorph, metabolite, hydrate, solvate or ester thereof, for the treatment of cancer, which cancer is selected from lung cancer, acute myeloid leukemia, lymphoma, glioblastoma, and prostate cancer.

In another aspect, the present invention provides methods of treating or preventing a disease or condition associated with inflammation, a metabolic disorder, infection or an immune disease or condition by administering to a subject having such a condition or disease, a therapeutically effective amount of a compound or composition of the invention.

In further embodiments, diseases or conditions, including chronic diseases, of humans or other species can be treated or prevented by inhibition of DHODH. These diseases or conditions include (1) inflammatory or allergic diseases such as systemic anaphylaxis and hypersensitivity responses, drug allergies, insect sting allergies and food allergies, (2) inflammatory bowel diseases, such as Crohn's disease, ulcerative colitis, ileitis and enteritis, (3) vaginitis, (4) psoriasis and inflammatory dermatoses such as dermatitis, eczema, atopic dermatitis, allergic contact dermatitis and urticaria, (5) vasculitis, (6) spondyloarthropathies, (7) scleroderma, (8) asthma and respiratory allergic diseases such as allergic asthma, allergic rhinitis, allergic conjunctivitis, hypersensitivity lung diseases and the like, and (9) autoimmune diseases, such as arthritis (including rheumatoid and psoriatic), systemic lupus erythematosus, type I diabetes, glomerulonephritis and the like, (10) graft rejection (including allograft rejection and graft-v-host disease), (11) other diseases in which undesired inflammatory responses are to be inhibited, e.g., atherosclerosis, myositis, neurological disorders such as stroke, ischemic reperfusion injury, traumatic brain injury and closed-head injuries, neurodegenerative diseases (e.g., Parkinson's disease), multiple sclerosis, Alzheimer's disease, encephalitis, meningitis, osteoporosis, gout, hepatitis, nephritis, gall bladder disease, sepsis, sarcoidosis, conjunctivitis, otitis, chronic obstructive pulmonary disease, sinusitis and Behcet's syndrome, and (12) immune diseases or conditions.

In another aspect, the present invention provides methods of treating or preventing viral infections.

In yet another aspect, the present invention provides methods of treating or preventing Malaria.

These disorders have been well characterized in humans, but also exist with a similar etiology in other mammals, and can be treated by administering pharmaceutical compositions of the present invention.

If it is stated “preventing or treating” “treatment or prophylaxis” treating/treatment is preferred.

The term “treating” or “treatment” as stated throughout this document is used conventionally, for example the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, improving the condition of a disease or disorder, such as a carcinoma.

The compounds of the present invention can be used in particular in therapy and prevention, *i.e.* prophylaxis, of tumour growth and metastases, especially in solid tumours of all indications and stages with or without pre-treatment of the tumour growth.

Generally, the use of chemotherapeutic agents and/or anti-cancer agents in combination with a compound or pharmaceutical composition of the present invention will serve to:

1. yield better efficacy in reducing the growth of a tumour or even eliminate the tumour as compared to administration of either agent alone,
2. provide for the administration of lesser amounts of the administered chemotherapeutic agents,
3. provide for a chemotherapeutic treatment that is well tolerated in the patient with fewer deleterious pharmacological complications than observed with single agent chemotherapies and certain other combined therapies,
4. provide for treating a broader spectrum of different cancer types in mammals, especially humans,
5. provide for a higher response rate among treated patients,
6. provide for a longer survival time among treated patients compared to standard chemotherapy treatments,
7. provide a longer time for tumour progression, and/or
8. yield efficacy and tolerability results at least as good as those of the agents used alone, compared to known instances where other cancer agent combinations produce antagonistic effects.

In addition, the compounds of general formula (I) of the present invention can also be used in combination with radiotherapy and/or surgical intervention.

In a further embodiment of the present invention, the compounds of general formula (I) of the present invention may be used to sensitize a cell to radiation, *i.e.* treatment of a cell with a compound of the present invention prior to radiation treatment of the cell renders the cell more susceptible to DNA damage and cell death than the cell would be in the absence of any treatment with a compound of the present invention. In one aspect, the cell is treated with at least one compound of general formula (I) of the present invention.

Thus, the present invention also provides a method of killing a cell, wherein a cell is administered one or more compounds of the present invention in combination with conventional radiation therapy.

The present invention also provides a method of rendering a cell more susceptible to cell death, wherein the cell is treated with one or more compounds of general formula (I) of the present invention prior to the treatment of the cell to cause or induce cell death. In one aspect, after the cell is treated with one or more compounds of general formula (I) of the present invention, the cell is treated with at least one compound, or at least one method, or a combination thereof, in order to cause DNA damage for the purpose of inhibiting the function of the normal cell or killing the cell.

In other embodiments of the present invention, a cell is killed by treating the cell with at least one DNA damaging agent, *i.e.* after treating a cell with one or more compounds of general formula (I) of the present invention to sensitize the cell to cell death, the cell is treated with at least one DNA damaging agent to kill the cell. DNA damaging agents useful in the present invention include, but are not limited to, chemotherapeutic agents (*e.g.* cis platin), ionizing radiation (X-rays, ultraviolet radiation), carcinogenic agents, and mutagenic agents.

In other embodiments, a cell is killed by treating the cell with at least one method to cause or induce DNA damage. Such methods include, but are not limited to, activation of a cell signalling pathway that results in DNA damage when the pathway is activated, inhibiting of a cell signalling pathway that results in DNA damage when the pathway is inhibited, and inducing a biochemical change in a cell, wherein the change results in DNA damage. By way of a non-limiting example, a DNA repair pathway in a cell can be inhibited, thereby preventing the repair of DNA damage and resulting in an abnormal accumulation of DNA damage in a cell.

In one aspect of the invention, a compound of general formula (I) of the present invention is administered to a cell prior to the radiation or other induction of DNA damage in the cell. In another aspect of the invention, a compound of general formula (I) of the present invention is administered to a cell concomitantly with the radiation or other induction of DNA damage in the cell. In yet another aspect of the invention, a compound of general formula (I) of the present invention is administered to a cell immediately after radiation or other induction of DNA damage in the cell has begun.

In another aspect, the cell is in vitro. In another embodiment, the cell is in vivo.

In accordance with a further aspect, the present invention provides compounds of general formula (I), as described *supra*, or tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides, particularly pharmaceutically acceptable salts thereof, or mixtures of same, for

use in the treatment or prophylaxis of diseases, in particular hyperproliferative and/or inflammatory disorders.

In accordance with a further aspect, the present invention provides compounds of general formula (I), as described *supra*, or tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides, for use in the treatment or prophylaxis of diseases, in particular hyperproliferative disorders, particularly benign hyperproliferative disorders, more particularly cancer.

The pharmaceutical activity of the compounds according to the invention can be explained by their activity as DHODH inhibitors.

In accordance with a further aspect, the present invention providesprovides the use of compounds of general formula (I), as described *supra*, or tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides, particularly pharmaceutically acceptable salts thereof, or mixtures of same, for the treatment or prophylaxis of diseases, in particular hyperproliferative and/or inflammatory disorders.

In accordance with a further aspect, the present invention provides the use of compounds of general formula (I), as described *supra*, or tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides, particularly pharmaceutically acceptable salts thereof, or mixtures of same, for the treatment or prophylaxis of diseases, in particular hyperproliferative disorders, particularly benign hyperproliferative disorders, more particularly cancer.

In accordance with a further aspect, the present invention provides the use of compounds of general formula (I), as described *supra*, or tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides, particularly pharmaceutically acceptable salts thereof, or mixtures of same, in a method of treatment or prophylaxis of diseases, in particular hyperproliferative and/or inflammatory disorders, particularly cancer.

In accordance with a further aspect, the present invention provides the use of compounds of general formula (I), as described *supra*, or tautomers, N-oxides, and salts thereof, or salts of tautomers or N-oxides, particularly pharmaceutically acceptable salts thereof, or mixtures of same, in a method of treatment or prophylaxis of diseases, in particular hyperproliferative disorders, particularly benign hyperproliferative disorders, more particularly cancer.

In accordance with a further aspect, the present invention provides the use of a compound of general formula (I), as described supra, or a tautomer, an N-oxide, and a salt thereof, or a salt of a tautomer or an N-oxide, particularly a pharmaceutically acceptable salt thereof, or a mixture of same, for the preparation of a medicament, for the prophylaxis or treatment of diseases, in particular hyperproliferative disorders, particularly benign hyperproliferative disorders, more particularly cancer.

In accordance with a further aspect, the present invention provides use of a compound of general formula (I), as described *supra*, or a tautomer, an N-oxide, and a salt thereof, or a salt

of a tautomer or an N-oxide, particularly a pharmaceutically acceptable salt thereof, or a mixture of same, for the preparation of a pharmaceutical composition, for the prophylaxis or treatment of diseases, in particular hyperproliferative and/or inflammatory disorders.

In accordance with a further aspect, the present invention provides use of a compound of general formula (I), as described supra, or a tautomer, an N-oxide, and a salt thereof, or a salt of a tautomer or an N-oxide, particularly a pharmaceutically acceptable salt thereof, or a mixture of same, for the preparation of a pharmaceutical composition, preferably a medicament, for the prophylaxis or treatment of diseases, in particular hyperproliferative disorders, particularly benign hyperproliferative disorders, more particularly cancer.

In accordance with a further aspect, the present invention provides a method of treatment or prophylaxis of diseases, in particular hyperproliferative and/or inflammatory disorders, comprising administering an effective amount of a compound of general formula (I), as described *supra*, or a tautomer, an N-oxide, and a salt thereof, or a salt of a tautomer or an N-oxide, particularly a pharmaceutically acceptable salt thereof, or a mixture of same.

In accordance with a further aspect, the present invention provides a method of treatment or prophylaxis of diseases, in particular hyperproliferative disorders, particularly benign hyperproliferative disorders, more particularly cancer, comprising administering an effective amount of a compound of general formula (I), as described supra, or a tautomer, an N-oxide, and a salt thereof, or a salt of a tautomer or an N-oxide, particularly a pharmaceutically acceptable salt thereof, or a mixture of same.

In accordance with a further aspect, the present invention provides pharmaceutical compositions, in particular a medicament, comprising a compound of general formula (I), as described *supra*, or a tautomer, an N-oxide, and a salt thereof, or a salt of a tautomer or an N-oxide, particularly a pharmaceutically acceptable salt, or a mixture of same, and one or more excipients), in particular one or more pharmaceutically acceptable excipient(s). Conventional procedures for preparing such pharmaceutical compositions in appropriate dosage forms can be utilized.

The present invention furthermore provides pharmaceutical compositions, in particular medicaments, which comprise at least one compound according to the invention, conventionally together with one or more pharmaceutically suitable excipients, and to their use for the above mentioned purposes.

It is possible for the compounds according to the invention to have systemic and/or local activity. For this purpose, they can be administered in a suitable manner, such as, for example, via the oral, parenteral, pulmonary, nasal, sublingual, lingual, buccal, rectal, vaginal, dermal, transdermal, conjunctival, otic route or as an implant or stent.

For these administration routes, it is possible for the compounds according to the invention to be administered in suitable administration forms.

For oral administration, it is possible to formulate the compounds according to the invention to dosage forms known in the art that deliver the compounds of the invention rapidly and/or in a modified manner, such as, for example, tablets (uncoated or coated tablets, for example with enteric or controlled release coatings that dissolve with a delay or are insoluble), orally-disintegrating tablets, films/wafers, films/lyophylisates, capsules (for example hard or soft gelatine capsules), sugar-coated tablets, granules, pellets, powders, emulsions, suspensions, aerosols or solutions. It is possible to incorporate the compounds according to the invention in crystalline and/or amorphised and/or dissolved form into said dosage forms.

Parenteral administration can be effected with avoidance of an absorption step (for example intravenous, intraarterial, intracardial, intraspinal or intralumbal) or with inclusion of absorption (for example intramuscular, subcutaneous, intracutaneous, percutaneous or intraperitoneal). Administration forms which are suitable for parenteral administration are, inter alia, preparations for injection and infusion in the form of solutions, suspensions, emulsions, lyophylisates or sterile powders.

Examples which are suitable for other administration routes are pharmaceutical forms for inhalation [inter alia powder inhalers, nebulizers], nasal drops, nasal solutions, nasal sprays; tablets/films/wafers/capsules for lingual, sublingual or buccal administration; suppositories; eye drops, eye ointments, eye baths, ocular inserts, ear drops, ear sprays, ear powders, ear-rinses, ear tampons; vaginal capsules, aqueous suspensions (lotions, mixturae agitandae), lipophilic suspensions, emulsions, ointments, creams, transdermal therapeutic systems (such as, for example, patches), milk, pastes, foams, dusting powders, implants or stents.

The compounds according to the invention can be incorporated into the stated administration forms. This can be effected in a manner known per se by mixing with pharmaceutically suitable excipients. Pharmaceutically suitable excipients include, inter alia,

- fillers and carriers (for example cellulose, microcrystalline cellulose (such as, for example, Avicel®), lactose, mannitol, starch, calcium phosphate (such as, for example, Di-Cafos®)),
- ointment bases (for example petroleum jelly, paraffins, triglycerides, waxes, wool wax, wool wax alcohols, lanolin, hydrophilic ointment, polyethylene glycols),
- bases for suppositories (for example polyethylene glycols, cacao butter, hard fat),
- solvents (for example water, ethanol, isopropanol, glycerol, propylene glycol, medium chain-length triglycerides fatty oils, liquid polyethylene glycols, paraffins),

- surfactants, emulsifiers, dispersants or wetters (for example sodium dodecyl sulfate), lecithin, phospholipids, fatty alcohols (such as, for example, Lanette®), sorbitan fatty acid esters (such as, for example, Span®), polyoxyethylene sorbitan fatty acid esters (such as, for example, Tween®), polyoxyethylene fatty acid glycerides (such as, for example, Cremophor®), polyoxethylene fatty acid esters, polyoxyethylene fatty alcohol ethers, glycerol fatty acid esters, poloxamers (such as, for example, Pluronic®),
- buffers, acids and bases (for example phosphates, carbonates, citric acid, acetic acid, hydrochloric acid, sodium hydroxide solution, ammonium carbonate, trometamol, triethanolamine),
- isotonicity agents (for example glucose, sodium chloride),
- adsorbents (for example highly-disperse silicas),
- viscosity-increasing agents, gel formers, thickeners and/or binders (for example polyvinylpyrrolidone, methylcellulose, hydroxypropylmethylcellulose, hydroxypropyl-cellulose, carboxymethylcellulose-sodium, starch, carbomers, polyacrylic acids (such as, for example, Carbopol®); alginates, gelatine),
- disintegrants (for example modified starch, carboxymethylcellulose-sodium, sodium starch glycolate (such as, for example, Explotab®), cross- linked polyvinylpyrrolidone, croscarmellose-sodium (such as, for example, AcDiSol®)),
- flow regulators, lubricants, glidants and mould release agents (for example magnesium stearate, stearic acid, talc, highly-disperse silicas (such as, for example, Aerosil®)),
- coating materials (for example sugar, shellac) and film formers for films or diffusion membranes which dissolve rapidly or in a modified manner (for example polyvinylpyrrolidones (such as, for example, Kollidon®), polyvinyl alcohol, hydroxypropylmethylcellulose, hydroxypropylcellulose, ethylcellulose, hydroxypropyl-methylcellulose phthalate, cellulose acetate, cellulose acetate phthalate, polyacrylates, polymethacrylates such as, for example, Eudragit®)),
- capsule materials (for example gelatine, hydroxypropylmethylcellulose),
- synthetic polymers (for example polylactides, polyglycolides, polyacrylates, polymethacrylates (such as, for example, Eudragit®), polyvinylpyrrolidones (such as, for example, Kollidon®), polyvinyl alcohols, polyvinyl acetates, polyethylene oxides, polyethylene glycols and their copolymers and blockcopolymers),

- plasticizers (for example polyethylene glycols, propylene glycol, glycerol, triacetine, triacetyl citrate, dibutyl phthalate),
- penetration enhancers,
- stabilisers (for example antioxidants such as, for example, ascorbic acid, ascorbyl palmitate, sodium ascorbate, butylhydroxyanisole, butylhydroxytoluene, propyl gallate),
- preservatives (for example parabens, sorbic acid, thiomersal, benzalkonium chloride, chlorhexidine acetate, sodium benzoate),
- colourants (for example inorganic pigments such as, for example, iron oxides, titanium dioxide),
- flavourings, sweeteners, flavour- and/or odour-masking agents.

The present invention furthermore relates to a pharmaceutical composition which comprise at least one compound according to the invention, conventionally together with one or more pharmaceutically suitable excipient(s), and to their use according to the present invention.

In accordance with another aspect, the present invention provides pharmaceutical combinations, in particular medicaments, comprising at least one compound of general formula (I) of the present invention and at least one or more further active ingredients, in particular for the treatment and/or prophylaxis of a hyperproliferative disorder, particularly cancer.

Particularly, the present invention provides a pharmaceutical combination, which comprises:

- one or more first active ingredients, in particular compounds of general formula (I) as defined *supra,* and
- one or more further active ingredients, in particular anti-cancer agents.

The term “combination” in the present invention is used as known to persons skilled in the art, it being possible for said combination to be a fixed combination, a non-fixed combination or a kit-of-parts.

A “fixed combination” in the present invention is used as known to persons skilled in the art and is defined as a combination wherein, for example, a first active ingredient, such as one or more compounds of general formula (I) of the present invention, and a further active ingredient are present together in one unit dosage or in one single entity. One example of a “fixed combination” is a pharmaceutical composition wherein a first active ingredient and a further active ingredient are present in admixture for simultaneous administration, such as in a formulation. Another example of a “fixed combination” is a pharmaceutical combination wherein a first active ingredient and a further active ingredient are present in one unit without being in admixture.

A non-fixed combination or “kit-of-parts” in the present invention is used as known to persons skilled in the art and is defined as a combination wherein a first active ingredient and a further active ingredient are present in more than one unit. One example of a non-fixed combination or kit-of-parts is a combination wherein the first active ingredient and the further active ingredient are present separately. It is possible for the components of the non-fixed combination or kit-of-parts to be administered separately, sequentially, simultaneously, concurrently or chronologically staggered.

The compounds of the present invention can be administered as the sole pharmaceutical agent or in combination with one or more other pharmaceutically active ingredients where the combination causes no unacceptable adverse effects. The present invention also provides such pharmaceutical combinations. For example, the compounds of the present invention can be combined with known anti-cancer agents.

Examples of anti-cancer agents include:

131I-chTNT, abarelix, abiraterone, aclarubicin, adalimumab, ado-trastuzumab emtansine, afatinib, aflibercept, aldesleukin, alectinib, alemtuzumab, alendronic acid, alitretinoin, altretamine, amifostine, aminoglutethimide, hexyl aminolevulinate, amrubicin, amsacrine, anastrozole, ancestim, anethole dithiolethione, anetumab ravtansine, angiotensin II, antithrombin III, aprepitant, arcitumomab, arglabin, arsenic trioxide, asparaginase, atezolizumab, axitinib, azacitidine, basiliximab, belotecan, bendamustine, besilesomab, belinostat, bevacizumab, bexarotene, bicalutamide, bisantrene, bleomycin, blinatumomab, bortezomib, buserelin, bosutinib, brentuximab vedotin, busulfan, cabazitaxel, cabozantinib, calcitonine, calcium folinate, calcium levofolinate, capecitabine, capromab, carbamazepine carboplatin, carboquone, carfilzomib, carmofur, carmustine, catumaxomab, celecoxib, celmoleukin, ceritinib, cetuximab, chlorambucil, chlormadinone, chlormethine, cidofovir, cinacalcet, cisplatin, cladribine, clodronic acid, clofarabine, cobimetinib, copanlisib, crisantaspase, crizotinib, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daratumumab, darbepoetin alfa, dabrafenib, dasatinib, daunorubicin, decitabine, degarelix, denileukin diftitox, denosumab, depreotide, deslorelin, dianhydrogalactitol, dexrazoxane, dibrospidium chloride, dianhydrogalactitol, diclofenac, dinutuximab, docetaxel, dolasetron, doxifluridine, doxorubicin, doxorubicin + estrone, dronabinol, eculizumab, edrecolomab, elliptinium acetate, elotuzumab, eltrombopag, endostatin, enocitabine, enzalutamide, epirubicin, epitiostanol, epoetin alfa, epoetin beta, epoetin zeta, eptaplatin, eribulin, erlotinib, esomeprazole, estradiol, estramustine, ethinylestradiol, etoposide, everolimus, exemestane, fadrozole, fentanyl, filgrastim, fluoxymesterone, floxuridine, fludarabine, fluorouracil, flutamide, folinic acid, formestane, fosaprepitant, fotemustine, fulvestrant, gadobutrol, gadoteridol, gadoteric acid meglumine, gadoversetamide, gadoxetic acid, gallium nitrate, ganirelix, gefitinib, gemcitabine, gemtuzumab, Glucarpidase, glutoxim,

GM-CSF, goserelin, granisetron, granulocyte colony stimulating factor, histamine dihydrochloride, histrelin, hydroxycarbamide, I-125 seeds, lansoprazole, ibandronic acid, ibritumomab tiuxetan, ibrutinib, idarubicin, ifosfamide, imatinib, imiquimod, improsulfan, indisetron, incadronic acid, ingenol mebutate, interferon alfa, interferon beta, interferon gamma, iobitridol, iobenguane (123I), iomeprol, ipilimumab, irinotecan, Itraconazole, ixabepilone, ixazomib, lanreotide, lansoprazole, lapatinib, lasocholine, lenalidomide, lenvatinib, lenograstim, lentinan, letrozole, leuprorelin, levamisole, levonorgestrel, levothyroxine sodium, lisuride, lobaplatin, lomustine, lonidamine, masoprocol, medroxyprogesterone, megestrol, melarsoprol, melphalan, mepitiostane, mercaptopurine, mesna, methadone, methotrexate, methoxsalen, methylaminolevulinate, methylprednisolone, methyltestosterone, metirosine, mifamurtide, miltefosine, miriplatin, mitobronitol, mitoguazone, mitolactol, mitomycin, mitotane, mitoxantrone, mogamulizumab, molgramostim, mopidamol, morphine hydrochloride, morphine sulfate, nabilone, nabiximols, nafarelin, naloxone + pentazocine, naltrexone, nartograstim, necitumumab, nedaplatin, nelarabine, neridronic acid, netupitant/palonosetron, nivolumab, pentetreotide, nilotinib, nilutamide, nimorazole, nimotuzumab, nimustine, nintedanib, nitracrine, nivolumab, obinutuzumab, octreotide, ofatumumab, olaparib, olaratumab, omacetaxine mepesuccinate, omeprazole, ondansetron, oprelvekin, orgotein, orilotimod, osimertinib, oxaliplatin, oxycodone, oxymetholone, ozogamicine, p53 gene therapy, paclitaxel, palbociclib, palifermin, palladium-103 seed, palonosetron, pamidronic acid, panitumumab, panobinostat, pantoprazole, pazopanib, pegaspargase, PEG-epoetin beta (methoxy PEG-epoetin beta), pembrolizumab, pegfilgrastim, peginterferon alfa-2b, pembrolizumab, pemetrexed, pentazocine, pentostatin, peplomycin, Perflubutane, perfosfamide, Pertuzumab, picibanil, pilocarpine, pirarubicin, pixantrone, plerixafor, plicamycin, poliglusam, polyestradiol phosphate, polyvinylpyrrolidone + sodium hyaluronate, polysaccharide-K, pomalidomide, ponatinib, porfimer sodium, pralatrexate, prednimustine, prednisone, procarbazine, procodazole, propranolol, quinagolide, rabeprazole, racotumomab, radium-223 chloride, radotinib, raloxifene, raltitrexed, ramosetron, ramucirumab, ranimustine, rasburicase, razoxane, refametinib, regorafenib, risedronic acid, rhenium-186 etidronate, rituximab, rolapitant, romidepsin, romiplostim, romurtide, rucaparib, samarium (153Sm) lexidronam, sargramostim, satumomab, secretin, siltuximab, sipuleucel-T, sizofiran, sobuzoxane, sodium glycididazole, sonidegib, sorafenib, stanozolol, streptozocin, sunitinib, talaporfin, talimogene laherparepvec, tamibarotene, tamoxifen, tapentadol, tasonermin, teceleukin, technetium (99mTc) nofetumomab merpentan, 99mTc-HYNIC-[Tyr3]-octreotide, tegafur, tegafur + gimeracil + oteracil, temoporfin, temozolomide, temsirolimus, teniposide, testosterone, tetrofosmin, thalidomide, thiotepa, thymalfasin, thyrotropin alfa, tioguanine, tocilizumab, topotecan, toremifene, tositumomab, trabectedin, trametinib, tramadol, trastuzumab, trastuzumab emtansine, treosulfan, tretinoin, trifluridine + tipiracil, trilostane, triptorelin, trametinib, trofosfamide, thrombopoietin, tryptophan, ubenimex, valatinib, valrubicin, vandetanib,

vapreotide, vemurafenib, vinblastine, vincristine, vindesine, vinflunine, vinorelbine, vismodegib, vorinostat, vorozole, yttrium-90 glass microspheres, zinostatin, zinostatin stimalamer, zoledronic acid, zorubicin.

Based upon standard laboratory techniques known to evaluate compounds useful for the treatment of hyperproliferative and/or inflammatory disorders, by standard toxicity tests and by standard pharmacological assays for the determination of treatment of the conditions identified above in mammals, and by comparison of these results with the results of known active ingredients or medicaments that are used to treat these conditions, the effective dosage of the compounds of the present invention can readily be determined for treatment of each desired indication. The amount of the active ingredient to be administered in the treatment of one of these conditions can vary widely according to such considerations as the particular compound and dosage unit employed, the mode of administration, the period of treatment, the age and sex of the patient treated, and the nature and extent of the condition treated.

The total amount of the active ingredient to be administered will generally range from about 0.001 mg/kg to about 200 mg/kg body weight per day, and preferably from about 0.01 mg/kg to about 20 mg/kg body weight per day. Clinically useful dosing schedules will range from one to three times a day dosing to once every four weeks dosing. In addition, it is possible for "drug holidays", in which a patient is not dosed with a drug for a certain period of time, to be beneficial to the overall balance between pharmacological effect and tolerability. It is possible for a unit dosage to contain from about 0.5 mg to about 1500 mg (*e.g.* about 0.5 mg to about 5 mg, about 5 mg to about 50 mg, about 50 mg to about 500 mg, about 500 mg to about 1500 mg, etc.) of active ingredient, and can be administered one or more times per day or less than once a day. The average daily dosage for administration by injection, including intravenous, intramuscular, subcutaneous and parenteral injections, and use of infusion techniques will preferably be from 0.01 to 200 mg/kg of total body weight. The average daily rectal dosage regimen will preferably be from 0.01 to 200 mg/kg of total body weight. The average daily vaginal dosage regimen will preferably be from 0.01 to 200 mg/kg of total body weight. The average daily topical dosage regimen will preferably be from 0.1 to 200 mg administered between one to four times daily. The transdermal concentration will preferably be that required to maintain a daily dose of from 0.01 to 200 mg/kg. The average daily inhalation dosage regimen will preferably be from 0.01 to 100 mg/kg of total body weight.

In other embodiemts of the invention the total amount of the active ingredient to be administered will generally range from 0.001 mg/kg to 200 mg/kg body weight per day, and preferably from 0.01 mg/kg to 20 mg/kg body weight per day. Clinically useful dosing schedules will range from one to three times a day dosing to once every four weeks dosing. In addition, it is possible for "drug holidays", in which a patient is not dosed with a drug for a certain period of time, to be beneficial to the overall balance between pharmacological effect

and tolerability. It is possible for a unit dosage to contain from 0.5 mg to 1500 mg of active ingredient, and can be administered one or more times per day or less than once a day.

Of course the specific initial and continuing dosage regimen for each patient will vary according to the nature and severity of the condition as determined by the attending diagnostician, the activity of the specific compound employed, the age and general condition of the patient, time of administration, route of administration, rate of excretion of the drug, drug combinations, and the like. The desired mode of treatment and number of doses of a compound of the present invention or a pharmaceutically acceptable salt or ester or composition thereof can be ascertained by those skilled in the art using conventional treatment tests.

EXPERIMENTAL SECTION

NMR peak forms are stated as they appear in the spectra, possible higher order effects have not been considered.

The ^{1}H-NMR data of selected examples are listed in the form of ^{1}H-NMR peaklists. For each signal peak the δ value in ppm is given, followed by the signal intensity, reported in round brackets. The δ value-signal intensity pairs from different peaks are separated by commas. Therefore, a peaklist is described by the general form: δ_1 (intensity$_1$), δ_2 (intensity$_2$), ... , δ_i (intensity$_i$), ... , δ_n (intensity$_n$).

The intensity of a sharp signal correlates with the height (in cm) of the signal in a printed NMR spectrum. When compared with other signals, this data can be correlated to the real ratios of the signal intensities. In the case of broad signals, more than one peak, or the center of the signal along with their relative intensity, compared to the most intense signal displayed in the spectrum, are shown. A ^{1}H-NMR peaklist is similar to a classical ^{1}H-NMR readout, and thus usually contains all the peaks listed in a classical NMR interpretation. Moreover, similar to classical ^{1}H-NMR printouts, peaklists can show solvent signals, signals derived from stereoisomers of target compounds (also the subject of the invention), and/or peaks of impurities. The peaks of stereoisomers, and/or peaks of impurities are typically displayed with a lower intensity compared to the peaks of the target compounds (e.g., with a purity of >90%). Such stereoisomers and/or impurities may be typical for the particular manufacturing process, and therefore their peaks may help to identify the reproduction of our manufacturing process on the basis of "by-product fingerprints". An expert who calculates the peaks of the target compounds by known methods (MestReC, ACD simulation, or by use of empirically evaluated expectation values), can isolate the peaks of target compounds as required, optionally using additional intensity filters. Such an operation would be similar to peak-picking in classical ^{1}H-NMR interpretation. A detailed description of the reporting of NMR data in the form of peaklists can be found in the publication "Citation of NMR Peaklist Data within Patent Applications" (cf.

Research Disclosure Database Number 605005, 2014, 01 Aug 2014, or http://www.researchdisclosure.com/searching-disclosures). In the peak picking routine, as described in the Research Disclosure Database Number 605005, the parameter "MinimumHeight" can be adjusted between 1% and 4%. Depending on the chemical structure and/or depending on the concentration of the measured compound it may be reasonable to set the parameter "MinimumHeight" <1%.

Chemical names were generated using the ACD/Name software from ACD/Labs. In some cases generally accepted names of commercially available reagents were used in place of ACD/Name generated names.

The following table 1 lists the abbreviations used in this paragraph and in the Examples section as far as they are not explained within the text body. Other abbreviations have their meanings customary *per se* to the skilled person.

Table 1: Abbreviations

Abbreviation	**Meaning**
aq.	aqueous
br	broad (^{1}H-NMR signal)
cat.	catalytic
$CDCl_3$	deuterated chloroform
CI	chemical ionisation
d	doublet
DAD	diode array detector
DCM	dichloromethane
d	doublet
dd	double-doublet
ddd	double-doublet-doublet
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
ELSD	Evaporative Light Scattering Detector
eq.	equivalent
ESI	electrospray (ES) ionisation
h	hour(s)
HATU	1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate
HPLC	high performance liquid chromatography
LC-MS	liquid chromatography mass spectrometry
m	multiplet

Abbreviation	Meaning
min	minute(s)
MS	mass spectrometry
NMR	nuclear magnetic resonance spectroscopy: chemical shifts (δ) are given in ppm. The chemical shifts were corrected by setting the DMSO signal to 2.50 ppm unless otherwise stated.
p	pentet
q	quartet
r.t. or rt or RT	room temperature
rac	racemic
Rt	retention time (as measured either with HPLC or UPLC) in minutes
s	singlet
t	triplet
td	triple-doublet
UPLC	ultra performance liquid chromatography

Other abbreviations have their meanings customary per se to the skilled person.

The various aspects and embodiments of the invention described in this application are illustrated by the following examples which are not meant to limit the invention in any way.

The example testing experiments described herein serve to illustrate the present invention and the invention is not limited to the examples given.

EXPERIMENTAL SECTION - GENERAL PART

All reagents, for which the synthesis is not described in the experimental part, are either commercially available, or are known compounds or may be formed from known compounds by known methods by a person skilled in the art.

The compounds and intermediates produced according to the methods of the invention may require purification. Purification of organic compounds is well known to the person skilled in the art and there may be several ways of purifying the same compound. In some cases, no purification may be necessary. In some cases, the compounds may be purified by crystallization. In some cases, impurities may be stirred out using a suitable solvent. In some cases, the compounds may be purified by chromatography, particularly flash column chromatography, using for example prepacked silica gel cartridges, e.g. Biotage SNAP cartidges KP-Sil® or KP-NH® in combination with a Biotage autopurifier system (SP4® or Isolera Four®) and eluents such as gradients of hexane/ethyl acetate or DCM/methanol. In

some cases, the compounds may be purified by preparative HPLC using for example a Waters autopurifier equipped with a diode array detector and/or on-line electrospray ionization mass spectrometer in combination with a suitable prepacked reverse phase column and eluents such as gradients of water and acetonitrile which may contain additives such as trifluoroacetic acid, formic acid or aqueous ammonia.

In some cases, purification methods as described above can provide those compounds of the present invention which possess a sufficiently basic or acidic functionality in the form of a salt, such as, in the case of a compound of the present invention which is sufficiently basic, a trifluoroacetate or formate salt for example, or, in the case of a compound of the present invention which is sufficiently acidic, an ammonium salt for example. A salt of this type can either be transformed into its free base or free acid form, respectively, by various methods known to the person skilled in the art, or be used as salts in subsequent biological assays. It is to be understood that the specific form (e.g. salt, free base etc.) of a compound of the present invention as isolated and as described herein is not necessarily the only form in which said compound can be applied to a biological assay in order to quantify the specific biological activity.

UPLC-MS Standard Procedures

Analytical UPLC-MS was performed as described below. The masses (m/z) are reported from the positive mode electrospray ionisation unless the negative mode is indicated (ESI-). In most of the cases method 1 is used. If not, it is indicated.

Method A (HPLC-MS):

Instrument: Waters Acquity UPLCMS SingleQuad; Column: Acquity UPLC BEH C18 1.7 µm, 50x2.1mm; eluent A: water + 0.1 vol % formic acid (99%), eluent B: acetonitrile; gradient: 0-1.6 min 1-99% B, 1.6-2.0 min 99% B; flow 0.8 ml/min; temperature: 60 ℃; DAD scan: 210-400 nm.

Method B (HPLC-MS):

Instrument: Waters Acquity UPLCMS SingleQuad; Column: Acquity UPLC BEH C18 1.7 µm, 50x2.1mm; eluent A: water + 0.2 vol % aqueous ammonia (32%), eluent B: acetonitrile; gradient: 0-1.6 min 1-99% B, 1.6-2.0 min 99% B; flow 0.8 ml/min; temperature: 60 ℃; DAD scan: 210-400 nm.

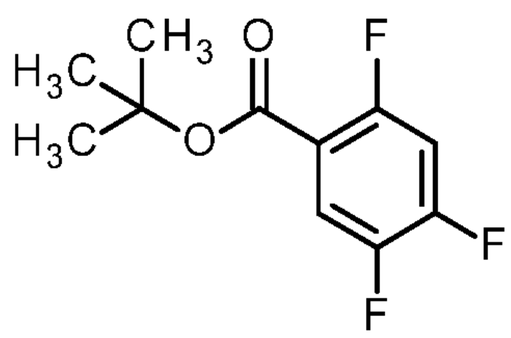
Method C (HPLC-MS):

Instrument: Waters Acquity; MS: Waters ZQ; Column: Acquity BEH C18 1.7µm, 50x2.1mm; eluent A: water + 0.1 vol % formic acid (99%), eluent B: acetonitrile; gradient:0-1.6min 1-99% B, 1.8-2.0min 99% B; tempersture: 60℃; flow: 0.8 m l/min; DAD scan: 210-400nm

EXPERIMENTAL SECTION – INTERMEDIATES

Intermediate 1

tert-butyl 2,4,5-trifluorobenzoate

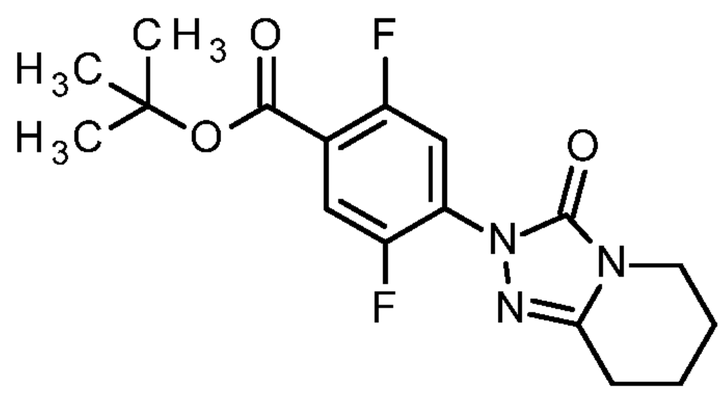


Under argon, to a solution of 2,4,5-trifluorobenzoic acid (101 g, 574 mmol) in 2-methylpropan-2-ol (200 ml) was added N,N-dimethylpyridin-4-amine (35 g, 287 mmol). Subsequently, di-tert-butyl dicarbonate (200 ml, 860 mmol) was added in portions. The resulting mixture was stirred at ambient temperature for two days to yield a clear colorless solution. The reaction mixture was poured into an aqueous sodium carbonate solution (1 N, 1.5 l), and the resulting mixture was extracted with tert-butyl methyl ether (3x 300 ml). The organic phases were concentrated and the observed crude product was purified by silica gel chromatography to yield tert-butyl 2,4,5-trifluorobenzoate (113 g, 85 %) as white crystals.

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.53 (s, 9 H), 7.68 (m, 1 H), 7.87 (m, 1 H).

Intermediate 2

tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate



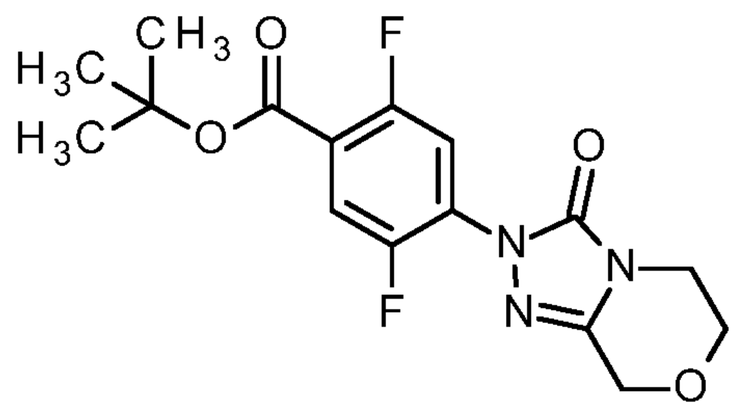
Under argon, to a solution of tert-butyl 2,4,5-trifluorobenzoate (intermediate 1) (50.0 g, 215 mmol) in acetonitrile (500 ml, 9.5 mol) was added 5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one [CAS 118801-67-5] (33.0 g, 237 mmol), and potassium carbonate (59.5 g, 431 mmol). The reaction mixture was stirred under reflux for three days. The mixture was then cooled to room temperature, poured into water (2 l) and the mixture was extracted with tert-butyl methyl ether (3x 500 ml). The organic phases were concentrated and the residue was purified twice by chromatography over silica gel to yield tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate 47.2 g (62 %).

LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 352.0 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.54 (s, 9 H), 1.73–1.92 (m, 4 H), 2.70 (m, 2 H), 3.56 (m, 2 H), 7.61 (m, 1 H), 7.78 (m, 1 H).

Intermediate 3

tert-butyl 2,5-difluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoate



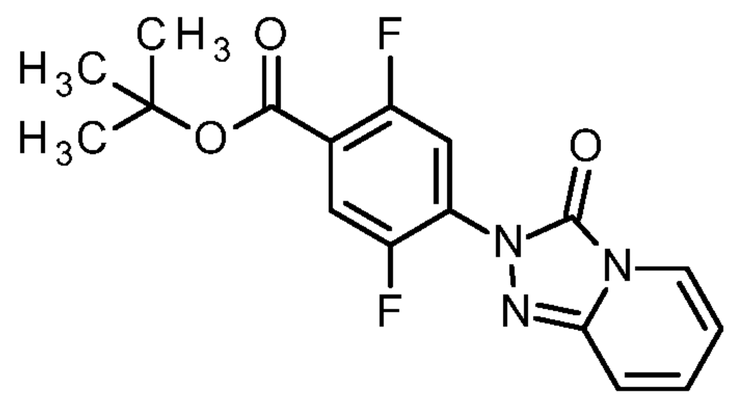
To a room temperature stirred solution of tert-butyl 2,4,5-trifluorobenzoate (intermediate 1) (1.16 g, 5.00 mmol) in anhydrous acetonitrile (12.5 ml) was added 2,5,6,8-tetrahydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-one [CAS 133365-36-3] (741 mg, 5.25 mmol) followed by dropwise addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (1.52 ml, 10.0 mmol). Following complete addition, the resulting mixture was heated at 85 °C for 16 hours, cooled to room temperature and concentrated under reduced pressure to give a dark brown oil (3.52 g). The residue was purified by flash column chromatography to give a waxy white solid (1.35 g, 98 % purity, 75 %).

LC-MS (method A): R_t = 1.15 min; MS (ESIpos): m/z = 354.2 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.60 (s, 9 H), 3.80 (dd, 2 H), 4.08 (dd, 2 H), 4.74 (s, 2 H), 7.45 (dd, 1 H), 7.73 (dd, 1 H).

Intermediate 4

tert-butyl 2,5-difluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate



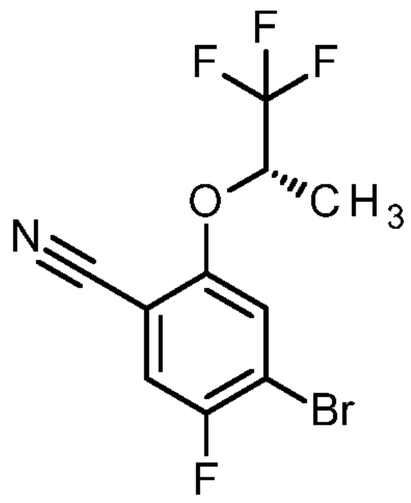
Tert-butyl 2,5-difluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate was prepared as described for tert-butyl 2,5-difluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoate (Intermediate 3) using tert-butyl 2,4,5-trifluorobenzoate (intermediate 1) and [1,2,4]triazolo[4,3-a]pyridin-3(2H)-one [CAS 6969-71-7] to yield the title compound (70 %).

MS (ESIpos): m/z = 348 $[M+H]^+$

^{1}H NMR (400 MHz, CDCl3) δ [ppm] 1.60 (s, 9H), 6.55 (ddd, 1H), 7.13 – 7.21 (m, 2H), 7.53 (dd, 1H), 7.76 (d, 1H), 7.81 (td, 1H).

Intermediate 5

4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile



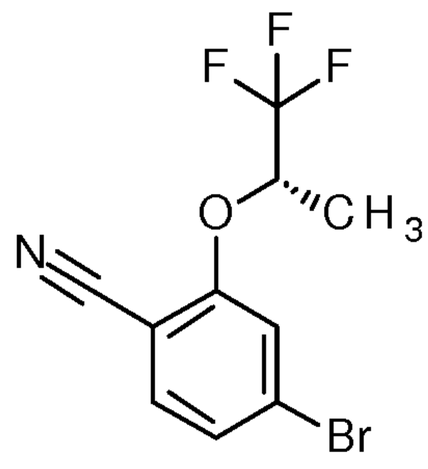
To a stirred suspension of 4-bromo-2,5-difluorobenzonitrile (5.0 g, 22.9 mmol) and potassium carbonate (9.5 g, 68.8 mmol) in N,N-dimethylformamide (45.9 ml) was added (S)-1,1,1-trifluoropropanol [CAS 3539-97-7] dropwise (2.88 g, 25.2 mmol). The resulting mixture was heated at 55 ℃ for for 15 hours and cooled to room temperature. Water (100 ml) was added to the mixture and extracted with diethyl ether (3 × 50 ml). The combined organic extracts were sequentially washed with water (2 × 100 ml), brine (100 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give an off white solid (6.93 g). The residue was purified by flash column chroamtography to give the ether as a white crystalline solid (5.90 g, 97 % purity, 80 %).

LC-MS (method A): R_t = 1.29 min; MS (ESIpos): m/z = 312.0 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.511 (4.41), 1.531 (15.64), 1.533 (16.00), 1.548 (15.84), 1.550 (15.83), 4.566 (1.08), 4.581 (2.68), 4.597 (3.18), 4.612 (2.62), 4.626 (1.01), 7.194 (5.27), 7.207 (7.60), 7.220 (7.57).

Intermediate 6

4-bromo-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile



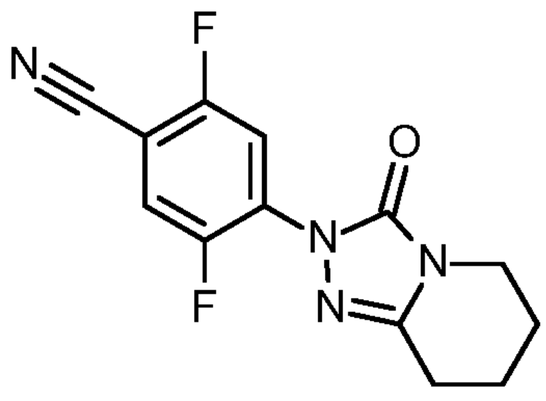
To a stirred suspension of 4-bromo-2-fluorobenzonitrile (5.00 g, 25.0 mmol) and potassium carbonate (10.4 g, 75.0 mmol) in N,N-dimethylformamide (50.0 ml) was added (S)-1,1,1-trifluoropropanol dropwise (3.14 g, 27.5 mmol). The resulting mixture was heated at 55 °C for two days and cooled to room temperature. Water (100 ml) was added to the mixture and extracted with diethyl ether (3 × 50 ml). The combined organic extracts were sequentially washed with water (2 × 100 ml), brine (100 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give a white solid 7.03 g (98 % purity, 94 %). The product was used directly in the next step without further purification.

LC-MS (method A): R_t = 1.27 min; MS (ESIpos): m/z = 294 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.368 (3.65), 1.415 (15.76), 1.427 (16.00), 1.428 (15.81), 1.984 (0.94), 4.525 (1.13), 4.538 (2.65), 4.550 (3.35), 4.562 (2.58), 4.574 (1.03), 7.019 (7.92), 7.022 (8.28), 7.073 (9.59), 7.089 (5.49), 7.092 (5.57), 7.105 (7.20), 7.108 (6.95).

Intermediate 7

2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile



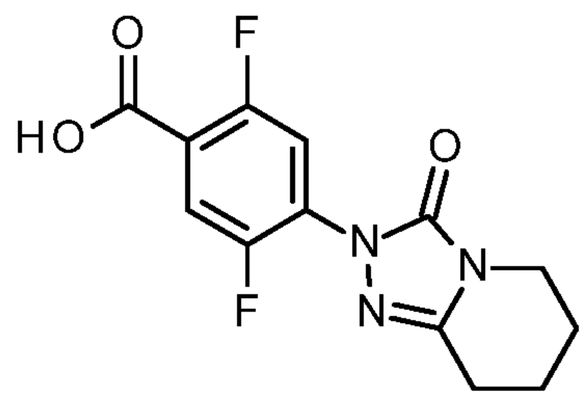
To a solution of 2,4,5-trifluorobenzonitrile (1.08 g, 6.9 mmol) and potassium carbonate (1.9 g, 13.8 mmol) in acetonitrile (25 ml) was added 5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one [CAS 118801-67-5] (1.05 g, 7.6 mmol), and the mixture was heated under reflux overnight. The mixture was then cooled to room temperature, poured into water (150 ml), and extracted with dichloromethane (3 x 300 ml). The organic phases were dried over sodium sulfate, and concentrated under reduced pressure, and the residue was purified by flash chromatography to yield the title compound as an off-white solid (1.06 g, 56%).

LC-MS (method A): R_t = 0.91 min; MS (ESIpos): m/z = 277 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.194 (16.00), 1.896 (1.10), 1.898 (1.22), 1.905 (1.49), 1.914 (3.31), 1.920 (3.80), 1.926 (4.48), 1.936 (4.46), 1.941 (5.07), 1.944 (3.41), 1.953 (2.17), 1.957 (2.32), 1.978 (2.44), 1.982 (2.02), 1.992 (4.35), 1.997 (4.41), 2.008 (4.81), 2.013 (3.80), 2.019 (2.76), 2.022 (3.01), 2.028 (1.50), 2.035 (1.36), 2.050 (0.42), 2.776 (7.63), 2.793 (13.88), 2.808 (8.54), 3.218 (5.28), 3.691 (9.78), 3.707 (15.57), 3.722 (6.87), 7.448 (5.53), 7.462 (5.56), 7.472 (5.65), 7.486 (5.47), 7.644 (5.43), 7.658 (5.52), 7.667 (5.42), 7.682 (5.28).

Intermediate 8

2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid

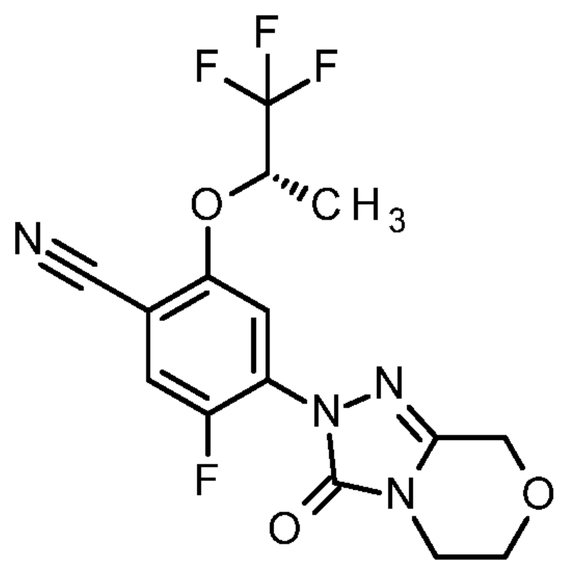


To a solution of 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile (intermediate 7) (4.3 g, 15.67 mmol) in ethanol (30 ml) was added aqueous sodium hydroxide (1 N, 300 ml) and the resulting suspension was heated to 85 °C for one hour. The resulting clear red solution was cooled to room temperature, adjusted to pH 1 with aqueous 1 N hydrochloric acid, and extracted with ethyl acetate. The organic phases were dried over sodium sulfate and concentrated under reduced pressure to yield a beige-brown solid (3.93 g, 85 %), which was used for the next step.

LC-MS (method A): R_t = 0.73 min; MS (ESIpos): m/z = 296 $[M+H]^+$

Intermediate 9

5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile



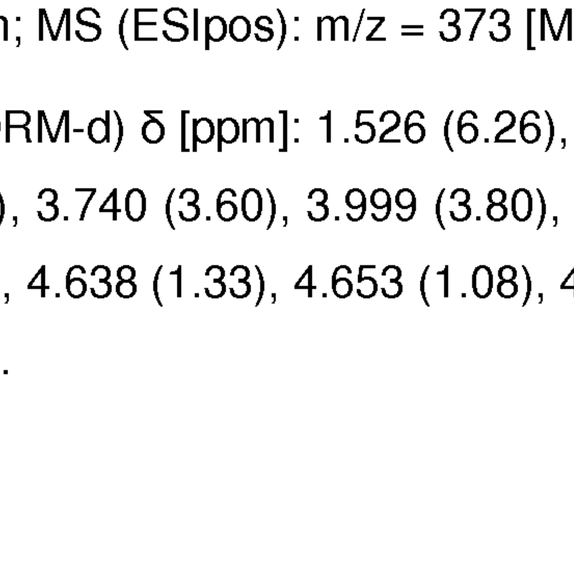
A mixture of 4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 5) (2.43 g, 7.79 mmol), 2,5,6,8-tetrahydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-one (1.0 g, 7.09 mmol), tris(dibenzylideneacetone)dipalladium(0) (195 mg, 0.21 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (369 mg, 0.64 mmol) and cesium carbonate (3.46 g, 10.6 mmol) were placed under an argon atmosphere. To this mixture was then added argon sparged 1,4-dioxane (14.2 ml) after which the resulting mixture was heated at 105 °C for two days and then cooled to room temperature. The mixture was diluted with ethyl acetate, filtered through a Celite plug and concentrated under reduced pressure to give foamy dark orange solid (3.54 g). The residue was purified by flash column chromatography to give the title compound as a yellow soild (2.53 g, 98 % purity, 94 %).

LC-MS (method B): R_t = 1.04 min; MS (ESIpos): m/z = 373 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.526 (6.26), 1.542 (8.45), 1.544 (7.59), 3.713 (2.80), 3.726 (3.96), 3.729 (2.71), 3.740 (3.60), 3.999 (3.80), 4.009 (2.74), 4.012 (3.99), 4.025 (3.13), 4.607 (0.44), 4.623 (1.07), 4.638 (1.33), 4.653 (1.08), 4.673 (16.00), 7.338 (3.00), 7.353 (3.00), 7.381 (3.98), 7.405 (4.00).

Intermediate 10

5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile



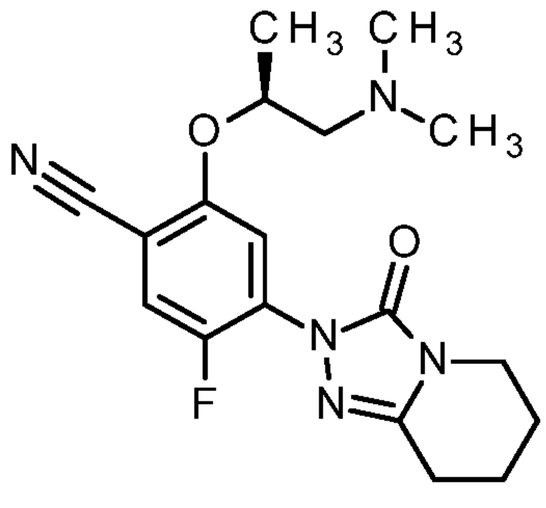
A mixture of 4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 5) (8.24 g, 26.4 mmol), 2,6,7,9-tetrahydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-3-one (intermediate 37) (3.72 g, 24.0 mmol), tris(dibenzylideneacetone)dipalladium(0) (659 mg, 720 µmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (1.25 g, 2.16 mmol) and cesium carbonate (11.7 g, 36.0 mmol) were placed under an argon atmosphere. To this mixture was then added argon sparged 1,4-dioxane (48 ml) after which the resulting mixture was heated at 105 °C for two days and then cooled to room tempera ture. The mixture was diluted with ethyl acetate, filtered through a Celite plug and concentrated under reduced pressure to give a dark foam (3.54 g). The residue was purified by flash column chromatography to give the title compound as a off-white soild (8.56 g, 90 %).

LC-MS (method A): R_t = 1.07 min; MS (ESIpos): m/z = 387.2 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.584 (3.78), 1.587 (1.48), 1.603 (6.18), 1.618 (6.41), 1.620 (6.42), 2.011 (0.70), 2.017 (0.65), 2.024 (1.24), 2.038 (1.84), 2.050 (1.28), 2.063 (0.74), 3.989 (2.42), 3.996 (1.08), 4.001 (1.79), 4.004 (1.76), 4.017 (2.33), 4.057 (2.76), 4.069 (2.30), 4.081 (2.72), 4.595 (16.00), 4.684 (0.45), 4.699 (1.08), 4.714 (1.33), 4.729 (1.04), 4.744 (0.41), 7.390 (3.04), 7.404 (3.01), 7.454 (4.08), 7.477 (4.04).

Intermediate 11

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3-a]pyridin-2(3H)-yl)benzonitrile



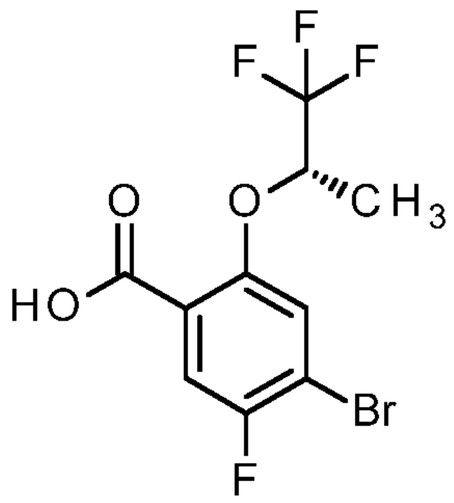
To a solution of (S)-(+)-1-dimethylamino-2-propanol (2.26 g, 25 mmol) in N,N-dimethylformamide (30 ml) was added sodium hydride (1.0 g, 60 % purity, 25.1 mmol) and the suspension was stirred at room temperature for one hour. A solution of 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile (intermediate 7) (3.46 g, 12.5 mmol) in N,N-dimethylformamide (30 ml) was then added dropwise, and the reaction mixture was stirred for three hours, then poured into water, and extracted with ethyl acetate. The organic phases were washed with brine, dried over sodium sulfate and concentrated

under reduced pressure. The residue was purified by flash chromatography to yield the title compound as a brown, foamy oil (2.1 g, 47 %).

LC-MS (method A): R_t = 0.52 min; MS (ESIpos): m/z = 360.2 $[M+H]^+$

Intermediate 12

4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid



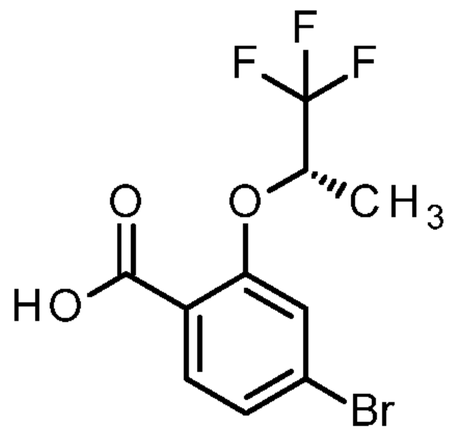
To a solution of 4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 5) (27.4 g, 87.9 mmol) in ethanol (90 ml) was added aqueous sodium hydroxide (2 N, 140 ml) and the resulting mixture was heated to 90 °C for 20 hours. The resulting solution was cooled to room temperature, diluted with water, and extracted with dichloromethane. The aqueous phase was acidified with 2 N aqueous hydrochloric acid (pH 2) upon which a white solid precipitated. The suspension was stirred for further 15 minutes, the solid was filtered off, washed with water and dried *in vacuo*. to yield an off-white solid (25.97 g, 89 %), which was used for the next step without further purification.

LC-MS (method A): R_t = 1.16 min; MS (ESIpos): m/z = 331 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.396 (15.96), 1.411 (16.00), 1.469 (0.69), 1.484 (0.45), 2.518 (3.48), 2.523 (2.36), 5.288 (1.19), 5.304 (2.89), 5.320 (3.73), 5.336 (2.70), 5.352 (1.05), 7.612 (11.35), 7.634 (11.12), 7.743 (7.88), 7.757 (7.91).

Intermediate 13

4-bromo-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid



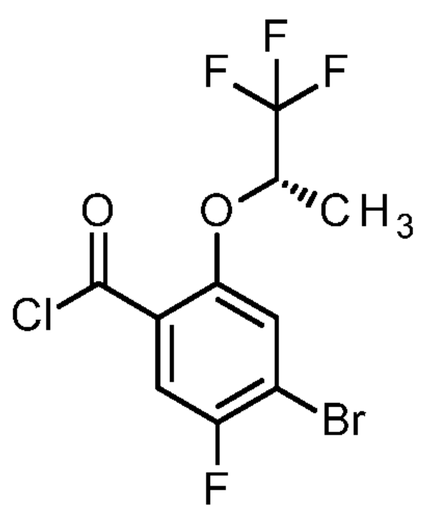
To a solution of 4-bromo-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 6) (5.00 g, 17.0 mmol) in ethanol (18 ml) was added aqueous sodium hydroxide (2 N, 28 ml) and the resulting mixture was heated to 90 °C for 21 ho urs. The resulting solution was cooled to room temperature, diluted with water, and extracted with dichloromethane. The aqueous phase was acidified with 2 N aqueous hydrochloric acid (pH 2) upon which a white solid precipitated. The suspension was stirred for further 15 minutes, the solid was filtered off, washed with water and dried *in vacuo*. to yield white solid 4.76 g (89 %), which was used for the next step without further purification.

LC-MS (method A): R_t = 1.15 min; MS (ESIneg): m/z = 311 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.403 (15.87), 1.419 (16.00), 2.518 (2.74), 2.523 (1.80), 5.352 (1.13), 5.368 (2.86), 5.383 (3.71), 5.400 (2.72), 5.416 (1.03), 7.299 (6.49), 7.304 (6.51), 7.320 (6.97), 7.324 (7.05), 7.584 (13.85), 7.596 (8.97), 7.600 (8.84), 7.605 (12.52).

Intermediate 14

4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl chloride



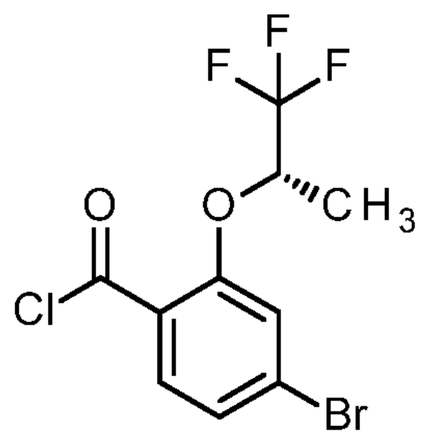
To a solution of 4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid (intermediate 12) (15.0 g, 45.3 mmol) in dichloromethane (230 ml) was added N,N-dimethylformamide (350 µl), followed by dropwise addition of ethanedioyl dichloride (4.7 ml, 54 mmol). The reaction mixture was stirred at room temperature for one hour, and concentrated under reduced pressure. The title compound was obtained as brown oil (15.84 g, quantitative), which was used for the next step without purification. For analytic, a small amount of the

product was treated with methanol, to yield the corresponding methyl ester, which was detected by LC-MS.

LC-MS (method A) [methyl ester]: R_t = 1.36 min; MS (ESIpos): m/z = 345 $[M+H]^+$

Intermediate 15

4-bromo-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl chloride

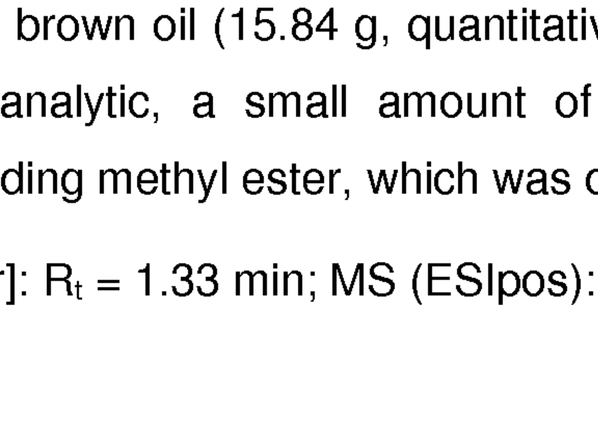


To a solution of 4-bromo-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid (intermediate 13) (2.6 g, 8.3 mmol) in dichloromethane (42 ml) was added N,N-dimethylformamide (870 µl), followed by dropwise addition of ethanedioyl dichloride (870 µl, 10 mmol). The reaction mixture was stirred at room temperature for one hour, and concentrated under reduced pressure. The title compound was obtained as brown oil (15.84 g, quantitative), which was used for the next step without purification. For analytic, a small amount of the product was treated with methanol, to yield the corresponding methyl ester, which was detected by LC-MS.

LC-MS (method A) [methyl ester]: R_t = 1.33 min; MS (ESIpos): m/z = 327 $[M+H]^+$

Intermediate 16

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid



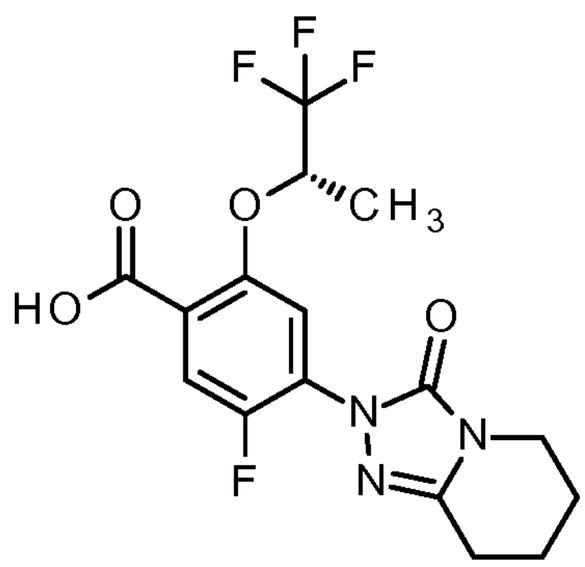
To a -10 ℃ stirred solution of (S)-(+)-2-pentanol (1.16 g, 13.2 mmol) in anhydrous tetrahydrofuran (13.2 ml) was added a 1.0 M solution of potassium 1,1,1,3,3,3-hexamethyldisilazan-2-ide in tetrahydrofuran dropwise (7.20 ml, 7.20 mmol). The resulting mixture was was then stirred at -10 ℃ for 1 hour, after which the resulting alkoxide solution was added dropwise to a stirred solution of tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 2) (2.11 g, 6.00 mmol) in anhydrous tetrahydrofuran (6.00 ml). The resulting orange solution was stirred at -10 ℃ for 2 hours and then concentrated under reduced pressure to give a orange solid. The residue was purified by flash column chromatography to give a mixture of esters as a colourless oil. The residue was suspended in a 4:1 ration of 1,4-dioxane/water (30.0 ml) after which lithium hydroxide (2.16 g, 90.0 mmol) was added in one portion. The resulting mixture was heated at 70 ℃ for 16 hours and cooled to room temperature. Water (20 ml) was added to the mixture followed by washing with diethyl ether (20 ml). The aqueous layer was acidified to pH 2.0 with concentrated hydrochloric acid and then extracted with diethyl ether (3 x 20 ml). The combined organic extracts were washed with brine (20 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give a cream solid. The residue was purified by flash column chromatography to give 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid as a cream solid (1.06 g, 48 %).

LC-MS (method A): R_t = 1.05 min; MS (ESIpos): m/z = 364 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.958 (6.44), 0.976 (15.81), 0.983 (0.74), 0.995 (7.41), 1.002 (0.81), 1.400 (0.49), 1.418 (0.89), 1.426 (0.78), 1.435 (16.00), 1.444 (1.77), 1.450 (15.70), 1.459 (1.02), 1.462 (1.04), 1.471 (0.41), 1.478 (1.05), 1.484 (0.68), 1.490 (0.68), 1.497 (0.84), 1.504 (0.84), 1.509 (0.68), 1.516 (0.45), 1.523 (0.87), 1.542 (0.50), 1.675 (0.56), 1.689 (0.98), 1.700 (0.47), 1.704 (0.57), 1.710 (0.90), 1.714 (0.89), 1.724 (1.46), 1.728 (0.53), 1.734 (0.83), 1.739 (0.76), 1.749 (1.27), 1.763 (0.57), 1.811 (0.71), 1.825 (0.85), 1.827 (0.85), 1.837 (0.71), 1.841 (0.83), 1.846 (0.58), 1.851 (0.76), 1.853 (0.79), 1.860 (0.58), 1.862 (0.60), 1.867 (0.68), 1.872 (0.50), 1.876 (0.48), 1.888 (0.49), 1.902 (0.78), 1.910 (0.62), 1.919 (1.38), 1.926 (1.59), 1.931 (1.81), 1.942 (1.81), 1.946 (2.01), 1.959 (0.85), 1.962 (0.92), 1.984 (0.96), 1.990 (0.88), 1.999 (1.79), 2.003 (1.85), 2.014 (1.99), 2.019 (1.58), 2.028 (1.19), 2.042 (0.52), 2.793 (3.08), 2.808 (5.61), 2.825 (3.35), 3.701 (3.92), 3.712 (9.14), 3.717 (6.28), 3.732 (2.69), 4.674 (0.99), 4.689 (1.93), 4.704 (1.90), 4.720 (0.95), 5.308 (1.24), 7.464 (3.89), 7.478 (3.90), 8.012 (4.97), 8.040 (4.91), 11.113 (0.43).

Intermediate 17

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid



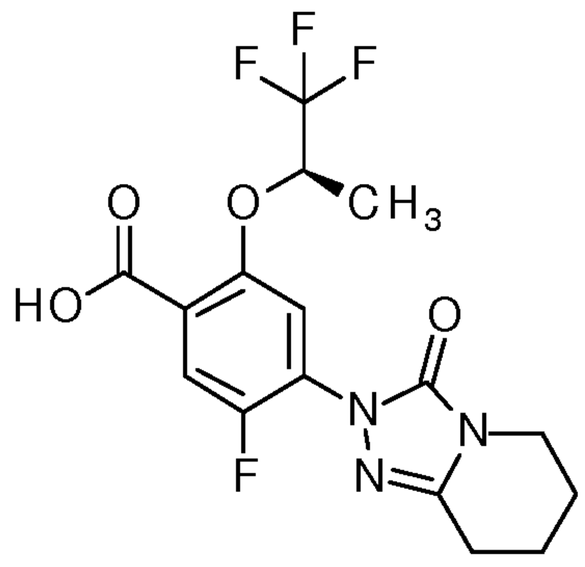
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (S)-1,1,1-trifluoropropanol [CAS 3539-97-7] (5.01 g, 44.0 mmol) and tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 2) (7.03 g, 20.0 mmol) to yield the title compound, 7.15 g (98 % purity, 90 %).

LC-MS (method A): R_t = 0.93 min; MS (ESIpos): m/z = 390 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.578 (0.49), 1.607 (15.92), 1.623 (16.00), 1.908 (1.01), 1.923 (2.89), 1.935 (4.07), 1.950 (4.27), 1.966 (2.10), 1.988 (2.08), 2.007 (4.12), 2.018 (4.38), 2.032 (2.70), 2.046 (1.12), 2.054 (0.61), 2.798 (5.21), 2.814 (10.12), 2.830 (5.64), 3.709 (6.22), 3.725 (10.71), 3.739 (4.89), 4.821 (1.08), 4.836 (2.54), 4.851 (3.26), 4.866 (2.46), 4.882 (1.00), 7.504 (6.48), 7.519 (6.42), 7.954 (6.94), 7.981 (6.82).

Intermediate 18

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid



5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid

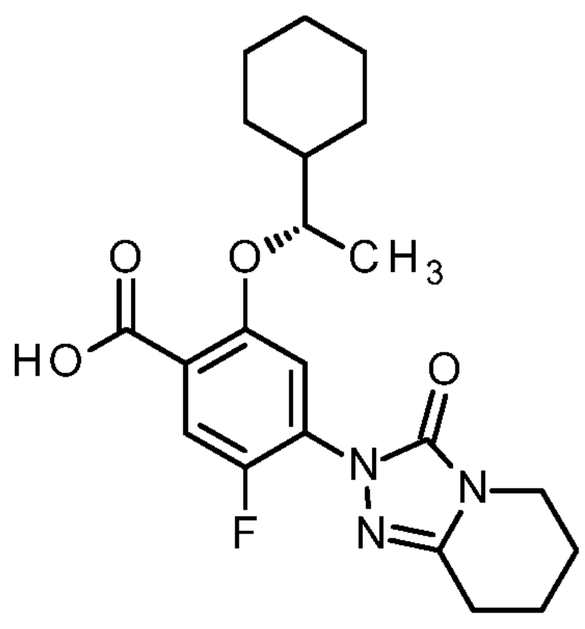
(Intermediate 16), using (R)-1,1,1-trifluoropropanol [CAS 17628-73-8] (714 mg, 6.26 mmol) and tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 2) (1.0 g, 2.85 mmol) to yield the title compound, 800 mg (72 %).

LC-MS (method A): R_t = 0.92 min; MS (ESIpos): m/z = 390 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.400 (15.93), 1.416 (16.00), 1.512 (1.30), 1.769 (0.97), 1.784 (2.84), 1.796 (4.11), 1.810 (4.29), 1.823 (2.12), 1.864 (2.02), 1.878 (4.18), 1.889 (4.40), 1.903 (2.82), 1.917 (1.14), 2.083 (9.11), 2.326 (0.48), 2.683 (4.64), 2.699 (9.32), 2.715 (5.05), 3.549 (5.37), 3.564 (9.81), 3.579 (4.60), 5.184 (1.05), 5.200 (2.59), 5.216 (3.40), 5.232 (2.48), 5.248 (1.00), 7.481 (6.42), 7.497 (6.44), 7.645 (7.67), 7.671 (7.48), 13.231 (1.18).

Intermediate 19

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid



2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (1S)-1-cyclohexylethanol (14.96 g, 116.7 mmol), tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 2) (20 g, 56.9 mmol) and to yield the title compound, and potassium 2-methylpropan-2-olate instead of potassium 1,1,1,3,3,3-hexamethyldisilazan-2-ide as base. The title compound was obtained as white solid, 13.03 g (57 %).

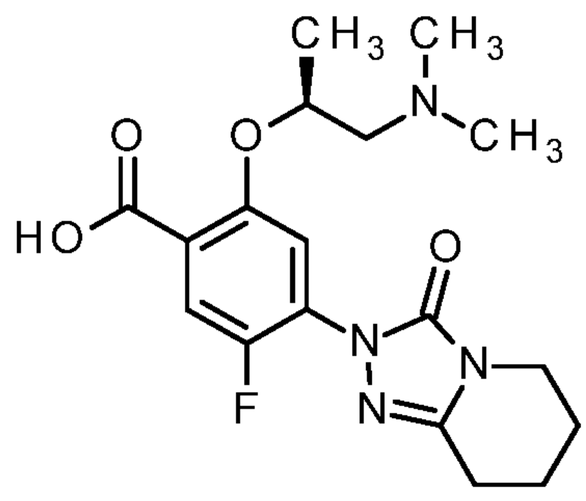
LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 404 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: -0.008 (0.83), 0.008 (0.90), 1.025 (0.44), 1.056 (1.55), 1.086 (2.87), 1.106 (2.47), 1.118 (3.29), 1.148 (3.68), 1.166 (15.87), 1.182 (16.00), 1.535 (1.26), 1.616 (1.40), 1.645 (1.48), 1.692 (4.71), 1.721 (4.07), 1.766 (0.90), 1.781 (2.33), 1.793 (3.31), 1.808 (3.63), 1.824 (2.93), 1.857 (2.93), 1.875 (3.52), 1.886 (3.49), 1.899 (2.18), 1.914

(0.86), 2.675 (3.71), 2.691 (7.09), 2.707 (3.89), 3.542 (4.20), 3.557 (7.48), 3.572 (3.50), 4.203 (0.54), 4.218 (1.95), 4.233 (2.74), 4.247 (1.91), 4.262 (0.51), 5.758 (0.53), 7.227 (4.58), 7.243 (4.56), 7.542 (5.25), 7.568 (5.18), 12.923 (4.84).

Intermediate 20

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid



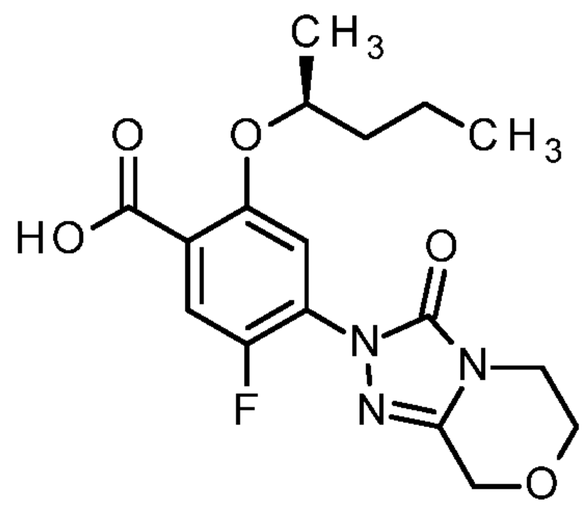
To a solution of 2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile (intermediate 11) (2.1 g, 5.84 mmol) in ethanol (12 ml) was added aqueous sodium hydroxide solution (120 ml, 1.0 M, 120 mmol), and the mixture was heated to 85 °C for seven hours . The mixture was then cooled to room temperature and extracted with ethyl acetate. The aqueous solution was then adjusted to pH 5 with 1 M aqueous hydrochloric acid and concentrated under reduced pressure. The residue was purified by reversed phase column chromatography (Biotage® SNAP ULTRA C18, water, acetonitrile 0 – 40 %) to yield the product as a beige solid (1.9 g, 86 %).

LC-MS (method B): R_t = 0.51 min; MS (ESIneg): m/z = 377 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.497 (4.39), 1.513 (4.38), 1.909 (0.76), 1.921 (1.07), 1.936 (1.12), 1.993 (1.11), 2.003 (1.14), 2.595 (16.00), 2.766 (0.86), 2.772 (0.98), 2.781 (1.40), 2.797 (3.05), 2.812 (1.46), 3.115 (0.65), 3.143 (0.81), 3.174 (0.57), 3.689 (1.55), 3.704 (2.60), 3.718 (1.30), 4.599 (0.48), 7.289 (1.65), 7.304 (1.61), 7.724 (1.76), 7.751 (1.72).

Intermediate 21

5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid

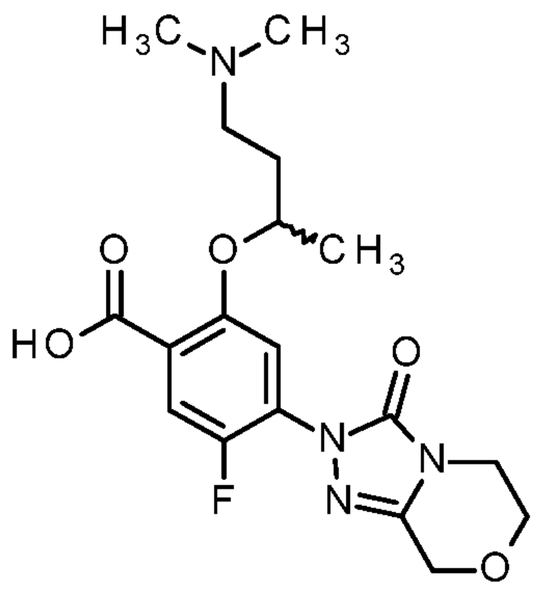


5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (S)-pentan-2-ol (440 µl, 4.0 mmol) and tert-butyl 2,5-difluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoate (intermediate 3) (650 mg, 1.84 mmol) to yield the title compound, 200 mg (30 %).

LC-MS (method A): R_t = 0.97 min; MS (ESIpos): m/z = 366.2 $[M+H]^+$

Intermediate 22

rac-2-{[(2S)-4-(dimethylamino)butan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoic acid

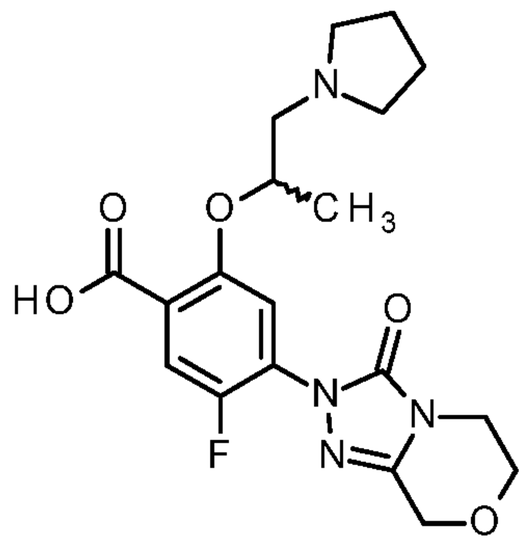


Rac-2-{[(2S)-4-(dimethylamino)butan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using rac-4-(dimethylamino)butan-2-ol (136 mg, 1.16 mmol) and tert-butyl 2,5-difluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoate (intermediate 3) (200 mg, 0.566 mmol) to yield the title compound, 64 mg (52 %).

LC-MS (method B): R_t = 0.49 min; MS (ESIpos): m/z = 395 $[M+H]^+$

Intermediate 23

rac-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzoic acid

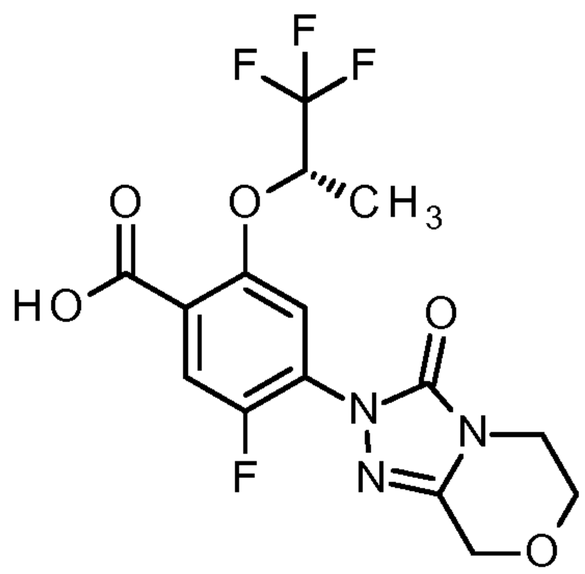


5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using rac-1-(pyrrolidin-1-yl)propan-2-ol (187 mg, 1.45 mmol) and tert-butyl 2,5-difluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoate (intermediate 3) (250 mg, 0.707 mmol) to yield the title compound, 117 mg (41 %).

LC-MS (method B): R_t = 0.52 min; MS (ESIpos): m/z = 407 $[M+H]^+$

Intermediate 24

5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid



Method 1:

5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (S)-1,1,1-trifluoropropanol [CAS 3539-97-7] (461 mg, 4.0 mmol) and

tert-butyl 2,5-difluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzoate (intermediate 3) (650 mg, 1.8 mmol) to yield the title compound, 356 mg (49 %).

Method 2:

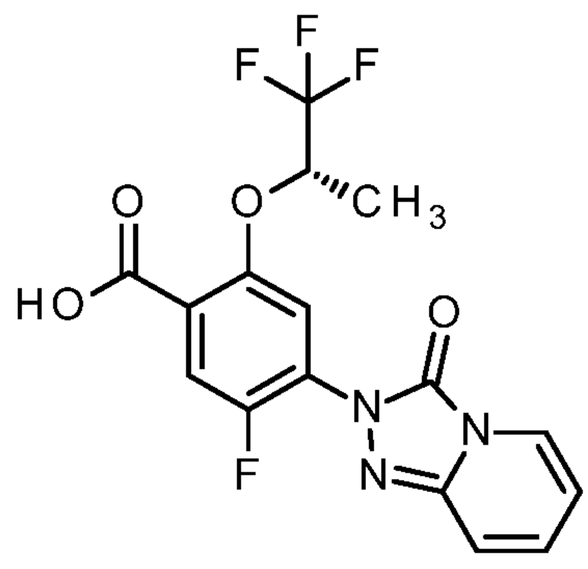
To a stirred suspension of 5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 9) (1.12 g, 3.0 mmol) in water (3.00 ml) was added concentrated sulfuric acid (8.40 ml, 158 mmol) and acetic acid (8.40 ml, 147 mmol). The resulting mixture was heated at 120 °C for 2 days and then cooled to room temperature. The mixture was poured onto ice water and extracted with diethyl ether (3 x 50 ml), after which the combined organic extracts were washed with 2.0 M aqueous sodium hydroxide (4 x 25 ml). The resulting aq. layer was acidified to pH 2.5 with concentrated aqueous hydrochloric acid and extracted with diethyl ether (3 x 50 ml). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure to give the acid as an off whtie solid (1.07 g, 98 % purity, 89 %).

LC-MS (method A): R_t = 0.84 min; MS (ESIpos): m/z = 392 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.400 (8.86), 1.416 (8.88), 1.513 (1.37), 2.083 (3.03), 2.326 (0.67), 2.331 (0.48), 2.518 (3.05), 2.522 (2.02), 2.668 (0.70), 2.673 (0.49), 3.653 (3.00), 3.666 (4.91), 3.680 (3.47), 4.016 (3.69), 4.030 (5.03), 4.043 (3.10), 4.736 (16.00), 5.177 (0.60), 5.193 (1.49), 5.209 (1.93), 5.225 (1.38), 5.241 (0.55), 7.484 (2.92), 7.499 (2.85), 7.640 (3.36), 7.666 (3.30).

Intermediate 25

5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid

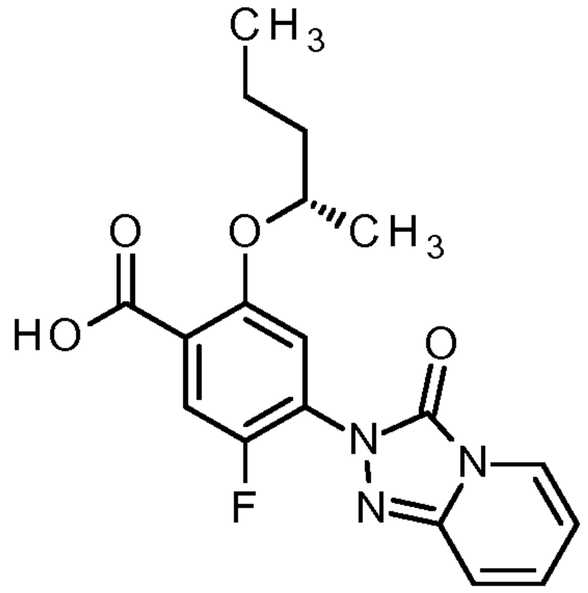


5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid

(Intermediate 16), using (S)-1,1,1-trifluoropropanol [CAS 3539-97-7] and tert-butyl 2,5-difluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 4).

Intermediate 26

5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid



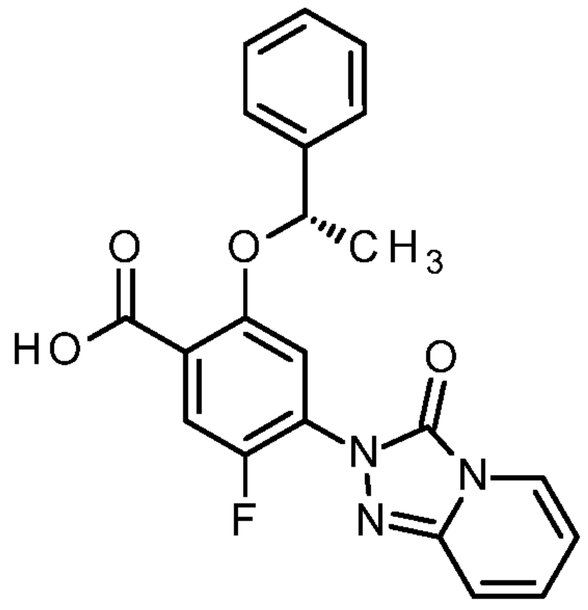
5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (S)-pentan-2-ol and tert-butyl 2,5-difluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 4).

MS (ESIneg): m/z = 358 $[M-H]^-$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 0.98 (t, 3H), 1.39 – 1.57 (m, 2H), 1.46 (d, 3H), 1.68 – 1.79 (m, 1H), 1.82 – 1.92 (m, 1H), 4.67 – 4.76 (m, 1H), 6.57 (ddd, 1H), 7.15 – 7.23 (m, 2H), 7.48 (d, 1H), 7.82 (td, 1H), 8.09 (d, 1H), 11.04 (br, 1H).

Intermediate 27

5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzoic acid



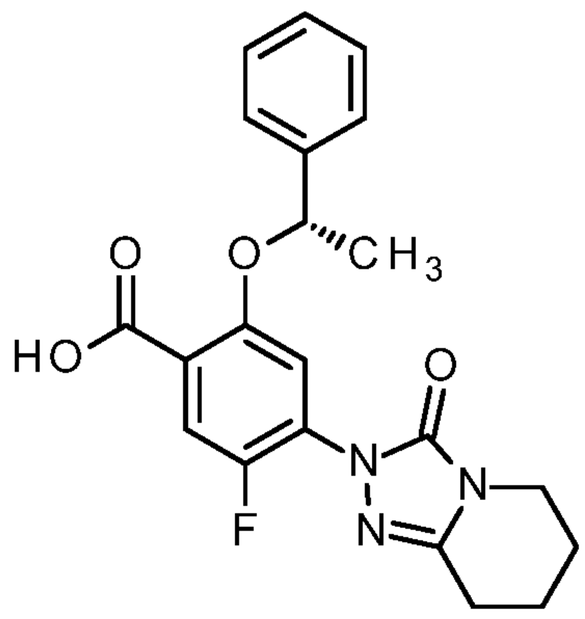
5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (1S)-1-phenylethanol and tert-butyl 2,5-difluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 4).

MS (ESIneg): m/z = 392 $[M-H]^-$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 1.83 (d, 3H), 5.63 (q, 1H), 6.55 (ddd, 1H), 7.11 – 7.22 (m, 2H), 7.29 – 7.41 (m, 5H), 7.44 (d, 1H), 7.79 (td, 1H), 8.05 (d, 1H), 11.04 (br, 1H).

Intermediate 28

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzoic acid



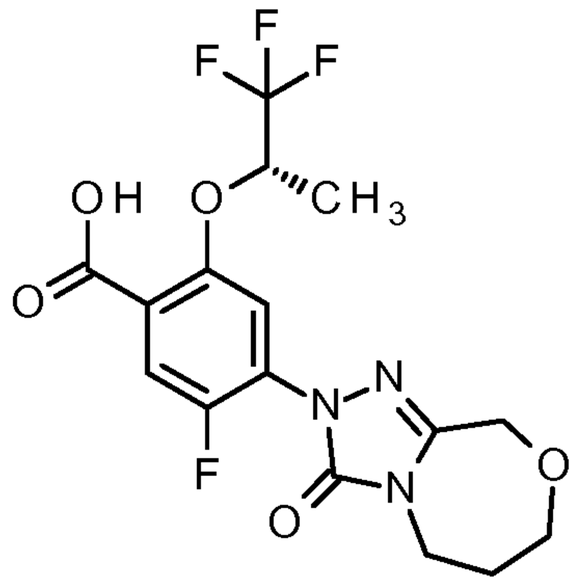
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzoic acid was prepared as described for 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (Intermediate 16), using (1S)-1-phenylethanol and tert-butyl 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoate (intermediate 2).

MS (ESIpos): m/z = 398 $[M+H]^+$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 1.80 (d, 3H), 1.86 – 1.94 (m, 2H), 1.94 – 2.02 (m, 2H), 2.76 (t, 2H), 3.65 – 3.71 (m, 2H), 5.61 (q, 1H), 7.30 – 7.40 (m, 5H), 7.45 (d, 1H), 7.98 (d, 1H).

Intermediate 29

5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid



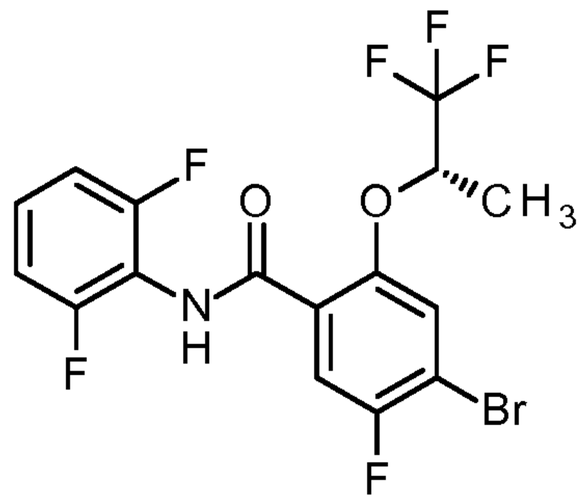
To a stirred suspension of 5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 10) (2.61 g, 6.76 mmol) in water (6.76 ml) was added concentrated. sulfuric acid (18.9 ml) and acetic acid (18.9 ml). The resulting mixture was heated at 120 ℃ for two days and then cooled to room temperature. The mixture was poured onto ice water and extracted with diethyl ether (3 x 100 ml), after which the combined organic extracts were washed with 2.0 M aqueous sodium hydroxide (4 x 50 ml). The resulting aqueous layer was acidified to pH 2.5 with concentrated hydrochloric acid and extracted with diethyl ether (3 x 100 ml). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure to give the acid as a beige solid (2.1 g, 85 % purity, 65 %). The material was used in the next step without further purification.

LC-MS (method A): R_t = 0.89 min; MS (ESIpos): m/z = 406 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.817 (0.46), 0.837 (0.88), 0.842 (0.90), 0.849 (0.81), 0.858 (0.73), 0.887 (0.43), 1.262 (1.08), 1.293 (0.99), 1.379 (0.51), 1.624 (9.21), 1.640 (9.17), 2.019 (3.78), 2.032 (1.73), 2.045 (2.48), 2.057 (1.91), 2.065 (1.03), 2.070 (1.21), 3.709 (0.48), 3.723 (0.65), 3.737 (0.45), 4.001 (2.93), 4.016 (2.36), 4.028 (3.00), 4.041 (0.80), 4.062 (3.28), 4.075 (3.04), 4.087 (3.03), 4.609 (16.00), 4.694 (2.34), 4.821 (0.61), 4.837 (1.44), 4.852 (1.82), 4.868 (1.38), 4.883 (0.56), 7.445 (3.54), 7.459 (3.54), 7.473 (0.55), 7.488 (0.51), 7.971 (0.86), 7.977 (4.10), 7.998 (0.88), 8.003 (4.03).

Intermediate 30

4-bromo-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



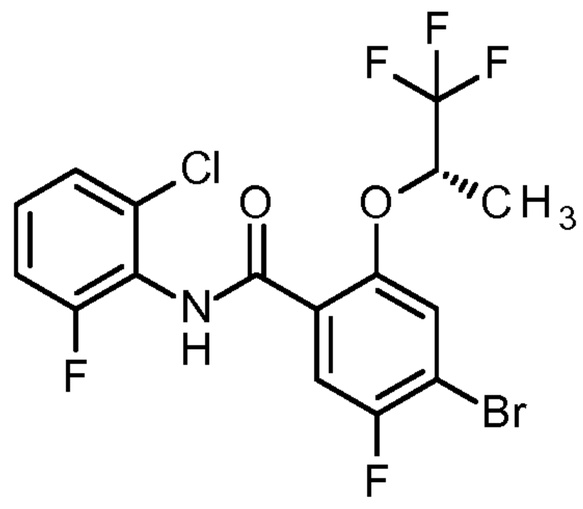
Under argon, a solution of 4-bromo-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl chloride (intermediate 14) (17.0 g, 48.6 mmol) in dichloromethane (200 ml) were added at room temperature to a solution of 2,6-difluoroaniline (5.8 ml, 54 mmol) and triethylamine (7.5 ml, 54 mmol) in dichloromethane (350 ml), and the mixture was stirred at room temperature for one hour. The reaction mixture was then concentrated under reduced pressure. The residue was dissolved in 150 ml of methanol and triturated with water (300 ml). The resulting solid was filtered, washed with water, and dried *in vacuo* to yield the title compound (20.6 g, 96 %) as off-white solid.

LC-MS (method A): R_t = 1.40 min; MS (ESIneg): m/z = 440 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.147 (1.01), 1.165 (1.91), 1.184 (1.01), 1.339 (0.56), 1.356 (0.62), 1.394 (0.97), 1.411 (1.35), 1.430 (16.00), 1.446 (15.69), 1.486 (0.42), 2.331 (0.97), 2.518 (4.44), 2.522 (3.02), 2.673 (0.97), 5.366 (1.11), 5.383 (2.64), 5.399 (3.30), 5.415 (2.46), 5.430 (1.04), 7.183 (4.93), 7.203 (10.41), 7.224 (6.52), 7.367 (1.18), 7.382 (2.50), 7.403 (3.68), 7.419 (1.98), 7.424 (1.91), 7.440 (0.83), 7.555 (7.05), 7.576 (6.98), 7.808 (6.25), 7.822 (6.18), 9.886 (0.42), 9.918 (10.17).

Intermediate 31

4-bromo-N-(2-chloro-6-fluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



4-bromo-N-(2-chloro-6-fluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide was prepared as described for 4-bromo-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide (Intermediate 30), using 4-bromo-5-fluoro-2-{[(2S)-1,1,1-

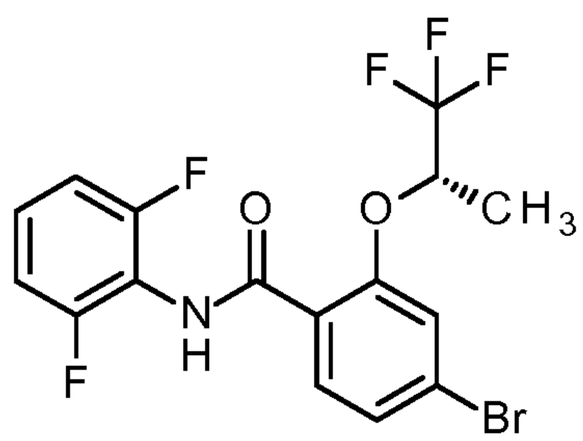
trifluoropropan-2-yl]oxy}benzoyl chloride (intermediate 14) (10.6 g, 30.3 mmol) and 2-chloro-6-fluoroaniline (4.86 g, 33.4 mmol) to yield the title compound, 12.5 g (90 %).

LC-MS (method A): R_t = 1.44 min; MS (ESIpos): m/z = 458 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.343 (1.25), 1.356 (1.38), 1.387 (1.01), 1.404 (1.10), 1.437 (16.00), 1.453 (15.85), 2.327 (0.96), 2.669 (0.99), 5.401 (1.31), 5.417 (2.76), 5.432 (3.40), 5.449 (2.53), 5.465 (1.17), 7.328 (1.83), 7.347 (4.04), 7.363 (2.55), 7.371 (2.93), 7.383 (2.30), 7.403 (4.05), 7.416 (5.56), 7.425 (9.27), 7.431 (9.39), 7.445 (2.51), 7.482 (0.62), 7.528 (5.87), 7.549 (5.79), 7.679 (0.57), 7.820 (5.53), 7.834 (5.48), 9.977 (10.39).

Intermediate 32

4-bromo-N-(2,6-difluorophenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



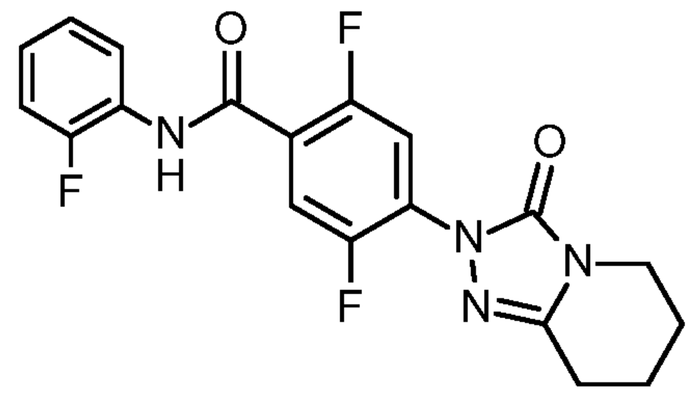
4-bromo-N-(2,6-difluorophenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide was prepared as described for 4-bromo-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide (Intermediate 30), using 4-bromo-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl chloride (intermediate 15) (2.65 g, 7.99 mmol) and 2,6-difluoroaniline (950 µl, 8.8 mmol) to yield the title compound, 3.11 g (92 %).

LC-MS (method A): R_t = 1.36 min; MS (ESIpos): m/z = 424 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.054 (0.42), 1.350 (0.40), 1.365 (0.42), 1.445 (16.00), 1.461 (15.92), 2.518 (4.30), 2.523 (2.73), 5.433 (1.17), 5.449 (2.71), 5.465 (3.50), 5.481 (2.57), 5.497 (1.09), 7.176 (4.91), 7.197 (10.19), 7.217 (6.29), 7.362 (4.96), 7.365 (4.80), 7.382 (7.32), 7.385 (6.93), 7.395 (4.03), 7.411 (2.04), 7.433 (0.82), 7.493 (7.91), 7.514 (5.84), 7.667 (8.70), 9.794 (12.87).

Intermediate 33

2,5-difluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



To a solution of 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 8) (195 mg, 660 µmol) in N,N-dimethylformamide (5 ml) was added 1-[bis(dimethylamino)methylene]-1H-[1,2,3]triazolo[4,5-b]pyridin-1-ium 3-oxide hexafluorophosphate (HATU) (502 mg, 1.32 mmol), and the mixture was stirred at room temperature for 15 minutes. Then, 2-fluoroaniline (80.7 mg, 727 µmol) and N-ethyl-N-isopropylpropan-2-amine (350 µl, 2.0 mmol) were added subsequently, and the reaction mixture was stirred at room temperature for four hours. The reaction solution was directly subjected to reversed phase column chromatography (Biotage® SNAP ULTRA C18, water, acetonitrile 10 – 90 %) to yield the product as a beige solid (110 mg, 43 %).

LC-MS (method A): R_t = 1.08 min; MS (ESIpos): m/z = 389.8 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.844 (0.47), 1.108 (8.91), 1.145 (0.50), 1.198 (0.42), 1.232 (0.92), 1.775 (1.68), 1.790 (4.64), 1.802 (6.53), 1.817 (6.65), 1.829 (3.29), 1.870 (3.21), 1.884 (6.59), 1.895 (7.01), 1.909 (4.27), 1.923 (1.68), 2.074 (7.34), 2.323 (1.28), 2.327 (1.68), 2.331 (1.23), 2.523 (4.80), 2.669 (1.90), 2.674 (1.59), 2.689 (7.65), 2.705 (15.02), 2.721 (8.15), 3.559 (9.08), 3.575 (16.00), 3.589 (7.23), 4.190 (0.84), 7.216 (1.90), 7.229 (5.00), 7.234 (5.72), 7.247 (6.51), 7.253 (7.20), 7.263 (4.94), 7.270 (4.22), 7.275 (5.36), 7.281 (2.23), 7.291 (5.31), 7.310 (2.29), 7.317 (4.75), 7.338 (2.32), 7.342 (1.95), 7.600 (3.24), 7.614 (3.60), 7.626 (3.55), 7.640 (3.24), 7.742 (3.55), 7.757 (3.80), 7.768 (3.80), 7.783 (3.49), 7.823 (2.18), 7.840 (3.85), 7.856 (2.12), 10.315 (8.04).

Intermediate 34

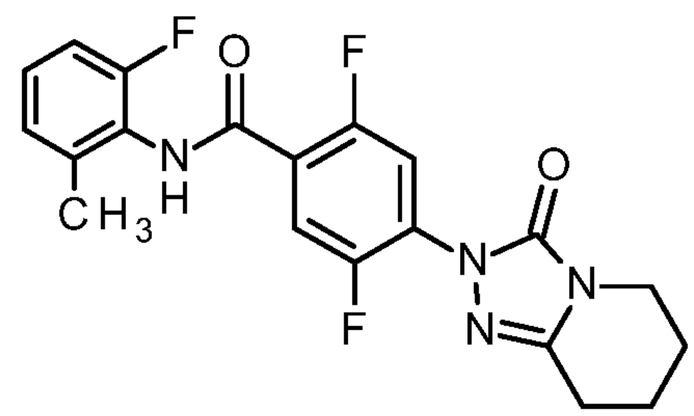
N-(2,6-difluorophenyl)-2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide

To a solution of 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 8) (195 mg, 660 µmol) in N,N-dimethylformamide (5 ml) was added 1-[bis(dimethylamino)methylene]-1H-[1,2,3]triazolo[4,5-b]pyridin-1-ium 3-oxide hexafluorophosphate (HATU) (502 mg, 1.32 mmol), and the mixture was stirred at room temperature for 15 minutes. Then, 2,6-difluoroaniline (93.8 mg, 727 µmol) and N-ethyl-N-isopropylpropan-2-amine (350 µl, 2.0 mmol) were added subsequently, and the reaction mixture was stirred at room temperature for four hours. The reaction solution was directly subjected to reversed phase column chromatography (Biotage® SNAP ULTRA C18, water, acetonitrile 10 – 90 %) to yield the product as a beige solid (292 mg, 40 % purity, 44 % yield).

LC-MS (method A): R_t = 0.99 min; MS (ESIpos): m/z = 407.8 $[M+H]^+$

Intermediate 35

2,5-difluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



To a solution of 2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 8) (1.4 g, 4.74 mmol) in N,N-dimethylformamide (110 ml) was added 1-[bis(dimethylamino)methylene]-1H-[1,2,3]triazolo[4,5-b]pyridin-1-ium 3-oxide hexafluorophosphate (HATU) (10.1 g, 26.6 mmol), and the mixture was stirred at room temperature for 15 minutes. Then, 2-fluoro-6-methylaniline (1.83 g, 14.6 mmol) and N-ethyl-N-isopropylpropan-2-amine (7.0 ml, 40 mmol) were added subsequently, and the reaction mixture was stirred at room temperature for four hours. The reaction solution was directly subjected to reversed phase column chromatography (Biotage® SNAP ULTRA C18, 0.1% aqueous ammonia, acetonitrile 1 – 100 %) to yield the product as a beige solid (1.1 g, 57 %).

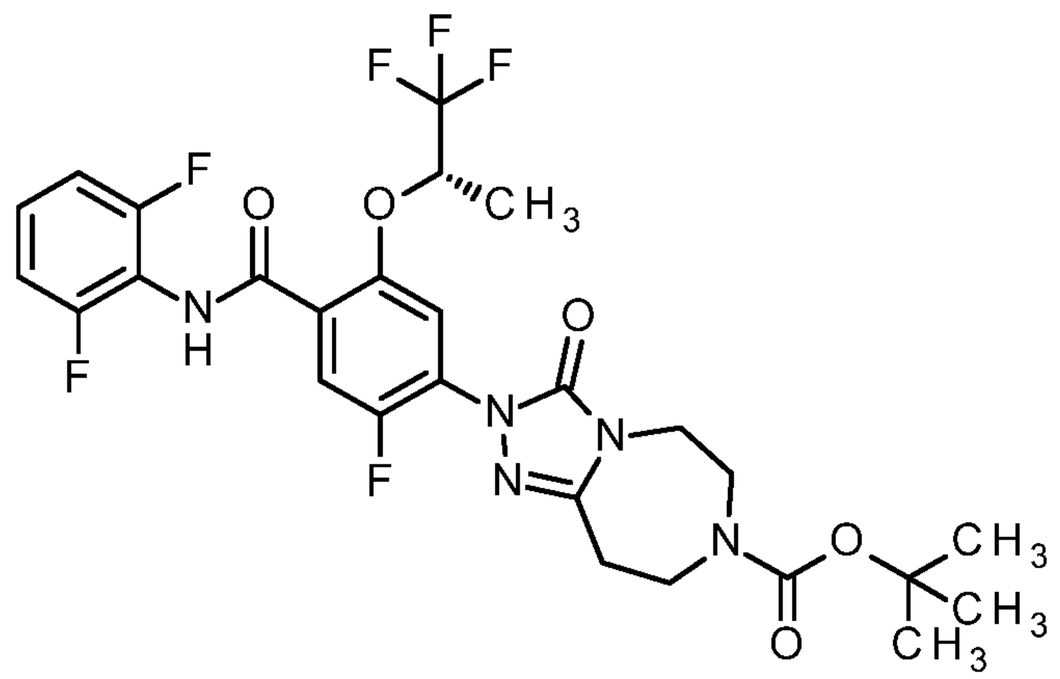
LC-MS (method A): R_t = 1.03 min; MS (ESIneg): m/z = 403.3 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.273 (0.85), 1.290 (0.98), 1.316 (0.46), 1.579 (0.83), 1.907 (0.43), 1.914 (0.55), 1.923 (1.11), 1.930 (1.33), 1.934 (1.51), 1.946 (1.48), 1.950 (1.61), 1.962 (0.70), 1.966 (0.76), 1.986 (0.85), 1.990 (0.77), 2.000 (1.48), 2.005 (1.53), 2.016 (1.58), 2.021 (1.29), 2.030 (0.97), 2.044 (0.43), 2.203 (2.58), 2.336 (16.00), 2.796 (2.27), 2.813 (4.24), 2.829 (2.49), 3.710 (3.20), 3.725 (4.84), 3.740 (2.05), 7.001 (0.69), 7.023 (1.39), 7.046

(0.86), 7.072 (1.29), 7.091 (1.72), 7.190 (0.87), 7.204 (0.96), 7.210 (1.30), 7.224 (1.29), 7.230 (0.65), 7.243 (0.59), 7.625 (1.26), 7.639 (1.27), 7.655 (1.27), 7.670 (1.24), 7.974 (0.80), 8.012 (0.86), 8.020 (1.51), 8.036 (1.31), 8.047 (1.29), 8.064 (1.25).

Intermediate 36

tert-butyl 2-(4-[(2,6-difluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-phenyl)-3-oxo-2,3,5,6,8,9-hexahydro-7H-[1,2,4]triazolo[4,3-d][1,4]diazepine-7-carboxylate



4-bromo-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide (intermediate 30) (100 mg, 226 µmol), tert-butyl 3-oxo-2,3,5,6,8,9-hexahydro-7H-[1,2,4]triazolo[4,3-d][1,4]diazepine-7-carboxylate [CAS 1424939-96-7] (86.3 mg, 339 µmol), tris(dibenzylideneacetone)dipalladium(0) (20.7 mg, 22.6 µmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (39.3 mg, 67.8 µmol), and cesium carbonate (147 mg, 452 µmol) were placed in a microwave vial under argon. Degassed dioxane (2.0 ml) was added, the vial was capped and the mixture was heated to 110 °C for 40 hours. The resulting suspension was filtered over celite, the filter cake was washed with ethyl acetate, and the filtrate was reduced under reduced pressure. The residue was purified by preparative HPLC to yield the title compound as beige crystalline solid (67.2 mg, 90 % purity, 43 %).

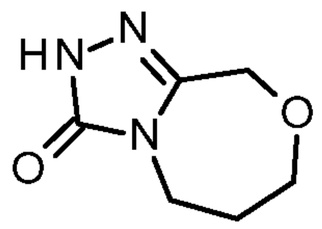
LC-MS (method A): R_t = 1.32 min; MS (ESIpos): m/z = 616.2 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.430 (1.97), 1.449 (16.00), 2.518 (1.77), 2.522 (1.16), 2.907 (0.55), 3.634 (0.66), 3.833 (0.70), 7.190 (0.52), 7.204 (0.70), 7.211 (1.04), 7.231 (0.64), 7.386 (0.40), 7.408 (0.40), 7.554 (0.62), 7.570 (1.11), 7.596 (0.67), 9.996 (1.53).

Intermediates 37–41 were prepared by methods described in the literature (the syntheses of similar triazolone derivatives are for example described in Chemische Berichte (1957), 90, 909-21; Journal of Medicinal Chemistry (1992), 35(1), 189-94; DE 19901846 A1).

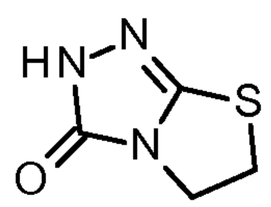
Intermediate 37

2,6,7,9-tetrahydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-3-one



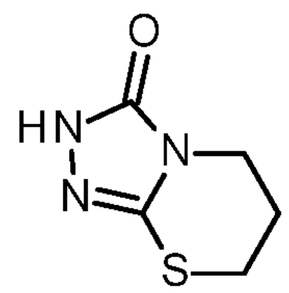
Intermediate 38

5,6-dihydro[1,3]thiazolo[2,3-c][1,2,4]triazol-3(2H)-one



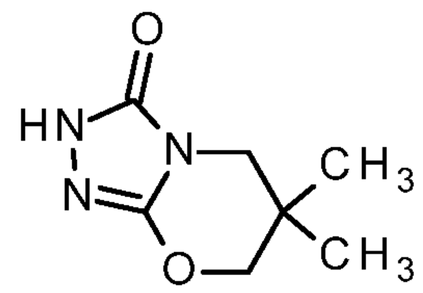
Intermediate 39

6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]thiazin-3(2H)-one



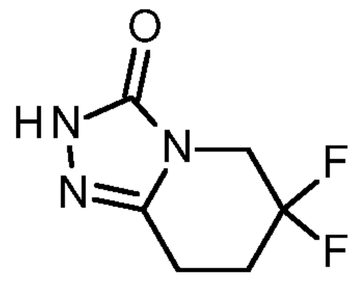
Intermediate 40

6,6-dimethyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-3(2H)-one



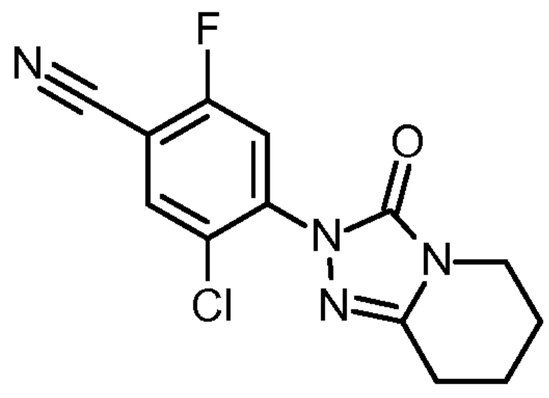
Intermediate 41

6,6-difluoro-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one



Intermediate 42

5-chloro-2-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile



A mixture of 5-chloro-2,4-difluorobenzonitrile [CAS 146780-26-9] (540 mg, 3.11 mmol), 5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one [CAS 118801-67-5] (476 mg, 3.42 mmol), and potassium carbonate (860 mg, 6.22 mmol) in acetonitrile (5.1 ml) was heated in an oil bath at 95 °C bath temperature for 3.5 hours. After cooling to room temperature, the mixture was poured into water, and the resulting mixture was extracted with dichloromethane. The organic fractions were dried over sodium sulfate and concentrated under reduced pressure to yield the crude product as yellow oil (1 g, 38 %-UV), which was used in the next step without purification.

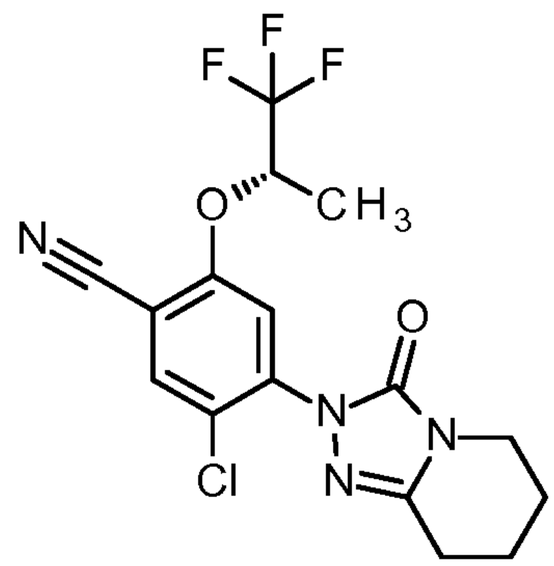
For analytical purpose, the reaction was repeated with 50.0 mg (288 µmol) of 5-chloro-2,4-difluorobenzonitrile, 5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one (44.1 mg, 317 µmol), and potassium carbonate (79.6 mg, 576 µmol) in 0.4 ml acetonitrile under the same conditions. The crude material was purified by preparative HPLC (XBridge Prep C18 5µ OBD; solvents: water (+0.1 % ammonia), acetonitrile; gradient 5 %-95 % acetonitrile in 10 min; flow: 30 ml/min) to afford 5-chloro-2-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile (16 mg, 19 % yield, 100 %-UV).

LC-MS (Method A): R_t = 0.93 min; MS (ESIpos): m/z = 293 $[M+H]^+$

^{1}H-NMR (500 MHz, DMSO-d6) δ [ppm]: -0.006 (0.53), 0.000 (13.44), 0.007 (0.47), 1.242 (0.55), 1.780 (1.49), 1.786 (1.73), 1.793 (4.36), 1.799 (4.35), 1.803 (5.95), 1.812 (4.83), 1.815 (6.38), 1.824 (2.21), 1.827 (2.42), 1.873 (2.41), 1.878 (2.20), 1.885 (5.83), 1.889 (5.08), 1.897 (6.55), 1.902 (4.54), 1.908 (4.03), 1.920 (1.58), 2.077 (1.08), 2.519 (1.18), 2.523 (0.96), 2.527 (0.73), 2.687 (8.10), 2.700 (15.19), 2.713 (7.92), 3.216 (0.91), 3.557 (8.68), 3.569 (16.00), 3.581 (7.93), 7.765 (10.96), 7.784 (11.13), 8.374 (10.26), 8.387 (10.04).

Intermediate 43

5-chloro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile

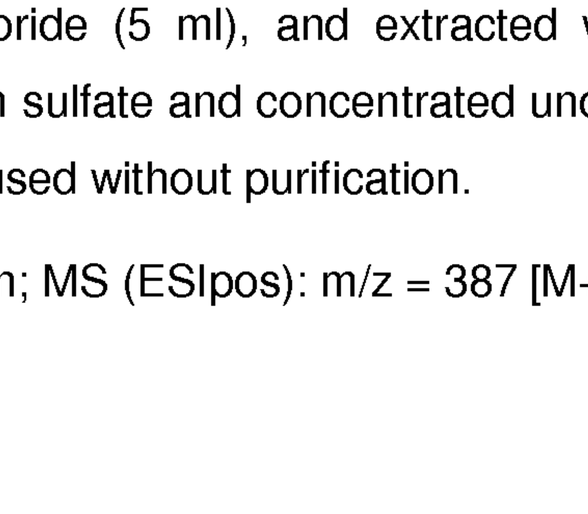


To a solution of (2S)-1,1,1-trifluoropropan-2-ol (468 mg, 4.10 mmol) in tetrahydrofuran (5 ml) was added in portions sodium hydride (164 mg, 60 % in mineral oil, 4.10 mmol) at 0 °C. After stirring for 30 min, a solution of 5-chloro-2-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzonitrile (intermediate 42, crude product from previous step, 1.00 g, 38 %-UV) and the mixture was stirred for 1.5 h at 0 °C. The mixture was then poured into saturated aqueous sodium chloride (5 ml), and extracted with ethyl acetate. The organic fractions were dried over sodium sulfate and concentrated under reduced pressure. The crude product (1.16 g, 50 %-UV) was used without purification.

LC-MS (Method A): R_t = 1.12 min; MS (ESIpos): m/z = 387 $[M+H]^+$

Intermediate 44

5-chloro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid

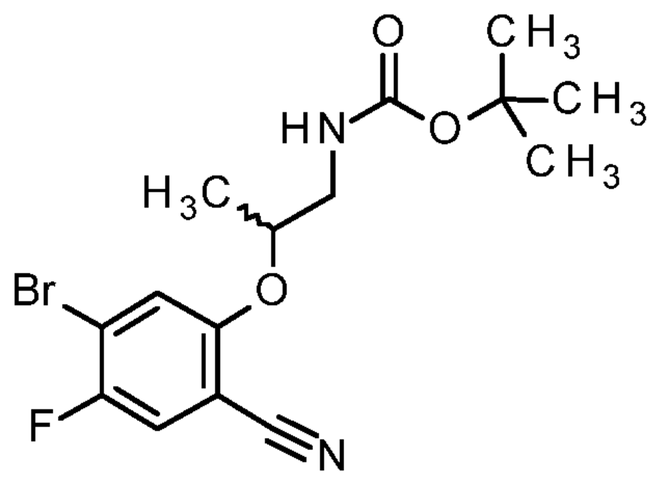


To a solution of 5-chloro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzonitrile (intermediate 43, crude product from previous step, 1.16 g, 50 %-UV) in ethanol (90 ml) was added aqueous sodium hydroxide (62 ml, 1.0 M, 62 mmol) and the mixture was stirred at 80 °C for 2 d. After cooling to room temperature, the reaction mixture was extracted twice with ethyl acetate. The organic phase was discarded, and the aqueous phase was then adjusted to an acidic pH using 1 N aqueous hydrochloric acid and extracted with ethyl acetate. The organic phases were dried over sodium sulfate and concentrated under reduced pressure to yield the crude product (0.73 g, 80 %-UV), which was used without further purification.

LC-MS (Method A): R_t = 0.93 min; MS (ESIneg): m/z = 404 $[M-H]^-$

Intermediate 45

rac-tert-butyl N-[2-(5-bromo-2-cyano-4-fluoro-phenoxy)propyl]carbamate



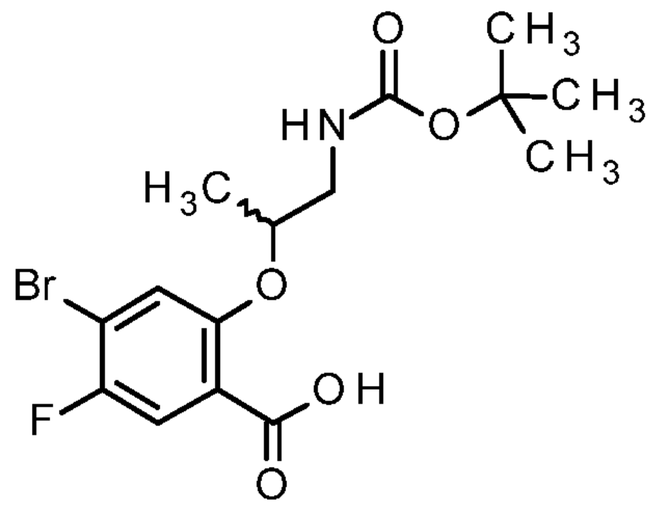
To a suspension of sodium hydride (4.04 g, 100 mmol, 60 % purity) in THF (25 mL) was added tert-butyl N-(2-hydroxypropyl)carbamate (8.84 g, 50.5 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 0.5 h, then a solution of 4-bro mo-2,5-difluorobenzonitrile (10 g, 45.9 mmol) in THF (25 mL) was added. The mixture was stirred at 0 °C for 0.5 h. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to give a residue, which was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 50/1 to 10/1) to give the desired product (13 g, 34.8 mmol, 76% yield) as a white solid.

MS ($M+H^+$): 397.1

^1H NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.33-7.30 (t, *J* = 6Hz, 1H), 7.27-7.24 (t, *J* = 6Hz, 1H), 4.99 (s, 1H), 4.57 (s, 1H), 3.53-3.48 (m, 1H), 3.33-3.28 (m, 1H), 1.62-1.45 (q, 9H), 1.36-1.26 (m, 3H).

Intermediate 46

rac-4-bromo-2-[2-(tert-butoxycarbonylamino)-1-methyl-ethoxy]-5-fluoro-benzoic acid



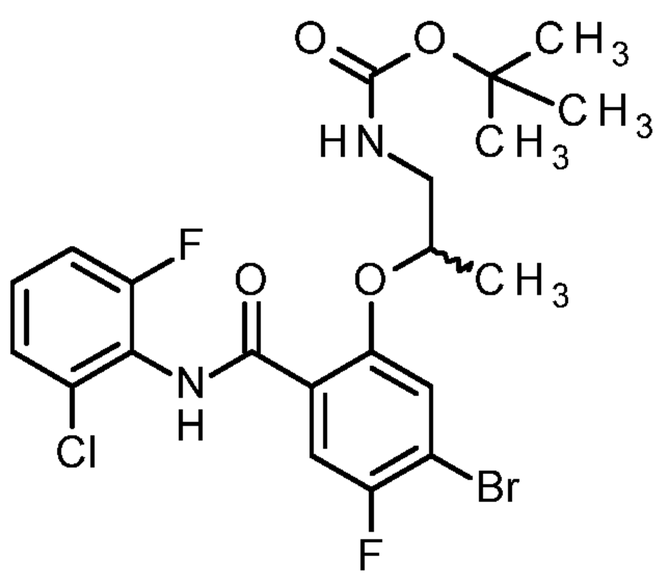
To a solution of tert-butyl N-[2-(5-bromo-2-cyano-4-fluoro-phenoxy)propyl]carbamate (13 g, 34.8 mmol) in ethanol (60 mL) was added sodium hydroxide (5 M in water, 69.7 mL) at 25 ℃, the resulting mixture was stirred at 90 ℃ for 12 h rs. The reaction mixture was evaporated under vacuum, the residue was diluted with water (60 mL), acidified to pH=4~5 with aq. hydrochloric acid (1 N), extracted with ethyl acetate three times. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the desired product (11 g, crude) as a yellow oil, which was used in next step without further purification.

MS ($M+H^+$): 336.2

^1H NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.84-7.82 (d, *J* = 8Hz, 1H), 7.31-7.29 (d, *J* = 8Hz, 1H), 5.16 (s, 1H), 4.70 (s, 1H), 3.53-3.50 (m, 1H), 3.40-3.34 (m, 1H), 1.44-1.39 (t, *J* = 10Hz, 9H), 1.32-1.25 (m,3H).

Intermediate 47

rac-tert-butyl (2-{5-bromo-2-[(2-chloro-6-fluorophenyl)carbamoyl]-4-fluorophenoxy}propyl) carbamate



Crude intermediate 46 (10 g, 25.5 mmol) and 2-chloro-6-fluoroaniline (3.71 g, 25.5 mmol) were suspended in pyridine (50 mL) was added phosphoryl chloride (15.6 g, 102 mmol, 9.5 mL) in one portion at 0 ℃ under nitrogen. The resulting m ixture was stirred at 25 ℃ for 10 min. The reaction mixture was quenched by addition of water (300 mL) and extracted with ethyl acetate (300 mLx2). The combined organic layers were washed with brine (150 mL x 2), dried over

sodium sulfate, filtered and concentrated under reduced pressure. Column chromatography (silica gel, petroleum ether/ethyl acetate = 50/1 to 5/1) afforded the desire product (8.22 g, 15.2 mmol, 59% yield, 96% purity).

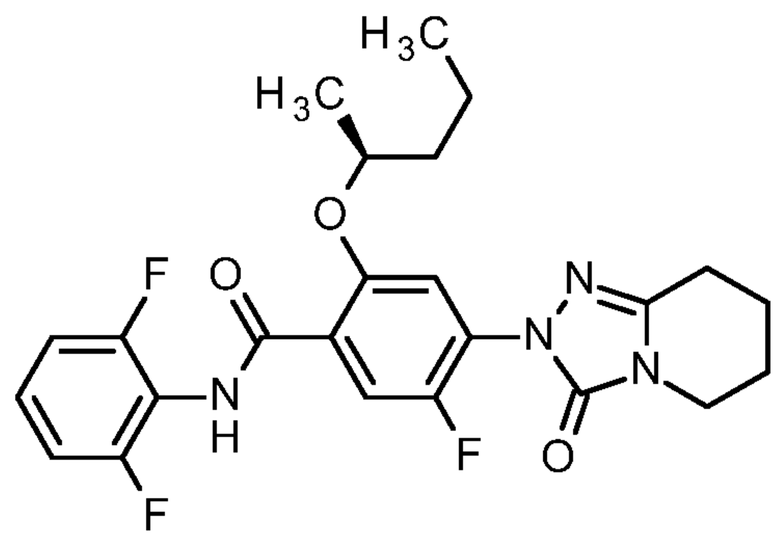
MS ($M+H^+$): 421.1

^1H NMR (400 MHz, $CDCl_3$) δ [ppm]: 9.46 (s, 1H), 8.06-8.03 (d, *J* = 12Hz, 1H), 7.31-7.28 (q, 2H), 7.26 (s, 1H), 7.25-7.13 (t, *J* = 24Hz, 1H), 4.92 (s, 1H), 4.78-4.73 (q, 1H), 3.50-3.47 (m, 2H), 1.58-1.42 (q, 3H), 1.38 (s, 9H).

EXPERIMENTAL SECTION – EXAMPLES

Example 1

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



To a 0 ℃ stirred solution of 5-fluoro-4-(3-oxo-5,6 ,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (intermediate 16) (100 mg, 275 µmol) and catalytic N,N-dimethylformamide in anhydrous dichloromethane (1.5 ml) was added oxalyl chloride (28 µl, 330 µmol). The resulting mixture was warmed to room temperature, stirred for 90 minutes and concentrated under reduced pressure. A solution of the residue in anhydrous dichloromethane (1.0 ml) was added dropwise to a 0 ℃ stirred solution of 2,6-difluoroaniline (39 mg, 303 µmol) and triethylamine (42 µl, 300 µmol) in anhydrous DCM (2.0 ml). Following complete addition, the mixture was warmed to room temperature and stirred for 1 hour. Aqueous 1.0 M hydrochloric acid was added to the mixture and extracted with dichloromethane. The combined organic extracts were washed with brine, dried (magnesium sulfate) and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/ethyl acetate) to give the desired product (111 mg, 85 %).

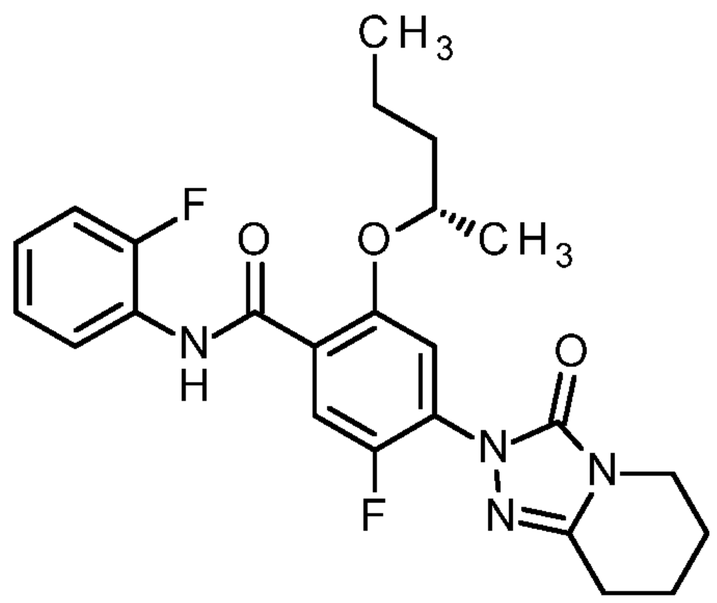
MS (ESIpos): m/z = 475 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 0.95 (t, 3H), 1.43 (d, 3H), 1.45 – 1.56 (m, 2H), 1.61 – 1.78 (m, 1H), 1.78 – 2.06 (m, 5H), 2.81 (t, 2H), 3.72 (t, 2H), 4.59 – 4.71 (m, 1H), 6.95 – 7.04 (m, 2H), 7.16 – 7.27 (m, 1H), 7.41 (d, 1H), 8.14 (d, 1H), 9.68 (s, 1H).

Examples 2–23 were prepared as described for example 1 from 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (intermediate 16) and the respective amines, as indicated. Products were purified by flash column chromatography or, if explicitely mentioned, by preparative HPLC.

Example 2

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



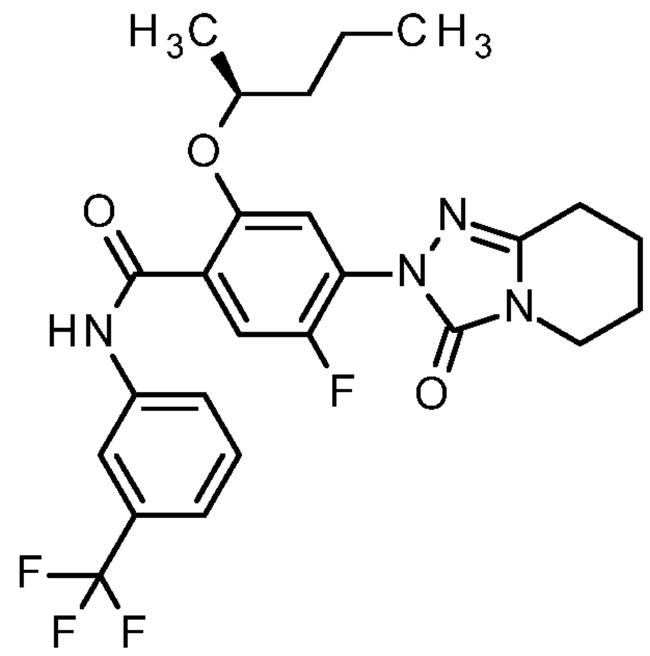
From intermediate 16 and 2-fluoroaniline.

LC-MS (method A): R_t = 1.46 min; MS (ESIpos): m/z = 457 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.875 (6.76), 0.894 (16.00), 0.912 (7.62), 1.346 (11.35), 1.361 (11.28), 1.389 (1.11), 1.397 (1.00), 1.408 (1.06), 1.427 (0.96), 1.446 (0.91), 1.452 (0.92), 1.470 (0.90), 1.670 (1.13), 1.695 (0.88), 1.790 (2.28), 1.798 (2.94), 1.803 (3.29), 1.814 (3.07), 1.818 (3.31), 1.829 (1.73), 1.833 (1.63), 1.866 (1.21), 1.871 (1.23), 1.881 (2.35), 1.885 (2.56), 1.897 (2.70), 1.902 (2.20), 1.911 (1.61), 2.518 (1.69), 2.523 (1.18), 2.692 (3.05), 2.708 (6.06), 2.725 (3.28), 3.559 (3.63), 3.575 (6.53), 3.590 (2.88), 4.725 (0.82), 4.740 (1.56), 4.755 (1.53), 7.173 (1.45), 7.178 (1.33), 7.186 (1.38), 7.192 (1.85), 7.197 (1.30), 7.205 (1.32), 7.210 (1.26), 7.221 (1.64), 7.225 (1.93), 7.241 (2.22), 7.245 (2.44), 7.260 (0.98), 7.264 (0.94), 7.333 (1.53), 7.337 (1.50), 7.353 (1.33), 7.357 (1.44), 7.362 (1.62), 7.366 (1.53), 7.382 (1.18), 7.386 (1.16), 7.486 (3.45), 7.501 (3.41), 7.883 (4.33), 7.911 (4.28), 8.358 (1.21), 8.362 (1.26), 8.378 (2.31), 8.382 (2.25), 8.398 (1.19), 8.402 (1.12), 10.342 (3.06), 10.348 (2.99).

Example 3

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[3-(trifluoromethyl)phenyl]benzamide



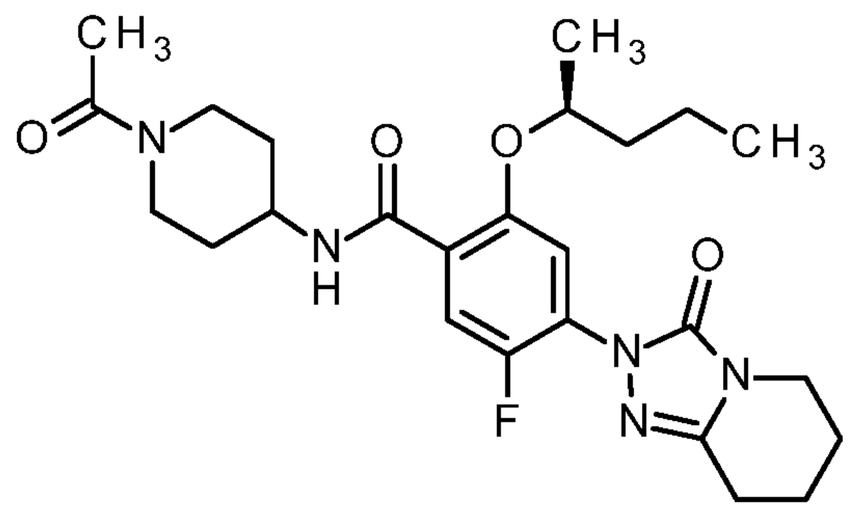
From intermediate 16 and 3-(trifluoromethyl)aniline.

MS (ESIpos): m/z = 507 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.00 (t, 3H), 1.47 (d, 3H), 1.49 – 1.57 (m, 2H), 1.64 – 2.05 (m, 6H), 2.81 (t, 2H), 3.72 (t, 2H), 4.60 – 4.73 (m, 1H), 7.35 – 7.42 (m, 2H), 7.49 (t, 1H), 7.86 (d, 1H), 7.93 (s, 1H), 8.15 (d, 1H), 10.4 (s, 1H).

Example 4

N-(1-acetylpiperidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 1-(4-aminopiperidin-1-yl)ethanone.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

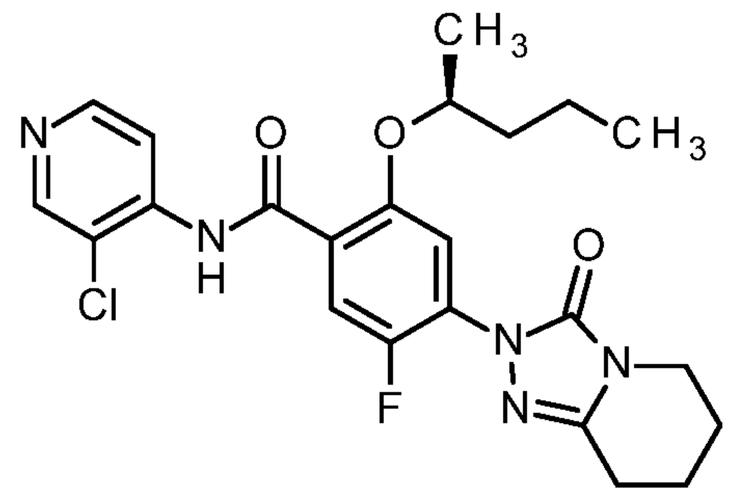
LC-MS (method A): R_t = 0.99 min; MS (ESIpos): m/z = 488 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.935 (1.11), 0.946 (1.23), 0.953 (2.59), 0.964 (2.55), 0.972 (1.38), 0.982 (1.24), 1.361 (2.55), 1.375 (4.76), 1.390 (3.06), 1.404 (0.96), 1.423 (0.84), 1.432 (0.82), 1.448 (0.64), 1.461 (0.52), 1.626 (0.45), 1.646 (0.60), 1.652 (0.68), 1.660

(0.70), 1.676 (0.56), 1.684 (0.44), 1.908 (0.72), 1.916 (0.86), 1.920 (0.96), 1.932 (0.99), 1.936 (1.05), 1.948 (0.47), 1.952 (0.50), 1.972 (0.55), 1.988 (0.95), 1.993 (1.00), 2.003 (1.08), 2.009 (0.94), 2.016 (0.88), 2.031 (0.54), 2.133 (16.00), 2.783 (1.51), 2.800 (2.90), 2.815 (1.68), 2.874 (0.54), 3.253 (0.64), 3.259 (0.42), 3.694 (1.93), 3.709 (3.09), 3.724 (1.36), 3.791 (0.45), 4.516 (0.43), 4.541 (0.72), 4.556 (1.22), 4.572 (0.94), 4.587 (0.47), 7.292 (1.89), 7.307 (1.87), 8.044 (1.37), 8.073 (1.35), 8.163 (0.53), 8.177 (0.52).

Example 5

N-(3-chloropyridin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 3-chloropyridin-4-amine.

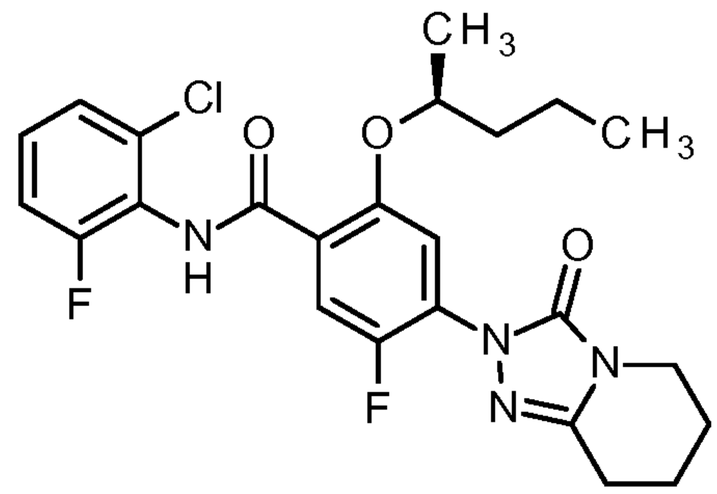
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method A): R_t = 1.28 min; MS (ESIpos): m/z = 474 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.929 (6.69), 0.947 (16.00), 0.965 (7.53), 1.259 (0.42), 1.282 (2.30), 1.391 (0.52), 1.409 (0.86), 1.416 (0.65), 1.424 (0.75), 1.427 (0.77), 1.435 (1.09), 1.442 (0.78), 1.452 (1.27), 1.462 (15.62), 1.471 (1.85), 1.477 (15.87), 1.489 (1.00), 1.496 (0.90), 1.501 (0.72), 1.509 (0.50), 1.515 (0.87), 1.529 (0.41), 1.534 (0.49), 1.665 (0.61), 1.679 (1.13), 1.689 (0.57), 1.694 (0.66), 1.699 (0.88), 1.704 (0.95), 1.714 (1.39), 1.719 (0.58), 1.724 (0.79), 1.728 (0.73), 1.739 (1.16), 1.753 (0.57), 1.914 (1.01), 1.926 (1.90), 1.931 (2.19), 1.939 (2.40), 1.944 (1.98), 1.948 (2.56), 1.952 (2.80), 1.956 (2.11), 1.961 (1.37), 1.965 (1.56), 1.969 (1.62), 1.979 (0.80), 1.990 (1.48), 2.004 (2.30), 2.009 (1.99), 2.019 (2.08), 2.024 (1.70), 2.034 (1.28), 2.047 (0.58), 2.803 (3.02), 2.819 (5.65), 2.836 (3.35), 3.713 (3.80), 3.729 (6.23), 3.744 (2.68), 4.655 (0.91), 4.671 (1.72), 4.687 (1.72), 4.703 (0.89), 7.467 (3.74), 7.481 (3.72), 8.101 (5.26), 8.130 (5.22), 8.463 (1.02), 8.476 (1.14), 8.589 (1.77), 8.626 (1.79), 8.640 (1.55), 10.429 (2.68).

Example 6

N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 2-chloro-6-fluoroaniline.

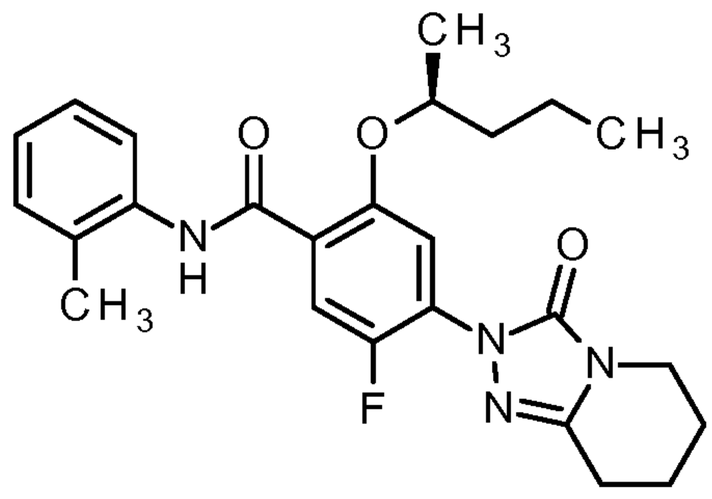
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method A): R_t = 1.35 min; MS (ESIpos): m/z = 491 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.937 (6.73), 0.955 (16.00), 0.974 (7.56), 1.414 (0.59), 1.432 (1.21), 1.444 (15.10), 1.459 (15.32), 1.473 (0.81), 1.476 (0.89), 1.486 (0.68), 1.491 (0.81), 1.500 (0.77), 1.505 (0.72), 1.511 (0.80), 1.518 (0.84), 1.525 (0.90), 1.530 (0.75), 1.538 (0.54), 1.544 (0.93), 1.558 (0.50), 1.563 (0.58), 1.577 (0.46), 1.629 (1.09), 1.670 (0.75), 1.685 (1.13), 1.696 (0.58), 1.700 (0.71), 1.705 (0.93), 1.710 (0.91), 1.719 (1.45), 1.724 (0.61), 1.730 (0.84), 1.734 (0.80), 1.744 (1.16), 1.759 (0.54), 1.846 (0.69), 1.860 (0.87), 1.872 (0.75), 1.876 (0.88), 1.881 (0.68), 1.888 (0.87), 1.897 (0.77), 1.902 (1.02), 1.907 (1.03), 1.911 (1.08), 1.920 (2.00), 1.933 (2.11), 1.945 (2.04), 1.948 (2.17), 1.960 (0.98), 1.964 (1.01), 1.985 (1.07), 2.000 (1.96), 2.004 (2.05), 2.015 (2.16), 2.020 (1.77), 2.029 (1.29), 2.043 (0.53), 2.801 (3.05), 2.818 (5.83), 2.834 (3.34), 3.711 (3.77), 3.727 (6.13), 3.741 (2.72), 4.663 (1.01), 4.679 (1.98), 4.694 (1.95), 4.709 (0.96), 7.107 (1.11), 7.110 (1.15), 7.128 (1.92), 7.131 (2.59), 7.151 (1.69), 7.155 (1.72), 7.195 (1.24), 7.209 (1.23), 7.215 (2.50), 7.229 (2.53), 7.236 (1.58), 7.249 (1.61), 7.280 (2.67), 7.294 (1.25), 7.297 (1.90), 7.300 (1.30), 7.418 (3.77), 7.433 (3.71), 8.152 (5.03), 8.181 (4.88), 9.727 (3.12).

Example 7

5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and o-toluidine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.36 min; MS (ESIpos): m/z = 453 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.929 (5.14), 0.947 (12.73), 0.965 (5.84), 1.419 (0.88), 1.426 (11.38), 1.442 (11.90), 1.452 (0.70), 1.459 (0.98), 1.473 (0.65), 1.478 (0.95), 1.484 (0.58), 1.492 (0.65), 1.497 (0.73), 1.503 (0.55), 1.516 (0.67), 1.582 (1.77), 1.640 (0.44), 1.655 (0.80), 1.670 (0.49), 1.674 (0.66), 1.679 (0.66), 1.689 (1.08), 1.695 (0.41), 1.699 (0.59), 1.704 (0.55), 1.714 (0.85), 1.728 (0.42), 1.819 (0.51), 1.833 (0.61), 1.836 (0.59), 1.845 (0.52), 1.849 (0.63), 1.853 (0.48), 1.858 (0.58), 1.861 (0.59), 1.867 (0.51), 1.874 (0.51), 1.879 (0.40), 1.895 (0.41), 1.908 (0.51), 1.913 (0.50), 1.922 (1.05), 1.929 (1.24), 1.934 (1.40), 1.945 (1.46), 1.949 (1.57), 1.961 (0.69), 1.965 (0.72), 1.986 (0.74), 1.992 (0.66), 2.001 (1.37), 2.006 (1.44), 2.016 (1.52), 2.021 (1.25), 2.031 (0.93), 2.044 (0.41), 2.355 (16.00), 2.801 (2.27), 2.817 (4.37), 2.833 (2.54), 3.712 (2.98), 3.727 (4.80), 3.743 (2.08), 4.637 (0.73), 4.652 (1.45), 4.668 (1.46), 4.683 (0.71), 7.098 (0.76), 7.102 (0.78), 7.117 (1.86), 7.120 (1.91), 7.135 (1.30), 7.138 (1.28), 7.232 (1.83), 7.252 (2.22), 7.290 (0.74), 7.404 (2.81), 7.419 (2.84), 8.010 (1.88), 8.028 (1.72), 8.030 (1.70), 8.167 (3.90), 8.196 (3.88), 9.656 (1.79).

Example 8

5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide

From intermediate 16 and 4-fluoro-2-methylaniline.

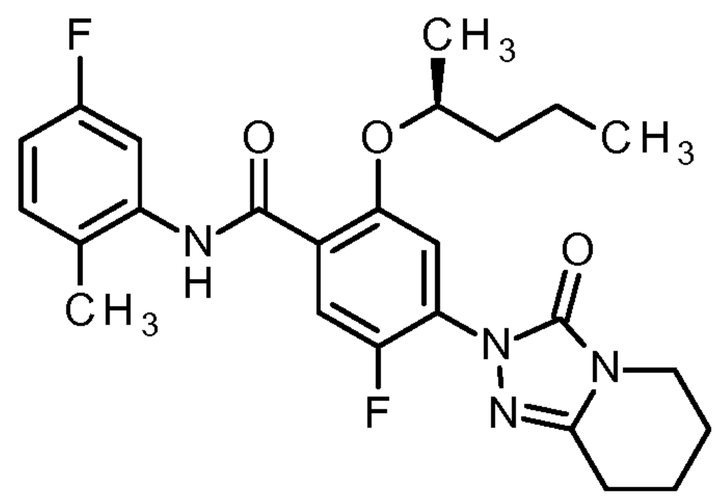
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.36 min; MS (ESIpos): m/z = 471 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.931 (4.92), 0.950 (12.09), 0.968 (5.64), 1.419 (0.81), 1.427 (11.60), 1.442 (11.68), 1.452 (0.73), 1.459 (0.90), 1.463 (0.75), 1.472 (0.67), 1.477 (0.95), 1.483 (0.60), 1.490 (0.62), 1.496 (0.78), 1.501 (0.52), 1.515 (0.65), 1.577 (5.23), 1.643 (0.40), 1.658 (0.73), 1.673 (0.45), 1.677 (0.64), 1.682 (0.62), 1.692 (1.04), 1.702 (0.57), 1.707 (0.53), 1.717 (0.83), 1.806 (0.49), 1.820 (0.62), 1.822 (0.61), 1.832 (0.50), 1.836 (0.61), 1.841 (0.47), 1.848 (0.59), 1.856 (0.50), 1.862 (0.51), 1.914 (0.44), 1.922 (1.01), 1.929 (1.20), 1.934 (1.36), 1.946 (1.39), 1.950 (1.52), 1.962 (0.66), 1.965 (0.71), 1.986 (0.71), 1.991 (0.64), 2.002 (1.34), 2.006 (1.40), 2.017 (1.50), 2.022 (1.23), 2.031 (0.91), 2.332 (16.00), 2.801 (2.22), 2.817 (4.18), 2.833 (2.46), 3.712 (2.81), 3.727 (4.58), 3.742 (2.00), 4.639 (0.72), 4.655 (1.44), 4.670 (1.44), 4.686 (0.70), 6.939 (2.37), 6.944 (1.08), 6.946 (1.12), 6.962 (1.97), 6.969 (1.21), 6.975 (1.03), 7.405 (2.76), 7.419 (2.77), 7.856 (1.10), 7.870 (1.32), 7.881 (1.32), 7.894 (1.10), 8.150 (3.76), 8.179 (3.68), 9.591 (1.88).

Example 9

5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 5-fluoro-2-methylaniline.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

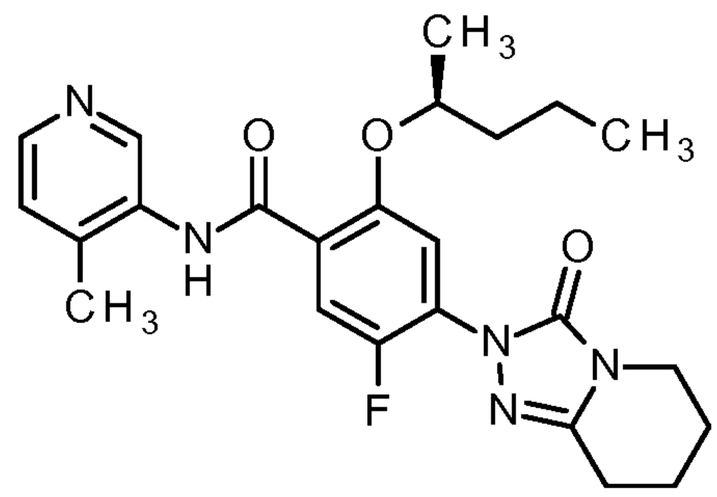
LC-MS (method A): R_t = 1.40 min; MS (ESIneg): m/z = 469 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.929 (6.51), 0.948 (16.00), 0.966 (7.35), 1.397 (0.48), 1.415 (0.87), 1.430 (14.73), 1.445 (14.06), 1.454 (1.16), 1.458 (1.00), 1.467 (0.87), 1.473 (1.17), 1.478 (0.79), 1.486 (0.79), 1.492 (0.99), 1.497 (0.66), 1.505 (0.45), 1.511

(0.83), 1.530 (0.47), 1.586 (8.72), 1.639 (0.55), 1.655 (0.99), 1.664 (0.46), 1.670 (0.59), 1.674 (0.83), 1.679 (0.78), 1.689 (1.31), 1.694 (0.50), 1.698 (0.70), 1.703 (0.66), 1.714 (1.07), 1.728 (0.49), 1.820 (0.60), 1.834 (0.76), 1.836 (0.73), 1.846 (0.64), 1.850 (0.74), 1.854 (0.59), 1.862 (0.71), 1.870 (0.61), 1.875 (0.63), 1.879 (0.50), 1.884 (0.50), 1.896 (0.51), 1.910 (0.64), 1.914 (0.62), 1.922 (1.30), 1.929 (1.54), 1.934 (1.72), 1.946 (1.77), 1.950 (1.91), 1.962 (0.83), 1.965 (0.88), 1.986 (0.91), 1.993 (0.83), 2.002 (1.69), 2.006 (1.78), 2.017 (1.90), 2.022 (1.54), 2.031 (1.13), 2.045 (0.48), 2.316 (15.27), 2.801 (2.86), 2.817 (5.28), 2.833 (3.11), 3.712 (3.54), 3.727 (5.83), 3.742 (2.50), 4.640 (0.90), 4.656 (1.79), 4.671 (1.80), 4.687 (0.87), 6.779 (1.00), 6.786 (1.08), 6.799 (1.92), 6.806 (2.07), 6.820 (1.12), 6.826 (1.17), 7.134 (1.45), 7.152 (1.58), 7.155 (1.47), 7.171 (1.27), 7.422 (3.43), 7.437 (3.47), 7.996 (1.87), 8.003 (1.86), 8.024 (1.89), 8.031 (1.84), 8.149 (4.55), 8.178 (4.52), 9.690 (2.14).

Example 10

5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 4-methylpyridin-3-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

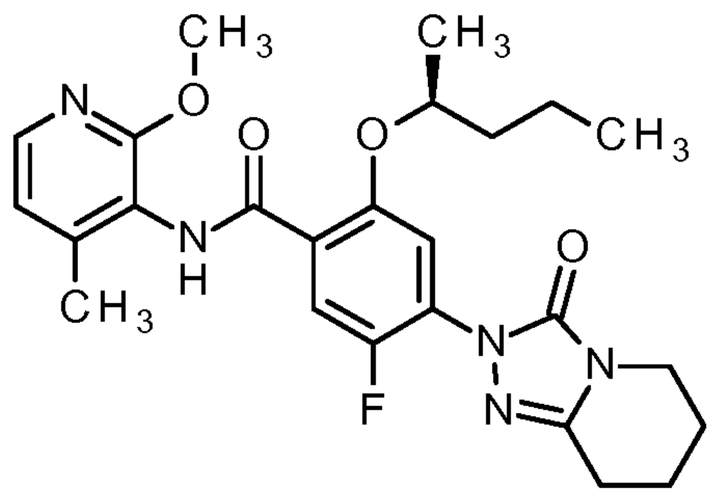
LC-MS (method A): R_t = 0.92 min; MS (ESIpos): m/z = 454 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.940 (4.74), 0.958 (11.64), 0.977 (5.45), 1.261 (0.41), 1.430 (0.69), 1.444 (10.59), 1.459 (10.71), 1.470 (1.00), 1.484 (0.68), 1.489 (0.97), 1.494 (0.62), 1.503 (0.67), 1.508 (0.80), 1.513 (0.58), 1.522 (0.42), 1.527 (0.72), 1.546 (0.48), 1.560 (0.43), 1.605 (1.27), 1.660 (0.55), 1.675 (0.79), 1.684 (0.42), 1.689 (0.50), 1.694 (0.69), 1.699 (0.64), 1.709 (1.05), 1.714 (0.43), 1.719 (0.58), 1.723 (0.55), 1.734 (0.85), 1.813 (0.48), 1.827 (0.63), 1.839 (0.50), 1.843 (0.61), 1.847 (0.45), 1.854 (0.59), 1.862 (0.50), 1.868 (0.49), 1.917 (0.49), 1.925 (1.05), 1.933 (1.22), 1.937 (1.39), 1.948 (1.39), 1.952 (1.50), 1.964 (0.69), 1.969 (0.73), 1.990 (0.75), 1.996 (0.69), 2.005 (1.36), 2.009 (1.42), 2.020 (1.50), 2.025 (1.23), 2.034 (0.91), 2.048 (0.40), 2.352 (16.00), 2.805 (2.18), 2.820 (4.09), 2.837 (2.36), 3.714

(2.77), 3.729 (4.41), 3.744 (1.94), 4.659 (0.69), 4.674 (1.38), 4.690 (1.36), 4.705 (0.68), 7.185 (2.04), 7.197 (2.07), 7.437 (2.63), 7.451 (2.61), 8.158 (3.51), 8.187 (3.38), 8.350 (2.62), 8.362 (2.53), 9.056 (4.07), 9.699 (1.94).

Example 11

5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 2-methoxy-4-methylpyridin-3-amine.

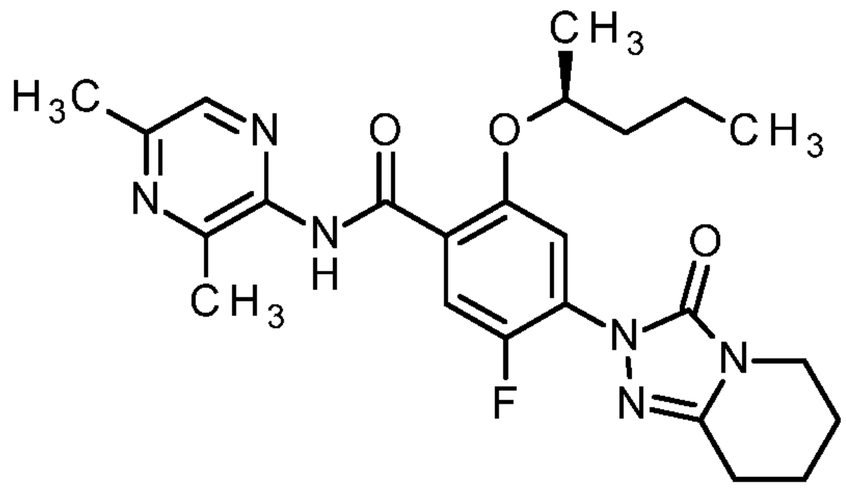
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 484 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.946 (2.63), 0.964 (6.58), 0.983 (2.99), 1.438 (5.62), 1.453 (5.79), 1.477 (0.40), 1.495 (0.44), 1.601 (1.14), 1.720 (0.54), 1.745 (0.43), 1.916 (0.46), 1.920 (0.54), 1.930 (0.75), 1.944 (0.72), 1.948 (0.78), 1.999 (0.67), 2.004 (0.72), 2.015 (0.75), 2.020 (0.62), 2.029 (0.46), 2.284 (9.26), 2.800 (1.13), 2.816 (2.12), 2.832 (1.25), 3.711 (1.45), 3.726 (2.32), 3.741 (1.02), 3.970 (16.00), 4.664 (0.73), 4.679 (0.72), 6.829 (1.38), 6.842 (1.43), 7.391 (1.43), 7.405 (1.44), 7.938 (1.92), 7.951 (1.85), 8.116 (1.95), 8.146 (1.95), 9.681 (1.15).

Example 12

N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 3,5-dimethylpyrazin-2-amine.

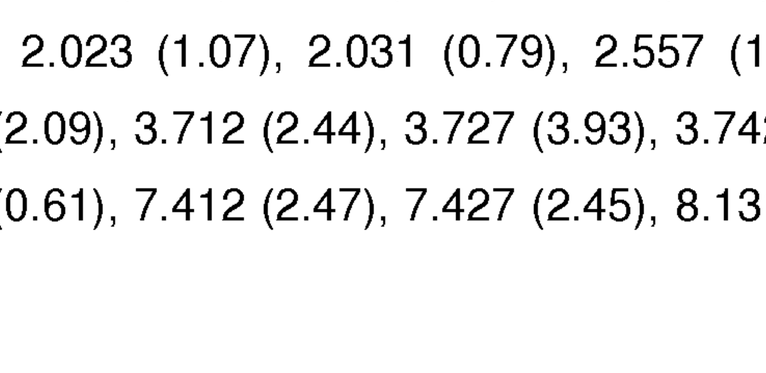
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.15 min; MS (ESIpos): m/z = 469 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.939 (4.46), 0.957 (10.95), 0.976 (5.06), 1.454 (9.68), 1.470 (10.05), 1.483 (0.51), 1.493 (0.84), 1.508 (0.70), 1.511 (0.66), 1.517 (0.51), 1.525 (0.64), 1.531 (0.64), 1.535 (0.53), 1.544 (0.44), 1.549 (0.74), 1.554 (0.44), 1.582 (2.57), 1.696 (0.64), 1.712 (0.40), 1.716 (0.57), 1.721 (0.54), 1.731 (0.90), 1.741 (0.52), 1.746 (0.48), 1.756 (0.76), 1.842 (0.45), 1.856 (0.56), 1.867 (0.46), 1.872 (0.54), 1.876 (0.41), 1.883 (0.52), 1.892 (0.44), 1.897 (0.47), 1.902 (0.43), 1.906 (0.62), 1.918 (0.80), 1.922 (0.95), 1.932 (1.30), 1.946 (1.26), 1.950 (1.33), 1.962 (0.60), 1.965 (0.62), 1.987 (0.65), 1.993 (0.60), 2.002 (1.20), 2.007 (1.25), 2.017 (1.33), 2.023 (1.07), 2.031 (0.79), 2.557 (14.74), 2.562 (16.00), 2.801 (1.88), 2.817 (3.63), 2.833 (2.09), 3.712 (2.44), 3.727 (3.93), 3.742 (1.71), 4.639 (0.63), 4.655 (1.26), 4.670 (1.24), 4.686 (0.61), 7.412 (2.47), 7.427 (2.45), 8.131 (3.31), 8.161 (3.30), 8.174 (3.72), 10.076 (1.90).

Example 13

5-fluoro-N-(5-methylpyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 5-methylpyrimidin-4-amine.

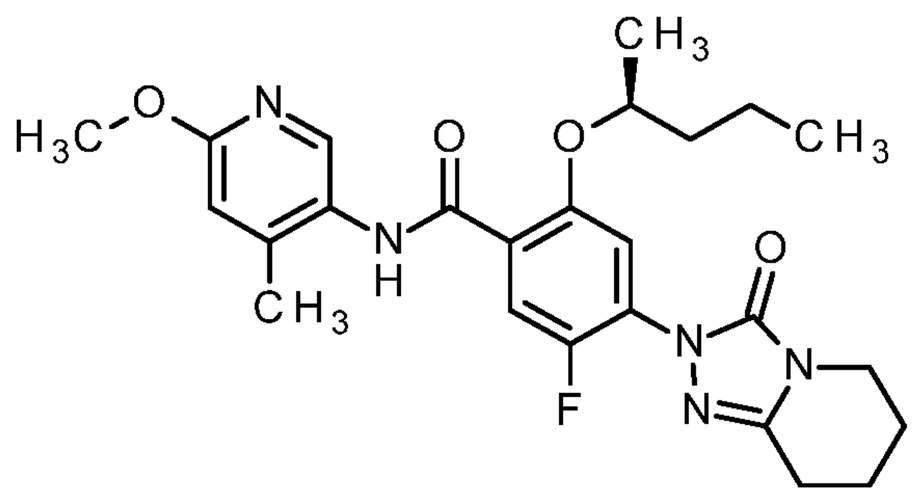
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method A): R_t = 1.07 min; MS (ESIpos): m/z = 455 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.950 (4.72), 0.968 (11.18), 0.986 (5.34), 1.464 (11.05), 1.480 (11.04), 1.490 (0.63), 1.498 (0.95), 1.513 (0.68), 1.516 (0.91), 1.523 (0.59), 1.531 (0.68), 1.537 (0.72), 1.542 (0.59), 1.550 (0.45), 1.556 (0.76), 1.570 (0.56), 1.575 (0.75), 1.594 (1.86), 1.694 (0.41), 1.708 (0.72), 1.723 (0.46), 1.728 (0.62), 1.733 (0.61), 1.743 (0.99), 1.747 (0.40), 1.753 (0.58), 1.758 (0.54), 1.768 (0.82), 1.866 (0.48), 1.880 (0.63), 1.891 (0.53), 1.896 (0.64), 1.900 (0.54), 1.908 (0.95), 1.915 (0.98), 1.922 (1.43), 1.931 (1.65), 1.936 (1.55), 1.947 (1.51), 1.951 (1.59), 1.955 (1.24), 1.963 (0.70), 1.967 (0.74), 1.988 (0.78), 2.003 (1.43), 2.008 (1.47), 2.018 (1.56), 2.023 (1.25), 2.032 (0.93), 2.047 (0.40), 2.318 (16.00), 2.802 (2.17), 2.818 (4.14), 2.834 (2.35), 2.877 (0.64), 3.101 (0.58), 3.712 (2.81), 3.727 (4.44), 3.742 (1.95), 4.648 (0.71), 4.663 (1.42), 4.679 (1.41), 4.694 (0.70), 7.437 (2.73), 7.452 (2.73), 8.114 (3.58), 8.143 (3.55), 8.560 (3.85), 8.929 (4.40), 10.249 (2.13).

Example 14

5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 6-methoxy-4-methylpyridin-3-amine.

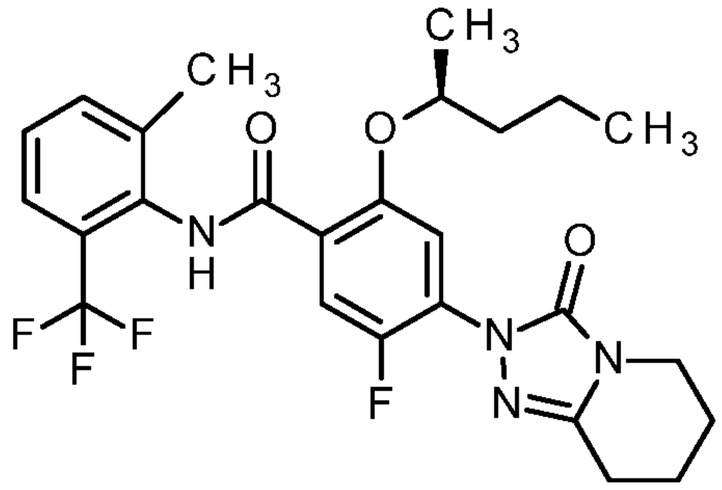
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.24 min; MS (ESIpos): m/z = 484 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.934 (2.43), 0.952 (6.05), 0.970 (2.77), 1.428 (5.60), 1.443 (5.62), 1.463 (0.45), 1.481 (0.42), 1.697 (0.53), 1.722 (0.43), 1.920 (0.49), 1.927 (0.58), 1.933 (0.65), 1.943 (0.67), 1.948 (0.72), 2.000 (0.64), 2.005 (0.68), 2.015 (0.72), 2.020 (0.59), 2.029 (0.44), 2.281 (7.18), 2.800 (1.03), 2.815 (2.00), 2.832 (1.16), 3.709 (1.33), 3.725 (2.13), 3.739 (0.96), 3.939 (16.00), 4.651 (0.69), 4.667 (0.70), 6.661 (2.10), 7.407 (1.34), 7.421 (1.33), 8.137 (1.86), 8.167 (1.77), 8.422 (2.61), 9.506 (1.09).

Example 15

5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 2-methyl-6-(trifluoromethyl)aniline.

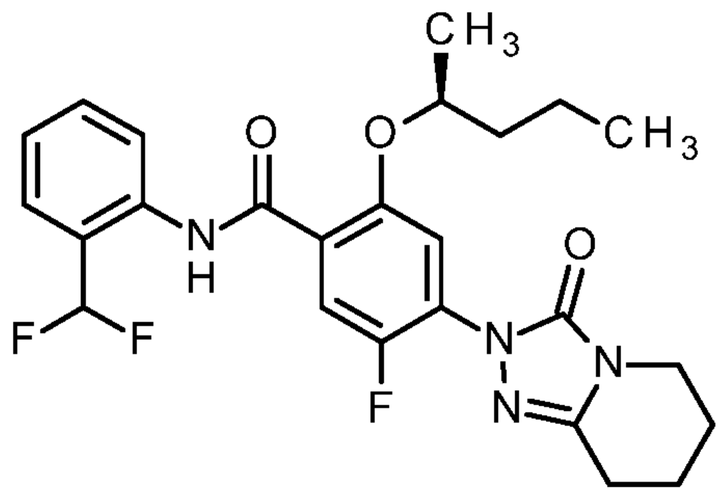
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method A): R_t = 1.41 min; MS (ESIpos): m/z = 521 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.915 (1.53), 0.932 (2.74), 0.950 (1.66), 1.411 (3.45), 1.425 (3.35), 1.454 (0.92), 1.570 (9.08), 1.615 (0.46), 1.631 (0.81), 1.646 (0.51), 1.650 (0.74), 1.655 (0.65), 1.665 (1.14), 1.670 (0.48), 1.674 (0.62), 1.680 (0.58), 1.689 (0.91), 1.705 (0.42), 1.796 (0.47), 1.819 (0.52), 1.829 (0.48), 1.908 (0.47), 1.915 (0.61), 1.923 (1.32), 1.931 (1.57), 1.936 (1.76), 1.947 (1.79), 1.951 (1.92), 1.963 (0.84), 1.966 (0.88), 1.988 (0.94), 1.993 (0.86), 2.002 (1.72), 2.007 (1.81), 2.018 (1.88), 2.023 (1.53), 2.032 (1.13), 2.045 (0.48), 2.321 (16.00), 2.804 (2.80), 2.820 (5.25), 2.836 (3.03), 3.715 (3.64), 3.731 (5.74), 3.746 (2.48), 4.656 (0.81), 4.672 (1.63), 4.687 (1.62), 4.702 (0.79), 7.322 (1.03), 7.341 (2.38), 7.361 (1.47), 7.401 (3.23), 7.416 (3.19), 7.506 (2.05), 7.525 (1.64), 7.552 (2.05), 7.571 (1.71), 8.152 (3.39), 8.181 (3.40), 9.766 (0.50).

Example 16

N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 2-(difluoromethyl)aniline.

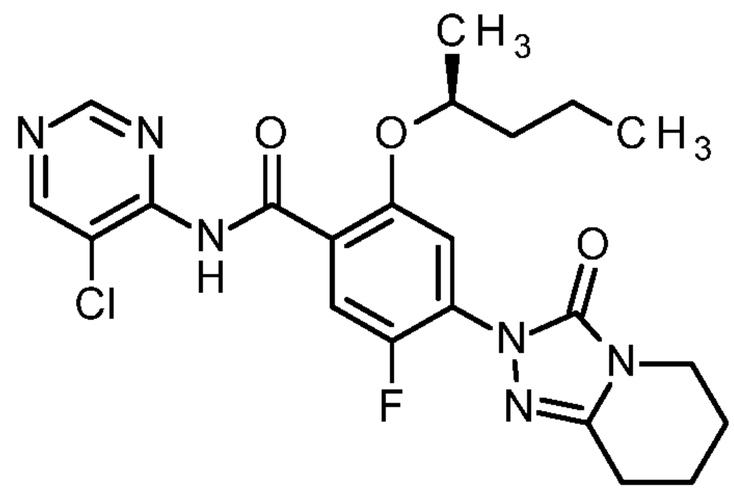
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.35 min; MS (ESIpos): m/z = 489 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.908 (6.25), 0.926 (15.09), 0.945 (7.37), 1.225 (0.41), 1.259 (0.70), 1.364 (0.46), 1.382 (0.80), 1.389 (0.59), 1.397 (0.77), 1.400 (0.83), 1.407 (1.25), 1.417 (12.87), 1.433 (12.64), 1.441 (1.71), 1.448 (0.86), 1.456 (0.90), 1.462 (0.95), 1.467 (0.71), 1.475 (0.53), 1.481 (0.87), 1.495 (0.42), 1.499 (0.48), 1.600 (16.00), 1.621 (1.11), 1.631 (0.54), 1.637 (0.64), 1.640 (0.80), 1.646 (0.79), 1.655 (1.18), 1.660 (0.54), 1.666 (0.67), 1.670 (0.64), 1.680 (0.92), 1.695 (0.44), 1.825 (0.54), 1.840 (0.72), 1.850 (0.62), 1.854 (0.73), 1.859 (0.62), 1.866 (0.72), 1.873 (0.66), 1.880 (0.63), 1.884 (0.52), 1.889 (0.50), 1.900 (0.61), 1.906 (0.57), 1.914 (0.95), 1.922 (1.46), 1.929 (1.73), 1.934 (1.94), 1.945 (1.97), 1.949 (2.11), 1.961 (0.96), 1.965 (1.00), 1.986 (1.02), 1.992 (0.95), 2.000 (1.90), 2.006 (2.01), 2.016 (2.10), 2.021 (1.73), 2.030 (1.28), 2.044 (0.54), 2.802 (3.02), 2.817 (5.72), 2.834 (3.25), 3.713 (3.70), 3.728 (6.16), 3.743 (2.70), 4.613 (0.79), 4.628 (1.58), 4.644 (1.59), 4.659 (0.79), 6.615 (1.84), 6.753 (3.62), 6.892 (1.75), 7.286 (1.13), 7.305 (2.40), 7.324 (1.44), 7.404 (3.60), 7.419 (3.60), 7.528 (1.21), 7.547 (2.08), 7.556 (2.52), 7.567 (1.24), 7.575 (2.03), 7.975 (2.34), 7.996 (2.11), 8.130 (4.67), 8.159 (4.69), 9.954 (2.50).

Example 17

N-(5-chloropyrimidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 5-chloropyrimidin-4-amine.

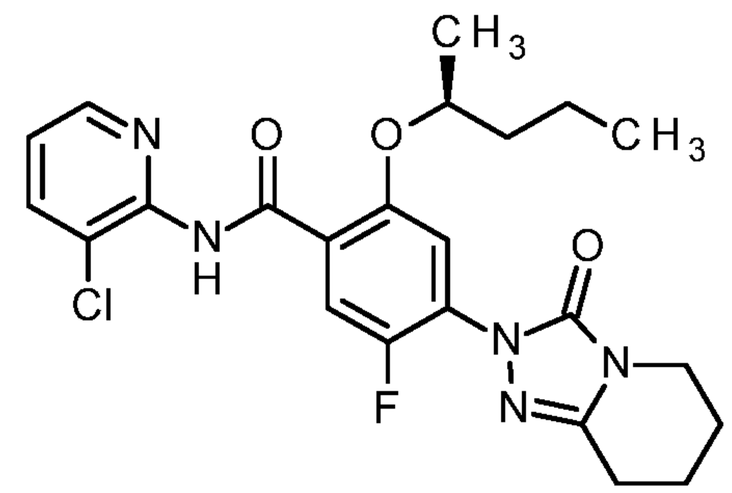
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method A): R_t = 1.14 min; MS (ESIpos): m/z = 475 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.931 (3.70), 0.950 (8.84), 0.969 (4.20), 1.261 (0.51), 1.416 (0.51), 1.432 (0.46), 1.435 (0.50), 1.442 (0.72), 1.450 (0.56), 1.461 (9.31), 1.476 (9.27), 1.486 (0.55), 1.494 (0.63), 1.500 (0.56), 1.505 (0.45), 1.518 (0.53), 1.575 (16.00), 1.582 (8.92), 1.679 (0.62), 1.699 (0.50), 1.704 (0.52), 1.714 (0.80), 1.724 (0.45), 1.728 (0.42), 1.739 (0.65), 1.908 (0.71), 1.917 (0.77), 1.925 (1.18), 1.934 (1.46), 1.939 (1.37), 1.948 (1.54), 1.952 (1.54), 1.956 (1.12), 1.964 (0.81), 1.968 (0.88), 1.982 (0.45), 1.989 (0.63), 2.003 (1.14), 2.009 (1.17), 2.019 (1.28), 2.024 (1.00), 2.033 (0.74), 2.803 (1.76), 2.819 (3.30), 2.835 (1.90), 3.712 (2.19), 3.727 (3.61), 3.742 (1.55), 4.662 (0.55), 4.678 (1.04), 4.693 (1.04), 4.709 (0.53), 7.473 (2.15), 7.488 (2.14), 8.140 (2.85), 8.169 (2.83), 8.669 (7.42), 9.008 (5.44), 10.680 (1.64).

Example 18

N-(3-chloropyridin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 3-chloropyridin-2-amine.

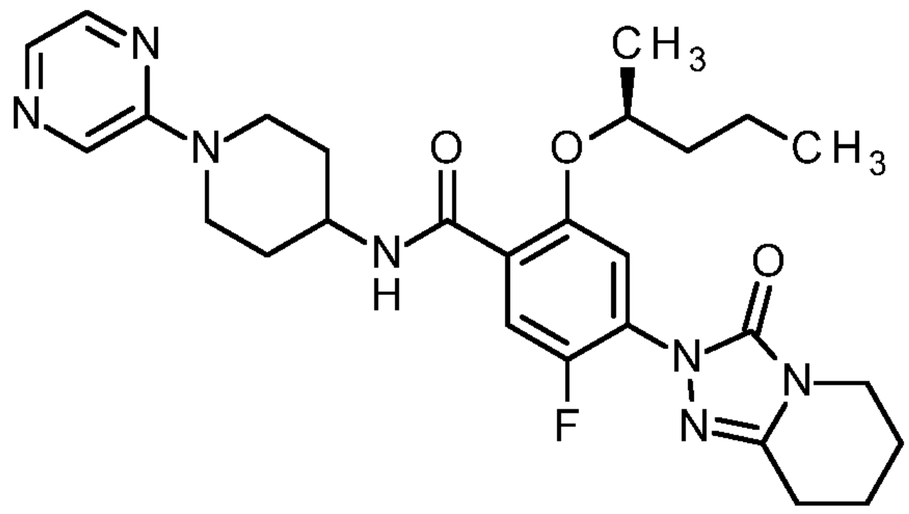
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.20 min; MS (ESIpos): m/z = 474 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.920 (6.70), 0.939 (16.00), 0.957 (7.63), 1.257 (0.54), 1.399 (0.56), 1.410 (0.43), 1.417 (0.94), 1.425 (0.76), 1.432 (1.07), 1.443 (15.74), 1.459 (15.85), 1.467 (1.16), 1.476 (0.99), 1.481 (0.99), 1.486 (0.80), 1.493 (0.91), 1.500 (0.89), 1.506 (0.95), 1.511 (0.81), 1.519 (0.56), 1.525 (0.94), 1.539 (0.47), 1.544 (0.54), 1.655 (0.65), 1.670 (1.14), 1.681 (0.61), 1.685 (0.74), 1.690 (0.94), 1.695 (0.99), 1.704 (1.46), 1.710 (0.68), 1.715 (0.87), 1.719 (0.85), 1.730 (1.19), 1.744 (0.59), 1.879 (0.75), 1.893 (0.93), 1.896 (1.01), 1.905 (1.19), 1.909 (1.63), 1.918 (2.34), 1.930 (2.86), 1.935 (2.42), 1.941 (2.61), 1.944 (2.88), 1.956 (1.62), 1.961 (1.28), 1.969 (0.81), 1.982 (1.18), 1.988 (1.11), 1.997 (2.14), 2.002 (2.24), 2.013 (2.35), 2.017 (1.96), 2.026 (1.46), 2.040 (0.66), 2.797 (3.07), 2.814 (5.99), 2.829 (3.43), 3.709 (3.89), 3.725 (6.43), 3.740 (2.86), 4.643 (1.00), 4.659 (1.94), 4.674 (1.91), 4.690 (0.98), 7.095 (3.31), 7.106 (3.37), 7.114 (3.66), 7.126 (3.66), 7.406 (3.92), 7.421 (3.90), 7.760 (3.83), 7.765 (3.65), 7.780 (3.51), 7.784 (3.68), 8.181 (4.98), 8.210 (5.09), 8.481 (3.09), 8.486 (3.25), 8.493 (3.20), 8.498 (2.97), 10.484 (3.08).

Example 19

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[1-(pyrazin-2-yl)piperidin-4-yl]benzamide



From intermediate 16 and 1-(pyrazin-2-yl)piperidin-4-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

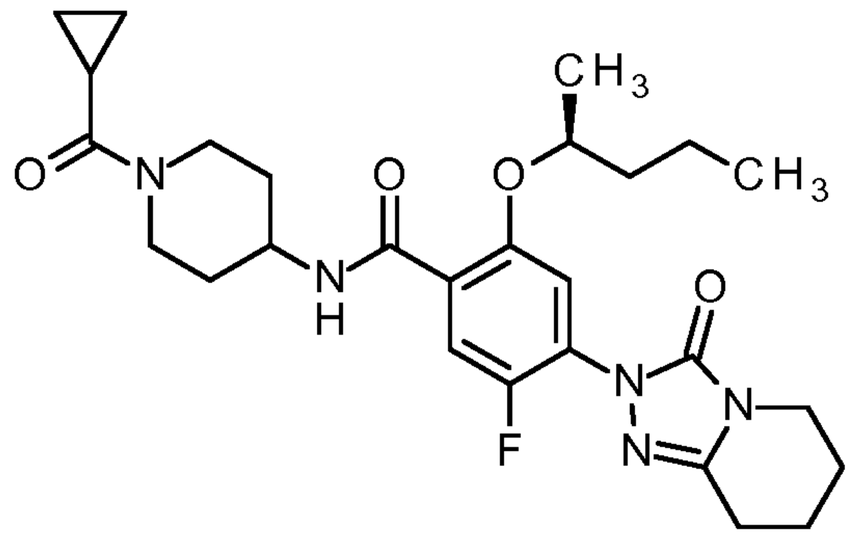
LC-MS (method B): R_t = 1.18 min; MS (ESIpos): m/z = 524 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.894 (6.91), 0.913 (16.00), 0.931 (7.84), 1.357 (15.59), 1.372 (15.66), 1.384 (0.86), 1.393 (0.92), 1.395 (0.93), 1.403 (1.21), 1.410 (0.79), 1.421 (1.25), 1.430 (0.56), 1.438 (1.28), 1.443 (0.88), 1.449 (0.83), 1.457 (1.01), 1.463 (1.05), 1.467 (0.82), 1.482 (1.24), 1.495 (1.09), 1.501 (1.03), 1.521 (1.82), 1.528 (1.51), 1.552 (1.84), 1.572 (0.67), 1.580 (0.82), 1.590 (1.02), 1.604 (0.96), 1.614 (0.58), 1.618 (0.75), 1.625

(1.20), 1.628 (1.01), 1.639 (2.21), 1.650 (4.72), 1.663 (1.77), 1.678 (0.75), 1.698 (0.86), 1.712 (1.09), 1.724 (0.89), 1.729 (1.03), 1.733 (0.75), 1.740 (1.01), 1.749 (0.73), 1.754 (0.82), 1.758 (0.59), 1.763 (0.53), 1.774 (0.53), 1.891 (0.61), 1.906 (1.73), 1.918 (2.34), 1.930 (2.36), 1.934 (2.50), 1.950 (1.20), 1.971 (1.24), 1.986 (2.30), 1.990 (2.40), 2.001 (2.53), 2.006 (2.08), 2.014 (1.77), 2.029 (0.67), 2.179 (1.65), 2.187 (1.64), 2.202 (1.54), 2.211 (1.49), 2.782 (3.36), 2.798 (6.55), 2.814 (3.65), 3.142 (1.66), 3.149 (1.87), 3.170 (2.09), 3.176 (3.46), 3.182 (2.07), 3.204 (1.93), 3.211 (1.61), 3.692 (4.15), 3.707 (6.96), 3.722 (3.05), 4.236 (0.56), 4.261 (3.66), 4.271 (2.25), 4.281 (2.15), 4.293 (2.97), 4.531 (1.11), 4.546 (2.07), 4.561 (2.04), 4.576 (1.06), 7.288 (4.32), 7.302 (4.24), 7.844 (5.22), 7.851 (5.51), 8.058 (5.55), 8.068 (3.56), 8.072 (4.06), 8.074 (3.78), 8.079 (3.56), 8.088 (5.35), 8.184 (2.24), 8.195 (6.10), 8.198 (6.16).

Example 20

N-[1-(cyclopropylcarbonyl)piperidin-4-yl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and (4-aminopiperidin-1-yl)(cyclopropyl)methanone.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

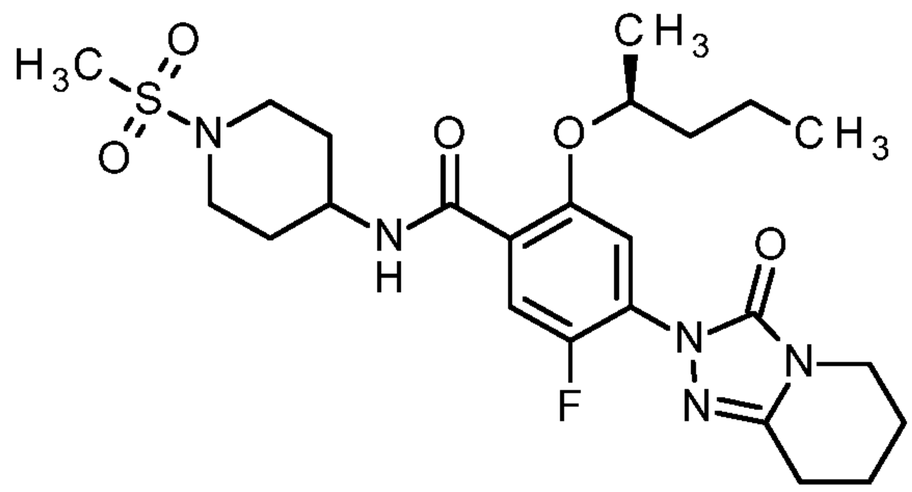
LC-MS (method B): R_t = 1.12 min; MS (ESIpos): m/z = 514 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.739 (2.24), 0.749 (8.60), 0.757 (9.81), 0.770 (8.61), 0.777 (10.19), 0.786 (2.76), 0.921 (6.84), 0.939 (13.91), 0.958 (10.83), 0.967 (11.75), 0.974 (9.50), 0.979 (11.09), 0.986 (8.74), 0.996 (2.88), 1.353 (11.57), 1.367 (12.46), 1.402 (4.89), 1.423 (5.15), 1.461 (3.04), 1.498 (0.88), 1.516 (0.48), 1.592 (0.85), 1.607 (1.46), 1.627 (1.89), 1.641 (2.60), 1.651 (1.80), 1.655 (1.67), 1.665 (2.00), 1.680 (0.97), 1.700 (1.40), 1.715 (2.14), 1.726 (1.82), 1.730 (2.06), 1.740 (3.55), 1.752 (4.51), 1.760 (4.46), 1.763 (3.17), 1.771 (6.46), 1.780 (2.57), 1.783 (3.26), 1.792 (3.20), 1.803 (1.33), 1.865 (9.27), 1.873 (2.21), 1.882 (2.04), 1.890 (4.00), 1.897 (4.77), 1.902 (5.26), 1.914 (5.46), 1.918 (5.68), 1.930 (2.67), 1.934 (2.75), 1.955 (2.83), 1.961 (2.75), 1.970 (5.28), 1.975 (5.53), 1.985 (5.99), 1.990 (5.16), 1.997

(4.69), 2.005 (2.88), 2.013 (2.73), 2.203 (1.47), 2.764 (7.72), 2.780 (14.85), 2.796 (8.44), 2.866 (0.99), 2.895 (1.68), 2.924 (1.02), 3.283 (1.01), 3.312 (1.67), 3.342 (0.98), 3.675 (9.57), 3.690 (16.00), 3.704 (6.90), 4.153 (1.54), 4.167 (1.65), 4.178 (2.27), 4.188 (2.49), 4.195 (2.83), 4.205 (2.81), 4.214 (2.18), 4.223 (2.36), 4.232 (1.77), 4.250 (0.95), 4.260 (0.48), 4.487 (1.54), 4.510 (1.86), 4.525 (3.68), 4.540 (5.10), 4.556 (4.74), 4.571 (2.42), 4.586 (0.53), 7.288 (9.79), 8.027 (11.72), 8.056 (11.80), 8.157 (4.23), 8.176 (4.12).

Example 21

5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 1-(methylsulfonyl)piperidin-4-amine.

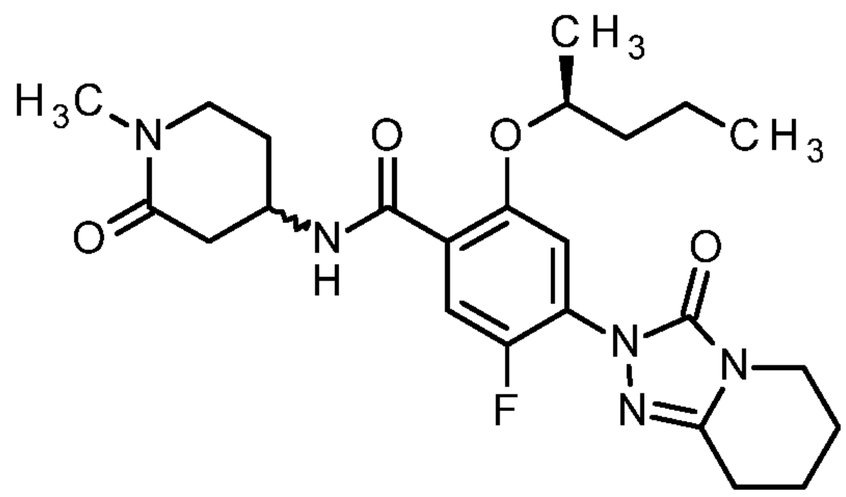
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.07 min; MS (ESIpos): m/z = 524 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.955 (2.98), 0.973 (7.37), 0.991 (3.43), 1.378 (6.54), 1.393 (6.64), 1.407 (0.42), 1.433 (0.51), 1.448 (0.49), 1.450 (0.53), 1.466 (0.61), 1.485 (0.46), 1.490 (0.44), 1.509 (0.44), 1.600 (1.54), 1.618 (0.94), 1.624 (1.00), 1.639 (0.55), 1.649 (0.47), 1.653 (0.49), 1.659 (0.66), 1.673 (0.67), 1.683 (0.41), 1.697 (0.53), 1.743 (0.46), 1.759 (0.42), 1.770 (0.41), 1.910 (0.68), 1.922 (0.91), 1.934 (0.93), 1.937 (0.99), 1.949 (0.46), 1.953 (0.47), 1.975 (0.49), 1.989 (0.89), 1.994 (0.95), 2.005 (0.99), 2.010 (0.81), 2.017 (0.64), 2.179 (0.63), 2.189 (0.64), 2.785 (1.37), 2.801 (2.70), 2.820 (16.00), 2.835 (0.78), 2.841 (0.81), 2.866 (1.36), 2.871 (1.29), 2.895 (0.79), 2.901 (0.66), 3.696 (1.69), 3.711 (2.82), 3.726 (1.24), 3.817 (1.00), 3.847 (0.93), 4.100 (0.43), 4.119 (0.43), 4.552 (0.44), 4.567 (0.85), 4.582 (0.85), 4.597 (0.43), 7.299 (1.76), 7.314 (1.72), 8.034 (2.31), 8.064 (2.24), 8.190 (0.77), 8.209 (0.76).

Example 22

5-fluoro-N-(1-methyl-2-oxopiperidin-(4R,S)-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide ,mixture of diastereomers



From intermediate 16 and rac-4-amino-1-methylpiperidin-2-one.

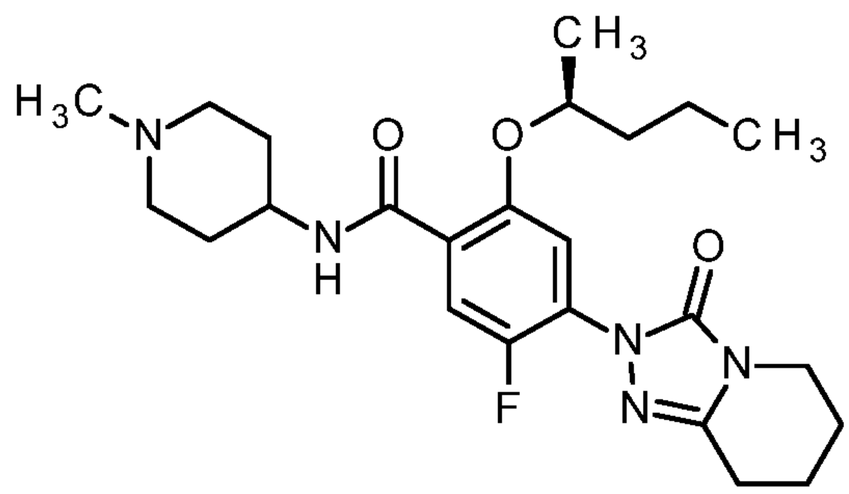
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 0.97 min; MS (ESIpos): m/z = 474 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.941 (1.17), 0.952 (1.22), 0.959 (2.87), 0.970 (2.72), 0.977 (1.37), 0.989 (1.22), 1.279 (16.00), 1.350 (2.40), 1.365 (4.96), 1.381 (2.72), 1.621 (1.15), 1.635 (0.69), 1.640 (0.47), 1.645 (0.41), 1.901 (0.44), 1.909 (0.70), 1.922 (0.96), 1.933 (0.88), 1.936 (0.88), 1.941 (0.69), 1.954 (0.45), 1.988 (0.66), 1.993 (0.68), 2.004 (0.72), 2.009 (0.58), 2.018 (0.42), 2.300 (0.45), 2.320 (0.41), 2.342 (0.48), 2.363 (0.48), 2.784 (1.03), 2.800 (2.04), 2.816 (1.52), 2.990 (7.27), 3.362 (0.42), 3.378 (0.78), 3.385 (0.42), 3.392 (0.44), 3.397 (0.44), 3.694 (1.26), 3.709 (2.09), 3.725 (0.90), 4.570 (0.43), 4.582 (0.41), 7.304 (1.27), 7.319 (1.24), 8.042 (1.74), 8.071 (1.70), 8.239 (0.55), 8.256 (0.53).

Example 23

5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From intermediate 16 and 1-methylpiperidin-4-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

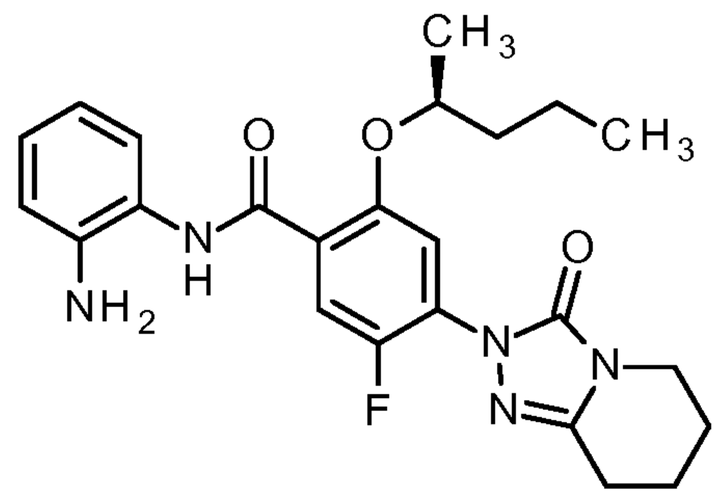
LC-MS (method B): R_t = 1.11 min; MS (ESIpos): m/z = 460 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.919 (4.45), 0.937 (10.63), 0.955 (5.06), 1.344 (9.61), 1.359 (9.80), 1.378 (0.64), 1.385 (0.48), 1.393 (0.54), 1.396 (0.55), 1.403 (0.72), 1.411 (0.52), 1.419 (0.61), 1.421 (0.73), 1.427 (0.48), 1.436 (0.59), 1.440 (0.67), 1.446 (0.53), 1.452 (0.54), 1.459 (0.60), 1.465 (0.65), 1.470 (0.51), 1.484 (0.66), 1.503 (0.64), 1.516 (0.55), 1.538 (1.01), 1.564 (1.07), 1.590 (0.80), 1.604 (0.81), 1.618 (0.46), 1.624 (0.67), 1.628 (0.54), 1.639 (0.96), 1.649 (0.59), 1.652 (0.56), 1.662 (0.75), 1.721 (0.48), 1.735 (0.63), 1.737 (0.61), 1.747 (0.53), 1.751 (0.62), 1.755 (0.48), 1.761 (0.58), 1.762 (0.58), 1.769 (0.45), 1.772 (0.47), 1.776 (0.49), 1.878 (0.52), 1.887 (1.10), 1.894 (1.33), 1.899 (1.48), 1.910 (1.51), 1.914 (1.58), 1.926 (0.75), 1.930 (0.78), 1.951 (0.81), 1.958 (0.79), 1.966 (1.50), 1.971 (1.55), 1.982 (1.65), 1.987 (1.37), 1.995 (1.08), 2.010 (0.77), 2.031 (1.40), 2.041 (1.27), 2.052 (1.16), 2.063 (1.19), 2.131 (0.68), 2.162 (1.17), 2.189 (0.67), 2.298 (16.00), 2.761 (2.44), 2.777 (4.83), 2.793 (3.09), 3.672 (2.59), 3.688 (4.25), 3.703 (1.92), 3.977 (0.48), 3.986 (0.46), 3.995 (0.48), 4.520 (0.68), 4.535 (1.29), 4.551 (1.27), 4.566 (0.65), 7.261 (2.67), 8.031 (3.34), 8.061 (3.30), 8.121 (1.02), 8.141 (1.00).

Examples 24–27 were prepared in analogy according to the general methods described above.

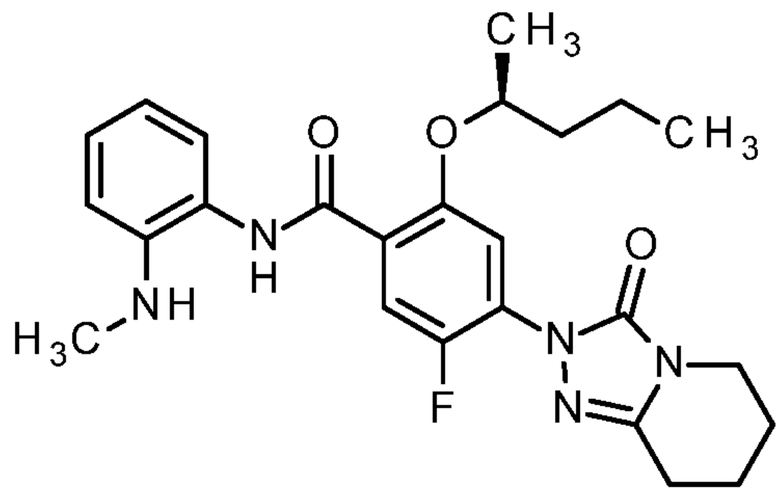
Example 24

N-(2-aminophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



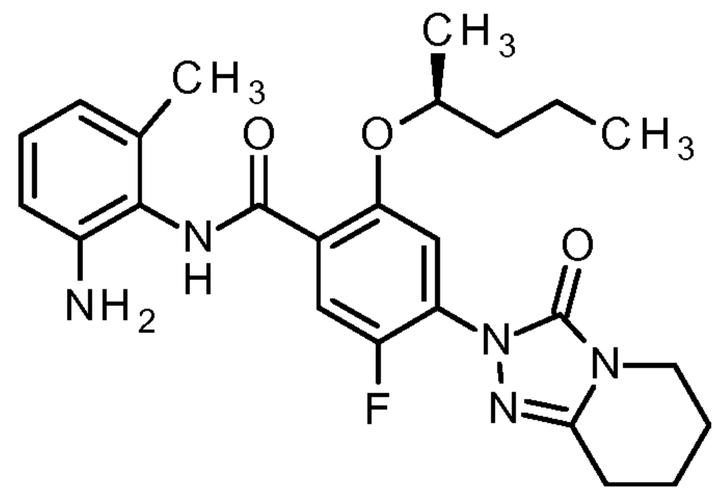
Example 25

5-fluoro-N-[2-(methylamino)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



Example 26

N-(2-amino-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide

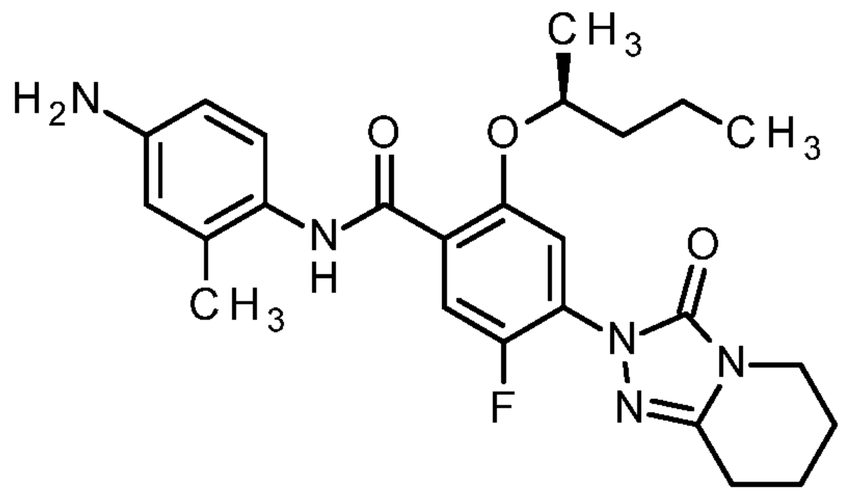


MS (ESIpos): m/z = 468.3 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: -0.149 (0.42), -0.008 (4.72), 0.008 (3.65), 0.146 (0.42), 0.863 (4.75), 0.882 (11.10), 0.900 (5.34), 1.275 (9.68), 1.290 (9.59), 1.323 (0.45), 1.341 (0.71), 1.356 (0.71), 1.366 (0.89), 1.374 (0.68), 1.384 (0.89), 1.403 (0.83), 1.415 (0.71), 1.423 (0.74), 1.428 (0.80), 1.447 (0.80), 1.527 (0.42), 1.541 (0.68), 1.561 (0.74), 1.575 (1.04), 1.585 (0.71), 1.599 (0.77), 1.655 (0.53), 1.670 (0.74), 1.685 (0.77), 1.695 (0.71), 1.710 (0.62), 1.730 (0.42), 1.794 (1.42), 1.806 (2.02), 1.821 (2.08), 1.833 (1.04), 1.888 (2.08), 1.898 (2.14), 1.912 (1.31), 2.146 (16.00), 2.368 (1.10), 2.525 (2.49), 2.671 (0.45), 2.691 (2.32), 2.706 (4.63), 2.723 (2.43), 3.557 (2.70), 3.572 (4.78), 3.587 (2.20), 4.560 (0.77), 4.575 (1.45), 4.590 (1.45), 4.605 (0.74), 4.874 (1.37), 6.458 (2.05), 6.476 (2.20), 6.583 (2.05), 6.601 (2.35), 6.886 (1.96), 6.906 (3.06), 6.925 (1.57), 7.301 (3.00), 7.316 (2.91), 7.641 (3.62), 7.667 (3.56), 9.262 (4.36).

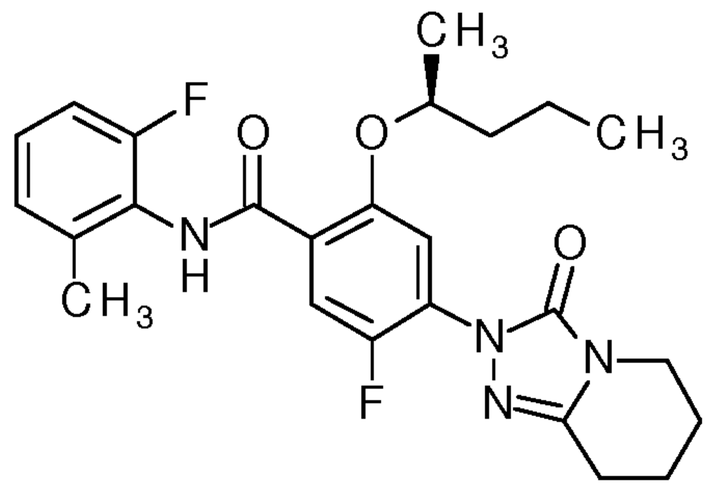
Example 27

N-(4-amino-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



Example 28

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



Example 28 was prepared as described for example 1 from 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzoic acid (intermediate 16) and 2-fluoro-6-methylaniline.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

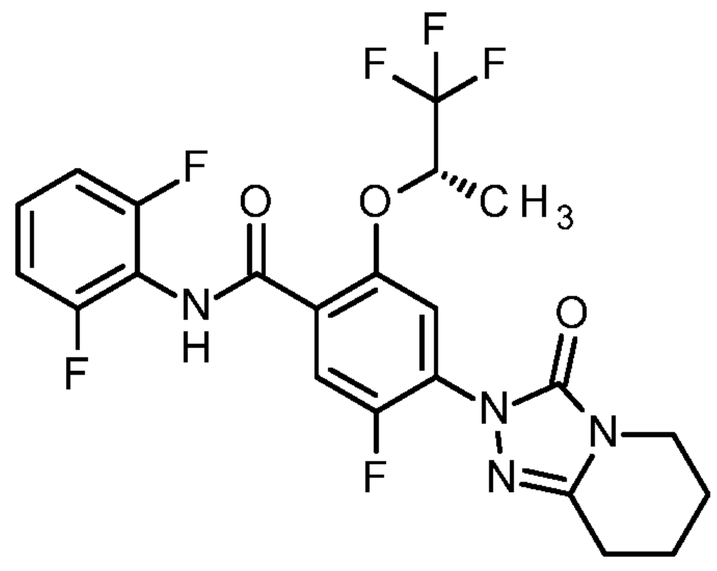
LC-MS (method A): R_t = 1.33 min; MS (ESIpos): m/z = 471.3 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.936 (5.02), 0.954 (12.41), 0.972 (5.77), 1.430 (11.33), 1.445 (11.53), 1.458 (0.59), 1.466 (0.57), 1.469 (0.63), 1.477 (0.49), 1.484 (0.61), 1.491 (0.54), 1.496 (0.48), 1.503 (0.61), 1.510 (0.57), 1.516 (0.61), 1.522 (0.49), 1.535 (0.64), 1.582 (4.28), 1.655 (0.40), 1.670 (0.72), 1.684 (0.44), 1.689 (0.63), 1.695 (0.58), 1.704 (1.04), 1.715 (0.57), 1.719 (0.54), 1.729 (0.83), 1.811 (0.48), 1.825 (0.61), 1.837 (0.52), 1.841 (0.61), 1.846 (0.44), 1.853 (0.58), 1.860 (0.46), 1.867 (0.49), 1.902 (0.44), 1.912 (0.44), 1.921 (1.01), 1.928 (1.20), 1.933 (1.35), 1.945 (1.39), 1.948 (1.50), 1.960 (0.66), 1.964 (0.69), 1.985 (0.71), 1.991 (0.63), 2.000 (1.32), 2.005 (1.39), 2.015 (1.48), 2.020 (1.21), 2.029 (0.90), 2.326 (16.00), 2.801 (2.19), 2.817 (4.23), 2.833 (2.45), 3.711 (2.82), 3.727 (4.62), 3.741 (2.00), 4.641 (0.70), 4.656 (1.38), 4.671 (1.36), 4.687 (0.68), 6.986 (0.71), 7.006 (1.53), 7.031 (0.92), 7.060

(1.26), 7.080 (1.83), 7.151 (1.05), 7.164 (1.09), 7.171 (1.44), 7.185 (1.42), 7.190 (0.67), 7.204 (0.62), 7.399 (2.84), 7.414 (2.80), 8.131 (3.86), 8.160 (3.73), 9.562 (2.06).

Example 29

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



To a 0 °C stirred solution of 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid (intermediate 17) (80.0 mg, 205 µmol) and catalytic N,N-dimethylformamide (3 drops) in anhydrous dichloromethane (1.5 ml) was added oxalyl chloride (21 µl, 250 µmol). The resulting mixture was warmed to room temperature, stirred for 90 minutes and concentrated under reduced pressure. A solution of the crude acid chloride in dichloromethane (1.0 ml) was then added dropwise to a 0 °C stirred solution of 2,6-difluoroaniline (29 mg, 226 µmol) and triethylamine (32 µl, 230 µmol) in anhydrous dichloromethane (2.0 ml). Following complete addition, the mixture was warmed to room temperature, stirred for 2 hours and concentrated under reduced pressure. The residue was dissolved in DMSO, filtered through a teflon filter and purified by reverse phase column chromatography (acetonitrile, 0.1 % aqueous formic acid) to give the amide as a white solid (88 mg, 86 %).

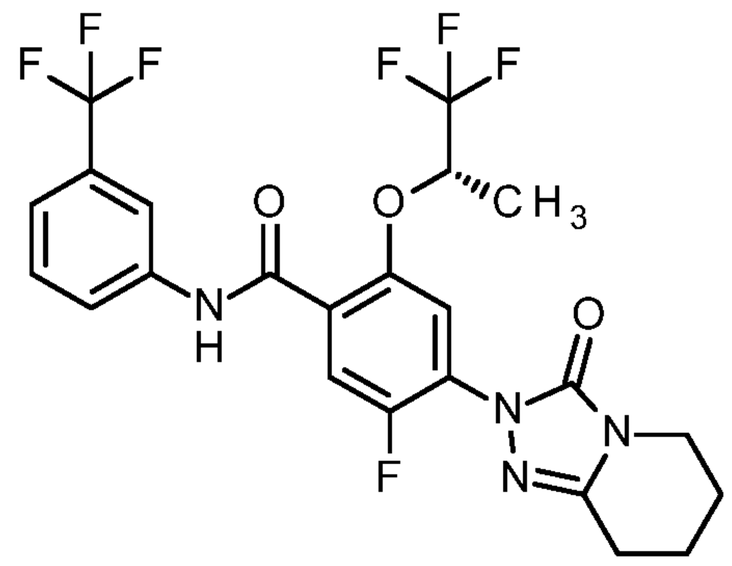
LC-MS (method A): R_t = 1.19 min; MS (ESIneg): m/z = 499 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.035 (0.67), 1.052 (1.37), 1.070 (0.72), 1.428 (16.00), 1.444 (15.78), 1.512 (0.72), 1.795 (3.93), 1.807 (5.48), 1.818 (5.46), 1.822 (5.57), 1.835 (2.76), 1.875 (2.76), 1.890 (5.66), 1.900 (5.84), 1.905 (4.85), 1.914 (3.60), 1.929 (1.37), 2.331 (0.92), 2.518 (5.21), 2.522 (3.46), 2.673 (1.15), 2.678 (0.76), 2.696 (6.07), 2.712 (11.84), 2.729 (6.22), 3.561 (7.12), 3.577 (12.72), 3.591 (5.80), 5.272 (1.15), 5.287 (2.63), 5.304 (3.39), 5.319 (2.47), 5.335 (1.03), 7.187 (4.79), 7.208 (9.78), 7.228 (6.02), 7.367 (1.03), 7.382 (2.36), 7.403 (3.28), 7.424 (1.73), 7.440 (0.72), 7.541 (5.75), 7.560 (8.40), 7.585 (6.27), 9.985 (10.67).

Examples 30–112 were prepared as described for example 29 from 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid (intermediate 17) and the respective amines, as indicated. Products were purified by flash column chromatography or, if explicitely mentioned, by preparative HPLC. Example 52 was prepared from example 51 by deprotection of the azetidine nitrogen, as described below.

Example 30

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[3-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 3-(trifluoromethyl)aniline.

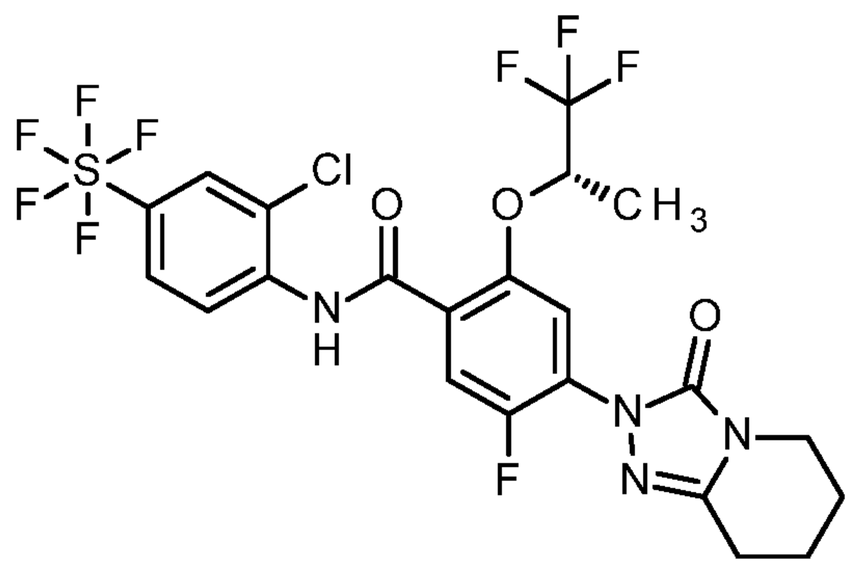
MS (ESIpos): m/z = 533 $(M+H)^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.851 (0.68), 1.172 (0.55), 1.233 (2.37), 1.404 (16.00), 1.420 (15.81), 1.796 (3.05), 1.808 (4.25), 1.823 (4.35), 1.835 (2.17), 1.890 (4.32), 1.901 (4.51), 1.929 (1.17), 1.987 (1.33), 2.006 (0.52), 2.322 (1.49), 2.326 (1.98), 2.331 (1.36), 2.522 (5.42), 2.537 (1.56), 2.664 (1.62), 2.669 (2.08), 2.673 (1.53), 2.697 (5.03), 2.713 (9.83), 2.730 (5.32), 3.562 (5.87), 3.577 (10.45), 3.592 (4.64), 5.246 (1.10), 5.262 (2.66), 5.278 (3.47), 5.294 (2.50), 5.309 (1.04), 7.464 (3.44), 7.483 (4.51), 7.527 (6.46), 7.542 (6.39), 7.587 (2.89), 7.607 (5.13), 7.626 (2.56), 7.652 (8.63), 7.678 (8.37), 7.835 (3.83), 7.856 (3.18), 8.173 (6.78), 10.616 (10.19).

Example 31

N-[2-chloro-4-(pentafluoro-lambda^6-sulfanyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide

301



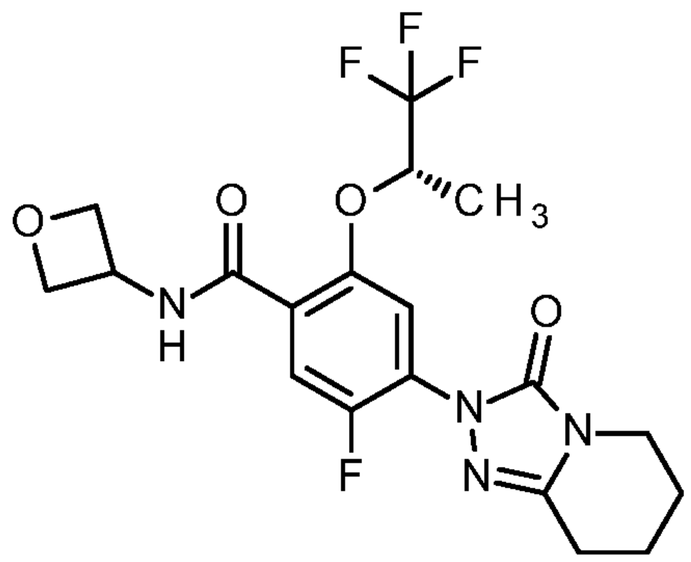
From intermediate 17 and 2-chloro-4-(pentafluoro-lambda6-sulfanyl)aniline.

LC-MS (method A): R_t = 1.54 min; MS (ESIpos): m/z = 625 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.421 (0.43), 1.623 (5.93), 1.656 (16.00), 1.673 (15.82), 1.914 (0.94), 1.929 (2.69), 1.941 (3.70), 1.953 (3.71), 1.957 (3.96), 1.969 (1.86), 1.972 (1.92), 1.994 (1.90), 2.000 (1.88), 2.009 (3.60), 2.014 (3.79), 2.024 (3.99), 2.029 (3.33), 2.038 (2.44), 2.052 (1.02), 2.805 (5.06), 2.821 (9.80), 2.838 (5.50), 3.713 (6.39), 3.729 (10.67), 3.744 (4.78), 4.879 (1.07), 4.895 (2.48), 4.910 (3.22), 4.926 (2.38), 4.941 (0.96), 7.542 (6.43), 7.556 (6.39), 7.708 (3.70), 7.715 (4.06), 7.732 (3.82), 7.738 (4.24), 7.839 (9.64), 7.845 (8.84), 8.086 (8.20), 8.114 (8.14), 8.727 (4.11), 8.750 (3.83), 9.870 (5.68).

Example 32

5-fluoro-N-(oxetan-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and oxetan-3-amine.

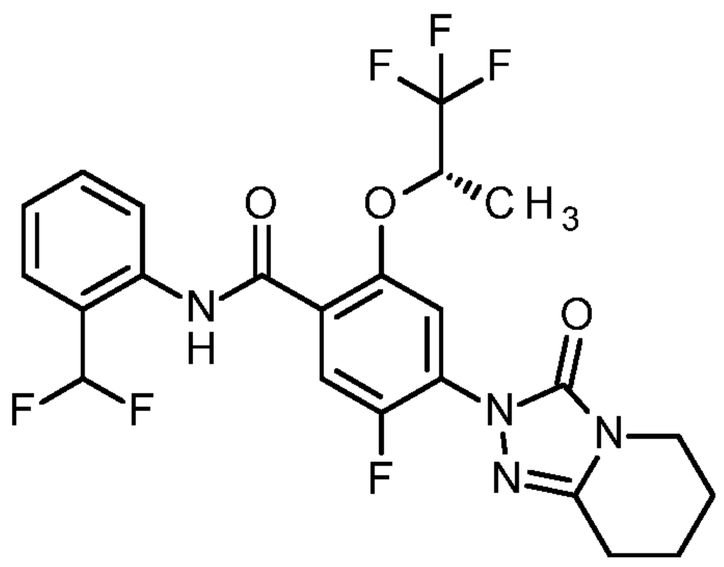
LC-MS (method A): R_t = 0.92 min; MS (ESIpos): m/z = 445 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.631 (15.14), 1.647 (16.00), 1.902 (0.83), 1.909 (1.06), 1.918 (2.41), 1.925 (2.82), 1.930 (3.26), 1.941 (3.31), 1.945 (3.53), 1.957 (1.59), 1.961 (1.66), 1.983 (1.64), 1.989 (1.61), 1.998 (3.18), 2.003 (3.32), 2.014 (3.61), 2.019 (2.89), 2.028 (2.22), 2.042 (0.93), 2.624 (3.46), 2.715 (0.82), 2.790 (4.94), 2.805 (9.55), 2.822 (5.51),

2.993 (1.49), 3.697 (6.16), 3.713 (9.97), 3.728 (4.49), 4.392 (0.50), 4.563 (5.46), 4.580 (10.99), 4.596 (6.03), 4.839 (0.98), 4.854 (2.28), 4.870 (2.97), 4.885 (2.19), 4.900 (0.88), 4.977 (3.73), 4.981 (3.73), 4.995 (7.31), 4.998 (7.15), 5.013 (3.94), 5.016 (4.02), 5.201 (0.60), 5.219 (1.71), 5.235 (3.29), 5.253 (3.05), 5.269 (1.38), 7.391 (6.46), 7.405 (6.37), 8.033 (8.67), 8.062 (8.84), 8.104 (2.07), 8.121 (2.03).

Example 33

N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



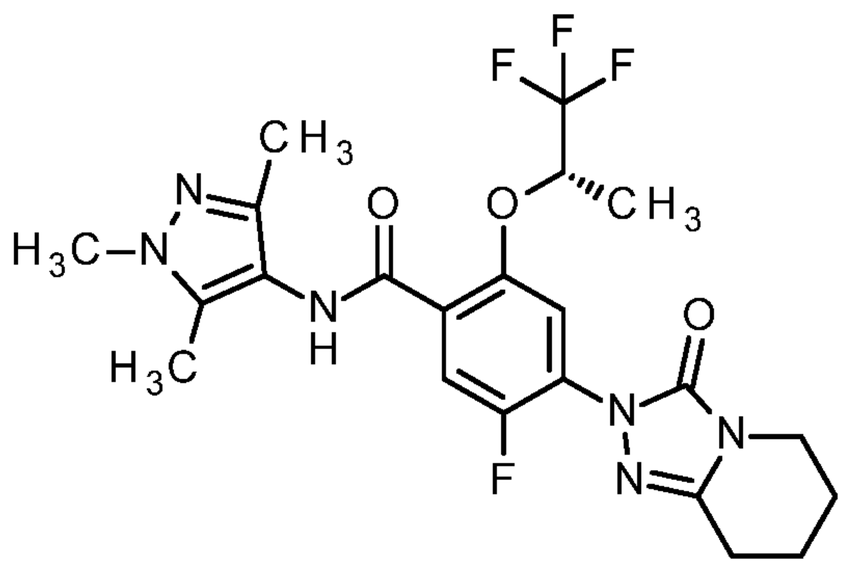
From intermediate 17 and 2-(difluoromethyl)aniline.

LC-MS (method A): R_t = 1.24 min; MS (ESIpos): m/z = 515 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.625 (15.67), 1.641 (16.00), 1.710 (0.58), 1.905 (1.16), 1.920 (3.18), 1.932 (4.51), 1.944 (4.50), 1.947 (4.77), 1.959 (2.44), 1.963 (2.46), 1.985 (2.34), 2.004 (4.62), 2.015 (4.86), 2.028 (3.12), 2.043 (1.34), 2.316 (0.45), 2.796 (5.56), 2.812 (10.82), 2.829 (6.17), 3.705 (6.59), 3.721 (11.38), 3.735 (5.40), 4.864 (1.06), 4.880 (2.49), 4.895 (3.25), 4.911 (2.46), 4.926 (1.07), 6.614 (3.39), 6.753 (6.73), 6.891 (3.29), 7.302 (2.16), 7.320 (4.82), 7.339 (2.98), 7.485 (6.25), 7.499 (6.34), 7.525 (2.39), 7.547 (7.45), 7.568 (5.51), 7.919 (4.68), 7.938 (4.17), 8.098 (7.10), 8.127 (6.95), 9.384 (4.86).

Example 34

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)benzamide



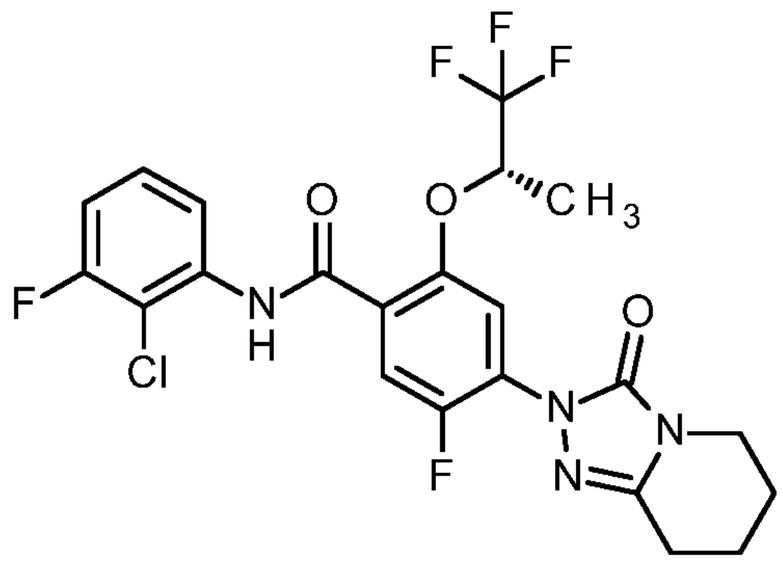
From intermediate 17 and 1,3,5-trimethyl-1H-pyrazol-4-amine.

LC-MS (method A): R_t = 0.97 min; MS (ESIpos): m/z = 497 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.463 (4.62), 1.479 (4.72), 1.761 (1.74), 1.775 (1.78), 1.844 (1.99), 2.007 (16.00), 2.625 (1.74), 2.640 (3.09), 2.656 (1.75), 3.532 (1.92), 3.546 (3.26), 3.561 (2.02), 3.584 (9.16), 4.733 (0.76), 4.748 (0.98), 4.763 (0.75), 7.108 (1.50), 7.284 (1.71), 7.946 (2.04), 7.976 (1.77), 8.376 (1.94).

Example 35

N-(2-chloro-3-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



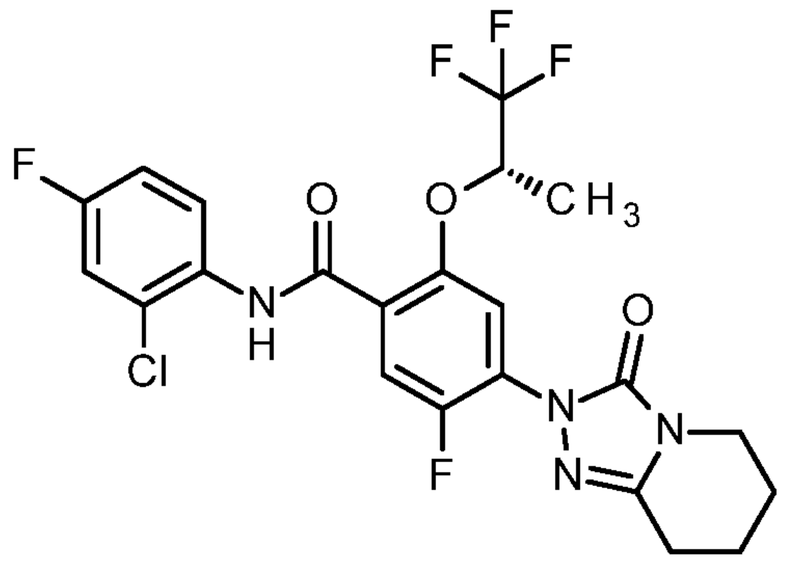
From intermediate 17 and 2-chloro-3-fluoroaniline.

LC-MS (method A): R_t = 1.36 min; MS (ESIpos): m/z = 517 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.571 (16.00), 1.657 (1.59), 1.673 (1.59), 2.807 (0.55), 2.822 (1.04), 2.839 (0.60), 3.716 (0.71), 3.731 (1.15), 3.746 (0.50), 6.975 (0.55), 6.979 (0.54), 7.295 (0.46), 7.310 (0.45), 7.515 (0.69), 7.529 (0.77), 8.099 (0.87), 8.128 (0.86), 8.357 (0.46), 8.378 (0.45), 9.748 (0.44).

Example 36

N-(2-chloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



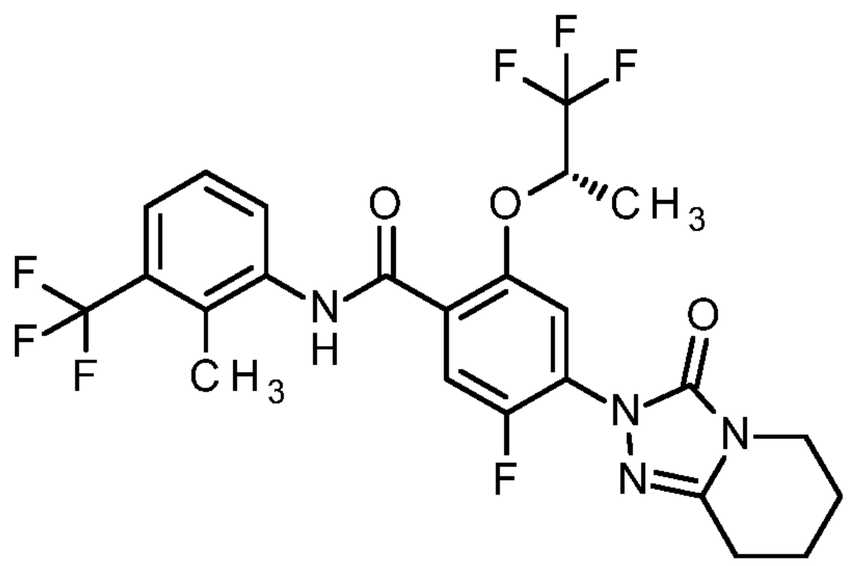
From intermediate 17 and 2-chloro-4-fluoroaniline.

LC-MS (method A): R_t = 1.35 min; MS (ESIpos): m/z = 517 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.574 (16.00), 1.647 (3.49), 1.662 (3.53), 1.929 (0.58), 1.941 (0.79), 1.953 (0.78), 1.956 (0.86), 1.972 (0.41), 1.993 (0.40), 2.009 (0.76), 2.013 (0.80), 2.019 (1.12), 2.024 (0.87), 2.029 (0.70), 2.038 (0.53), 2.805 (1.20), 2.821 (2.28), 2.837 (1.33), 3.714 (1.55), 3.730 (2.55), 3.744 (1.11), 4.887 (0.57), 4.903 (0.74), 4.918 (0.55), 7.039 (0.48), 7.046 (0.53), 7.058 (0.53), 7.062 (0.56), 7.065 (0.61), 7.069 (0.61), 7.081 (0.49), 7.089 (0.54), 7.176 (1.26), 7.183 (1.16), 7.197 (1.25), 7.204 (1.15), 7.498 (1.48), 7.512 (1.50), 8.106 (1.91), 8.135 (1.83), 8.448 (0.98), 8.462 (1.01), 8.471 (0.99), 8.485 (0.94), 9.613 (1.04).

Example 37

5-fluoro-N-[2-methyl-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



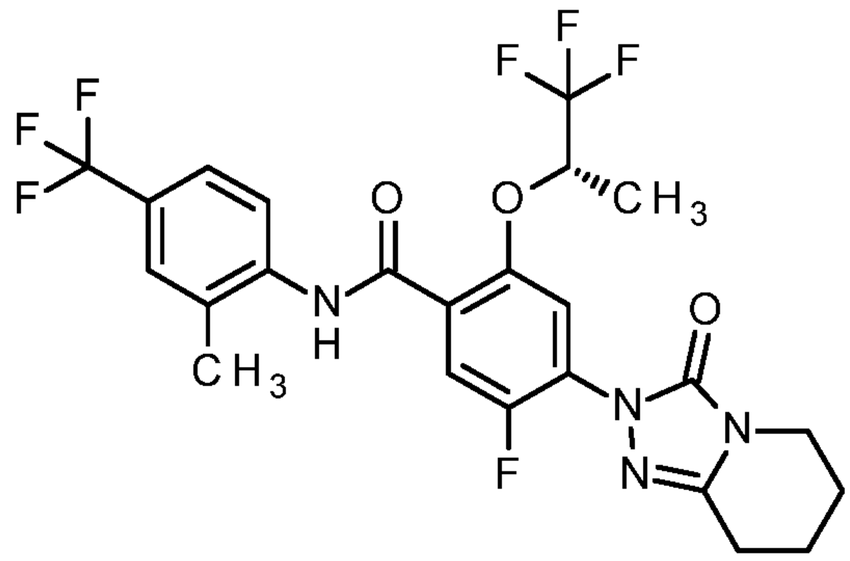
From intermediate 17 and 2-methyl-3-(trifluoromethyl)aniline.

LC-MS (method A): R_t = 1.36 min; MS (ESIpos): m/z = 547 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.577 (16.00), 1.644 (2.65), 1.660 (2.67), 1.933 (0.46), 1.945 (0.63), 1.956 (0.63), 1.960 (0.69), 2.013 (0.61), 2.018 (0.68), 2.028 (0.69), 2.033 (0.57), 2.042 (0.43), 2.407 (3.39), 2.810 (0.92), 2.826 (1.80), 2.842 (1.05), 3.717 (1.15), 3.733 (1.93), 3.748 (0.86), 4.927 (0.42), 4.942 (0.54), 4.958 (0.41), 5.310 (0.41), 7.360 (0.76), 7.380 (0.44), 7.497 (1.12), 7.511 (1.11), 7.535 (0.85), 7.555 (0.68), 7.983 (0.74), 8.003 (0.70), 8.153 (1.37), 8.181 (1.34), 9.136 (0.83).

Example 38

5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



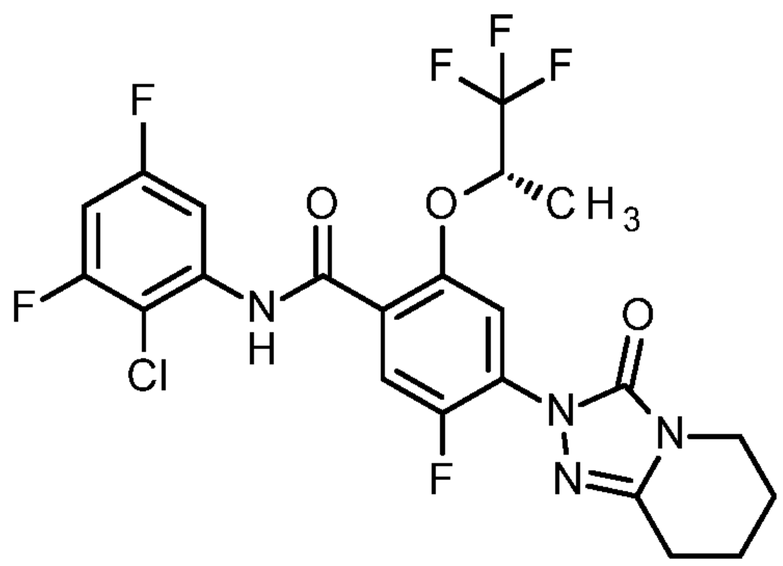
From intermediate 17 and 2-methyl-4-(trifluoromethyl)aniline.

LC-MS (method A): R_t = 1.39 min; MS (ESIpos): m/z = 547 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.572 (16.00), 1.628 (1.48), 1.644 (1.48), 2.374 (3.61), 2.809 (0.53), 2.825 (1.01), 2.841 (0.59), 3.717 (0.68), 3.732 (1.13), 3.748 (0.48), 7.499 (0.63), 7.507 (0.71), 7.522 (0.84), 8.132 (0.78), 8.161 (0.77), 8.185 (0.43), 8.206 (0.40), 9.156 (0.43).

Example 39

N-(2-chloro-3,5-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



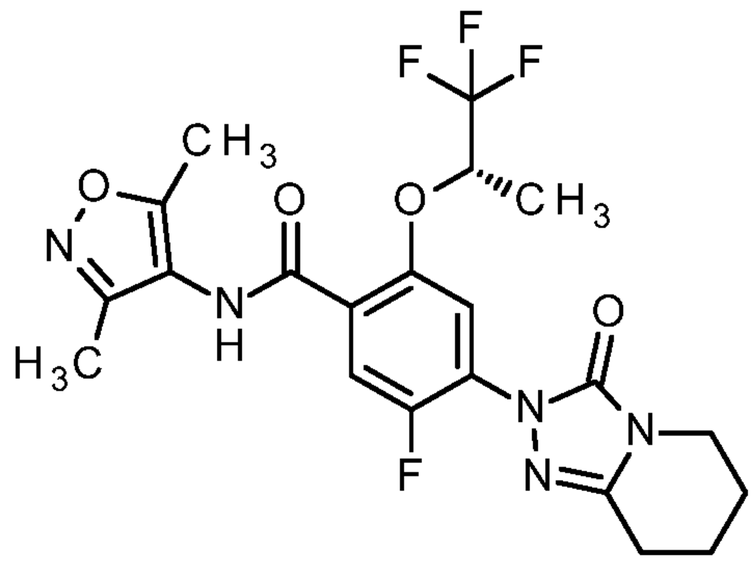
From intermediate 17 and 2-chloro-3,5-difluoroaniline.

LC-MS (method A): R_t = 1.43 min; MS (ESIpos): m/z = 535 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.571 (16.00), 1.657 (0.75), 1.674 (0.75), 2.823 (0.49), 3.731 (0.56), 8.076 (0.44), 8.105 (0.45).

Example 40

N-(3,5-dimethyl-1,2-oxazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



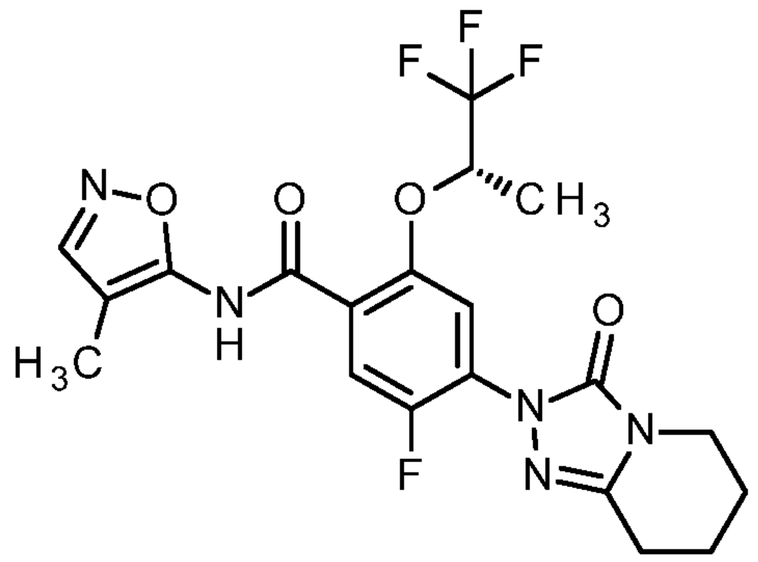
From intermediate 17 and 3,5-dimethyl-1,2-oxazol-4-amine.

LC-MS (method A): R_t = 1.05 min; MS (ESIneg): m/z = 482 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.599 (10.02), 1.656 (3.90), 1.672 (3.91), 1.931 (0.67), 1.938 (0.78), 1.943 (0.89), 1.954 (0.90), 1.958 (0.96), 1.970 (0.42), 1.974 (0.45), 1.997 (0.47), 2.002 (0.44), 2.011 (0.88), 2.018 (1.08), 2.026 (0.95), 2.032 (0.77), 2.041 (0.57), 2.204 (0.58), 2.235 (16.00), 2.378 (11.94), 2.806 (1.42), 2.822 (2.62), 2.839 (1.55), 3.712 (1.74), 3.727 (2.76), 3.743 (1.22), 4.919 (0.60), 4.934 (0.79), 4.949 (0.57), 7.477 (1.73), 7.491 (1.74), 8.123 (2.47), 8.152 (2.50), 8.553 (1.23).

Example 41

5-fluoro-N-(4-methyl-1,2-oxazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



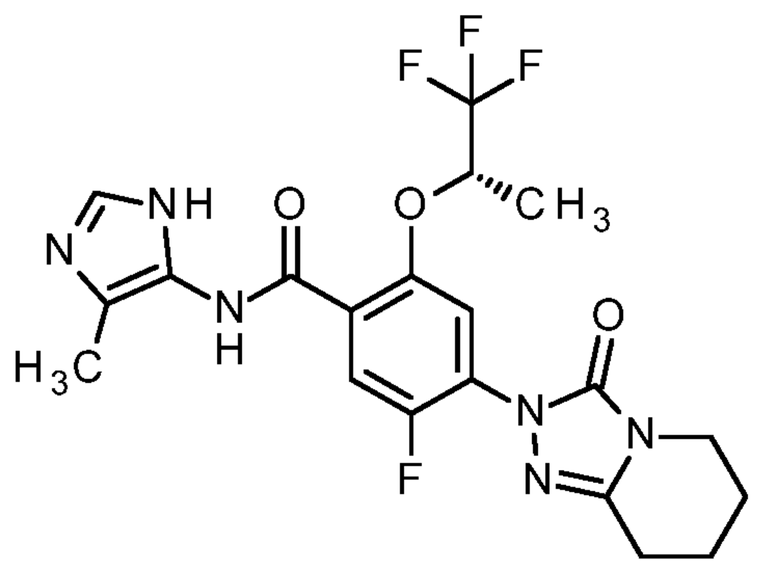
From intermediate 17 and 4-methyl-1,2-oxazol-5-amine.

LC-MS (method A): R_t = 1.07 min; MS (ESIneg): m/z = 468 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.000 (3.05), 1.183 (0.56), 1.419 (1.13), 1.434 (1.18), 1.500 (16.00), 1.862 (0.90), 1.873 (0.57), 1.932 (0.69), 1.944 (0.57), 2.105 (0.45), 2.717 (0.52), 2.733 (0.95), 2.749 (0.56), 2.977 (0.62), 3.631 (0.62), 3.646 (1.02), 3.661 (0.44), 7.268 (0.40), 7.277 (0.41), 7.452 (0.42).

Example 42

5-fluoro-N-(4-methyl-1H-imidazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 4-methyl-1H-imidazol-5-amine.

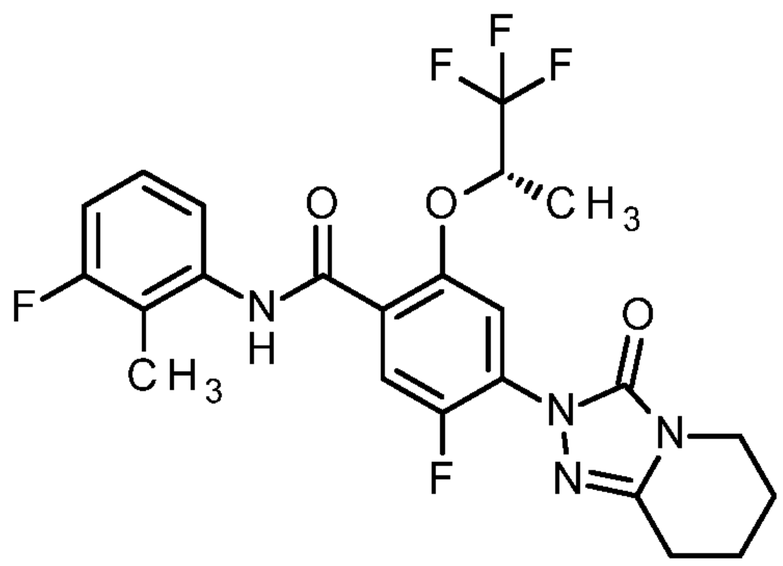
LC-MS (method A): R_t = 0.78 min; MS (ESIpos): m/z = 469.2 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.184 (0.68), 1.533 (0.84), 1.549 (0.77), 1.580 (3.47), 1.589 (6.33), 1.595 (4.79), 1.605 (6.10), 1.852 (2.06), 1.863 (2.83), 1.878 (2.87), 1.895 (1.40), 1.937 (2.77), 1.948 (2.73), 1.961 (1.66), 1.975 (0.62), 2.159 (1.26), 2.294 (10.47), 2.373 (1.94), 2.378 (1.35), 2.401 (6.22), 2.571 (16.00), 2.726 (2.76), 2.741 (5.10), 2.757 (2.60), 2.924

(0.48), 3.629 (3.04), 3.635 (2.70), 3.645 (4.93), 3.650 (3.79), 3.659 (2.75), 3.728 (0.70), 4.805 (0.49), 4.821 (0.67), 4.837 (0.83), 4.852 (1.08), 4.868 (1.18), 4.883 (0.85), 6.931 (0.49), 7.386 (1.14), 7.401 (1.64), 7.406 (2.32), 7.420 (2.23), 7.453 (0.59), 7.744 (0.60), 7.917 (1.53), 7.945 (2.75), 8.019 (3.33), 8.031 (1.41), 8.059 (1.26), 8.164 (0.73), 8.187 (0.94), 9.012 (2.30), 9.047 (0.75), 9.433 (1.76).

Example 43

5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



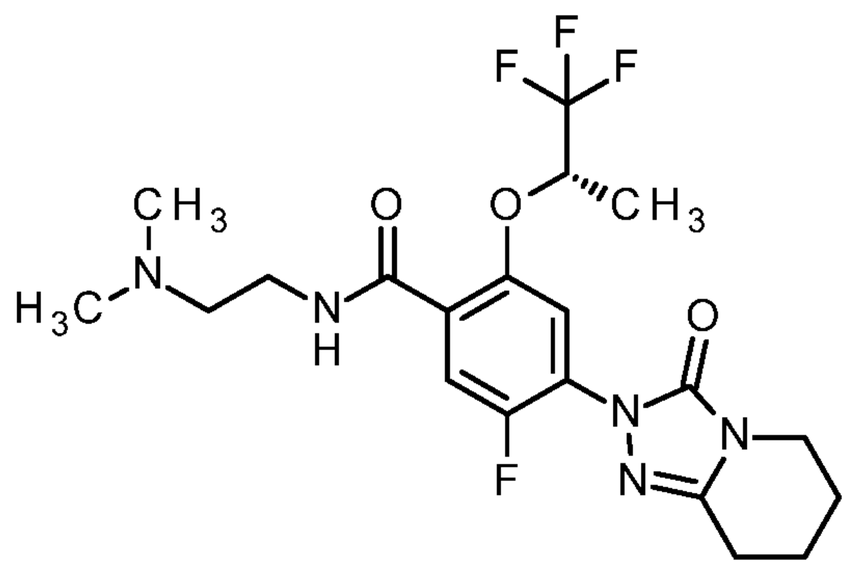
From intermediate 17 and 3-fluoro-2-methylaniline.

LC-MS (method A): R_t = 1.27 min; MS (ESIpos): m/z = 497 $[M-H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.504 (16.00), 1.554 (3.10), 1.570 (3.08), 1.854 (0.54), 1.866 (0.72), 1.877 (0.73), 1.881 (0.78), 1.934 (0.71), 1.939 (0.74), 1.949 (0.79), 1.954 (0.64), 1.963 (0.48), 2.142 (4.42), 2.146 (4.41), 2.730 (1.10), 2.747 (2.14), 2.762 (1.23), 3.638 (1.42), 3.654 (2.31), 3.669 (1.01), 4.824 (0.50), 4.840 (0.65), 4.855 (0.48), 6.833 (0.44), 6.855 (0.89), 6.877 (0.51), 7.133 (0.62), 7.149 (0.62), 7.407 (1.30), 7.422 (1.30), 7.605 (0.93), 7.625 (0.86), 8.061 (1.61), 8.091 (1.62), 9.008 (0.83).

Example 44

N-[2-(dimethylamino)ethyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



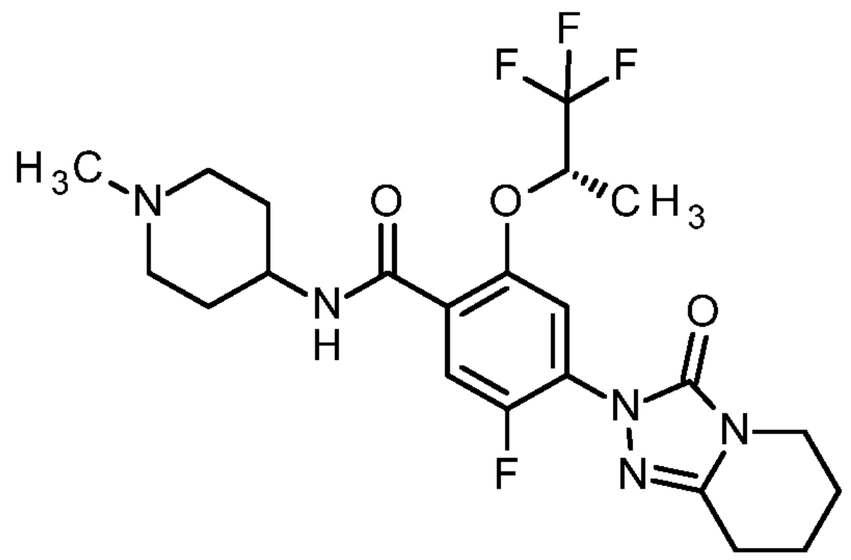
From intermediate 17 and N,N-dimethylethane-1,2-diamine.

LC-MS (method B): R_t = 1.04 min; MS (ESIpos): m/z = 459.8 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.436 (0.45), 1.449 (0.75), 1.464 (0.62), 1.523 (13.22), 1.539 (13.33), 1.824 (0.94), 1.830 (1.22), 1.838 (2.56), 1.846 (3.02), 1.851 (3.46), 1.862 (3.45), 1.866 (3.76), 1.878 (1.73), 1.882 (1.83), 1.903 (1.86), 1.910 (1.81), 1.919 (3.39), 1.923 (3.56), 1.934 (3.73), 1.939 (3.12), 1.945 (2.26), 1.948 (2.32), 1.962 (1.07), 2.247 (0.41), 2.366 (16.00), 2.655 (2.48), 2.711 (5.18), 2.726 (9.50), 2.742 (5.45), 2.810 (1.37), 2.854 (1.32), 3.034 (1.50), 3.598 (2.63), 3.608 (2.70), 3.620 (7.79), 3.636 (10.88), 3.650 (4.81), 4.715 (0.99), 4.731 (2.28), 4.746 (3.01), 4.762 (2.20), 4.777 (0.89), 7.282 (6.13), 7.296 (6.17), 7.886 (1.28), 7.899 (2.19), 7.911 (1.23), 7.937 (6.99), 7.966 (6.77).

Example 45

5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 1-methylpiperidin-4-amine.

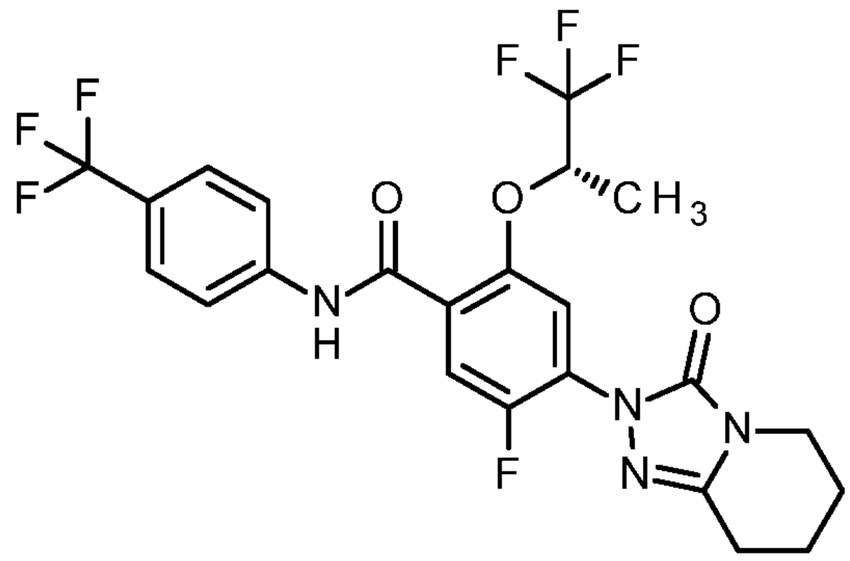
LC-MS (method A): R_t = 0.72 min; MS (ESIpos): m/z = 486.1 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.510 (13.94), 1.526 (13.91), 1.647 (1.39), 1.671 (1.57), 1.824 (0.89), 1.831 (1.11), 1.839 (2.41), 1.847 (2.81), 1.852 (3.22), 1.863 (3.26), 1.867 (3.54), 1.879 (1.60), 1.883 (1.72), 1.905 (1.71), 1.911 (1.63), 1.920 (3.19), 1.925 (3.34),

1.935 (3.53), 1.940 (2.89), 1.949 (2.27), 1.963 (1.05), 1.994 (1.47), 2.010 (0.95), 2.032 (2.32), 2.068 (1.25), 2.254 (1.85), 2.345 (16.00), 2.550 (0.58), 2.712 (4.93), 2.728 (9.27), 2.744 (5.48), 2.811 (0.50), 2.893 (1.77), 2.918 (1.64), 3.033 (0.54), 3.619 (6.19), 3.635 (10.03), 3.650 (4.44), 3.919 (0.45), 3.936 (0.86), 3.945 (1.06), 3.954 (0.94), 3.963 (1.06), 3.973 (0.84), 3.990 (0.44), 4.713 (0.93), 4.728 (2.21), 4.743 (2.85), 4.759 (2.09), 4.774 (0.85), 7.273 (6.29), 7.287 (6.21), 7.434 (2.21), 7.453 (2.17), 7.968 (8.02), 7.997 (7.92).

Example 46

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[4-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



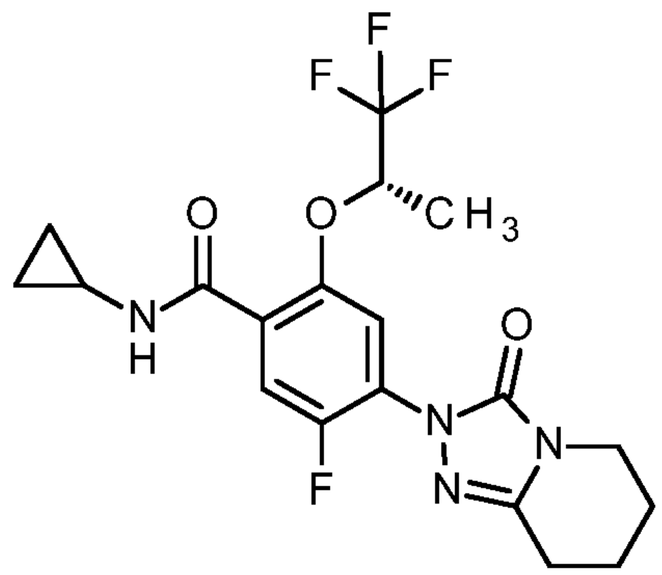
From intermediate 17 and 4-(trifluoromethyl)aniline.

LC-MS (method A): R_t = 1.38 min; MS (ESIpos): m/z = 533 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.513 (16.00), 1.585 (3.48), 1.599 (3.49), 1.857 (0.66), 1.862 (0.66), 1.867 (0.88), 1.875 (0.79), 1.879 (0.95), 1.936 (0.82), 1.941 (0.76), 1.948 (0.99), 1.953 (0.69), 1.960 (0.57), 2.732 (1.29), 2.745 (2.43), 2.758 (1.38), 3.638 (1.63), 3.651 (2.69), 3.663 (1.23), 4.853 (0.54), 4.865 (0.69), 4.877 (0.51), 7.406 (1.56), 7.417 (1.53), 7.550 (1.68), 7.567 (2.06), 7.711 (1.94), 7.728 (1.53), 8.089 (1.84), 8.113 (1.77), 9.557 (1.01).

Example 47

N-cyclopropyl-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



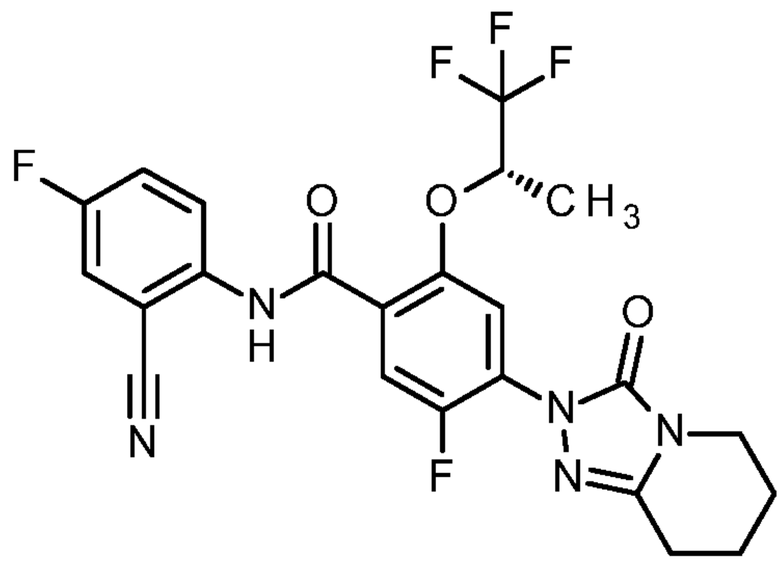
From intermediate 17 and cyclopropanamine.

LC-MS (method A): R_t = 1.04 min; MS (ESIpos): m/z = 429.2 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.500 (0.91), 0.503 (0.94), 0.508 (0.86), 0.510 (0.93), 0.514 (0.96), 0.516 (0.89), 0.526 (0.42), 0.777 (0.46), 0.781 (1.02), 0.785 (1.02), 0.799 (1.23), 0.801 (0.76), 1.483 (2.67), 1.498 (2.76), 1.515 (16.00), 1.838 (0.43), 1.845 (0.49), 1.850 (0.58), 1.861 (0.58), 1.865 (0.64), 1.918 (0.57), 1.923 (0.59), 1.933 (0.64), 1.939 (0.51), 2.710 (0.94), 2.726 (1.77), 2.742 (1.04), 2.903 (0.61), 2.913 (0.60), 3.617 (1.19), 3.633 (1.90), 3.648 (0.85), 4.694 (0.45), 4.709 (0.59), 4.725 (0.43), 7.251 (1.25), 7.265 (1.21), 8.001 (1.54), 8.030 (1.52).

Example 48

N-(2-cyano-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



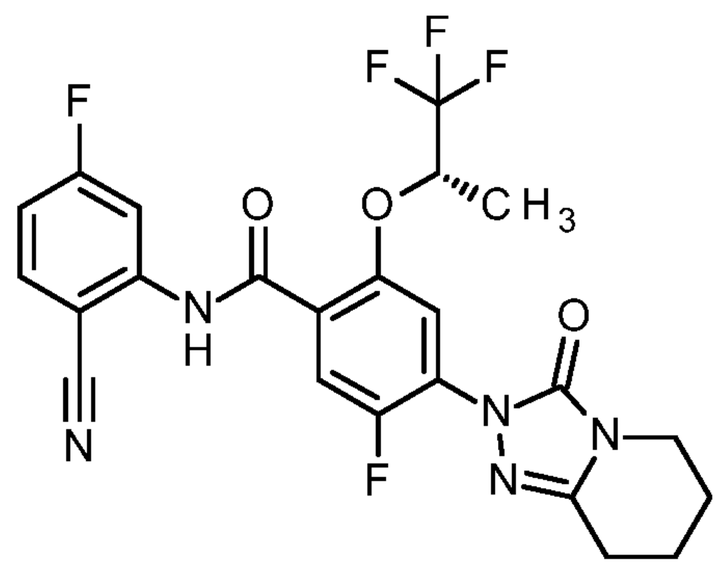
From intermediate 17 and 2-amino-5-fluorobenzonitrile.

LC-MS (method A): R_t = 1.21 min; MS (ESIpos): m/z = 508 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.497 (16.00), 1.674 (1.05), 1.690 (1.06), 2.747 (0.72), 2.762 (0.42), 3.638 (0.48), 3.653 (0.79), 7.269 (0.42), 7.288 (0.41), 7.439 (0.50), 7.453 (0.55), 8.016 (0.63), 8.044 (0.64).

Example 49

N-(2-cyano-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



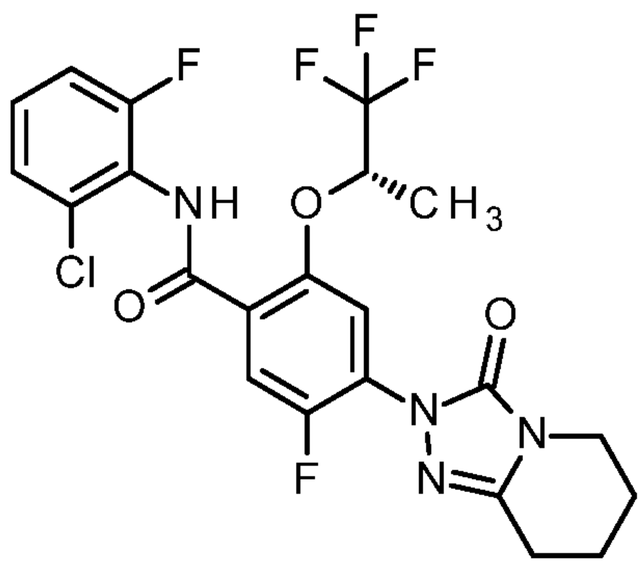
From intermediate 17 and 2-amino-4-fluorobenzonitrile.

LC-MS (method A): R_t = 1.25 min; MS (ESIpos): m/z = 508 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.496 (16.00), 1.695 (1.63), 1.711 (1.65), 1.882 (0.41), 1.949 (0.40), 2.731 (0.60), 2.747 (1.13), 2.763 (0.67), 3.638 (0.72), 3.654 (1.21), 3.669 (0.52), 7.450 (0.81), 7.465 (0.77), 7.543 (0.55), 7.557 (0.56), 7.564 (0.54), 7.579 (0.52), 7.983 (1.04), 8.012 (1.02), 8.334 (0.47), 8.340 (0.50), 8.362 (0.48), 8.368 (0.47), 9.792 (0.48).

Example 50

N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



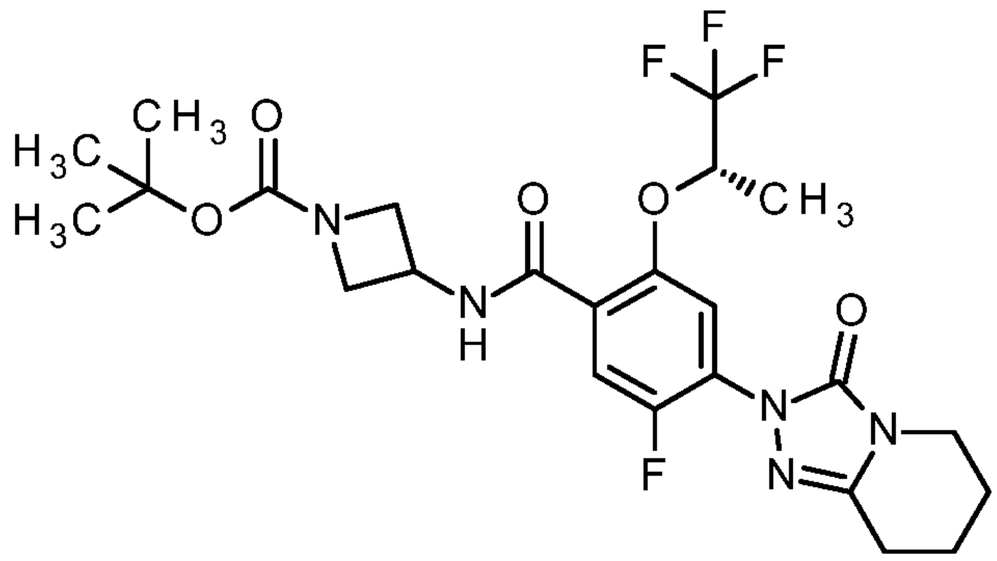
From intermediate 17 and 2-chloro-6-fluoroaniline.

LC-MS (method A): R_t = 1.24 min; MS (ESIpos): m/z = 517 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.260 (2.60), 1.566 (15.66), 1.651 (15.46), 1.667 (16.00), 1.914 (0.91), 1.920 (1.16), 1.928 (2.65), 1.936 (3.12), 1.941 (3.61), 1.953 (3.68), 1.956 (3.99), 1.960 (2.64), 1.968 (1.74), 1.972 (1.87), 1.993 (1.84), 1.999 (1.68), 2.009 (3.52), 2.014 (3.68), 2.024 (3.94), 2.030 (3.17), 2.035 (2.27), 2.038 (2.38), 2.045 (1.34), 2.052 (1.06), 2.807 (5.60), 2.824 (10.65), 2.840 (6.20), 3.713 (7.20), 3.729 (11.72), 3.744 (5.11), 4.918 (1.08), 4.934 (2.52), 4.949 (3.27), 4.964 (2.42), 4.979 (0.98), 7.006 (0.73), 7.109 (2.08), 7.112 (2.21), 7.129 (3.34), 7.133 (4.49), 7.136 (2.62), 7.152 (2.91), 7.156 (3.08), 7.216 (2.02), 7.230 (1.97), 7.237 (4.68), 7.250 (4.82), 7.257 (3.44), 7.281 (5.08), 7.285 (6.29), 7.288 (5.16), 7.302 (2.07), 7.305 (2.58), 7.308 (2.15), 7.502 (6.93), 7.516 (6.96), 7.528 (0.77), 8.170 (7.37), 8.199 (7.34), 9.033 (4.66).

Example 51

tert-butyl 3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}azetidine-1-carboxylate



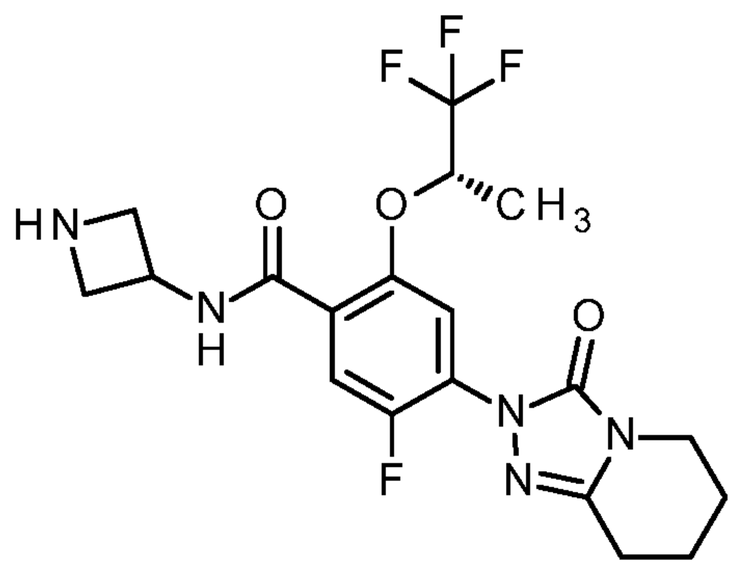
From intermediate 17 and tert-butyl 3-aminoazetidine-1-carboxylate.

LC-MS (method A): R_t = 1.18 min; MS (ESIpos): m/z = 544 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.378 (16.00), 1.403 (1.63), 1.420 (1.61), 2.518 (0.78), 2.523 (0.58), 2.682 (0.48), 2.698 (0.94), 2.715 (0.51), 3.547 (0.56), 3.563 (1.01), 3.577 (0.44), 7.458 (0.74), 7.473 (0.73), 7.499 (0.96), 7.525 (0.93), 8.786 (0.50), 8.803 (0.49).

Example 52

N-(azetidin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



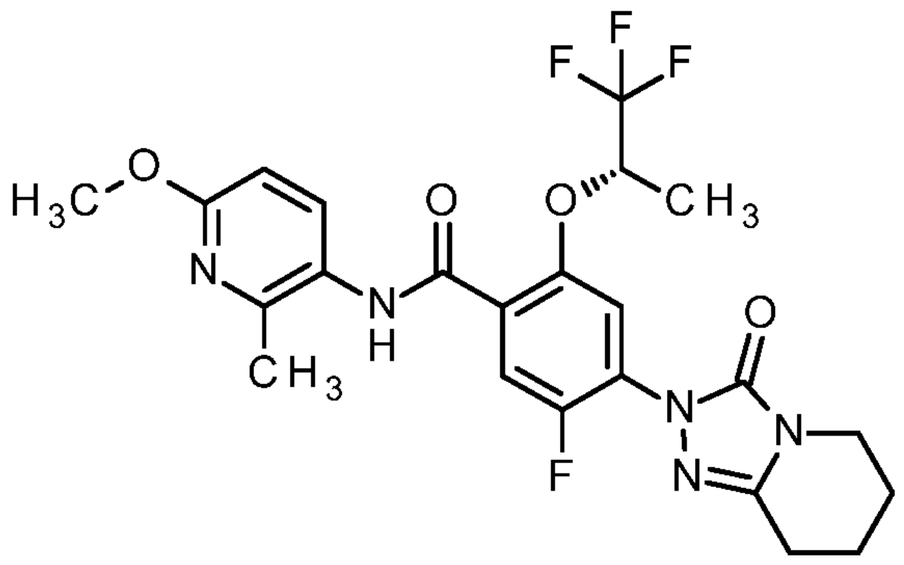
To a room temperature stirred solution of tert-butyl 3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}azetidine-1-carboxylate (example 51) (56.3 mg, 0.10 mmol, 1.00 eq.) in dichloromethane (0.50 ml) was added trifluoroacetic acid (0.12 ml). The resulting mixture was stirred at room temperature for 1 hour and then concentrated under reduced pressure to give a colourless oil. The residue was dissolved in DMSO, filtered through a teflon filter and purified by reverse phase column chromatography (15-55% acetonitrile, 0.1 % aqueous ammonia) to give the title compound as an off white solid (13.7 mg, 28 %).

LC-MS (method A): R_t = 0.70 min; MS (ESIpos): m/z = 444.4 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.000 (0.53), 0.811 (0.53), 1.149 (0.41), 1.158 (4.66), 1.165 (0.51), 1.175 (10.45), 1.184 (2.82), 1.193 (5.41), 1.209 (0.72), 1.227 (0.68), 1.543 (7.53), 1.560 (10.35), 1.567 (15.08), 1.583 (14.09), 1.827 (1.49), 1.843 (4.17), 1.854 (5.70), 1.866 (5.72), 1.870 (6.08), 1.882 (2.89), 1.886 (2.94), 1.909 (2.90), 1.914 (3.11), 1.923 (5.48), 1.928 (6.01), 1.939 (5.94), 1.943 (5.34), 1.950 (3.77), 1.957 (3.65), 1.966 (1.52), 1.978 (0.53), 1.994 (0.51), 2.557 (16.00), 2.646 (1.88), 2.668 (0.63), 2.715 (7.65), 2.731 (14.31), 2.747 (8.08), 2.875 (1.09), 2.923 (1.23), 2.949 (1.37), 3.053 (1.23), 3.456 (0.48), 3.621 (7.02), 3.629 (4.80), 3.636 (11.70), 3.646 (7.94), 3.651 (5.79), 3.664 (5.24), 3.681 (1.74), 3.728 (1.76), 3.742 (1.83), 3.750 (1.84), 3.763 (1.74), 3.888 (0.46), 3.901 (0.51), 3.913 (0.50), 3.927 (0.46), 4.019 (0.43), 4.031 (0.43), 4.044 (0.43), 4.092 (2.78), 4.259 (1.38), 4.267 (1.42), 4.279 (2.25), 4.286 (2.20), 4.301 (1.42), 4.308 (1.37), 4.326 (1.13), 4.339 (1.96), 4.363 (3.16), 4.387 (1.91), 4.412 (0.55), 4.513 (0.48), 4.727 (1.11), 4.742 (2.83), 4.758 (3.88), 4.774 (3.33), 4.791 (1.91), 4.811 (0.67), 4.859 (0.84), 4.877 (1.45), 4.895 (1.40), 4.912 (0.72), 6.931 (0.80), 7.309 (3.42), 7.318 (6.51), 7.323 (4.29), 7.332 (7.15), 7.346 (1.20), 7.454 (0.97), 7.876 (6.03), 7.904 (5.98), 7.936 (1.78), 7.945 (1.02), 7.955 (6.56), 7.974 (0.89), 7.984 (5.05), 8.106 (2.92), 8.123 (2.87), 8.287 (1.33).

Example 53

5-fluoro-N-(6-methoxy-2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 6-methoxy-2-methylpyridin-3-amine.

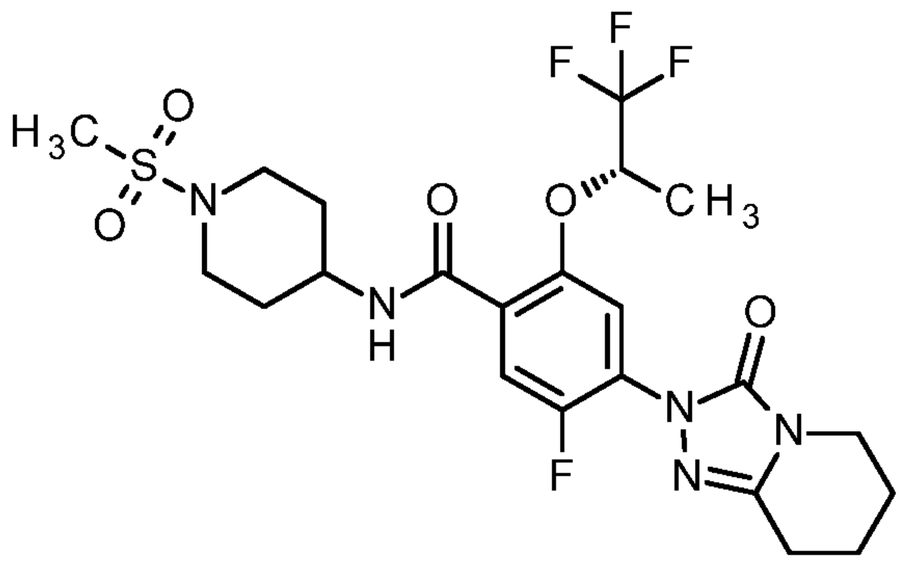
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.24 min; MS (ESIneg): m/z = 508 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.579 (0.96), 1.638 (3.37), 1.654 (3.40), 1.929 (0.54), 1.937 (0.63), 1.941 (0.73), 1.953 (0.75), 1.957 (0.81), 2.010 (0.72), 2.015 (0.77), 2.018 (0.99), 2.025 (0.81), 2.030 (0.66), 2.039 (0.49), 2.446 (9.49), 2.806 (1.15), 2.822 (2.19), 2.838 (1.29), 3.713 (1.47), 3.729 (2.42), 3.744 (1.05), 3.934 (16.00), 4.906 (0.55), 4.922 (0.73), 4.938 (0.52), 6.634 (1.37), 6.655 (1.41), 7.473 (1.49), 7.487 (1.49), 7.931 (1.72), 7.953 (1.62), 8.140 (1.97), 8.169 (1.91), 8.946 (1.11).

Example 54

5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 1-(methylsulfonyl)piperidin-4-amine.

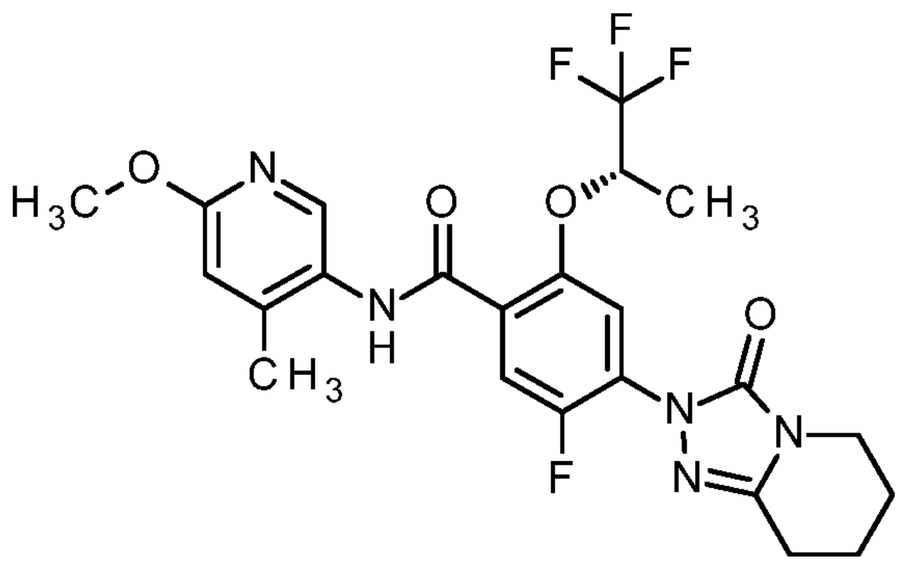
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.06 min; MS (ESIpos): m/z = 551 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.595 (6.63), 1.612 (4.96), 1.630 (0.60), 1.639 (0.80), 1.918 (0.68), 1.930 (0.91), 1.941 (0.92), 1.945 (1.00), 1.957 (0.43), 1.962 (0.47), 1.984 (0.46), 1.990 (0.45), 1.998 (0.91), 2.003 (0.96), 2.014 (1.01), 2.017 (0.95), 2.028 (0.61), 2.140 (0.42), 2.165 (0.79), 2.791 (1.40), 2.806 (2.89), 2.817 (16.00), 2.822 (2.10), 2.838 (0.44), 2.845 (0.75), 2.850 (0.48), 2.874 (1.33), 2.898 (0.48), 2.904 (0.72), 3.698 (1.75), 3.713 (2.94), 3.728 (1.27), 3.801 (0.98), 3.832 (0.94), 4.093 (0.43), 4.111 (0.43), 4.817 (0.68), 4.832 (0.87), 4.847 (0.64), 7.362 (1.90), 7.376 (1.87), 7.549 (0.76), 7.567 (0.75), 8.050 (2.34), 8.079 (2.33).

Example 55

5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 6-methoxy-4-methylpyridin-3-amine.

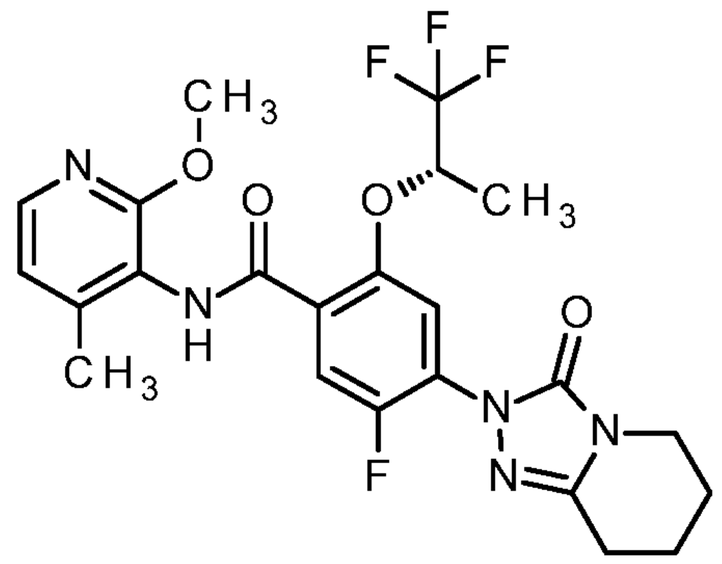
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.20 min; MS (ESIpos): m/z = 511 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.599 (0.49), 1.637 (3.77), 1.653 (3.74), 1.927 (0.60), 1.935 (0.70), 1.939 (0.82), 1.951 (0.83), 1.955 (0.90), 1.971 (0.42), 1.993 (0.42), 2.008 (0.80), 2.013 (0.85), 2.017 (1.34), 2.023 (0.91), 2.028 (0.74), 2.037 (0.54), 2.261 (8.80), 2.805 (1.25), 2.820 (2.43), 2.836 (1.39), 3.711 (1.62), 3.726 (2.64), 3.741 (1.15), 3.940 (16.00), 4.896 (0.61), 4.911 (0.80), 4.927 (0.58), 6.666 (2.45), 7.473 (1.64), 7.488 (1.65), 8.132 (2.12), 8.161 (2.11), 8.335 (2.99), 8.875 (1.25).

Example 56

5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 2-methoxy-4-methylpyridin-3-amine.

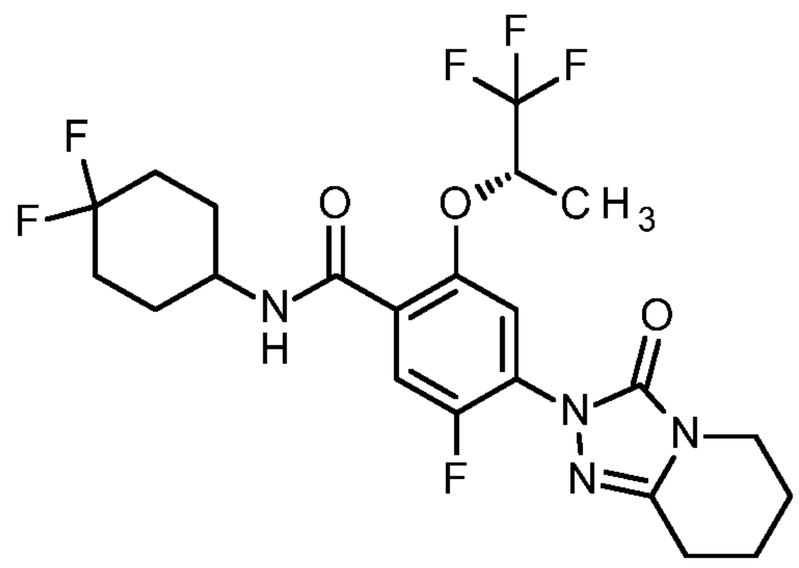
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.22 min; MS (ESIneg): m/z = 508 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.605 (0.71), 1.652 (3.93), 1.669 (3.92), 1.927 (0.63), 1.934 (0.73), 1.939 (0.86), 1.951 (0.86), 1.955 (0.94), 1.967 (0.40), 1.971 (0.44), 1.992 (0.44), 1.998 (0.41), 2.007 (0.84), 2.012 (0.89), 2.017 (0.63), 2.023 (0.94), 2.028 (0.76), 2.036 (0.57), 2.278 (11.08), 2.805 (1.33), 2.821 (2.56), 2.837 (1.48), 3.713 (1.74), 3.728 (2.82), 3.743 (1.22), 3.958 (16.00), 4.919 (0.64), 4.935 (0.83), 4.950 (0.60), 6.826 (1.67), 6.838 (1.71), 7.464 (1.73), 7.479 (1.68), 7.954 (2.20), 7.967 (2.13), 8.128 (2.21), 8.157 (2.19), 8.972 (1.33).

Example 57

N-(4,4-difluorocyclohexyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 4,4-difluorocyclohexanamine.

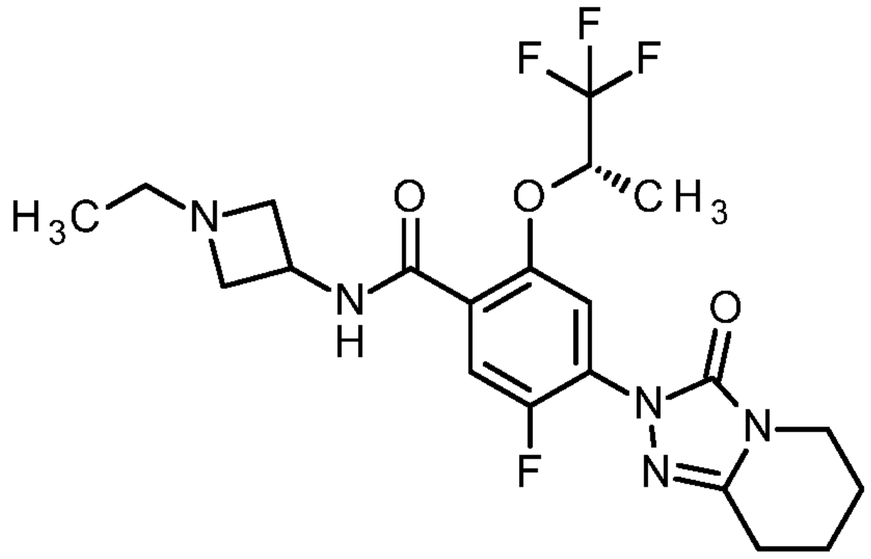
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 507 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.261 (0.55), 1.580 (16.00), 1.589 (13.98), 1.605 (12.82), 1.626 (2.04), 1.650 (1.01), 1.847 (0.51), 1.881 (1.07), 1.903 (1.26), 1.909 (1.53), 1.918 (2.73), 1.925 (2.88), 1.930 (3.15), 1.941 (3.16), 1.945 (3.53), 1.957 (2.21), 1.961 (2.26), 1.984 (1.89), 1.989 (1.77), 1.998 (2.93), 2.003 (2.85), 2.014 (2.88), 2.019 (2.37), 2.028 (1.73), 2.042 (0.76), 2.100 (2.55), 2.120 (3.85), 2.142 (2.59), 2.174 (0.57), 2.791 (4.12), 2.806 (7.78), 2.823 (4.59), 3.698 (5.24), 3.713 (8.51), 3.728 (3.72), 4.084 (0.90), 4.102 (0.91), 4.796 (0.84), 4.811 (1.95), 4.827 (2.57), 4.842 (1.85), 4.857 (0.73), 7.357 (5.44), 7.372 (5.39), 7.498 (1.71), 7.517 (1.67), 7.529 (0.60), 8.055 (6.90), 8.084 (6.82).

Example 58

N-(1-ethylazetidin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



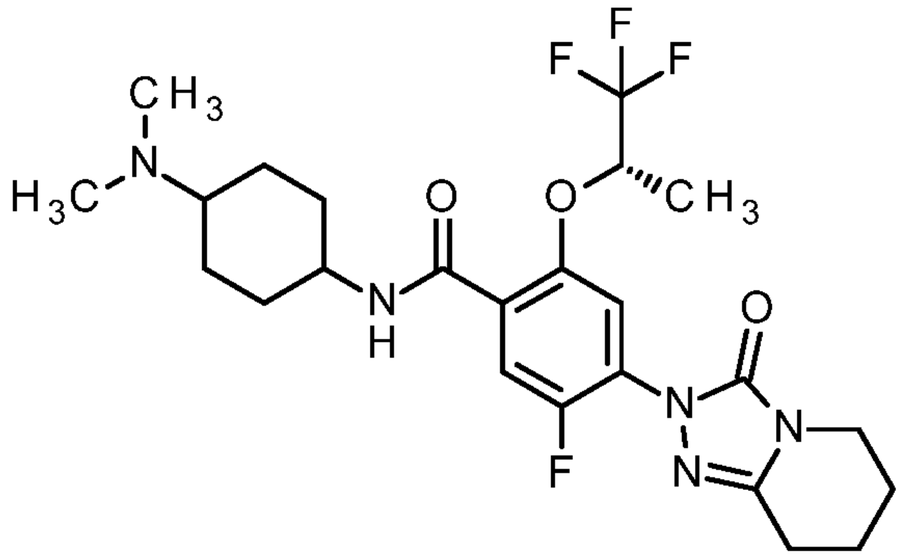
From intermediate 17 and 1-ethylazetidin-3-amine.

LC-MS (method A): R_t = 0.75 min; MS (ESIpos): m/z = 472 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.972 (7.23), 0.990 (16.00), 1.008 (7.51), 1.450 (0.44), 1.466 (0.47), 1.608 (10.98), 1.625 (11.42), 1.902 (0.62), 1.909 (0.81), 1.917 (1.78), 1.925 (2.14), 1.930 (2.38), 1.941 (2.49), 1.945 (2.59), 1.957 (1.13), 1.961 (1.20), 1.983 (1.22), 1.990 (1.23), 1.998 (2.38), 2.003 (2.44), 2.014 (2.59), 2.019 (2.08), 2.028 (1.53), 2.042 (0.63), 2.463 (1.44), 2.480 (4.24), 2.499 (4.10), 2.517 (1.32), 2.789 (3.85), 2.806 (7.19), 2.822 (5.32), 2.836 (2.60), 2.853 (1.44), 2.886 (2.16), 3.110 (2.62), 3.698 (4.87), 3.713 (8.03), 3.728 (3.47), 3.763 (2.51), 3.781 (4.08), 3.784 (4.03), 3.801 (2.45), 4.723 (1.31), 4.740 (2.43), 4.758 (2.40), 4.775 (1.22), 4.803 (0.72), 4.818 (1.70), 4.834 (2.21), 4.849 (1.61), 4.865 (0.65), 7.006 (0.41), 7.360 (4.90), 7.374 (4.76), 7.528 (0.42), 7.827 (1.52), 7.845 (1.50), 8.039 (6.09), 8.067 (5.99).

Example 59

N-[4-(dimethylamino)cyclohexyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and N,N-dimethylcyclohexane-1,4-diamine.

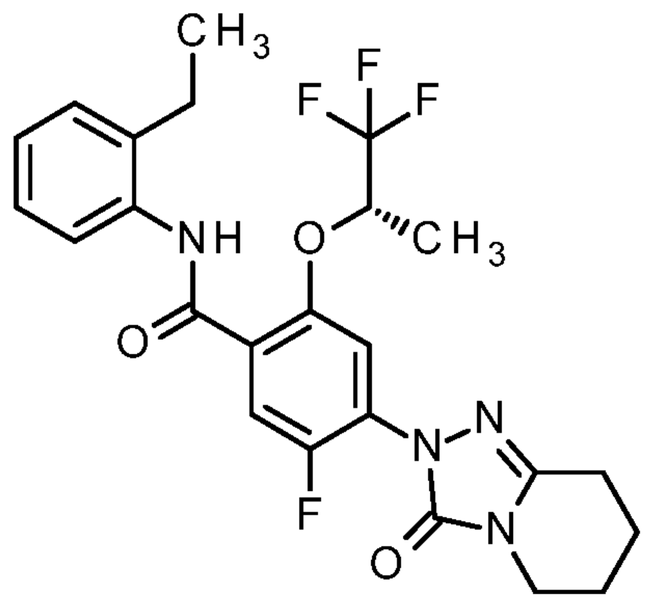
LC-MS (method A): R_t = 0.77 min; MS (ESIneg): m/z = 512 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.240 (0.49), 1.249 (0.55), 1.255 (0.58), 1.264 (0.58), 1.270 (0.59), 1.278 (0.61), 1.285 (0.61), 1.293 (0.57), 1.466 (0.83), 1.496 (0.79), 1.571 (4.85), 1.587 (4.91), 1.908 (0.81), 1.920 (1.12), 1.931 (1.13), 1.935 (1.21), 1.947 (0.55), 1.951 (0.57), 1.973 (0.57), 1.979 (0.56), 1.988 (1.10), 1.993 (1.16), 2.003 (1.24), 2.010 (1.73), 2.018 (0.88), 2.024 (0.66), 2.033 (0.87), 2.042 (0.84), 2.049 (0.80), 2.057 (0.72), 2.067 (0.73), 2.074 (0.74), 2.189 (0.88), 2.197 (0.91), 2.221 (0.88), 2.229 (0.82), 2.447 (16.00), 2.780 (1.59), 2.796 (3.13), 2.812 (1.77), 3.686 (1.98), 3.702 (3.36), 3.717 (1.47), 3.910 (0.50), 3.919 (0.40), 3.929 (0.50), 4.791 (0.78), 4.806 (1.00), 4.822 (0.73), 7.333 (2.17), 7.348 (2.13), 7.437 (0.91), 7.457 (0.89), 8.043 (2.63), 8.072 (2.57), 8.574 (2.09).

Example 60

N-(2-ethylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide

320



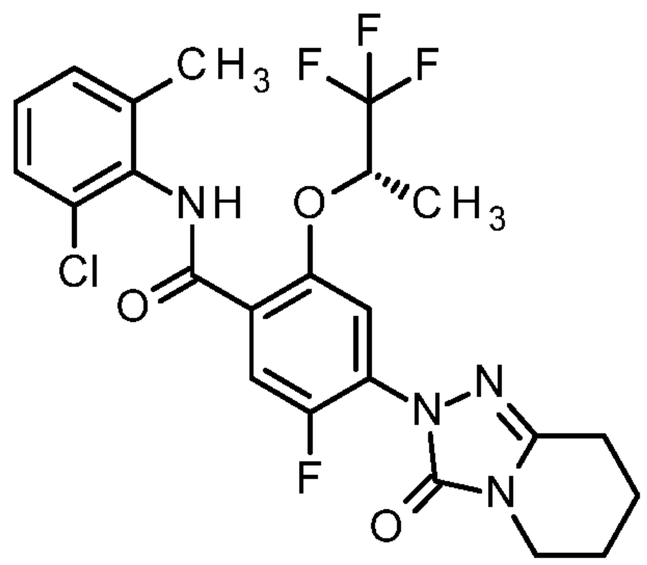
From intermediate 17 and 2-ethylaniline.

LC-MS (method A): R_t = 1.31 min; MS (ESIpos): m/z = 493 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.226 (5.00), 1.245 (10.79), 1.264 (5.32), 1.579 (16.00), 1.619 (6.34), 1.635 (6.33), 1.928 (1.08), 1.941 (1.49), 1.956 (1.59), 1.972 (0.76), 1.993 (0.77), 2.009 (1.47), 2.014 (1.51), 2.024 (1.62), 2.038 (0.97), 2.052 (0.40), 2.639 (1.25), 2.657 (3.50), 2.676 (3.34), 2.695 (1.07), 2.805 (2.14), 2.822 (4.13), 2.838 (2.33), 3.715 (2.70), 3.730 (4.44), 3.745 (1.98), 4.871 (0.44), 4.887 (1.05), 4.903 (1.34), 4.918 (1.00), 7.188 (0.58), 7.204 (1.84), 7.223 (1.55), 7.226 (1.49), 7.257 (1.44), 7.295 (2.09), 7.471 (2.68), 7.485 (2.61), 7.814 (2.01), 7.834 (1.68), 8.139 (3.15), 8.167 (3.08), 9.016 (1.80).

Example 61

N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 2-chloro-6-methylaniline.

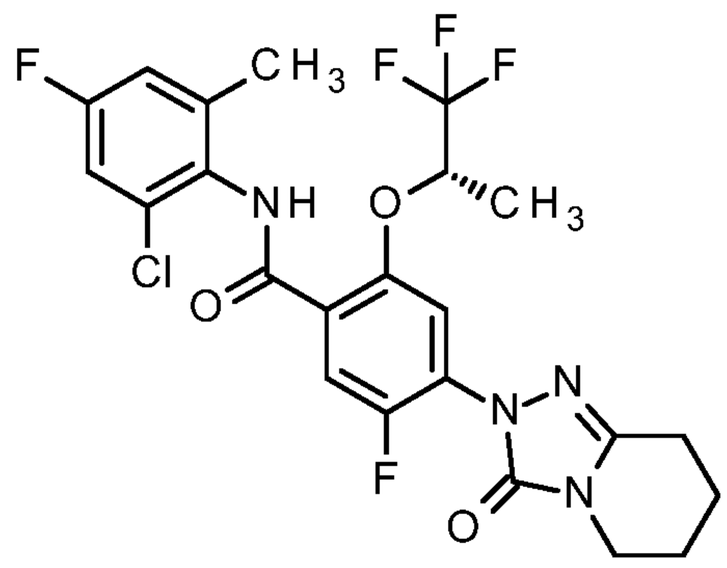
LC-MS (method A): R_t = 1.28 min; MS (ESIneg): m/z = 511 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.652 (6.60), 1.668 (6.61), 1.918 (0.48), 1.926 (1.08), 1.938 (1.46), 1.949 (1.45), 1.953 (1.58), 1.965 (0.69), 1.969 (0.75), 1.991 (0.75), 1.997 (0.71), 2.006 (1.43), 2.011 (1.50), 2.021 (1.58), 2.026 (1.27), 2.035 (0.95), 2.049 (0.40), 2.318

(16.00), 2.804 (2.17), 2.820 (4.13), 2.836 (2.38), 3.711 (2.69), 3.727 (4.55), 3.742 (1.96), 4.929 (0.43), 4.944 (1.03), 4.959 (1.33), 4.975 (0.98), 7.155 (0.85), 7.174 (2.83), 7.193 (3.57), 7.198 (1.99), 7.202 (2.55), 7.218 (0.76), 7.222 (0.52), 7.315 (1.63), 7.319 (1.67), 7.333 (1.20), 7.338 (1.22), 7.475 (2.72), 7.489 (2.72), 8.157 (3.48), 8.186 (3.42), 8.987 (2.03).

Example 62

N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



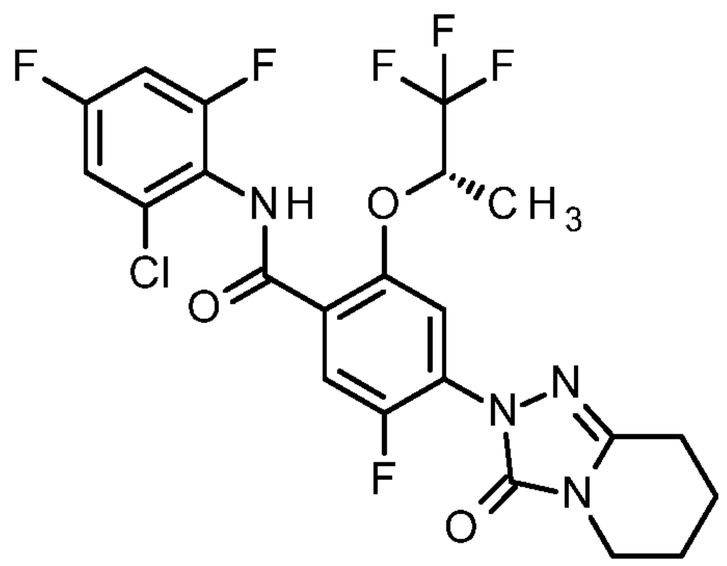
From intermediate 17 and 2-chloro-4-fluoro-6-methylaniline.

LC-MS (method A): R_t = 1.30 min; MS (ESIpos): m/z = 531 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.576 (16.00), 1.653 (5.89), 1.669 (5.93), 1.930 (0.98), 1.942 (1.33), 1.954 (1.31), 1.957 (1.44), 1.973 (0.69), 1.995 (0.68), 2.010 (1.30), 2.014 (1.37), 2.025 (1.47), 2.030 (1.17), 2.039 (0.88), 2.310 (14.34), 2.807 (2.01), 2.824 (3.83), 2.840 (2.23), 3.715 (2.54), 3.730 (4.23), 3.745 (1.83), 4.927 (0.40), 4.942 (0.95), 4.958 (1.24), 4.973 (0.91), 6.935 (1.08), 6.941 (1.19), 6.957 (1.08), 6.964 (1.16), 7.073 (1.29), 7.080 (1.19), 7.093 (1.31), 7.100 (1.17), 7.479 (2.56), 7.493 (2.55), 8.144 (3.18), 8.172 (3.23), 8.885 (1.84).

Example 63

N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



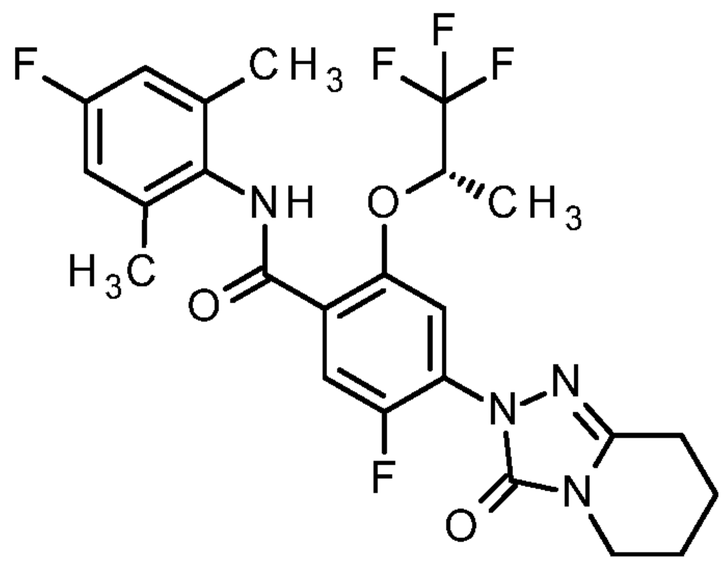
From intermediate 17 and 2-chloro-4,6-difluoroaniline.

LC-MS (method A): R_t = 1.28 min; MS (ESIpos): m/z = 535 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.595 (9.60), 1.645 (15.98), 1.662 (16.00), 1.911 (0.94), 1.927 (2.68), 1.939 (3.69), 1.951 (3.67), 1.954 (3.96), 1.970 (1.88), 1.992 (1.88), 2.007 (3.61), 2.012 (3.78), 2.022 (4.01), 2.027 (3.24), 2.037 (2.42), 2.051 (1.01), 2.626 (0.75), 2.805 (5.37), 2.821 (10.44), 2.837 (5.90), 3.711 (6.68), 3.726 (11.35), 3.741 (4.92), 4.917 (1.06), 4.932 (2.48), 4.948 (3.22), 4.963 (2.38), 4.978 (0.96), 6.888 (2.03), 6.895 (2.27), 6.911 (2.80), 6.916 (2.94), 6.918 (2.89), 6.933 (2.04), 6.940 (2.18), 7.067 (2.50), 7.071 (2.82), 7.074 (2.87), 7.077 (2.61), 7.086 (2.64), 7.090 (2.78), 7.093 (2.89), 7.097 (2.37), 7.501 (6.61), 7.515 (6.57), 8.148 (7.17), 8.176 (7.23), 8.926 (5.40).

Example 64

5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 4-fluoro-2,6-dimethylaniline.

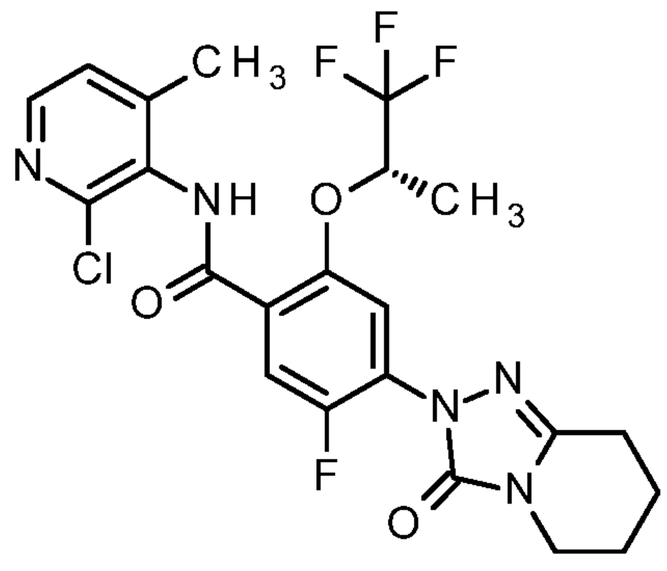
LC-MS (method A): R_t = 1.28 min; MS (ESIpos): m/z = 511 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.606 (1.52), 1.643 (3.27), 1.658 (3.29), 1.929 (0.54), 1.937 (0.62), 1.941 (0.72), 1.953 (0.73), 1.957 (0.80), 2.010 (0.71), 2.015 (0.74), 2.025 (0.79), 2.030 (0.64), 2.039 (0.48), 2.252 (16.00), 2.806 (1.16), 2.823 (2.17), 2.839 (1.28), 3.714

(1.48), 3.729 (2.41), 3.744 (1.04), 4.939 (0.53), 4.955 (0.69), 4.970 (0.50), 6.830 (2.17), 6.853 (2.15), 7.457 (1.45), 7.471 (1.46), 8.143 (1.96), 8.171 (1.93), 8.645 (0.92).

Example 65

N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



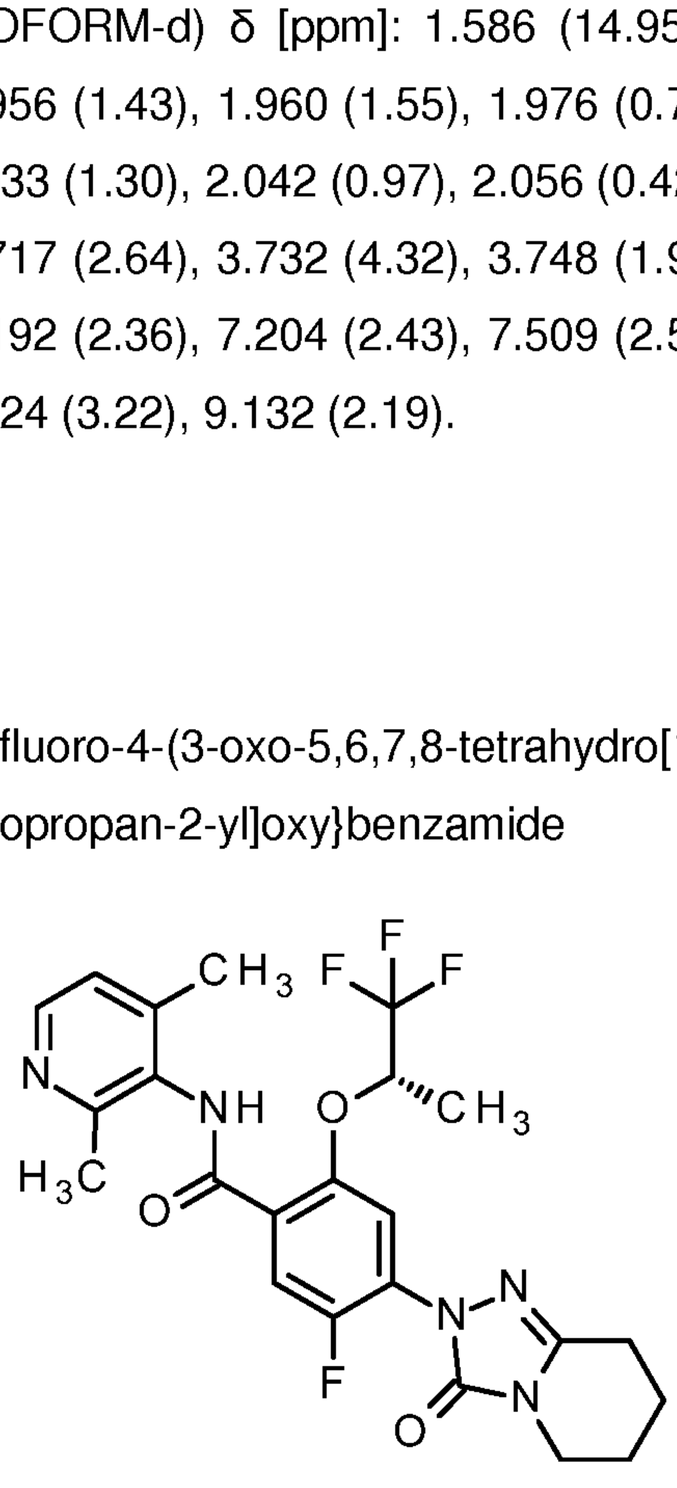
From intermediate 17 and 2-chloro-4-methylpyridin-3-amine.

LC-MS (method A): R_t = 1.11 min; MS (ESIneg): m/z = 512 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.586 (14.95), 1.677 (6.12), 1.693 (6.15), 1.933 (1.03), 1.945 (1.40), 1.956 (1.43), 1.960 (1.55), 1.976 (0.73), 1.998 (0.74), 2.013 (1.40), 2.017 (1.46), 2.028 (1.55), 2.033 (1.30), 2.042 (0.97), 2.056 (0.42), 2.349 (16.00), 2.810 (2.06), 2.827 (4.02), 2.843 (2.31), 3.717 (2.64), 3.732 (4.32), 3.748 (1.94), 4.950 (0.43), 4.965 (0.97), 4.981 (1.27), 4.996 (0.93), 7.192 (2.36), 7.204 (2.43), 7.509 (2.59), 7.523 (2.58), 8.149 (3.33), 8.178 (3.33), 8.212 (3.22), 8.224 (3.22), 9.132 (2.19).

Example 66

N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



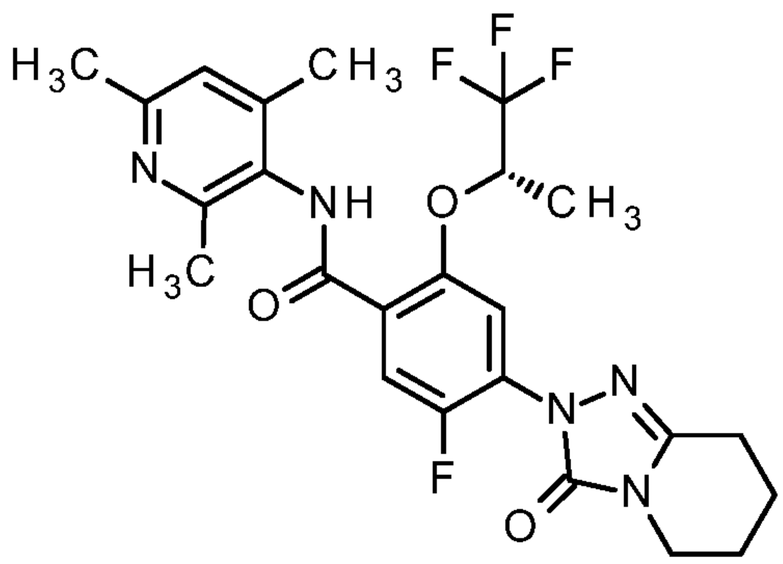
From intermediate 17 and 2,4-dimethylpyridin-3-amine.

LC-MS (method A): R_t = 0.81 min; MS (ESIpos): m/z = 494 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.608 (9.87), 1.662 (6.35), 1.678 (6.30), 1.934 (1.08), 1.947 (1.51), 1.962 (1.62), 1.978 (0.81), 2.000 (0.77), 2.019 (1.54), 2.030 (1.61), 2.045 (1.02), 2.058 (0.44), 2.281 (14.78), 2.515 (16.00), 2.626 (2.90), 2.812 (2.01), 2.829 (3.91), 2.845 (2.27), 3.719 (2.48), 3.734 (4.23), 3.750 (1.93), 4.944 (0.43), 4.959 (0.98), 4.974 (1.27), 4.990 (0.92), 7.083 (2.08), 7.096 (2.10), 7.488 (2.53), 7.502 (2.50), 8.159 (3.07), 8.188 (3.08), 8.334 (2.74), 8.346 (2.63), 8.836 (2.11).

Example 67

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-N-(2,4,6-trimethylpyridin-3-yl)benzamide



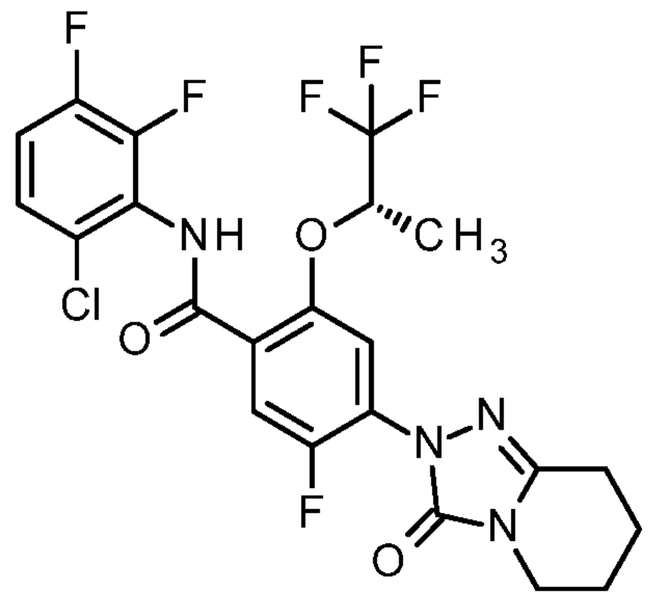
From intermediate 17 and 2,4,6-trimethylpyridin-3-amine.

LC-MS (method A): R_t = 0.79 min; MS (ESIneg): m/z = 506 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.442 (7.39), 1.458 (7.49), 1.729 (2.46), 1.742 (2.56), 1.801 (2.53), 1.812 (2.60), 2.043 (15.52), 2.285 (16.00), 2.328 (15.22), 2.430 (0.46), 2.594 (2.48), 2.609 (4.67), 2.625 (2.61), 3.500 (2.78), 3.516 (4.81), 3.530 (2.46), 4.737 (0.56), 4.753 (1.22), 4.768 (1.56), 4.783 (1.18), 4.798 (0.52), 6.016 (0.59), 6.788 (4.69), 7.071 (1.94), 7.283 (2.70), 7.922 (2.73), 7.950 (2.73), 8.072 (1.90), 8.584 (3.19).

Example 68

N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



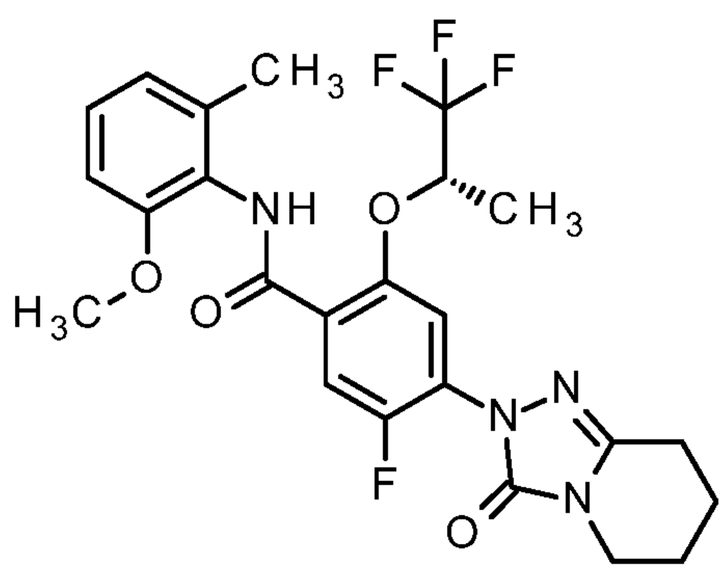
From intermediate 17 and 6-chloro-2,3-difluoroaniline.

LC-MS (method A): R_t = 1.28 min; MS (ESIpos): m/z = 535 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.636 (4.25), 1.653 (16.00), 1.670 (15.48), 1.910 (1.06), 1.926 (2.96), 1.938 (4.26), 1.952 (4.46), 1.968 (2.29), 1.991 (2.20), 2.010 (4.36), 2.021 (4.58), 2.033 (2.92), 2.048 (1.20), 2.803 (4.90), 2.819 (9.54), 2.836 (5.29), 3.709 (5.79), 3.724 (9.99), 3.739 (4.77), 4.932 (1.04), 4.948 (2.42), 4.964 (3.13), 4.979 (2.35), 4.994 (0.98), 7.081 (1.26), 7.103 (3.33), 7.123 (3.55), 7.146 (1.94), 7.211 (2.32), 7.216 (2.47), 7.223 (2.75), 7.228 (2.62), 7.233 (2.05), 7.238 (1.92), 7.245 (1.84), 7.250 (1.72), 7.516 (5.83), 7.530 (5.84), 8.162 (6.02), 8.191 (6.02), 9.091 (5.61).

Example 69

5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 17 and 2-methoxy-6-methylaniline.

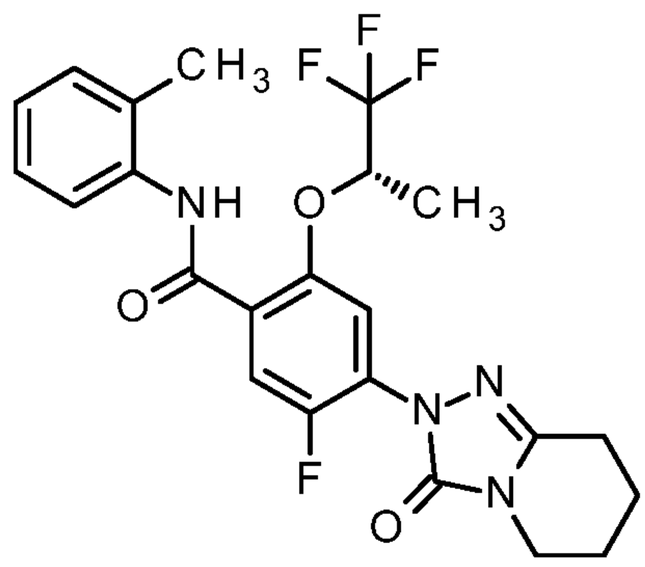
LC-MS (method A): R_t = 1.25 min; MS (ESIneg): m/z = 507 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.720 (5.68), 1.736 (5.77), 2.008 (1.06), 2.020 (1.49), 2.035 (1.57), 2.047 (0.77), 2.051 (0.79), 2.073 (0.77), 2.092 (1.52), 2.103 (1.60), 2.116 (1.00), 2.131 (0.41), 2.375 (13.05), 2.886 (1.84), 2.902 (3.60), 2.918 (2.03), 3.795 (2.23), 3.810

(3.83), 3.825 (1.78), 3.906 (16.00), 5.003 (0.92), 5.018 (1.20), 5.033 (0.89), 6.880 (1.63), 6.901 (1.81), 6.975 (1.59), 6.994 (1.82), 7.250 (1.45), 7.290 (1.14), 7.363 (1.94), 7.532 (2.27), 7.547 (2.29), 8.229 (2.61), 8.258 (2.58), 8.977 (2.03).

Example 70

5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



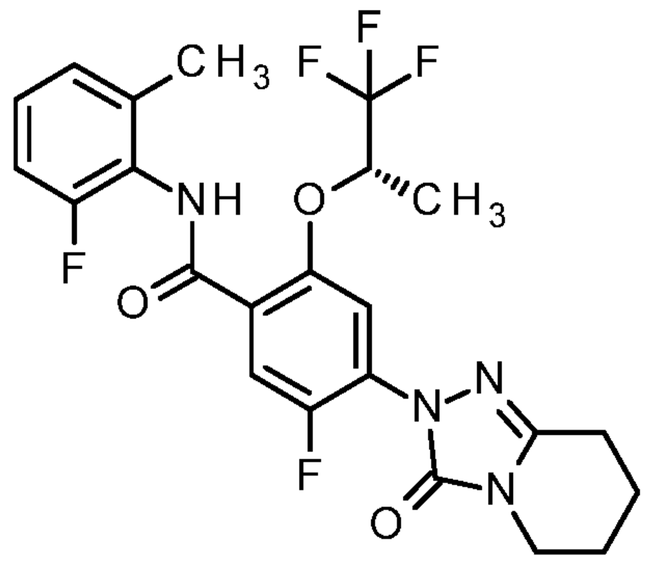
From intermediate 17 and o-toluidine.

MS (ESIpos): m/z = 479 $(M+H)^+$

^{1}H NMR (300 MHz, CDCl3) δ [ppm] 1.62 (d, 3H), 1.86 – 2.06 (m, 4H), 2.31 (s, 3H), 2.81 (t, 2H), 3.71 (t, 2H), 4.82 – 4.97 (m, 1H), 7.13 (t, 1H), 7.20 – 7.30 (m, 2H), 7.46 (d, 1H), 7.89 (d, 1H), 8.14 (d, 1H), 9.02 (s, 1H).

Example 71

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



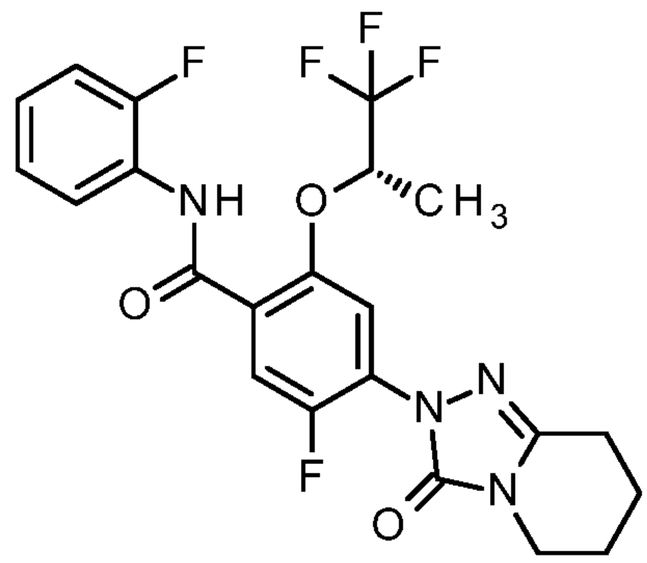
From intermediate 17 and 2-fluoro-6-methylaniline.

MS (ESIpos): m/z = 497 $(M+H)^+$

^{1}H NMR (300 MHz, CDCl3) δ [ppm] 1.66 (d, 3H), 1.90 – 2.08 (m, 4H), 2.33 (s, 3H), 2.83 (t, 2H), 3.74 (t, 2H), 4.87 – 5.02 (m, 1H), 6.97 – 7.12 (m, 2H), 7.21 (dd, 1H), 7.50 (d, 1H), 8.17 (d, 1H), 8.18 (s, 1H).

Example 72

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



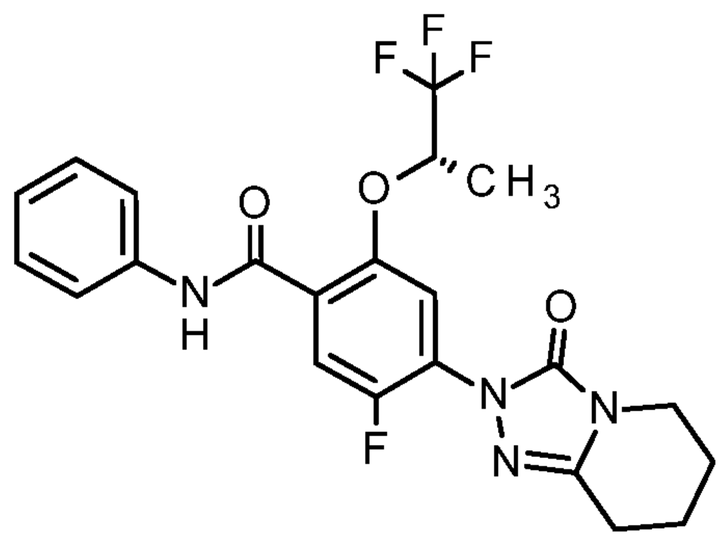
From intermediate 17 and 2-fluoroaniline.

MS (ESIpos): m/z = 483 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.66 (d, 3H), 1.87 – 2.06 (m, 4H), 2.81 (t, 2H), 3.72 (t, 2H), 4.85 – 5.00 (m, 1H), 7.03 – 7.22 (m, 3H), 7.49 (d, 1H), 8.16 (d, 1H), 8.54 (td, 1H), 9.77 (s, 1H).

Example 73

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-phenyl-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



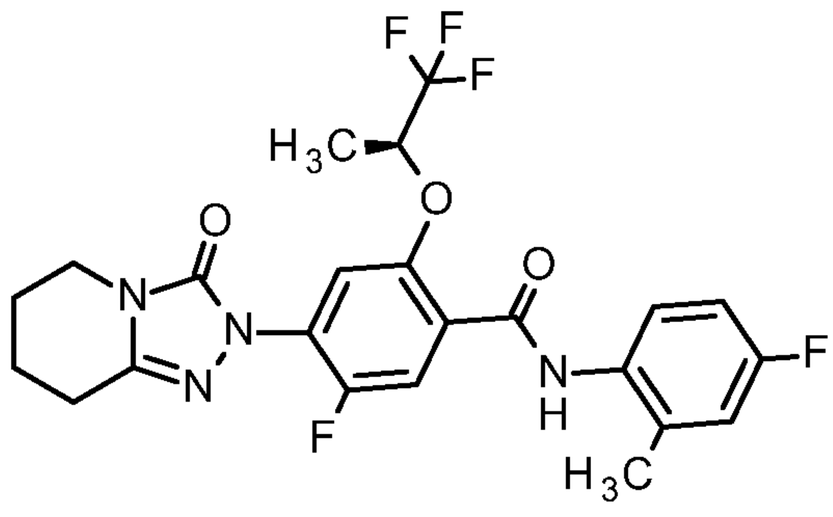
From intermediate 17 and aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.25 min; MS (ESIpos): m/z = 465 $[M+H]^+$

Example 74

5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



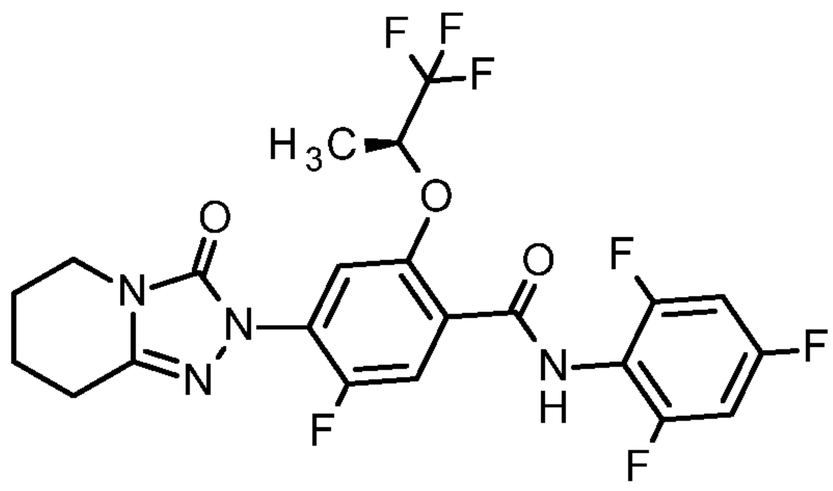
From intermediate 17 and 4-fluoro-2-methylaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.26 min; MS (ESIpos): m/z = 497 $[M+H]^+$

Example 75

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,4,6-trifluorophenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



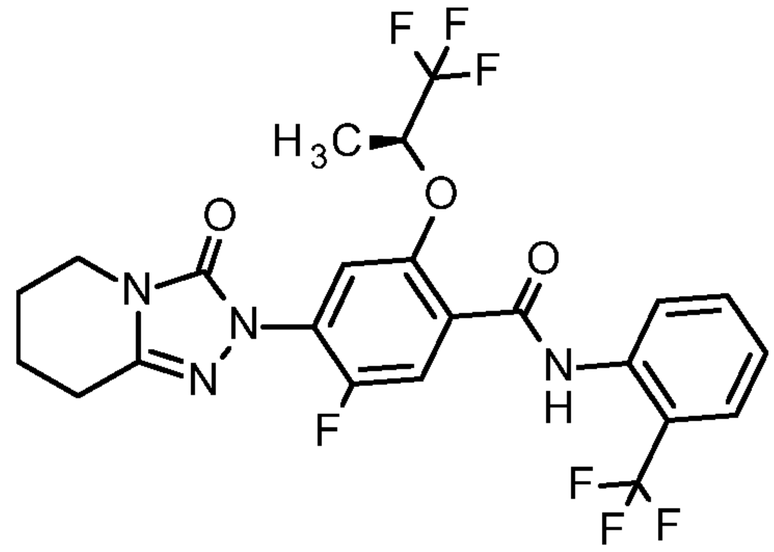
From intermediate 17 and 2,4,6-trifluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.23 min; MS (ESIpos): m/z = 519 $[M+H]^+$

Example 76

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[2-(trifluoromethyl)phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



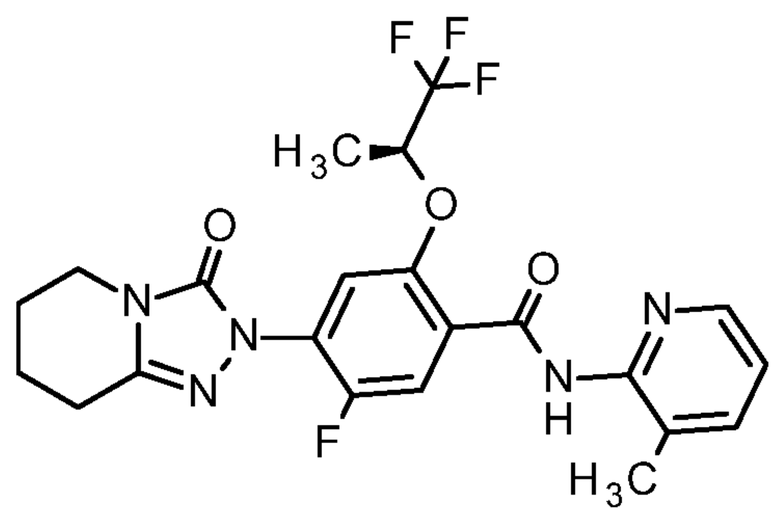
From intermediate 17 and 2-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.32 min; MS (ESIpos): m/z = 533 $[M+H]^+$

Example 77

5-fluoro-N-(3-methylpyridin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



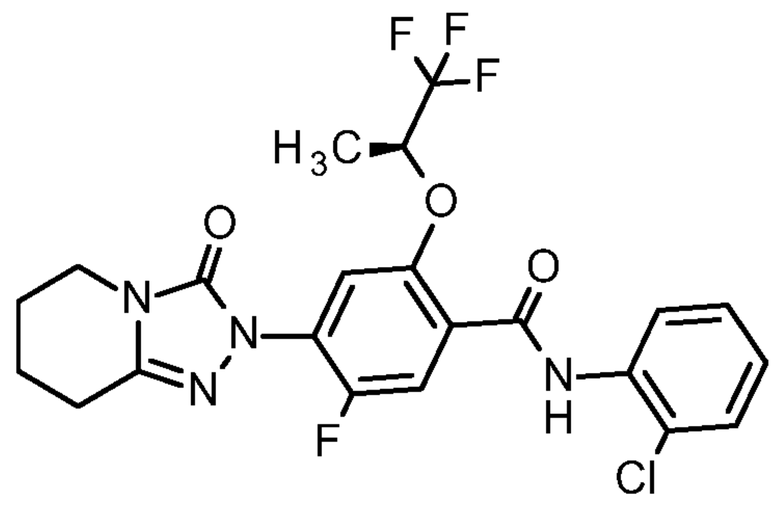
From intermediate 17 and 3-methylpyridin-2-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.00 min; MS (ESIpos): m/z = 480 $[M+H]^+$

Example 78

N-(2-chlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



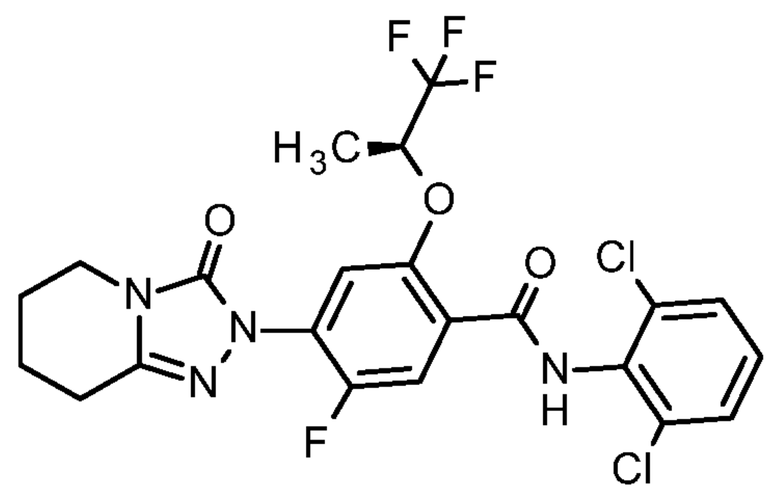
From intermediate 17 and 2-chloroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.35 min; MS (ESIpos): m/z = 500 $[M+H]^+$

Example 79

N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



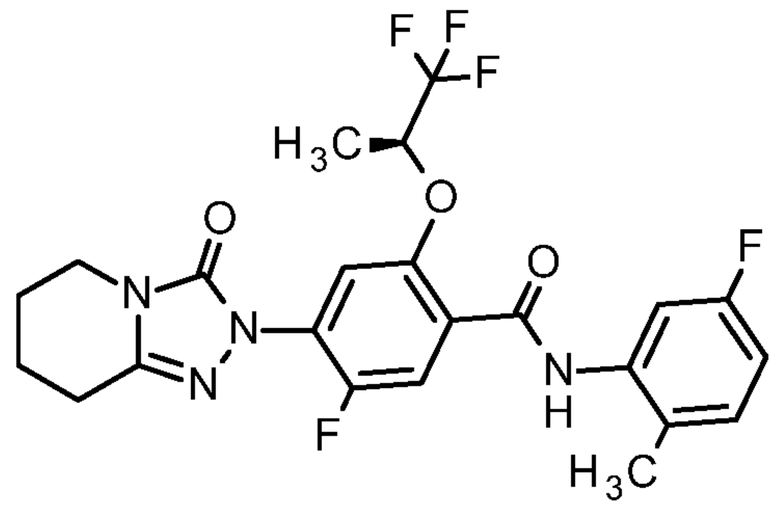
From intermediate 17 and 2,6-dichloroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.27 min; MS (ESIpos): m/z = 534 $[M+H]^+$

Example 80

5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



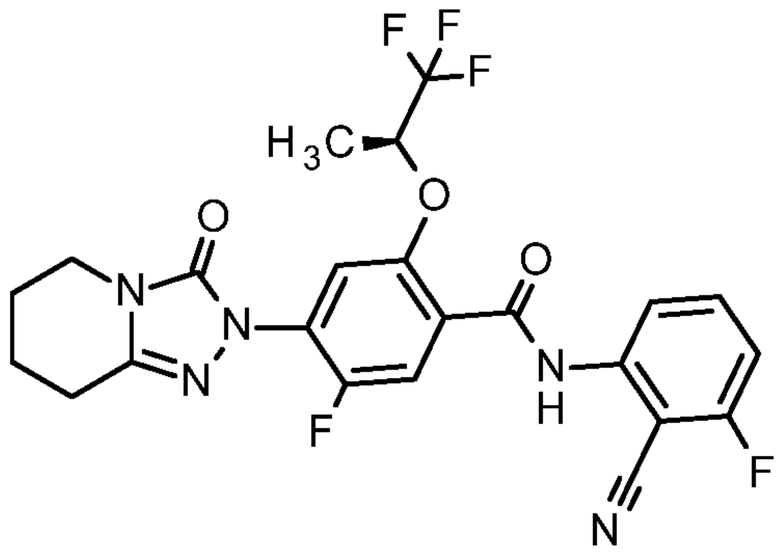
From intermediate 17 and 5-fluoro-2-methylaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.30 min; MS (ESIpos): m/z = 497 $[M+H]^+$

Example 81

N-(2-cyano-3-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



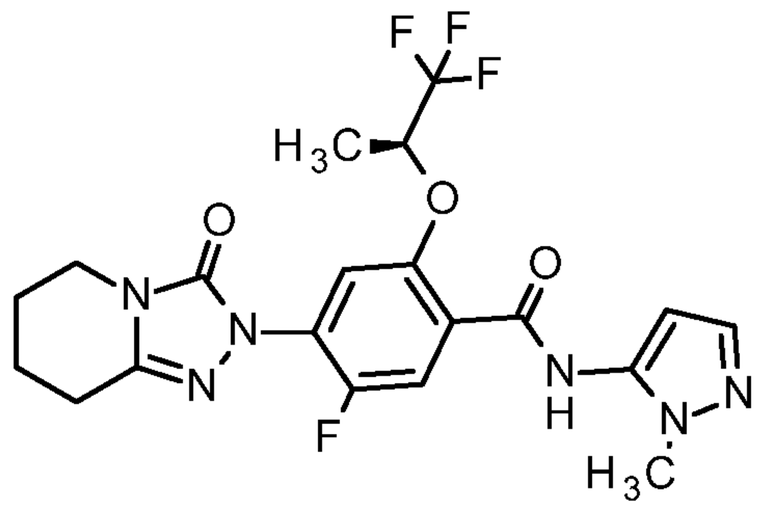
From intermediate 17 and 2-amino-6-fluorobenzonitrile.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.24 min; MS (ESIpos): m/z = 508 $[M+H]^+$

Example 82

5-fluoro-N-(1-methyl-1H-pyrazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



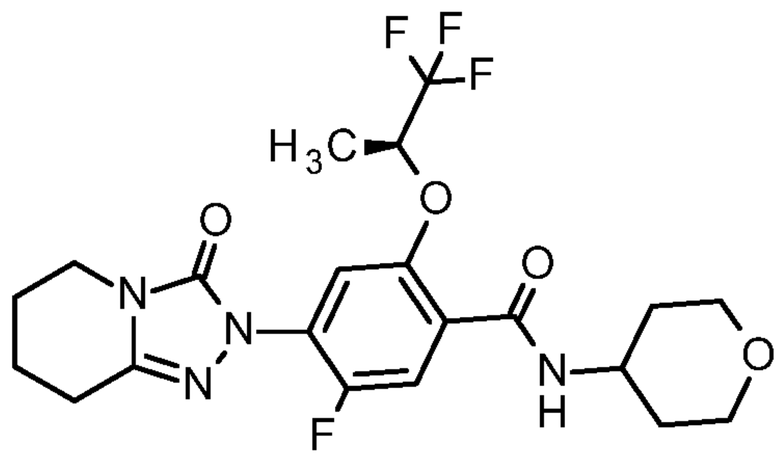
From intermediate 17 and 1-methyl-1H-pyrazol-5-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.99 min; MS (ESIpos): m/z = 469 $[M+H]^+$

Example 83

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(tetrahydro-2H-pyran-4-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



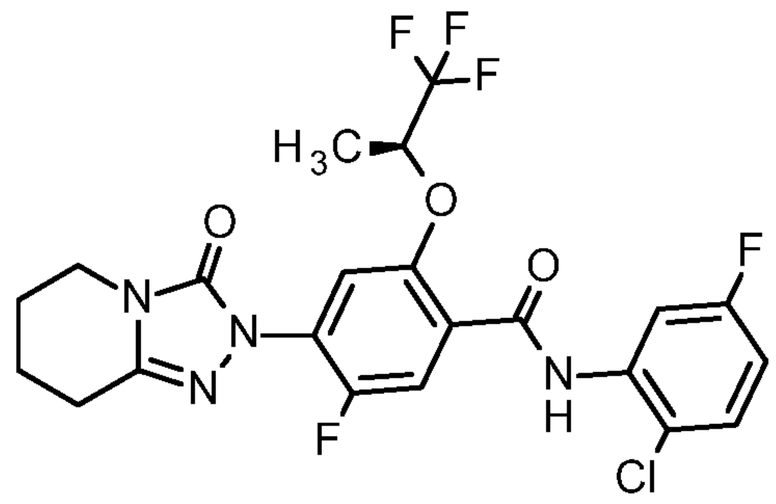
From intermediate 17 and tetrahydro-2H-pyran-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.01 min; MS (ESIpos): m/z = 473 $[M+H]^+$

Example 84

N-(2-chloro-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



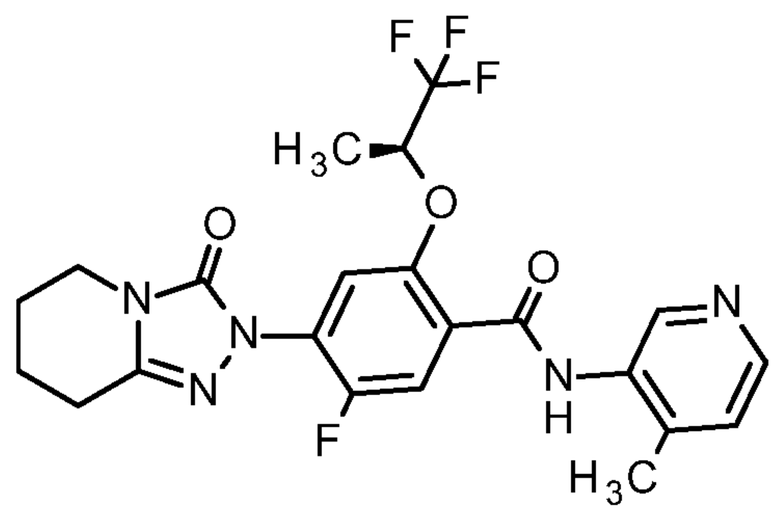
From intermediate 17 and 2-chloro-5-fluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.41 min; MS (ESIpos): m/z = 518 $[M+H]^+$

Example 85

5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



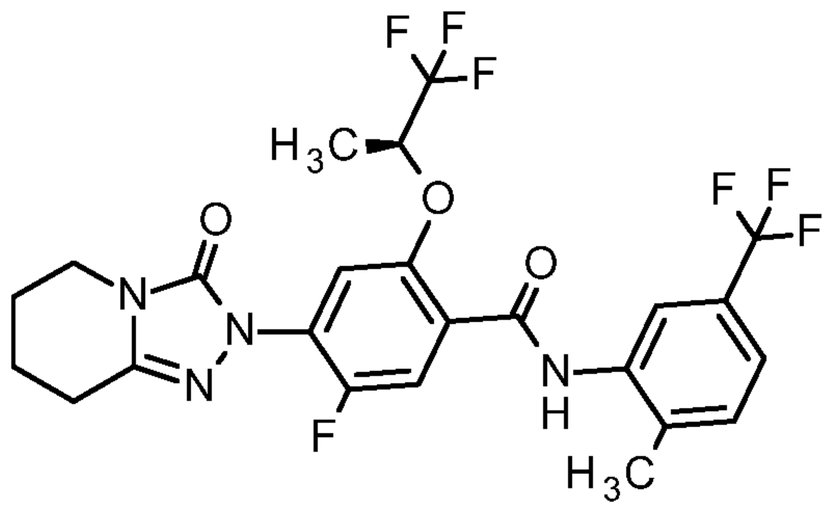
From intermediate 17 and 4-methylpyridin-3-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.83 min; MS (ESIpos): m/z = 480 $[M+H]^+$

Example 86

5-fluoro-N-[2-methyl-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



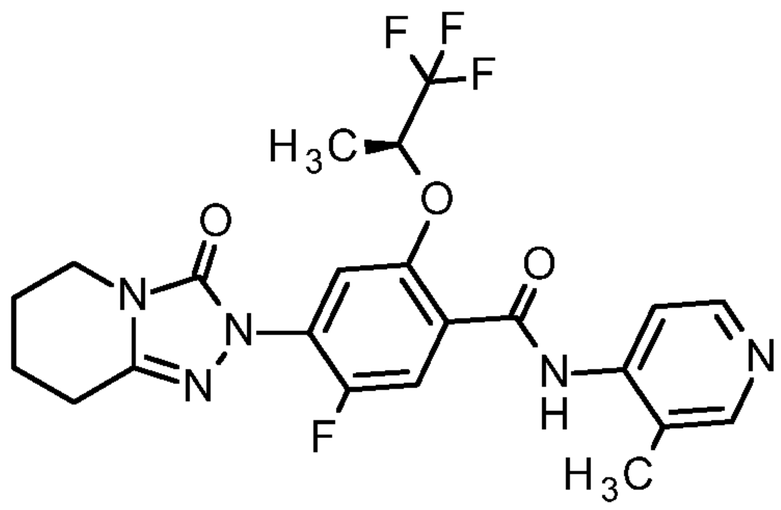
From intermediate 17 and 2-methyl-5-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.39 min; MS (ESIpos): m/z = 547 $[M+H]^+$

Example 87

5-fluoro-N-(3-methylpyridin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



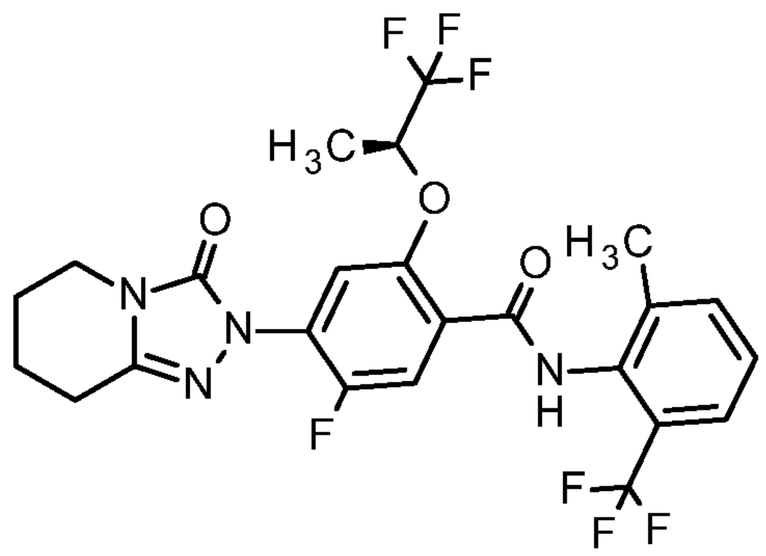
From intermediate 17 and 3-methylpyridin-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.78 min; MS (ESIpos): m/z = 480 $[M+H]^+$

Example 88

5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



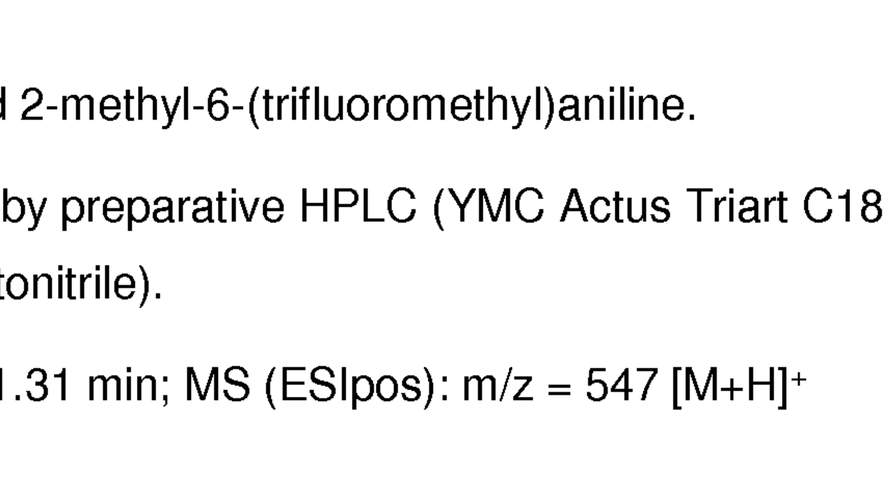
From intermediate 17 and 2-methyl-6-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.31 min; MS (ESIpos): m/z = 547 $[M+H]^+$

Example 89

N-(1,3-dimethyl-1H-pyrazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



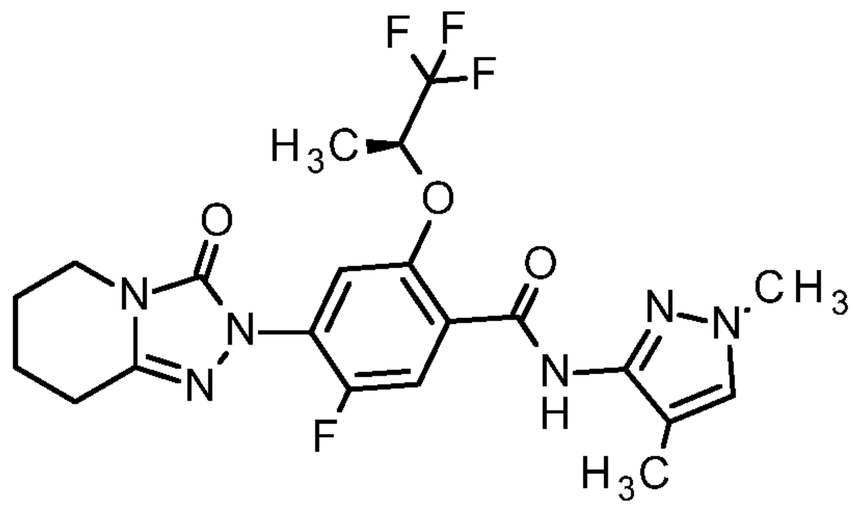
From intermediate 17 and 1,3-dimethyl-1H-pyrazol-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.00 min; MS (ESIpos): m/z = 483 $[M+H]^+$

Example 90

N-(1,4-dimethyl-1H-pyrazol-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



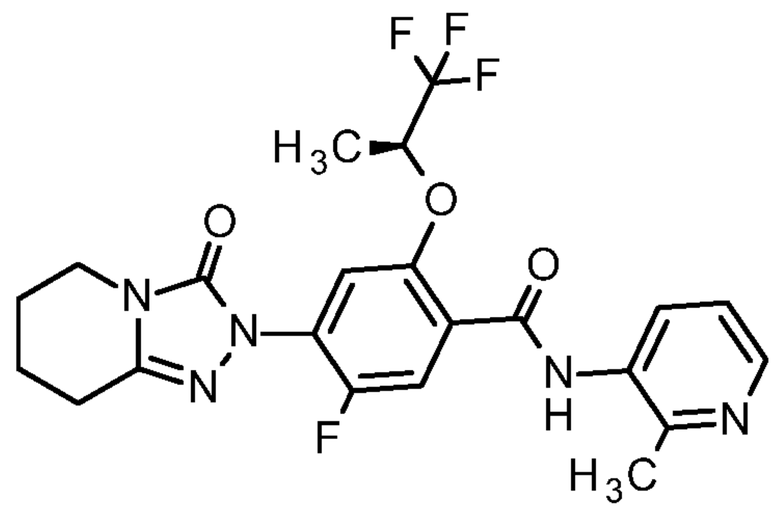
From intermediate 17 and 1,4-dimethyl-1H-pyrazol-3-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.02 min; MS (ESIpos): m/z = 483 $[M+H]^+$

Example 91

5-fluoro-N-(2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



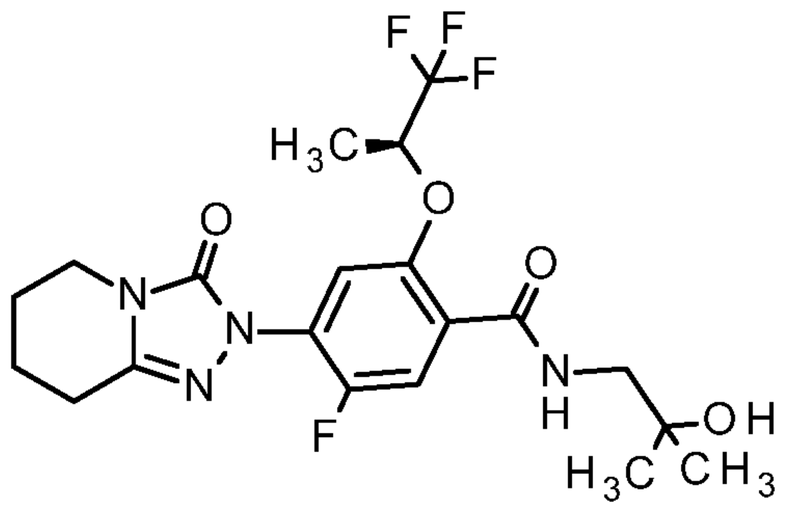
From intermediate 17 and 2-methylpyridin-3-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.83 min; MS (ESIpos): m/z = 480 $[M+H]^+$

Example 92

5-fluoro-N-(2-hydroxy-2-methylpropyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



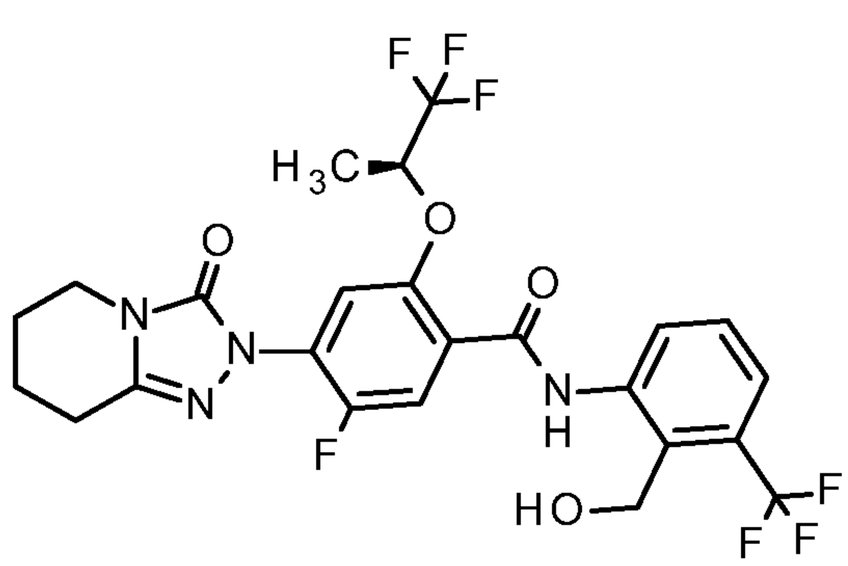
From intermediate 17 and 1-amino-2-methylpropan-2-ol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.96 min; MS (ESIpos): m/z = 461 $[M+H]^+$

Example 93

5-fluoro-N-[2-(hydroxymethyl)-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



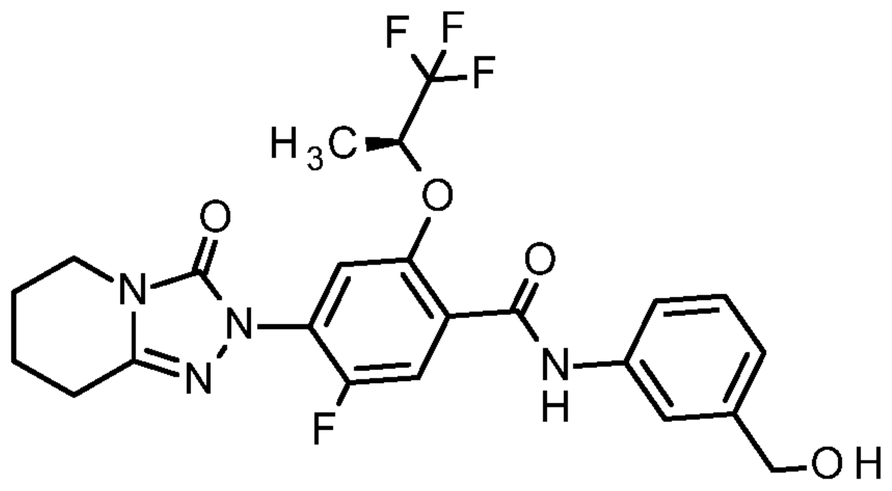
From intermediate 17 and [2-amino-6-(trifluoromethyl)phenyl]methanol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.23 min; MS (ESIpos): m/z = 563 $[M+H]^+$

Example 94

5-fluoro-N-[3-(hydroxymethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



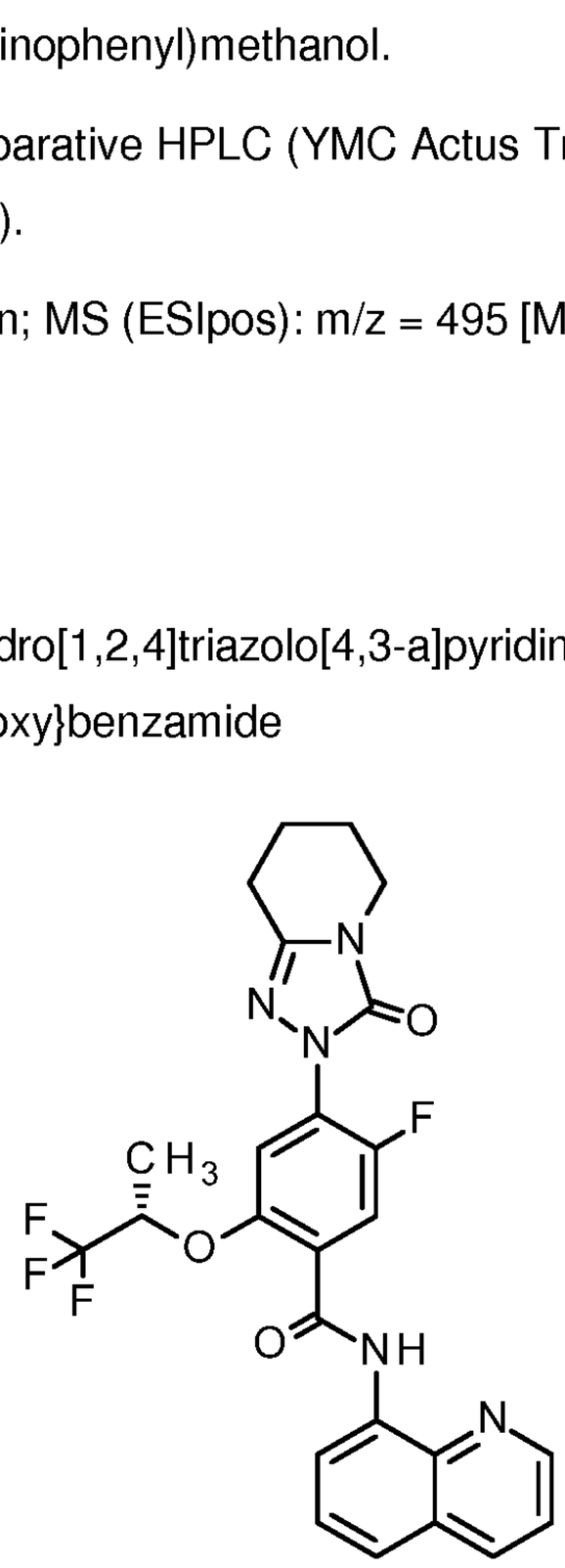
From intermediate 17 and (3-aminophenyl)methanol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.06 min; MS (ESIpos): m/z = 495 $[M+H]^+$

Example 95

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-8-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



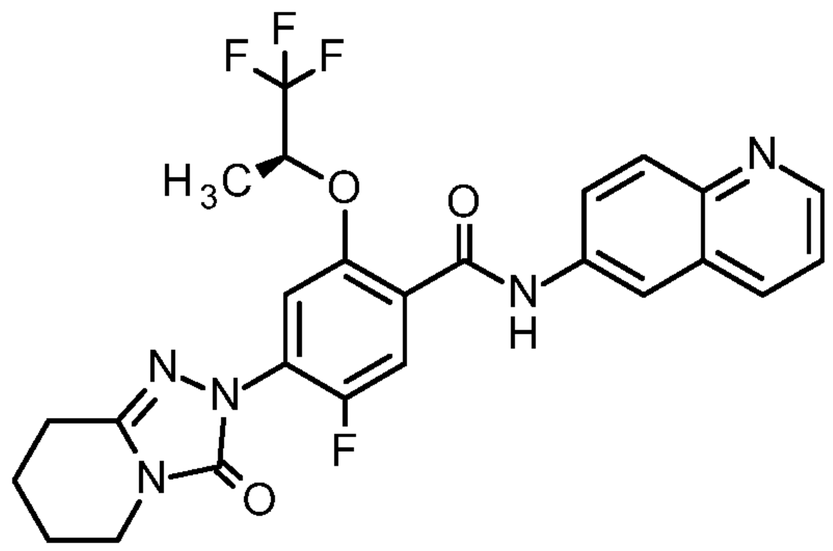
From intermediate 17 and quinolin-8-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.39 min; MS (ESIpos): m/z = 516 $[M+H]^+$

Example 96

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-6-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



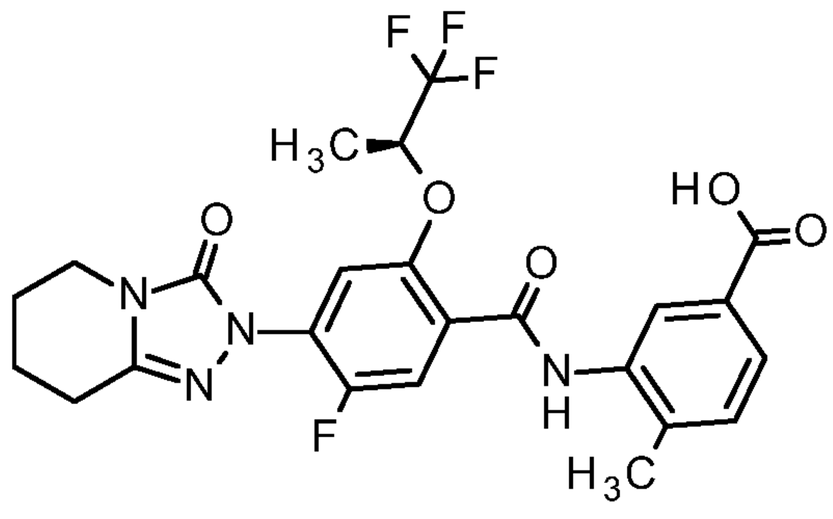
From intermediate 17 and quinolin-6-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.96 min; MS (ESIpos): m/z = 516 $[M+H]^+$

Example 97

3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}-4-methylbenzoic acid



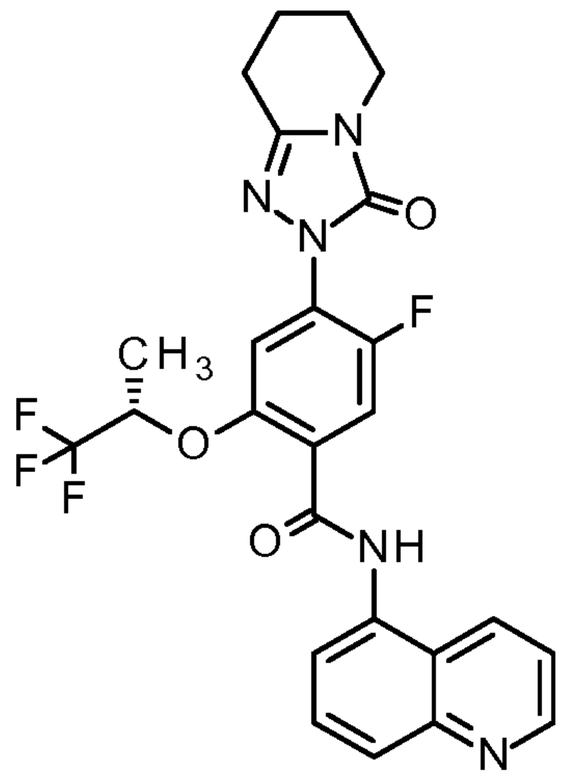
From intermediate 17 and 3-amino-4-methylbenzoic acid.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.10 min; MS (ESIpos): m/z = 523 $[M+H]^+$

Example 98

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-5-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



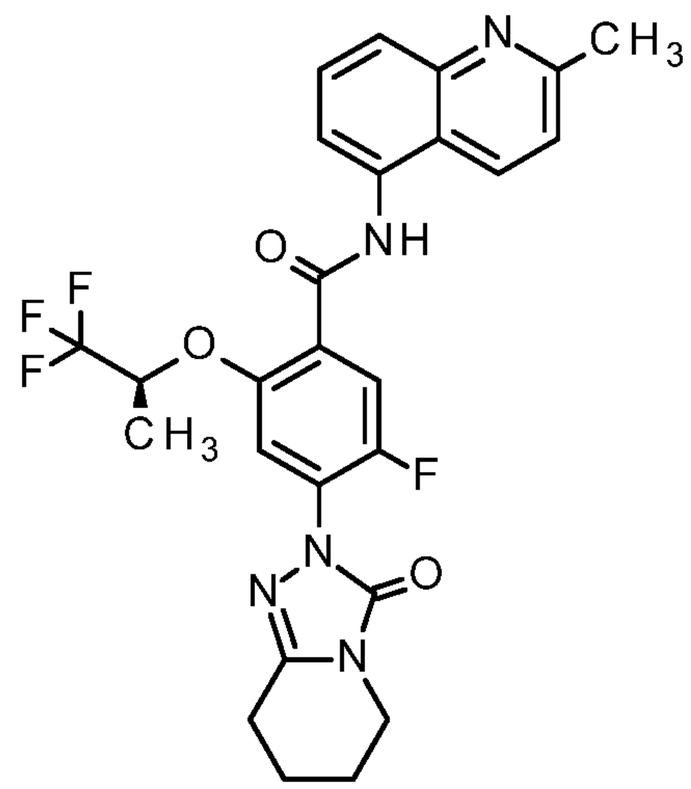
From intermediate 17 and quinolin-5-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.96 min; MS (ESIpos): m/z = 516 $[M+H]^+$

Example 99

5-fluoro-N-(2-methylquinolin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



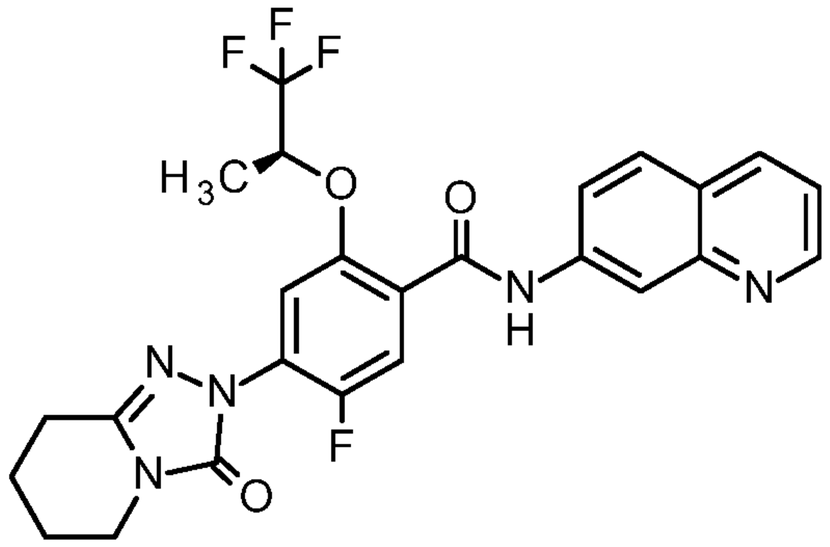
From intermediate 17 and 2-methylquinolin-5-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.89 min; MS (ESIpos): m/z = 530 $[M+H]^+$

Example 100

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-7-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



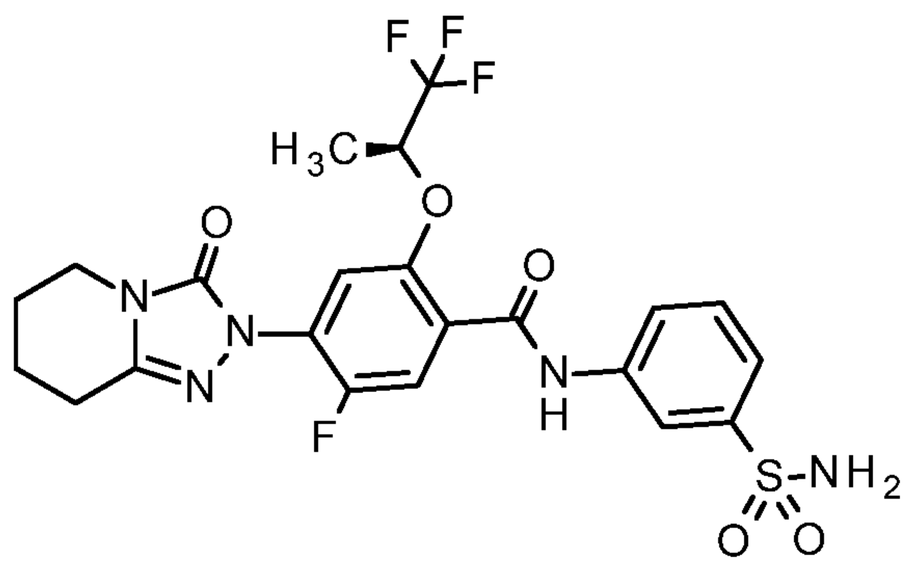
From intermediate 17 and quinolin-7-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.93 min; MS (ESIpos): m/z = 516 $[M+H]^+$

Example 101

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(3-sulfamoylphenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



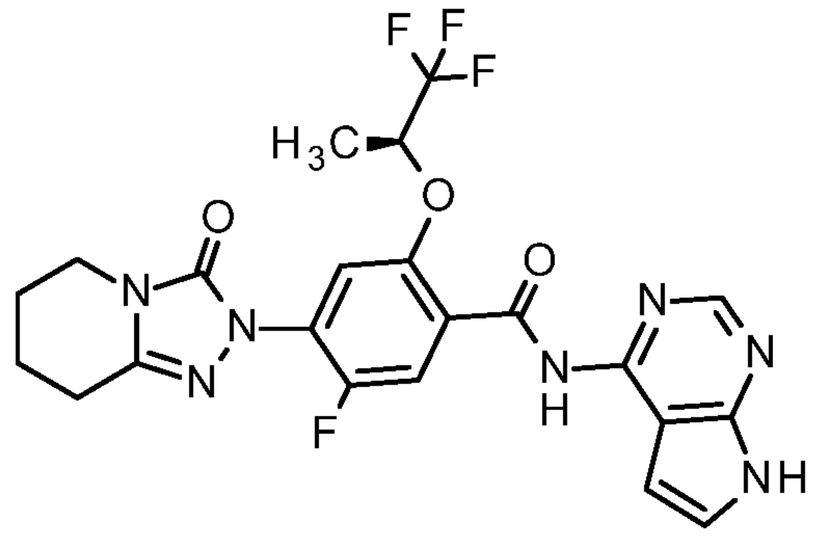
From intermediate 17 and 3-aminobenzenesulfonamide.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.02 min; MS (ESIpos): m/z = 544 $[M+H]^+$

Example 102

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



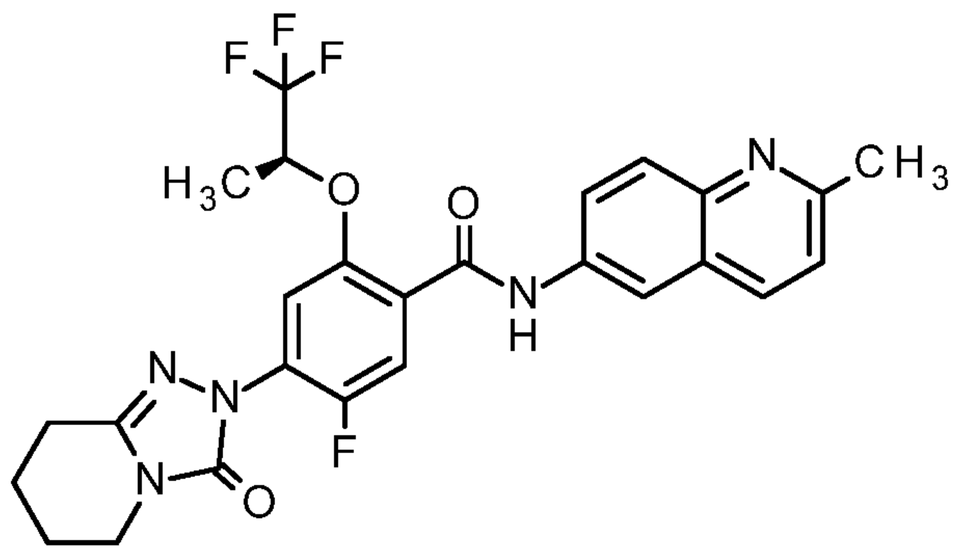
From intermediate 17 and 7H-pyrrolo[2,3-d]pyrimidin-4-amine

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.96 min; MS (ESIpos): m/z = 506 $[M+H]^+$

Example 103

5-fluoro-N-(2-methylquinolin-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



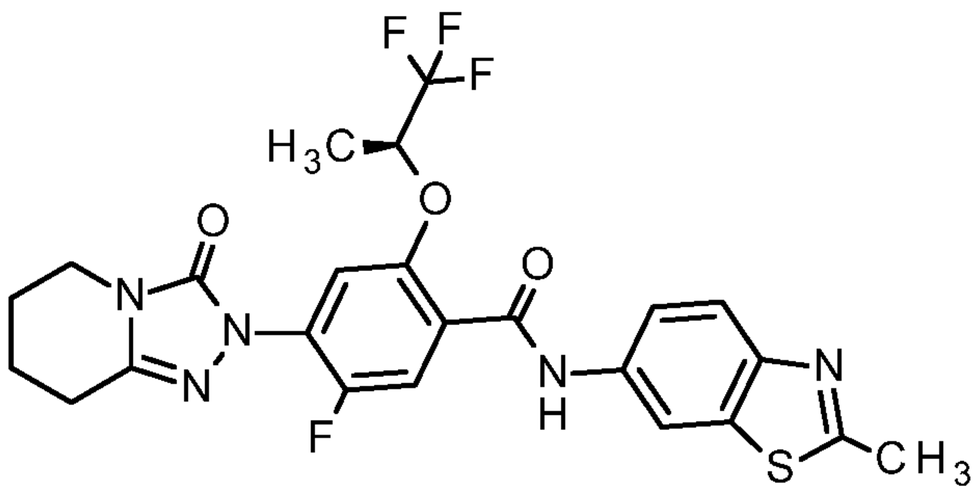
From intermediate 17 and 2-methylquinolin-6-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.89 min; MS (ESIpos): m/z = 530 $[M+H]^+$

Example 104

5-fluoro-N-(2-methyl-1,3-benzothiazol-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



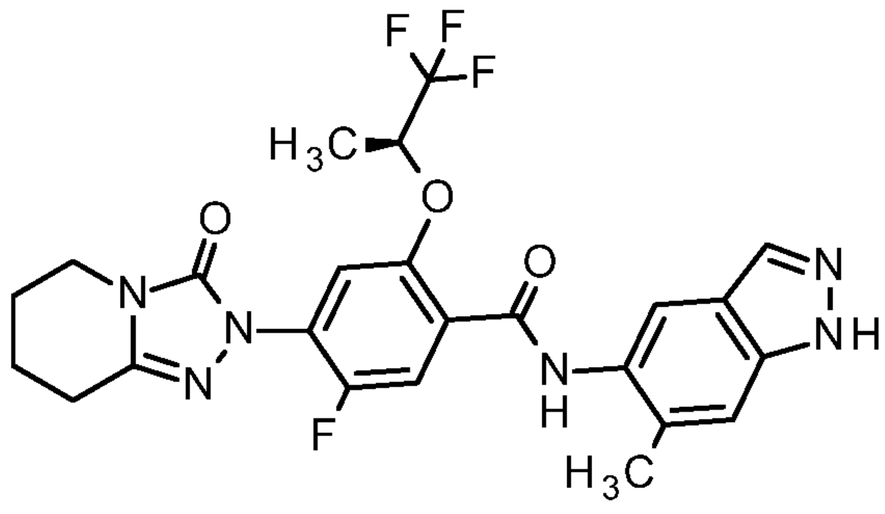
From intermediate 17 and 2-methyl-1,3-benzothiazol-6-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.23 min; MS (ESIpos): m/z = 536 $[M+H]^+$

Example 105

5-fluoro-N-(6-methyl-1H-indazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



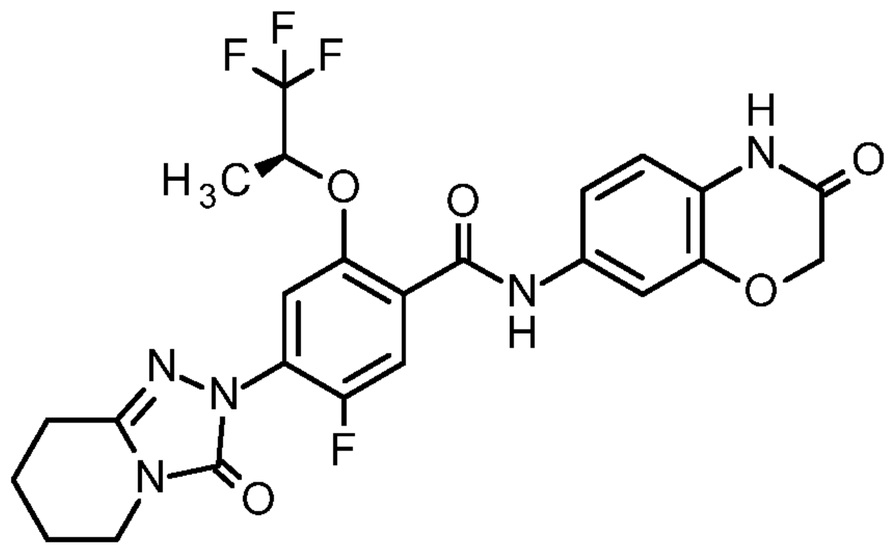
From intermediate 17 and 6-methyl-1H-indazol-5-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.05 min; MS (ESIpos): m/z = 519 $[M+H]^+$

Example 106

5-fluoro-N-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



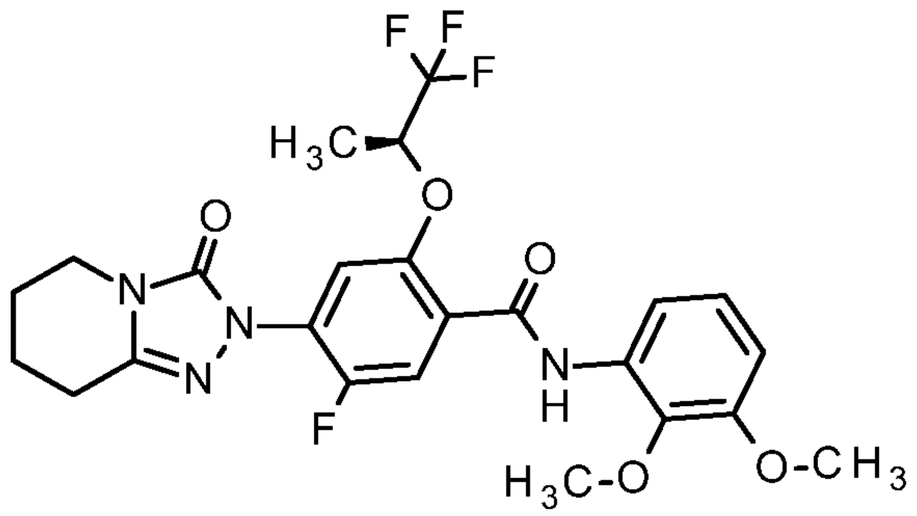
From intermediate 17 and 7-amino-2H-1,4-benzoxazin-3(4H)-one.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.03 min; MS (ESIpos): m/z = 536 $[M+H]^+$

Example 107

N-(2,3-dimethoxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



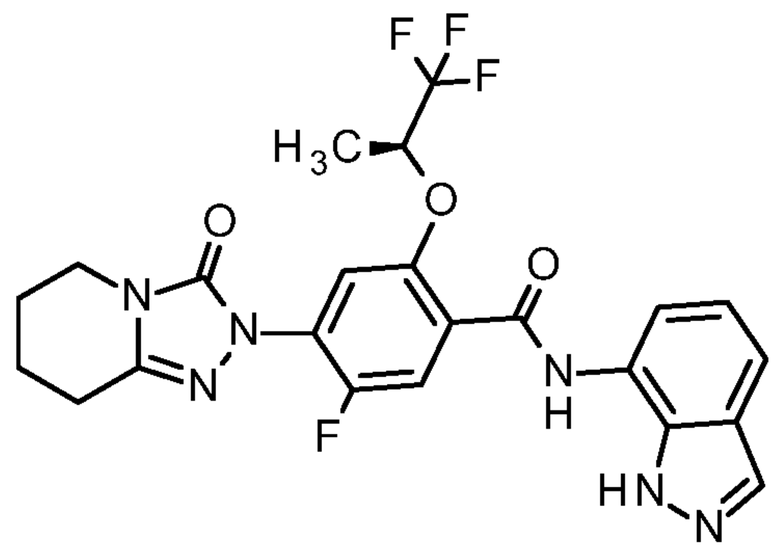
From intermediate 17 and 2,3-dimethoxyaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.31 min; MS (ESIpos): m/z = 525 $[M+H]^+$

Example 108

5-fluoro-N-(1H-indazol-7-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



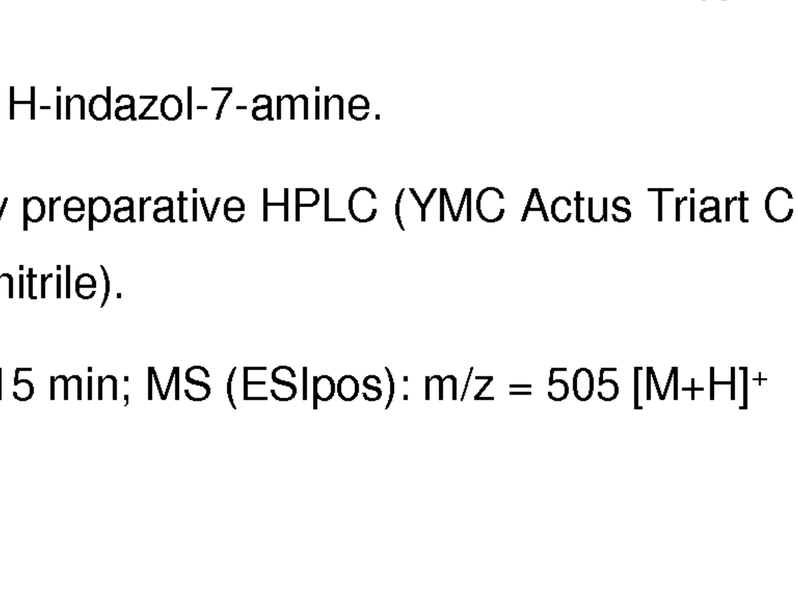
From intermediate 17 and 1H-indazol-7-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.15 min; MS (ESIpos): m/z = 505 $[M+H]^+$

Example 109

5-fluoro-N-[1-(4-fluorophenyl)cyclopropyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



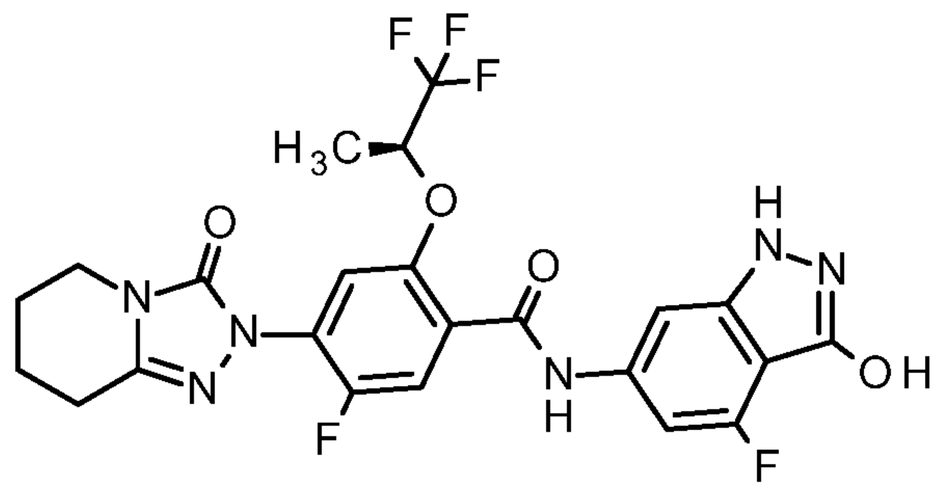
From intermediate 17 and 1-(4-fluorophenyl)cyclopropanamine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.29 min; MS (ESIpos): m/z = 523 $[M+H]^+$

Example 110

5-fluoro-N-(4-fluoro-3-hydroxy-1H-indazol-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



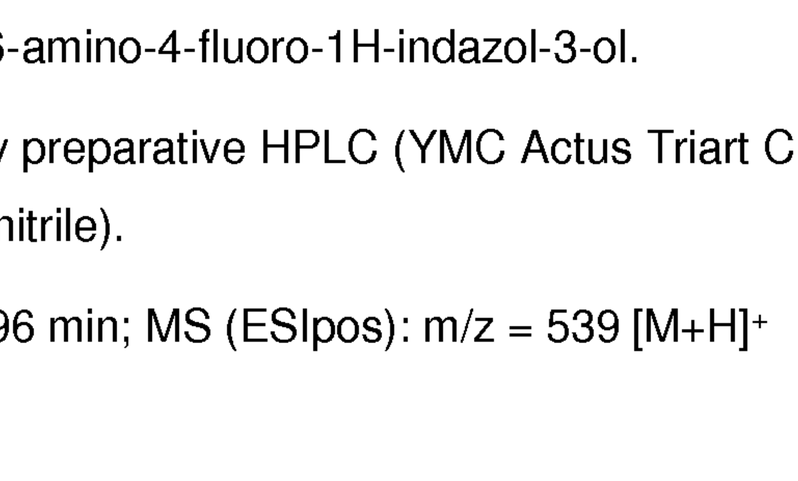
From intermediate 17 and 6-amino-4-fluoro-1H-indazol-3-ol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.96 min; MS (ESIpos): m/z = 539 $[M+H]^+$

Example 111

5-fluoro-N-[(1S,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



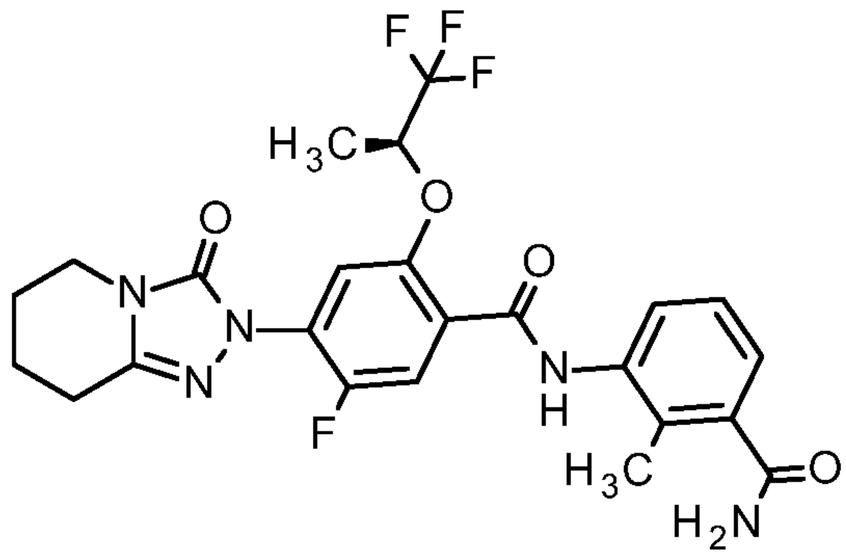
From intermediate 17 and (1S,2S)-1-aminoindan-2-ol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.14 min; MS (ESIpos): m/z = 521 $[M+H]^+$

Example 112

N-(3-carbamoyl-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



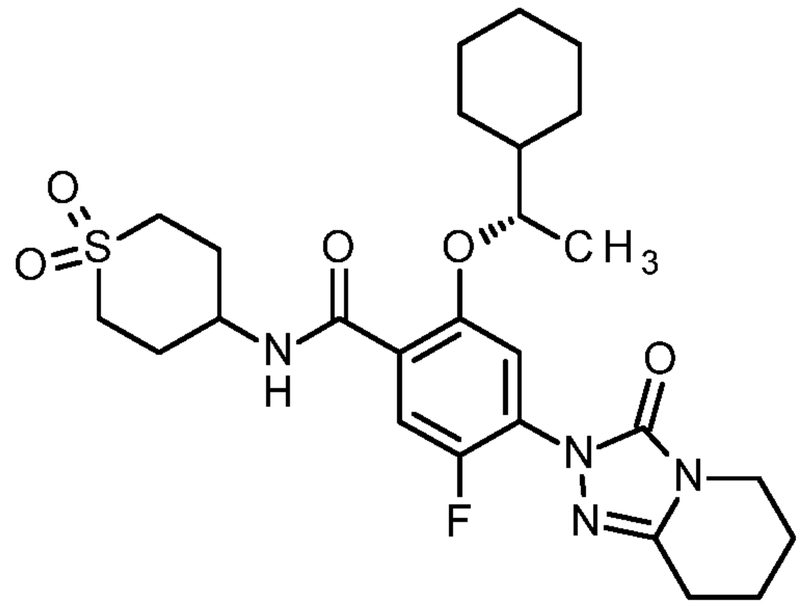
From intermediate 17 and 3-amino-2-methylbenzamide.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.95 min; MS (ESIpos): m/z = 522 $[M+H]^+$

Example 113

2-[(1S)-1-cyclohexylethoxy]-N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



To a solution of 2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 19) (100 mg, 248 µmol) in dichloromethane (1.0 ml) was added two drops of N,N-dimethylformamide. The solution was cooled to 0 °C and oxalyl chloride (34 .6 mg, 273 µmol) was slowly added. The reaction was then warmed to room temperature and stirred for 90 minutes. The solvent was removed under reduced pressure and the residue was re-dissolved in dichloromethane (2.0 ml) and added dropwise to a cooled (0 °C) solution of tetrahydro-2H-thiopyran-4-amine 1,1-dioxide (40.7 mg, 273 µmol) and triethylamine (38 µl, 270 µmol) in dichloromethane (2.0 ml). The mixture was warmed to room temperature and stirred for one hour. Then, the solvent was removed under reduced pressure and the residue was purified by preparative HPLC (X-Bridge

Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile), to yield the title compound (90 mg, 67 %) as a solid.

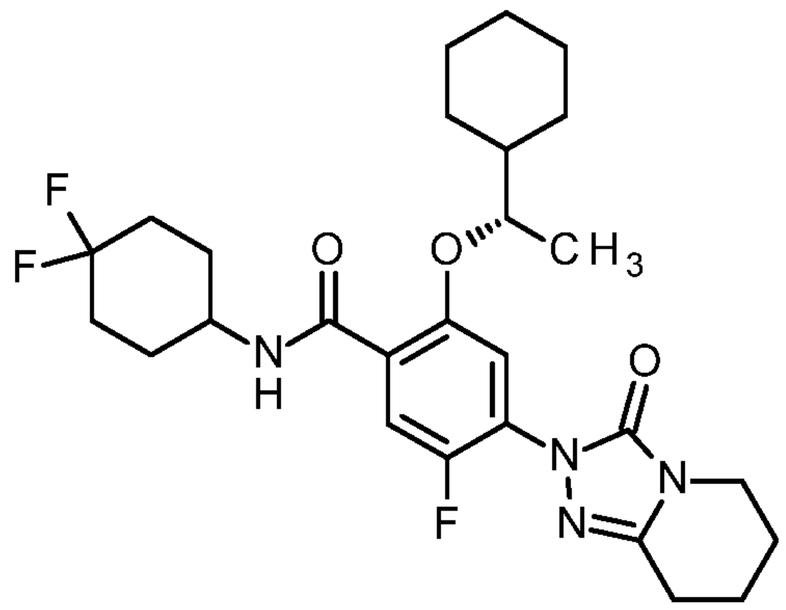
LC-MS (method A): R_t = 1.13 min; MS (ESIpos): m/z = 536 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.993 (0.97), 1.001 (0.94), 1.024 (1.23), 1.031 (1.16), 1.073 (1.11), 1.080 (1.06), 1.103 (1.81), 1.109 (1.58), 1.132 (1.83), 1.159 (2.02), 1.192 (16.00), 1.207 (15.54), 1.220 (1.40), 1.228 (1.22), 1.559 (0.98), 1.566 (1.00), 1.573 (0.99), 1.624 (1.13), 1.658 (1.62), 1.702 (3.47), 1.732 (1.88), 1.770 (0.90), 1.779 (1.94), 1.786 (2.30), 1.791 (2.69), 1.802 (2.75), 1.806 (2.85), 1.818 (1.95), 1.822 (2.10), 1.855 (2.20), 1.859 (2.40), 1.869 (3.17), 1.874 (3.14), 1.884 (2.92), 1.890 (2.39), 1.899 (1.73), 1.905 (0.96), 1.966 (1.39), 1.978 (1.48), 1.994 (1.59), 2.003 (1.63), 2.019 (0.90), 2.149 (1.26), 2.158 (1.81), 2.164 (1.88), 2.173 (1.74), 2.178 (1.52), 2.183 (1.51), 2.188 (1.38), 2.193 (1.38), 2.198 (1.29), 2.208 (0.91), 2.540 (1.18), 2.672 (3.37), 2.688 (6.60), 2.704 (3.61), 3.090 (1.33), 3.098 (1.72), 3.127 (2.11), 3.133 (2.37), 3.141 (1.80), 3.279 (1.62), 3.308 (2.42), 3.342 (1.21), 3.539 (3.92), 3.554 (7.13), 3.568 (3.12), 4.149 (0.85), 4.155 (1.13), 4.165 (0.99), 4.175 (1.13), 4.282 (1.76), 4.297 (2.63), 4.312 (1.76), 7.240 (4.66), 7.256 (4.66), 7.501 (6.75), 7.528 (6.43), 8.224 (3.25), 8.244 (3.16).

Examples 114–138 were prepared as described for example 113 from 2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 19) and the respective amines, as indicated. Products were purified by flash column chromatography or, if explicitely mentioned, by preparative HPLC.

Example 114

2-[(1S)-1-cyclohexylethoxy]-N-(4,4-difluorocyclohexyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 4,4-difluorocyclohexanamine.

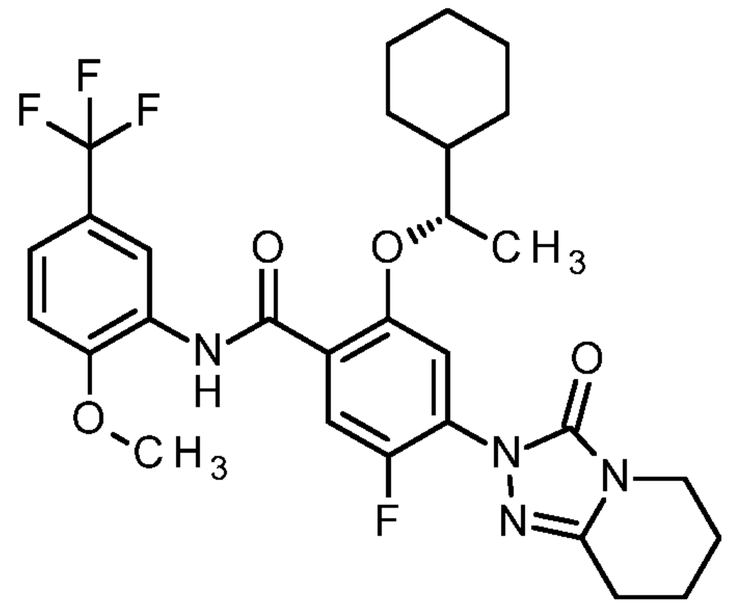
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.14 min; MS (ESIpos): m/z = 522 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.003 (0.99), 1.011 (0.95), 1.033 (1.26), 1.040 (1.18), 1.079 (1.06), 1.088 (1.21), 1.099 (1.04), 1.111 (1.53), 1.117 (1.48), 1.130 (1.44), 1.139 (1.44), 1.153 (2.22), 1.165 (1.46), 1.175 (1.73), 1.180 (1.94), 1.199 (16.00), 1.214 (15.48), 1.230 (1.11), 1.536 (1.92), 1.542 (2.21), 1.548 (2.02), 1.567 (2.68), 1.572 (2.53), 1.578 (2.19), 1.593 (1.26), 1.599 (1.19), 1.608 (1.15), 1.616 (1.06), 1.627 (1.17), 1.657 (1.54), 1.703 (3.79), 1.731 (1.93), 1.770 (0.95), 1.779 (2.01), 1.786 (2.40), 1.791 (2.75), 1.802 (2.79), 1.806 (2.90), 1.818 (1.58), 1.822 (1.64), 1.835 (1.43), 1.855 (1.92), 1.859 (2.16), 1.869 (3.64), 1.873 (3.75), 1.884 (3.24), 1.889 (2.77), 1.899 (2.47), 1.905 (2.30), 1.913 (2.32), 1.934 (2.76), 1.957 (2.22), 2.014 (2.22), 2.030 (2.85), 2.041 (2.37), 2.052 (1.84), 2.075 (0.84), 2.540 (1.46), 2.672 (3.45), 2.688 (6.74), 2.704 (3.68), 3.539 (4.39), 3.554 (7.73), 3.569 (3.86), 3.974 (0.93), 3.992 (0.91), 4.312 (1.77), 4.328 (2.63), 4.342 (1.75), 7.257 (4.67), 7.272 (4.65), 7.544 (7.00), 7.572 (6.60), 8.111 (3.23), 8.130 (3.16).

Example 115

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methoxy-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 2-methoxy-5-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

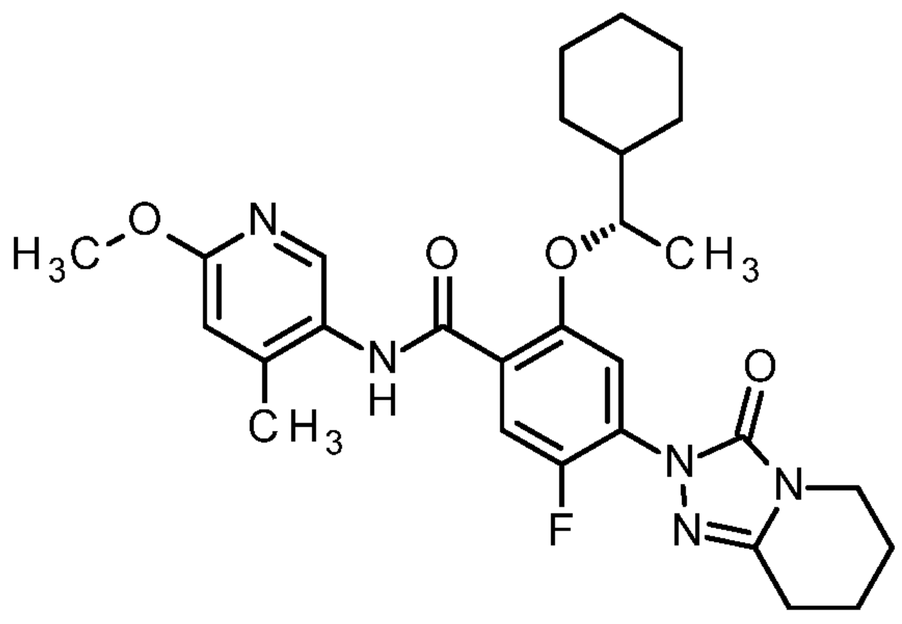
LC-MS (method A): R_t = 1.59 min; MS (ESIpos): m/z = 578 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.382 (6.95), 1.397 (6.77), 1.774 (1.31), 1.783 (1.65), 1.813 (1.01), 1.934 (1.00), 1.946 (1.03), 1.950 (1.11), 2.001 (1.35), 2.007 (1.43), 2.017 (1.25), 2.022 (0.96), 2.801 (1.54), 2.817 (2.95), 2.833 (1.69), 3.713 (1.92), 3.729 (3.21), 3.743 (1.39), 3.995 (16.00), 4.386 (1.00), 6.981 (1.43), 7.002 (1.61), 7.353 (0.93), 7.355 (0.99), 7.359

(1.06), 7.360 (1.14), 7.364 (2.07), 7.374 (1.03), 7.379 (2.67), 8.127 (2.63), 8.156 (2.60), 8.995 (1.83), 9.001 (1.79), 10.429 (1.57).

Example 116

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 6-methoxy-4-methylpyridin-3-amine.

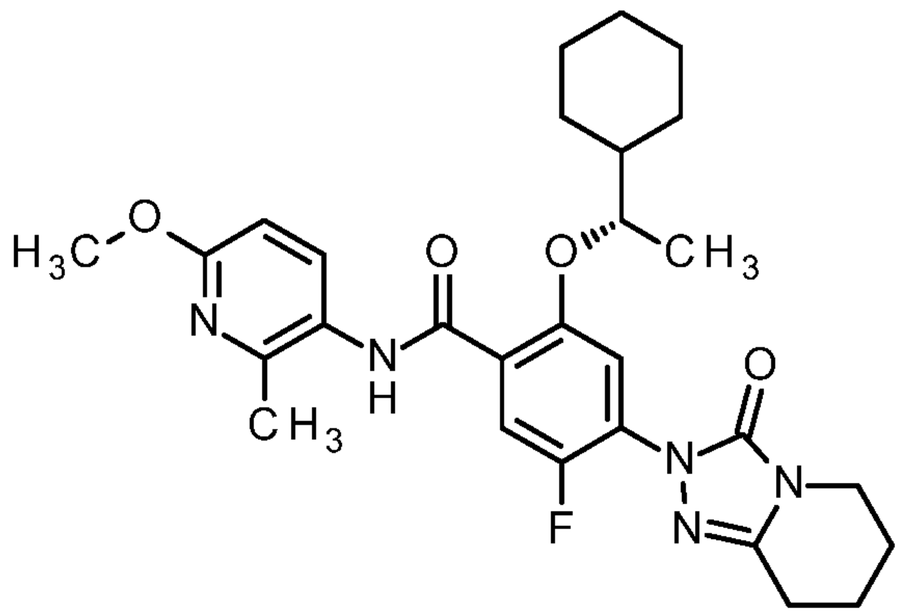
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.39 min; MS (ESIpos): m/z = 525 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.368 (5.19), 1.383 (5.27), 1.612 (2.02), 1.948 (1.08), 2.273 (7.42), 2.274 (7.97), 2.800 (1.09), 2.817 (2.10), 2.832 (1.21), 3.710 (1.39), 3.725 (2.28), 3.740 (0.99), 3.939 (16.00), 6.665 (2.17), 6.667 (1.81), 7.384 (1.37), 7.399 (1.34), 8.128 (1.94), 8.157 (1.92), 8.341 (2.75), 9.497 (1.20).

Example 117

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxy-2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 6-methoxy-2-methylpyridin-3-amine.

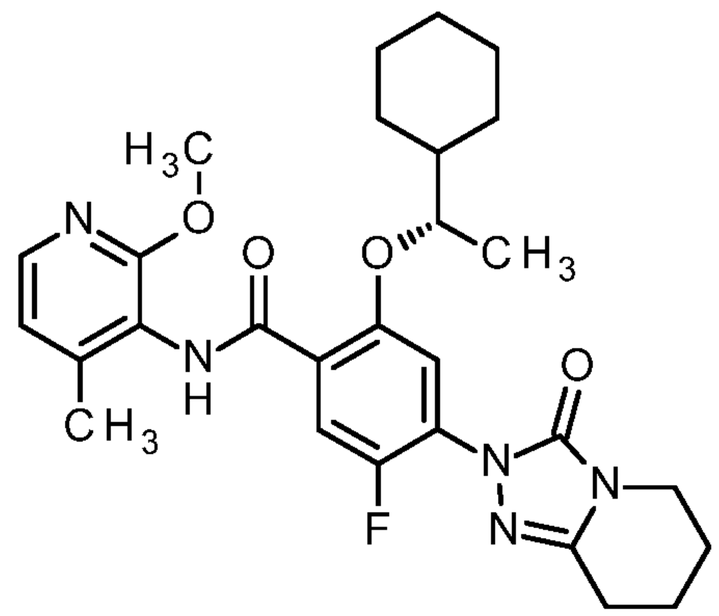
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.43 min; MS (ESIpos): m/z = 525 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.371 (4.50), 1.386 (4.74), 2.468 (8.80), 2.801 (1.00), 2.817 (1.92), 2.834 (1.12), 3.712 (1.28), 3.727 (2.08), 3.742 (0.91), 3.931 (16.00), 6.634 (1.22), 6.655 (1.25), 7.381 (1.26), 7.395 (1.24), 7.996 (1.68), 8.018 (1.56), 8.134 (1.80), 8.164 (1.75), 9.556 (1.07).

Example 118

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 2-methoxy-4-methylpyridin-3-amine.

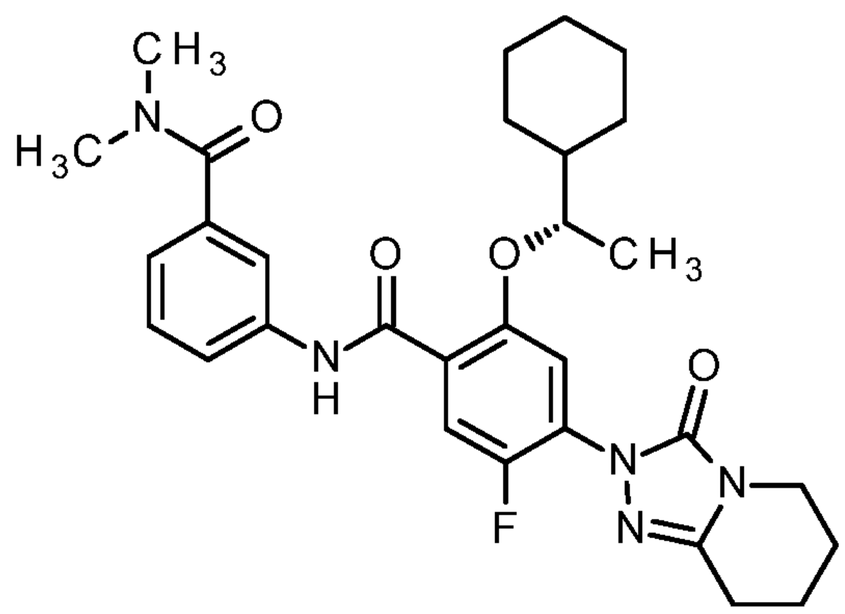
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.41 min; MS (ESIpos): m/z = 525 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.371 (5.34), 1.387 (5.54), 1.620 (1.18), 2.014 (1.13), 2.282 (9.70), 2.800 (1.15), 2.817 (2.25), 2.832 (1.31), 3.711 (1.49), 3.726 (2.44), 3.741 (1.08), 3.959 (16.00), 6.830 (1.47), 6.843 (1.52), 7.371 (1.46), 7.386 (1.44), 7.943 (1.98), 7.956 (1.95), 8.122 (2.03), 8.151 (2.05), 9.606 (1.27).

Example 119

2-[(1S)-1-cyclohexylethoxy]-N-[3-(dimethylcarbamoyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 3-amino-N,N-dimethylbenzamide.

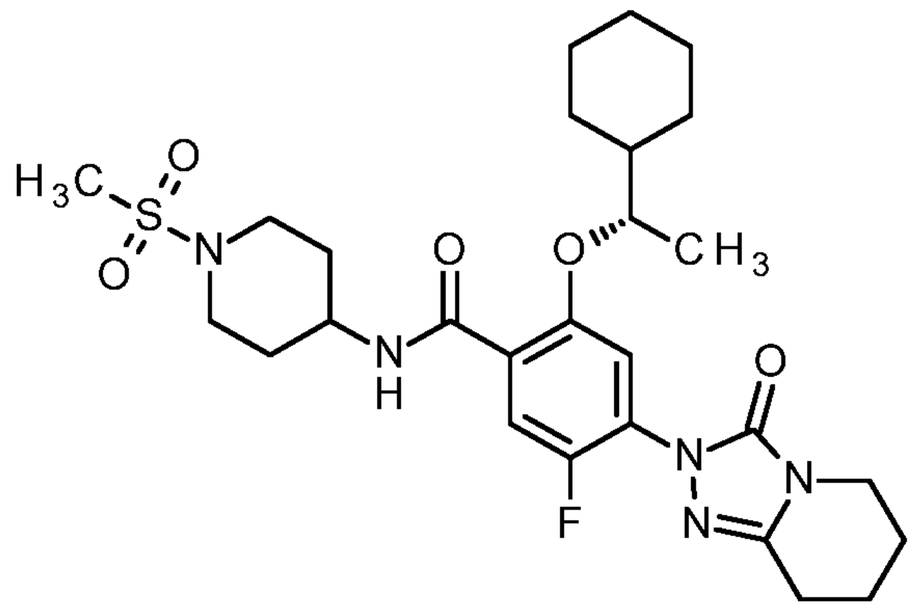
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.28 min; MS (ESIpos): m/z = 551 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.133 (1.32), 1.140 (1.25), 1.155 (1.32), 1.164 (1.60), 1.178 (1.01), 1.190 (1.85), 1.217 (1.15), 1.267 (1.06), 1.276 (1.38), 1.284 (1.35), 1.290 (1.18), 1.297 (1.04), 1.307 (1.12), 1.315 (1.03), 1.390 (15.78), 1.406 (16.00), 1.627 (3.39), 1.734 (1.25), 1.741 (1.39), 1.749 (1.08), 1.778 (1.29), 1.796 (3.56), 1.825 (2.88), 1.919 (1.59), 1.926 (1.87), 1.931 (2.14), 1.943 (2.23), 1.946 (2.38), 1.950 (1.66), 1.959 (1.08), 1.963 (1.14), 1.984 (1.73), 1.990 (1.96), 1.998 (2.92), 2.004 (2.75), 2.014 (2.89), 2.019 (2.75), 2.026 (2.31), 2.028 (2.29), 2.798 (3.31), 2.813 (6.43), 2.830 (3.67), 3.039 (6.90), 3.129 (6.84), 3.709 (4.18), 3.724 (6.99), 3.739 (3.00), 4.418 (1.58), 4.433 (2.34), 4.449 (1.50), 7.196 (1.92), 7.199 (2.71), 7.202 (2.04), 7.215 (2.44), 7.219 (3.37), 7.221 (2.32), 7.362 (4.22), 7.377 (4.26), 7.389 (2.80), 7.409 (4.80), 7.428 (2.76), 7.584 (1.98), 7.587 (2.30), 7.590 (2.27), 7.592 (2.17), 7.604 (1.64), 7.607 (1.75), 7.610 (1.96), 7.613 (1.73), 7.818 (3.10), 7.822 (4.79), 7.827 (3.01), 8.125 (5.73), 8.154 (5.81), 10.181 (3.75).

Example 120

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 1-(methylsulfonyl)piperidin-4-amine.

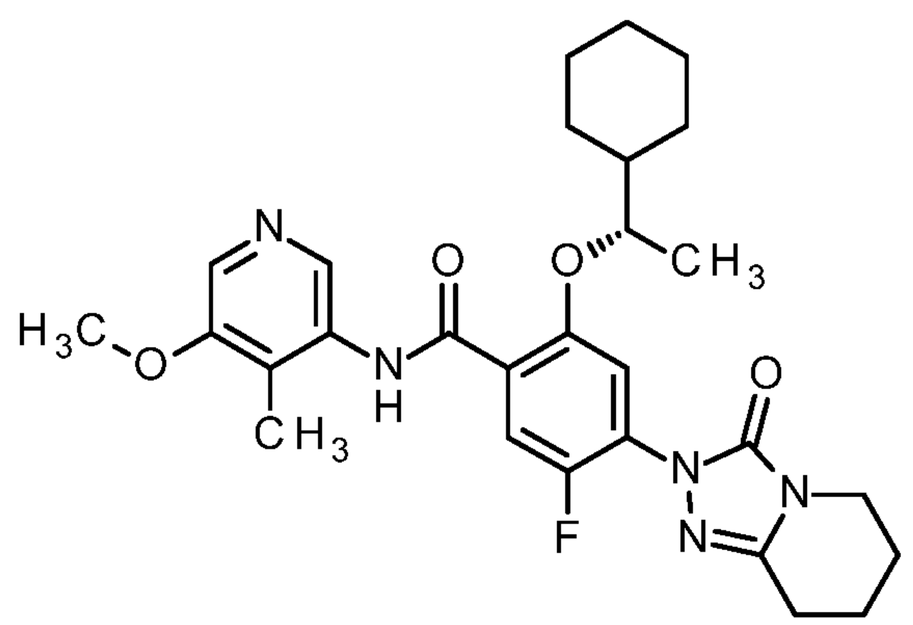
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.20 min; MS (ESIpos): m/z = 565 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.315 (6.10), 1.331 (6.01), 1.615 (2.10), 1.909 (0.97), 1.916 (1.07), 1.921 (1.07), 1.933 (1.05), 1.936 (1.19), 2.784 (1.27), 2.800 (2.49), 2.816 (3.13), 2.819 (16.00), 2.851 (1.75), 2.857 (1.27), 3.695 (1.59), 3.710 (2.66), 3.725 (1.16), 4.347 (1.00), 7.291 (1.61), 8.035 (2.20), 8.065 (2.20).

Example 121

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 5-methoxy-4-methylpyridin-3-amine.

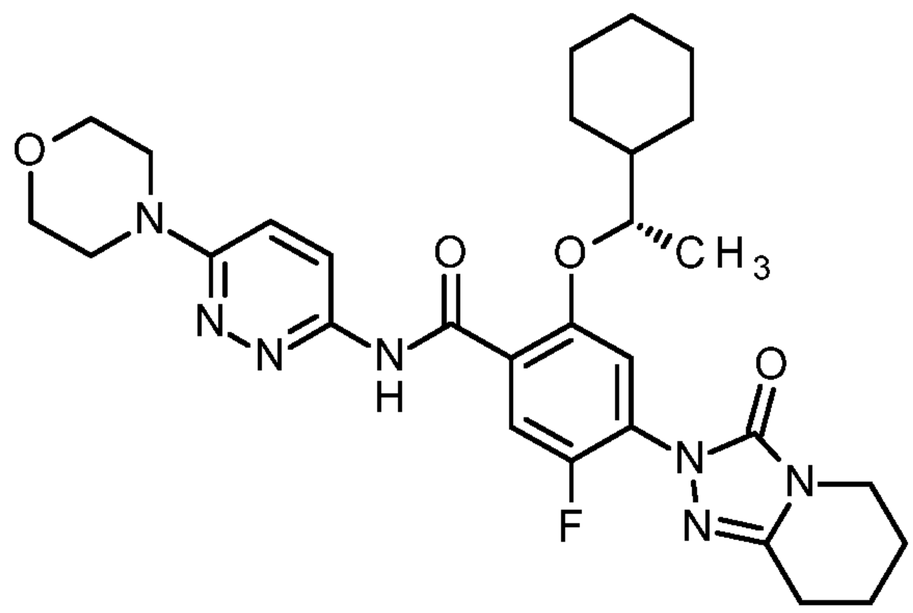
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method A): R_t = 1.20 min; MS (ESIpos): m/z = 524 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.298 (6.59), 1.313 (6.91), 1.683 (1.19), 1.868 (1.13), 1.873 (1.32), 1.924 (1.17), 1.930 (1.08), 1.940 (1.06), 2.150 (14.84), 2.726 (1.50), 2.742 (2.88), 2.758 (1.65), 3.634 (1.87), 3.650 (3.14), 3.665 (1.32), 3.893 (16.00), 4.360 (1.00), 7.338 (1.81), 7.353 (1.81), 8.042 (3.18), 8.063 (2.46), 8.093 (2.49), 8.677 (2.37), 9.646 (1.54).

Example 122

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[6-(morpholin-4-yl)pyridazin-3-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 6-(morpholin-4-yl)pyridazin-3-amine.

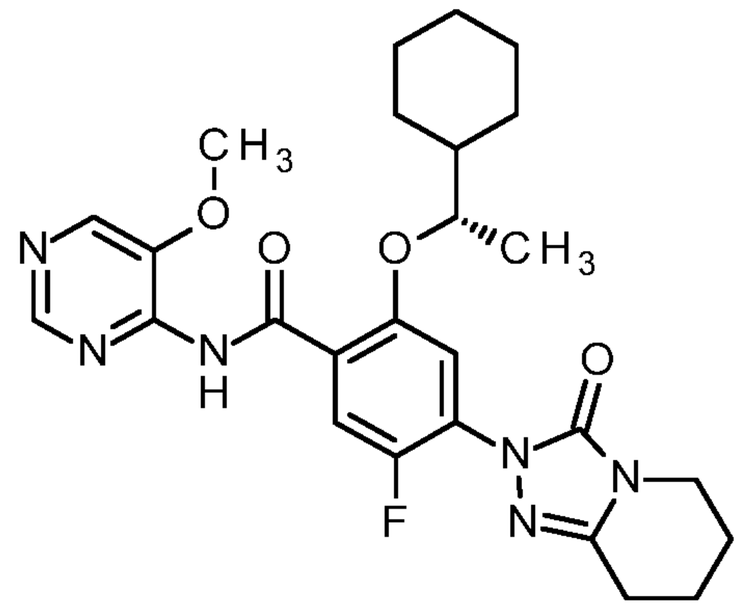
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.30 min; MS (ESIpos): m/z = 567 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.085 (1.31), 1.095 (1.47), 1.117 (2.32), 1.123 (2.56), 1.137 (1.05), 1.147 (2.08), 1.155 (2.37), 1.160 (1.99), 1.168 (0.99), 1.183 (0.93), 1.191 (0.91), 1.259 (1.62), 1.290 (2.08), 1.323 (1.66), 1.409 (15.58), 1.425 (16.00), 1.674 (1.14), 1.704 (1.04), 1.749 (2.09), 1.756 (2.11), 1.781 (3.03), 1.799 (1.96), 1.808 (1.87), 1.831 (1.06), 1.839 (0.99), 1.847 (1.01), 1.925 (1.94), 1.933 (2.50), 1.938 (2.97), 1.948 (3.79), 1.952 (3.95), 1.964 (1.87), 1.968 (1.89), 1.989 (2.19), 2.003 (2.58), 2.009 (2.71), 2.018 (3.20), 2.024 (2.38), 2.034 (1.68), 2.805 (3.84), 2.820 (7.56), 2.837 (4.22), 3.709 (6.23), 3.717 (10.39), 3.720 (10.18), 3.732 (14.91), 3.747 (3.82), 3.882 (8.63), 3.896 (9.39), 3.906 (6.47), 4.405 (1.64), 4.421 (2.51), 4.437 (1.63), 7.006 (0.57), 7.301 (2.87), 7.381 (4.86), 7.395 (4.80), 8.046 (6.81), 8.076 (6.86), 8.737 (3.23), 8.762 (3.05), 11.073 (1.18).

Example 123

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methoxypyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 6-(morpholin-4-yl)pyridazin-3-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.14 min; MS (ESIpos): m/z = 511 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.031 (0.48), 1.038 (0.47), 1.067 (0.83), 1.098 (0.74), 1.132 (0.50), 1.163 (0.59), 1.185 (0.91), 1.205 (0.83), 1.213 (0.58), 1.228 (0.66), 1.237 (0.70), 1.245 (0.41), 1.258 (0.53), 1.383 (7.29), 1.399 (7.32), 1.688 (1.41), 1.727 (0.48), 1.747 (0.94), 1.754 (1.09), 1.779 (1.74), 1.803 (1.09), 1.918 (0.84), 1.925 (1.01), 1.930 (1.15), 1.941 (1.29), 1.945 (1.44), 1.957 (1.07), 1.960 (1.06), 1.983 (0.98), 1.988 (1.04), 1.997 (1.42), 2.012 (1.24), 2.017 (1.02), 2.026 (0.74), 2.796 (1.71), 2.812 (3.28), 2.829 (1.90), 3.707 (2.10), 3.722 (3.52), 3.737 (1.52), 4.033 (16.00), 4.392 (0.75), 4.408 (1.10), 4.424 (0.72), 7.390 (2.08), 7.405 (2.06), 8.140 (2.99), 8.169 (2.95), 8.263 (2.87), 8.772 (4.28), 10.731 (1.73).

Example 124

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methoxypyrimidin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide

From intermediate 19 and 2-methoxypyrimidin-5-amine.

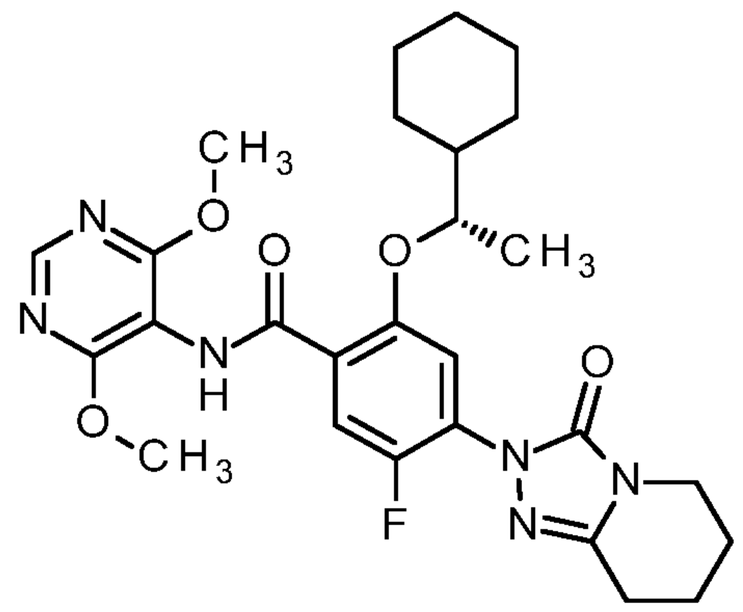
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.29 min; MS (ESIpos): m/z = 512 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.393 (5.54), 1.409 (5.64), 2.801 (1.12), 2.817 (2.12), 2.834 (1.25), 3.712 (1.40), 3.728 (2.35), 3.743 (1.00), 4.045 (16.00), 7.393 (1.42), 7.408 (1.42), 8.121 (2.01), 8.150 (1.97), 8.866 (10.12), 10.079 (1.31).

Example 125

2-[(1S)-1-cyclohexylethoxy]-N-(4,6-dimethoxypyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 4,6-dimethoxypyrimidin-5-amine.

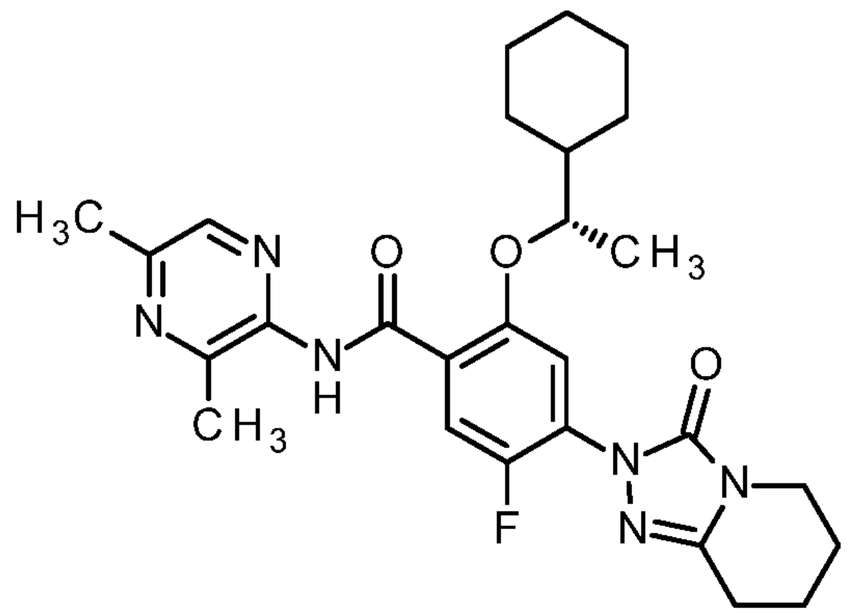
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.2 % aqueous ammonia, acetonitrile).

LC-MS (method B): R_t = 1.33 min; MS (ESIpos): m/z = 541 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.205 (0.43), 1.359 (2.94), 1.375 (2.89), 1.662 (0.91), 1.767 (0.61), 1.792 (0.60), 1.925 (0.45), 1.937 (0.46), 1.940 (0.49), 1.977 (0.43), 1.991 (0.52), 1.997 (0.56), 2.007 (0.67), 2.012 (0.64), 2.018 (0.40), 2.794 (0.66), 2.810 (1.31), 2.825 (0.74), 3.703 (0.83), 3.718 (1.41), 3.733 (0.61), 4.020 (16.00), 4.419 (0.50), 7.360 (0.82), 7.374 (0.83), 8.107 (1.03), 8.136 (1.03), 8.380 (2.30), 9.304 (0.82).

Example 126

2-[(1S)-1-cyclohexylethoxy]-N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 3,5-dimethylpyrazin-2-amine.

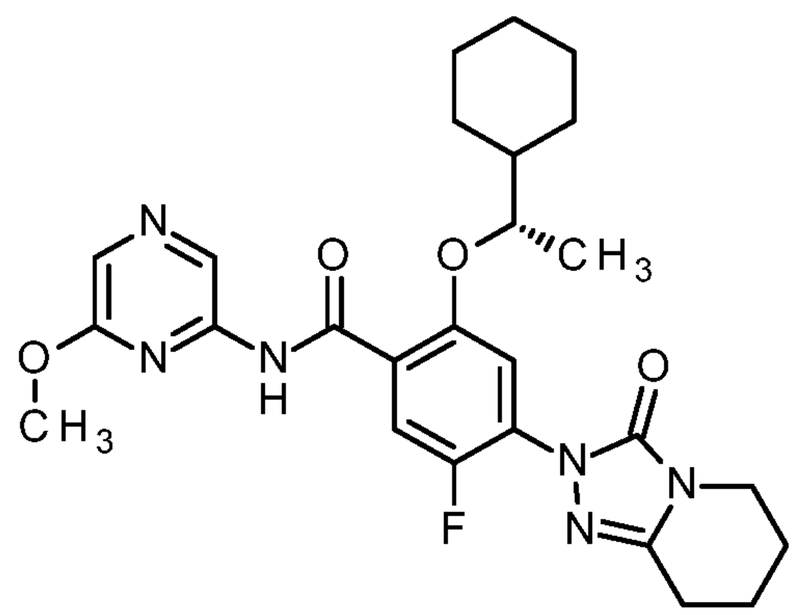
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.32 min; MS (ESIpos): m/z = 510 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.126 (0.59), 1.157 (0.53), 1.181 (0.45), 1.203 (0.77), 1.228 (0.75), 1.234 (0.66), 1.243 (0.52), 1.251 (0.51), 1.260 (0.75), 1.274 (0.41), 1.396 (4.90), 1.412 (4.84), 1.702 (0.48), 1.745 (0.55), 1.770 (0.98), 1.785 (0.74), 1.795 (0.81), 1.908 (0.54), 1.923 (0.84), 1.935 (0.96), 1.947 (0.93), 1.951 (0.98), 1.966 (0.77), 1.987 (0.60), 2.002 (1.07), 2.007 (1.07), 2.018 (0.89), 2.023 (0.70), 2.032 (0.51), 2.565 (16.00), 2.803 (1.09), 2.819 (2.09), 2.836 (1.18), 3.713 (1.36), 3.729 (2.24), 3.744 (0.98), 4.427 (0.52), 4.442 (0.74), 4.457 (0.49), 7.394 (1.34), 7.409 (1.33), 8.122 (1.70), 8.151 (1.71), 8.172 (1.55), 10.087 (1.09).

Example 127

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxypyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 6-methoxypyrazin-2-amine.

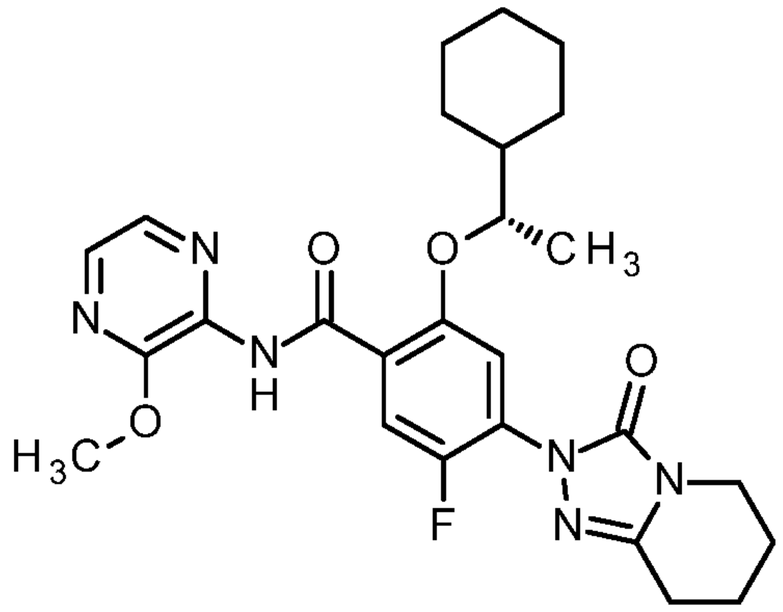
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.47 min; MS (ESIpos): m/z = 511 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.174 (0.85), 1.205 (1.29), 1.232 (1.01), 1.250 (0.49), 1.261 (0.74), 1.405 (6.24), 1.421 (6.21), 1.622 (0.41), 1.692 (0.43), 1.722 (0.42), 1.782 (0.82), 1.805 (0.78), 1.815 (0.79), 1.830 (0.48), 1.839 (0.54), 1.850 (0.55), 1.874 (0.41), 1.925 (0.64), 1.933 (0.75), 1.937 (0.83), 1.948 (0.85), 1.952 (0.91), 1.964 (0.42), 1.968 (0.45), 1.990 (0.47), 2.005 (1.03), 2.010 (1.16), 2.019 (1.17), 2.025 (0.94), 2.035 (0.74), 2.040 (0.60), 2.047 (0.57), 2.803 (1.29), 2.820 (2.44), 2.836 (1.42), 3.714 (1.66), 3.729 (2.70), 3.744 (1.15), 3.953 (16.00), 4.458 (0.57), 4.473 (0.83), 4.489 (0.55), 7.414 (1.62), 7.428 (1.59), 8.043 (3.93), 8.143 (2.27), 8.172 (2.20), 9.260 (3.63), 10.567 (1.22).

Example 128

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methoxypyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 3-methoxypyrazin-2-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

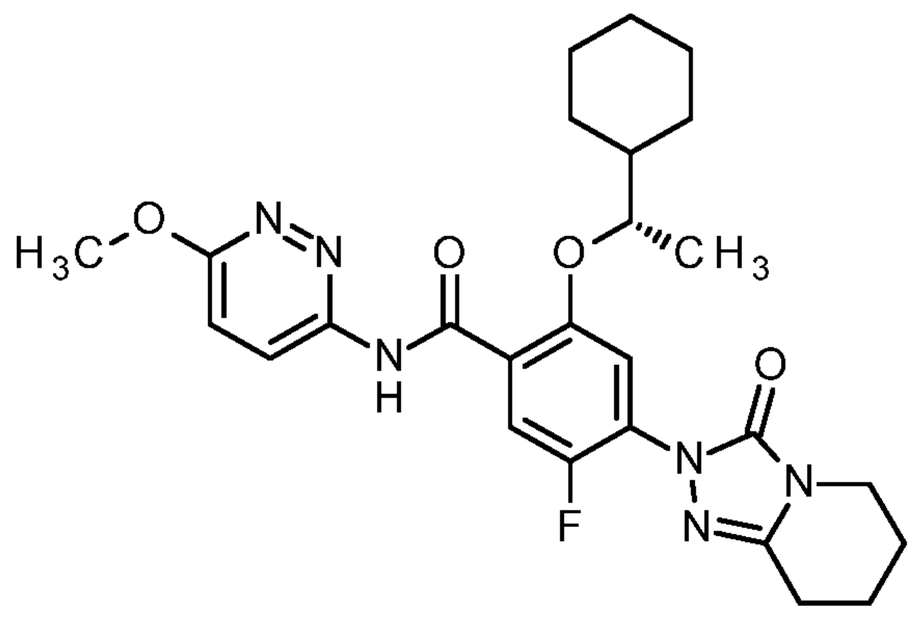
LC-MS (method A): R_t = 1.34 min; MS (ESIpos): m/z = 512 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.036 (0.79), 1.041 (0.60), 1.049 (0.57), 1.079 (0.89), 1.112 (0.97), 1.135 (0.55), 1.143 (0.58), 1.166 (0.70), 1.192 (1.34), 1.221 (0.88), 1.229 (0.71), 1.252 (0.86), 1.259 (0.80), 1.278 (3.86), 1.296 (0.56), 1.397 (6.33), 1.412 (6.33), 1.682 (0.57), 1.713 (0.66), 1.748 (0.72), 1.756 (0.69), 1.791 (2.14), 1.817 (1.64), 1.903 (0.41), 1.919 (1.04), 1.931 (1.47), 1.946 (1.63), 1.962 (1.17), 1.983 (1.86), 2.002 (2.29), 2.012 (2.41), 2.040 (0.58), 2.798 (1.63), 2.814 (3.19), 2.830 (1.79), 3.710 (1.95), 3.725 (3.34), 3.740 (1.56), 4.091

(16.00), 4.400 (0.78), 4.416 (1.16), 4.431 (0.77), 7.374 (1.89), 7.389 (1.90), 7.837 (1.71), 7.844 (1.91), 8.064 (1.59), 8.071 (1.60), 8.156 (2.14), 8.185 (2.12), 10.658 (1.61).

Example 129

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxypyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 6-methoxypyridazin-3-amine.

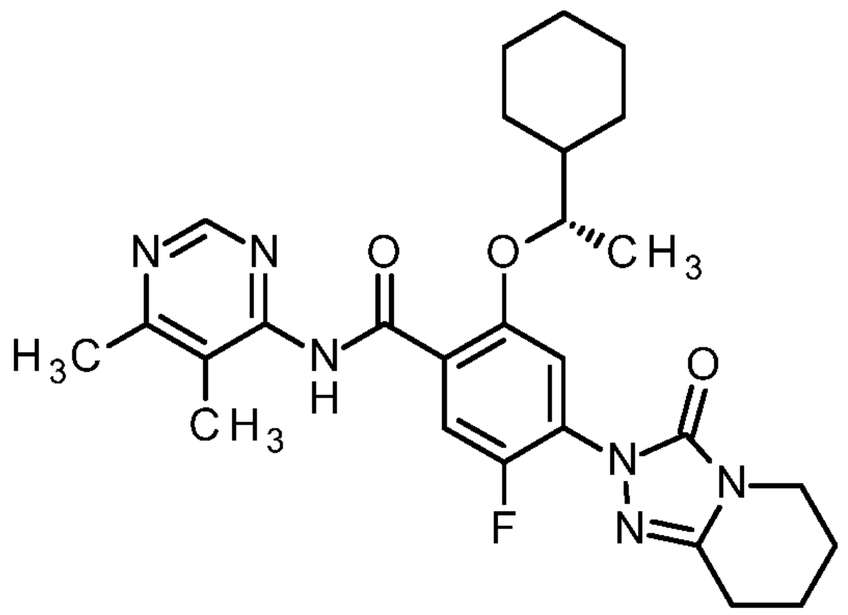
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.40 min; MS (ESIpos): m/z = 511 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.149 (0.81), 1.181 (0.83), 1.445 (5.28), 1.461 (5.44), 1.946 (0.73), 1.950 (0.78), 2.002 (0.83), 2.007 (0.87), 2.017 (1.07), 2.023 (0.90), 2.802 (1.11), 2.818 (2.14), 2.834 (1.23), 3.713 (1.43), 3.729 (2.30), 3.744 (1.01), 4.127 (16.00), 4.436 (0.88), 7.036 (1.70), 7.059 (1.69), 7.061 (1.63), 7.387 (1.42), 7.402 (1.42), 8.105 (1.96), 8.135 (1.92), 8.587 (2.83), 8.610 (2.65), 10.991 (1.13).

Example 130

2-[(1S)-1-cyclohexylethoxy]-N-(5,6-dimethylpyrimidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 5,6-dimethylpyrimidin-4-amine.

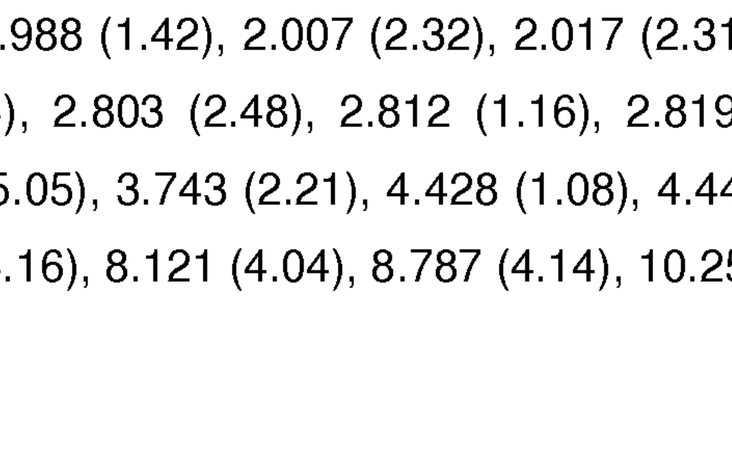
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.28 min; MS (ESIpos): m/z = 509 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.121 (0.74), 1.129 (0.69), 1.152 (1.26), 1.179 (1.50), 1.206 (1.45), 1.212 (1.37), 1.224 (0.79), 1.239 (1.12), 1.247 (1.04), 1.255 (1.08), 1.263 (1.35), 1.271 (1.08), 1.278 (0.96), 1.287 (0.80), 1.294 (0.76), 1.302 (0.67), 1.369 (0.96), 1.385 (1.02), 1.406 (11.40), 1.421 (11.11), 1.681 (0.88), 1.713 (0.91), 1.729 (0.64), 1.737 (0.66), 1.744 (0.66), 1.773 (2.00), 1.798 (2.32), 1.908 (0.46), 1.924 (1.28), 1.936 (1.70), 1.947 (1.79), 1.951 (1.88), 1.967 (1.14), 1.988 (1.42), 2.007 (2.32), 2.017 (2.31), 2.029 (1.16), 2.047 (0.47), 2.238 (16.00), 2.598 (11.14), 2.803 (2.48), 2.812 (1.16), 2.819 (4.69), 2.836 (2.72), 3.713 (3.07), 3.720 (0.91), 3.728 (5.05), 3.743 (2.21), 4.428 (1.08), 4.444 (1.61), 4.459 (1.06), 7.408 (2.90), 7.423 (2.92), 8.093 (4.16), 8.121 (4.04), 8.787 (4.14), 10.250 (1.31).

Example 131

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyrimidin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 4-methylpyrimidin-5-amine.

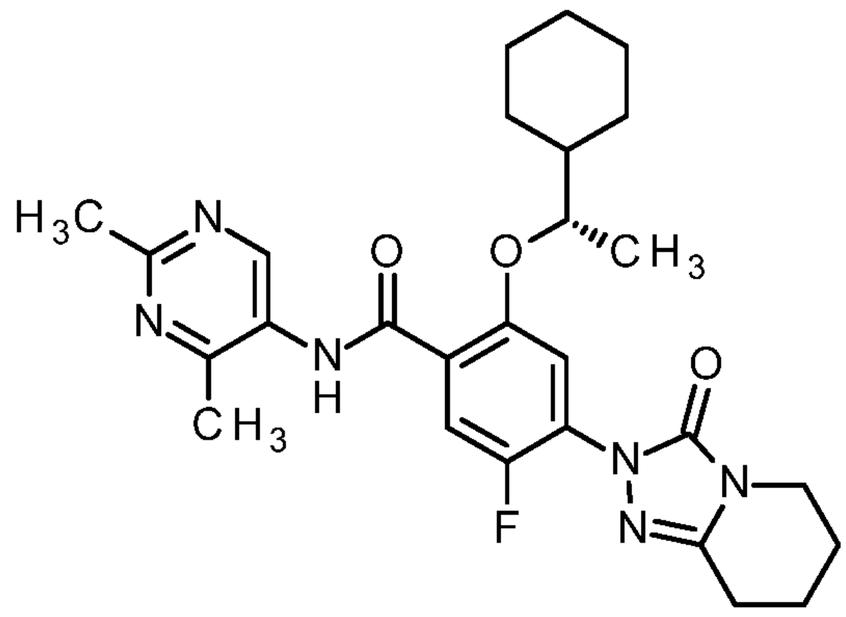
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.21 min; MS (ESIpos): m/z = 495 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.036 (0.42), 1.068 (0.56), 1.074 (0.56), 1.100 (0.64), 1.123 (0.52), 1.132 (0.68), 1.138 (0.62), 1.145 (0.54), 1.153 (0.63), 1.161 (0.61), 1.183 (0.82), 1.214 (0.85), 1.245 (0.91), 1.254 (0.71), 1.261 (1.29), 1.399 (6.46), 1.414 (6.67), 1.595 (5.20), 1.695 (0.72), 1.715 (0.83), 1.723 (0.94), 1.731 (0.86), 1.740 (0.94), 1.754 (0.86), 1.762 (0.97), 1.776 (1.24), 1.804 (0.62), 1.928 (0.80), 1.941 (1.05), 1.952 (1.19), 1.956 (1.36), 1.968 (0.97), 1.993 (0.94), 1.999 (0.97), 2.007 (1.26), 2.013 (1.16), 2.023 (1.10), 2.028 (0.92), 2.037 (0.67), 2.580 (16.00), 2.809 (1.55), 2.824 (2.90), 2.840 (1.64), 3.102 (0.42), 3.717 (1.93), 3.733 (3.14), 3.748 (1.38), 4.447 (0.69), 4.463 (1.02), 4.479 (0.65), 7.445 (1.85), 7.459 (1.84), 8.139 (2.52), 8.168 (2.48), 8.935 (3.62), 9.325 (2.90), 9.764 (1.57).

Example 132

2-[(1S)-1-cyclohexylethoxy]-N-(2,4-dimethylpyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 2,4-dimethylpyrimidin-5-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.2 % aqueous ammonia, acetonitrile).

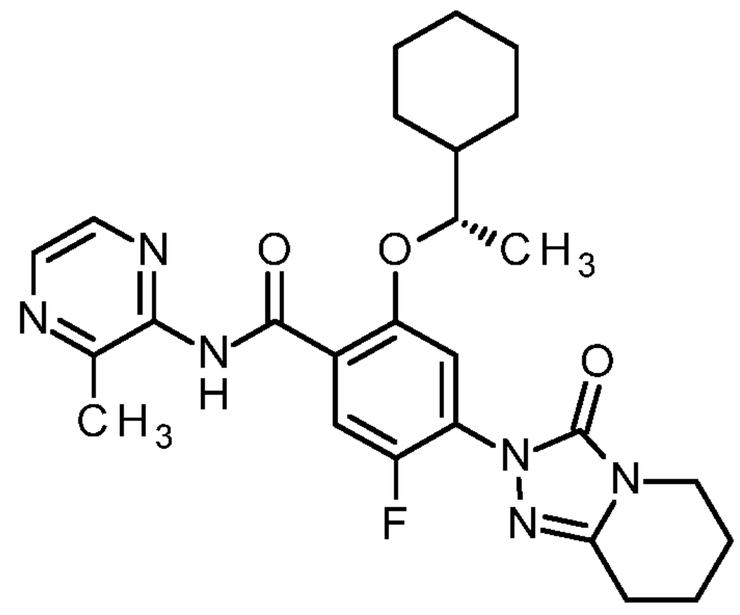
LC-MS (method B): R_t = 1.23 min; MS (ESIpos): m/z = 509 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.060 (0.45), 1.066 (0.45), 1.114 (0.60), 1.142 (0.76), 1.177 (0.77), 1.210 (0.75), 1.217 (0.47), 1.240 (0.71), 1.260 (0.69), 1.388 (6.64), 1.404 (6.66), 1.618 (1.40), 1.688 (0.69), 1.701 (0.68), 1.710 (0.75), 1.717 (0.87), 1.725 (0.80), 1.736 (0.72), 1.749 (0.69), 1.768 (1.15), 1.798 (0.60), 1.925 (0.73), 1.937 (1.02), 1.948 (1.30), 1.952 (1.44), 1.964 (0.77), 1.990 (0.90), 2.004 (1.01), 2.009 (1.01), 2.019 (1.04), 2.024 (0.85), 2.033

(0.62), 2.527 (16.00), 2.725 (12.54), 2.805 (1.47), 2.820 (2.85), 2.836 (1.62), 3.713 (1.89), 3.729 (3.04), 3.744 (1.33), 4.438 (0.67), 4.454 (1.00), 4.470 (0.64), 7.428 (1.78), 7.443 (1.78), 8.131 (2.56), 8.160 (2.52), 9.102 (3.75), 9.689 (1.62).

Example 133

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 3-methylpyrazin-2-amine.

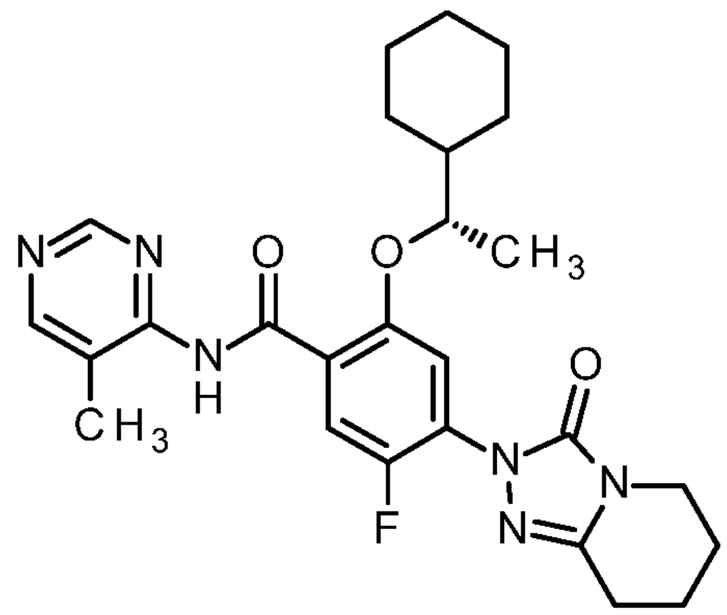
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.24 min; MS (ESIpos): m/z = 495 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.102 (0.63), 1.110 (0.58), 1.133 (1.08), 1.140 (0.90), 1.156 (0.59), 1.164 (1.04), 1.171 (0.94), 1.181 (0.59), 1.194 (0.60), 1.204 (1.17), 1.209 (1.14), 1.218 (0.53), 1.233 (1.23), 1.242 (0.93), 1.249 (0.86), 1.264 (0.90), 1.273 (0.67), 1.281 (0.60), 1.289 (0.49), 1.405 (9.32), 1.421 (9.40), 1.623 (0.60), 1.673 (0.71), 1.706 (0.72), 1.714 (0.61), 1.722 (0.42), 1.730 (0.41), 1.737 (0.50), 1.743 (0.69), 1.760 (1.44), 1.766 (1.62), 1.780 (1.73), 1.789 (1.61), 1.798 (1.24), 1.924 (0.97), 1.932 (1.16), 1.937 (1.31), 1.948 (1.34), 1.952 (1.44), 1.968 (0.90), 1.988 (1.12), 1.994 (0.91), 2.009 (1.88), 2.018 (1.86), 2.033 (0.88), 2.608 (16.00), 2.805 (2.03), 2.820 (3.89), 2.837 (2.21), 3.714 (2.51), 3.730 (4.21), 3.744 (1.81), 4.435 (0.96), 4.450 (1.39), 4.465 (0.92), 7.408 (2.54), 7.423 (2.52), 8.126 (3.34), 8.155 (3.34), 8.298 (1.88), 8.304 (2.07), 8.389 (2.50), 8.395 (2.21), 10.183 (2.08).

Example 134

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methylpyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 5-methylpyrimidin-4-amine.

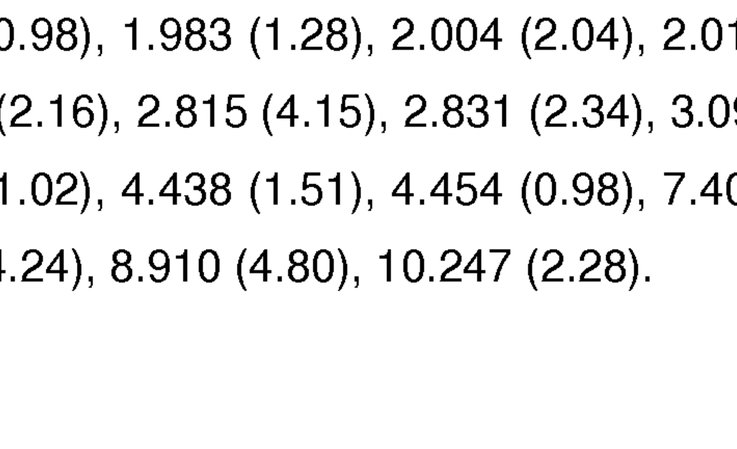
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.2 % aqueous ammonia, acetonitrile).

LC-MS (method B): R_t = 1.22 min; MS (ESIpos): m/z = 495 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.110 (0.74), 1.118 (0.66), 1.141 (1.27), 1.148 (0.99), 1.165 (1.10), 1.172 (1.23), 1.188 (1.05), 1.195 (1.14), 1.202 (0.80), 1.217 (0.89), 1.221 (0.90), 1.238 (0.85), 1.245 (0.97), 1.253 (0.88), 1.263 (0.93), 1.270 (0.82), 1.276 (0.71), 1.285 (0.60), 1.294 (0.52), 1.402 (9.98), 1.418 (9.92), 1.700 (2.07), 1.729 (0.56), 1.736 (0.54), 1.764 (1.73), 1.772 (1.75), 1.788 (1.89), 1.911 (0.52), 1.920 (1.08), 1.927 (1.31), 1.932 (1.46), 1.943 (1.49), 1.947 (1.59), 1.963 (0.98), 1.983 (1.28), 2.004 (2.04), 2.014 (2.19), 2.025 (1.01), 2.042 (0.40), 2.313 (16.00), 2.799 (2.16), 2.815 (4.15), 2.831 (2.34), 3.097 (0.64), 3.708 (2.76), 3.723 (4.43), 3.739 (1.96), 4.423 (1.02), 4.438 (1.51), 4.454 (0.98), 7.409 (2.73), 7.424 (2.70), 8.099 (3.71), 8.128 (3.65), 8.562 (4.24), 8.910 (4.80), 10.247 (2.28).

Example 135

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 4-methylpyridazin-3-amine.

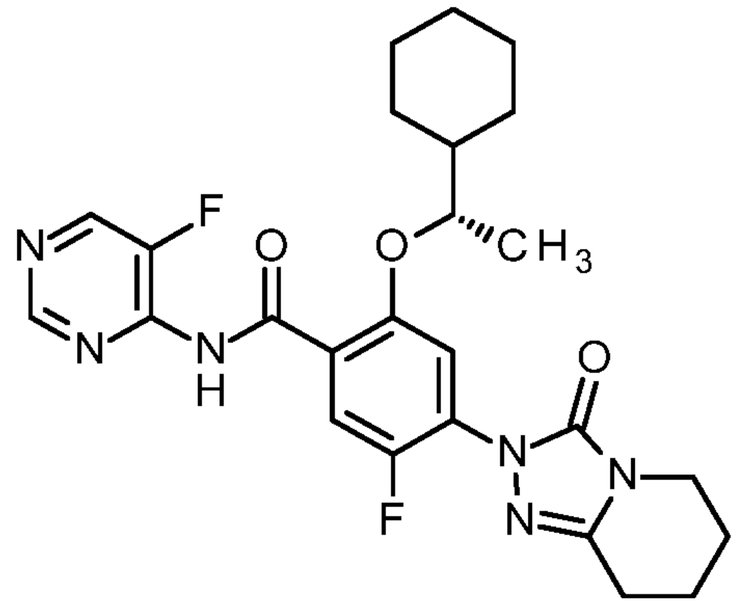
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.19 min; MS (ESIpos): m/z = 495 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.100 (0.44), 1.129 (1.24), 1.158 (1.74), 1.190 (1.61), 1.223 (1.78), 1.227 (1.79), 1.240 (1.27), 1.249 (1.61), 1.263 (2.61), 1.271 (2.03), 1.294 (1.33), 1.302 (1.23), 1.326 (0.48), 1.433 (13.98), 1.448 (13.80), 1.664 (3.93), 1.765 (2.70), 1.800 (3.50), 1.829 (1.51), 1.911 (0.65), 1.926 (1.69), 1.939 (2.22), 1.950 (2.30), 1.953 (2.42), 1.969 (1.17), 1.991 (1.46), 2.005 (3.08), 2.010 (3.13), 2.020 (2.83), 2.026 (2.45), 2.035 (2.34), 2.398 (16.00), 2.807 (3.36), 2.823 (6.46), 2.839 (3.67), 3.717 (4.19), 3.732 (7.02), 3.747 (3.04), 4.440 (1.41), 4.456 (2.03), 4.470 (1.36), 7.006 (0.53), 7.420 (5.35), 7.435 (5.86), 7.529 (0.58), 8.093 (5.55), 8.121 (5.47), 8.971 (2.05), 8.983 (2.01), 10.558 (2.28).

Example 136

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-fluoropyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 5-fluoropyrimidin-4-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

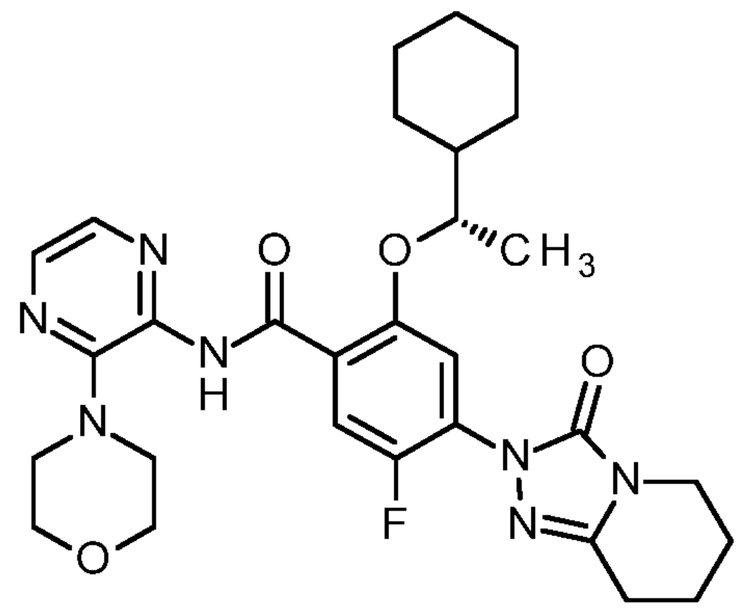
LC-MS (method A): R_t = 1.27 min; MS (ESIneg): m/z = 497 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.059 (1.01), 1.067 (0.98), 1.088 (1.15), 1.097 (1.31), 1.111 (1.20), 1.119 (1.05), 1.128 (0.99), 1.136 (1.24), 1.142 (1.47), 1.149 (1.34), 1.157 (0.71), 1.173 (1.01), 1.180 (1.48), 1.188 (0.73), 1.204 (0.55), 1.211 (0.91), 1.233 (0.84), 1.240 (0.84), 1.256 (1.15), 1.264 (1.62), 1.271 (1.51), 1.277 (1.29), 1.287 (1.08), 1.295 (1.23), 1.303 (1.12), 1.308 (1.03), 1.316 (0.63), 1.327 (0.40), 1.400 (16.00), 1.415 (15.57), 1.634 (2.45), 1.691 (1.18), 1.722 (1.07), 1.784 (3.55), 1.796 (2.87), 1.803 (2.96), 1.907 (0.59), 1.914 (0.78),

1.922 (1.74), 1.929 (2.09), 1.934 (2.34), 1.946 (2.42), 1.950 (2.61), 1.962 (1.49), 1.966 (1.81), 1.986 (1.79), 1.993 (1.57), 2.002 (3.11), 2.007 (3.37), 2.016 (3.58), 2.022 (2.33), 2.028 (1.53), 2.031 (1.57), 2.045 (0.67), 2.801 (3.70), 2.817 (7.06), 2.834 (4.10), 3.710 (4.73), 3.726 (7.62), 3.741 (3.34), 4.435 (1.55), 4.451 (2.33), 4.467 (1.52), 7.430 (4.52), 7.444 (4.54), 8.145 (6.44), 8.174 (6.34), 8.551 (5.33), 8.558 (5.23), 8.890 (5.58), 8.895 (5.48), 10.794 (2.81).

Example 137

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[3-(morpholin-4-yl)pyrazin-2-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 3-(morpholin-4-yl)pyrazin-2-amine.

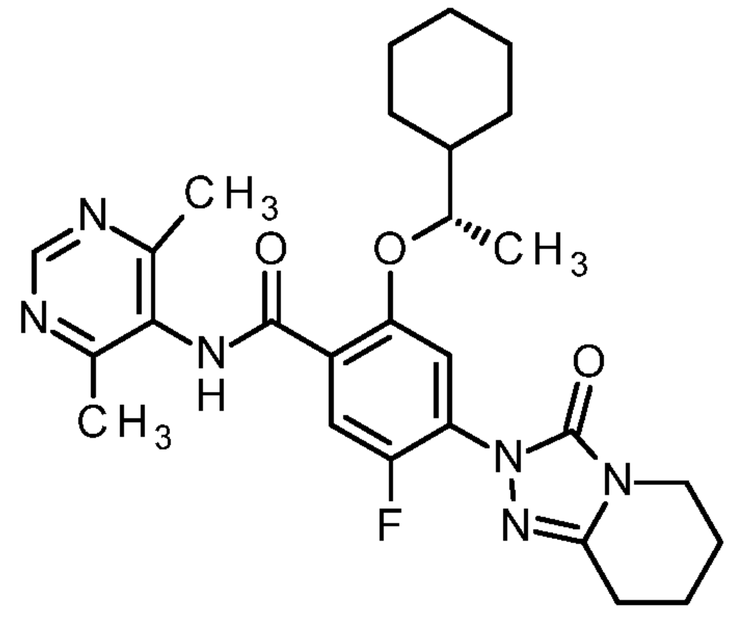
The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.27 min; MS (ESIneg): m/z = 564 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.016 (0.54), 1.048 (1.86), 1.079 (2.64), 1.109 (2.34), 1.123 (2.56), 1.154 (2.83), 1.180 (2.10), 1.213 (1.21), 1.245 (0.63), 1.261 (0.97), 1.369 (3.14), 1.385 (4.62), 1.390 (15.80), 1.406 (16.00), 1.637 (2.07), 1.667 (2.27), 1.695 (2.32), 1.729 (3.97), 1.737 (4.24), 1.760 (3.18), 1.833 (0.43), 1.912 (2.02), 1.926 (2.99), 1.938 (3.99), 1.950 (4.06), 1.953 (3.87), 1.965 (1.59), 1.991 (1.56), 2.005 (2.95), 2.011 (2.96), 2.021 (3.20), 2.026 (2.57), 2.035 (1.88), 2.049 (0.77), 2.803 (3.99), 2.812 (2.63), 2.819 (7.65), 2.828 (1.57), 2.835 (4.32), 3.273 (0.95), 3.285 (1.46), 3.306 (2.14), 3.319 (2.79), 3.328 (2.15), 3.359 (2.03), 3.368 (2.80), 3.382 (2.35), 3.403 (1.46), 3.414 (1.01), 3.704 (0.96), 3.716 (5.16), 3.731 (8.33), 3.746 (3.55), 3.784 (0.71), 3.792 (1.12), 3.812 (4.20), 3.821 (7.47), 3.826 (6.26), 3.830 (6.33), 3.836 (7.10), 3.845 (3.71), 3.865 (0.89), 3.873 (0.54), 4.354 (0.44), 4.369 (1.73), 4.385 (2.60), 4.400 (1.73), 4.415 (0.45), 4.485 (0.41), 7.006 (0.48), 7.390 (4.67), 7.405 (4.61), 7.449 (0.81), 7.463 (0.79), 7.529 (0.48), 8.014 (1.32), 8.041 (1.08), 8.072 (5.79), 8.079 (8.31), 8.107 (8.60), 8.113 (6.24), 8.156 (6.14), 8.185 (6.20), 10.210 (3.81).

Example 138

2-[(1S)-1-cyclohexylethoxy]-N-(4,6-dimethylpyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 19 and 4,6-dimethylpyrimidin-5-amine.

The product was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile).

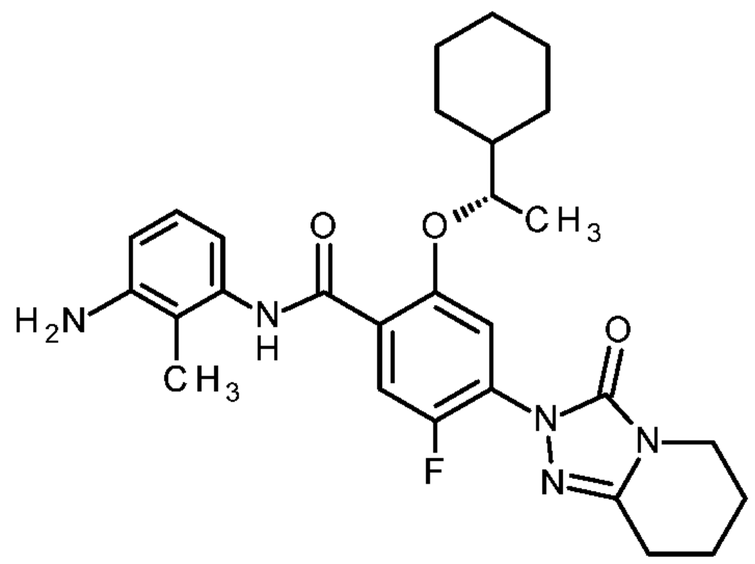
LC-MS (method A): R_t = 1.18 min; MS (ESIpos): m/z = 509 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.388 (3.64), 1.404 (3.60), 1.588 (0.60), 1.720 (0.64), 1.756 (0.60), 1.930 (0.52), 1.942 (0.79), 1.953 (0.67), 1.957 (0.70), 1.973 (0.52), 2.009 (0.53), 2.014 (0.57), 2.024 (0.58), 2.029 (0.49), 2.506 (16.00), 2.810 (0.81), 2.826 (1.58), 2.843 (0.89), 3.719 (1.03), 3.734 (1.69), 3.750 (0.75), 4.495 (0.55), 7.433 (1.00), 7.447 (0.99), 8.127 (1.39), 8.156 (1.37), 8.909 (2.11), 9.558 (0.93).

Examples 139–147 were prepared in analogy according to the general methods described above.

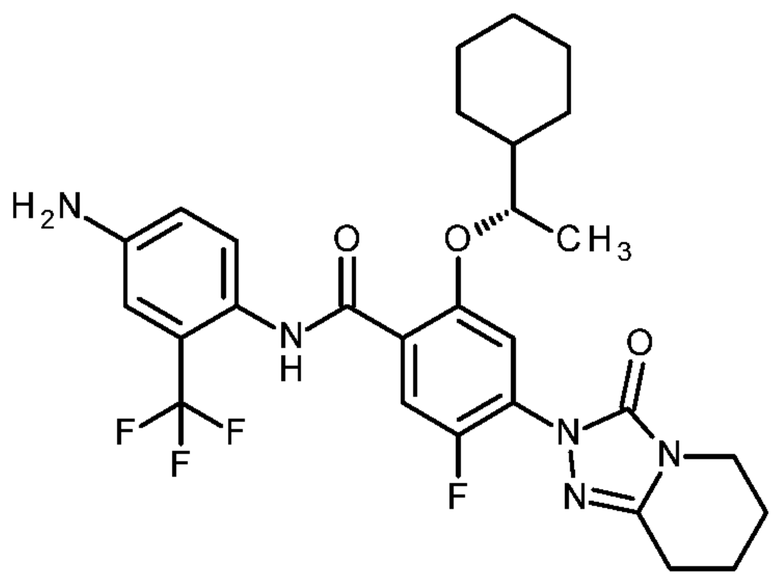
Example 139

N-(3-amino-2-methylphenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



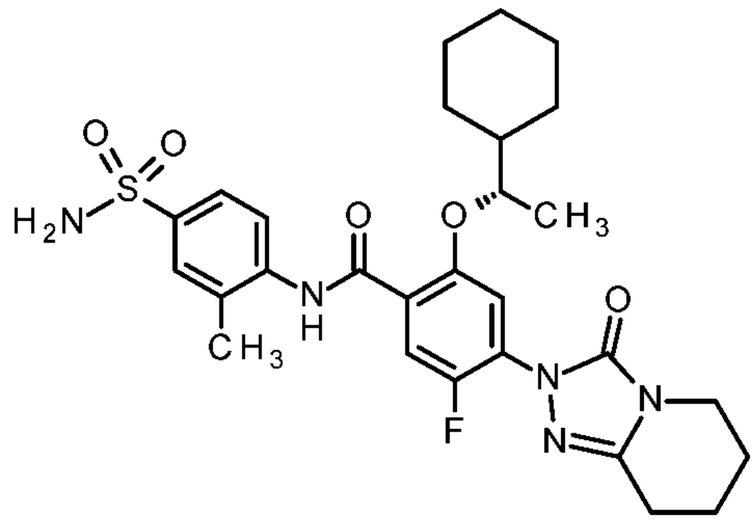
Example 140

N-[4-amino-2-(trifluoromethyl)phenyl]-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



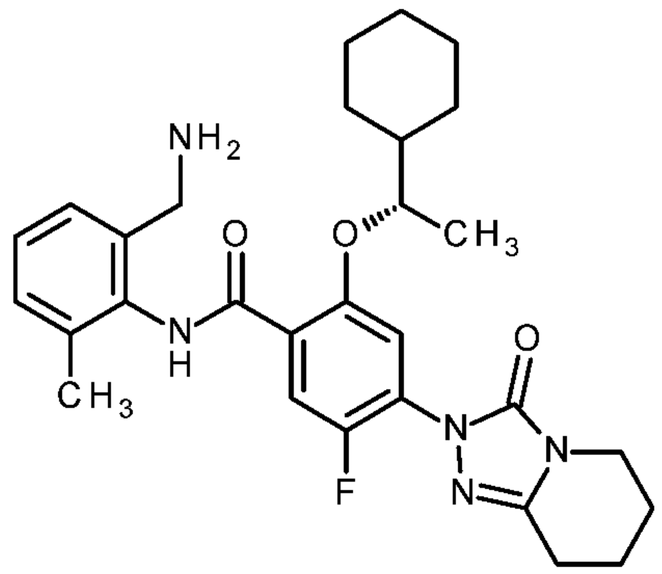
Example 141

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methyl-4-sulfamoylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



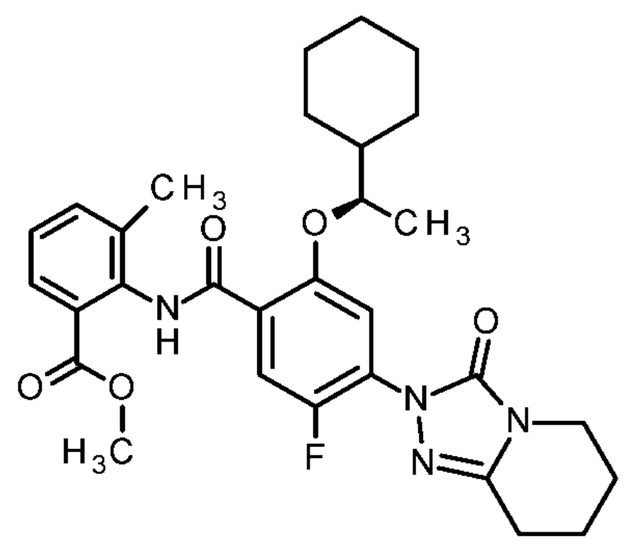
Example 142

N-[2-(aminomethyl)-6-methylphenyl]-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



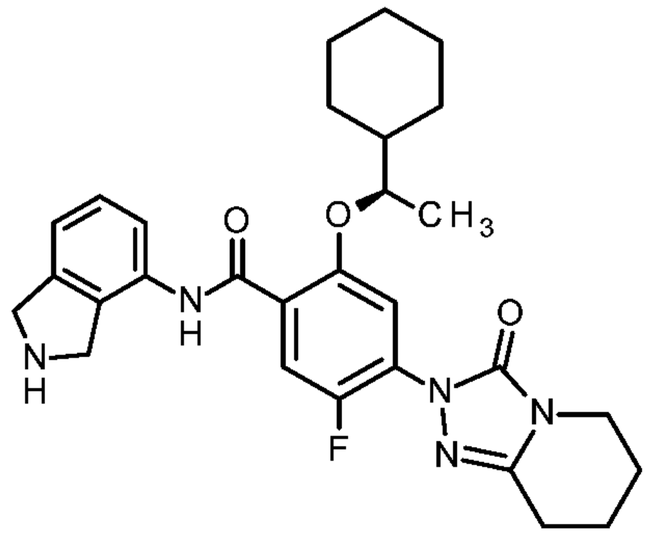
Example 143

Methyl 2-({2-[(1R)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoate



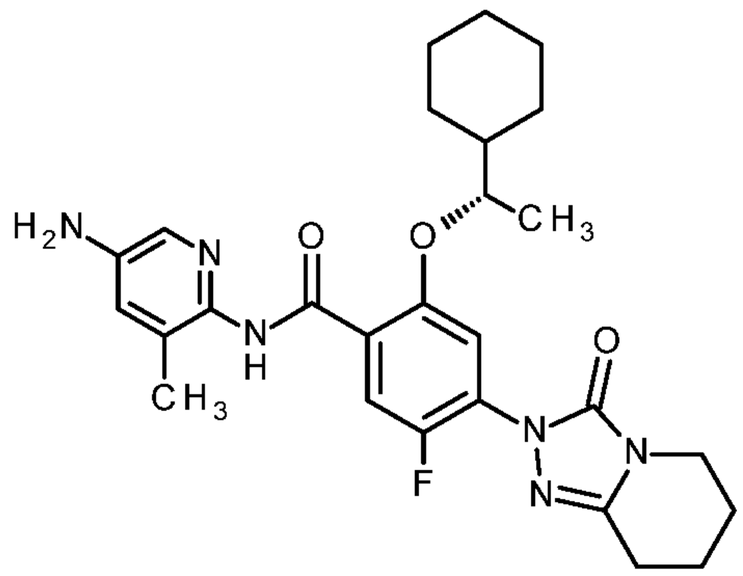
Example 144

2-[(1R)-1-cyclohexylethoxy]-N-(2,3-dihydro-1H-isoindol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



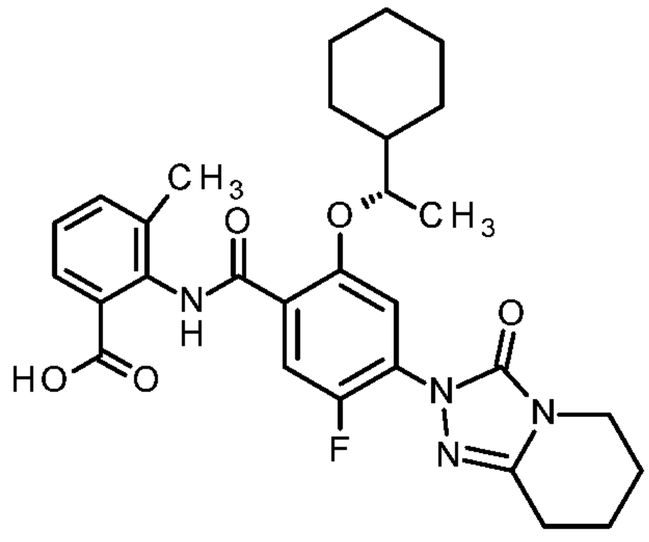
Example 145

N-(5-amino-3-methylpyridin-2-yl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



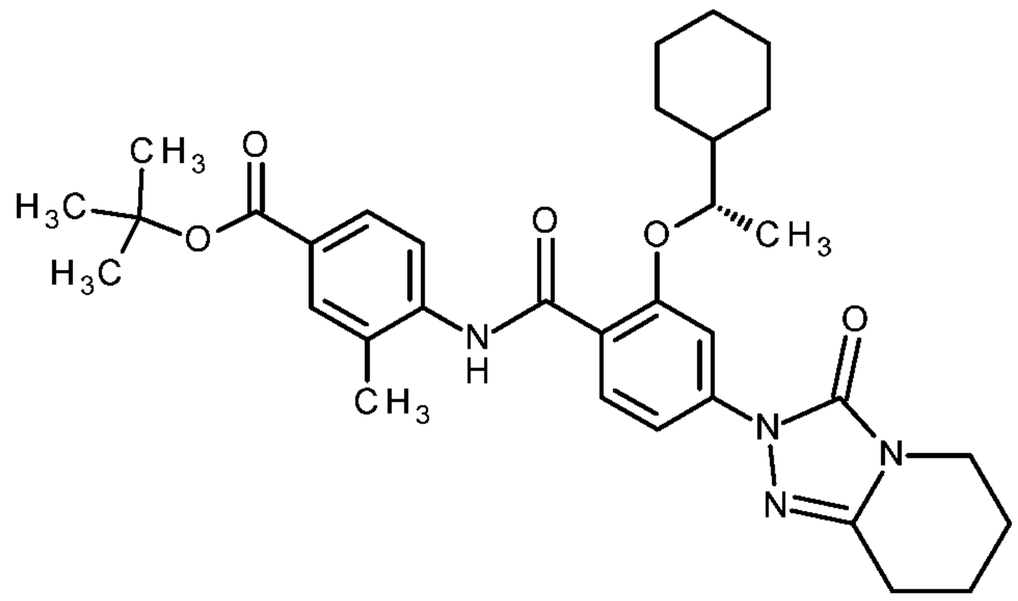
Example 146

2-({2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoic acid



Example 147

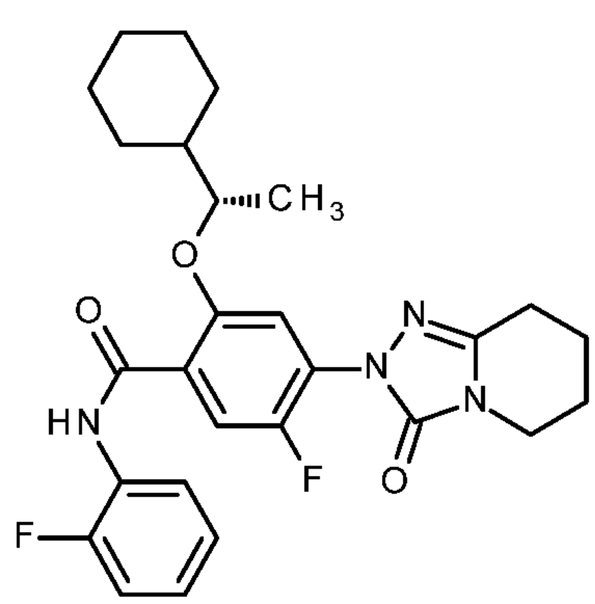
tert-butyl 4-({2-[(1S)-1-cyclohexylethoxy]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoate



Examples 148–179 were prepared as described for example 113 from 2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 19) and the respective amines, as indicated. Products were purified by flash column chromatography or, if explicitely mentioned, by preparative HPLC.

Example 148

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



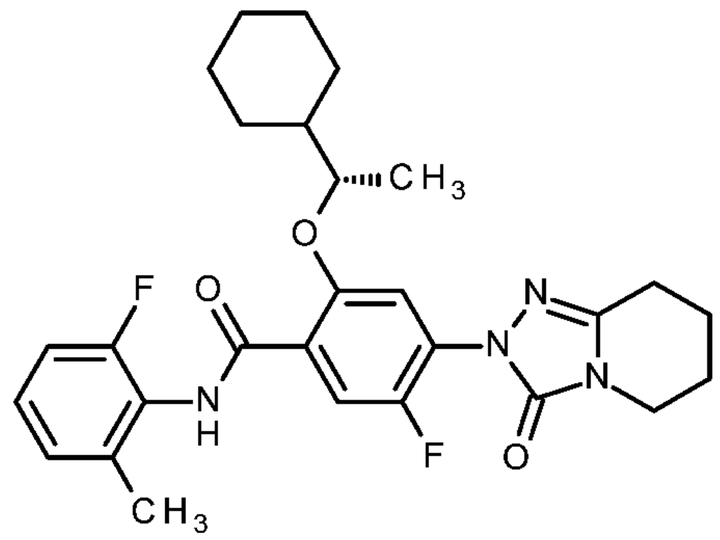
From intermediate 19 and 2-fluoroaniline.

MS (ESIpos): m/z = 497 $(M+H)^+$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 0.96 - 1.21 (m, 3H), 1.21 - 1.35 (m, 2H), 1.38 (d, 3H), 1.65 – 1.86 (m, 5H), 1.89 – 1.97 (m, 2H), 1.97 – 2.04 (m, 3H), 2.81 (t, 2H), 3.72 (t, 2H), 4.35 – 4.44 (m, 1H), 7.03 – 7.21 (m, 3H), 7.36 (d, 1H), 8.16 (d, 1H), 8.61 (td, 1H), 10.4 (s, 1H).

Example 149

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



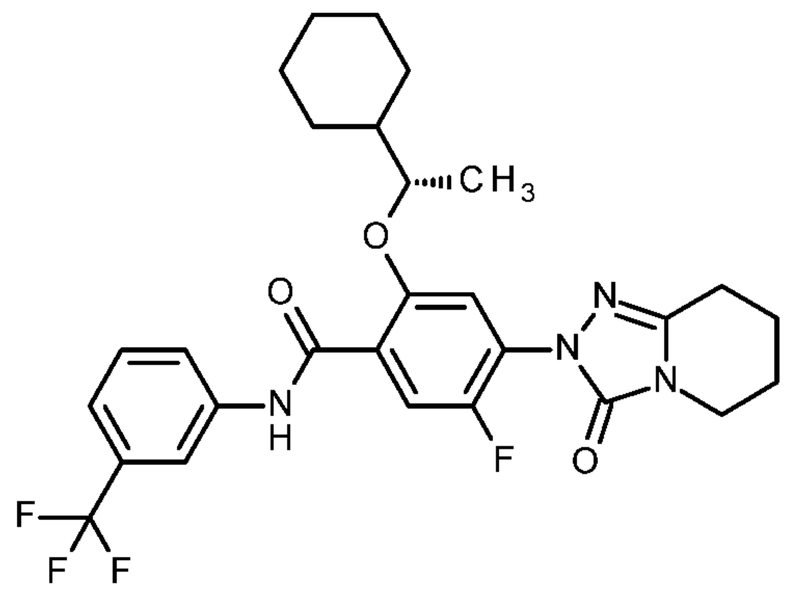
From intermediate 19 and 2-fluoro-6-methylaniline.

MS (ESIpos): m/z = 511 $(M+H)^+$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 0.97 – 1.31 (m, 5H), 1.37 (d, 3H), 1.62 – 1.80 (m, 5H), 1.89 – 2.05 (m, 5H), 2.31 (s, 3H), 2.81 (t, 2H), 3.72 (t, 2H), 4.38 – 4.47 (m, 1H), 7.00 (td, 1H), 7.06 (d, 1H), 7.17 (dd, 1H), 7.38 (d, 1H), 8.14 (d, 1H), 9.52 (s, 1H).

Example 150

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[3-(trifluoromethyl)phenyl]benzamide



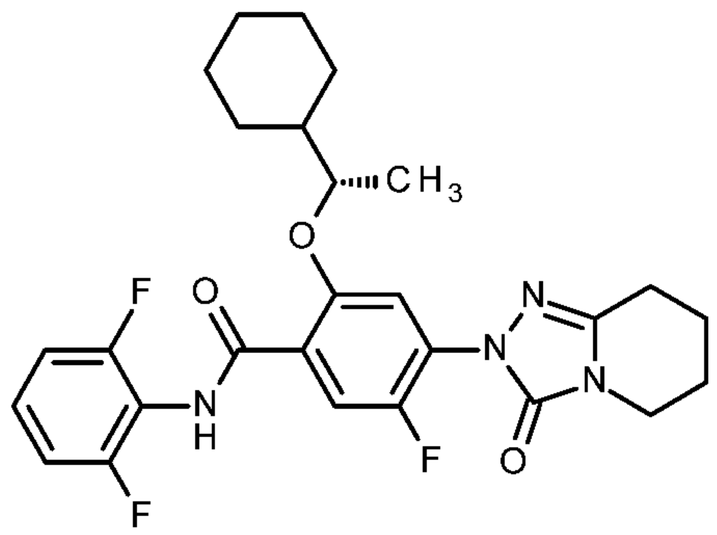
From intermediate 19 and 3-(trifluoromethyl)aniline.

MS (ESIpos): m/z = 547 $(M+H)^+$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 1.06 – 1.36 (m, 5H), 1.40 (d, 3H), 1.68 – 1.86 (5H, m), 1.88 – 1.97 (2H, m), 1,97 – 2.07 (m, 3H), 2.81 (t, 2H), 3.72 (t, 2H), 4.40 – 4.48 (m, 1H), 7.37 – 7.41 (m, 2H), 7.49 (t, 1H), 7.88 – 7.93 (m, 2H), 8.14 (d, 1H), 10.3 (s, 1H).

Example 151

2-[(1S)-1-cyclohexylethoxy]-N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



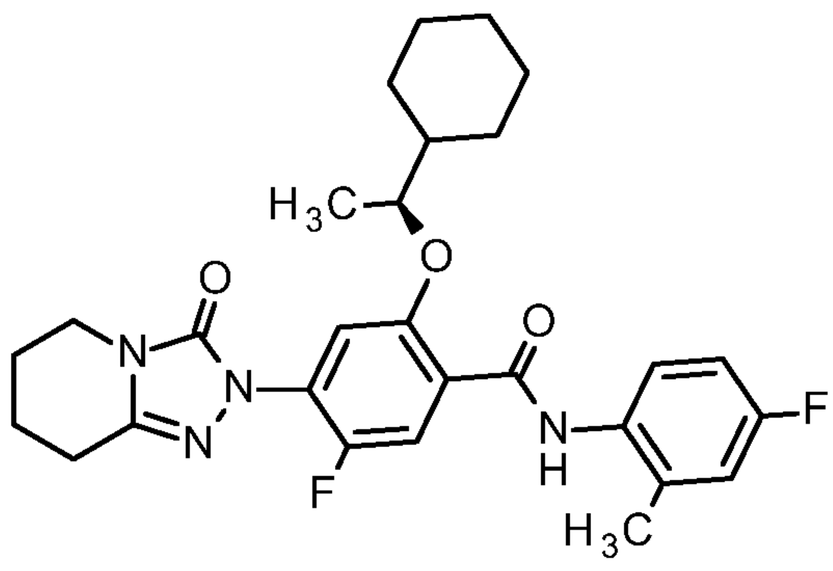
From intermediate 19 and 2,6-difluoroaniline.

MS (ESIpos): m/z = 515 $(M+H)^+$

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] 0.97 – 1.33 (m, 5H), 1.38 (d, 3H), 1.64 – 1.82 (m, 5H), 1.89 – 1.96 (m, 2H), 1.96 – 2.05 (m, 3H), 2.81 (t, 2H), 3.71 (t, 2H), 4.38 – 4.46 (m, 1H), 6.96 – 7.04 (m, 2H), 7.17 – 7.25 (m, 1H), 7.39 (d, 1H), 8.14 (d, 1H), 9.63 (s, 1H).

Example 152

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



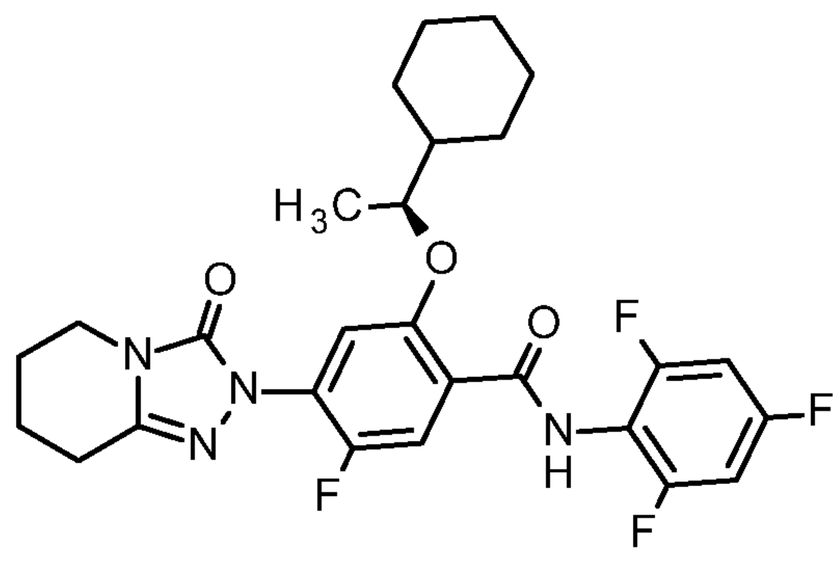
From intermediate 19 and 4-fluoro-2-methylaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.52 min; MS (ESIpos): m/z = 511 $[M+H]^+$

Example 153

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,4,6-trifluorophenyl)benzamide



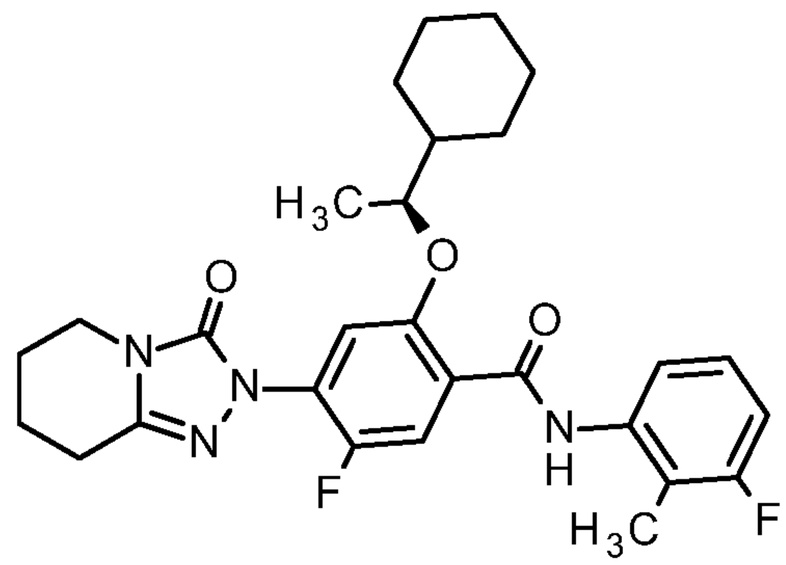
From intermediate 19 and 2,4,6-trifluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.50 min; MS (ESIpos): m/z = 533 $[M+H]^+$

Example 154

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



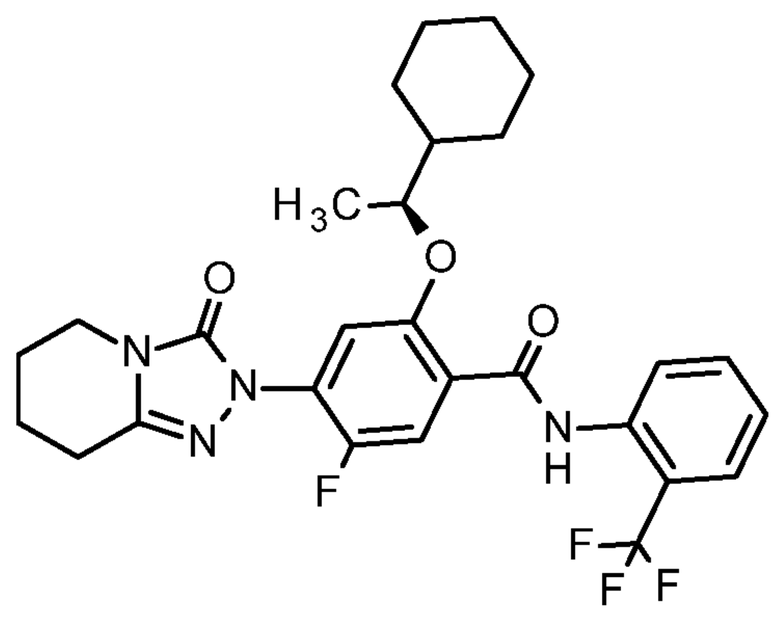
From intermediate 19 and 3-fluoro-2-methylaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.55 min; MS (ESIpos): m/z = 511 $[M+H]^+$

Example 155

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[2-(trifluoromethyl)phenyl]benzamide



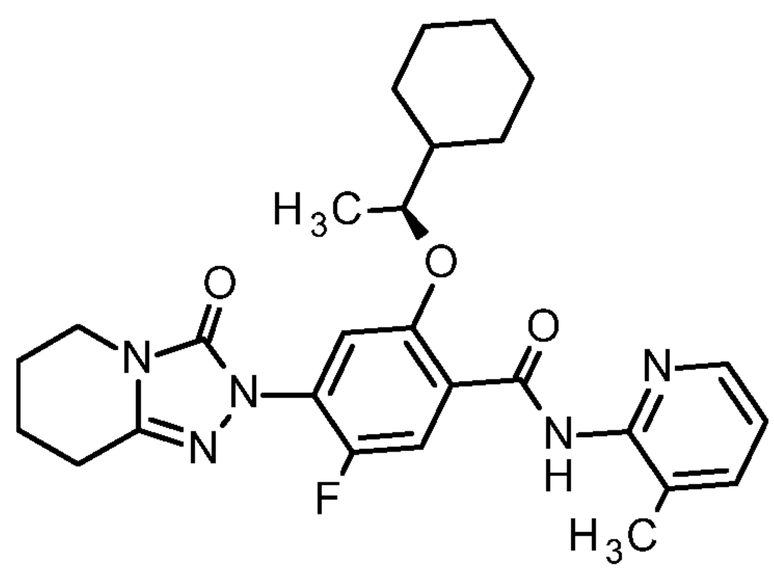
From intermediate 19 and 1-methyl-2-(trifluoromethyl)benzene.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.58 min; MS (ESIpos): m/z = 547 $[M+H]^+$

Example 156

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyridin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



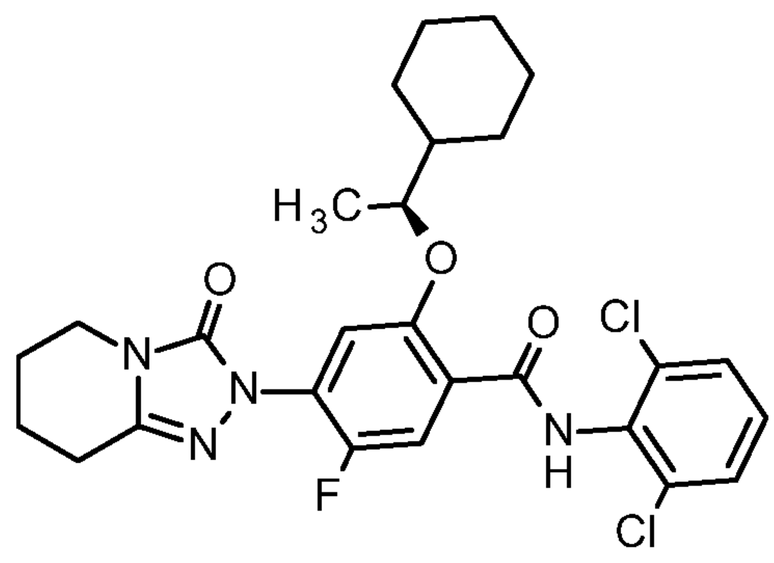
From intermediate 19 and 2,3-dimethylpyridine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.26 min; MS (ESIpos): m/z = 494 $[M+H]^+$

Example 157

2-[(1S)-1-cyclohexylethoxy]-N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



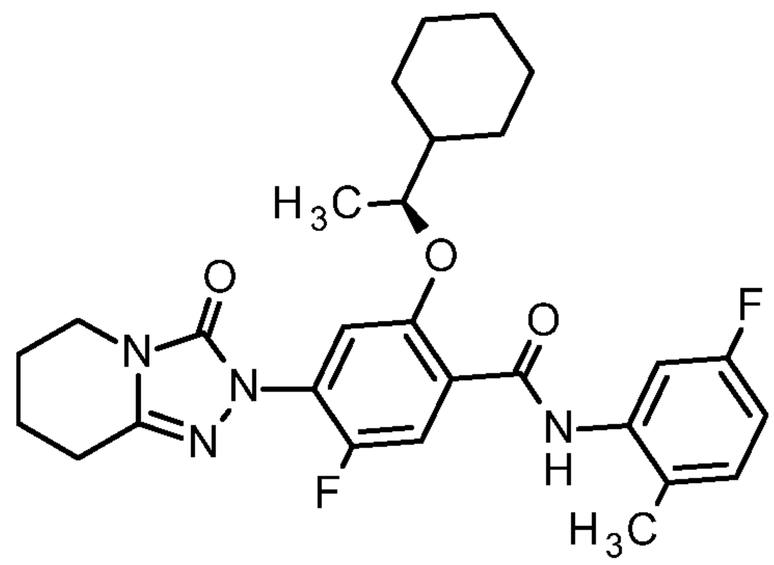
From intermediate 19 and 1,3-dichloro-2-methylbenzene.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.54 min; MS (ESIpos): m/z = 548 $[M+H]^+$

Example 158

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



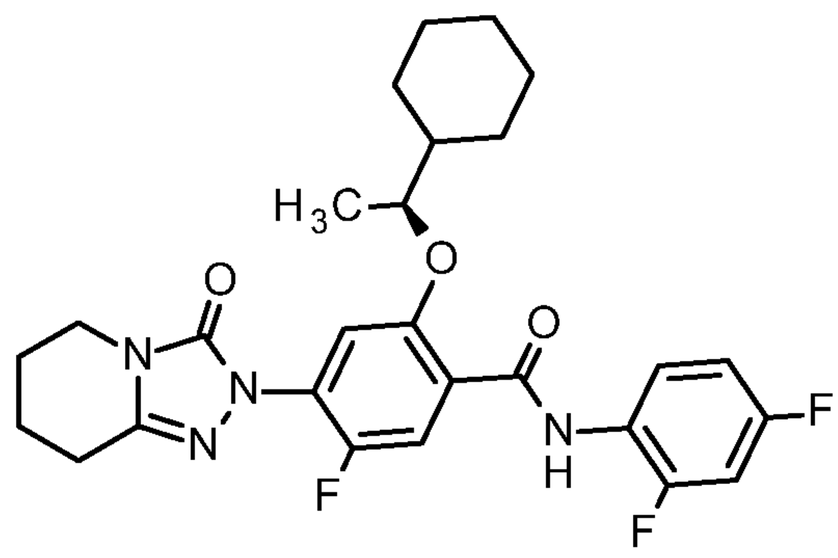
From intermediate 19 and 5-fluoro-2-methylaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.56 min; MS (ESIpos): m/z = 511 $[M+H]^+$

Example 159

2-[(1S)-1-cyclohexylethoxy]-N-(2,4-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



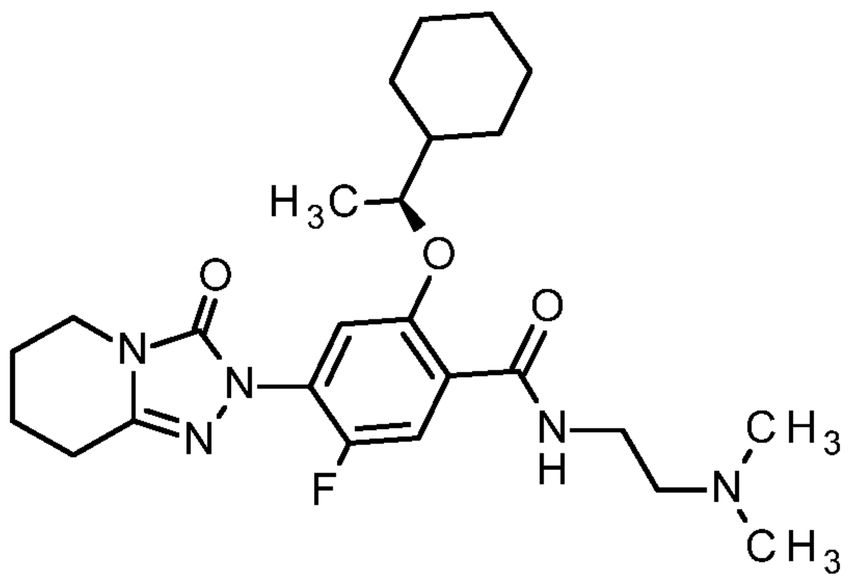
From intermediate 19 and 2,4-difluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.60 min; MS (ESIpos): m/z = 515 $[M+H]^+$

Example 160

2-[(1S)-1-cyclohexylethoxy]-N-[2-(dimethylamino)ethyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



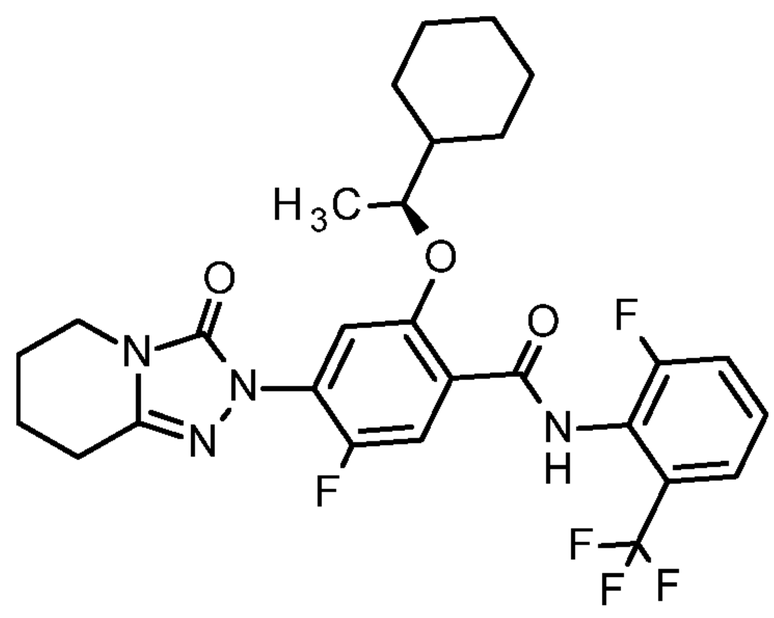
From intermediate 19 and N,N-dimethylethane-1,2-diamine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.86 min; MS (ESIpos): m/z = 474 $[M+H]^+$

Example 161

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-fluoro-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



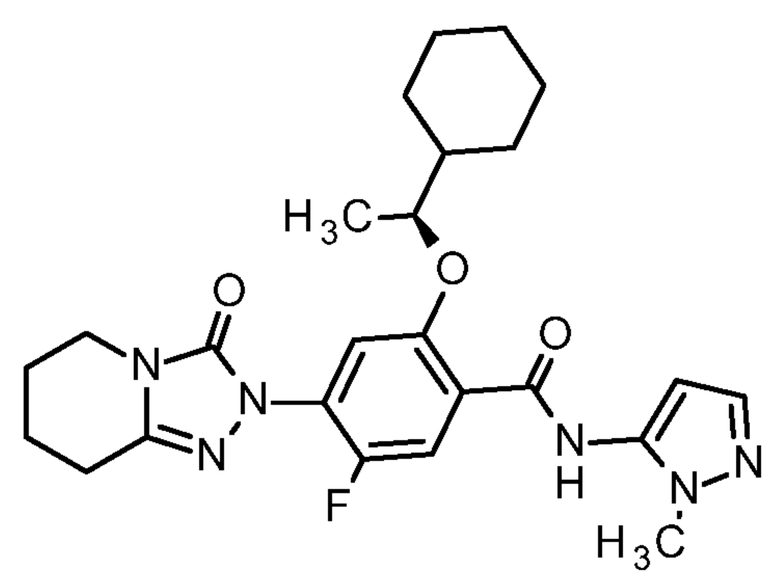
From intermediate 19 and 2-fluoro-6-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.53 min; MS (ESIpos): m/z = 565 $[M+H]^+$

Example 162

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(1-methyl-1H-pyrazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



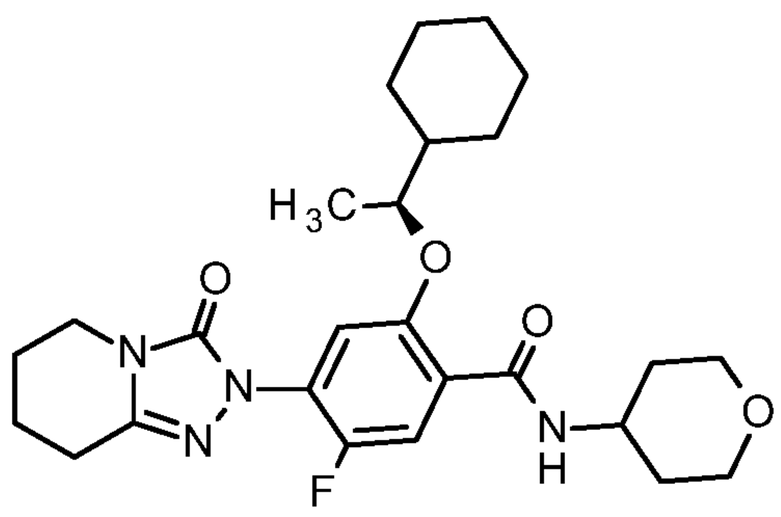
From intermediate 19 and 1-methyl-1H-pyrazol-5-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.24 min; MS (ESIpos): m/z = 483 $[M+H]^+$

Example 163

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(tetrahydro-2H-pyran-4-yl)benzamide



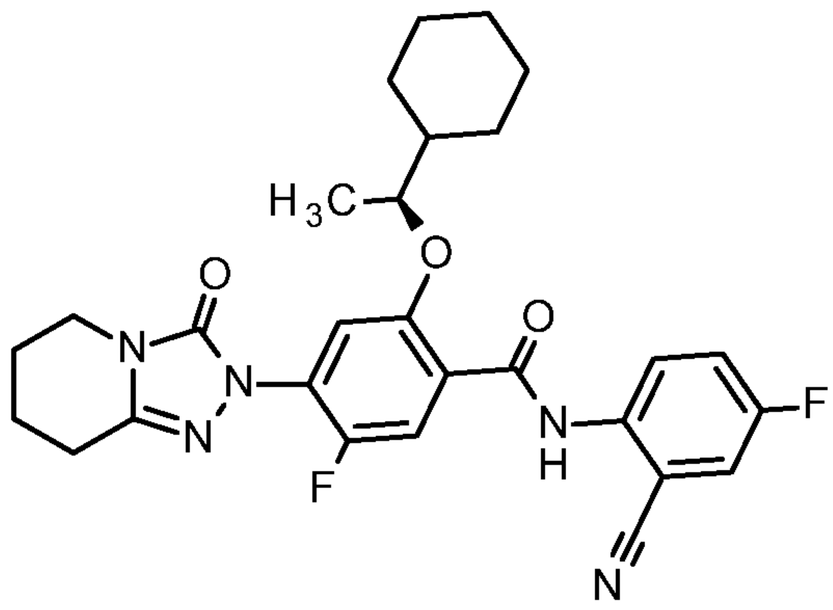
From intermediate 19 and tetrahydro-2H-pyran-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.27 min; MS (ESIpos): m/z = 487 $[M+H]^+$

Example 164

N-(2-cyano-4-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



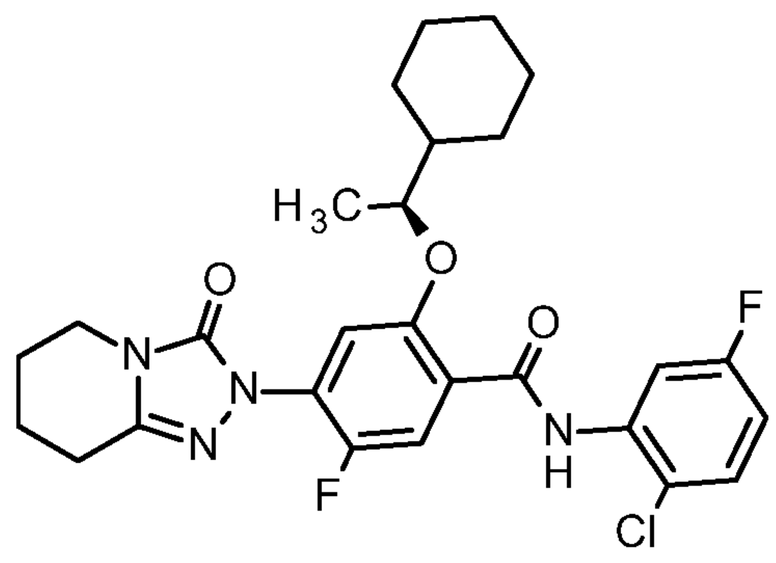
From intermediate 19 and 2-amino-5-fluorobenzonitrile.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.49 min; MS (ESIpos): m/z = 522 $[M+H]^+$

Example 165

N-(2-chloro-5-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



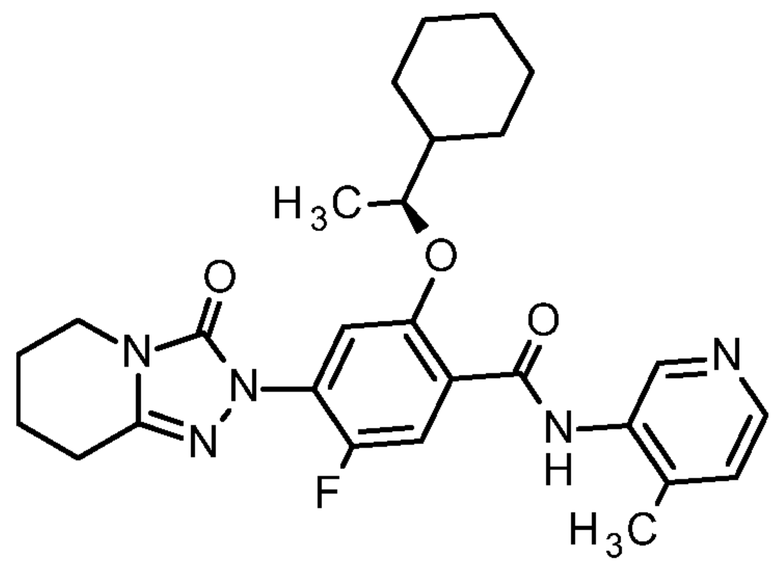
From intermediate 19 and 2-chloro-5-fluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.67 min; MS (ESIpos): m/z = 532 $[M+H]^+$

Example 166

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



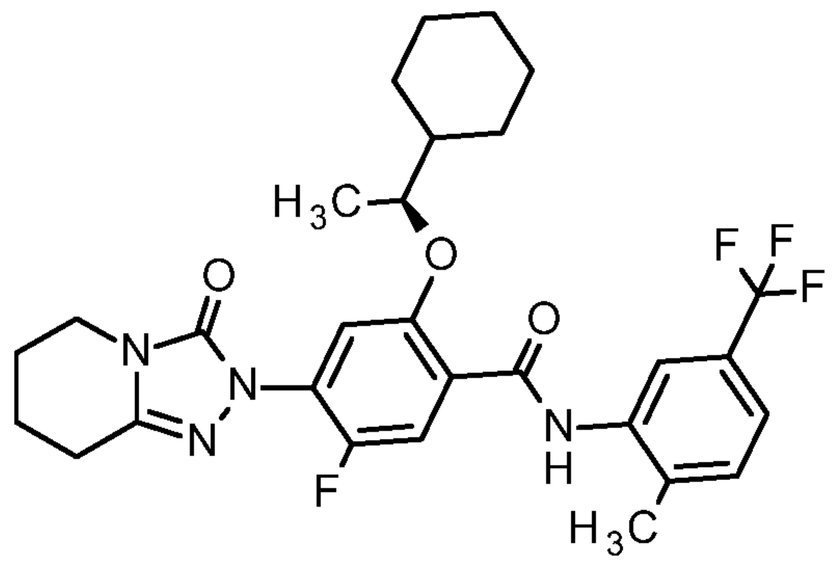
From intermediate 19 and 4-methylpyridin-3-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.08 min; MS (ESIpos): m/z = 494 $[M+H]^+$

Example 167

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



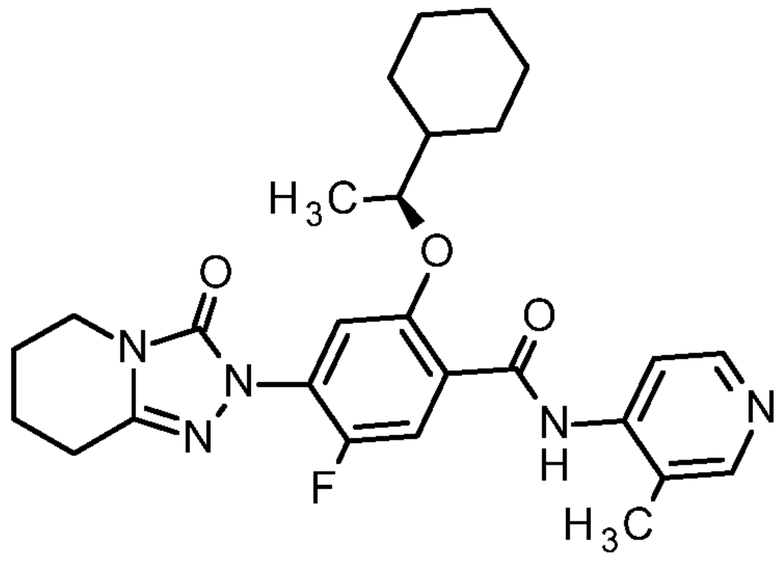
From intermediate 19 and 2-methyl-5-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.62 min; MS (ESIpos): m/z = 561 $[M+H]^+$

Example 168

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyridin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



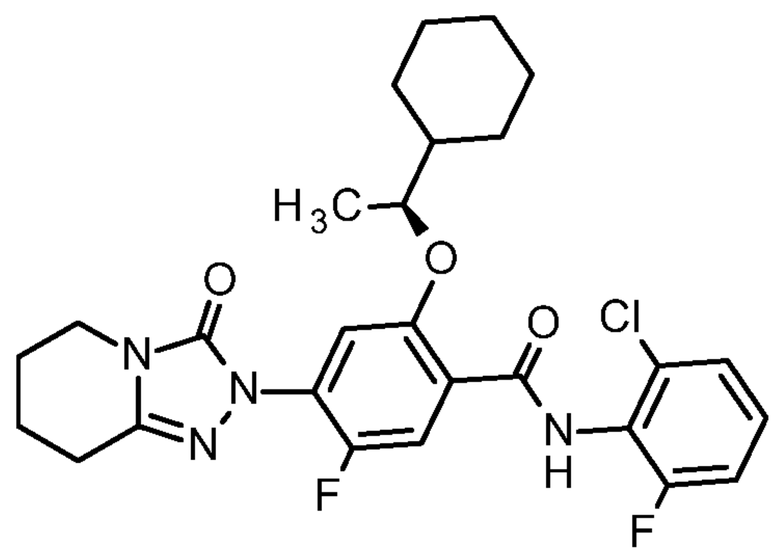
From intermediate 19 and 3-methylpyridin-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.96 min; MS (ESIpos): m/z = 494 $[M+H]^+$

Example 169

N-(2-chloro-6-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



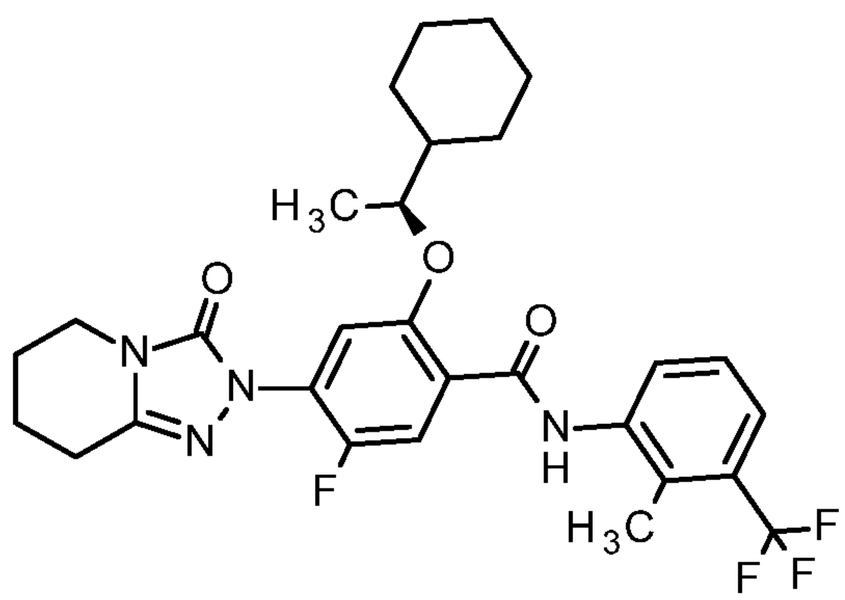
From intermediate 19 and 2-chloro-6-fluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.51 min; MS (ESIpos): m/z = 532 $[M+H]^+$

Example 170

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



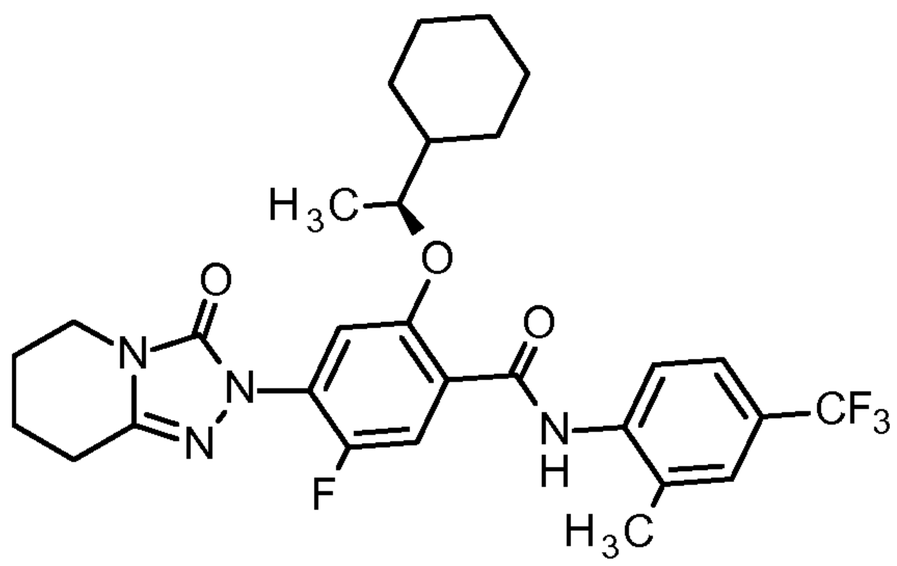
From intermediate 19 and 2-methyl-3-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.62 min; MS (ESIpos): m/z = 561 $[M+H]^+$

Example 171

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



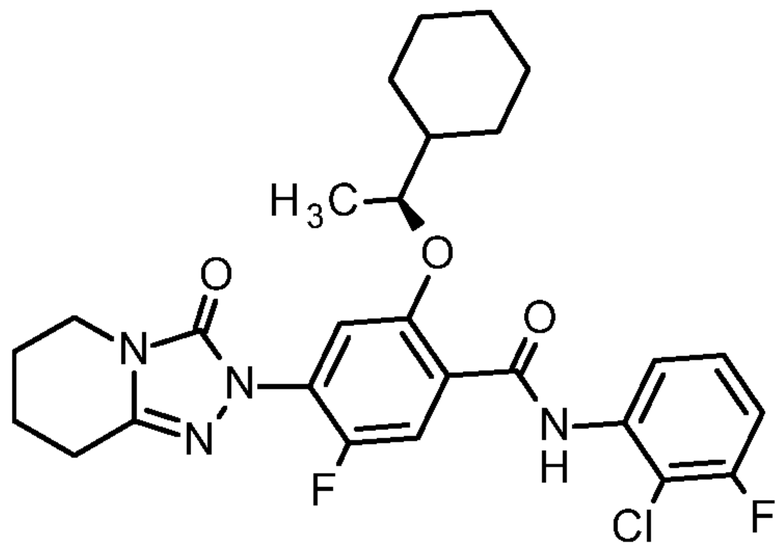
From intermediate 19 and 2-methyl-4-(trifluoromethyl)aniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.64 min; MS (ESIpos): m/z = 561 $[M+H]^+$

Example 172

N-(2-chloro-3-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



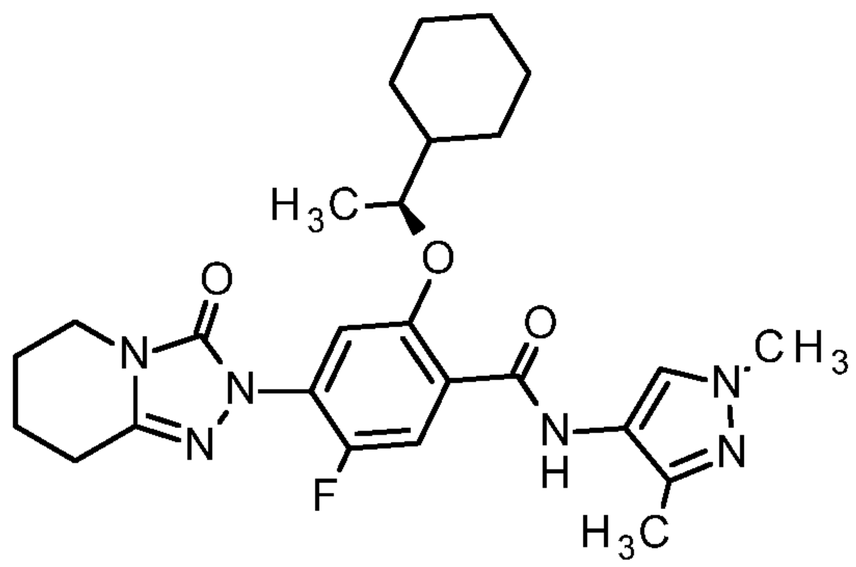
From intermediate 19 and 2-chloro-3-fluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.64 min; MS (ESIpos): m/z = 532 $[M+H]^+$

Example 173

2-[(1S)-1-cyclohexylethoxy]-N-(1,3-dimethyl-1H-pyrazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



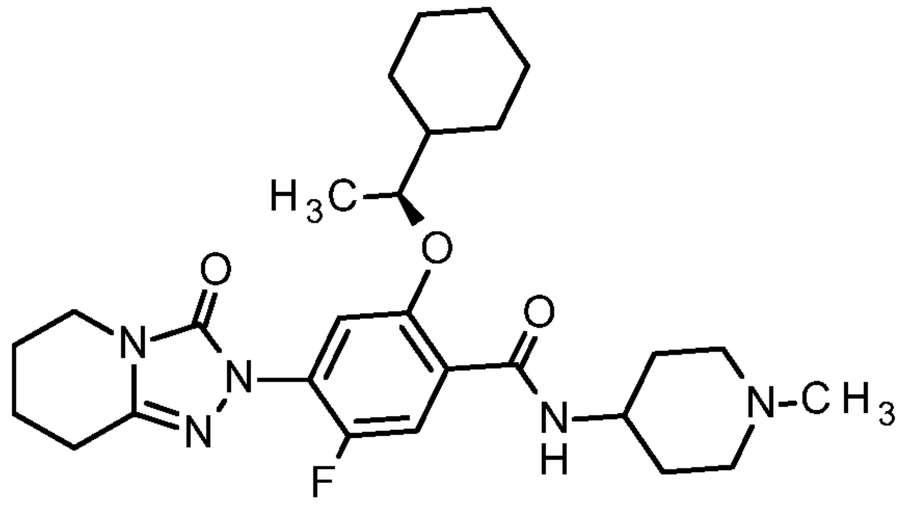
From intermediate 19 and 1,3-dimethyl-1H-pyrazol-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.25 min; MS (ESIpos): m/z = 497 $[M+H]^+$

Example 174

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



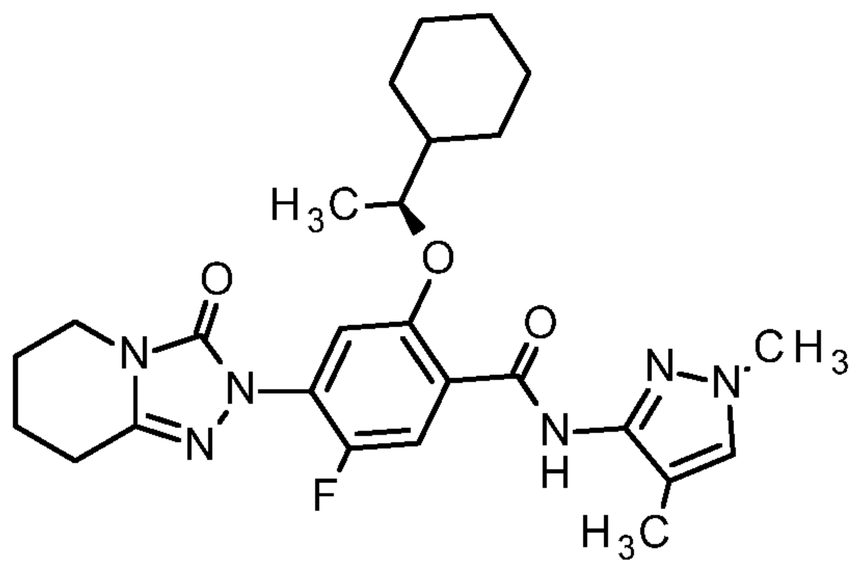
From intermediate 19 and 1-methylpiperidin-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 0.85 min; MS (ESIpos): m/z = 500 $[M+H]^+$

Example 175

2-[(1S)-1-cyclohexylethoxy]-N-(1,4-dimethyl-1H-pyrazol-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



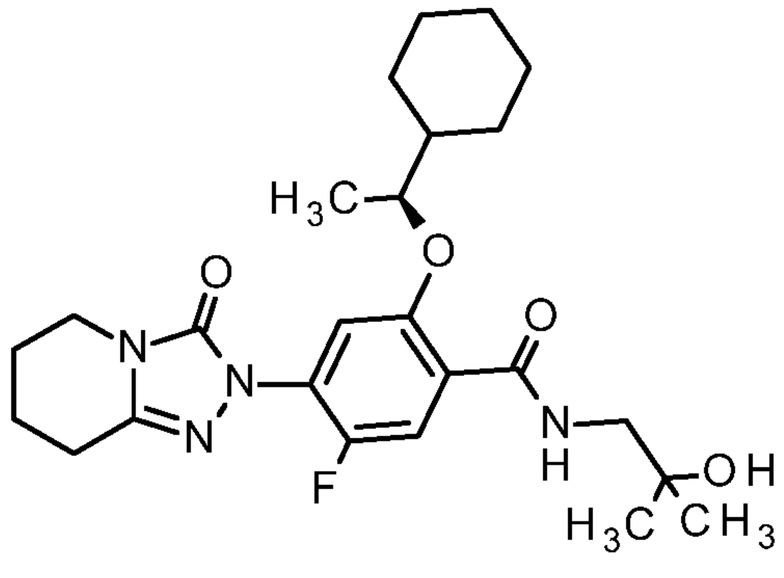
From intermediate 19 and 1,4-dimethyl-1H-pyrazol-3-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.29 min; MS (ESIpos): m/z = 497 $[M+H]^+$

Example 176

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-hydroxy-2-methylpropyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



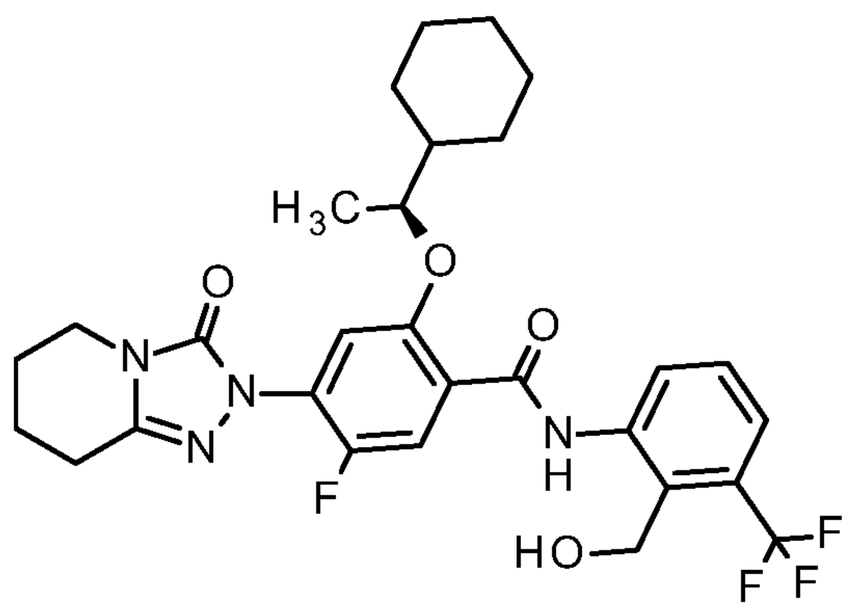
From intermediate 19 and 1-amino-2-methylpropan-2-ol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.21 min; MS (ESIpos): m/z = 475 $[M+H]^+$

Example 177

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-(hydroxymethyl)-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



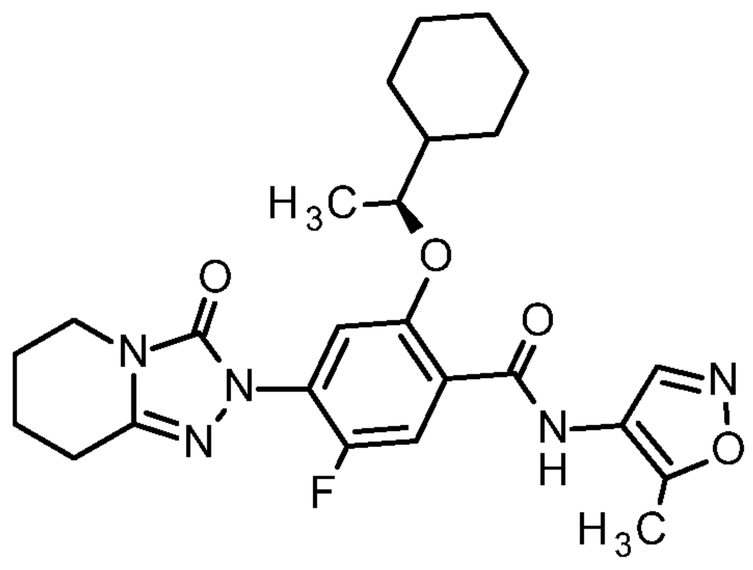
From intermediate 19 and [2-amino-6-(trifluoromethyl)phenyl]methanol.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.45 min; MS (ESIpos): m/z = 577 $[M+H]^+$

Example 178

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methyl-1,2-oxazol-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



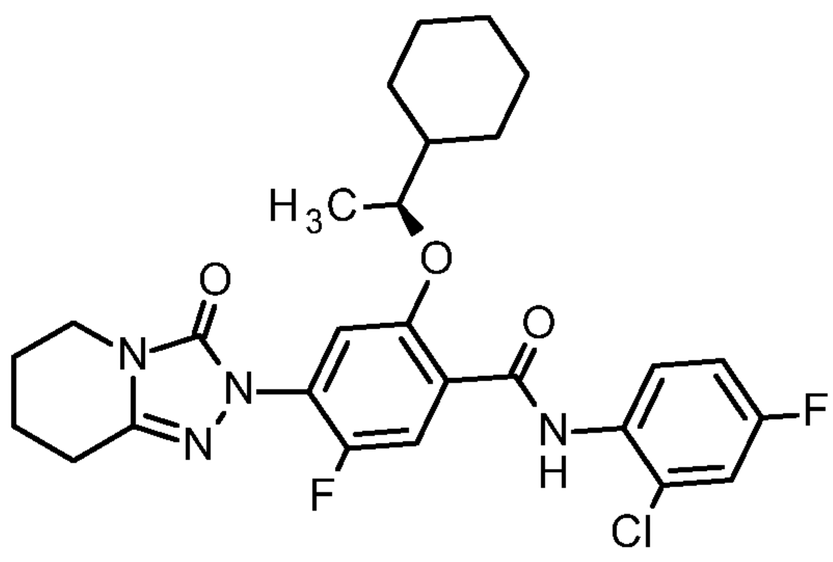
From intermediate 19 and 5-methyl-1,2-oxazol-4-amine.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.33 min; MS (ESIpos): m/z = 484 $[M+H]^+$

Example 179

N-(2-chloro-4-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



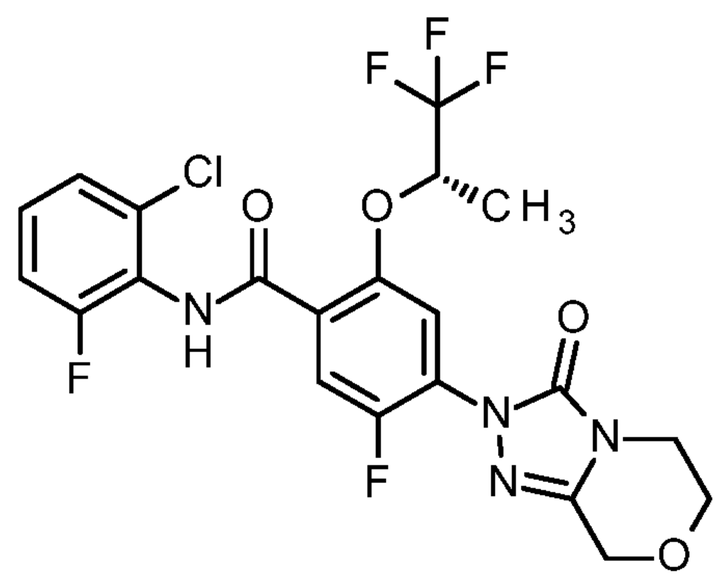
From intermediate 19 and 2-chloro-4-fluoroaniline.

The product was purified by preparative HPLC (YMC Actus Triart C18 100x30 mm 5µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method C): R_t = 1.64 min; MS (ESIpos): m/z = 532 $[M+H]^+$

Example 180

N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



To a 0 ℃ stirred solution of 5-fluoro-4-(3-oxo-5,6 -dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid (intermediate 24) (74.3 mg, 190 µmol) and DMF (3 drops) in anhydrous dichloromethane (0.95 ml) was added oxalyl chloride dropwise (28,9 mg, 0.23 mmol). The resulting mixture was warmed to room temperature, stirred for one hour and concentrated under reduced pressure. A solution of the crude acid chloride in dichloromethane (0.63 ml) was then added dropwise to a 0 ℃ stirred solution of 2-chloro-6-fluoraniline (30.4 mg, 0.21 mmol) and triethylamine (21.1 mg, 0.21 mmol) in dichloromethane (0.70 ml). Following complete addition, the mixture was warmed to room temperature and stirred for one hour. Aqueous hydrochloric acid (1.0 M, 10 ml) was added to

the residue and extracted with dichloromethane (3 x 10 ml). The combined organic extracts were washed with brine (10 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give a pale yellow oil. The residue was purified by reverse phase column chromatography (acetonitrile, 0.1 % aqueous formic acid) to give the amide as a white solid (73.3 mg, 66 %).

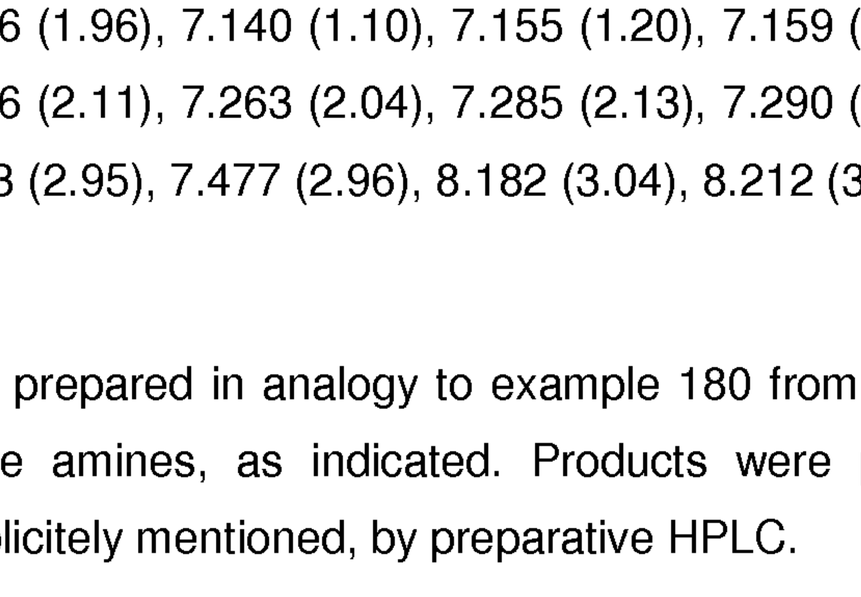
LC-MS (method A): Rt = 1.18 min; MS (ESIpos): m/z = 519 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.572 (8.35), 1.659 (7.01), 1.676 (7.05), 3.807 (2.84), 3.820 (4.22), 3.834 (3.51), 4.086 (3.74), 4.098 (3.02), 4.100 (4.34), 4.113 (2.89), 4.772 (16.00), 4.911 (0.46), 4.927 (1.09), 4.942 (1.41), 4.958 (1.09), 4.973 (0.42), 7.112 (0.89), 7.116 (0.94), 7.133 (1.48), 7.136 (1.96), 7.140 (1.10), 7.155 (1.20), 7.159 (1.25), 7.222 (0.85), 7.235 (0.84), 7.242 (1.98), 7.256 (2.11), 7.263 (2.04), 7.285 (2.13), 7.290 (2.75), 7.305 (0.88), 7.309 (1.07), 7.312 (0.89), 7.463 (2.95), 7.477 (2.96), 8.182 (3.04), 8.212 (3.06), 9.021 (2.04).

Examples 181–243 were prepared in analogy to example 180 from the respective carboxylic acids and the respective amines, as indicated. Products were purified by flash column chromatography or, if explicitely mentioned, by preparative HPLC.

Example 181

5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



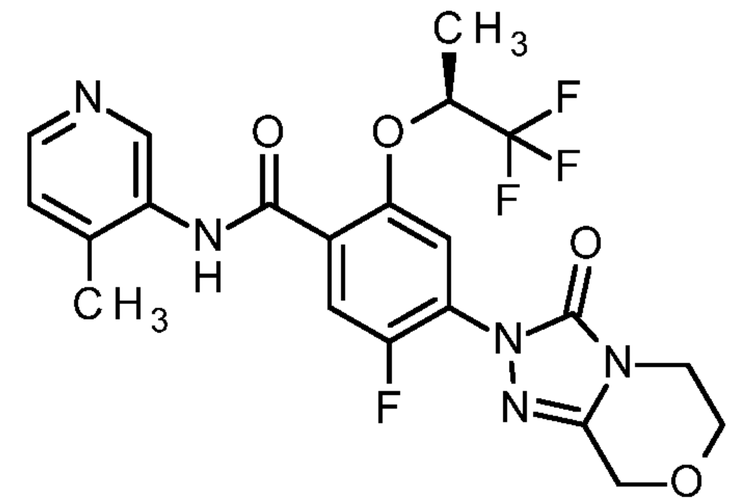
From Intermediate 24 and 6-methoxy-4-methylpyridin-3-amine.

LC-MS (method A): Rt = 1.07 min; MS (ESIpos): m/z = 512 $[M-H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.589 (0.76), 1.647 (4.45), 1.663 (4.41), 2.019 (0.46), 2.266 (9.79), 3.806 (1.68), 3.819 (2.50), 3.833 (2.13), 3.949 (16.00), 4.086 (2.25), 4.097 (1.77), 4.101 (2.57), 4.114 (1.78), 4.770 (9.83), 4.889 (0.68), 4.905 (0.87), 4.920 (0.65), 6.676 (2.54), 7.439 (1.87), 7.454 (1.85), 8.146 (2.51), 8.174 (2.44), 8.343 (3.08), 8.868 (1.38).

Example 182

5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 24 and 4-methylpyridin-3-amine.

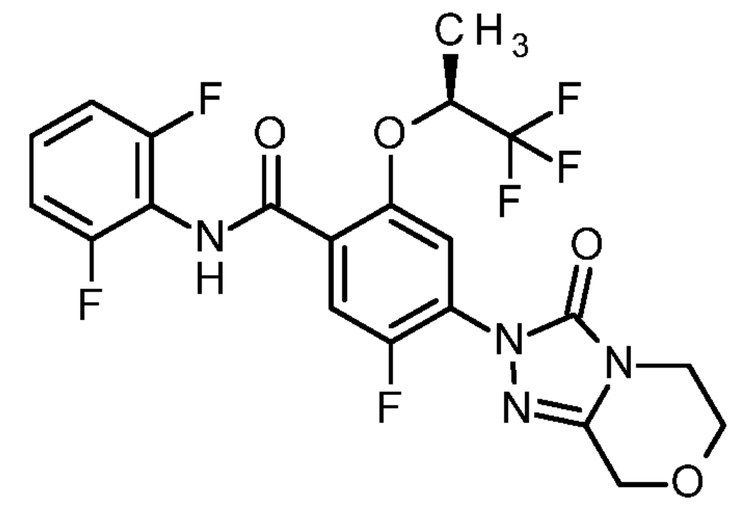
The product was purified by preparative HPLC (Chromatorex C18 125x30 mm 10µm, 0.1 % aqueous ammonia, acetonitrile).

LC-MS (method B): R_t = 0.96 min; MS (ESIneg): m/z = 480 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.076 (2.64), 1.094 (2.55), 1.435 (6.35), 1.451 (6.32), 1.996 (1.77), 2.085 (0.54), 2.280 (16.00), 2.331 (0.50), 2.518 (3.12), 2.523 (2.07), 2.674 (0.48), 2.950 (5.52), 3.670 (2.13), 3.683 (3.60), 3.697 (2.44), 4.032 (2.62), 4.046 (3.73), 4.058 (2.18), 4.754 (10.85), 5.311 (0.41), 5.327 (1.01), 5.343 (1.28), 5.359 (0.94), 7.312 (2.44), 7.324 (2.48), 7.571 (2.59), 7.585 (2.57), 7.686 (3.14), 7.698 (0.80), 7.711 (3.14), 8.304 (3.42), 8.316 (3.37), 8.572 (5.57), 10.014 (3.83).

Example 183

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 24 and 2,6-difluoroaniline.

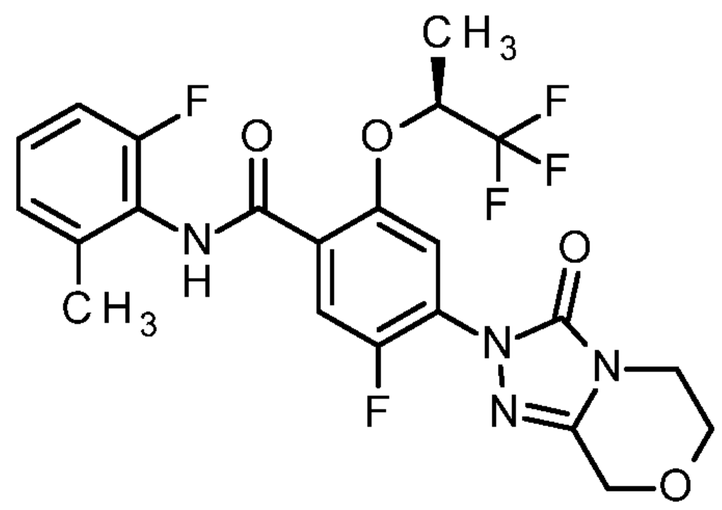
The product was purified by preparative HPLC (Chromatorex C18 125x30 mm 10µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.13 min; MS (ESIpos): m/z = 503 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.432 (8.16), 1.448 (8.08), 2.084 (16.00), 2.327 (0.50), 2.523 (1.83), 2.531 (0.50), 2.669 (0.47), 3.668 (3.16), 3.681 (5.53), 3.695 (3.55), 4.029 (3.95), 4.043 (5.85), 4.056 (3.34), 4.752 (14.13), 5.265 (0.57), 5.280 (1.33), 5.296 (1.72), 5.312 (1.27), 5.328 (0.52), 7.191 (2.47), 7.212 (5.08), 7.232 (3.16), 7.372 (0.57), 7.388 (1.25), 7.409 (1.77), 7.425 (0.97), 7.430 (0.96), 7.446 (0.41), 7.573 (3.33), 7.584 (5.08), 7.608 (3.29), 10.008 (3.86).

Example 184

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 24 and 2-fluoro-6-methylaniline.

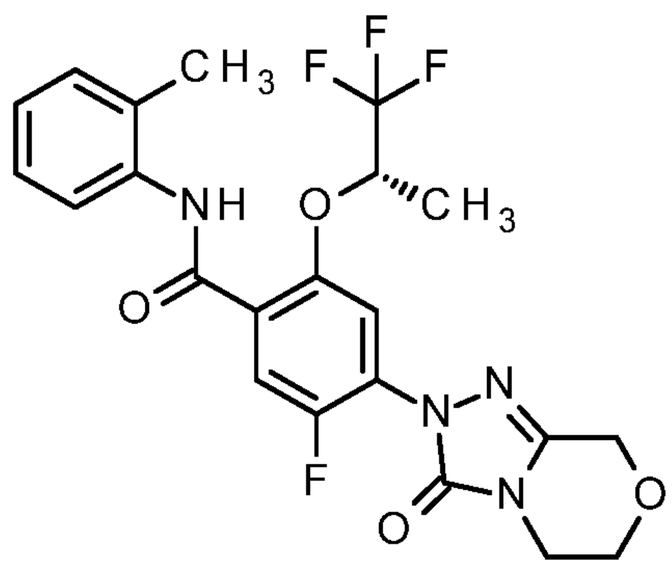
The product was purified by preparative HPLC (Chromatorex C18 125x30 mm 10µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.16 min; MS (ESIpos): m/z = 499 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.431 (7.00), 1.447 (7.01), 2.085 (5.21), 2.272 (16.00), 2.518 (2.28), 2.523 (1.65), 3.669 (2.26), 3.682 (3.84), 3.696 (2.61), 4.031 (2.78), 4.045 (4.01), 4.058 (2.37), 4.753 (12.11), 5.307 (0.44), 5.323 (1.10), 5.339 (1.43), 5.356 (1.02), 5.759 (1.00), 7.100 (0.91), 7.117 (2.32), 7.121 (2.26), 7.134 (2.50), 7.143 (1.39), 7.227 (1.08), 7.241 (1.18), 7.247 (1.56), 7.261 (1.20), 7.266 (0.77), 7.281 (0.63), 7.566 (6.67), 7.580 (3.00), 7.590 (3.68), 9.828 (4.20).

Example 185

5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



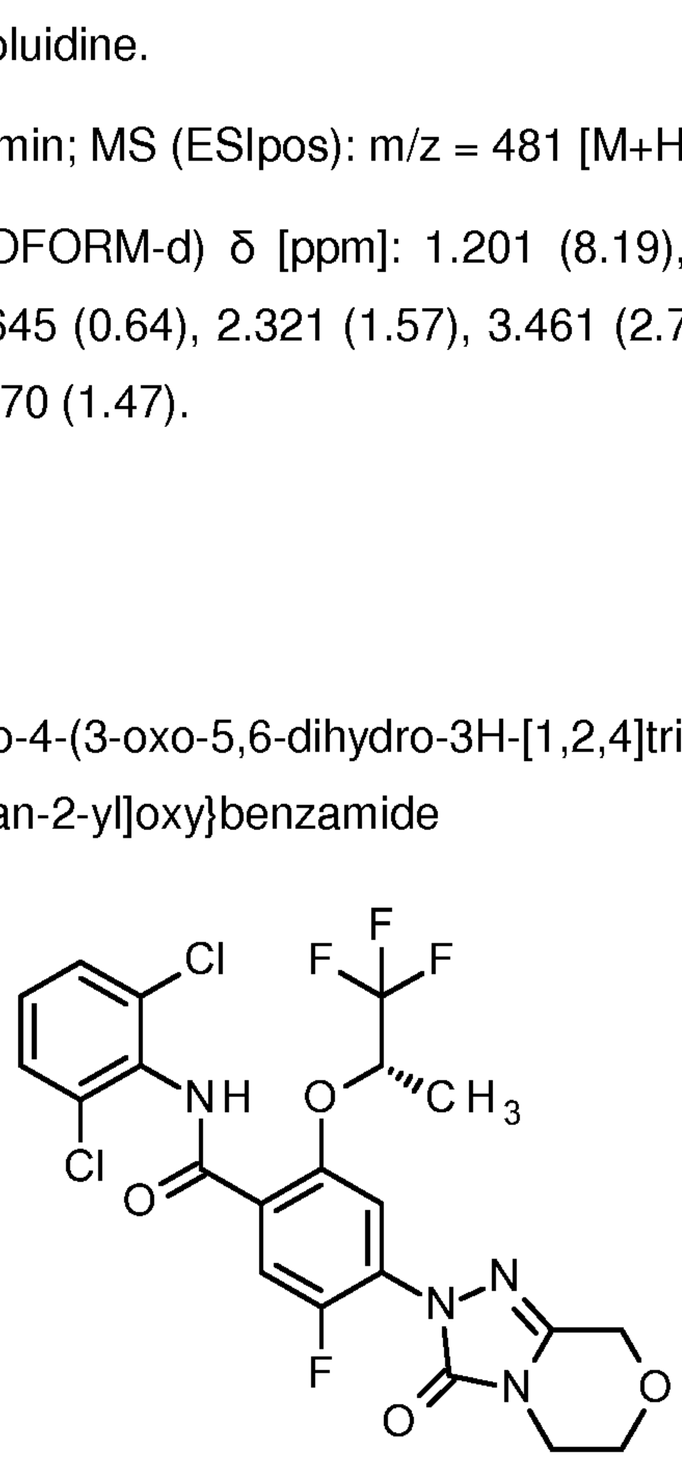
From Intermediate 24 and o-toluidine.

LC-MS (method A): R_t = 1.21 min; MS (ESIpos): m/z = 481 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.201 (8.19), 1.218 (16.00), 1.235 (8.73), 1.580 (1.03), 1.629 (0.64), 1.645 (0.64), 2.321 (1.57), 3.461 (2.72), 3.479 (8.01), 3.496 (7.46), 3.514 (2.60), 4.100 (0.40), 4.770 (1.47).

Example 186

N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



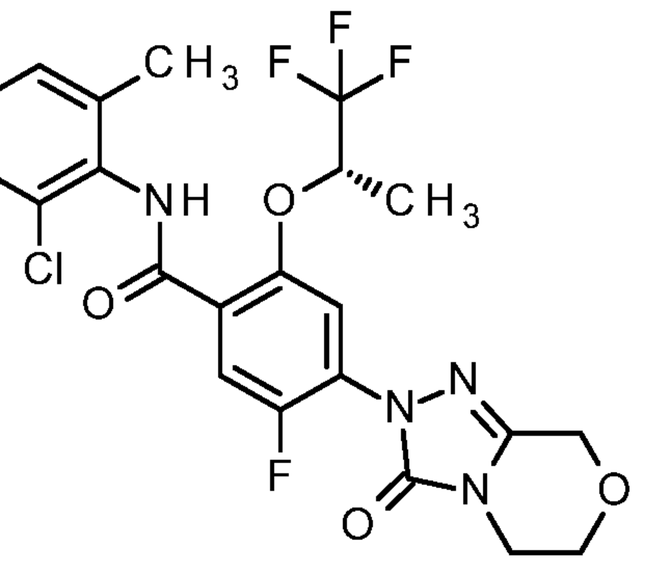
From Intermediate 24 and 2,6-dichloroaniline.

LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 535 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.512 (12.67), 1.524 (12.83), 3.655 (5.00), 3.664 (8.25), 3.674 (5.40), 3.934 (5.57), 3.944 (8.21), 3.954 (4.80), 4.616 (16.00), 4.783 (1.04), 4.795 (2.13), 4.807 (2.67), 4.819 (2.06), 4.830 (0.98), 7.065 (2.09), 7.081 (4.28), 7.097 (2.87), 7.121 (4.39), 7.312 (4.64), 7.322 (4.44), 8.032 (3.80), 8.055 (3.79), 8.922 (5.01).

Example 187

N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



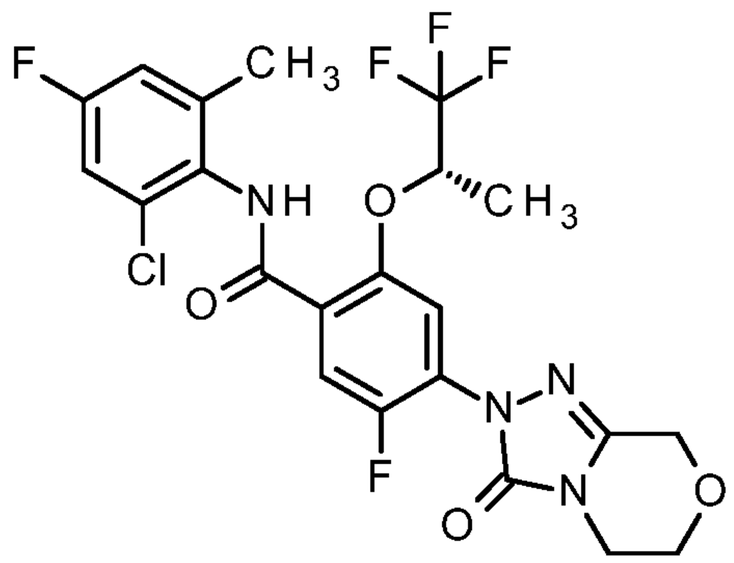
From Intermediate 24 and 2-chloro-6-methylaniline.

LC-MS (method A): R_t = 1.23 min; MS (ESIpos): m/z = 515 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.735 (6.96), 1.749 (7.00), 2.080 (0.70), 2.396 (16.00), 3.870 (2.70), 3.880 (4.17), 3.891 (3.27), 4.149 (3.28), 4.160 (4.25), 4.170 (2.78), 4.833 (12.96), 5.011 (0.46), 5.023 (1.08), 5.036 (1.39), 5.048 (1.03), 5.061 (0.42), 7.239 (0.98), 7.255 (3.10), 7.279 (2.25), 7.281 (2.64), 7.294 (0.96), 7.353 (1.66), 7.395 (1.85), 7.398 (1.84), 7.410 (1.51), 7.413 (1.45), 7.520 (2.83), 7.531 (2.84), 8.240 (3.29), 8.263 (3.33), 9.058 (2.51).

Example 188

N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 24 and 2-chloro-4-fluoro-6-methylaniline.

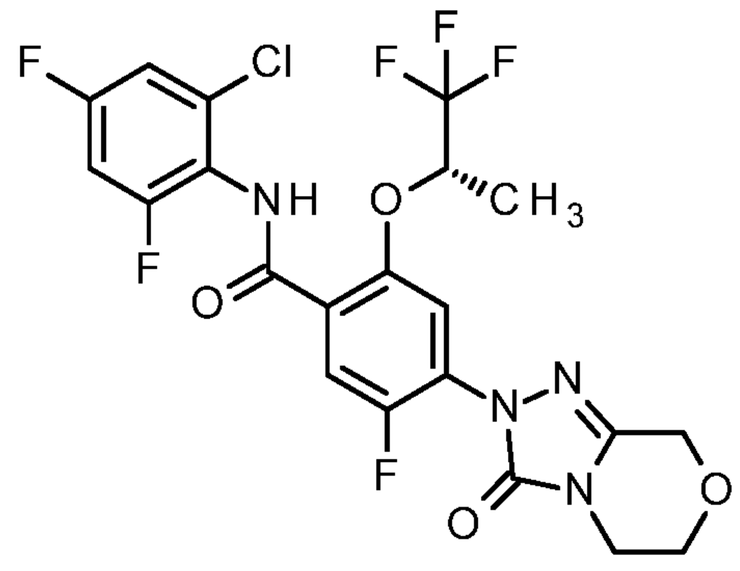
LC-MS (method A): R_t = 1.25 min; MS (ESIneg): m/z = 531 $[M-H]^-$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.657 (7.02), 1.670 (7.36), 2.010 (0.44), 2.306 (16.00), 3.801 (2.85), 3.811 (4.07), 3.822 (3.42), 4.081 (3.56), 4.092 (4.15), 4.103 (2.90), 4.762 (14.32), 4.926 (0.45), 4.939 (1.06), 4.951 (1.36), 4.963 (1.00), 4.975 (0.40), 6.935 (1.25), 6.941

(1.36), 6.953 (1.27), 6.959 (1.34), 7.073 (1.50), 7.078 (1.42), 7.089 (1.51), 7.094 (1.37), 7.440 (2.95), 7.452 (2.90), 8.149 (3.65), 8.171 (3.51), 8.874 (2.19).

Example 189

N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



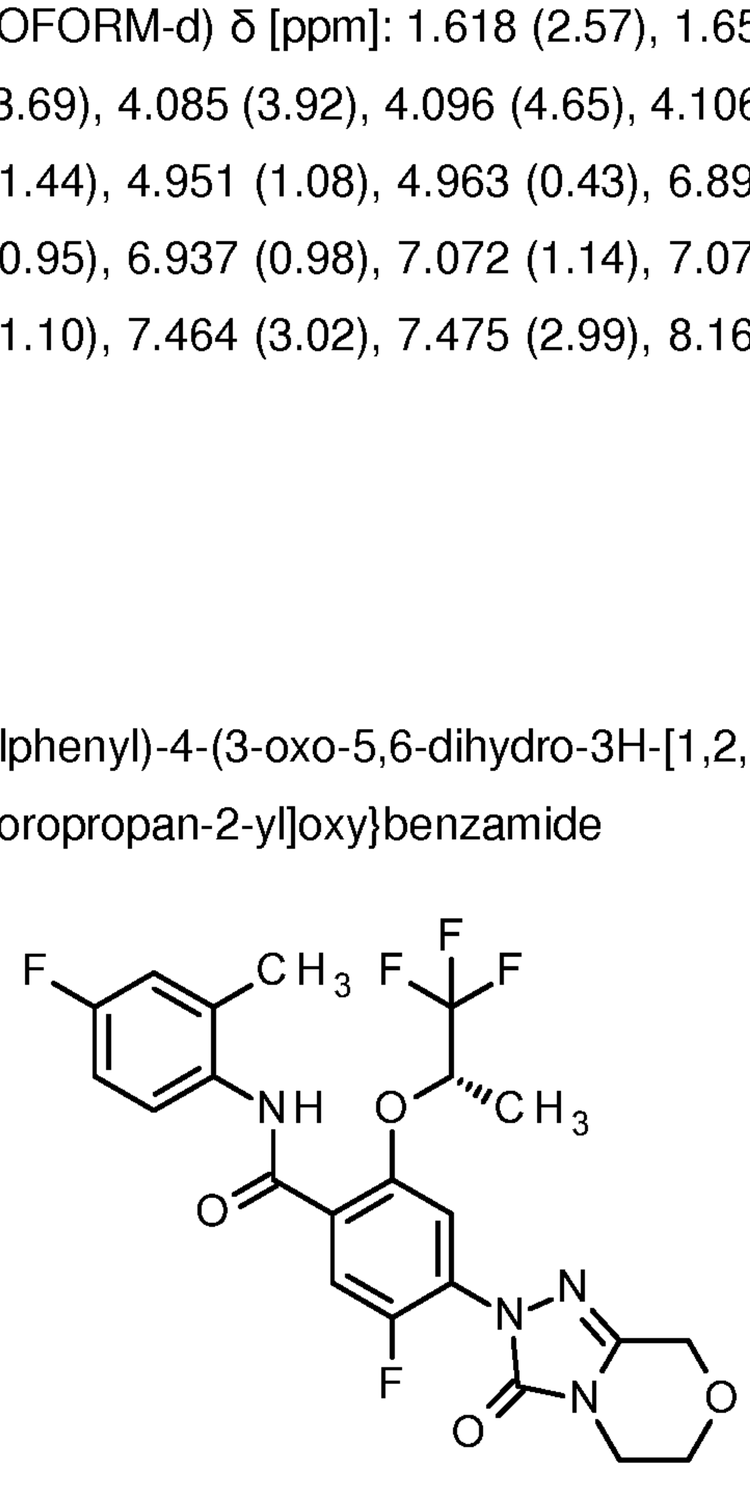
From Intermediate 24 and 2-chloro-4,6-difluoroaniline.

LC-MS (method A): R_t = 1.23 min; MS (ESIpos): m/z = 537 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.618 (2.57), 1.654 (7.69), 1.667 (7.60), 3.804 (3.07), 3.814 (4.58), 3.825 (3.69), 4.085 (3.92), 4.096 (4.65), 4.106 (3.17), 4.766 (16.00), 4.914 (0.54), 4.927 (1.14), 4.939 (1.44), 4.951 (1.08), 4.963 (0.43), 6.895 (0.93), 6.901 (1.02), 6.914 (1.29), 6.918 (1.37), 6.931 (0.95), 6.937 (0.98), 7.072 (1.14), 7.077 (1.47), 7.081 (1.21), 7.088 (1.21), 7.093 (1.46), 7.097 (1.10), 7.464 (3.02), 7.475 (2.99), 8.161 (3.32), 8.183 (3.26), 8.913 (2.62).

Example 190

5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



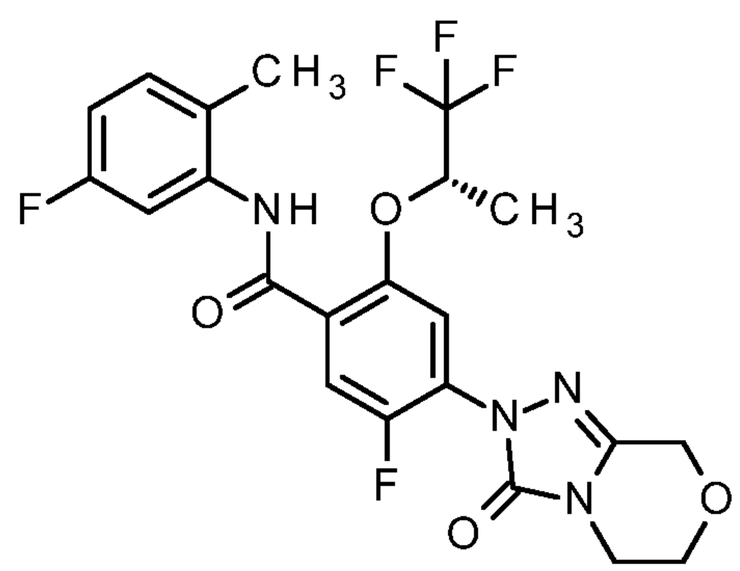
From Intermediate 24 and 4-fluoro-2-methylaniline.

LC-MS (method A): R_t = 1.18 min; MS (ESIpos): m/z = 499 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.047 (0.59), 1.466 (7.05), 1.480 (7.07), 1.526 (0.70), 2.131 (16.00), 3.632 (2.72), 3.642 (4.20), 3.653 (3.23), 3.913 (3.33), 3.925 (4.31), 3.935 (2.80), 4.593 (12.98), 4.714 (0.47), 4.727 (1.11), 4.739 (1.47), 4.751 (1.06), 4.764 (0.44), 6.764 (0.54), 6.770 (0.95), 6.786 (3.95), 6.803 (3.10), 7.106 (2.57), 7.281 (2.79), 7.559 (1.06), 7.570 (1.34), 7.576 (1.12), 7.586 (1.18), 7.973 (3.21), 7.996 (3.20), 8.784 (2.24).

Example 191

5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



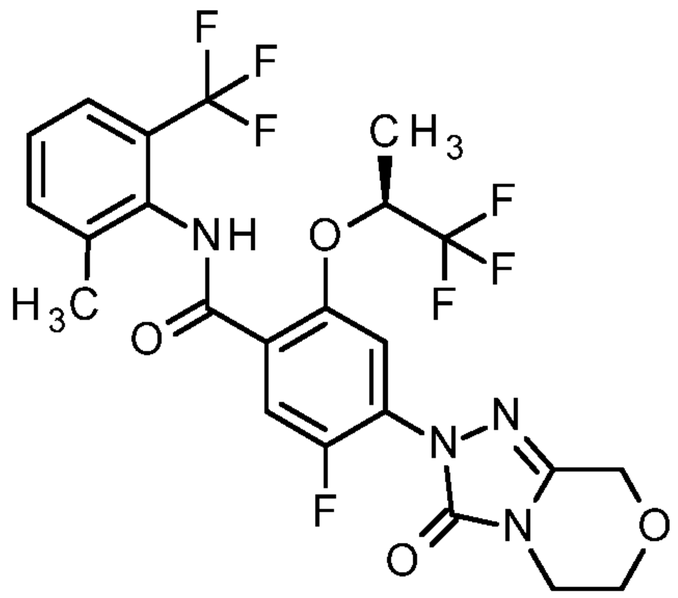
From Intermediate 24 and 5-fluoro-2-methylaniline.

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 499 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.625 (7.46), 1.638 (7.49), 1.667 (0.69), 2.010 (0.50), 2.276 (14.37), 3.798 (3.15), 3.808 (4.50), 3.819 (3.76), 4.080 (4.03), 4.089 (3.35), 4.091 (4.61), 4.101 (3.31), 4.759 (16.00), 4.869 (0.51), 4.882 (1.19), 4.893 (1.52), 4.906 (1.20), 4.919 (0.46), 6.807 (0.90), 6.812 (0.98), 6.824 (1.76), 6.829 (1.83), 6.840 (1.01), 6.846 (1.01), 7.150 (1.37), 7.163 (1.53), 7.166 (1.44), 7.179 (1.23), 7.456 (3.10), 7.467 (3.06), 7.875 (1.63), 7.880 (1.66), 7.896 (1.67), 7.901 (1.61), 8.125 (3.49), 8.147 (3.56), 9.049 (2.13).

Example 192

5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



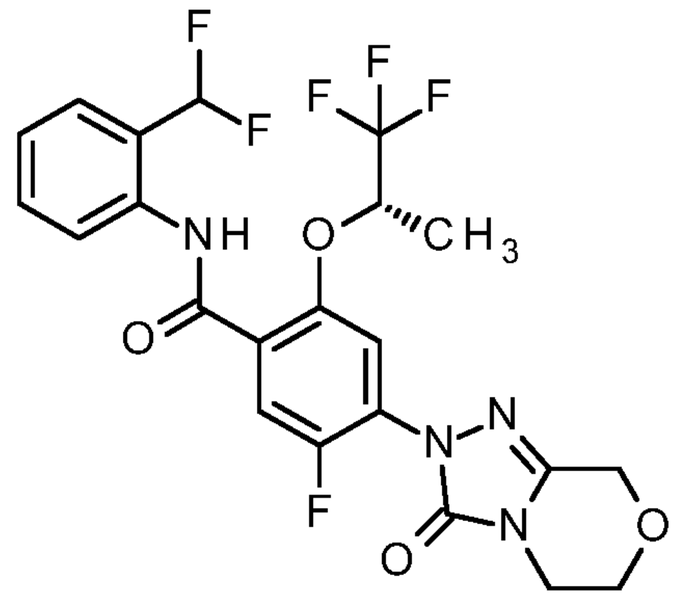
From Intermediate 24 and 2-methyl-6-(trifluoromethyl)aniline.

LC-MS (method A): R_t = 1.18 min; MS (ESIpos): m/z = 549 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.640 (2.42), 1.651 (2.43), 1.672 (2.39), 2.200 (8.34), 2.325 (16.00), 3.800 (2.97), 3.811 (4.44), 3.821 (3.63), 4.078 (3.97), 4.089 (4.62), 4.099 (3.28), 4.140 (0.55), 4.761 (15.84), 4.929 (0.48), 4.941 (1.13), 4.953 (1.45), 4.965 (1.08), 4.977 (0.43), 6.698 (0.49), 6.713 (1.00), 6.729 (0.54), 7.201 (0.80), 7.215 (0.75), 7.318 (0.83), 7.334 (0.84), 7.341 (1.05), 7.356 (2.33), 7.371 (1.40), 7.440 (3.15), 7.450 (3.08), 7.511 (2.01), 7.526 (1.66), 7.554 (2.01), 7.570 (1.73), 8.168 (0.75), 8.190 (0.74).

Example 193

N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 24 and 2-(difluoromethyl)aniline.

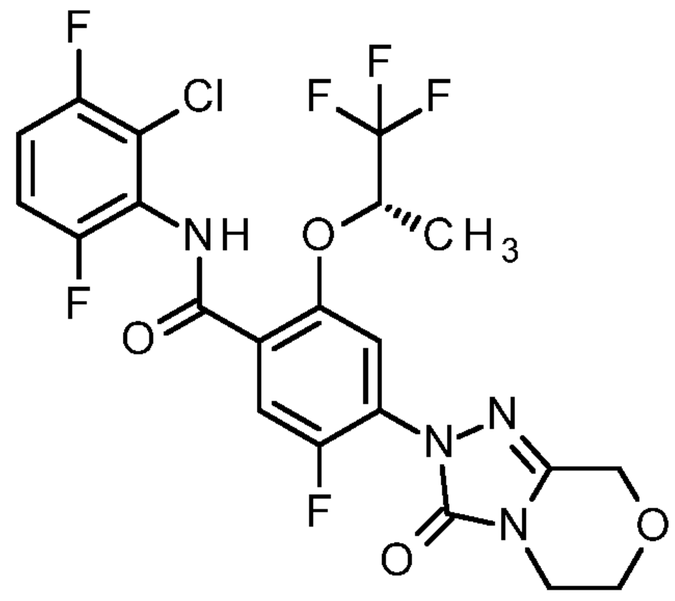
LC-MS (method A): R_t = 1.20 min; MS (ESIpos): m/z = 517 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.633 (7.89), 1.647 (8.28), 2.620 (0.41), 3.801 (3.22), 3.811 (4.97), 3.821 (3.82), 4.080 (4.09), 4.091 (5.05), 4.101 (3.38), 4.761 (16.00), 4.858 (0.51), 4.870 (1.18), 4.883 (1.54), 4.895 (1.15), 4.908 (0.53), 6.640 (1.65), 6.750 (3.26), 6.861

(1.55), 7.308 (1.06), 7.324 (2.31), 7.339 (1.36), 7.455 (3.09), 7.466 (3.04), 7.533 (1.06), 7.549 (4.62), 7.564 (3.35), 7.933 (2.12), 7.949 (1.94), 8.113 (3.35), 8.135 (3.35), 9.379 (2.25).

Example 194

N-(2-chloro-3,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



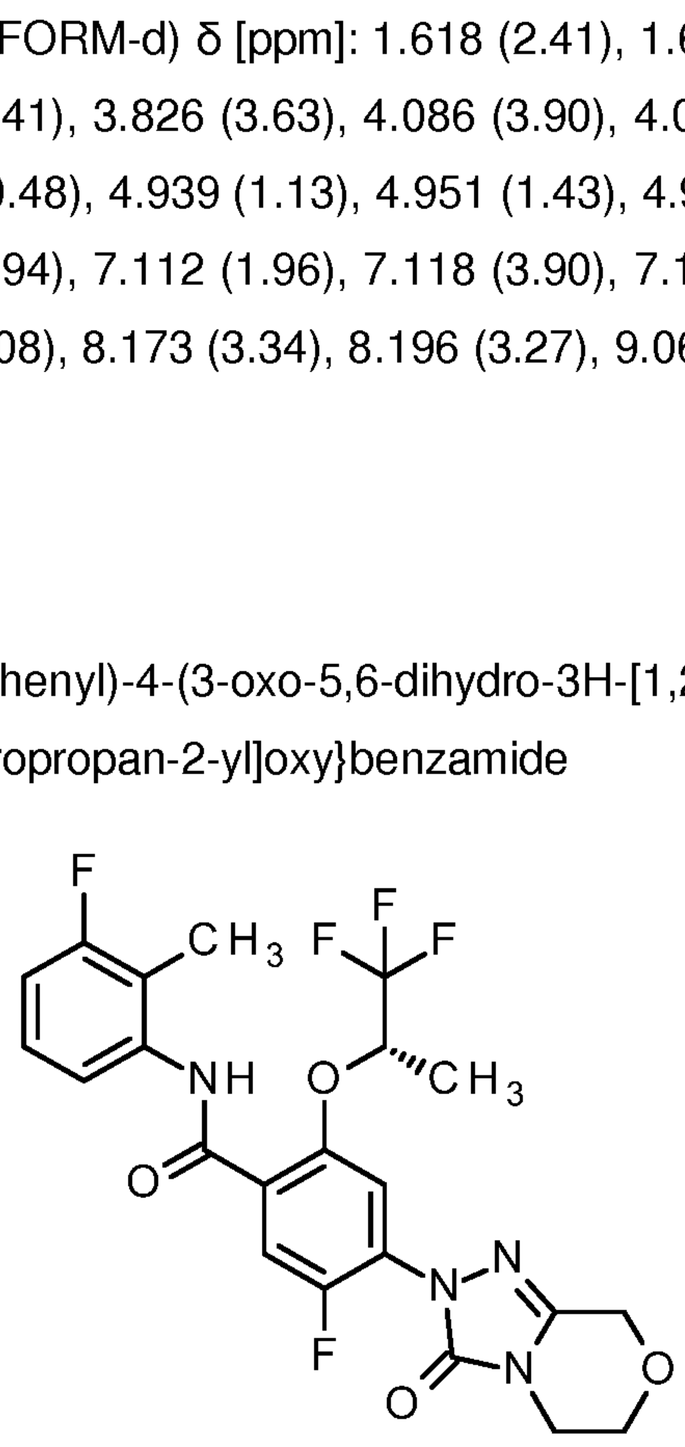
From Intermediate 24 and 2-chloro-3,6-difluoroaniline.

LC-MS (method A): R_t = 1.21 min; MS (ESIpos): m/z = 535 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.618 (2.41), 1.664 (7.49), 1.677 (7.43), 2.622 (0.78), 3.805 (3.02), 3.816 (4.41), 3.826 (3.63), 4.086 (3.90), 4.094 (3.26), 4.097 (4.53), 4.107 (3.15), 4.768 (16.00), 4.927 (0.48), 4.939 (1.13), 4.951 (1.43), 4.964 (1.07), 4.976 (0.43), 7.094 (0.41), 7.102 (2.02), 7.107 (1.94), 7.112 (1.96), 7.118 (3.90), 7.121 (1.79), 7.128 (2.15), 7.132 (1.88), 7.477 (3.19), 7.488 (3.08), 8.173 (3.34), 8.196 (3.27), 9.064 (2.29).

Example 195

5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



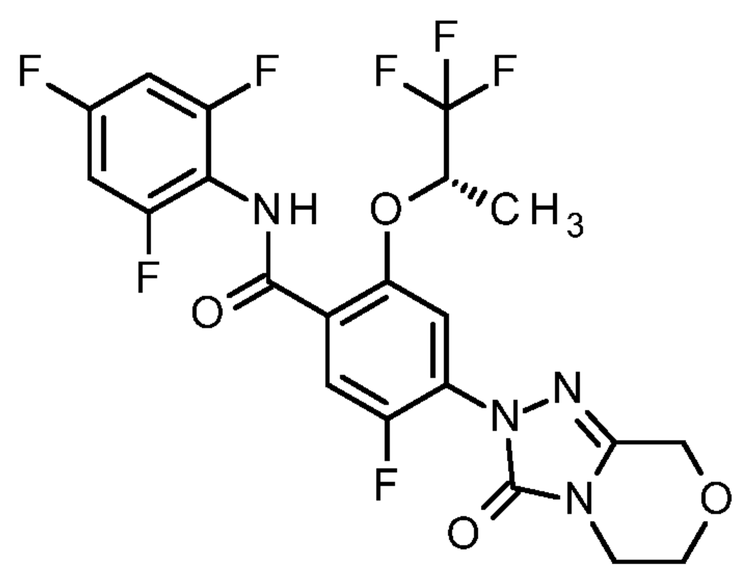
From Intermediate 24 and 3-fluoro-2-methylaniline.

LC-MS (method A): R_t = 1.24 min; MS (ESIpos): m/z = 499 $[M+H]^+$

^{1}H-NMR (500 MHz, CHLOROFORM-d) δ [ppm]: 1.454 (7.49), 1.467 (7.52), 1.824 (1.58), 2.035 (10.57), 2.039 (10.63), 3.611 (3.16), 3.621 (4.59), 3.632 (3.81), 3.893 (4.07), 3.905 (4.72), 3.915 (3.36), 4.573 (16.00), 4.706 (0.51), 4.718 (1.22), 4.730 (1.51), 4.743 (1.13), 4.756 (0.45), 6.730 (1.14), 6.747 (2.23), 6.765 (1.26), 7.009 (0.75), 7.025 (1.51), 7.038 (1.52), 7.054 (0.71), 7.094 (2.16), 7.281 (3.07), 7.493 (2.38), 7.510 (2.19), 7.954 (3.66), 7.977 (3.54), 8.894 (2.40).

Example 196

5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-N-(2,4,6-trifluoro-phenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



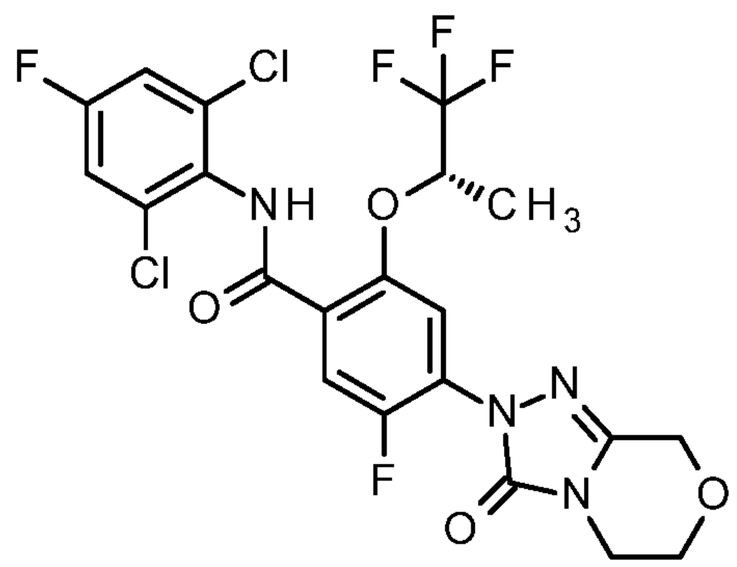
From Intermediate 24 and 2,4,6-trifluoroaniline.

LC-MS (method A): R_t = 1.18 min; MS (ESIpos): m/z = 519 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.645 (7.52), 1.661 (7.40), 2.016 (3.38), 3.801 (2.97), 3.814 (4.46), 3.817 (3.24), 3.827 (3.72), 4.082 (3.87), 4.093 (3.20), 4.096 (4.54), 4.109 (3.09), 4.766 (16.00), 4.881 (0.48), 4.896 (1.12), 4.912 (1.44), 4.927 (1.08), 4.943 (0.45), 6.772 (1.14), 6.777 (2.61), 6.785 (0.48), 6.796 (3.50), 6.798 (3.48), 6.810 (0.51), 6.817 (2.76), 6.822 (1.13), 7.459 (3.11), 7.473 (3.08), 8.140 (3.54), 8.169 (3.53), 8.846 (2.50).

Example 197

N-(2,6-dichloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



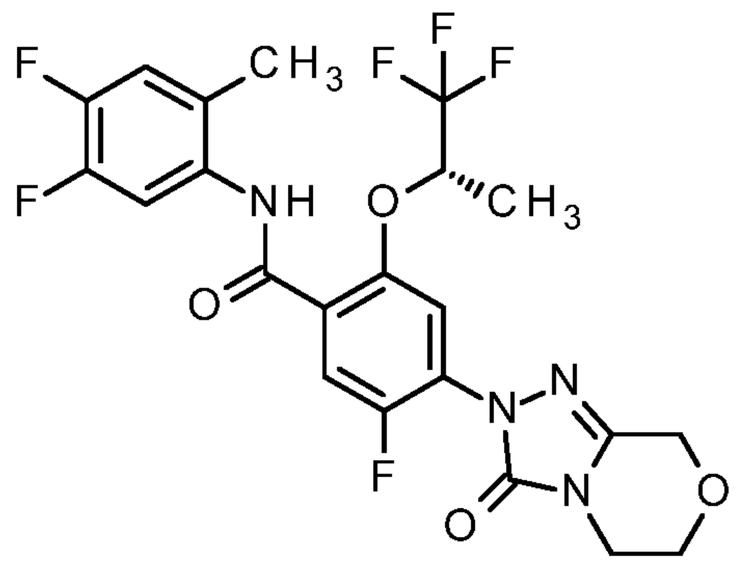
From Intermediate 24 and 2,6-dichloro-4-fluoroaniline.

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 553 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.578 (16.00), 1.660 (6.41), 1.676 (6.62), 3.807 (2.38), 3.820 (3.89), 3.834 (3.08), 4.087 (3.02), 4.101 (4.08), 4.114 (2.58), 4.771 (12.23), 4.923 (0.42), 4.939 (1.02), 4.955 (1.35), 4.969 (1.01), 4.985 (0.43), 7.202 (6.80), 7.221 (6.95), 7.462 (2.56), 7.476 (2.59), 8.168 (2.91), 8.196 (2.92), 8.971 (2.37).

Example 198

N-(4,5-difluoro-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



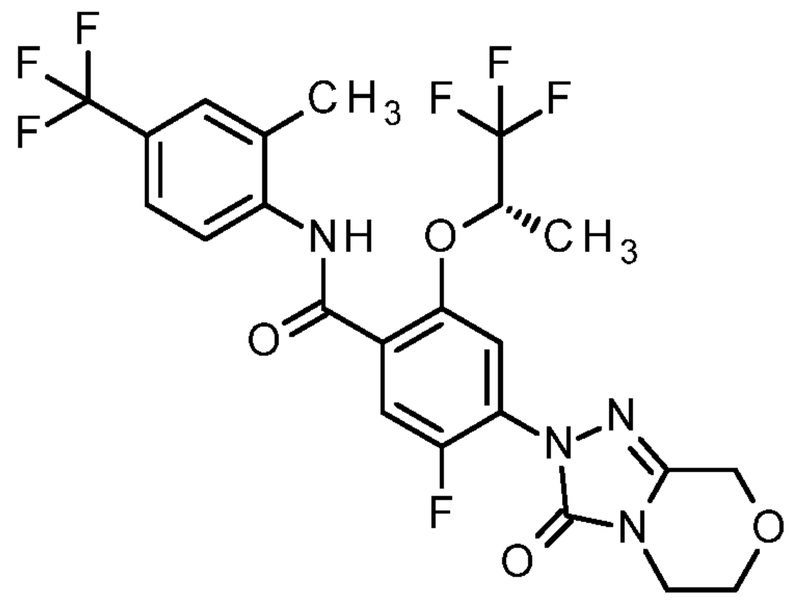
From Intermediate 24 and 4,5-difluoro-2-methylaniline.

LC-MS (method A): R_t = 1.27 min; MS (ESIpos): m/z = 517 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.629 (7.16), 1.644 (11.48), 2.259 (13.55), 3.798 (2.87), 3.811 (4.36), 3.825 (3.59), 4.081 (3.82), 4.092 (3.22), 4.095 (4.45), 4.108 (3.06), 4.761 (16.00), 4.870 (0.52), 4.886 (1.19), 4.901 (1.54), 4.917 (1.13), 4.932 (0.46), 7.005 (1.22), 7.026 (1.35), 7.032 (1.35), 7.053 (1.21), 7.452 (3.11), 7.467 (3.07), 7.854 (1.50), 7.873 (1.58), 7.884 (1.57), 7.904 (1.51), 8.122 (3.76), 8.151 (3.76), 8.984 (2.18).

Example 199

5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



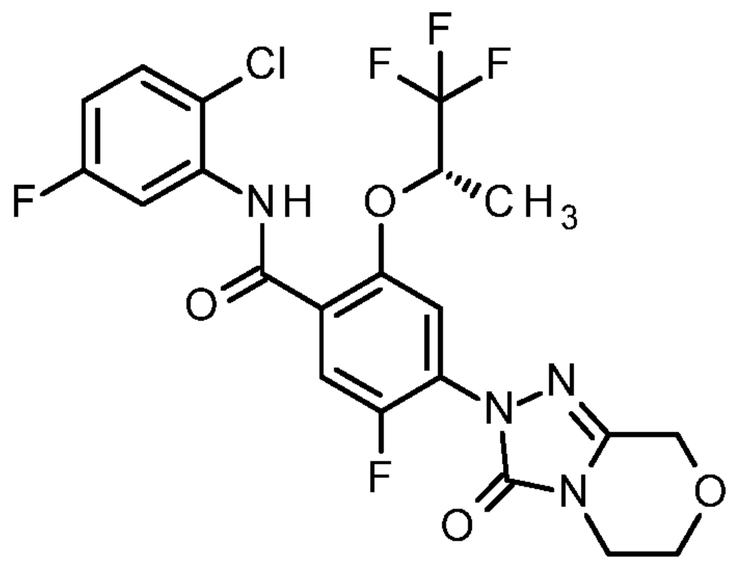
From Intermediate 24 and 2-methyl-4-(trifluoromethyl)aniline.

LC-MS (method A): R_t = 1.37 min; MS (ESIpos): m/z = 549 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.615 (5.42), 1.636 (6.64), 1.651 (6.69), 2.375 (16.00), 3.805 (2.71), 3.818 (4.12), 3.820 (3.03), 3.832 (3.51), 4.086 (3.71), 4.097 (2.93), 4.100 (4.26), 4.112 (2.98), 4.768 (15.76), 4.877 (0.45), 4.893 (1.09), 4.908 (1.42), 4.924 (1.05), 4.939 (0.43), 7.474 (2.92), 7.488 (3.03), 7.501 (2.85), 7.516 (1.45), 7.537 (1.39), 8.140 (3.29), 8.169 (3.27), 8.183 (2.01), 8.204 (1.84), 9.144 (2.03).

Example 200

N-(2-chloro-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 24 and 2-chloro-5-fluoroaniline.

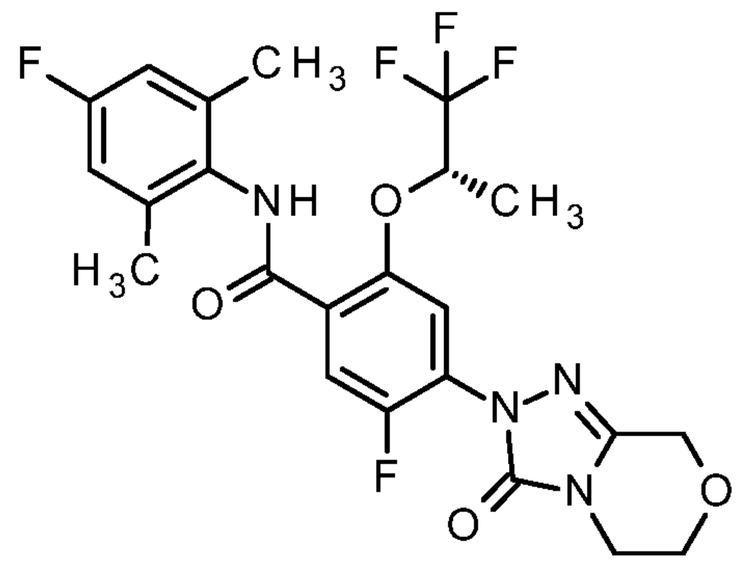
LC-MS (method A): R_t = 1.36 min; MS (ESIneg): m/z = 517 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.632 (3.35), 1.656 (7.36), 1.672 (7.40), 3.801 (2.95), 3.814 (4.44), 3.817 (3.14), 3.827 (3.70), 4.081 (3.86), 4.091 (3.09), 4.095 (4.58), 4.107

(3.19), 4.763 (16.00), 4.850 (0.51), 4.865 (1.20), 4.881 (1.57), 4.897 (1.15), 4.912 (0.47), 6.804 (1.19), 6.812 (1.31), 6.822 (1.26), 6.826 (1.41), 6.830 (1.42), 6.834 (1.47), 6.845 (1.29), 6.852 (1.38), 7.351 (2.42), 7.365 (2.43), 7.373 (2.34), 7.387 (2.22), 7.482 (3.21), 7.496 (3.23), 8.091 (4.10), 8.120 (4.07), 8.418 (2.00), 8.425 (2.01), 8.445 (2.02), 8.452 (1.99), 9.751 (1.99).

Example 201

5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



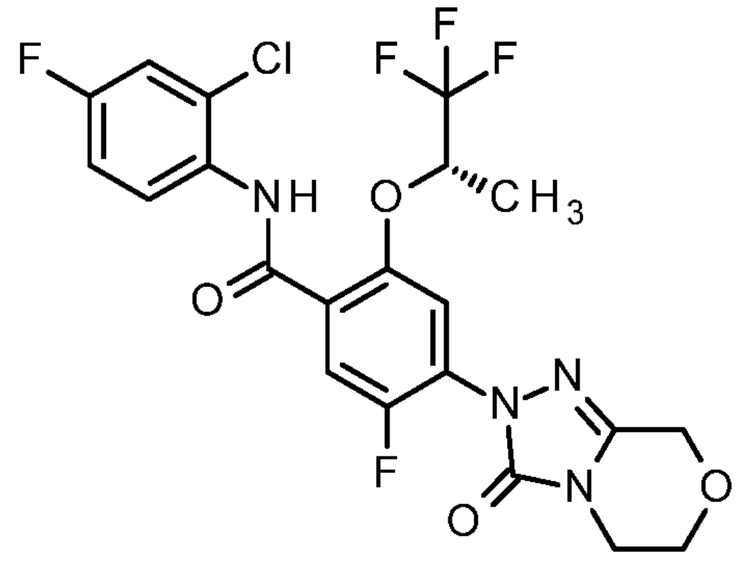
From Intermediate 24 and 4-fluoro-2,6-dimethylaniline.

LC-MS (method A): R_t = 1.23 min; MS (ESIpos): m/z = 513 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.644 (3.44), 1.660 (3.50), 2.248 (16.00), 3.793 (1.21), 3.805 (1.97), 3.819 (1.50), 4.074 (1.59), 4.088 (2.05), 4.101 (1.29), 4.758 (6.48), 4.933 (0.56), 4.948 (0.73), 4.964 (0.54), 6.825 (2.24), 6.848 (2.24), 7.419 (1.51), 7.433 (1.52), 8.140 (1.58), 8.169 (1.56), 8.637 (1.09).

Example 202

N-(2-chloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



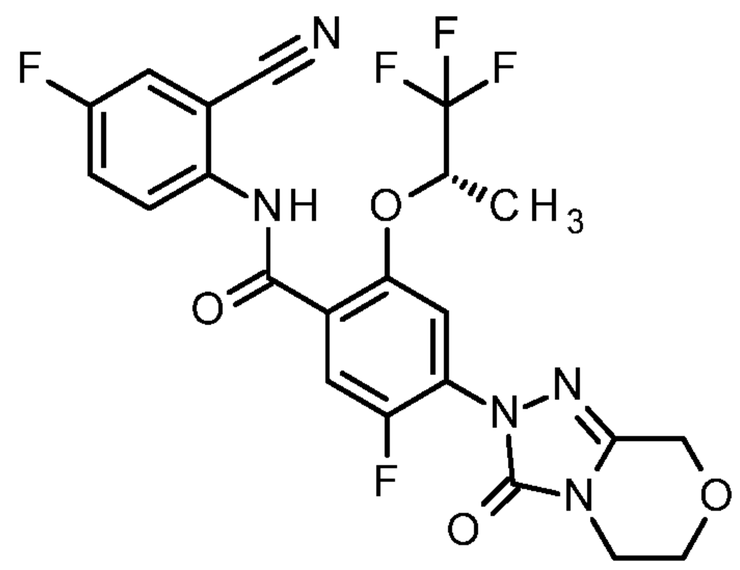
From Intermediate 24 and 2-chloro-4-fluoroaniline.

LC-MS (method A): R_t = 1.32 min; MS (ESIneg): m/z = 517 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.842 (0.76), 0.849 (0.72), 1.261 (0.69), 1.293 (0.67), 1.584 (12.78), 1.655 (6.46), 1.672 (6.45), 3.807 (2.75), 3.819 (4.01), 3.822 (2.89), 3.833 (3.56), 4.085 (3.77), 4.096 (2.90), 4.099 (4.19), 4.112 (2.96), 4.768 (16.00), 4.860 (0.46), 4.876 (1.05), 4.891 (1.39), 4.907 (1.02), 4.922 (0.41), 7.042 (0.89), 7.049 (1.02), 7.062 (0.99), 7.065 (1.07), 7.069 (1.16), 7.072 (1.17), 7.084 (0.93), 7.092 (1.04), 7.179 (2.51), 7.186 (2.21), 7.200 (2.56), 7.207 (2.28), 7.468 (2.86), 7.481 (2.83), 8.117 (3.64), 8.147 (3.54), 8.451 (1.95), 8.464 (1.94), 8.473 (1.90), 8.488 (1.84), 9.605 (1.93).

Example 203

N-(2-cyano-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



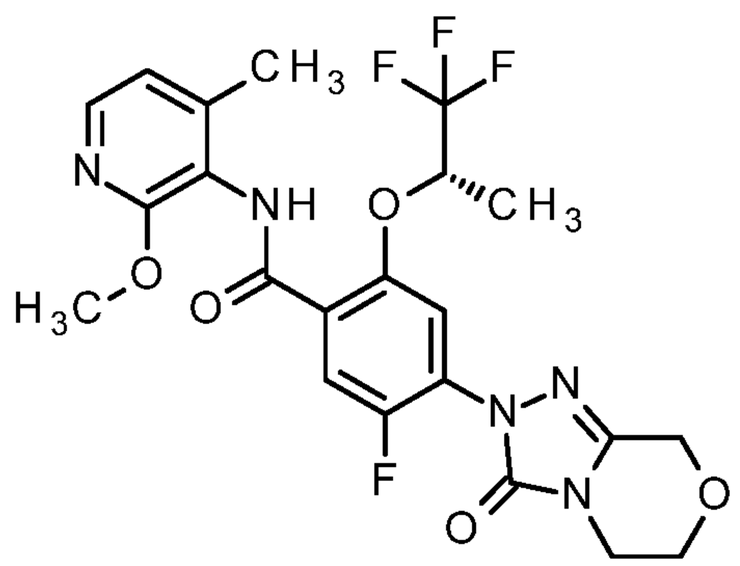
From Intermediate 24 and 2-amino-5-fluorobenzonitrile.

LC-MS (method A): R_t = 1.17 min; MS (ESIpos): m/z = 510 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.610 (1.66), 1.755 (6.55), 1.772 (6.62), 2.016 (0.58), 3.803 (2.77), 3.816 (4.06), 3.819 (2.87), 3.830 (3.45), 4.084 (3.72), 4.095 (2.95), 4.098 (4.20), 4.110 (2.94), 4.767 (16.00), 4.860 (0.45), 4.876 (1.05), 4.891 (1.37), 4.907 (1.00), 4.922 (0.40), 7.341 (1.11), 7.348 (2.45), 7.352 (1.88), 7.360 (1.44), 7.367 (2.47), 7.371 (1.91), 7.374 (1.49), 7.381 (0.88), 7.393 (1.19), 7.401 (0.78), 7.480 (3.06), 7.494 (3.09), 8.101 (3.86), 8.129 (3.83), 8.423 (1.38), 8.435 (1.41), 8.445 (1.35), 8.457 (1.34), 9.741 (2.16).

Example 204

5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



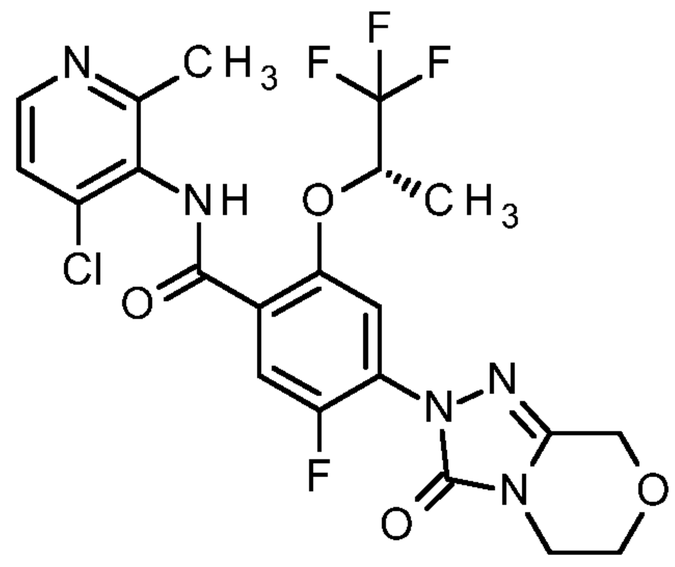
From Intermediate 24 and 2-methoxy-4-methylpyridin-3-amine.

LC-MS (method A): R_t = 1.10 min; MS (ESIneg): m/z = 510 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.656 (3.88), 1.672 (3.93), 2.010 (1.01), 2.273 (10.82), 3.798 (1.46), 3.811 (2.26), 3.825 (1.82), 3.956 (16.00), 4.077 (1.92), 4.088 (1.73), 4.091 (2.33), 4.104 (1.52), 4.762 (7.99), 4.913 (0.63), 4.928 (0.82), 4.943 (0.61), 6.824 (1.63), 6.837 (1.66), 7.426 (1.68), 7.440 (1.69), 7.953 (2.05), 7.967 (2.04), 8.135 (2.05), 8.163 (2.06), 8.960 (1.38).

Example 205

N-(4-chloro-2-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



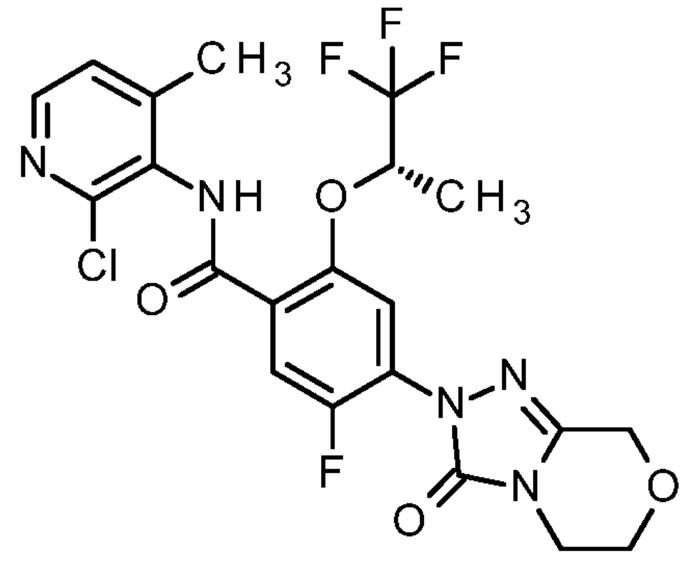
From Intermediate 24 and 4-chloro-2-methylpyridin-3-amine.

LC-MS (method A): R_t = 0.99 min; MS (ESIpos): m/z = 516 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.675 (5.82), 1.691 (5.88), 2.017 (0.50), 2.574 (16.00), 2.719 (0.49), 3.810 (2.35), 3.823 (3.44), 3.826 (2.47), 3.837 (3.00), 4.090 (3.16), 4.100 (2.50), 4.103 (3.53), 4.117 (2.49), 4.774 (13.95), 4.957 (0.91), 4.972 (1.18), 4.988 (0.85), 7.321 (2.24), 7.334 (2.29), 7.472 (2.56), 7.486 (2.55), 8.091 (0.59), 8.172 (3.42), 8.201 (3.38), 8.379 (2.74), 8.392 (2.66), 9.046 (2.06).

Example 206

N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



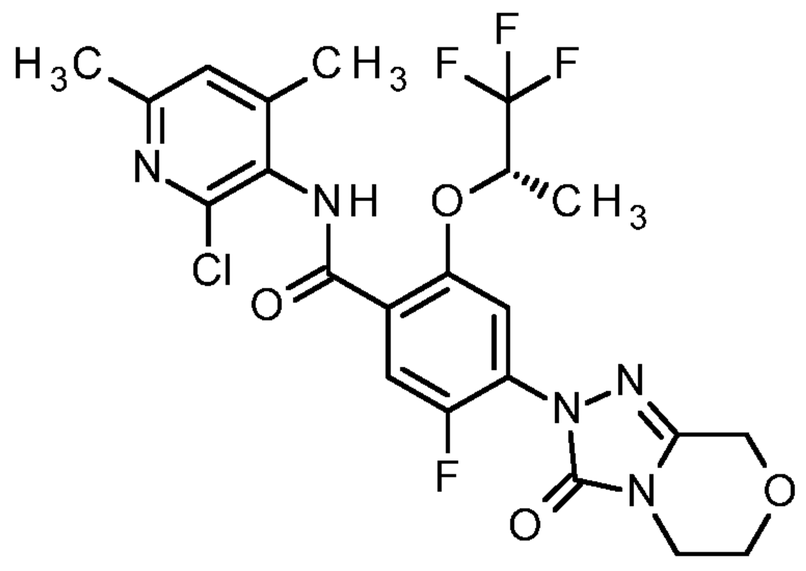
From Intermediate 24 and 2-chloro-4-methylpyridin-3-amine.

LC-MS (method A): R_t = 1.04 min; MS (ESIpos): m/z = 516 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.681 (5.98), 1.696 (5.99), 2.013 (2.42), 2.346 (16.00), 3.805 (2.42), 3.817 (3.57), 3.820 (2.60), 3.831 (3.03), 4.084 (3.25), 4.095 (2.62), 4.098 (3.63), 4.111 (2.57), 4.768 (13.88), 4.958 (0.94), 4.973 (1.22), 4.988 (0.88), 7.194 (2.25), 7.206 (2.29), 7.468 (2.62), 7.481 (2.60), 8.036 (0.44), 8.156 (3.46), 8.184 (3.45), 8.212 (3.12), 8.224 (3.06), 9.121 (2.17).

Example 207

N-(2-chloro-4,6-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



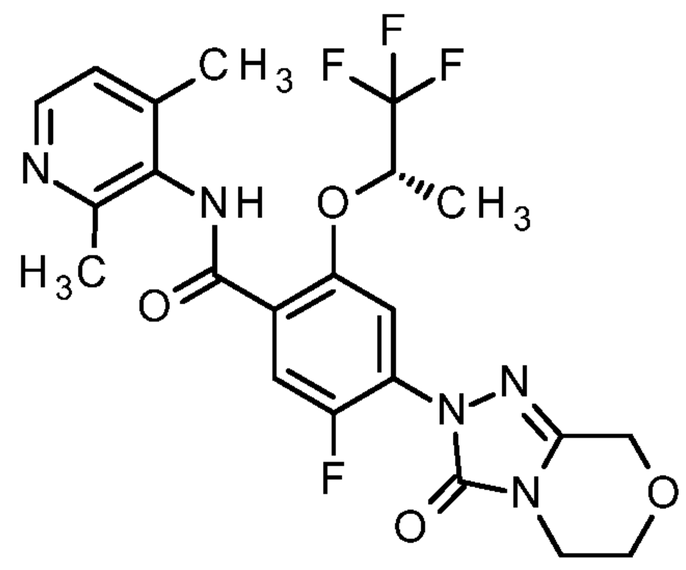
From Intermediate 24 and 2-chloro-4,6-dimethylpyridin-3-amine.

LC-MS (method A): R_t = 1.11 min; MS (ESIneg): m/z = 528 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.667 (6.25), 1.683 (6.32), 2.008 (0.54), 2.290 (16.00), 2.514 (15.66), 3.796 (2.39), 3.809 (3.70), 3.823 (2.98), 4.077 (3.06), 4.088 (2.77), 4.091 (3.77), 4.104 (2.50), 4.761 (13.11), 4.927 (0.41), 4.943 (0.99), 4.958 (1.26), 4.974 (0.93), 7.048 (4.33), 7.451 (2.66), 7.465 (2.64), 8.144 (3.40), 8.172 (3.39), 9.017 (2.45).

Example 208

N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



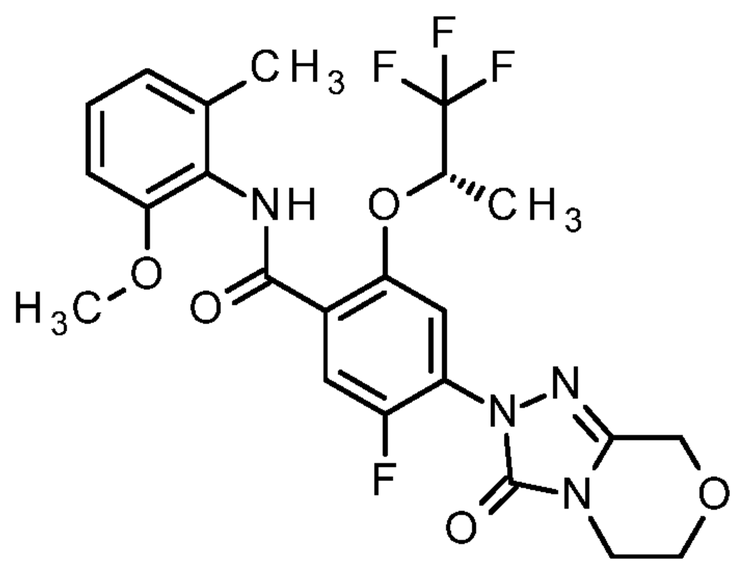
From Intermediate 24 and 2,4-dimethylpyridin-3-amine.

LC-MS (method A): R_t = 0.73 min; MS (ESIpos): m/z = 496 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.671 (6.70), 1.687 (6.81), 1.795 (0.64), 2.295 (15.58), 2.533 (16.00), 3.812 (2.68), 3.824 (3.93), 3.827 (2.79), 3.838 (3.35), 4.092 (3.56), 4.103 (2.85), 4.106 (4.01), 4.119 (2.85), 4.776 (15.04), 4.939 (0.44), 4.955 (1.03), 4.970 (1.36), 4.985 (0.98), 5.001 (0.40), 7.115 (1.84), 7.128 (1.88), 7.454 (2.90), 7.468 (2.89), 8.172 (3.93), 8.200 (3.86), 8.345 (2.84), 8.358 (2.77), 8.839 (2.13).

Example 209

5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



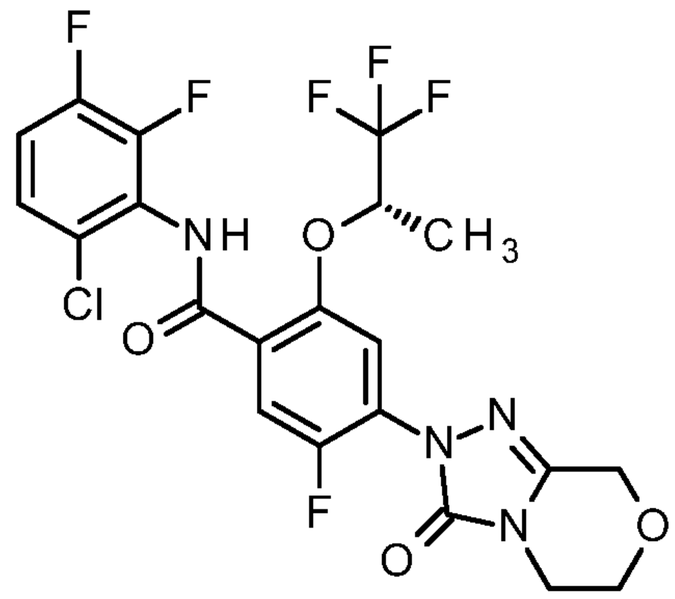
From Intermediate 24 and 2-methoxy-6-methylaniline.

LC-MS (method A): R_t = 1.19 min; MS (ESIpos): m/z = 511 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.637 (4.76), 1.653 (4.83), 2.283 (11.55), 3.798 (1.85), 3.812 (3.58), 3.818 (16.00), 3.824 (2.91), 4.076 (2.24), 4.090 (2.88), 4.103 (1.82), 4.762 (8.99), 4.900 (0.77), 4.915 (1.01), 4.931 (0.75), 6.793 (1.33), 6.813 (1.47), 6.887 (1.31), 6.906 (1.49), 7.164 (1.31), 7.184 (2.04), 7.204 (1.03), 7.407 (2.00), 7.421 (2.00), 8.150 (2.41), 8.179 (2.39), 8.871 (1.60).

Example 210

N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



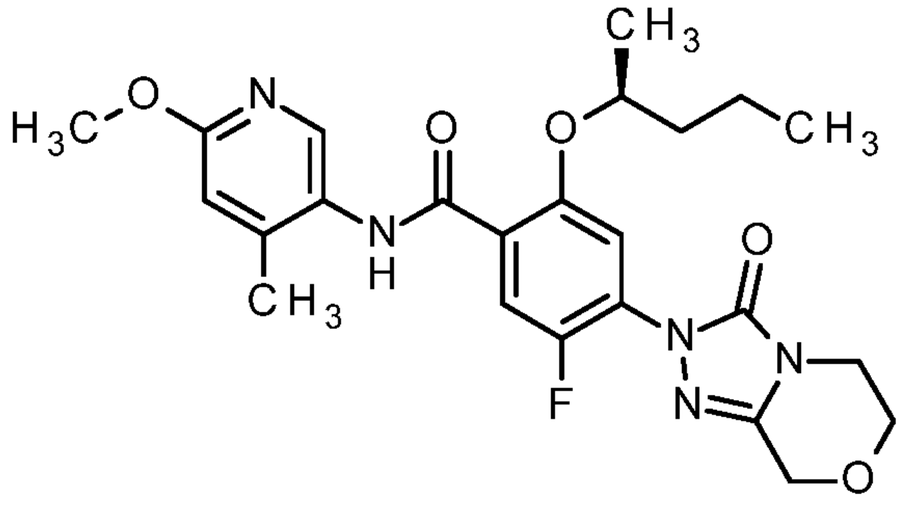
From Intermediate 24 and 6-chloro-2,3-difluoroaniline.

LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 537 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.566 (16.00), 1.666 (4.53), 1.682 (4.58), 3.808 (1.78), 3.821 (2.75), 3.835 (2.22), 4.088 (2.30), 4.103 (2.82), 4.116 (1.84), 4.774 (9.28), 4.938 (0.72), 4.953 (0.94), 4.969 (0.71), 7.090 (0.45), 7.113 (1.12), 7.133 (1.16), 7.136 (0.85), 7.155 (0.72), 7.218 (0.76), 7.224 (0.79), 7.230 (0.92), 7.236 (0.85), 7.241 (0.66), 7.247 (0.65), 7.253 (0.72), 7.259 (0.81), 7.481 (1.90), 7.495 (1.91), 8.183 (2.21), 8.212 (2.18), 9.079 (1.53).

Example 211

5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



From Intermediate 21 and 6-methoxy-4-methylpyridin-3-amine.

The product was purified by preparative HPLC (Chromatorex C18 125x30 mm 10µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.20 min; MS (ESIneg): m/z = 484 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.858 (2.70), 0.876 (6.35), 0.894 (3.04), 1.292 (5.45), 1.306 (5.50), 1.371 (0.52), 1.390 (0.57), 1.404 (0.61), 1.423 (0.47), 1.428 (0.44), 1.447 (0.45), 1.582 (0.41), 1.597 (0.55), 1.621 (0.43), 1.693 (0.41), 1.709 (0.41), 2.210 (0.59), 2.250 (9.42), 2.518 (1.10), 2.522 (0.71), 3.659 (1.35), 3.672 (2.28), 3.686 (1.59), 3.835 (16.00), 3.866 (1.04), 4.022 (1.70), 4.036 (2.38), 4.048 (1.42), 4.560 (0.41), 4.575 (0.77), 4.591 (0.77), 4.743 (6.99), 6.777 (2.95), 7.371 (1.65), 7.386 (1.64), 7.673 (2.19), 7.699 (2.11), 8.193 (3.65), 9.668 (2.60).

Example 212

N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide

The product was purified by preparative HPLC (Chromatorex C18 125x30 mm 10µm, 0.1 % aqueous formic acid, acetonitrile).

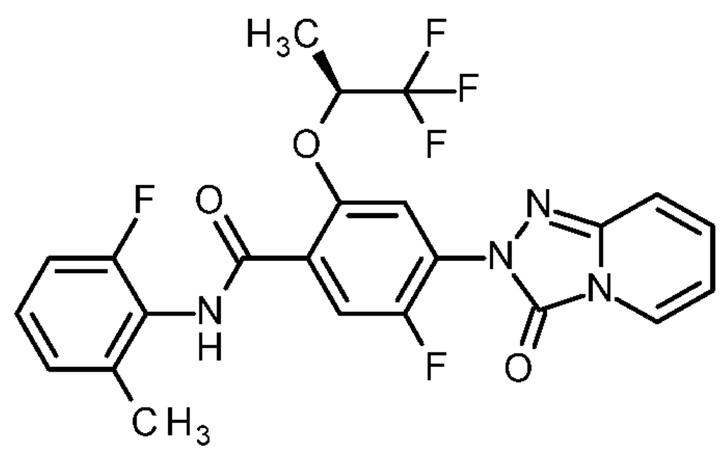
From Intermediate 21 and 2-chloro-6-fluoroaniline.

LC-MS (method A): R_t = 1.30 min; MS (ESIpos): m/z = 493 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.860 (6.38), 0.878 (15.05), 0.897 (7.24), 0.921 (0.42), 1.290 (0.75), 1.311 (8.08), 1.325 (8.15), 1.351 (1.04), 1.369 (0.96), 1.376 (1.07), 1.391 (1.01), 1.408 (1.04), 1.427 (0.89), 1.440 (0.87), 1.446 (0.93), 1.465 (0.89), 1.484 (0.54), 1.560 (0.47), 1.574 (0.76), 1.595 (0.91), 1.607 (1.11), 1.619 (0.89), 1.632 (0.79), 1.741 (0.51), 1.756 (0.75), 1.771 (0.85), 1.815 (0.47), 2.084 (1.18), 2.250 (0.71), 2.518 (3.68), 2.523 (2.36), 3.662 (3.26), 3.674 (5.56), 3.688 (3.73), 3.834 (1.16), 4.022 (4.19), 4.036 (5.89), 4.049 (3.47), 4.597 (0.75), 4.612 (1.38), 4.627 (1.35), 4.642 (0.73), 4.724 (0.88), 4.748 (16.00), 7.338 (0.82), 7.358 (2.07), 7.377 (1.45), 7.382 (1.75), 7.406 (2.04), 7.421 (4.15), 7.441 (4.64), 7.447 (3.87), 7.463 (1.29), 7.662 (2.75), 7.688 (2.69), 9.843 (6.16).

Example 213

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 25 and 2-fluoro-6-methylaniline.

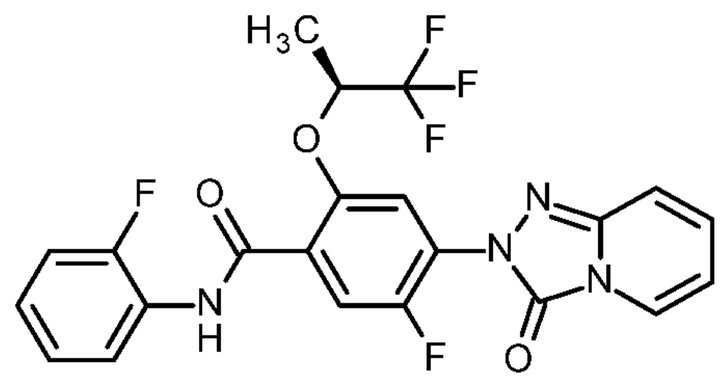
MS (ESIpos): m/z = 493 $(M+H)^+$

^{1}H NMR (400 MHz, CHLOROFORM-d) δ [ppm] 8.87 (s, 1H), 8.22 (d, 1H), 7.83 (dt, 1H), 7.49 (d, 1H), 7.25 – 7.13 (m, 3H), 7.12 – 6.95 (m, 2H), 6.59 (ddd, 1H), 4.95 (p, 1H), 2.32 (s, 3H), 1.67 (d, 3H).

Example 214

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide

407



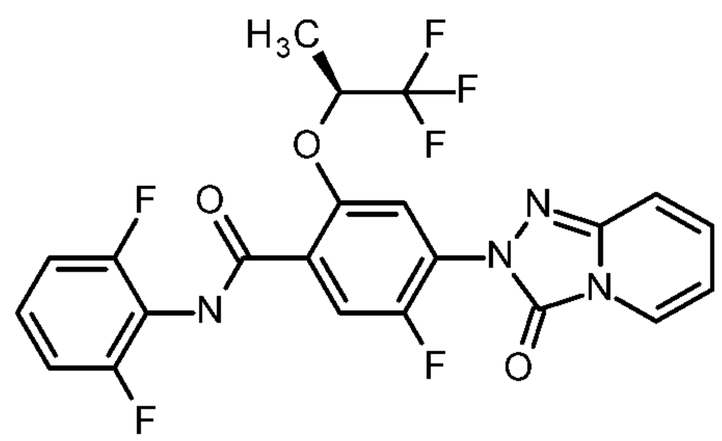
From Intermediate 25 and 2-fluoroaniline.

MS (ESIpos): m/z = 479 $(M+H)^+$

^{1}H NMR (400 MHz, CHLOROFORM-d) δ [ppm] 9.78 (s, 1H), 8.55 (t, 1H), 8.24 (d, 1H), 7.83 (dd, 1H), 7.51 (d, 1H), 7.25 – 7.13 (m, 6H), 7.13 – 7.06 (m, 2H), 6.59 (ddd, 1H), 4.95 (p, 1H), 1.68 (d, 3H).

Example 215

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



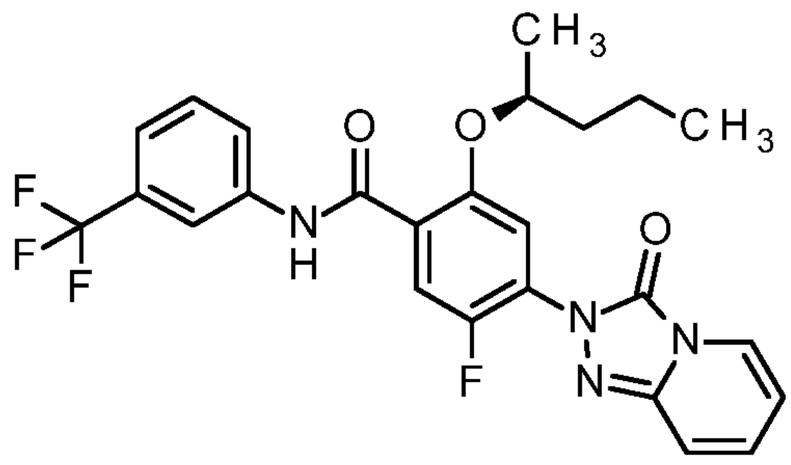
From Intermediate 25 and 2,6-difluoroaniline.

MS (ESIpos): m/z = 497 $(M+H)^+$

^{1}H NMR (400 MHz, CHLOROFORM-d) δ [ppm] 8.97 (s, 1H), 8.23 (d, 1H), 7.83 (dd, 1H), 7.51 (d, 1H), 7.23 (d, 22H), 7.01 (t, 2H), 6.59 (ddd, 1H), 4.94 (p, 1H), 1.66 (d, 3H).

Example 216

5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[3-(trifluoromethyl)phenyl]benzamide



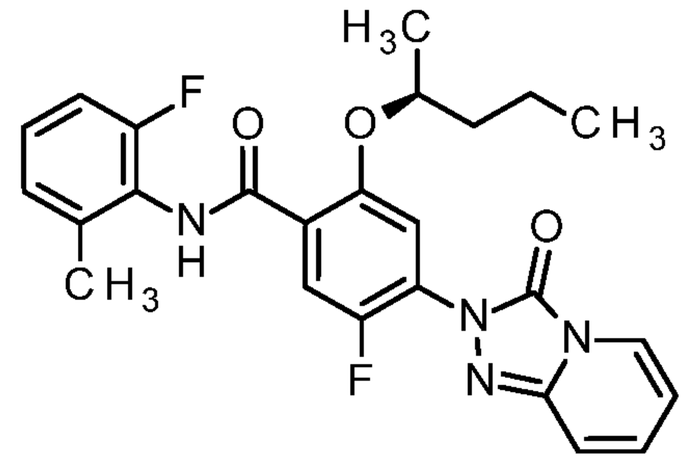
From Intermediate 26 and 3-(trifluoromethyl)aniline.

MS (ESIpos): m/z = 503 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.00 (t, 3H), 1.42 – 1.67 (m, 2H) 1.49 (d, 3H), 1.72 – 1.86 (m, 1H), 1.87 – 2.00 (m, 1H), 4.63 – 4.76 (m, 1H), 6.57 (dd, 1H), 7.17 – 7.22 (m, 2H), 7.36 – 7.45 (m, 2H), 7.50 (t, 1H), 7.80 – 7.89 (m, 2H), 7.94 (s, 1H), 8.22 (d, 1H), 10.34 (s, 1H).

Example 217

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



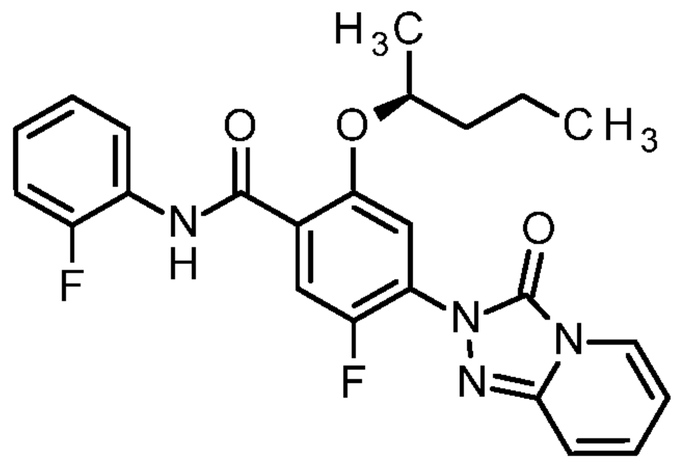
From Intermediate 26 and 2-fluoro-6-methylaniline.

MS (ESIpos): m/z = 467 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 0.95 (t, 3H), 1.36 – 1.58 (m, 2H) 1.45 (d, 3H), 1.63 – 1.78 (m, 1H), 1.80 – 1.94 (m, 1H), 2.33 (s, 3H), 4.62 – 4.73 (m, 1H), 6.53 – 6.60 (m, 1H), 7.01 (t, 1H), 7.07 (d, 1H), 7.13 – 7.24 (m, 3H), 7.43 (d, 1H), 7.84 (td, 1H), 8.20 (d, 1H), 9.56 (s, 1H).

Example 218

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



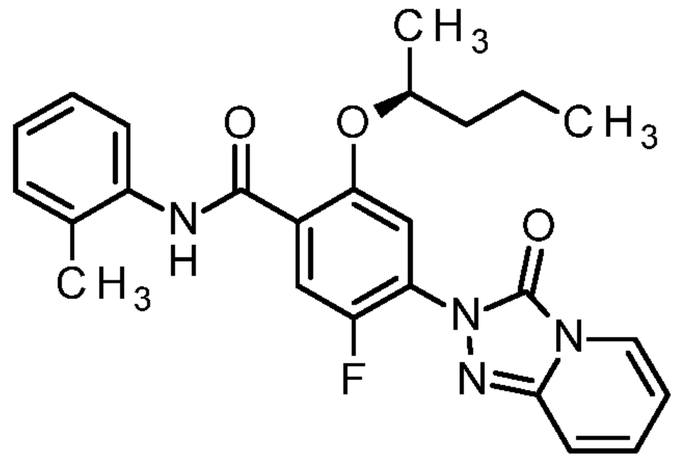
From Intermediate 26 and 2-fluoroaniline.

MS (ESIpos): m/z = 453 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 0.96 (t, 3H), 1.35 – 1.60 (m, 2H) 1.47 (d, 3H), 1.66 – 1.79 (m, 1H), 1.88 – 2.03 (m, 1H), 4.62 – 4.75 (m, 1H), 6.57 (dd, 1H), 7.03 – 7.23 (m, 5H), 7.42 (d, 1H), 7.84 (td, 1H), 8.24 (d, 1H), 8.63 (dt, 1H), 10.48 (s, 1H).

Example 219

5-fluoro-N-(2-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



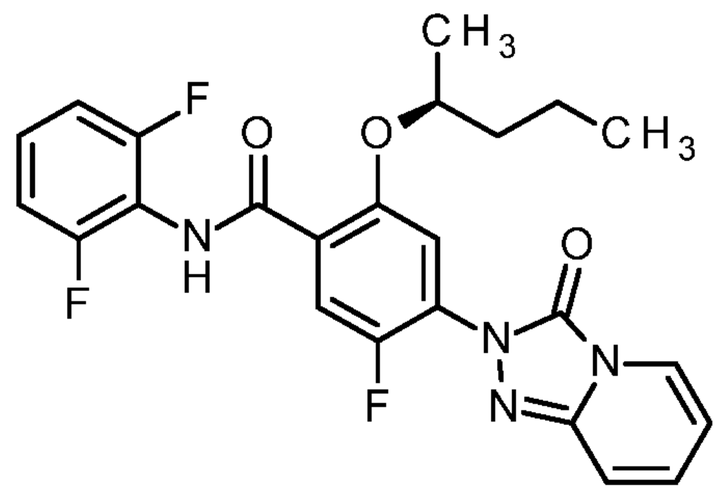
From Intermediate 26 and o-toluidine.

MS (ESIpos): m/z = 449 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 0.95 (t, 3H), 1.37 – 1.57 (m, 2H) 1.45 (d, 3H), 1.62 – 1.76 (m, 1H), 1.80 – 1.95 (m, 1H), 2.36 (s, 3H), 4.61 – 4.73 (m, 1H), 6.54 – 6.60 (m, 1H), 7.12 (dt, 1H), 7.18 – 7.21 (m, 2H), 7.22 – 7.31 (m, 2H), 7.43 (d, 1H), 7.84 (td, 1H), 8.02 (d, 1H), 8.24 (d, 1H), 9.65 (s, 1H).

Example 220

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide



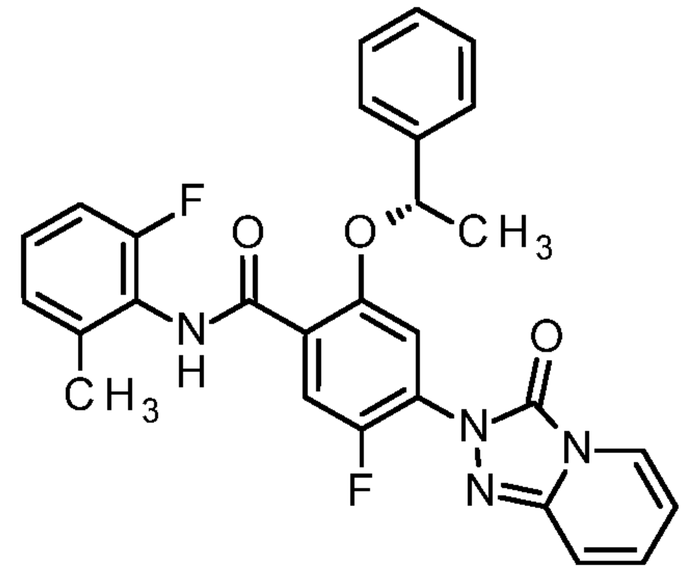
From Intermediate 26 and 2,6-difluoroaniline.

MS (ESIpos): m/z = 471 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 0.96 (t, 3H), 1.37 – 1.57 (m, 2H) 1.46 (d, 3H), 1.64 – 1.79 (m, 1H), 1.81 – 1.96 (m, 1H), 4.61 – 4.74 (m, 1H), 6.53 – 6.60 (m, 1H), 6.96 – 7.06 (m, 2H), 7.15 – 7.29 (m, 3H), 7.43 (d, 1H), 7.83 (td, 1H), 8.21 (d, 1H), 9.68 (s, 1H).

Example 221

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



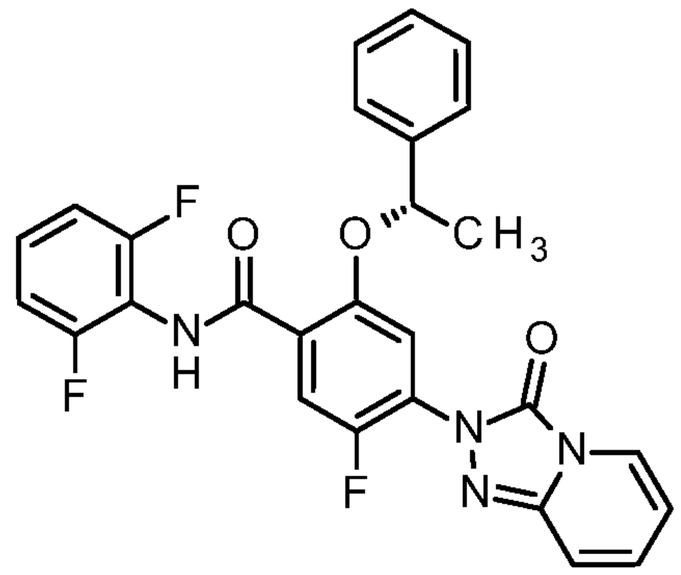
From Intermediate 27 and 2-fluoro-6-methylaniline.

MS (ESIpos): m/z = 501 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.81 (d, 3H), 2.32 (s, 3H), 5.62 (q, 1H), 6.54 (dd, 1H), 6.98 – 7.10 (m, 2H), 7.13 – 7.45 (m, 9H), 7.80 (td, 1H), 8.18 (d, 1H), 9.62 (s, 1H).

Example 222

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



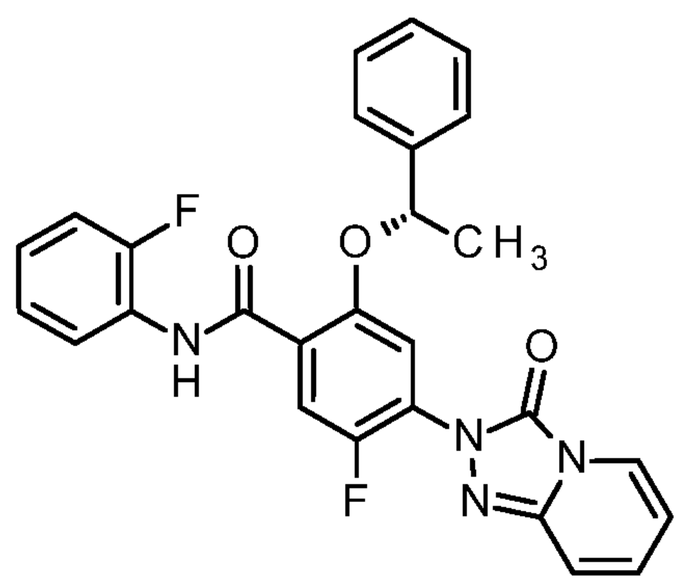
From Intermediate 27 and 2,6-difluoroaniline.

MS (ESIpos): m/z = 505 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.82 (d, 3H), 5.62 (q, 1H), 6.54 (dd, 1H), 6.98 – 7.07 (m, 2H), 7.13 – 7.18 (m, 2H), 7.19 – 7.45 (m, 7H), 7.79 (td, 1H), 8.18 (d, 1H), 9.74 (s, 1H).

Example 223

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



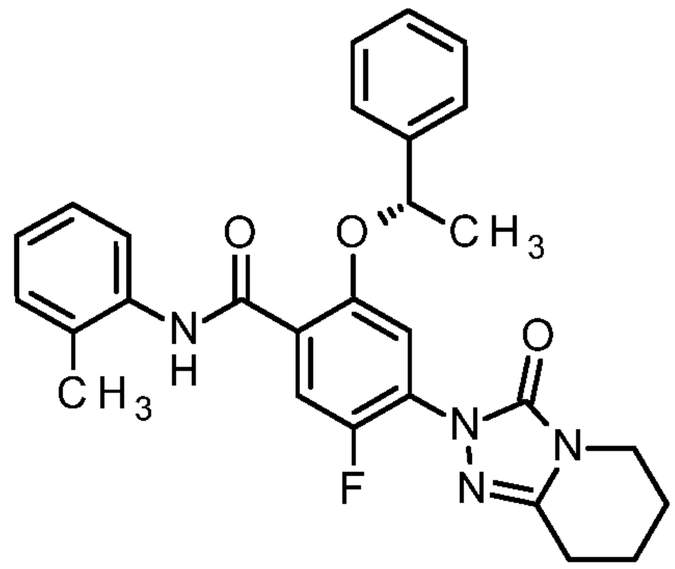
From Intermediate 27 and 2-fluoroaniline.

MS (ESIpos): m/z = 487 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.86 (d, 3H), 5.62 (q, 1H), 6.53 (dd, 1H), 7.05 – 7.44 (m, 11H), 7.79 (td, 1H), 8.20 (d, 1H), 8.65 (dt, 1H), 10.55 (s, 1H).

Example 224

5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



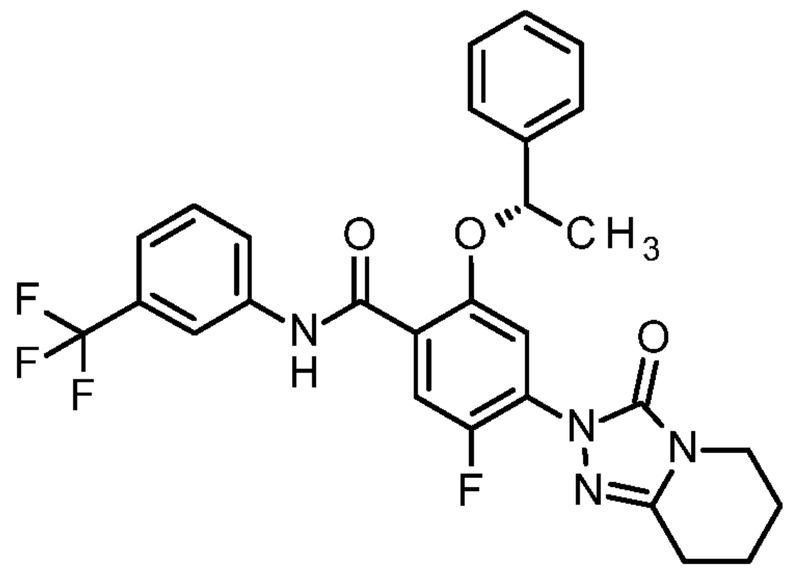
From Intermediate 28 and o-toluidine.

MS (ESIpos): m/z = 487 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.78 (d, 3H), 1.84 – 2.02 (m, 4H), 2.20 (s, 3H), 2.77 (t, 2H), 3.69 (t, 2H), 5.62 (q, 1H), 7.07 – 7.14 (m, 1H), 7.17 – 7.22 (m, 1H), 7.23 – 7.41 (m, 7H), 8.02 (d, 1H), 8.15 (d, 1H), 9.66 (s, 1H).

Example 225

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]-N-[3-(trifluoromethyl)phenyl]benzamide



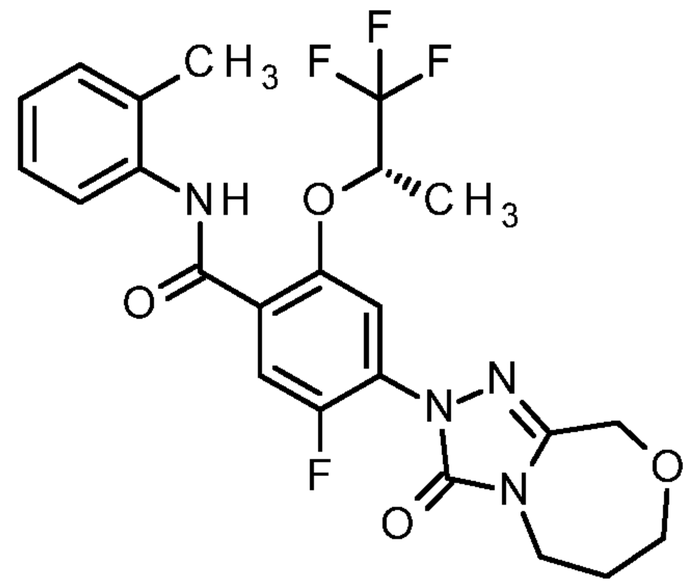
From Intermediate 28 and 3-(trifluoromethyl)aniline.

MS (ESIpos): m/z = 541 $(M+H)^+$

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 1.86 (d, 3H), 1.88 – 2.04 (m, 4H), 2.79 (t, 2H), 3.70 (t, 2H), 5.61 (q, 1H), 7.32 – 7.49 (m, 8H), 7.67 (s, 1H), 7.77 (d, 1H), 8.13 (d, 1H), 10.2 (s, 1H).

Example 226

5-fluoro-N-(2-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



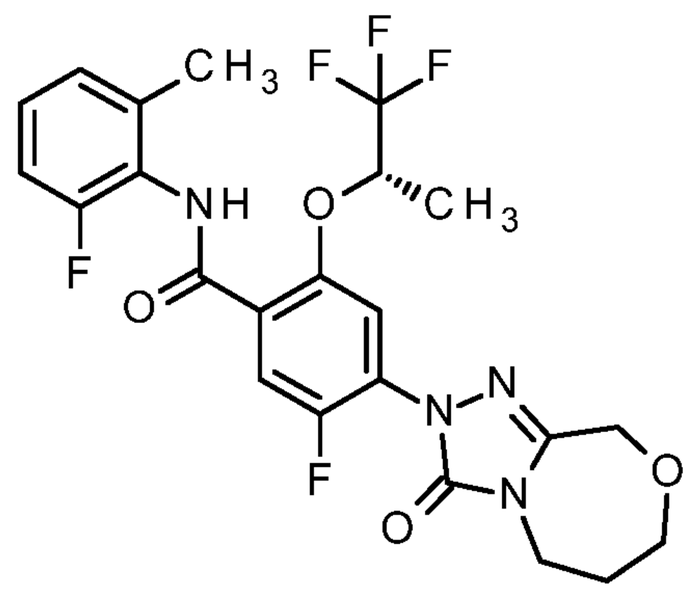
From Intermediate 29 and o-toluidine.

LC-MS (method A): R_t = 1.24 min; MS (ESIpos): m/z = 495 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.627 (6.76), 1.643 (6.70), 2.015 (1.54), 2.021 (0.72), 2.034 (1.36), 2.047 (1.95), 2.059 (1.37), 2.072 (0.70), 2.320 (16.00), 4.005 (2.37), 4.017 (1.90), 4.019 (1.90), 4.031 (2.29), 4.064 (2.68), 4.076 (2.49), 4.089 (2.54), 4.613 (13.95), 4.868 (0.48), 4.884 (1.09), 4.899 (1.43), 4.914 (1.03), 4.930 (0.42), 7.125 (0.70), 7.128 (0.76), 7.147 (1.88), 7.162 (1.38), 7.166 (1.35), 7.242 (2.22), 7.249 (1.37), 7.261 (1.53), 7.287 (0.76), 7.402 (2.86), 7.416 (2.87), 7.885 (2.00), 7.905 (1.72), 8.149 (3.58), 8.177 (3.55), 9.022 (1.83).

Example 227

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-fluoro-6-methylaniline.

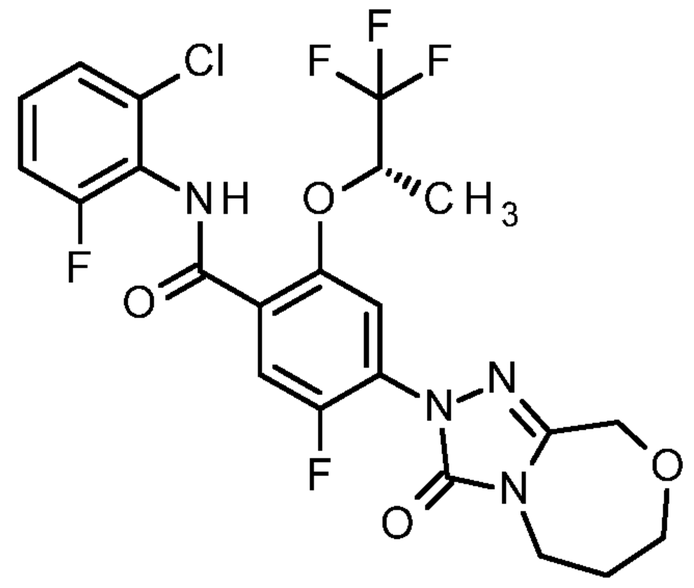
LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 513 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.649 (6.36), 1.665 (6.38), 2.015 (0.99), 2.020 (0.65), 2.033 (1.26), 2.046 (1.85), 2.059 (1.31), 2.072 (0.67), 2.314 (16.00), 2.628 (0.56), 4.004 (2.24), 4.016 (1.83), 4.031 (2.21), 4.064 (2.56), 4.076 (2.37), 4.088 (2.50), 4.615 (13.93), 4.898 (0.43), 4.913 (1.00), 4.929 (1.31), 4.945 (0.96), 6.991 (0.76), 7.012 (1.53), 7.035 (0.95), 7.063

(1.34), 7.082 (1.82), 7.171 (0.99), 7.185 (1.05), 7.191 (1.44), 7.205 (1.39), 7.211 (0.72), 7.224 (0.64), 7.404 (2.82), 7.417 (2.84), 8.155 (3.59), 8.183 (3.51), 8.864 (2.01).

Example 228

N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



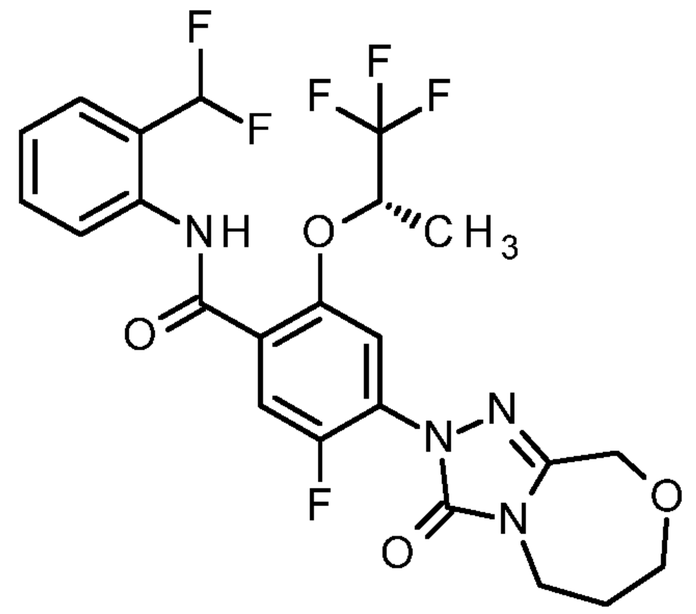
From Intermediate 29 and 2-chloro-6-fluoroaniline.

LC-MS (method A): R_t = 1.23 min; MS (ESIpos): m/z = 533 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.660 (8.08), 1.676 (8.12), 2.025 (0.84), 2.038 (1.70), 2.050 (2.45), 2.063 (1.75), 2.076 (0.88), 4.008 (2.75), 4.020 (2.31), 4.023 (2.31), 4.034 (2.71), 4.067 (3.17), 4.079 (3.09), 4.092 (3.03), 4.619 (16.00), 4.912 (0.54), 4.927 (1.25), 4.943 (1.62), 4.958 (1.20), 4.974 (0.49), 7.112 (0.98), 7.115 (1.06), 7.132 (1.69), 7.135 (2.25), 7.138 (1.30), 7.155 (1.38), 7.159 (1.40), 7.221 (0.95), 7.234 (0.93), 7.241 (2.15), 7.254 (2.22), 7.262 (1.93), 7.285 (2.42), 7.288 (3.20), 7.307 (1.27), 7.311 (1.05), 7.427 (3.39), 7.441 (3.36), 8.179 (3.32), 8.208 (3.34), 9.022 (2.47).

Example 229

N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



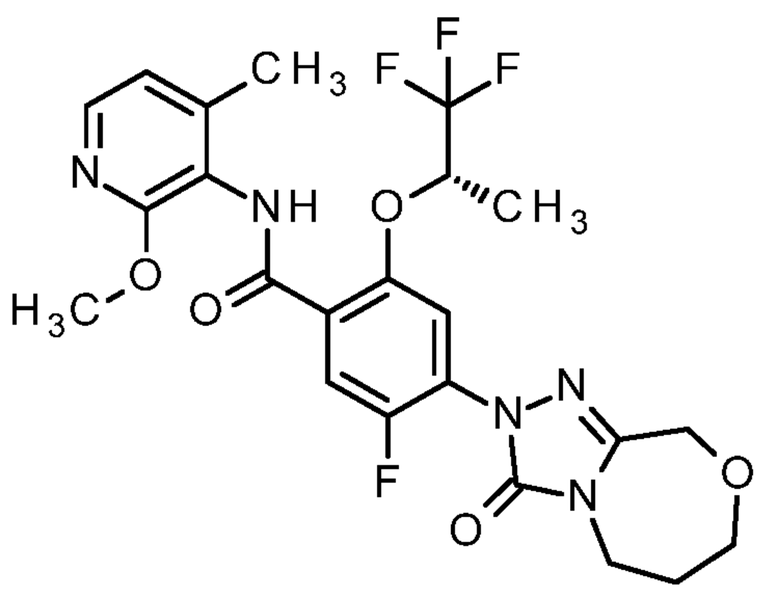
From Intermediate 29 and 2-(difluoromethyl)aniline.

LC-MS (method A): R_t = 1.23 min; MS (ESIpos): m/z = 531 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.633 (8.00), 1.650 (7.36), 2.018 (0.79), 2.031 (1.59), 2.044 (2.31), 2.056 (1.65), 2.069 (0.84), 4.001 (2.65), 4.014 (2.20), 4.016 (2.20), 4.028 (2.61), 4.061 (3.03), 4.073 (2.91), 4.086 (2.92), 4.611 (16.00), 4.855 (0.48), 4.870 (1.14), 4.886 (1.47), 4.901 (1.11), 4.916 (0.46), 6.612 (1.68), 6.751 (3.35), 6.889 (1.63), 7.306 (0.93), 7.324 (2.10), 7.343 (1.29), 7.420 (3.07), 7.434 (3.04), 7.529 (1.00), 7.549 (4.40), 7.568 (3.14), 7.931 (1.94), 7.951 (1.76), 8.108 (3.60), 8.136 (3.50), 9.380 (2.06).

Example 230

5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-methoxy-4-methylpyridin-3-amine.

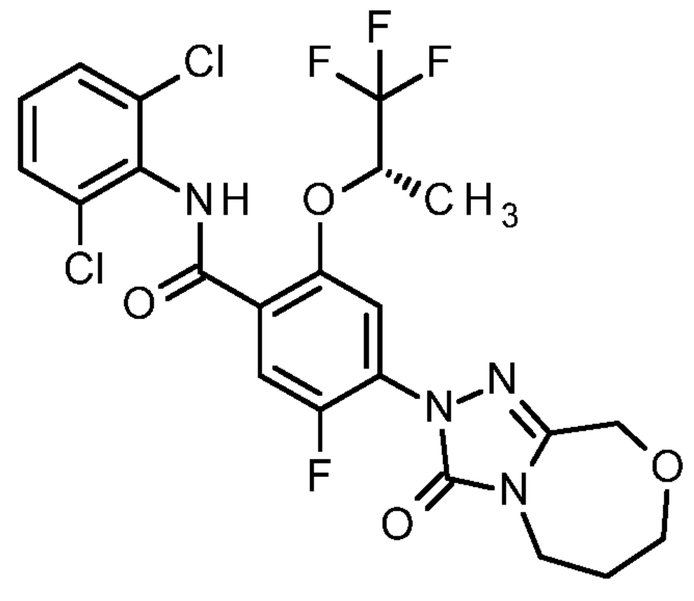
LC-MS (method A): R_t = 1.09 min; MS (ESIneg): m/z = 524 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.583 (0.47), 1.632 (0.48), 1.660 (4.31), 1.676 (4.25), 2.017 (1.16), 2.023 (0.46), 2.037 (0.87), 2.049 (1.24), 2.061 (0.88), 2.074 (0.44), 2.126 (0.87), 2.277 (11.34), 2.629 (0.52), 3.960 (16.00), 3.977 (1.50), 4.007 (1.42), 4.019 (1.20), 4.033 (1.43), 4.065 (1.65), 4.078 (1.59), 4.091 (1.52), 4.617 (8.14), 4.915 (0.65), 4.931 (0.84),

4.946 (0.62), 6.827 (1.72), 6.840 (1.73), 7.393 (1.74), 7.407 (1.72), 7.957 (2.23), 7.970 (2.10), 8.136 (2.13), 8.164 (2.07), 8.963 (1.46).

Example 231

N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2,6-dichloroaniline.

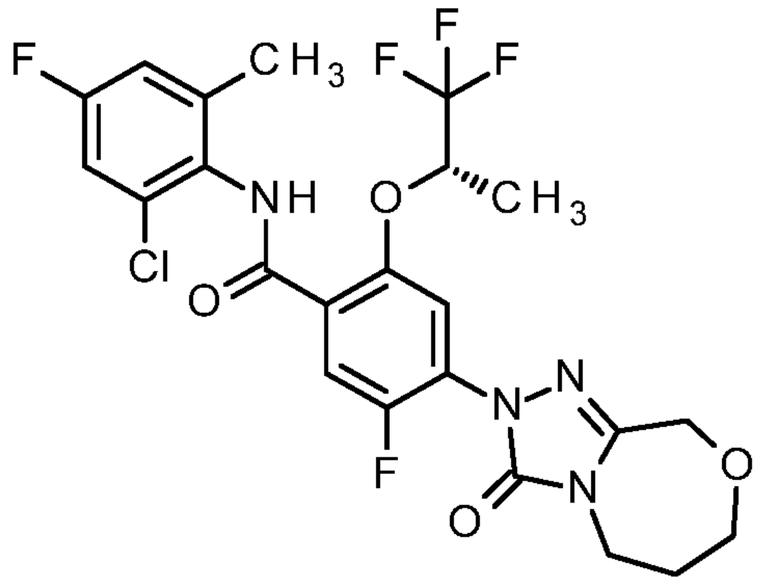
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 549 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.661 (9.55), 1.677 (8.61), 2.017 (1.63), 2.023 (0.81), 2.037 (1.57), 2.049 (2.31), 2.061 (1.63), 2.074 (0.83), 4.007 (2.63), 4.019 (2.13), 4.021 (2.14), 4.033 (2.59), 4.065 (3.04), 4.078 (2.87), 4.090 (2.92), 4.617 (16.00), 4.926 (0.51), 4.941 (1.22), 4.957 (1.58), 4.972 (1.18), 4.988 (0.47), 7.211 (1.95), 7.231 (3.26), 7.251 (2.88), 7.419 (11.00), 7.439 (9.09), 8.179 (3.72), 8.207 (3.63), 9.072 (2.64).

Example 232

N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-chloro-4-fluoro-6-methylaniline.

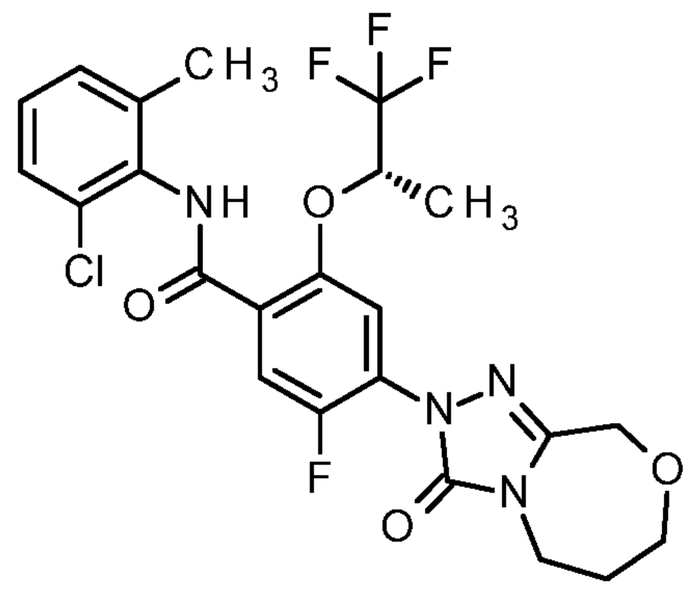
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.29 min; MS (ESIneg): m/z = 545 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.656 (7.01), 1.672 (7.02), 2.011 (0.83), 2.017 (0.80), 2.031 (1.55), 2.043 (2.16), 2.055 (1.53), 2.068 (0.74), 2.306 (16.00), 4.001 (2.48), 4.015 (2.14), 4.027 (2.34), 4.060 (2.75), 4.073 (2.71), 4.085 (2.54), 4.598 (0.54), 4.603 (1.21), 4.611 (13.04), 4.922 (0.46), 4.938 (1.08), 4.953 (1.40), 4.969 (1.03), 4.984 (0.41), 6.932 (1.25), 6.939 (1.40), 6.955 (1.27), 6.962 (1.37), 7.070 (1.49), 7.077 (1.40), 7.090 (1.52), 7.097 (1.36), 7.402 (2.87), 7.416 (2.84), 8.143 (3.47), 8.171 (3.52), 8.875 (2.31).

Example 233

N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-chloro-6-methylaniline.

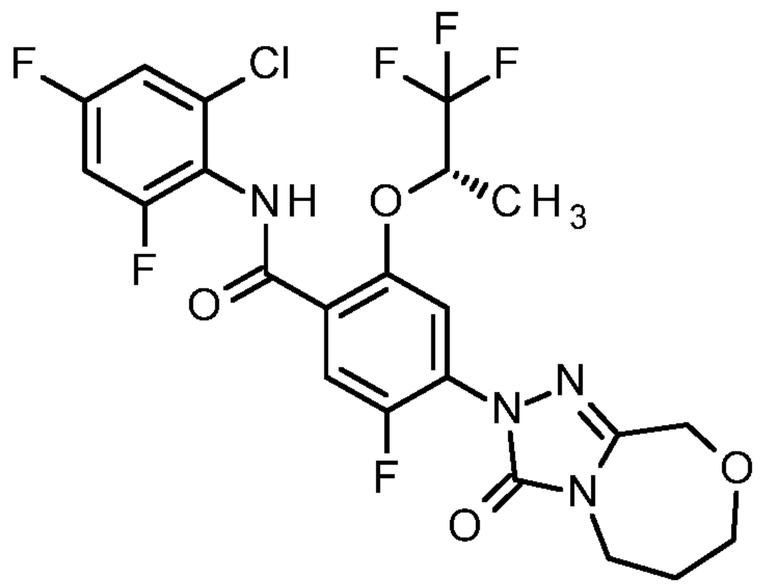
The product was purified by reverse phase column chromatography (Chromatorex C18 10µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 529 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.658 (6.92), 1.674 (6.94), 2.012 (1.83), 2.018 (0.73), 2.032 (1.41), 2.044 (2.05), 2.056 (1.48), 2.070 (0.74), 2.318 (16.00), 4.003 (2.29), 4.015 (1.98), 4.029 (2.29), 4.062 (2.51), 4.074 (2.61), 4.086 (2.46), 4.613 (11.95), 4.924 (0.43), 4.940 (1.05), 4.955 (1.36), 4.970 (1.01), 4.985 (0.41), 7.158 (0.79), 7.177 (2.68), 7.196 (3.65), 7.204 (2.74), 7.219 (0.82), 7.316 (1.70), 7.321 (1.71), 7.335 (1.28), 7.339 (1.28), 7.402 (2.72), 7.416 (2.71), 8.163 (3.23), 8.191 (3.18), 8.977 (2.28).

Example 234

N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c-][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-chloro-4,6-difluoroaniline.

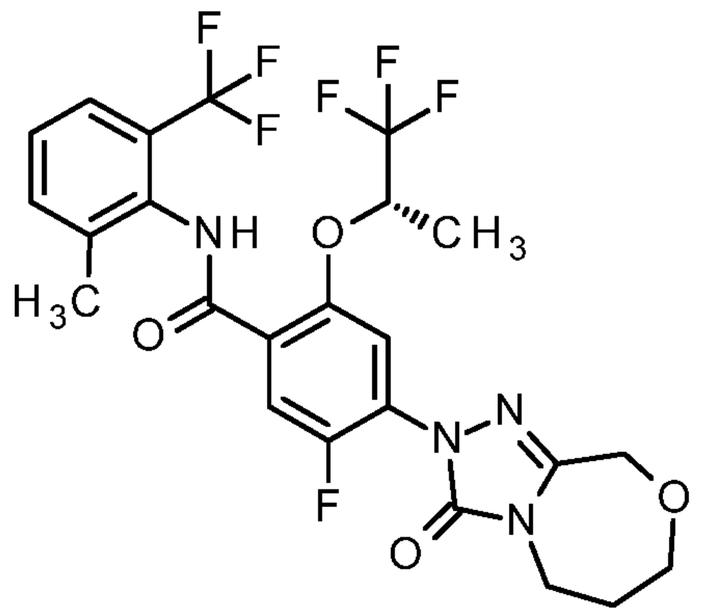
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 551 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.622 (1.96), 1.652 (9.37), 1.667 (9.40), 2.019 (0.97), 2.033 (2.05), 2.044 (2.93), 2.056 (2.15), 2.070 (1.03), 4.002 (3.18), 4.015 (2.87), 4.028 (3.20), 4.062 (3.46), 4.074 (3.77), 4.087 (3.38), 4.613 (16.00), 4.911 (0.59), 4.927 (1.40), 4.942 (1.82), 4.957 (1.36), 4.972 (0.56), 6.889 (1.05), 6.896 (1.17), 6.912 (1.61), 6.917 (1.75), 6.933 (1.09), 6.940 (1.17), 7.067 (1.32), 7.073 (1.86), 7.079 (1.40), 7.088 (1.40), 7.093 (1.88), 7.098 (1.32), 7.424 (3.60), 7.438 (3.60), 8.153 (3.80), 8.181 (3.78), 8.916 (3.39).

Example 235

5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-methyl-6-(trifluoromethyl)aniline.

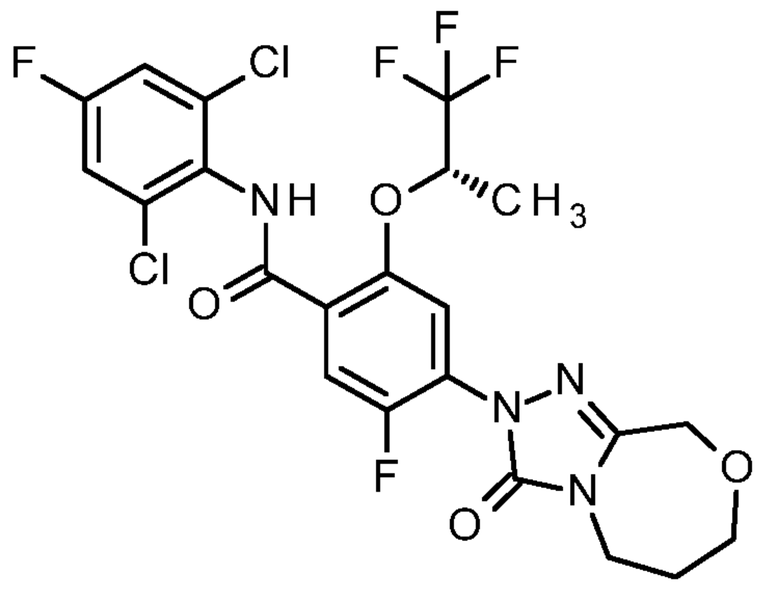
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.30 min; MS (ESIpos): m/z = 563 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.533 (0.71), 1.549 (0.75), 1.604 (3.81), 1.640 (3.52), 1.655 (3.37), 2.023 (0.94), 2.037 (1.88), 2.048 (2.56), 2.060 (1.80), 2.073 (0.83), 2.326 (16.00), 4.007 (2.87), 4.020 (2.59), 4.033 (2.62), 4.065 (3.08), 4.077 (3.23), 4.089 (2.78), 4.608 (1.67), 4.616 (12.95), 4.922 (0.49), 4.937 (1.16), 4.953 (1.50), 4.968 (1.11), 4.983 (0.45), 7.338 (1.02), 7.357 (2.33), 7.377 (1.48), 7.399 (3.00), 7.412 (2.98), 7.511 (2.17), 7.530 (1.74), 7.554 (2.16), 7.573 (1.77), 8.163 (1.12), 8.191 (1.10).

Example 236

N-(2,6-dichloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2,6-dichloro-4-fluoroaniline.

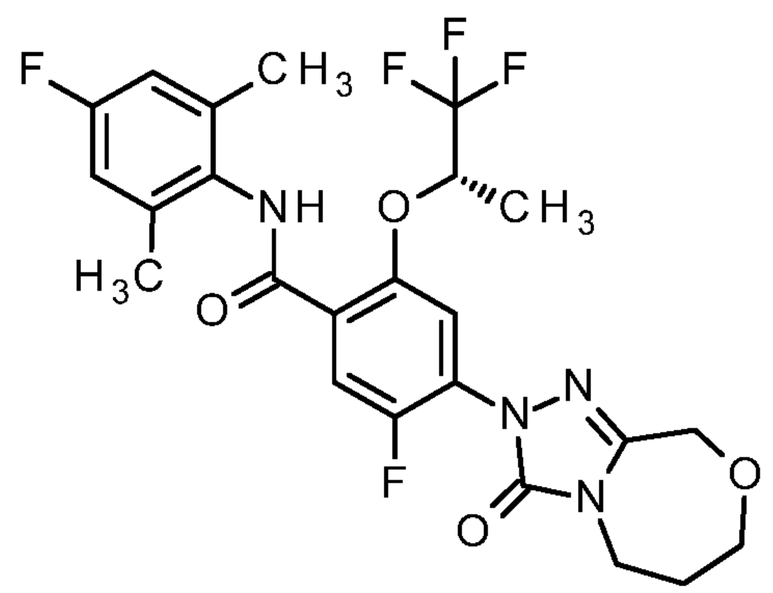
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.29 min; MS (ESIpos): m/z = 567 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.532 (0.51), 1.548 (0.52), 1.605 (2.70), 1.657 (7.33), 1.674 (7.43), 2.016 (0.51), 2.022 (0.80), 2.035 (1.57), 2.048 (2.22), 2.060 (1.57), 2.073 (0.80), 4.005 (2.58), 4.017 (2.09), 4.019 (2.14), 4.031 (2.46), 4.064 (3.01), 4.077 (2.76), 4.089 (2.78), 4.608 (1.52), 4.615 (16.00), 4.925 (0.49), 4.940 (1.15), 4.956 (1.50), 4.971 (1.12), 4.986 (0.45), 7.198 (10.53), 7.218 (10.12), 7.423 (3.20), 7.437 (3.20), 8.159 (4.00), 8.188 (4.08), 8.972 (2.62).

Example 237

5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 4-fluoro-2,6-dimethylaniline.

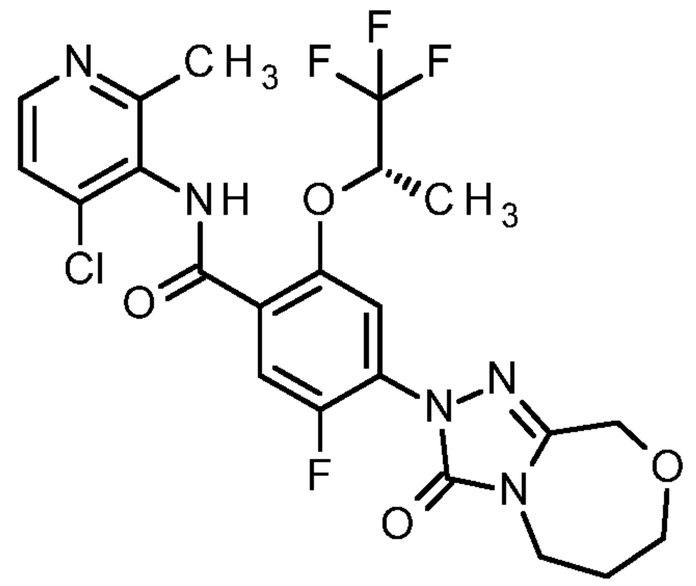
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): Rt = 1.26 min; MS (ESIpos): m/z = 527 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.603 (3.10), 1.650 (3.46), 1.666 (3.46), 2.037 (0.73), 2.049 (1.05), 2.061 (0.75), 2.253 (16.00), 4.007 (1.19), 4.022 (1.01), 4.034 (1.17), 4.067 (1.33), 4.079 (1.32), 4.091 (1.27), 4.617 (6.53), 4.934 (0.55), 4.950 (0.70), 4.965 (0.53), 6.832 (2.23), 6.854 (2.22), 7.381 (1.44), 7.395 (1.43), 8.150 (1.79), 8.179 (1.77), 8.635 (1.05).

Example 238

N-(4-chloro-2-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 4-chloro-2-methylpyridin-3-amine.

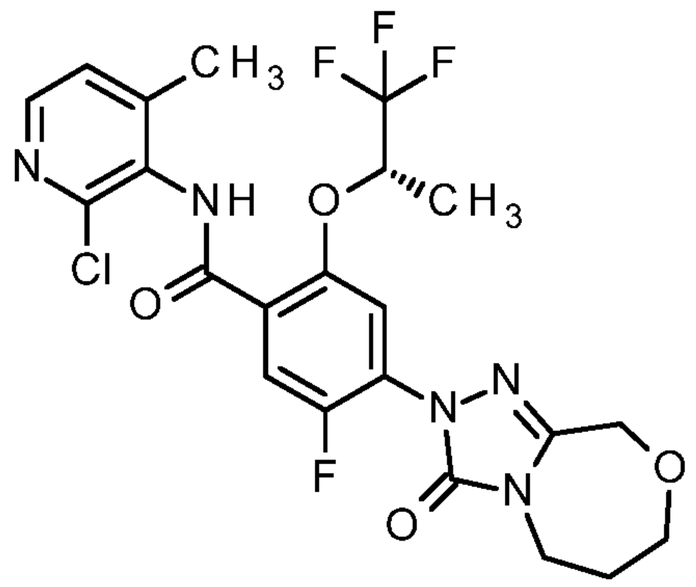
The product was purified by reverse phase column chromatography (Chromatorex C18 10µm, 0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.03 min; MS (ESIpos): m/z = 530 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.682 (7.70), 1.698 (7.71), 2.019 (0.85), 2.030 (0.99), 2.044 (1.84), 2.055 (2.55), 2.067 (1.84), 2.081 (0.94), 2.500 (0.40), 2.665 (8.57), 4.013 (2.72), 4.026 (2.35), 4.039 (2.65), 4.072 (3.15), 4.084 (3.11), 4.097 (2.97), 4.623 (16.00), 4.953 (0.47), 4.968 (1.09), 4.984 (1.40), 4.999 (1.04), 5.014 (0.42), 7.454 (4.21), 7.468 (3.35), 7.529 (0.41), 8.167 (4.09), 8.195 (4.12), 8.411 (1.92), 8.425 (1.88), 9.122 (2.05).

Example 239

N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-chloro-4-methylpyridin-3-amine.

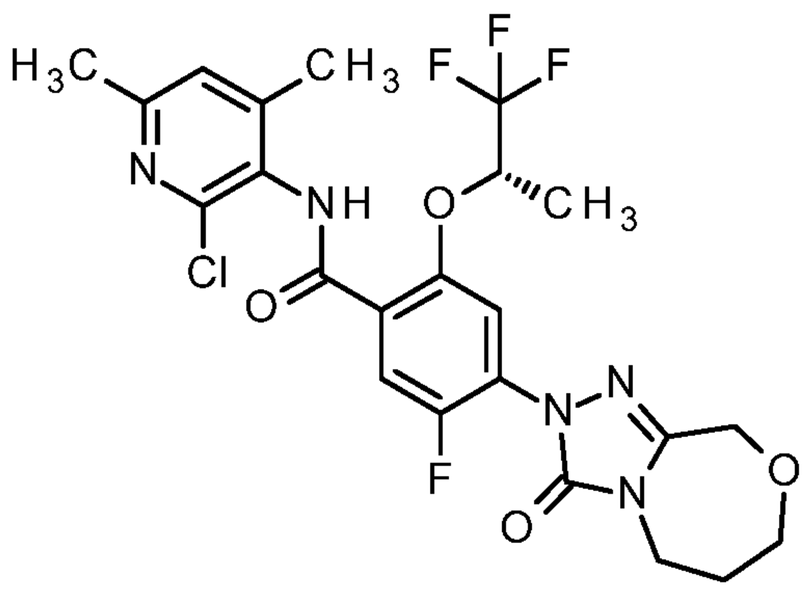
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.08 min; MS (ESIneg): m/z = 528 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.613 (0.48), 1.629 (0.53), 1.684 (5.61), 1.700 (5.68), 2.016 (1.37), 2.052 (1.84), 2.349 (16.00), 4.010 (1.87), 4.023 (1.83), 4.036 (1.91), 4.068 (2.32), 4.081 (2.47), 4.093 (2.31), 4.620 (11.21), 4.959 (0.75), 4.974 (0.98), 4.990 (0.74), 7.196 (1.58), 7.207 (1.65), 7.433 (2.10), 7.447 (2.13), 8.157 (3.76), 8.184 (3.78), 8.215 (1.40), 8.227 (1.41), 9.123 (2.16).

Example 240

N-(2-chloro-4,6-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-chloro-4,6-dimethylpyridin-3-amine.

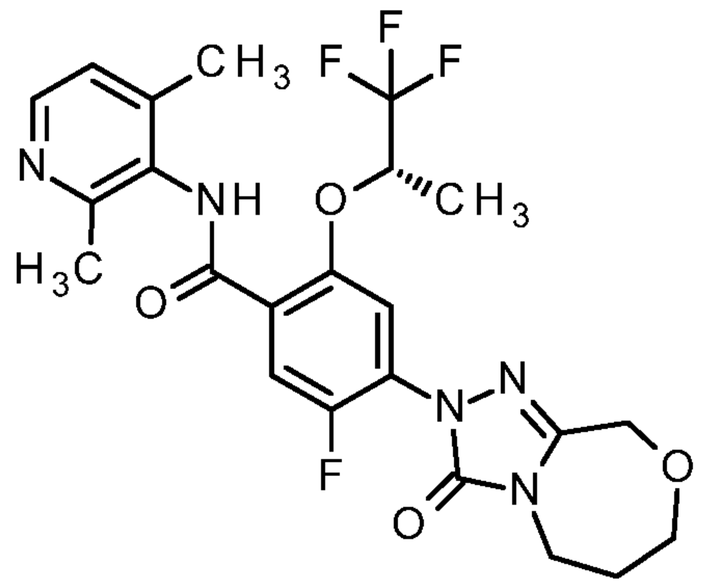
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.14 min; MS (ESIneg): m/z = 542 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.670 (8.31), 1.686 (8.36), 2.011 (2.57), 2.043 (3.09), 2.054 (2.31), 2.299 (15.28), 2.531 (12.01), 4.001 (3.22), 4.014 (3.15), 4.027 (3.22), 4.060 (3.64), 4.073 (4.08), 4.085 (3.55), 4.611 (16.00), 4.932 (0.52), 4.946 (1.21), 4.962 (1.58), 4.977 (1.19), 4.992 (0.50), 7.060 (3.90), 7.418 (3.53), 7.432 (3.52), 8.040 (0.58), 8.142 (5.13), 8.170 (5.21), 9.026 (3.03).

Example 241

N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2,4-dimethylpyridin-3-amine.

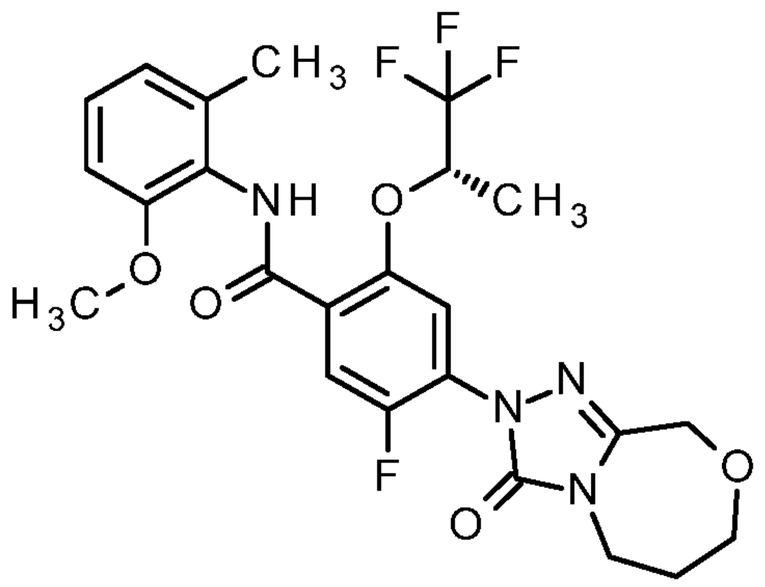
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 0.80 min; MS (ESIpos): m/z = 510 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.641 (3.60), 1.670 (7.51), 1.686 (6.85), 2.030 (0.63), 2.044 (1.25), 2.056 (1.80), 2.068 (1.29), 2.081 (0.65), 2.284 (14.66), 2.517 (16.00), 2.628 (3.85), 4.014 (2.01), 4.026 (1.68), 4.041 (1.98), 4.072 (2.29), 4.084 (2.22), 4.098 (2.19), 4.623 (12.19), 4.954 (0.91), 4.969 (1.20), 4.984 (0.89), 7.006 (0.43), 7.091 (1.99), 7.103 (2.01), 7.411 (2.57), 7.425 (2.54), 7.529 (0.45), 8.128 (0.45), 8.171 (3.30), 8.198 (3.19), 8.340 (2.78), 8.353 (2.73), 8.828 (2.01).

Example 242

5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 2-methoxy-6-methylaniline.

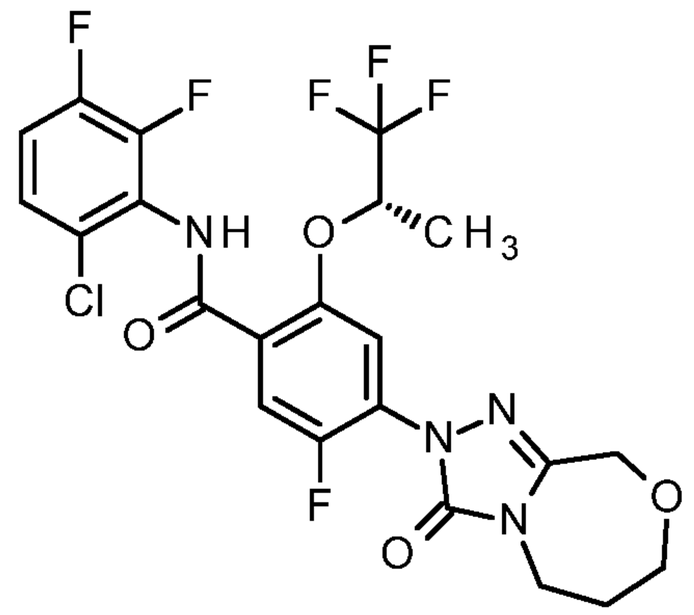
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.23 min; MS (ESIpos): m/z = 525 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.636 (4.51), 1.652 (4.58), 2.008 (1.69), 2.012 (0.50), 2.026 (0.94), 2.038 (1.32), 2.049 (0.96), 2.062 (0.47), 2.282 (11.94), 3.817 (16.00), 3.996 (1.45), 4.010 (1.28), 4.022 (1.41), 4.056 (1.66), 4.069 (1.70), 4.081 (1.61), 4.607 (8.30), 4.903 (0.70), 4.919 (0.90), 4.934 (0.68), 6.791 (1.26), 6.811 (1.39), 6.885 (1.27), 6.904 (1.45), 7.162 (1.27), 7.183 (1.99), 7.202 (1.00), 7.373 (1.87), 7.387 (1.85), 8.144 (2.67), 8.172 (2.64), 8.875 (1.62).

Example 243

N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From Intermediate 29 and 6-chloro-2,3-difluoroaniline.

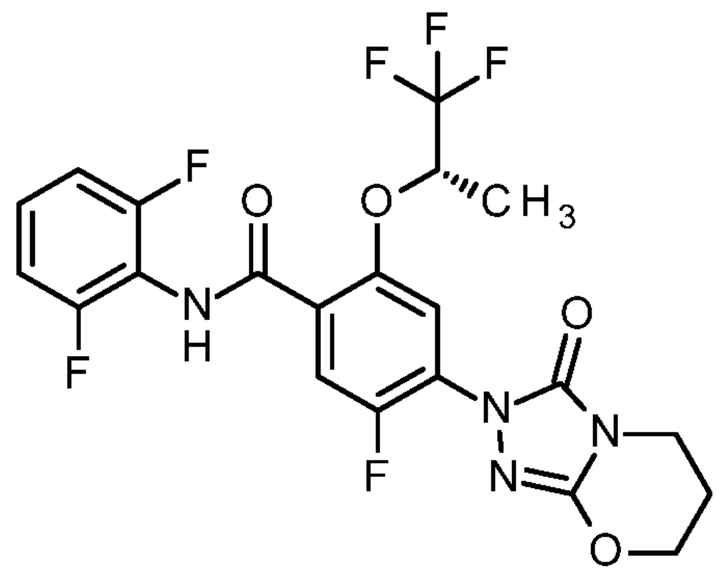
The product was purified by reverse phase column chromatography (0.1 % aqueous formic acid, acetonitrile).

LC-MS (method A): R_t = 1.26 min; MS (ESIpos): m/z = 551 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.636 (0.42), 1.664 (7.49), 1.680 (7.54), 2.018 (1.00), 2.025 (0.83), 2.038 (1.59), 2.050 (2.16), 2.062 (1.52), 2.076 (0.77), 4.008 (2.44), 4.022 (2.01), 4.034 (2.39), 4.067 (2.92), 4.079 (2.71), 4.092 (2.75), 4.619 (16.00), 4.926 (0.48), 4.941 (1.13), 4.957 (1.46), 4.972 (1.07), 4.988 (0.43), 7.088 (0.79), 7.107 (0.99), 7.110 (1.88), 7.130 (2.08), 7.134 (1.38), 7.153 (1.31), 7.216 (1.41), 7.222 (1.31), 7.228 (1.64), 7.234 (1.40), 7.239 (1.09), 7.245 (1.01), 7.251 (1.11), 7.256 (1.03), 7.442 (3.17), 7.456 (3.19), 8.177 (4.04), 8.205 (3.89), 9.081 (2.44).

Example 244

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



A solution of 4-bromo-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide (intermediate 30) (100 mg, 226 µmol), 6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-3(2H)-one (CAS 133365-37-4) (47.9 mg, 339 µmol), tris(dibenzylideneacetone)dipalladium(0) (20.7 mg, 22.6 µmol), 4,5-bis(diphenylphosphino)9,9-dimethylxanthene (39.3 mg, 67.8 µmol), and cesium carbonate (147 mg, 452 µmol) in dimethyl sulfoxide was heated to 110 °C for seventeen hours. The mixture was filtered over celite, the filter cace was washed with ethyl acetate, and the combined filtrate was concentrated under reduced pressure. The residue was purified by by preparative HPLC (X-Bridge Prep C18 5µm, 0.1 % aqueous formic acid, acetonitrile) to yield the title compound as light yellow solid 54.0 mg (97 % purity, 46 % yield).

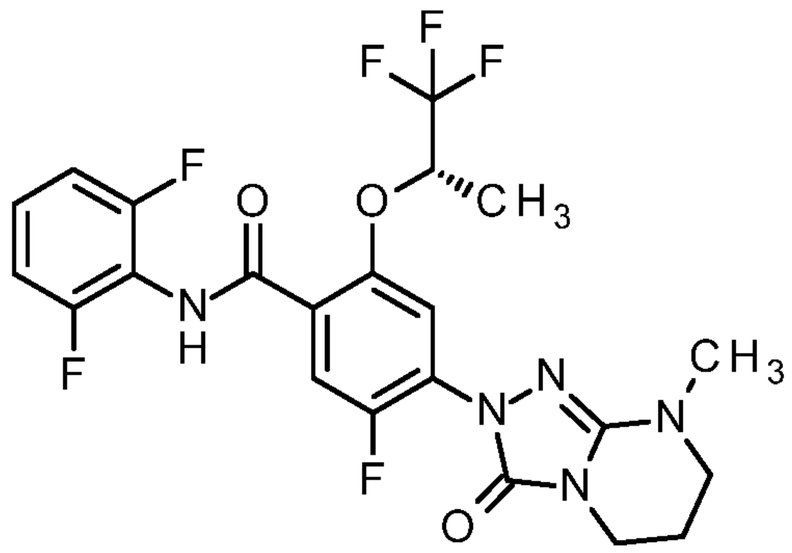
LC-MS (method A): R_t = 1.14 min; MS (ESIpos): m/z = 503 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.137 (0.72), 1.232 (0.96), 1.427 (16.00), 1.442 (16.00), 2.084 (1.05), 2.123 (1.93), 2.137 (5.55), 2.150 (6.91), 2.164 (5.71), 2.178 (1.93), 2.322 (1.77), 2.326 (2.41), 2.331 (1.77), 2.453 (0.80), 2.522 (6.91), 2.664 (1.77), 2.668 (2.41), 2.673 (1.69), 3.288 (1.05), 3.292 (0.80), 3.673 (6.59), 3.688 (13.51), 3.703 (6.19), 4.442 (7.64), 4.456 (9.89), 4.468 (7.40), 5.260 (1.13), 5.276 (2.65), 5.292 (3.30), 5.309 (2.49), 5.324 (1.05), 5.758 (1.85), 7.188 (4.82), 7.208 (10.05), 7.228 (6.19), 7.368 (1.29), 7.385 (2.57), 7.405 (3.46), 7.426 (2.09), 7.442 (1.05), 7.492 (5.95), 7.507 (5.87), 7.544 (6.43), 7.568 (6.27), 9.950 (14.71).

Examples 245–257 were prepared in analogy to example 244 from the respective aryl bromides and the respective triazolone derivative, as indicated.

Example 245

N-(2,6-difluorophenyl)-5-fluoro-4-(8-methyl-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyrimidin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



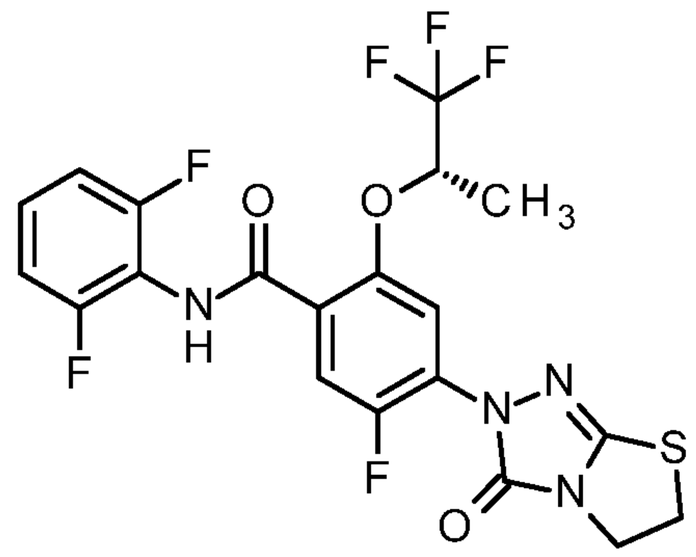
From intermediate 30 and 8-methyl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidin-3(2H)-one (CAS 425706-28-1).

LC-MS (method A): R_t = 1.17 min; MS (ESIpos): m/z = 516 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.432 (3.75), 1.447 (3.73), 2.019 (0.42), 2.033 (1.19), 2.047 (1.62), 2.061 (1.25), 2.076 (0.43), 2.084 (0.40), 2.518 (2.12), 2.522 (1.48), 2.754 (0.61), 2.876 (16.00), 3.221 (1.71), 3.235 (2.27), 3.249 (1.64), 3.564 (1.59), 3.579 (3.07), 3.594 (1.52), 5.261 (0.62), 5.277 (0.81), 5.293 (0.59), 7.189 (1.14), 7.209 (2.41), 7.230 (1.51), 7.385 (0.59), 7.405 (0.84), 7.422 (0.59), 7.426 (0.54), 7.499 (1.39), 7.517 (2.25), 7.543 (1.52), 9.895 (3.63).

Example 246

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro[1,3]thiazolo[2,3-c][1,2,4]triazol-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 30 and 5,6-dihydro[1,3]thiazolo[2,3-c][1,2,4]triazol-3(2H)-one (intermediate 38).

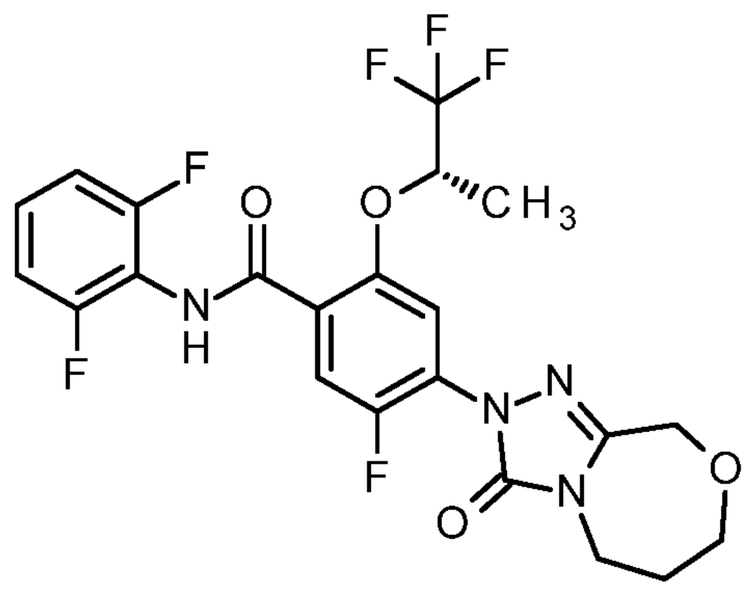
LC-MS (method A): R_t = 1.19 min; MS (ESIpos): m/z = 505 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.137 (0.63), 1.382 (0.93), 1.398 (1.23), 1.427 (16.00), 1.443 (15.90), 1.525 (6.17), 2.084 (6.10), 2.331 (1.43), 2.518 (8.73), 2.522 (5.53), 2.539 (0.77), 2.673 (1.40), 3.452 (3.43), 3.936 (3.47), 3.941 (3.80), 3.956 (11.37), 3.973 (10.07), 4.018 (9.50), 4.035 (9.70), 4.050 (3.37), 4.055 (2.93), 5.274 (1.17), 5.290 (2.63), 5.305 (3.37), 5.321

(2.50), 5.337 (1.03), 5.748 (1.57), 5.758 (2.80), 7.188 (4.80), 7.209 (10.03), 7.229 (6.20), 7.348 (0.57), 7.369 (1.57), 7.386 (2.53), 7.406 (3.57), 7.427 (2.37), 7.443 (1.20), 7.554 (6.90), 7.560 (8.63), 7.568 (6.83), 7.585 (6.57), 9.979 (14.40).

Example 247

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



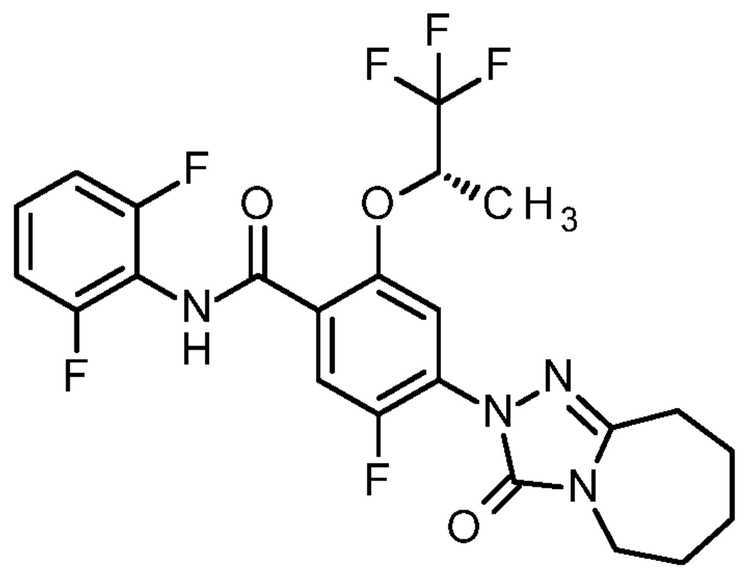
From intermediate 30 and 2,6,7,9-tetrahydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-3-one (intermediate 37).

LC-MS (method A): R_t = 1.17 min; MS (ESIpos): m/z = 517 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.137 (0.66), 1.430 (9.62), 1.446 (9.54), 1.882 (3.57), 2.084 (4.92), 2.518 (5.90), 2.522 (3.86), 2.673 (0.89), 3.922 (4.07), 3.934 (4.07), 3.947 (3.97), 3.969 (4.20), 3.981 (4.92), 3.993 (3.97), 4.606 (16.00), 5.293 (0.64), 5.308 (1.56), 5.324 (1.99), 5.340 (1.48), 5.355 (0.58), 5.758 (1.43), 7.190 (2.87), 7.211 (5.96), 7.231 (3.72), 7.371 (0.69), 7.387 (1.48), 7.408 (2.10), 7.424 (1.25), 7.445 (0.52), 7.579 (4.07), 7.603 (6.23), 7.616 (3.76), 10.000 (8.44).

Example 248

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7,8,9-tetrahydro-3H-[1,2,4]triazolo[4,3-a]azepin-2(5H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



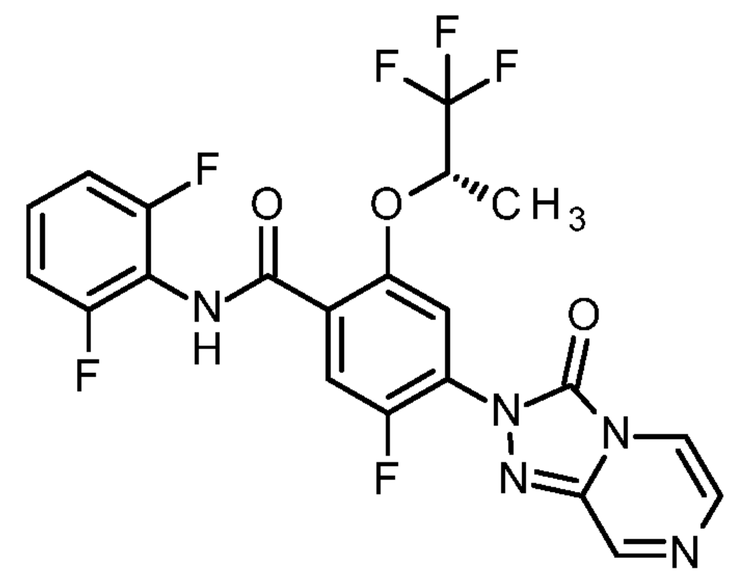
From intermediate 30 and 2,5,6,7,8,9-hexahydro-3H-[1,2,4]triazolo[4,3-a]azepin-3-one (CAS 27182-43-0).

LC-MS (method A): R_t = 1.27 min; MS (ESIpos): m/z = 515 $[M+H]^+$

^{1}H-NMR (500 MHz, DMSO-d6) δ [ppm]: 1.236 (0.52), 1.432 (16.00), 1.445 (15.91), 1.646 (6.57), 1.691 (10.32), 1.811 (5.58), 2.084 (0.42), 2.358 (2.11), 2.361 (2.86), 2.365 (2.30), 2.518 (8.96), 2.522 (6.52), 2.539 (1.17), 2.631 (2.16), 2.635 (2.91), 2.638 (2.25), 2.756 (6.52), 2.768 (6.05), 2.778 (6.24), 3.362 (0.66), 3.776 (6.38), 5.301 (1.08), 5.314 (2.49), 5.326 (3.28), 5.339 (2.39), 5.351 (1.03), 5.759 (0.99), 7.156 (0.52), 7.171 (0.89), 7.194 (4.74), 7.211 (9.57), 7.227 (5.82), 7.353 (1.03), 7.371 (3.61), 7.384 (5.87), 7.392 (6.33), 7.407 (3.80), 7.424 (2.16), 7.437 (0.99), 7.470 (0.84), 7.479 (1.08), 7.487 (1.27), 7.497 (0.75), 7.562 (6.19), 7.574 (6.85), 7.581 (8.54), 7.859 (0.89), 7.875 (0.84), 9.978 (13.75), 10.210 (0.42).

Example 249

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyrazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



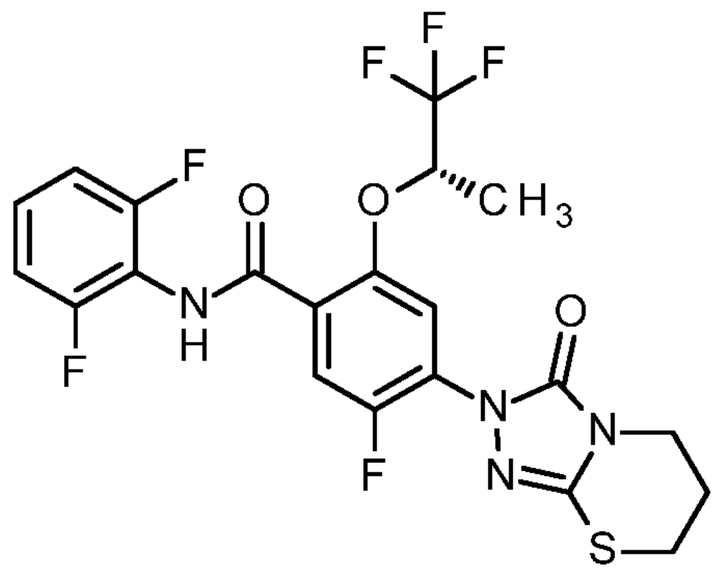
From intermediate 30 and [1,2,4]triazolo[4,3-a]pyrazin-3(2H)-one (CAS 53975-75-0).

LC-MS (method A): R_t = 1.17 min; MS (ESIpos): m/z = 498 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.137 (0.81), 1.232 (0.49), 1.449 (13.73), 1.465 (13.73), 1.906 (0.81), 2.084 (11.86), 2.336 (1.38), 2.518 (16.00), 2.522 (10.72), 2.539 (1.38), 2.678 (1.30), 3.283 (0.41), 3.371 (0.89), 5.242 (1.06), 5.258 (2.36), 5.274 (2.92), 5.290 (2.11), 5.305 (0.81), 7.202 (4.30), 7.222 (8.69), 7.242 (5.52), 7.381 (1.06), 7.397 (2.11), 7.418 (3.01), 7.435 (1.54), 7.439 (1.62), 7.455 (0.73), 7.642 (9.75), 7.654 (10.15), 7.680 (6.09), 7.704 (8.20), 7.715 (5.36), 7.998 (5.93), 8.002 (5.85), 8.010 (5.60), 8.014 (5.44), 9.056 (8.61), 9.061 (8.28), 10.106 (9.75).

Example 250

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]thiazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



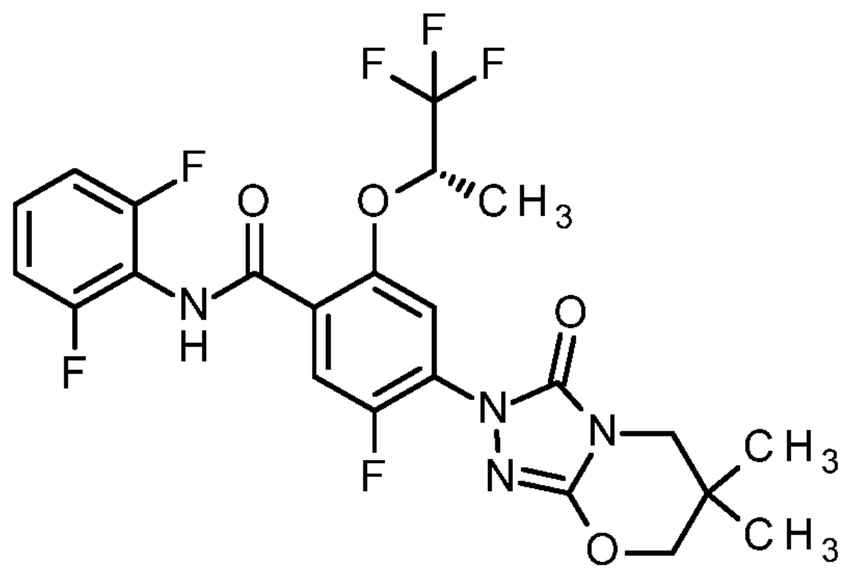
From intermediate 30 and 6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]thiazin-3(2H)-one (intermediate 39).

LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 519 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.427 (7.80), 1.443 (7.64), 1.647 (0.82), 2.074 (16.00), 2.216 (2.42), 2.228 (3.38), 2.241 (2.53), 2.327 (0.87), 2.669 (0.84), 3.221 (3.81), 3.234 (3.84), 3.248 (3.49), 3.564 (0.46), 3.693 (3.23), 3.708 (5.12), 3.723 (2.99), 5.282 (0.59), 5.298 (1.28), 5.314 (1.63), 5.330 (1.20), 5.345 (0.52), 7.189 (2.42), 7.210 (4.79), 7.230 (3.02), 7.346 (0.70), 7.364 (1.58), 7.386 (2.14), 7.407 (1.88), 7.427 (1.52), 7.443 (0.98), 7.549 (2.96), 7.568 (4.22), 7.594 (3.00), 9.987 (6.52).

Example 251

N-(2,6-difluorophenyl)-4-(6,6-dimethyl-3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-2(3H)-yl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



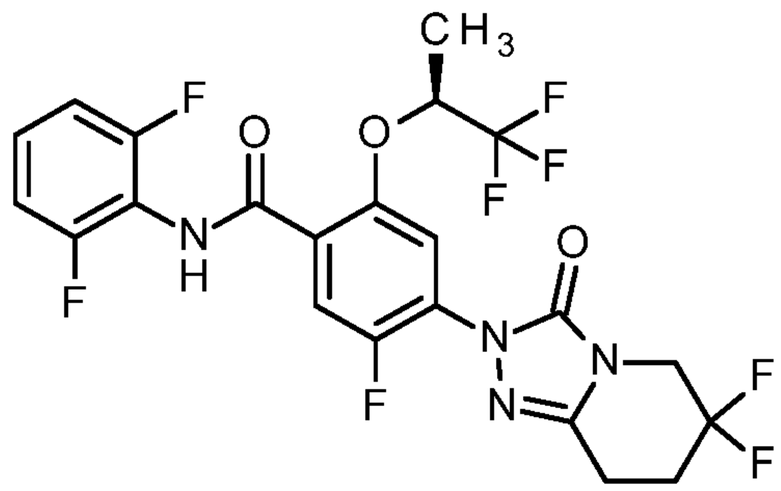
From intermediate 30 and 6,6-dimethyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-3(2H)-one (intermediate 40).

LC-MS (method A): Rt = 1.25 min; MS (ESIpos): m/z = 531 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.080 (16.00), 1.430 (2.47), 1.446 (2.47), 2.518 (2.20), 2.523 (1.57), 3.464 (4.00), 4.154 (4.37), 5.312 (0.52), 5.758 (1.46), 7.189 (0.76), 7.209 (1.56), 7.230 (0.97), 7.385 (0.45), 7.406 (0.54), 7.531 (0.95), 7.546 (1.91), 7.572 (1.03), 9.949 (2.24).

Example 252

4-(6,6-difluoro-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,6-difluoro-phenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 30 and 6,6-difluoro-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one (intermediate 41).

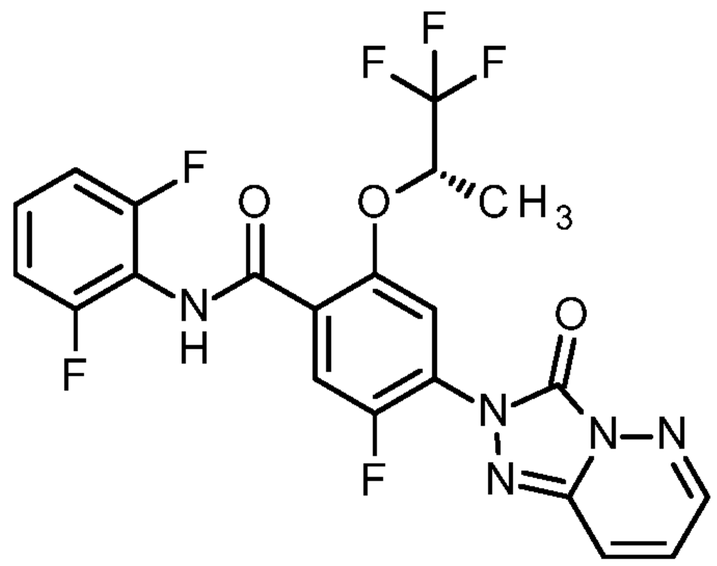
LC-MS (method A): R_t = 1.25 min; MS (ESIpos): m/z = 537 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.429 (16.00), 1.445 (15.89), 1.717 (0.89), 2.074 (1.68), 2.327 (2.32), 2.424 (1.54), 2.442 (3.29), 2.459 (5.29), 2.539 (2.14), 2.669 (2.07), 2.729 (3.79), 2.810 (0.43), 2.888 (4.36), 2.962 (6.14), 2.979 (11.50), 2.996 (5.29), 4.058 (4.96), 4.089 (9.86), 4.121 (4.75), 5.275 (1.11), 5.290 (2.61), 5.306 (3.32), 5.321 (2.50), 5.337 (1.07), 6.875 (0.46), 6.916 (0.50), 7.191 (4.71), 7.212 (10.00), 7.232 (6.43), 7.329 (0.50), 7.349 (0.82), 7.388

(3.29), 7.409 (3.93), 7.426 (2.75), 7.569 (5.93), 7.588 (8.29), 7.614 (6.32), 7.662 (0.57), 7.705 (0.64), 7.951 (0.75), 10.014 (4.89).

Example 253

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-b]pyridazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



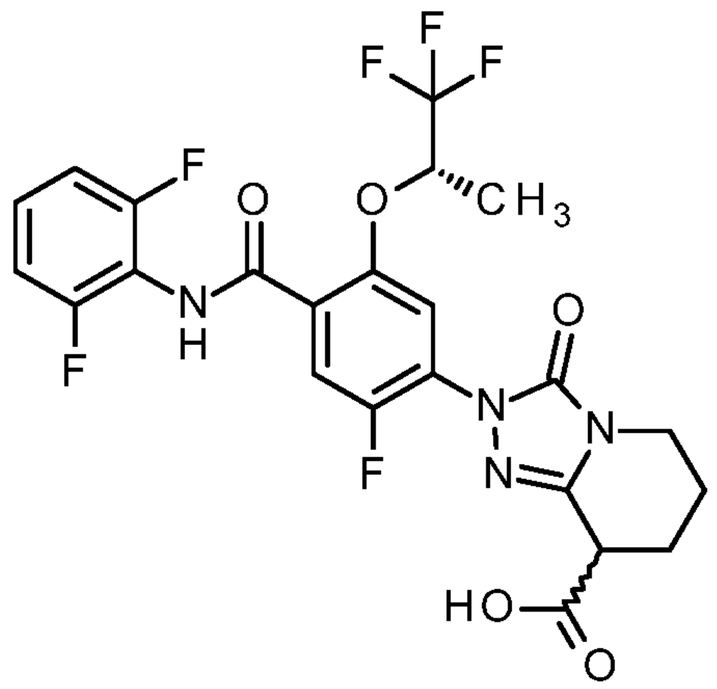
From intermediate 30 and [1,2,4]triazolo[4,3-b]pyridazin-3(2H)-one (CAS 33050-35-0).

LC-MS (method A): R_t = 1.14 min; MS (ESIpos): m/z = 498 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.137 (1.07), 1.233 (1.15), 1.448 (9.81), 1.464 (9.73), 1.907 (0.74), 2.084 (13.69), 2.115 (0.41), 2.332 (2.97), 2.336 (1.32), 2.518 (16.00), 2.522 (10.56), 2.539 (1.07), 2.669 (4.21), 2.673 (3.05), 2.678 (1.32), 5.259 (0.74), 5.274 (1.57), 5.290 (1.98), 5.306 (1.48), 5.322 (0.58), 5.758 (11.22), 7.201 (2.97), 7.221 (6.10), 7.242 (3.88), 7.255 (4.62), 7.265 (4.04), 7.279 (4.04), 7.289 (4.45), 7.381 (0.66), 7.396 (1.48), 7.418 (2.06), 7.438 (1.07), 7.454 (0.49), 7.658 (4.04), 7.682 (4.12), 7.707 (3.71), 7.721 (3.63), 7.939 (3.71), 7.942 (3.79), 7.963 (3.55), 7.966 (3.30), 8.372 (4.45), 8.375 (4.37), 8.382 (4.54), 8.385 (4.12), 10.085 (7.01).

Example 254

2-(4-[(2,6-difluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-(R,S)-carboxylic acid, mixture of diastereomers



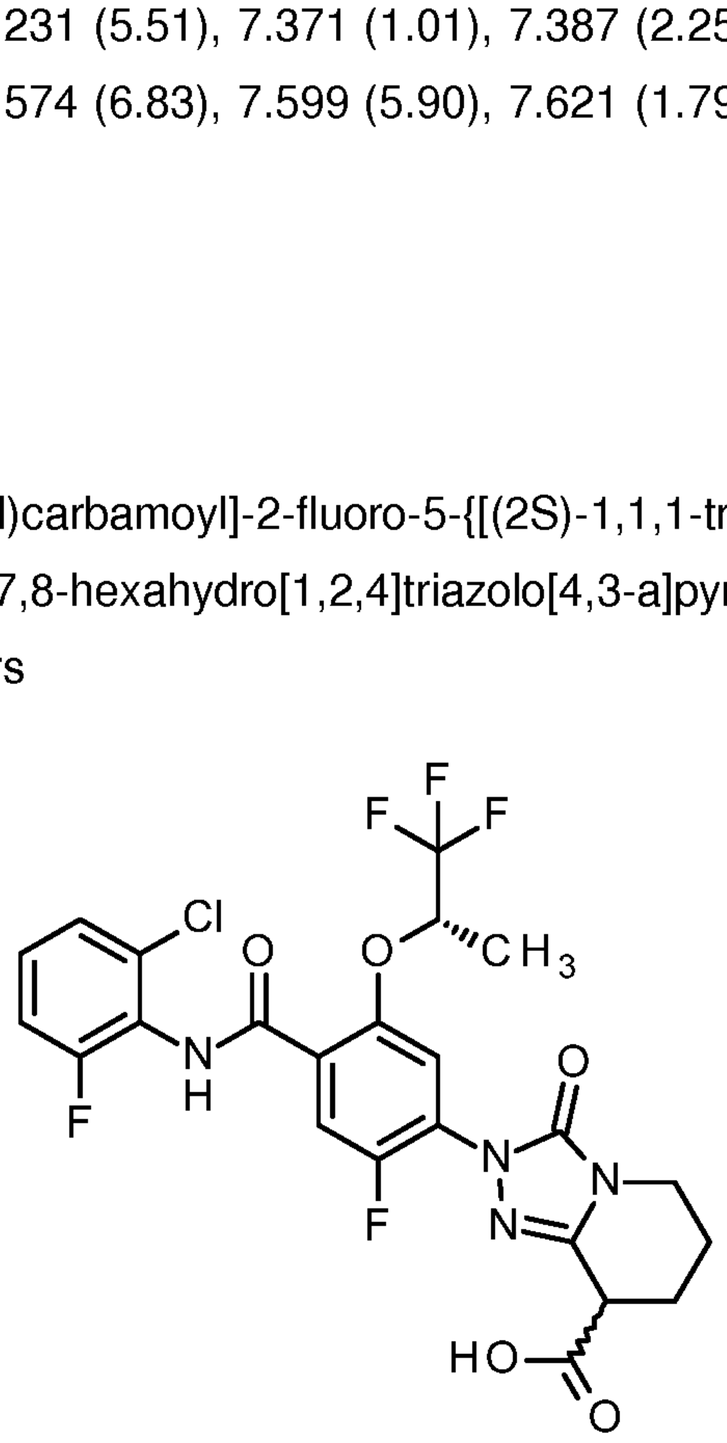
From intermediate 30 and rac-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8carboxylic acid (CAS 1432681-89-4).

LC-MS (method A): R_t = 1.06 min; MS (ESIpos): m/z = 498 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.421 (7.84), 1.435 (13.20), 1.449 (7.69), 1.914 (3.73), 1.928 (5.59), 1.943 (4.58), 2.066 (3.96), 2.080 (5.13), 2.095 (3.65), 2.322 (3.03), 2.326 (4.12), 2.331 (3.11), 2.539 (16.00), 2.664 (3.11), 2.668 (4.19), 2.673 (3.18), 3.513 (2.25), 3.530 (2.87), 3.546 (3.18), 3.561 (3.65), 3.577 (2.17), 3.622 (2.02), 3.635 (3.73), 3.650 (2.80), 3.666 (2.41), 3.680 (1.24), 3.824 (2.49), 3.838 (4.58), 3.852 (2.41), 5.299 (1.79), 5.315 (2.25), 5.326 (1.79), 7.190 (4.35), 7.211 (8.85), 7.231 (5.51), 7.371 (1.01), 7.387 (2.25), 7.407 (3.18), 7.423 (1.86), 7.547 (4.97), 7.556 (4.97), 7.574 (6.83), 7.599 (5.90), 7.621 (1.79), 7.641 (1.01), 9.998 (7.22), 10.003 (7.15).

Example 255

2-(4-[(2-chloro-6-fluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-(R,S)-carboxylic acid, mixture of diastereomers



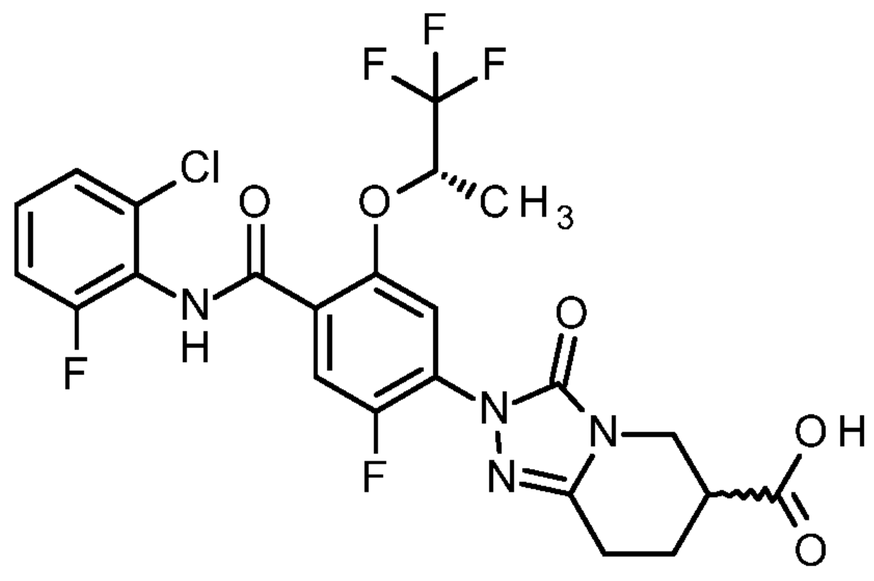
From intermediate 31 and rac-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-carboxylic acid (CAS 1432681-89-4).

LC-MS (method A): R_t = 1.11 min; MS (ESIpos): m/z = 561 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.428 (3.62), 1.441 (5.29), 1.455 (3.34), 1.931 (2.09), 2.083 (16.00), 2.322 (2.23), 2.326 (2.92), 2.331 (2.23), 2.522 (7.93), 2.539 (1.39), 2.665 (2.37), 2.669 (3.06), 2.673 (2.23), 3.538 (0.97), 3.552 (1.11), 3.568 (1.25), 3.637 (1.39), 3.653 (0.97), 3.668 (0.83), 3.843 (0.97), 3.857 (1.81), 5.326 (0.83), 5.342 (0.97), 5.755 (6.68), 7.355 (1.53), 7.371 (0.97), 7.378 (1.11), 7.388 (0.83), 7.408 (1.53), 7.421 (1.81), 7.433 (3.06), 7.438 (3.62), 7.551 (3.76), 7.575 (2.92), 10.062 (3.48).

Example 256

2-(4-[(2-chloro-6-fluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-6-(R,S)-carboxylic acid, mixture of diastereomers



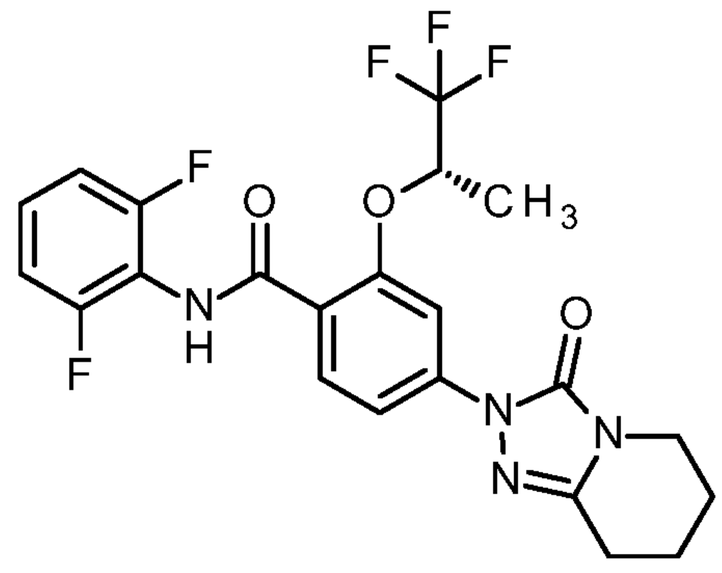
From intermediate 31 and rac-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-6-carboxylic acid (CAS 1432680-45-9).

LC-MS (method A): R_t = 1.14 min; MS (ESIpos): m/z = 561 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.137 (0.53), 1.232 (1.26), 1.432 (3.97), 1.448 (3.97), 1.967 (0.46), 1.988 (0.60), 2.001 (0.46), 2.085 (3.83), 2.157 (0.53), 2.323 (2.98), 2.327 (4.10), 2.331 (2.91), 2.518 (16.00), 2.523 (10.51), 2.540 (1.06), 2.665 (3.04), 2.669 (4.17), 2.673 (2.98), 2.734 (0.66), 2.750 (1.26), 2.770 (0.79), 2.793 (0.53), 3.046 (0.46), 3.659 (0.60), 3.678 (0.60), 3.689 (0.99), 3.708 (0.99), 3.751 (0.79), 3.764 (0.86), 3.782 (0.46), 3.796 (0.46), 5.333 (0.53), 5.348 (0.66), 5.363 (0.53), 5.759 (6.08), 7.335 (0.46), 7.353 (0.93), 7.370 (0.60), 7.377 (0.73), 7.407 (0.93), 7.421 (1.06), 7.431 (1.92), 7.438 (2.38), 7.452 (0.46), 7.540 (1.45), 7.565 (1.92), 7.573 (1.45), 10.053 (3.37).

Example 257

N-(2,6-difluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



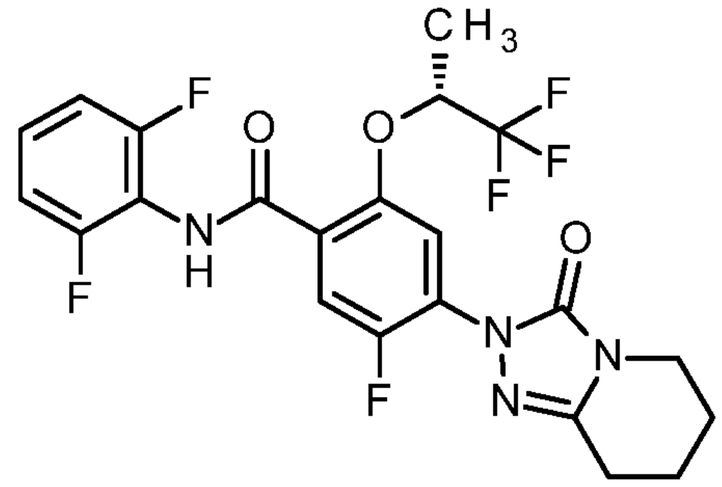
From intermediate 32 and 5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one.

LC-MS (method A): R_t = 1.25 min; MS (ESIneg): m/z = 481 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.138 (0.43), 1.231 (0.38), 1.432 (1.08), 1.447 (1.13), 1.489 (15.78), 1.504 (15.73), 1.556 (4.63), 1.646 (2.96), 1.794 (3.93), 1.806 (5.66), 1.817 (5.93), 1.882 (5.98), 1.893 (5.87), 2.084 (3.61), 2.349 (2.10), 2.443 (0.43), 2.518 (8.78), 2.523 (5.93), 2.541 (1.29), 2.718 (6.30), 2.734 (12.93), 2.750 (6.84), 3.317 (2.21), 3.376 (1.13), 3.565 (7.70), 3.581 (13.85), 3.596 (6.09), 5.272 (1.13), 5.288 (2.64), 5.304 (3.45), 5.319 (2.59), 5.336 (1.13), 5.758 (2.26), 7.180 (4.85), 7.200 (9.86), 7.221 (6.20), 7.373 (3.18), 7.385 (4.26), 7.395 (5.71), 7.409 (2.26), 7.430 (0.97), 7.478 (0.54), 7.489 (0.59), 7.570 (0.59), 7.587 (0.65), 7.711 (3.77), 7.732 (7.27), 7.772 (6.73), 7.792 (3.56), 7.828 (7.92), 7.854 (0.59), 7.874 (0.48), 8.296 (0.59), 9.685 (16.00).

Example 258

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



To a solution of 5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzoic acid (intermediate 18) (100 mg, 257 µmol) in dichloromethane (1 ml) was added 1-chloro-N,N,2-trimethylprop-1-en-1-amine (100 µl, 770 µmol) and the solution was stirred at room temperature for thirty minutes. Then, pyridine (100 µl, 1.3 mmol) and a solution of 2,6-difluoroaniline (55 µl, 510 µmol) in dichloromethane (1 ml) were added subsequently and the reaction was stirred for one hour at room temperature. The reaction mixture was concentrated under reduced pressure and the residue was purified by preparative HPLC (X-Bridge Prep C18 5µm, 0.1 % aqueous formic acid, acetonitrile) to yield the title compound as white solid (83 mg, 98 % purity, 63 %).

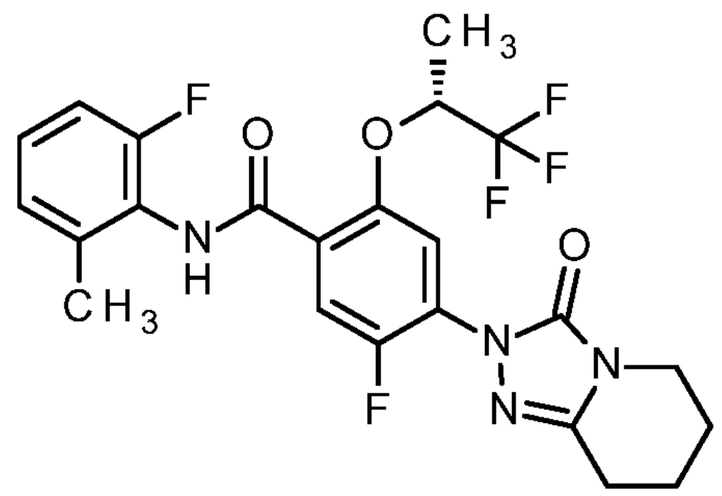
LC-MS (method A): R_t = 1.19 min; MS (ESIpos): m/z = 501 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.428 (16.00), 1.444 (16.00), 1.795 (3.75), 1.807 (5.19), 1.822 (5.33), 1.834 (2.59), 1.875 (2.59), 1.889 (5.33), 1.900 (5.48), 1.913 (3.46), 1.928 (1.30), 2.518 (6.92), 2.523 (4.76), 2.674 (1.44), 2.696 (5.77), 2.712 (11.53), 2.728 (6.05), 3.289 (0.86), 3.385 (0.72), 3.388 (0.72), 3.561 (6.92), 3.577 (12.54), 3.591 (5.62), 5.270 (1.15), 5.286 (2.59), 5.302 (3.32), 5.318 (2.45), 5.333 (1.01), 7.189 (4.90), 7.209 (10.09), 7.229 (6.34), 7.370 (1.15), 7.385 (2.45), 7.406 (3.46), 7.422 (1.73), 7.427 (1.87), 7.443 (0.72), 7.542 (6.05), 7.560 (9.23), 7.585 (6.77), 9.986 (8.22).

Examples 259–260 were prepared as described for example 258 from intermediate 18 and the respective amines, as indicated.

Example 259

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



From intermediate 18 and 2-fluoro-6-methylaniline.

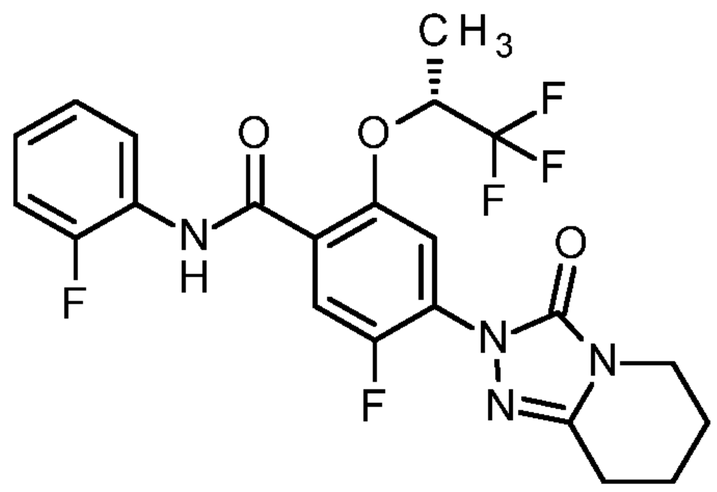
LC-MS (method A): R_t = 1.22 min; MS (ESIpos): m/z = 497 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.429 (7.04), 1.445 (7.00), 1.782 (0.45), 1.797 (1.26), 1.809 (1.73), 1.821 (1.75), 1.824 (1.77), 1.836 (0.87), 1.878 (0.88), 1.892 (1.80), 1.902 (1.84), 1.916 (1.11), 1.931 (0.43), 2.271 (16.00), 2.518 (0.99), 2.523 (0.63), 2.699 (2.09), 2.715 (4.12),

2.730 (2.18), 3.564 (2.48), 3.579 (4.38), 3.594 (1.92), 5.316 (0.46), 5.332 (1.11), 5.348 (1.44), 5.364 (1.04), 5.380 (0.40), 7.100 (0.93), 7.116 (2.35), 7.120 (2.28), 7.133 (2.52), 7.143 (1.42), 7.226 (1.11), 7.240 (1.21), 7.246 (1.58), 7.260 (1.22), 7.266 (0.77), 7.280 (0.65), 7.538 (3.17), 7.545 (4.27), 7.552 (3.11), 7.569 (3.69), 9.810 (4.16).

Example 260

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide



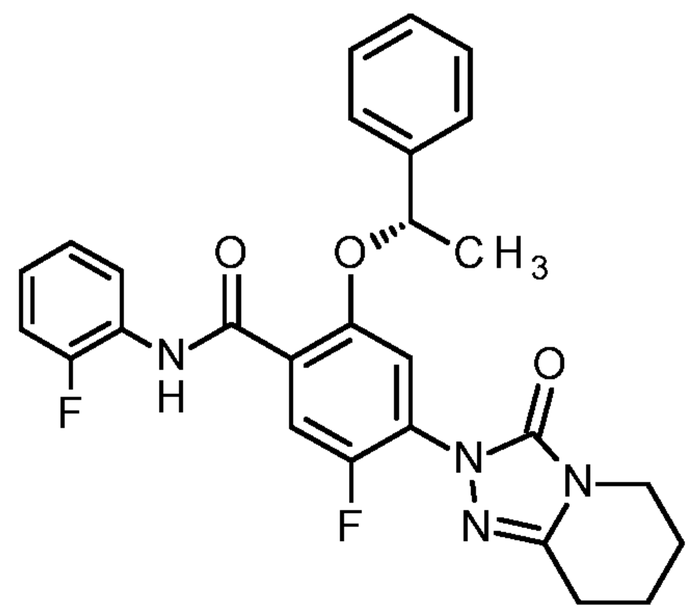
From intermediate 18 and 2-fluoroaniline.

LC-MS (method A): R_t = 1.29 min; MS (ESIpos): m/z = 483 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.470 (16.00), 1.486 (15.97), 1.796 (3.46), 1.808 (4.90), 1.823 (5.00), 1.836 (2.48), 1.877 (2.43), 1.891 (5.02), 1.902 (5.19), 1.915 (3.20), 1.930 (1.23), 2.518 (5.17), 2.523 (3.39), 2.699 (5.52), 2.715 (10.83), 2.731 (5.81), 3.564 (6.48), 3.580 (11.55), 3.594 (5.26), 5.387 (1.08), 5.404 (2.59), 5.420 (3.37), 5.435 (2.47), 5.451 (0.99), 7.188 (0.74), 7.202 (2.23), 7.208 (2.74), 7.216 (5.36), 7.219 (6.08), 7.226 (7.55), 7.237 (5.33), 7.240 (5.26), 7.253 (1.42), 7.295 (2.71), 7.301 (2.45), 7.314 (2.04), 7.322 (2.98), 7.329 (1.73), 7.333 (1.80), 7.341 (1.25), 7.346 (1.68), 7.588 (6.24), 7.602 (6.13), 7.728 (7.09), 7.754 (7.02), 8.057 (2.09), 8.063 (1.88), 8.077 (3.68), 8.082 (3.10), 8.089 (1.94), 8.101 (1.87), 10.024 (9.27).

Example 261

5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



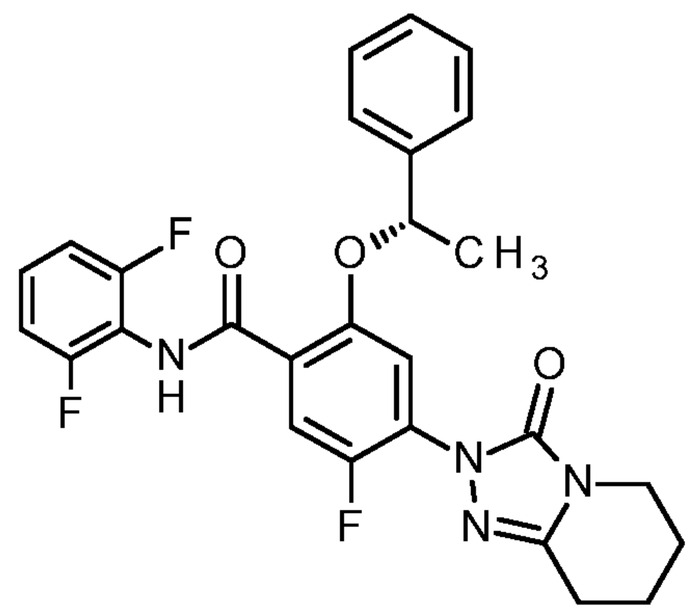
To a solution of 2,5-difluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide (intermediate 33) (62.0 mg, 160 µmol) in N,N-dimethylformamide (1.3 ml) were added (1S)-1-phenylethanol (58.5 mg, 479 µmol) and cesium carbonate (156 mg, 479 µmol) and the mixture was stirred at 100 °C for four hours. After cooling to room temperature, brine (5 ml) was added and the mixture was extracted with ethyl acetate (3 x 5 ml). The combined organic phases were dried over magnesium sulfate, concentrated under reduced pressure and the residue was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile) to yield the title compound as white solid (28 mg, 98 % purity, 35 %).

LC-MS (method A): R_t = 1.43 min; MS (ESIpos): m/z = 492 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.108 (9.31), 1.684 (15.15), 1.700 (15.18), 1.750 (1.42), 1.765 (3.80), 1.777 (5.46), 1.788 (5.41), 1.792 (5.57), 1.804 (2.86), 1.844 (2.84), 1.859 (5.73), 1.869 (5.78), 1.874 (4.94), 1.883 (3.58), 1.898 (1.40), 2.327 (0.75), 2.523 (2.55), 2.645 (6.08), 2.661 (12.21), 2.677 (6.69), 3.522 (6.93), 3.537 (12.37), 3.552 (5.73), 5.755 (1.35), 5.770 (4.13), 5.786 (4.09), 5.801 (1.28), 7.183 (0.99), 7.188 (1.12), 7.196 (1.21), 7.202 (3.06), 7.207 (2.87), 7.215 (2.89), 7.221 (3.97), 7.226 (2.92), 7.234 (3.16), 7.240 (4.13), 7.247 (4.30), 7.261 (5.84), 7.266 (5.54), 7.276 (7.46), 7.281 (4.36), 7.291 (3.67), 7.294 (5.51), 7.298 (3.49), 7.330 (8.96), 7.341 (11.41), 7.345 (10.26), 7.349 (16.00), 7.355 (11.25), 7.367 (9.58), 7.385 (2.44), 7.389 (2.35), 7.439 (12.21), 7.457 (8.32), 7.808 (7.39), 7.836 (7.18), 8.301 (2.35), 8.305 (2.45), 8.321 (4.36), 8.325 (4.31), 8.340 (2.24), 8.345 (2.12), 10.402 (6.71), 10.407 (6.65).

Example 262

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



To a solution of (1S)-1-phenylethanol (53.4 mg, 437 µmol) in N,N-dimethylformamide (1.2 ml) was added sodium hydride (17.5 mg, 60 % dispersion in mineral oil, 437 µmol) and the reaction mixture was stirred at room temperature for one hour. Then, (N-(2,6-difluorophenyl)-2,5-difluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide (60 mg, 146 µmol) (intermediate 34) in N,N-dimethylformamide (0.5 ml) was added and the mixture was stirred at 80 ℃ for three hours. After cooling to room temperature, brine (5 ml) was added and the mixture was extracted with ethyl acetate (3 x 5 ml). The combined organic phases were dried over magnesium sulfate, concentrated under reduced pressure and the residue was purified by preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous formic acid, acetonitrile) to yield the title compound as white solid (7 mg, 97 % purity, 9 %).

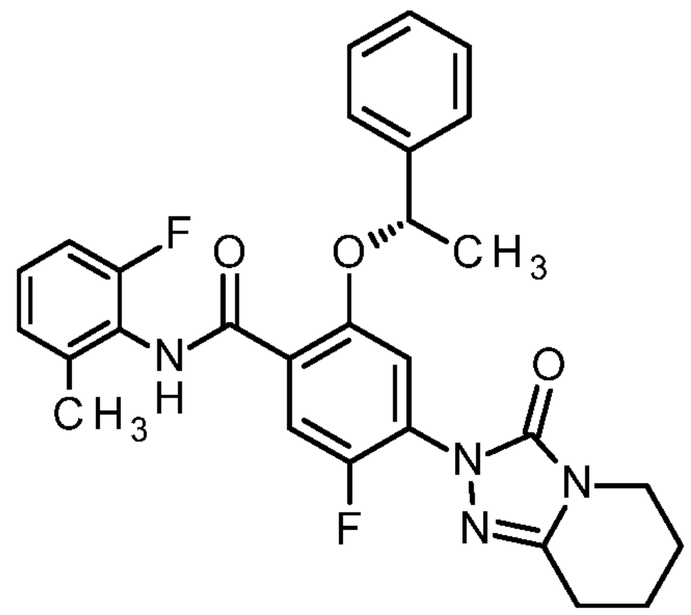
LC-MS (method A): R_t = 1.31 min; MS (ESIneg): m/z = 507 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.860 (0.50), 0.967 (1.86), 1.031 (0.50), 1.047 (0.50), 1.107 (5.71), 1.145 (1.74), 1.209 (0.99), 1.232 (1.74), 1.353 (0.37), 1.388 (0.37), 1.594 (7.57), 1.610 (7.57), 1.768 (1.86), 1.780 (2.48), 1.795 (2.73), 1.862 (2.60), 1.872 (2.85), 2.318 (1.61), 2.323 (3.60), 2.327 (5.09), 2.332 (3.60), 2.337 (1.49), 2.518 (16.00), 2.523 (11.29), 2.647 (2.73), 2.664 (8.56), 2.669 (6.70), 2.673 (4.71), 2.679 (4.47), 2.697 (0.87), 2.713 (0.37), 3.291 (0.74), 3.373 (0.37), 3.504 (1.12), 3.522 (3.35), 3.538 (5.95), 3.552 (2.85), 3.565 (0.99), 4.190 (0.50), 5.646 (1.74), 5.663 (1.74), 7.219 (2.48), 7.240 (5.21), 7.249 (2.23), 7.260 (6.20), 7.268 (5.21), 7.273 (3.84), 7.285 (3.10), 7.322 (4.22), 7.341 (6.82), 7.359 (3.10), 7.391 (0.62), 7.407 (1.24), 7.428 (1.86), 7.449 (1.12), 7.465 (5.09), 7.483 (3.60), 7.573 (2.85), 7.600 (2.85), 9.955 (7.19).

Examples 263–267 were prepared as described for example 262 from the respective difluorobenzamide derivatives and the respective alcohols, as indicated.

Example 263

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide



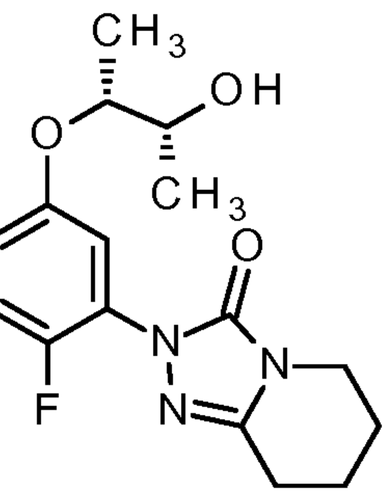
From intermediate 35 and (1S)-1-phenylethanol.

LC-MS (method A): R_t = 1.30 min; MS (ESIpos): m/z = 505 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 0.968 (0.56), 1.028 (0.60), 1.043 (0.61), 1.108 (4.21), 1.145 (0.41), 1.209 (0.46), 1.591 (6.83), 1.607 (6.79), 1.767 (1.12), 1.779 (1.52), 1.794 (1.60), 1.806 (0.83), 1.845 (0.76), 1.860 (1.64), 1.871 (1.64), 1.884 (1.02), 1.899 (0.41), 2.293 (16.00), 2.323 (0.50), 2.327 (0.71), 2.332 (0.50), 2.518 (1.88), 2.523 (1.37), 2.644 (1.83), 2.660 (3.88), 2.669 (1.31), 2.677 (2.15), 3.520 (2.21), 3.535 (3.97), 3.550 (1.74), 5.628 (0.45), 5.643 (1.55), 5.659 (1.57), 5.675 (0.43), 7.133 (1.75), 7.152 (3.22), 7.170 (1.16), 7.209 (2.76), 7.224 (2.78), 7.244 (1.09), 7.249 (0.61), 7.252 (0.96), 7.257 (1.32), 7.264 (1.95), 7.270 (2.61), 7.276 (1.72), 7.285 (1.45), 7.289 (1.98), 7.292 (1.12), 7.297 (0.68), 7.326 (2.76), 7.345 (4.69), 7.363 (2.18), 7.466 (4.18), 7.484 (3.29), 7.488 (2.36), 7.549 (3.69), 7.575 (3.55), 9.803 (3.93).

Example 264

5-fluoro-N-(2-fluoro-6-methylphenyl)-2-{[(2R,3R)-3-hydroxybutan-2-yl]oxy}-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



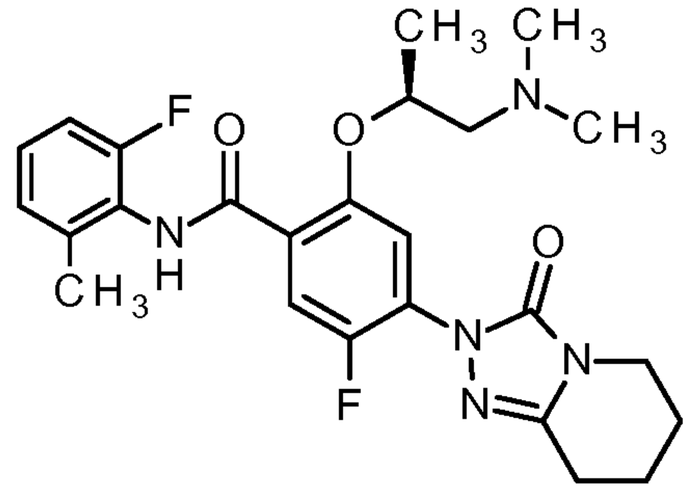
From intermediate 35 and (2R,3R)-butane-2,3-diol.

LC-MS (method A): R_t = 1.04 min; MS (ESIpos): m/z = 473 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.108 (16.00), 1.124 (0.43), 1.141 (0.40), 1.273 (0.41), 1.289 (0.41), 2.269 (1.07), 2.693 (0.92), 3.576 (0.42), 4.189 (1.37).

Example 265

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



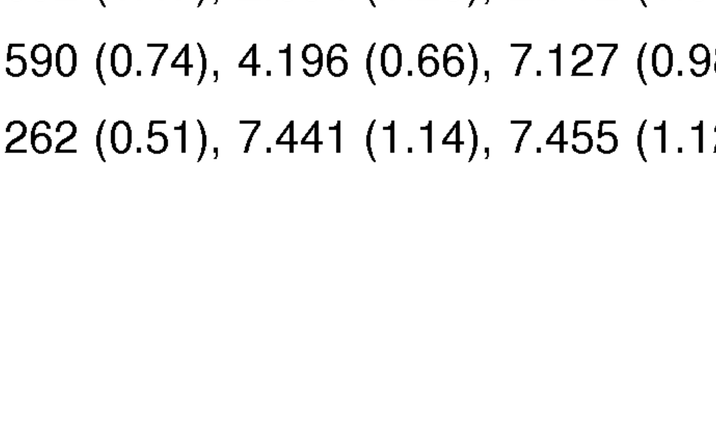
From intermediate 35 and (2S)-1-(dimethylamino)propan-2-ol.

LC-MS (method A): R_t = 0.74 min; MS (ESIpos): m/z = 486 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.108 (16.00), 1.370 (3.52), 1.385 (3.55), 1.792 (0.46), 1.804 (0.64), 1.819 (0.66), 1.882 (0.63), 1.887 (0.68), 1.898 (0.79), 1.911 (0.43), 2.022 (12.64), 2.253 (6.24), 2.285 (0.46), 2.295 (0.51), 2.318 (0.62), 2.327 (0.69), 2.518 (0.69), 2.523 (0.45), 2.658 (0.51), 2.680 (0.58), 2.692 (1.47), 2.694 (1.25), 2.712 (1.91), 2.728 (0.85), 3.301 (0.55), 3.559 (0.94), 3.575 (1.66), 3.590 (0.74), 4.196 (0.66), 7.127 (0.98), 7.146 (1.47), 7.228 (0.44), 7.242 (0.47), 7.248 (0.61), 7.262 (0.51), 7.441 (1.14), 7.455 (1.12), 7.647 (1.53), 7.674 (1.47), 10.530 (1.44).

Example 266

2-{[(2R)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



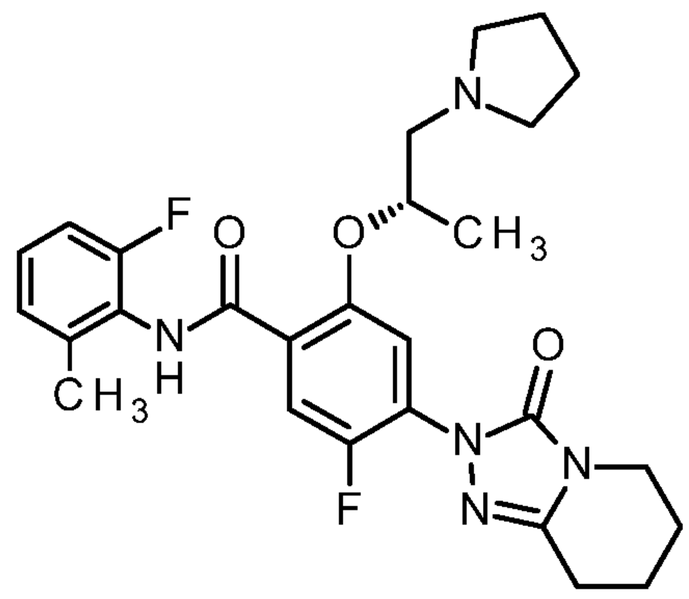
From intermediate 35 and (2R)-1-(dimethylamino)propan-2-ol.

LC-MS (method A): R_t = 0.68 min; MS (ESIpos): m/z = 486 $[M+H]^+$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.108 (16.00), 1.371 (0.58), 1.386 (0.58), 2.021 (2.22), 2.253 (1.09), 2.693 (0.42), 4.190 (0.61).

Example 267

5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzamide



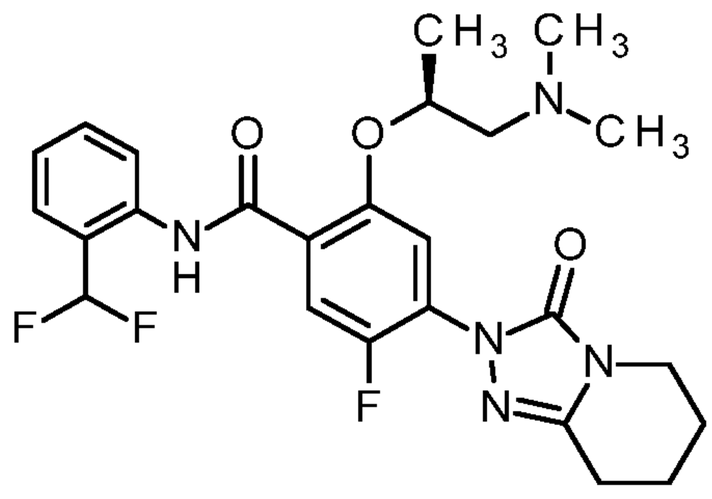
From intermediate 35 and (2S)-1-(pyrrolidin-1-yl)propan-2-ol.

LC-MS (method B): R_t = 1.30 min; MS (ESIneg): m/z = 510 $[M-H]^-$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.133 (1.05), 1.263 (2.49), 1.323 (0.95), 1.335 (1.19), 1.339 (1.19), 1.354 (0.91), 1.359 (1.00), 1.379 (0.47), 1.464 (0.47), 1.484 (1.01), 1.489 (0.87), 1.513 (11.32), 1.528 (11.00), 1.599 (1.41), 1.912 (0.49), 1.920 (1.08), 1.927 (1.30), 1.933 (1.44), 1.943 (1.49), 1.947 (1.60), 1.959 (0.71), 1.963 (0.75), 1.984 (0.78), 1.990 (0.69), 1.998 (1.42), 2.003 (1.49), 2.014 (1.56), 2.019 (1.30), 2.028 (0.95), 2.042 (0.41), 2.254 (0.71), 2.274 (1.40), 2.289 (1.65), 2.309 (0.93), 2.327 (16.00), 2.364 (1.17), 2.372 (1.24), 2.395 (1.33), 2.404 (1.27), 2.425 (0.92), 2.444 (1.69), 2.459 (1.37), 2.480 (0.66), 2.799 (2.32), 2.815 (4.36), 2.831 (2.58), 3.053 (1.20), 3.077 (1.33), 3.084 (1.19), 3.109 (1.15), 3.708 (2.90), 3.724 (4.83), 3.739 (2.09), 4.548 (0.45), 4.556 (0.62), 4.563 (0.57), 4.572 (0.90), 4.580 (0.56), 4.587 (0.61), 4.596 (0.43), 6.957 (0.77), 6.978 (1.59), 7.001 (0.96), 7.038 (1.38), 7.057 (1.92), 7.134 (1.01), 7.148 (1.08), 7.155 (1.44), 7.168 (1.42), 7.174 (0.69), 7.188 (0.63), 7.362 (2.98), 7.376 (2.98), 7.960 (3.79), 7.988 (3.75), 10.744 (2.04).

Example 268

N-[2-(difluoromethyl)phenyl]-2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



To a solution of 2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoic acid (intermediate 20) (100 mg, 264 µmol) in N,N-dimethylformamide (5 ml) was added 1-[bis(dimethylamino)methylene]-1H-[1,2,3]triazolo[4,5-b]pyridin-1-ium 3-oxide hexafluorophosphate (HATU) (201 mg, 529 µmol) and the mixture was stirred at room temperature for 15 minutes. Then, 2-(difluoromethyl)aniline hydrochloride (94.9 mg, 529 µmol) and N,N-diisopropylethylamine (280 µl, 1.6 mmol) were added and the reaction was stirred at room temperature for three hours. The crude reaction solution was subjected to preparative HPLC (X-Bridge Prep C18 5µm OBD, 0.1 % aqueous ammonia, acetonitrile) to yield the title compound (60 mg, 45 %).

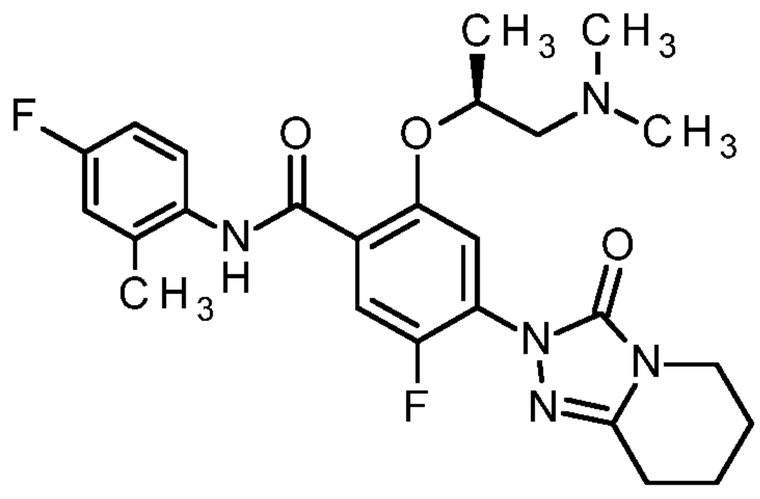
LC-MS (method B): R_t = 1.23 min; MS (ESIpos): m/z = 504 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.474 (5.30), 1.490 (5.28), 1.600 (2.88), 1.921 (0.64), 1.934 (0.89), 1.948 (0.95), 1.965 (0.45), 1.985 (0.46), 2.004 (0.90), 2.015 (0.96), 2.029 (0.59), 2.110 (16.00), 2.285 (0.57), 2.294 (0.61), 2.317 (0.67), 2.327 (0.65), 2.769 (0.65), 2.792 (0.81), 2.800 (1.77), 2.815 (2.55), 2.824 (0.86), 2.832 (1.47), 3.709 (1.58), 3.724 (2.65), 3.739 (1.19), 4.613 (0.44), 6.725 (0.79), 6.864 (1.51), 7.003 (0.75), 7.338 (0.49), 7.357 (1.11), 7.376 (0.68), 7.421 (1.64), 7.436 (1.63), 7.501 (0.45), 7.520 (0.92), 7.539 (0.51), 7.626 (1.10), 7.638 (1.14), 7.657 (0.92), 8.013 (1.90), 8.042 (1.87), 10.669 (1.08).

Examples 269–278 were prepared as described for example 268 from the respective benzoic acid derivatives and the respective amines, as indicated.

Example 269

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



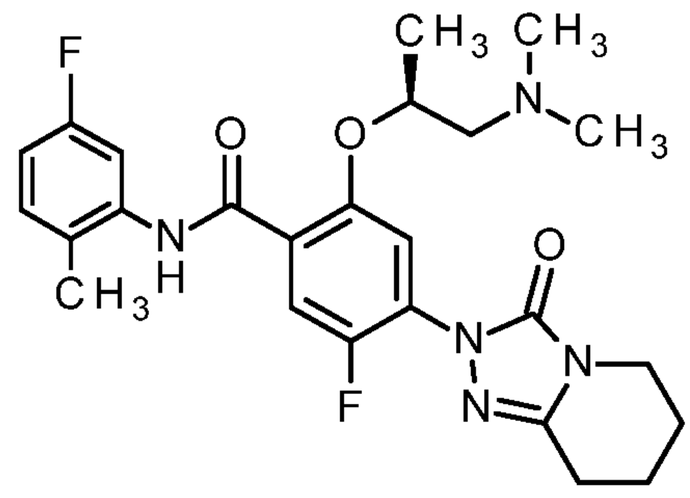
From intermediate 20 and 4-fluoro-2-methylaniline.

LC-MS (method B): R_t = 1.23 min; MS (ESIpos): m/z = 486 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.473 (4.17), 1.488 (4.19), 1.603 (2.03), 1.920 (0.45), 1.932 (0.63), 1.943 (0.69), 1.947 (0.69), 1.999 (0.61), 2.004 (0.63), 2.014 (0.68), 2.028 (0.42), 2.111 (16.00), 2.291 (0.61), 2.301 (0.68), 2.315 (6.67), 2.323 (0.90), 2.333 (0.70), 2.731 (0.64), 2.754 (0.65), 2.764 (0.56), 2.786 (0.58), 2.798 (0.94), 2.814 (1.81), 2.830 (1.02), 3.707 (1.15), 3.722 (1.90), 3.737 (0.85), 6.916 (0.45), 6.924 (0.64), 6.949 (0.65), 6.956 (0.45), 6.972 (0.60), 6.979 (0.44), 7.392 (1.24), 7.407 (1.23), 7.447 (0.61), 7.460 (0.63), 7.468 (0.59), 7.482 (0.56), 8.010 (1.45), 8.039 (1.44), 10.336 (0.86).

Example 270

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 20 and 5-fluoro-2-methylaniline.

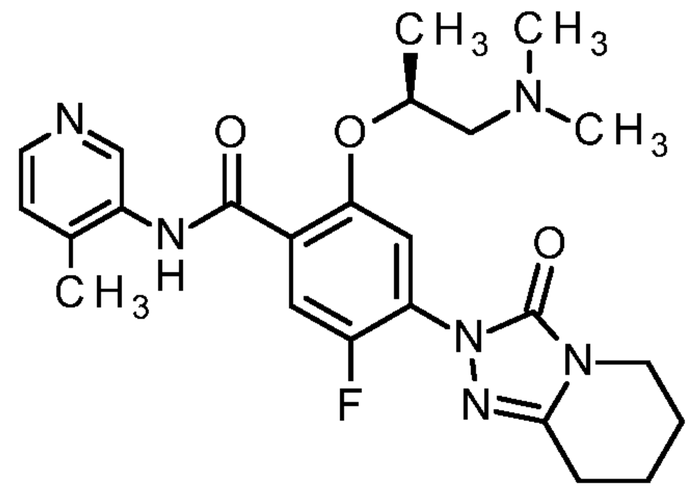
LC-MS (method B): R_t = 1.26 min; MS (ESIpos): m/z = 486 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.468 (5.82), 1.483 (5.75), 1.602 (3.25), 1.920 (0.60), 1.933 (0.83), 1.944 (0.83), 1.947 (0.90), 1.963 (0.43), 1.984 (0.49), 2.000 (0.81), 2.004 (0.85), 2.015 (0.91), 2.029 (0.55), 2.152 (16.00), 2.301 (7.13), 2.330 (0.56), 2.341 (0.57), 2.363 (0.66), 2.373 (0.63), 2.735 (0.71), 2.757 (0.73), 2.767 (0.63), 2.789 (0.70), 2.798 (1.28), 2.814 (2.43), 2.831 (1.37), 3.708 (1.56), 3.723 (2.57), 3.738 (1.15), 6.820 (0.41), 6.826 (0.46), 6.840 (0.85), 6.847 (0.92), 6.861 (0.48), 6.868 (0.49), 7.155 (0.68), 7.171 (0.75), 7.176 (0.70), 7.192

(0.61), 7.428 (1.65), 7.442 (1.64), 7.544 (0.78), 7.551 (0.79), 7.570 (0.79), 7.577 (0.78), 8.044 (1.88), 8.073 (1.86), 10.214 (0.91).

Example 271

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



From intermediate 20 and 4-methylpyridin-3-amine.

LC-MS (method B): R_t = 0.99 min; MS (ESIpos): m/z = 469 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.494 (5.60), 1.509 (5.68), 1.653 (2.09), 1.922 (0.67), 1.934 (0.93), 1.946 (0.94), 1.949 (1.00), 1.965 (0.48), 1.986 (0.48), 2.006 (0.95), 2.016 (1.01), 2.030 (0.62), 2.111 (16.00), 2.279 (0.65), 2.287 (0.65), 2.311 (0.73), 2.320 (0.73), 2.341 (10.04), 2.758 (0.70), 2.783 (0.77), 2.791 (0.75), 2.800 (1.37), 2.816 (3.14), 2.833 (1.48), 3.709 (1.62), 3.724 (2.77), 3.739 (1.24), 4.597 (0.58), 7.197 (1.39), 7.209 (1.43), 7.412 (1.74), 7.426 (1.73), 7.993 (1.89), 8.022 (1.92), 8.366 (1.83), 8.379 (1.82), 8.608 (3.02), 10.662 (1.14).

Example 272

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide

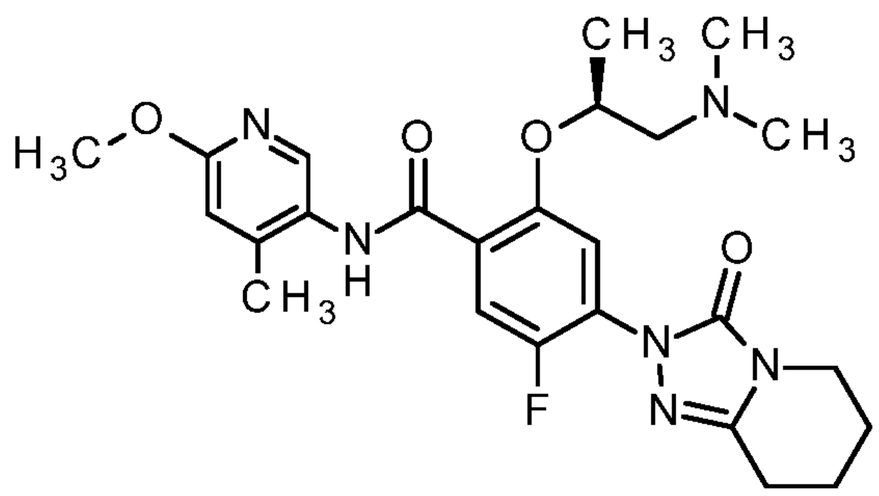
From intermediate 20 and 3,5-dimethylpyrazin-2-amine.

LC-MS (method B): R_t = 1.02 min; MS (ESIpos): m/z = 484 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.496 (5.32), 1.511 (5.37), 1.640 (0.98), 1.920 (0.71), 1.932 (0.98), 1.947 (1.05), 1.963 (0.50), 1.984 (0.51), 2.003 (1.00), 2.014 (1.05), 2.028 (0.64), 2.120 (16.00), 2.274 (0.65), 2.282 (0.73), 2.306 (0.77), 2.314 (0.74), 2.554 (9.81), 2.562 (10.77), 2.798 (1.36), 2.814 (2.80), 2.830 (1.49), 2.843 (0.77), 2.850 (0.66), 2.875 (0.65), 3.707 (1.63), 3.722 (2.76), 3.737 (1.22), 4.589 (0.56), 7.399 (1.72), 7.413 (1.71), 7.957 (1.89), 7.986 (1.89), 8.171 (2.73), 11.249 (1.26).

Example 273

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



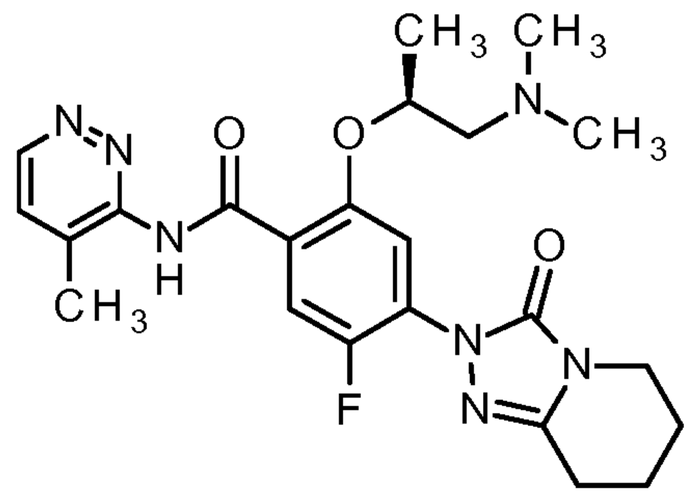
From intermediate 20 and 6-methoxy-4-methylpyridin-3-amine.

LC-MS (method B): R_t = 1.12 min; MS (ESIpos): m/z = 499 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.482 (4.25), 1.497 (4.28), 1.659 (1.33), 1.916 (0.49), 1.928 (0.67), 1.939 (0.69), 1.943 (0.73), 1.995 (0.65), 2.000 (0.68), 2.010 (0.72), 2.015 (0.60), 2.024 (0.44), 2.104 (16.00), 2.262 (0.80), 2.271 (7.61), 2.294 (0.73), 2.303 (0.70), 2.735 (0.63), 2.759 (0.65), 2.767 (0.57), 2.794 (1.20), 2.810 (1.92), 2.826 (1.07), 3.703 (1.19), 3.718 (2.02), 3.733 (0.90), 3.874 (0.53), 3.926 (11.06), 4.569 (0.47), 6.661 (1.99), 7.383 (1.33), 7.397 (1.36), 7.966 (1.57), 7.994 (1.53), 8.091 (2.43), 10.536 (1.13).

Example 274

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



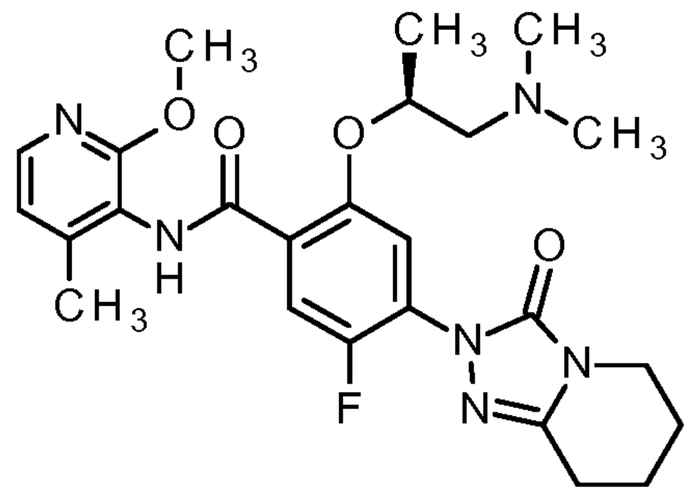
From intermediate 20 and 4-methylpyridazin-3-amine.

LC-MS (method B): R_t = 0.90 min; MS (ESIpos): m/z = 470 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.282 (16.00), 1.509 (1.84), 1.525 (1.86), 2.171 (1.13), 2.381 (2.30), 2.819 (0.70), 2.836 (0.41), 3.712 (0.50), 3.727 (0.77), 7.424 (0.48), 7.438 (0.48), 7.923 (0.50), 7.951 (0.49), 8.947 (0.63), 8.960 (0.61).

Example 275

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



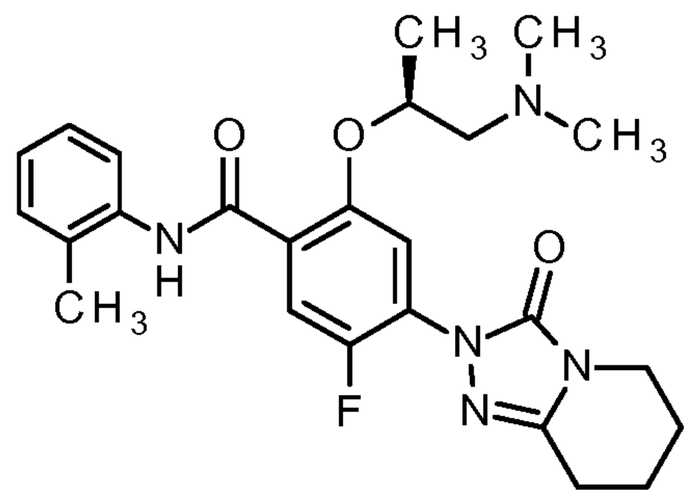
From intermediate 20 and 2-methoxy-4-methylpyridin-3-amine.

LC-MS (method B): R_t = 1.11 min; MS (ESIpos): m/z = 499 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.479 (5.44), 1.494 (5.36), 1.591 (3.64), 1.921 (0.55), 1.928 (0.66), 1.933 (0.74), 1.945 (0.76), 1.948 (0.83), 2.000 (0.73), 2.005 (0.76), 2.015 (0.80), 2.020 (0.67), 2.029 (0.49), 2.127 (5.59), 2.289 (9.73), 2.800 (1.32), 2.808 (0.60), 2.815 (2.31), 2.832 (1.34), 3.709 (1.53), 3.724 (2.49), 3.739 (1.08), 3.966 (16.00), 6.822 (1.45), 6.835 (1.47), 7.385 (1.25), 7.400 (1.25), 7.943 (1.92), 7.956 (1.89), 7.978 (2.10), 8.007 (2.09), 10.367 (0.56).

Example 276

2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide



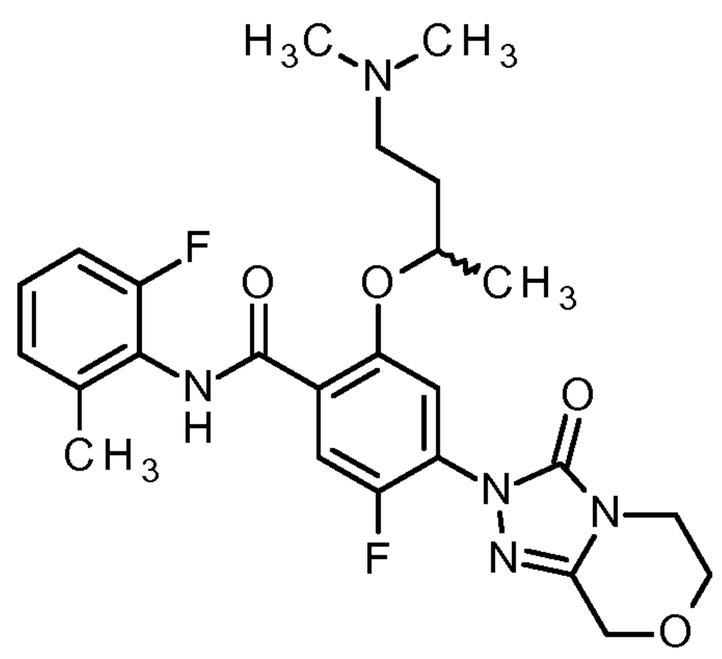
From intermediate 20 and o-toluidine.

LC-MS (method B): R_t = 1.21 min; MS (ESIpos): m/z = 468 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 1.261 (2.04), 1.471 (6.60), 1.487 (6.67), 1.590 (12.40), 1.923 (1.43), 1.929 (2.04), 1.941 (1.69), 1.945 (2.37), 1.949 (2.12), 1.961 (1.11), 1.986 (1.14), 2.001 (2.17), 2.017 (2.19), 2.027 (1.38), 2.155 (2.74), 2.342 (16.00), 2.626 (13.58), 2.720 (0.46), 2.781 (1.79), 2.798 (3.48), 2.816 (4.71), 2.832 (2.54), 3.697 (1.92), 3.710 (3.65), 3.712 (3.76), 3.725 (5.21), 3.740 (2.01), 7.006 (1.06), 7.128 (0.70), 7.144 (2.01), 7.162 (1.44), 7.166 (1.38), 7.222 (1.09), 7.241 (4.26), 7.259 (3.18), 7.413 (1.46), 7.428 (1.46), 7.452 (1.06), 7.466 (1.03), 7.476 (1.01), 7.490 (0.98), 7.528 (1.11), 7.649 (1.64), 7.663 (1.67), 7.672 (1.29), 7.687 (1.03), 8.044 (0.88), 8.072 (0.86).

Example 277

rac-2-{[4-(dimethylamino)butan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzamide



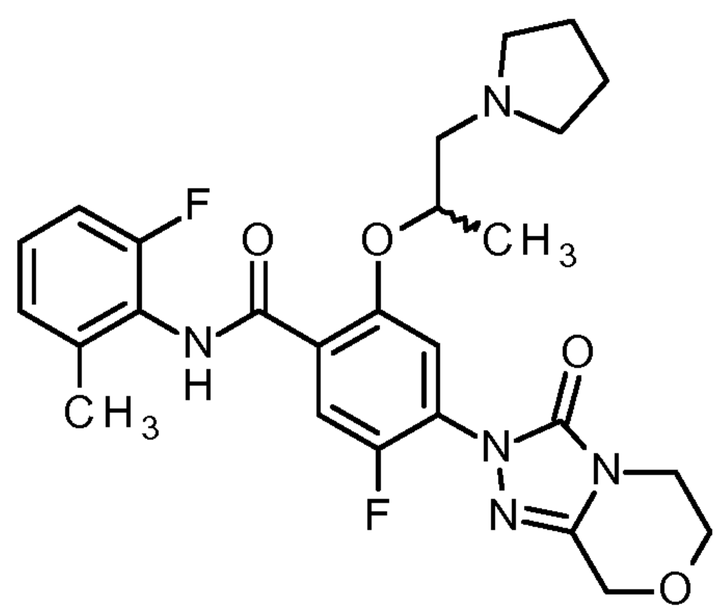
From intermediate 22 and 2-fluoro-6-methylaniline.

LC-MS (method B): R_t = 1.14 min; MS (ESIpos): m/z = 502 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.000 (0.60), 1.007 (2.18), 1.162 (1.63), 1.229 (2.62), 1.250 (14.10), 1.267 (1.43), 1.484 (6.89), 1.499 (7.10), 2.113 (2.61), 2.257 (0.68), 2.287 (16.00), 2.314 (0.70), 2.790 (10.53), 3.206 (1.04), 3.225 (1.65), 3.244 (0.92), 3.768 (2.24), 3.780 (3.49), 3.795 (2.69), 4.051 (2.94), 4.061 (2.75), 4.065 (3.56), 4.077 (2.35), 4.739 (12.57), 4.757 (0.82), 4.771 (0.78), 4.786 (0.45), 6.947 (0.73), 6.969 (1.38), 6.973 (1.26), 6.992 (0.88), 7.064 (1.35), 7.083 (1.86), 7.148 (0.95), 7.163 (1.02), 7.168 (1.35), 7.182 (1.29), 7.188 (0.69), 7.203 (0.60), 7.356 (2.24), 7.370 (2.24), 7.495 (0.44), 8.011 (3.22), 8.039 (3.17), 9.058 (2.34).

Example 278

rac-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzamide



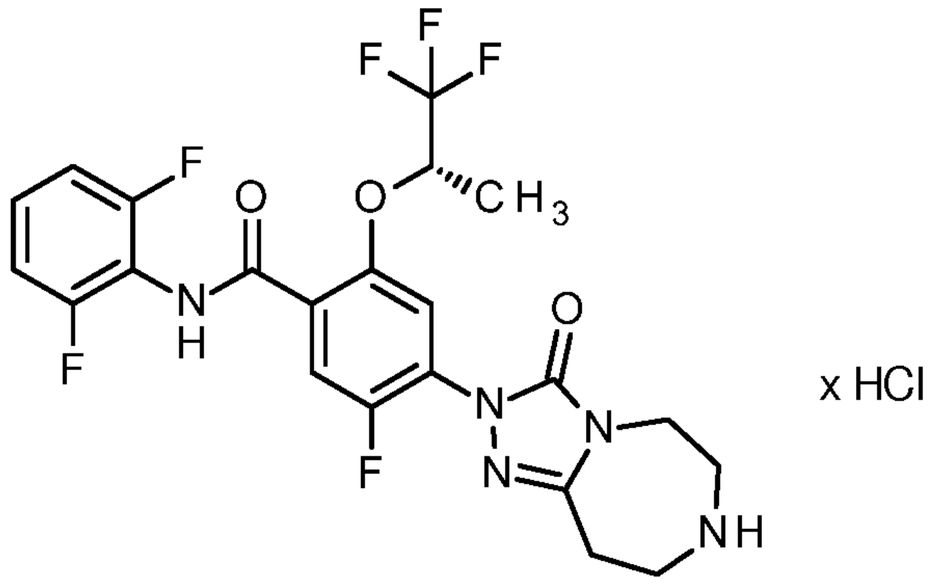
From intermediate 23 and 2-fluoro-6-methylaniline.

LC-MS (method B): R_t = 1.27 min; MS (ESIpos): m/z = 514 $[M+H]^+$

^{1}H-NMR (400 MHz, CHLOROFORM-d) δ [ppm]: 0.134 (3.48), 0.888 (0.66), 1.262 (7.42), 1.290 (0.45), 1.327 (1.01), 1.339 (1.19), 1.358 (0.93), 1.518 (8.47), 1.533 (8.12), 1.586 (2.79), 2.279 (1.26), 2.293 (1.41), 2.328 (16.00), 2.369 (0.75), 2.377 (0.76), 2.400 (0.84), 2.408 (0.83), 2.429 (0.77), 2.447 (1.42), 2.462 (1.21), 3.064 (0.64), 3.088 (0.83), 3.120 (0.60), 3.801 (2.82), 3.814 (4.27), 3.828 (3.43), 4.080 (3.64), 4.091 (3.07), 4.094 (4.36), 4.107 (2.92), 4.566 (0.64), 4.766 (14.33), 6.960 (0.82), 6.982 (1.68), 7.006 (1.17), 7.042 (1.27), 7.061 (1.77), 7.140 (0.91), 7.154 (1.00), 7.160 (1.30), 7.174 (1.28), 7.180 (0.64), 7.194 (0.55), 7.334 (1.43), 7.348 (1.43), 7.971 (1.88), 7.999 (1.85), 10.754 (1.46).

Example 279

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7,8,9-tetrahydro-3H-[1,2,4]triazolo[4,3-d][1,4]diazepin-2(5H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide, salt with hydrochloric acid



x HCl

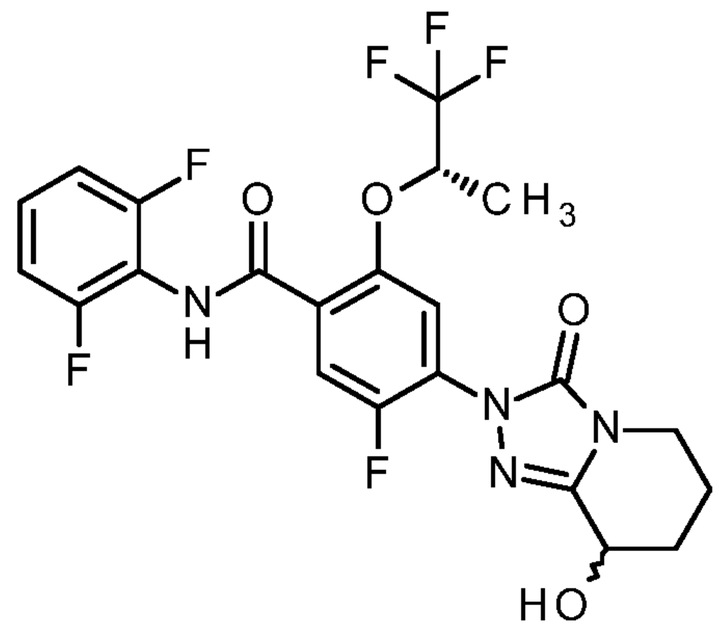
Intermediate 36 was treated with a solution of hydrochloric acid in dioxane (4 M, 1 ml) and the mixture was stirred at room temperature for two hours. The resulting suspension was concentrated under reduced pressure to obtain the title compound as yellow solid (53 mg, 95 % purity, 91 %)

LC-MS (method A): R_t = 0.89 min; MS (ESIneg): m/z = 514 $[M-H]^-$

^{1}H-NMR (400 MHz, DMSO-d6) δ [ppm]: 1.231 (0.70), 1.268 (0.64), 1.434 (13.39), 1.450 (13.32), 1.671 (0.89), 1.907 (0.57), 2.323 (2.61), 2.327 (3.63), 2.331 (2.61), 2.387 (0.76), 2.518 (16.00), 2.523 (10.65), 2.665 (2.68), 2.669 (3.70), 2.673 (2.61), 3.164 (4.14), 3.180 (4.53), 3.188 (5.04), 3.445 (4.65), 3.565 (14.02), 3.589 (0.45), 4.081 (5.04), 4.101 (4.72), 5.239 (0.89), 5.254 (2.17), 5.271 (2.74), 5.287 (2.04), 5.302 (0.83), 5.762 (0.57), 7.020 (3.38), 7.148 (3.95), 7.196 (4.33), 7.216 (8.67), 7.236 (5.48), 7.275 (3.44), 7.341 (0.45), 7.377 (1.27), 7.393 (2.80), 7.414 (3.63), 7.430 (1.85), 7.434 (1.85), 7.451 (0.76), 7.526 (5.23), 7.541 (5.23), 7.595 (5.80), 7.619 (5.61), 9.431 (3.76), 10.024 (12.56).

Example 280

N-(2,6-difluorophenyl)-5-fluoro-4-[(8R,S)-8-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide, mixture of diastereomers



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	449

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	449

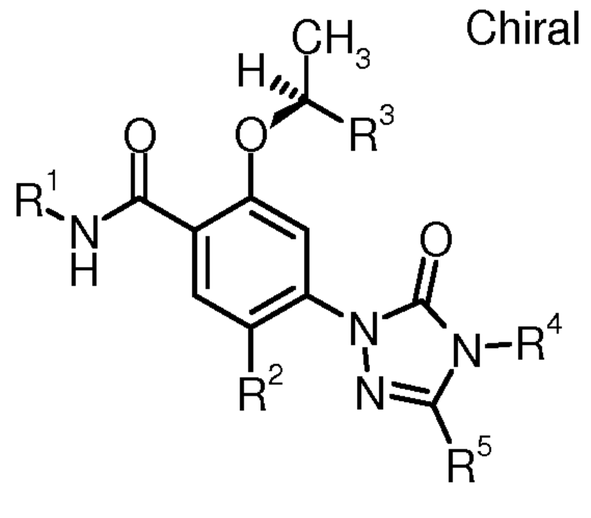
NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

CLAIMS

1. A compound of general formula (I)



(I),

in which

R^1 represents a group selected from

a C_1-C_8-alkyl group, which is optionally substituted with a group selected from

C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times with one or more substituents independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_8-haloalkyl group,

a C_3-C_8-cycloalkyl group, whch is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenyl group and a -$N(R^7)(R^8)$ group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group,

a -(C_1-C_6-alkyl)-$C(=O)N(R^7)(R^8)$ group,

a 4- to 7-membered, optionally unsaturated, heterocyclic group, which is connected to the rest of the molecule via a carbon atom, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a-$C(=O)O(C_1$-C_4-alkyl) group, a -$C(=O)(C_1$-C_6-alkyl) group, a -$C(=O)(C_3$-C_6-cycloalkyl) group, a -$S(=O)_2(C_1$-C_6-alkyl) group and a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, aryl, -O-aryl, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8),), -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-O-(C_2-C_6-alkenyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -N(O)$_2$, -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or wherein two vicinal substituents of said phenyl groups may form together a 5- or 6-membered, optionally heterocyclic, aromatic or non-aromatic ring, having optionally 1-3 heteroatoms independently selected from -N=, -NH-, -N(R^7)-, -O-, -S-, and optionally containing a C(=O) group, and wherein the so formed ring is optionally substituted one or two times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(O)OH, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8)

and

a monocyclic or bicyclic heteroaryl group which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

R^2 represents a hydrogen atom or a halogen atom,

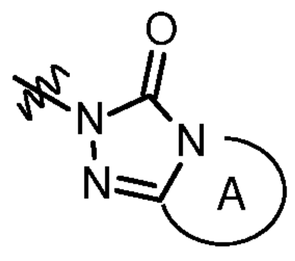
R^3 represents a group selected from

a C_1-C_6-alkyl group,

a C_3-C_8-cycloalkyl group,

a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group,
a C_2-C_6-alkenyl group,
a C_2-C_6-alkinyl group,
a C_4-C_8-cycloalkenyl group,
a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group,
a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group, wherein
said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group and wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
a phenyl group,
which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_6-alkyl), -N(O)$_2$, and -N(R^7)(R^8),

R^4 and R^5 jointly form a 5- to 6-membered, optionally unsaturated, heterocyclic ring A of partial formula (i)



(i)

whereby ring A in addition to the two mandatory atoms, the nitrogen atom and the carbon atom bridging the two rings, bears additional 3 to 6 members selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -S(=O)(=NR^{14})-, -N=, -N(R^7)-, -C(=O)-, -CH=, -CR^{11}=, -C(R^{12})$_2$-, -C(H)(R^{13})-,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-hydroxyalkyl group, a haloalkyl group, a aryl group, a (C_1-C_6-alkyl)-aryl group, and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_6-alkyl, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), and -C(=O)OR^6-,

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^9 and R^{10} together with the nitrogen to which they are attached represent a nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8)

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, -(C_1-C_6-alkyl)-aryl, -aryl-(C_1-C_6-alkyl), C_3-C_8-cycloalkyl, C_1-C_6-alkoxy, -O(C_2-C_6-alkenyl), C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, aryl, -O-aryl, cyano, -C(=O)OR^6-, hydroxy, -SH, -S-(C_1-C_6-alkyl), -S-(C_2-C_6-alkenyl), S(=O)$_2$(C_1-C_6-alkyl), -S(=O)$_2$-(C_2-C_6-alkenyl), -N(O)$_2$, and -N(R^7)(R^8),

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

R^{15} represents a group selected from

a C_1-C_6-alkyl group and a benzyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

2. The compound according to claim 1, wherein

R^1 represents a group selected from

a C_1-C_8-alkyl group, which is optionally substituted with a group selected from

C_3-C_8-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a C_2-C_8-haloalkyl group,

a C_3-C_8-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenyl group anda -$N(R^7)(R^8)$ group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_4-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_6-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group,

a -(C_1-C_6-alkyl)-$C(=O)N(R^7)(R^8)$ group,

a 4- to 7-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 7-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -$C(=O)O(C_1$-C_4-alkyl) group, a -$C(=O)(C_1$-C_6-alkyl) group, a -$C(=O)(C_3$-C_6-cycloalkyl) group, a -$S(=O)_2(C_1$-C_6-alkyl) group and

a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a 5- to 7-membered heterocycloalkenyl group, which is connected to the rest of the molecule via a carbon atom of said 5- to 7-membered heterocycloalkenyl group and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_6-alkyl) group,a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_6-alkyl) group and a oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group, which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_6-alkyl, C_3-C_8-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-hydroxyalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_3-C_8-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_6-alkyl)-N(R^7)(R^8), -(C_1-C_6-alkyl)-C(=O)OR^6, -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

an indanyl group, a tetralinyl group wherein said indanyl- or tetralinyl group is optionally substituted one or two times, each substituent independently selected from a halogen atom, a C_1-C_6-alkyl group, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group,a hydroxy group and a -N(R^7)(R^8) group,

and

a monocyclic or bicyclic heteroaryl group, which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_6-alky groupl, a C_1-C_6-haloalkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-alkoxy group, a C_1-C_6-haloalkoxy group, a C_3-C_8-cycloalkoxy group, a cyano group, a hydroxy group and a -N(R^7)(R^8) group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_8-cycloalkyl group, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a C_2-C_6-alkinyl group,

a C_4-C_8-cycloalkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,
a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group, a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,
a -(C_1-C_6-alkyl)-(4- to 7-membered nitrogen containing heterocycloalkyl) group and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,and
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
a phenyl group,wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_4-haloalkyl, C_1-C_3-alkoxy and hydroxy,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,
or
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
-N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_6-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_6-alkyl group, a C_2-C_6-hydroxyalkyl group and a -(C_2-C_6-alkyl)-N(R^9)(R^{10}) group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,
wherein said 4- to 7-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^9 and R^{10} together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 7-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

R^{15} represents a group selected from
a C_1-C_6-alkyl group and a benzyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

3. The compound according to claim 1, wherein

R^1 represents a group selected from

a C_1-C_6-alkyl group, which is optionally substituted with a group selected from

C_3-C_6-cycloalkyl, phenyl and monocyclic or bicyclic heteroaryl,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-haloalkyl group,

a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a hydroxy group, a phenylgroup and a -N(R^7)(R^8) group,

wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group,a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group and a hydroxy group,

a C_2-C_6-cyanoalkyl group,

a C_2-C_6-hydroxyalkyl group,

a (C_2-C_3-hydroxyalkyl)-O-(C_2-C_6-alky)- group,

a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,

a -(C_1-C_6-alkyl)-C(=O)N(R^7)(R^8) group,

a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group,a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and oxo (=O) group,

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a 5- to 6-membered heterocycloalkenyl group, which is connected to the rest of the molecule via a carbon atom of said 5- to 6-membered heterocycloalkenyl group, and which is optionally substituted one or two times, each substituent

independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroaryl group,a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and oxo (=O) group, and

wherein said 5- to 6-membered heteroaryl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

a phenyl group,which is optionally substituted, one, two, three, four or five times, each substituent independently selected from a halogen atom or a group selected from

C_1-C_3-alkyl, C_3-C_6-cycloalkyl, C_1-C_3-haloalkyl, C_1-C_3-hydroxyalkyl, C_1-C_3-alkoxy, C_1-C_3-haloalkoxy, C_3-C_6-cycloalkoxy, hydroxy, cyano, -C(=O)OR^6, -C(=O)N(R^7)(R^8), -N(R^7)(R^8), -(C_1-C_3-alkyl)-N(R^7)(R^8), -(C_1-C_3-alkyl)-C(=O)OR^6, -(C_1-C_3-alkyl)-C(=O)N(R^7)(R^8), -S(=O)$_2$N(R^7)(R^8), -S(=O)$_2$(C_1-C_3-alkyl), -S(=O)(=NR^{14})(C_1-C_3-alkyl), -P(=O)(C_1-C_3-alkyl)$_2$ and SF_5,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from

-CH_2-N(R^7)-CH_2-, -CH_2-O-CH_2-, -O-CH_2-C(=O)-NH- and -NH-C(=O)-NH-,

an indanyl group, a tetralinyl group which are optionally substituted one or two times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group, a C_3-C_6-cycloalkoxy group, a cyano group, ahydroxy group and a -N(R^7)(R^8) group,

and

a monocyclic or bicyclic heteroaryl group,

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_3-C_6-cycloalky groupl, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group, a C_3-C_6-cycloalkoxy group, a cyano group, a hydroxy group and a -N(R^7)(R^8) group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl, a C_2-C_6-alkinyl group,

a C_4-C_6-cycloalkenyl group, a (C_1-C_6-alkyl)-N(R^7)R^8 group,

a -(C_1-C_6-alkyl)-N(H)C(=O)R^6 group, a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} group,
a -(C_1-C_6-alkyl)-(4- to 6-membered nitrogen containing heterocycloalkyl) group and
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a C_1-C_3-alkyl group,
and
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is connected to the alkyl group via a carbon atom of the heterocycloalkyl group,
and
a phenyl group,wherein said phenyl group is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom or a group selected from
C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and hydroxy,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-CH_2-X^1-X^2-X^3-X^4-X^5-#,
*-CH(R^{13})-X^1-X^2-X^3-#,
*-CH=CH-CH(R^{13})-X^3-#,
*-CH=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-N=C(R^{11})-C(R^{11})=C(R^{11})-#,
*-CH=N-C(R^{11})=C(R^{11})-#,
*-CH=C(R^{11})-N=C(R^{11})-#,
and
*-CH=C(R^{11})-C(R^{11})=N-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,
and in which groups
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),
and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,
or
one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
-N(R^7)-, -O-, -S-, -S(=O)-, -S(=O)(=NR^{14})- and -S(=O)$_2$-,
and one of X^1, X^2, X^3, X^4 and X^5 represents a group selected from
C(R^{12})$_2$ and CH(R^{13}),

and the remaining of X^1, X^2, X^3, X^4 and X^5 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or a group selected from
a C_1-C_3-alkyl group, a C_2-C_3-hydroxyalkyl group and a -(C_2-C_3-alkyl)-N(R^9)(R^{10}),
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 6-membered heterocycloalkyl group,
wherein said 4- to 6-membered nitrogen containing heterocycloalkyl group is optionally substituted with a group selected from
C_1-C_3-alkyl, -S(=O)$_2$(C_1-C_3-alkyl) and -C(=O)O(C_1-C_4-alkyl),

R^9 and R^{10} represent, independently from each occurrence, a hydrogen atom or a C_1-C_3-alkyl group,
or
R^9 and R^{10} together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a group selected from
a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-alkoxy group, a C_1-C_3-haloalkoxy group and a cyano group,

R^{12} represents, independently from each occurrence, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group, a -C(=O)OR^6 group and a -C(=O)N(R^7)(R^8) group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)(C_1-C_3-haloalkyl) group,

R^{15} represents a group selected from
a C_1-C_4-alkyl group and a benzyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

4. The compound according to claim 1, wherein

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and –a $N(R^7)(R^8)$ group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
a C_2-C_6-hydroxyalkyl group,
a -(C_2-C_6-alkyl)-$N(R^7)(R^8)$ group,
a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alkyl group, a 5- to 6-membered heteroary groupl, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -$S(=O)_2$(C_1-C_3-alkyl) group and a oxo (=O) group,
a phenyl group, which is optionally substituted, one, two, three or four times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-haloalkyl group, a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a cyano group, a hydroxy group, a -C(=O)OR^6 group, a -C(=O)$N(R^7)(R^8)$group, a -$N(R^7)(R^8)$ group, a -(C_1-C_3-alkyl)-$N(R^7)(R^8)$ group, a -$S(=O)_2N(R^7)(R^8)$ group and a SF_5 group,
or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,
an indanyl group which is optionally substituted with a hydroxy group
and
a monocyclic or bicyclic heteroaryl group,
which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom,a C_1-C_3-alkyl group, a C_1-C_3-alkoxy group, a hydroxy group and a-$N(R^7)(R^8)$ group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from
a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,
a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, (C_1-C_6-alkyl)-$N(R^7)R^8$ group,
a -(C_1-C_6-alkyl)-$N(H)C(=O)OR^{15}$ group and a phenyl group,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-CH_2-X^1-X^2-#,
*-CH_2-X^1-X^2-X^3-#,
*-CH_2-X^1-X^2-X^3-X^4-#,
*-$CH(R^{13})$-X^1-X^2-X^3-#,
*-CH=CH-$CH(R^{13})$-X^3-#,
*-$CH=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,
*-$N=C(R^{11})$-$C(R^{11})=C(R^{11})$-#,
and
*-$CH=C(R^{11})$-$N=C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
or
one of X^1, X^2, X^3 and X^4 represents a group selected from
-$N(R^7)$-, -O-, -S- and -$S(=O)(=NR^{14})$-,
X^1, X^2, X^3 and X^4 represents a $C(R^{12})_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence, a hydrogen atom or
a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents a hydrogen atom,

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group and a -C(=O)OR^6 group,

R^{14} represents a hydrogen atom or a group selected from
a cyano group and a -C(=O)CF_3 group,

R^{15} represents a C_1-C_4-alkyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

5. The compound according to claim 1, wherein

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from cyclopropyl and cyclohexyl, and which is optionally substituted, one or two times, each substituent independently selected from a halogen atom, a phenyl group and a -N(R^7)(R^8) group,
wherein said phenyl substituent is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom,
a C_2-C_6-hydroxyalkyl group,
a -(C_2-C_6-alkyl)-N(R^7)(R^8) group,
a 4- to 6-membered heterocycloalkyl group, which is connected to the rest of the molecule via a carbon atom of said 4- to 6-membered heterocycloalkyl group, and which is selected from azetidinyl, oxetanyl, tetrahydro-2H-pyranyl, tetrahydro-2H-thiopyranyl and piperidinyl,and which is optionally substituted one or two times, each substituent independently selected from a C_1-C_3-alky groupl, a 5- to 6-membered heteroaryl group, a -C(=O)O(C_1-C_4-alkyl) group, a -C(=O)(C_1-C_3-alkyl) group, a -C(=O)(C_3-C_6-cycloalkyl) group, a -S(=O)$_2$(C_1-C_3-alkyl) group and a oxo (=O) group,
a phenyl group, which is optionally substituted, one, two or three times, each substituent independently selected from a halogen atom, a C_1-C_3-alky groupl, a

C_1-C_3-haloalkyl group,a C_1-C_3-hydroxyalkyl group, a C_1-C_3-alkoxy group, a hydroxy group, a cyano group, a -C(=O)OR^6 group, a -C(=O)$N(R^7)(R^8)$ group, a -$N(R^7)(R^8)$ group, a -(C_1-C_3-alkyl)-$N(R^7)(R^8)$ group,a -$S(=O)_2N(R^7)(R^8)$ group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH_2-$N(R^7)$-CH_2- and -O-CH_2-C(=O)-NH-,

an indanyl group which is optionally substituted with a hydroxy group

and

a monocyclic or bicyclic heteroaryl group,

which is selected from imidazolyl, 1,2-oxazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrazinyl, pyrimidinyl, indazolyl, 1,3-benzothiazolyl, pyrrolo[2,3-d]pyrimidinyl and quinolinyl, and

which is optionally substituted one, two or three times, each substituent independently selected from a halogen atom or a group selected from C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy and -$N(R^7)(R^8)$,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from

a C_1-C_6-alkyl group, a C_3-C_6-cycloalkyl group, a C_1-C_6-haloalkyl group,

a C_1-C_6-hydroxyalkyl group, a C_2-C_6-alkenyl group, a (C_1-C_6-alkyl)-$N(R^7)R^8$ group,

a -(C_1-C_6-alkyl)-N(H)C(=O)OR^{15} and a phenyl group,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

*-$CH(R^{13})$-X^1-X^2-X^3-#,

*-CH=CH-$CH(R^{13})$-X^3-#,

*-CH=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

*-N=$C(R^{11})$-$C(R^{11})$=$C(R^{11})$-#,

and

*-CH=$C(R^{11})$-N=$C(R^{11})$-#,

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

and in which groups
one of X^1, X^2, X^3 and X^4 represents a group selected from
$C(R^{12})_2$ and $CH(R^{13})$,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,
or
one of X^1, X^2, X^3 and X^4 represents a group selected from
$-N(R^7)-$, -O-, -S- and $-S(=O)(=NH)-$,
and one of X^1, X^2, X^3 and X^4 represents a $C(R^{12})_2$ group,
and the remaining of X^1, X^2, X^3 and X^4 each represent a CH_2 group,

R^6 represents a hydrogen atom or a group selected from
a C_1-C_4-alkyl group and a benzyl group,

R^7 and R^8 represent, independently from each occurrence,a hydrogen atom or
a C_1-C_3-alkyl group,
or
R^7 and R^8 together with the nitrogen to which they are attached represent a
nitrogen containing 4- to 6-membered heterocycloalkyl group,

R^{11} represents a hydrogen atom,

R^{12} represent, identically or differently, a hydrogen atom, a halogen atom or
a C_1-C_3-alkyl group,

R^{13} represents a group selected from
a hydroxy group and a $-C(=O)OR^6$ group,

R^{15} represents a C_1-C_4-alkyl group,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

6. The compound according to claim 1, wherein

R^1 represents a group selected from
a C_3-C_6-cycloalkyl group, which is selected from a cyclopropyl group and a cyclohexyl group,

which C_3-C_6-cycloalkyl group is optionally substituted, one or two times, each substituent independently selected from a fluorine atom, a phenyl group and a dimethylamino group,

wherein said phenyl substituent is optionally substituted with a fluorine atom

a 2-hydroxy-2-methylpropyl group,

a 2-(dimethylamino)ethyl group,

a 4- to 6-membered heterocycloalkyl group, which is selected from azetidin-3-yl, oxetan-3-yl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-thiopyran-4-yl and piperidin-4-yl, and

which is optionally substituted one or two times, each substituent independently selected from a group selected from a methyl group, an ethyl group, a pyrazinyl group, a *tert*-butoxycarbonyl group, a acetyl group, a 1-cyclopropanecarbonyl group, amethylsulfonyl group and a oxo (=O) group,

a phenyl group, which, is optionally substituted, one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, an ethyl group, a difluoromethyl group, a trifluoromethyl group, a hydroxymethyl group, a methoxy group, a hydroxy group, a cyano group,a -C(=O)OH group,a $-C(=O)OCH_3$ group, a $-C(=O)OC(CH_3)$, group, a $-C(=O)NH_2$ group, a-$C(=O)N(CH_3)_2$ group, an amino group, a methylamino group, an aminomethyl group,a $-S(=O)_2NH_2$ group and a SF_5 group,

or in which two substituents of said phenyl group, when they are attached to adjacent ring atoms, are optionally linked to one another in such a way that they jointly form a group selected from -CH-CH_2-NH-CH_2- and -O-CH_2-C(=O)-NH-,

a 2-hydroxyindan-1-yl group and

a monocyclic or bicyclic heteroaryl group,

which is selected from

imidazol-4-yl, 1,2-oxazol-4-yl, 1,2-oxazol-5-yl, pyrazol-3-yl, pyrazol-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyrazinyl, pyrimidin-4-yl, pyrimidin-5-yl, indazol-5-yl, indazol-6-yl, indazol-7-yl, 1,3-benzothiazol-6-yl, pyrrolo[2,3-d]pyrimidin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl, and

which is optionally substituted one, two or three times, each substituent independently selected from a fluorine atom, a chlorine atom, a methyl group, a methoxy group, a hydroxy group and a morpholin-4-yl group,

R^2 represents a hydrogen atom or a chlorine atom or a fluorine atom,

R^3 represents a group selected from
propyl, cyclohexyl, trifluoromethyl, 1-hydroxyethyl, allyl, aminomethyl, (dimethylamino)methyl, (tert-butoxycarbonylamino)methyl, 2-(dimethylamino)ethyl, pyrrolidin-1-yl-methyl and phenyl,

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from
*-$(CH_2)_2$-S-#,
*-$(CH_2)_4$-#,
*-CH_2-C(H)(C(=O)OH)-$(CH_2)_2$-#,
*-CH_2-CF_2-$(CH_2)_2$-#,
*-$(CH_2)_3$-C(H)(C(=O)OH)-#,
*-CH(OH)-$(CH_2)_3$-#,
*-CH_2-CH(OH)-$(CH_2)_2$-#,
*-$(CH_2)_2$-CH(OH)-CH_2-#,
*-$(CH_2)_3$-C(H)(OH)-#,
*-CH=CH-CH(OH)-CH_2-#,
*-CH_2-C$(CH_3)_2$-CH_2-O-#,
*-$(CH_2)_2$-O-CH_2-#,
*-$(CH_2)_3$-O-#,
*-$(CH_2)_3$-N(CH_3)-#,
*-$(CH_2)_3$-S-#,
*-$(CH_2)_3$-S(=O)(=NH)-,#
*-$(CH_2)_5$-#,
*-$(CH_2)_3$-O-CH_2-#,
*-$(CH_2)_2$-N(H)-$(CH_2)_2$-#
*-CH=CH-CH=CH-#,
*-N=CH-CH=CH-#,
and
*-CH=CH-N=CH-#,
in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

7. The compound according to claim 1 which is selected from the group consisting of:

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[3-(trifluoromethyl)phenyl]benzamide,
N-(1-acetylpiperidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(3-chloropyridin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(5-methylpyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(5-chloropyrimidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(3-chloropyridin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[1-(pyrazin-2-yl)piperidin-4-yl]benzamide,
N-[1-(cyclopropylcarbonyl)piperidin-4-yl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(1-methyl-2-oxopiperidin-(4R,S)-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide, mixture of diastereomers,
5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-aminophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-[2-(methylamino)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-amino-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(4-amino-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[3-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-chloro-4-(pentafluoro-lambda6-sulfanyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(oxetan-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)benzamide,
N-(2-chloro-3-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-3,5-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(3,5-dimethyl-1,2-oxazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methyl-1,2-oxazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methyl-1H-imidazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(dimethylamino)ethyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[4-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-cyclopropyl-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
tert-butyl 3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}azetidine-1-carboxylate,
N-(azetidin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

N-(4,4-difluorocyclohexyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(1-ethylazetidin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[4-(dimethylamino)cyclohexyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-ethylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-N-(2,4,6-trimethylpyridin-3-yl)benzamide,
N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-phenyl-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,4,6-trifluoro-phenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[2-(trifluoromethyl)-phenyl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-methylpyridin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-3-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(1-methyl-1H-pyrazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(tetrahydro-2H-pyran-4-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-methylpyridin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(1,3-dimethyl-1H-pyrazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(1,4-dimethyl-1H-pyrazol-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-hydroxy-2-methylpropyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-(hydroxymethyl)-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[3-(hydroxymethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-8-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-6-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
3-{[5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzoyl]amino}-4-methylbenzoic acid,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-5-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylquinolin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(quinolin-7-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(3-sulfamoyl-phenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(7H-pyrrolo[2,3-d]-pyrimidin-4-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methylquinolin-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methyl-1,3-benzothiazol-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methyl-1H-indazol-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,3-dimethoxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(1H-indazol-7-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[1-(4-fluorophenyl)cyclopropyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-3-hydroxy-1H-indazol-6-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[(1S,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(3-carbamoyl-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,

2-[(1S)-1-cyclohexylethoxy]-N-(4,4-difluorocyclohexyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methoxy-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxy-2-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-[3-(dimethylcarbamoyl)phenyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[1-(methylsulfonyl)piperidin-4-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[6-(morpholin-4-yl)pyridazin-3-yl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methoxypyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methoxypyrimidin-5-yl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(4,6-dimethoxypyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxypyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methoxypyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(6-methoxypyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(5,6-dimethylpyrimidin-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyrimidin-5-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(2,4-dimethylpyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyrazin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methylpyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-fluoropyrimidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[3-(morpholin-4-yl)pyrazin-2-yl]-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(4,6-dimethylpyrimidin-5-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(3-amino-2-methylphenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-[4-amino-2-(trifluoromethyl)phenyl]-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-methyl-4-sulfamoylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-[2-(aminomethyl)-6-methylphenyl]-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
methyl 2-({2-[(1R)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoate,
2-[(1R)-1-cyclohexylethoxy]-N-(2,3-dihydro-1H-isoindol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(5-amino-3-methylpyridin-2-yl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-({2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoic acid,
tert-butyl 4-({2-[(1S)-1-cyclohexylethoxy]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)benzoyl}amino)-3-methylbenzoate,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[3-(trifluoromethyl)phenyl]benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,4,6-trifluorophenyl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-[2-(trifluoromethyl)phenyl]benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyridin-2-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(2,4-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]-triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-[2-(dimethylamino)ethyl]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-fluoro-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(1-methyl-1H-pyrazol-5-yl)-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(tetrahydro-2H-pyran-4-yl)benzamide,
N-(2-cyano-4-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-5-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetra-hydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-5-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(3-methylpyridin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide
N-(2-chloro-6-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,

2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-3-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(1,3-dimethyl-1H-pyrazol-4-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(1-methylpiperidin-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-N-(1,4-dimethyl-1H-pyrazol-3-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(2-hydroxy-2-methylpropyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-[2-(hydroxymethyl)-3-(trifluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-[(1S)-1-cyclohexylethoxy]-5-fluoro-N-(5-methyl-1,2-oxazol-4-yl)-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-4-fluorophenyl)-2-[(1S)-1-cyclohexylethoxy]-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-3,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(3-fluoro-2-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-N-(2,4,6-trifluoro-phenyl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(4,5-difluoro-2-methylphenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamid,e
5-fluoro-N-[2-methyl-4-(trifluoromethyl)phenyl]-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-5-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-cyano-4-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide
N-(4-chloro-2-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c]-[1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]-N-[3-(trifluoro-methyl)phenyl]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(2S)-pentan-2-yloxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenyl-ethoxy]benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenyl-ethoxy]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenyl-ethoxy]-N-[3-(trifluoromethyl)phenyl]benzamide,
5-fluoro-N-(2-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

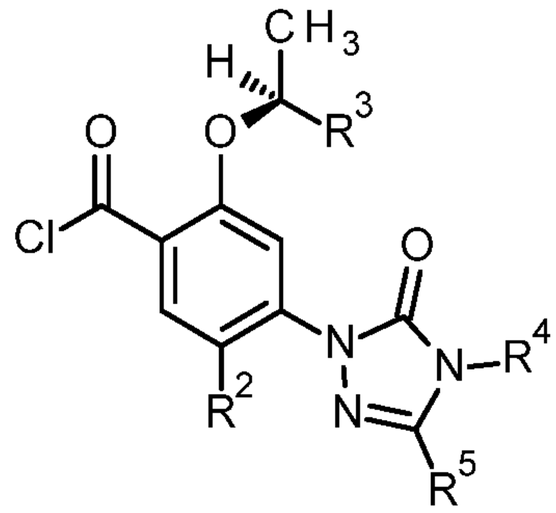
N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichlorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-fluoro-6-methylphenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-6-methylphenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-[2-methyl-6-(trifluoromethyl)phenyl]-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-dichloro-4-fluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(4-fluoro-2,6-dimethylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(4-chloro-2-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4-methylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c]-[1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2-chloro-4,6-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,4-dimethylpyridin-3-yl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-methoxy-6-methylphenyl)-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(6-chloro-2,3-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]-oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamid,e
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(8-methyl-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyrimidin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6-dihydro[1,3]thiazolo[2,3-c][1,2,4]triazol-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-3H,5H-[1,2,4]triazolo[3,4-c][1,4]oxazepin-2(9H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7,8,9-tetrahydro-3H-[1,2,4]triazolo[4,3-a]azepin-2(5H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-a]pyrazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]thiazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-4-(6,6-dimethyl-3-oxo-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]oxazin-2(3H)-yl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
4-(6,6-difluoro-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-N-(2,6-difluorophenyl)-5-fluoro-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo[1,2,4]triazolo[4,3-b]pyridazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
2-(4-[(2,6-difluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-(R,S)-carboxylic acid, mixture of diastereomers,
2-(4-[(2-chloro-6-fluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-8-(R,S)-carboxylic acid, mixture of diastereomers,
2-(4-[(2-chloro-6-fluorophenyl)carbamoyl]-2-fluoro-5-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}-phenyl)-3-oxo-2,3,5,6,7,8-hexahydro[1,2,4]triazolo[4,3-a]pyridine-6-(R,S)-carboxylic acid, mixture of diastereomers,
N-(2,6-difluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2R)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-fluoro-N-(2-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-[(1S)-1-phenylethoxy]benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-2-{[(2R,3R)-3-hydroxybutan-2-yl]oxy}-4-(3-oxo-5,6,7,8-

tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2R)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzamide,
N-[2-(difluoromethyl)phenyl]-2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(5-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-N-(3,5-dimethylpyrazin-2-yl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
2-{[(2S)-1-(dimethylamino)propan-2-yl]oxy}-5-fluoro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide,
rac-2-{[4-(dimethylamino)butan-2-yl]oxy}-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)benzamide,
rac-5-fluoro-N-(2-fluoro-6-methylphenyl)-4-(3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]-oxazin-2(8H)-yl)-2-{[1-(pyrrolidin-1-yl)propan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(3-oxo-6,7,8,9-tetrahydro-3H-[1,2,4]triazolo[4,3-d][1,4]-diazepin-2(5H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-[(8R,S)-8-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3-a]pyridin-2(3H)-yl]-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide, mixture of diastereomers,
5-chloro-N-(2,6-difluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(2-chloro-6-fluorophenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,

5-chloro-N-[1-(4-fluorophenyl)cyclopropyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-[2-(difluoromethyl)phenyl]-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(4-methylpyridazin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(6-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(2-methoxy-4-methylpyridin-3-yl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
5-chloro-N-(4-fluoro-2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide
5-chloro-N-(2-methylphenyl)-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluoro-4-hydroxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluoro-3-hydroxyphenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(8-imino-3,8-dioxo-5,6,7,8-tetrahydro-8λ^6-[1,2,4]triazolo-[3,4-b][1,3]thiazin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(7-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(6-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]-pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(6-hydroxy-3-oxo-5,6-dihydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
N-(2,6-difluorophenyl)-5-fluoro-4-(8-hydroxy-3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)-2-{[(2S)-1,1,1-trifluoropropan-2-yl]oxy}benzamide,
rac-tert-butyl [2-{2-[(2-chloro-6-fluorophenyl)carbamoyl]-4-fluoro-5-(3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)phenoxy}propyl]carbamate, and
rac-2-{[1-aminopropan-2-yl]oxy}-N-(2-chloro-6-fluorophenyl)-5-fluoro-4-(3-oxo-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)benzamide, salt with hydrochloric acid,
or a tautomer, an N-oxide, or a salt thereof, or a salt of a tautomer or an N-oxide of said compound.

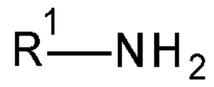
8. A method of preparing a compound of general formula (I) according to any one of claims 1 to 7, said method comprising the step of allowing an intermediate compound of general formula (IX) :



(IX),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) according to any one of claims 1 to 7,

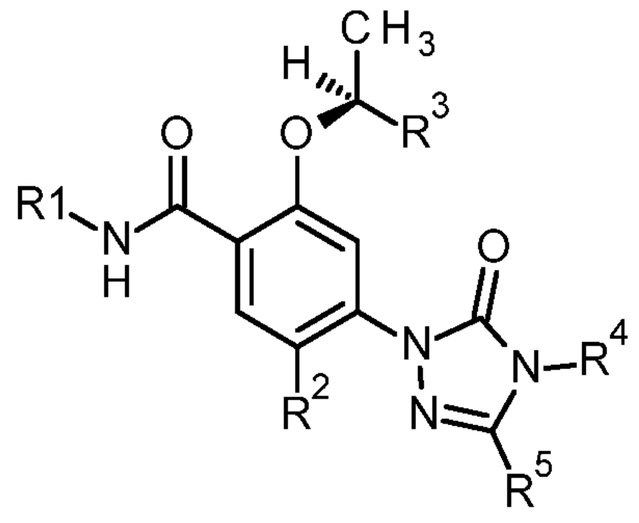
to react with a compound of general formula (X) :



(X),

in which R^1 is as defined for the compound of general formula (I) according to any one of claims 1 to 7,

thereby giving a compound of general formula (I) :



(I),

in which R^1, R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) according to any one of claims 1 to 7,

then optionally converting said compound into solvates, salts and/or solvates of such salts using the corresponding (i) solvents and/or (ii) bases or acids.

9. A compound of general formula (I) according to any one of claims 1 to 7 for use in the treatment or prophylaxis of a disease.

10. A pharmaceutical composition comprising a compound of general formula (I) according to any one of claims 1 to 7 and one or more pharmaceutically acceptable excipients.

11. A pharmaceutical combination comprising:

- one or more first active ingredients, in particular compounds of general formula (I) according to any one of claims 1 to 7, and
- one or more further active ingredients in particular anti-cancer agents.

12. Use of a compound of general formula (I) according to any one of claims 1 to 7 for the treatment or prophylaxis of a disease.

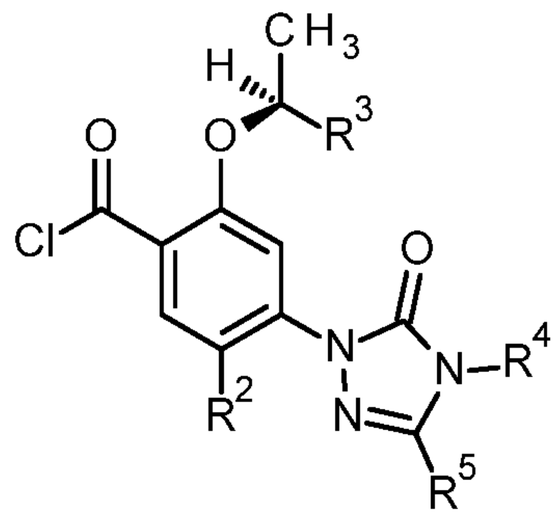
13. Use according to claim 9 or 12, wherein the disease is a hyperproliverative or an inflammatory disorder.

14. Use according to claim 13, wherein the disease is cancer.

15. Use according to claim 14 wherein the cancer disease is selected from a solid tumor, leukemia and lymphoma.

16. Use according to claim 15, wherein the cancer disease is selected from lung cancer, glioblastoma, prostate cancer, acute myeloid leukemia and lymphoma.

17. Use of a compound of general formula (IX) :

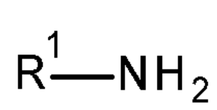


(IX),

in which R^2, R^3, R^4 and R^5 are as defined for the compound of general formula (I) according to any one of claims 1 to 7,

for the preparation of a compound of general formula (I) according to any one of claims 1 to 7.

18. Use of a compound of general formula (X) :



(X),

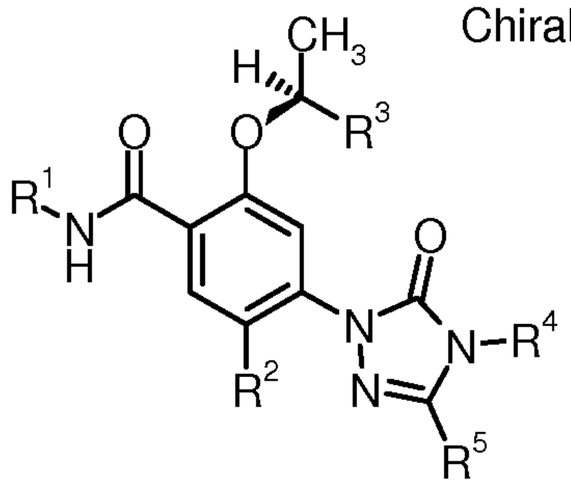
in which R^1 is as defined for the compound of general formula (I) according to any one of claims 1 to 7,

for the preparation of a compound of general formula (I) according to any one of claims 1 to 7.

19. A method of treating lymphoma in a subject, the method comprising administering to the subject an effective amount of a compound of any one of claims 1-7.

20. A method of reducing proliferation of a cell, the method comprising contacting the cell with an effective amount of a compound of any one of claims 1-7.

21. A process for the production of a compound of general formula (I)



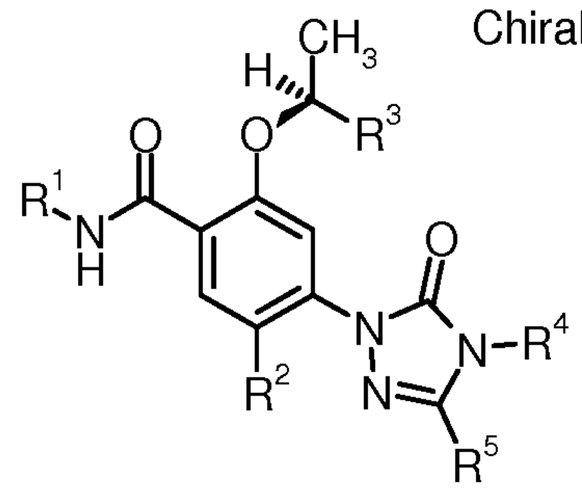
(I),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form together with the nitrogen atom and the carbon atom to which they are attached a 5 to 7 membered saturated or partially unsaturated heterocyclic ring that is substituted once with a hydroxy group,

by reacting a compound auf general formula (Ia)



(Ia),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

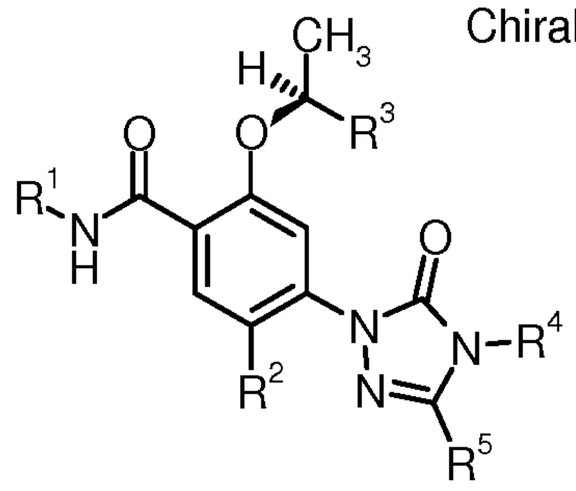
and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

with a suitable microorganism, under suitable conditions and in a suitable medium,

to form those compounds of general formula (I), as defined supra.

22. A process for the production of a compound of general formula (I) according to claim 21,



(I),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH(OH)-X^1-X^2-#,

*-CH_2-CH(OH)-X^2-#,

*-CH(OH)-X^1-X^2-X^3-#,

*-CH_2-CH(OH)-X^2-X^3-#,

*-CH_2-X^1-CH(OH)-X^3-#,

*-CH=CH-CH(OH)-X^3-#,

*-CH(OH)-X^1-X^2-X^3-X^4-#,

*-CH_2-CH(OH)-X^2-X^3-X^4-#,

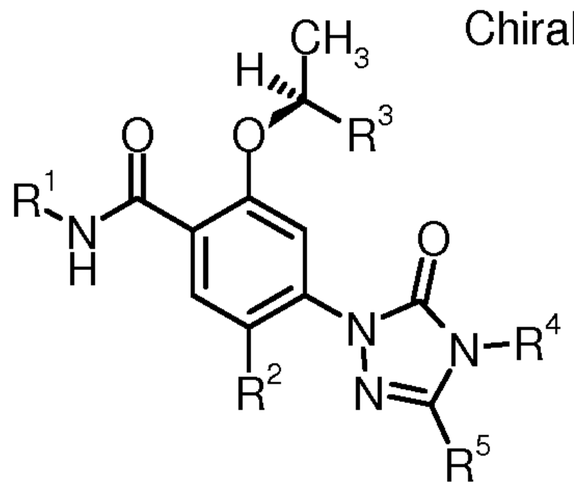
*-CH_2-X^1-CH(OH)-X^3-X^4-#,

*-CH_2-X^1-X^2-CH(OH)-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

by reacting a compound auf general formula (Ia)



(Ia),

in which

R^1, R^2, R^3 are as defined in any one of claims 1-6 and

R^4 and R^5 are linked to one another in such a way that they jointly form a group selected from

*-CH_2-X^1-X^2-#,

*-CH_2-X^1-X^2-X^3-#,

*-CH_2-X^1-X^2-X^3-X^4-#,

and X^1, X^2, X^3 and X^4 are –CH_2-

in which groups "*" represents the point of attachment of R^4 to the rest of the molecule, and "#" represents the point of attachment of R^5 to the rest of the molecule,

with a suitable microorganism, under suitable conditions and in a suitable medium, to form those compounds of general formula (I), as defined supra.

23. A process according to claim 21 or 22, wherein the microorganism is a modified E. coli stem that hosts the genomic sequence Seq. ID No. 1 or Seq. ID No. 2, as defined herein.

24. A process according to claim 21-23 wherein the suitable conditions are aerobic conditions, a temperature range of 20°-30°C and the suitable me dium is a buffer solution, a nutrition solution and optionally a complexing agent.

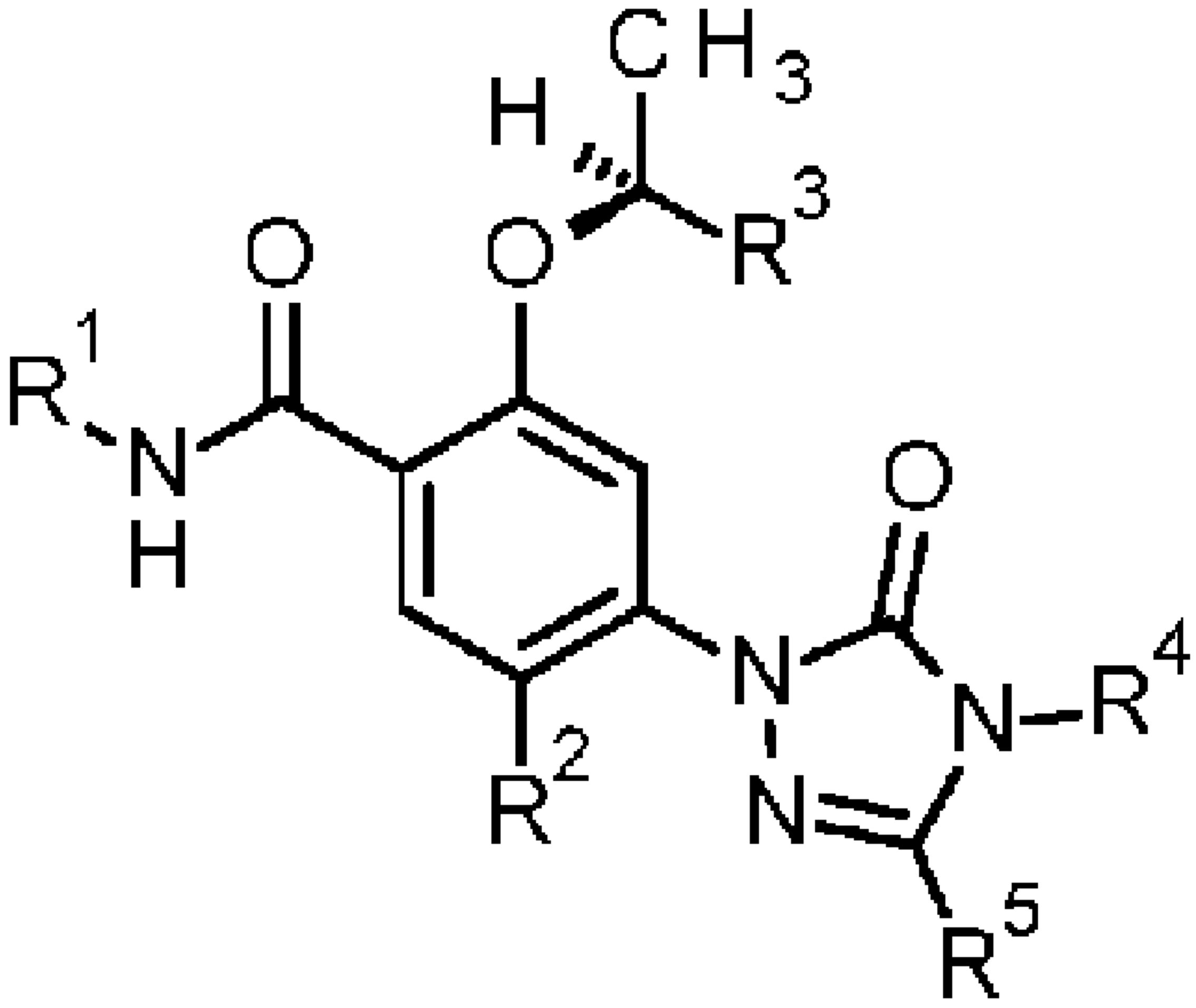
25. A microorganism, preferred E. coli, hosting nucleic acid sequence Seq. ID No. 1.

26. A microorganism, preferred E. coli, hosting nucleic acid sequence Seq. ID No. 2.

27. Use of nucleic acid sequence Seq. ID No. 1 or nucleic acid sequence Seq. ID No. 2

for the preparation of a microorganism suitable for the production of a compound of formula (I) according to claim 1.

28. A compound of formula (I) according to claim 1 obtained by a method according to claims 21-24.



(I)