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(54) **SUBSTITUTED 6,7-DIHYDRO-5H-BENZO[7]ANNULENE DERIVATIVES, PROCESSES FOR THEIR PREPARATION AND THERAPEUTIC USES THEREOF**

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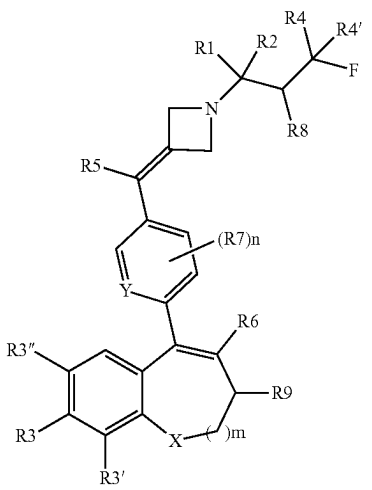
(57) **ABSTRACT**

The present invention relates to compounds of formula (I), or pharmaceutically acceptable salts thereof: (I), wherein R1 and R2 represent hydrogen or deuterium; R3 represents hydrogen, —COOH or —OH; R3' and R3" represent hydrogen, methyl, methoxy, chlorine, fluorine or cyano; R4 and R4' represent hydrogen or fluorine; R5 represents hydrogen, fluorine or ($C_1$-$C_3$)alkyl; R6 represents phenyl, fused phenyl, bicyclic group comprising 5 to 12 carbon atoms, heteroaryl group comprising 2 to 9 carbon atoms and comprising from 1 to 3 heteroatoms, cycloalkyl group comprising 3 to 7 carbon atoms, ($C_3$-$C_6$)cycloalkyl($C_1$-$C_3$)alkyl group, 4 to 7 membered-heterocycloalkyl group comprising 1 or 2 heteroatoms, ($C_1$-$C_6$)alkyl, and phenyl($C_1$-$C_2$)alkyl group; X represents —$CH_2$—, —O— or —S—; Y represents —CH═, —N═ or —CR"═, wherein R" represents ($C_1$-$C_3$)alkyl, halogen, cyano, or ($C_1$-$C_3$)fluoroalkyl; R7 represents ($C_1$-$C_3$)alkyl, halogen atom, cyano, or ($C_1$-$C_3$)fluoroalkyl; R8 represents hydrogen or fluorine; R9 represents hydrogen, ($C_1$-$C_3$)alkyl or a cyclopropyl; n is 0, 1 or 2; and m is 0 or 1. Further disclosed are process for preparing the same, pharmaceutical compositions comprising them as well as said compounds of formula (I) for use as an inhibitor and degrader of estrogen receptors, in particular in the treatment of ovulatory dysfunction, cancer, endometriosis, osteoporosis, benign prostatic hypertrophy or inflammation.

(I)



# SUBSTITUTED 6,7-DIHYDRO-5H-BENZO[7]ANNULENE DERIVATIVES, PROCESSES FOR THEIR PREPARATION AND THERAPEUTIC USES THEREOF

**[0001]** Disclosed herein are novel substituted 6,7-dihydro-5H-benzo[7]annulene derivatives, the processes for their preparation, as well as the therapeutic uses thereof, in particular as anticancer agents via selective antagonism and degradation of estrogen receptors.

**[0002]** The Estrogen Receptors (ER) belong to the steroid/nuclear receptor superfamily involved in the regulation of eukaryotic gene expression, cellular proliferation and differentiation in target tissues. ERs are in two forms: the estrogen receptor alpha (ERα) and the estrogen receptor beta (ERβ) respectively encoded by the ESR1 and the ESR2 genes. ERα and ERβ are ligand-activated transcription factors which are activated by the hormone estrogen (the most potent estrogen produced in the body is 17β-estradiol). In the absence of hormone, ERs are largely located in the cytosol of the cell. When the hormone estrogen binds to ERs, ERs migrate from the cytosol to the nucleus of the cell, form dimers and then bind to specific genomic sequences called Estrogen Response Elements (ERE). The DNA/ER complex interacts with co-regulators to modulate the transcription of target genes.

**[0003]** ERα is mainly expressed in reproductive tissues such as uterus, ovary, breast, bone and white adipose tissue. Abnormal ERα signaling leads to development of a variety of diseases, such as cancers, metabolic and cardiovascular diseases, neurodegenerative diseases, inflammation diseases and osteoporosis.

**[0004]** ERα is expressed in not more than 10% of normal breast epithelium but approximately 50-80% of breast tumors. Such breast tumors with high level of ERα are classified as ERα-positive breast tumors. The etiological role of estrogen in breast cancer is well established and modulation of ERα signaling remains the mainstay of breast cancer treatment for the majority ERα-positive breast tumors. Currently, several strategies for inhibiting the estrogen axis in breast cancer exist, including: 1—blocking estrogen synthesis by aromatase inhibitors that are used to treat early and advanced ERα-positive breast cancer patients; 2—antagonizing estrogen ligand binding to ERα by tamoxifen which is used to treat ERα-positive breast cancer patients in both pre- and post-menopausal setting; 3—antagonizing and downregulating ERα levels by fulvestrant, which is used to treat breast cancer in patients that have progressed despite endocrine therapies such as tamoxifen or aromatase inhibitors.

**[0005]** Although these endocrine therapies have contributed enormously to reduction in breast cancer development, about more than one-third of ERα-positive patients display de novo resistance or develop resistance over time to such existing therapies. Several mechanisms have been described to explain resistance to such hormone therapies. For example, hypersensitivity of ERα to low estrogen level in treatment with aromatase inhibitors, the switch of tamoxifen effects from antagonist to agonist effects in tamoxifen treatments or multiple growth factor receptor signaling pathways. Acquired mutations in ERα occurring after initiation of hormone therapies may also play a role in treatment failure and cancer progression. Certain mutations in ERα, particularly those identified in the Ligand Binding Domain (LBD), result in the ability to bind to DNA in the absence of ligand and confer hormone independence in cells harboring such mutant receptors.

**[0006]** Most of the endocrine therapy resistance mechanisms identified rely on ERα-dependent activity. One of the new strategies to counterforce such resistance is to shut down the ERα signaling by removing ERα from the tumor cells using Selective Estrogen Receptors Degraders (SERDs). Clinical and preclinical data showed that a significant number of the resistance pathways can be circumvented by the use of SERDs.

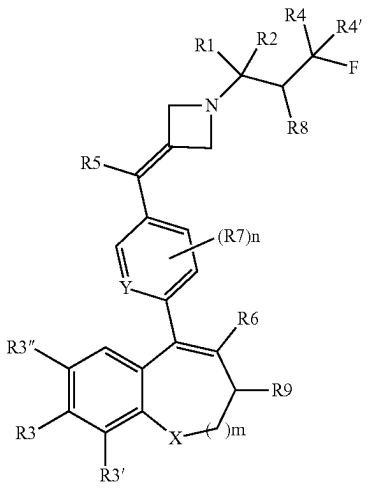
**[0007]** There is still a need to provide SERDs with good degradation efficacy.

**[0008]** Documents WO2017/140669 and WO2018/091153 disclose some substituted 6,7-dihydro-5H-benzo[7]annulene compounds and substituted N-(3-fluoropropyl)-pyrrolidine derivatives useful as SERDs.

**[0009]** The inventors have now found novel compounds able to selectively antagonize and degrade the estrogen receptors (SERDs compounds), for use for example in cancer treatment.

**[0010]** Disclosed herein are compounds of the formula (I), or pharmaceutically acceptable salts thereof:

(I)




wherein:

**[0011]** R1 and R2 independently represent a hydrogen atom or a deuterium atom;

**[0012]** R3 represents a hydrogen atom, a —COOH group or a —OH group;

**[0013]** R3' and R3" independently represent a hydrogen atom, a methyl group, a methoxy group, a chlorine atom, a fluorine atom or a cyano group;

**[0014]** R4 and R4' independently represent a hydrogen atom or a fluorine atom;

**[0015]** R5 represents a hydrogen atom, a fluorine atom or a ($C_1$-$C_3$)alkyl group;

**[0016]** R6 represents a group selected from:

**[0017]** a phenyl group, said phenyl group being optionally substituted by 1 to 3 substituents independently selected from a halogen atom; a ($C_1$-$C_6$)alkyl group, optionally substituted with a cyano group or a —OH group; a ($C_1$-$C_6$)fluoroalkyl group; a ($C_3$-$C_6$)cycloalkyl group; a ($C_1$-$C_6$)alkoxy group; a ($C_1$-

$C_6$)fluoroalkoxy group; a cyano group; a trifluoromethylsulfonyl group; a ($C_1$-$C_4$)alkylthio group; a ($C_1$-$C_4$)fluoroalkylthio group; a ($C_1$-$C_4$)alkylsulfonyl group and a —OH group;

**[0018]** a fused phenyl group, selected from phenyl groups fused with a ($C_3$-$C_6$)cycloalkyl, said ($C_3$-$C_6$)cycloalkyl optionally comprises an unsaturation, and wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group;

**[0019]** a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group;

**[0020]** a bicyclic group comprising 5 to 12 carbon atoms, optionally comprising 1 to 2 unsaturations; optionally substituted with 1 to 4 substituents independently selected from: a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group and an oxo group;

**[0021]** a heteroaryl group comprising 2 to 9 carbon atoms and comprising from 1 to 3 heteroatoms independently selected from oxygen, nitrogen and sulfur, and at least 5 atoms including carbon atoms and heteroatoms, such as a pyridyl group, said heteroaryl group being optionally substituted with 1 to 3 substituents independently selected from a halogen atom, a ($C_1$-$C_6$)alkyl group, a ($C_1$-$C_6$)fluoroalkyl group, a ($C_1$-$C_6$)alkoxy group, a ($C_1$-$C_6$)fluoroalkoxy group, a cyano group, a carbamoyl group and a —OH group;

**[0022]** a cycloalkyl group comprising 3 to 7 carbon atoms, said cycloalkyl group being saturated or partially saturated and being optionally substituted with 1 to 4 substituents independently selected from:

**[0023]** a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group, an oxo group,

**[0024]** a ($C_3$-$C_6$)cycloalkyl group and a phenyl group, said ($C_3$-$C_6$)cycloalkyl or phenyl groups being optionally substituted with one or two halogen atom(s) or ($C_1$-$C_3$)alkyl group(s);

**[0025]** a ($C_3$-$C_6$)cycloalkyl($C_1$-$C_3$)alkyl group, optionally substituted on the cycloalkyl with 1 to 4 substituents independently selected from: a fluorine atom, a —OH group, a ($C_1$-$C_4$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)fluoroalkoxy group and an oxo group;

**[0026]** a 4 to 7 membered-heterocycloalkyl group comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulfur, such as a tetrahydropyranyl group, said heterocycloalkyl group being saturated or partially saturated and being optionally substituted with 1 to 3 substituents independently selected from: a fluorine atom, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)fluoroalkoxy group, an oxo group, a ($C_1$-$C_3$)alkoxy group, and a —OH group;

**[0027]** a ($C_1$-$C_6$)alkyl group, such as an isobutyl group, a methyl group or an ethyl group, said alkyl group being optionally substituted with 1 to 4 substituents independently selected from: a fluorine atom, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group and a —OH group; and

**[0028]** a phenyl($C_1$-$C_2$)alkyl group, said phenyl group being optionally substituted with 1 to 3 substituents independently selected from a halogen atom; a ($C_1$-$C_3$)alkyl group; a ($C_1$-$C_3$)fluoroalkyl group; a ($C_1$-$C_3$)alkoxy group; a ($C_1$-$C_3$)fluoroalkoxy group; a cyano group; and a —OH group;

**[0029]** X represents —$CH_2$—, —O— or —S—;

**[0030]** Y represents —CH═, —N═ or —CR"═, wherein R" represents a ($C_1$-$C_3$)alkyl group, a halogen atom, such as a fluorine or a chlorine atom, a cyano group, or a ($C_1$-$C_3$)fluoroalkyl group, such as trifluoromethyl;

**[0031]** R7 independently represents a ($C_1$-$C_3$)alkyl group such as methyl, a halogen atom such as a fluorine atom, a cyano group, or a ($C_1$-$C_3$)fluoroalkyl group such as trifluoromethyl;

**[0032]** R8 represents a hydrogen atom or a fluorine atom;

**[0033]** R9 represents a hydrogen atom, a ($C_1$-$C_3$)alkyl group or a cyclopropyl;

**[0034]** n is 0, 1 or 2; and

**[0035]** m is 0 or 1.

**[0036]** The compounds of formula (I) can contain one or more asymmetric carbon atoms. They may therefore exist in the form of enantiomers.

**[0037]** The compounds of formula (I) may be present as well under tautomer forms.

**[0038]** The compounds of formula (I) may exist in the form of bases, acids, zwitterion or of addition salts with acids or bases. Hence, herein are provided compounds of formula (I) or pharmaceutically acceptable salts thereof.

**[0039]** These salts may be prepared with pharmaceutically acceptable acids or bases, although the salts of other acids or bases useful, for example, for purifying or isolating the compounds of formula (I) are also provided.

**[0040]** Among suitable salts of the compounds of formula (I), hydrochloride may be cited.

**[0041]** As used herein, the terms below have the following definitions unless otherwise mentioned throughout the instant specification:

**[0042]** a halogen atom: a fluorine, a chlorine, a bromine or an iodine atom, and in particular a fluorine and a chlorine atom;

**[0043]** an oxo: a "═O" group;

**[0044]** an alkyl group: a linear or branched saturated hydrocarbon-based aliphatic group comprising, unless otherwise mentioned, from 1 to 6 carbon atoms (noted "($C_1$-$C_6$)alkyl"). By way of examples, mention may be made of, but not limited to: methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, hexyl and isohexyl groups, and the like;

**[0045]** a cycloalkyl group: a monocyclic alkyl group comprising, unless otherwise mentioned, from 3 to 7 carbon atoms, saturated or partially unsaturated and unsubstituted or substituted. By way of examples, mention may be made of, but not limited to: cyclopro-

pyl, cyclobutyl, cyclopentyl, cyclobutenyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl and cycloheptenyl groups and the like, in particular a cyclopentyl, a cyclohexyl or a cyclohexenyl;

**[0046]** a cycloalkylalkyl group: an alkyl group substituted with a cyclic alkyl group as defined above. Mention may be made of, but not limited to: cyclobutylmethyl;

**[0047]** a heterocycloalkyl group: a 4 to 7-membered cycloalkyl group or in particular a 4 to 6-membered cycloalkyl, saturated or partially unsaturated, comprising 1 to 2 heteroatoms independently selected from oxygen, nitrogen and sulfur, in particular being oxygen or nitrogen. By way of examples, mention may be made of, but not limited to: morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, aziridinyl, oxanyl, oxetanyl, tetrahydropyranyl, morpholinyl, tetrahydrofuranyl, oxepanyl, diazepanyl, dioxanyl, tetrahydropyranyl and tetrahydrothiopyranyl. The heterocycloalkyl is advantageously tetrahydropyranyl.

**[0048]** a fluoroalkyl group: an alkyl group as previously defined where the alkyl group is substituted with at least one fluorine atom. In other terms, at least one hydrogen atom of the alkyl group is replaced by a fluorine atom. By way of example, mention may be made of $—CH_2F$, $—CHF_2$, $—CH_2CHF_2$, $—CH_2CH_2F$ and the like. When all the hydrogen atoms belonging to the alkyl group are replaced by fluorine atoms, the fluoroalkyl group can be named perfluoroalkyl group. By way of example, mention may be made of trifluoromethyl group or trifluoroethyl group and the like, and in particular trifluoromethyl group;

**[0049]** an alkoxy group: an —O-alkyl group where the alkyl group is as previously defined. By way of examples, mention may be made of, but not limited to: methoxy, ethoxy, propoxy, isopropoxy, linear, secondary or tertiary butoxy, isobutoxy, pentoxy or hexoxy groups, and the like;

**[0050]** a fluoroalkoxy group: an —O-alkyl group where the alkyl group is as previously defined and where the alkyl group is substituted with at least one fluorine atom. In other terms, at least one hydrogen atom of the alkyl group is replaced by a fluorine atom. By way of example, mention may be made of $—OCH_2F$, $—OCHF_2$, $—OCH_2CH_2F$ and the like. When all the hydrogen atoms belonging to the alkyl group are replaced by fluorine atoms, the fluoroalkoxy group can be named perfluoroalkoxy group. By way of example, mention may be made of trifluoromethoxy group and the like;

**[0051]** a $(C_1$-$C_4)$alkylthio group also named $(C_1$-$C_4)$ alkylsulfanyl: a —S-alkyl group where the alkyl group is as previously defined. By way of examples, mention may be made of, but not limited to: methylthio, ethylthio, propylthio, isopropylthio, linear, secondary or tertiary butylthio, isobutylthio, and the like;

**[0052]** a $(C_1$-$C_4)$alkylsulfonyl group: a $—SO_2$-alkyl group where the alkyl group is as previously defined. By way of examples, mention may be made of, but not limited to: $—SO_2CH_3$, $—SO_2CH_2CH_3$ and the like;

**[0053]** $(C_1$-$C_4)$fluoroalkylthio group also named a $(C_1$-$C_4)$fluoroalkylsulfanyl group: a —S-fluoroalkyl group where the fluoroalkyl group is as previously defined. By way of examples, mention may be made of, but not limited to: fluoromethylthio, difluoromethylthio, trifluoromethylthio and the like;

**[0054]** a fused phenyl group: a bicyclic radical comprising from 8 to 10 carbon atoms and that contains a phenyl moiety. Said phenyl moiety may be fused to a $(C_3$-$C_6)$cycloalkyl group, i.e. the phenyl moiety may share a bond with said $(C_3$-$C_6)$cycloalkyl group. The fused phenyl group may be bound to the rest of the molecule by its phenyl moiety. It may be substituted. Examples are, but not limited to, indanyl, bicyclo[4.2.0]octa-1(6),2,4-trienyl, tetrahydronaphthalenyl and the like;

**[0055]** a phenyl group fused with a hetero$(C_4$-$C_6)$cycloalkyl: a bicyclic radical comprising from 7 to 10 carbon atoms and that contains a phenyl moiety. Said phenyl moiety may be fused to a hetero$(C_4$-$C_6)$cycloalkyl group, i.e. the phenyl moiety may share a bond with said hetero$(C_4$-$C_6)$cycloalkyl group. The fused phenyl group may be bound to the rest of the molecule by its phenyl moiety. It may be substituted. Examples are, but are not limited to a chromanyl group, in particular a chroman-8-yl group and the like;

**[0056]** a heteroaryl group: a 5 to 10-membered cyclic aromatic group containing between 2 and 9 carbon atoms and containing between 1 and 3 heteroatoms, such as nitrogen, oxygen or sulfur. Such nitrogen atom may be substituted with an oxygen atom in order to form a —N—O bond. Such —N—O bond can be in a form of a N-oxide (—N+—O—). Said heteroaryl group may be monocyclic or bicyclic. By way of examples of heteroaryl groups, mention may be made of, but not limited to: thiophene, furan, thiadiazole, thiazole, imidazole, pyridazine, triazine, pyrazine, oxadiazole, pyrazole, isothiazole, oxazole, isoxazole, pyridine, pyrimidine, benzotriazole, benzoxazole, pyrrolo[2,3-b] pyridine, benzimidazole, benzoxadiazole, benzothiazole, benzothiadiazole, benzofuran, indole, isoquinoline, indazole, benzisoxazole, benzisothiazole, pyridone groups and the like. The heteroaryl is advantageously pyridine, pyrrole, imidazole, pyrazine, furane, thiazole, pyrazole, thiadiazole, pyridazine, pyridone and pyrimidine, and more particularly pyridine;

**[0057]** a bicyclic group, generally comprising 5 to 12 carbon atoms, is a hydrocarbon group selected from groups comprising two rings connected through:

**[0058]** a single common atom: a "spirobicyclic ring". Such spiro bicyclic alkyl generally comprises 5 to 11 carbon atoms referring to a "spiro$(C_5$-$C_{11})$bicyclic ring". The rings may be saturated or partially unsaturated. Such spirobicyclic ring may be unsubstituted or substituted, in particular by at least one $(C_1$-$C_3)$ alkyl group such as methyl or a fluorine. By way of examples of spiro$(C_5$-$C_{11})$bicyclic ring as for the definition of R6, mention may be made of, but not limited to: spiro[2.3]hexane, spiro[3.3]heptane, spiro [3.3]heptene, spiro[2.5]octane and 7-azaspiro[3.5] nonane. The spiro$(C_5$-$C_{11})$bicyclic ring is advantageously spiro[2.3]hexane, spiro[3.3]heptane or spiro [3.3]heptene still for the R6 group;

**[0059]** two common atoms. In that case the bicyclic group comprises 7 to 12 carbon atoms and optionally comprises 1 to 2 unsaturations. By way of examples of such bicyclic groups, mention may be made of, but not limited to: cis-1,3a,4,5,6,6a-hexahydropen-

talenyl group, bicyclo[3.1.0]hexan-1-yl, bicyclo[4.1.0]heptanyl and octahydropentalenyl,

**[0060]** three or more common atoms. In that case the bicyclic group comprises 6 to 10 carbon atoms, such bicyclic group may be referred to as a "bridged ($C_6$-$C_{10}$)cycloalkyl" group, the rings share three or more atoms and the bridge contains at least one atom, for example 1, 2 or 3 atoms and preferentially 1 atom. By way of examples of such bridged cycloalkyl groups, mention may be made of, but not limited to bicyclo[3.2.1]octan-3-yl and bicyclo[2.2.1]heptan-2-yl.

**[0061]** a zwitterion means: a globally neutral molecule with a positive and a negative electrical charge and having an acidic group and a basic group.

**[0062]** In another embodiment, in the compounds of formula (I) as defined above, R1 and R2 are a hydrogen atom.

**[0063]** In another embodiment, in the compounds of formula (I) as defined above, R3 is —COOH.

**[0064]** In another embodiment, in the compounds of formula (I) as defined above, R3' and R3" represent a hydrogen atom.

**[0065]** In another embodiment, in the compounds of formula (I) as defined above, X represents —$CH_2$—.

**[0066]** In another embodiment, in the compounds of formula (I) as defined above, R4 and R4' represent a hydrogen atom.

**[0067]** In another embodiment, in the compounds of formula (I) as defined above, R5 represents a hydrogen atom.

**[0068]** In another embodiment, in the compounds of formula (I) as defined above, R5 represents a hydrogen atom, a —$NH_2$ group, a methyl group, a methoxy group, an ethoxy group.

**[0069]** In another embodiment, in the compounds of formula (I) as defined above, R6 represents a phenyl group, said phenyl group being optionally substituted with 1 to 3 substituents independently selected from a chlorine atom, a fluorine atom, a methyl group, an ethyl group, a trifluoromethyl group, a cyclopropyl group, a methoxy group, a trifluoromethoxy group, a 1,1-difluoroethyl group, a difluoromethyl group, a difluoromethoxy group, a fluoromethyl group and a cyano group.

**[0070]** In another embodiment, in the compounds of formula (I) as defined above, R6 represents a fused phenyl group, selected from a bicyclo[4.2.0]octatrienyl group, an indanyl group or a tetrahydronaphthalenyl group, optionally substituted with one or two fluorine atom or R6 represents a chromanyl group.

**[0071]** In another embodiment, in the compounds of formula (I) as defined above, R6 represents a bicyclic group selected from a bicyclo[4.1.0]heptanyl, a bicyclo[3.1.0]hexanyl, a spiro[2.3]hexanyl and a bicyclo[3.2.1]octan-3-yl, optionally substituted with 1 to 4 substituents independently selected from: a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group and an oxo group; advantageously said bicyclic group is unsubstituted.

**[0072]** In another embodiment, in the compounds of formula (I) as defined above, R6 represents a cycloalkyl chosen from a cyclohexyl or a cyclopropyl group, said cycloalkyl being optionally substituted with 1 to 4 substituents independently selected from:

**[0073]** a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group, an oxo group

**[0074]** a ($C_3$-$C_6$)cycloalkyl group and a phenyl group said ($C_3$-$C_6$)cycloalkyl or phenyl group being optionally substituted with one or two halogen atom(s) or ($C_1$-$C_3$)alkyl group(s),

said cycloalkyl being advantageously substituted with 1 to 2 substituents independently selected from:

**[0075]** a methyl group, a phenyl group and

**[0076]** a cyclohexyl group substituted by two halogen atoms, in particular fluor atoms.

**[0077]** In another embodiment, in the compounds of formula (I) as defined above, R7 independently represents a methyl group, a cyano group, a trifluoromethyl group or a fluorine atom and n is 0, 1 or 2.

**[0078]** In another embodiment, in the compounds of formula (I) as defined above, Y represents —CH═, —N═ or —CR"═, R" representing a fluorine atom, a cyano group, or a trifluoromethyl group.

**[0079]** In another embodiment, in the compounds of formula (I) as defined above, m is 1.

**[0080]** In another embodiment, in the compounds of formula (I) as defined above, R6 represents a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group.

**[0081]** In another embodiment, in the compounds of formula (I) as defined above, R6 represents a phenyl group, said phenyl group being optionally substituted by 1 to 3 substituents independently selected from a halogen atom; a ($C_1$-$C_6$)alkyl group, optionally substituted with a cyano group or a —OH group; a ($C_1$-$C_6$)fluoroalkyl group; a ($C_3$-$C_6$)cycloalkyl group; a ($C_1$-$C_6$)alkoxy group; a ($C_1$-$C_6$)fluoroalkoxy group; a cyano group; a trifluoromethylsulfonyl group; a ($C_1$-$C_4$)alkylthio group; a ($C_1$-$C_4$)fluoroalkylthio group; a ($C_1$-$C_4$)alkylsulfonyl group and a —OH group; wherein said phenyl is substituted by at least one trifluoromethoxy group, by at least one 1,1-difluoroethyl group, by at least one difluoromethyl group, by at least one difluoromethoxy group or by at least one fluoromethyl group.

**[0082]** In another embodiment, in the compounds of formula (I) as defined above, R3 is a COOH group and R6 is a phenyl group, said phenyl group being optionally substituted with 1 to 3 substituents independently selected from a chlorine atom, a fluorine atom, a methyl group, an ethyl group, a trifluoromethyl group, a cyclopropyl group, a methoxy group, a trifluoromethoxy group, a 1,1-difluoroethyl group, a difluoromethyl group, a difluoromethoxy group, a fluoromethyl group and a cyano group, wherein said phenyl is substituted by at least one trifluoromethoxy group, by at least one 1,1-difluoroethyl group, by at least one difluoromethyl group, by at least one difluoromethoxy group or by at least one fluoromethyl group. In such embodiment, R3' and R3" are in particular hydrogen atoms. Still in such embodiment, R1, R2, R4, R4', R5, R8 and R9 are hydrogen atoms. In such embodiment, Y is a —CH═ group, m is equal to 1 and n is equal to 0. Still in such embodiment, X is a —$CH_2$— group.

**[0083]** Among the compounds of formula (I) described herein, mention may be made in particular of the following

compounds or a pharmaceutically acceptable salt thereof, in particular hydrochloride salt thereof:

**[0084]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-6-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (1)

**[0085]** 8-(3,4-difluoro-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (2)

**[0086]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (3)

**[0087]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-6-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (4)

**[0088]** 8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (5)

**[0089]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-6-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (6)

**[0090]** 8-(3-fluoro-2-methoxy-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (7)

**[0091]** 8-(3-ethyl-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (8)

**[0092]** 8-(2-fluoro-6-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (9)

**[0093]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-mesityl-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (10)

**[0094]** 8-(2-chloro-4,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (11)

**[0095]** 8-(3-fluoro-2,4-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (12)

**[0096]** 8-(3-chloro-2,4-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (13)

**[0097]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4,6-dimethylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (14)

**[0098]** 8-(2-(1,1-difluoroethyl)-4-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (15)

**[0099]** 8-(2-chloro-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (16)

**[0100]** 8-(2-chloro-6-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (17)

**[0101]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4-methoxy-2,6-dimethylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (18)

**[0102]** 8-(4-ethyl-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (19)

**[0103]** 8-(2-fluoro-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (20)

**[0104]** 8-(2-chloro-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (21)

**[0105]** 8-(2-fluoro-6-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (22)

**[0106]** 8-(2-chloro-6-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (23)

**[0107]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-3-(trifluoromethoxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (24)

**[0108]** 8-(2-ethyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (25)

**[0109]** 8-(2-fluoro-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (26)

**[0110]** 8-(4-fluoro-2,5-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (27)

**[0111]** 8-(4-(difluoromethyl)-3-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (28)

**[0112]** 8-(4-(difluoromethyl)-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (29)

**[0113]** 8-(2-(difluoromethyl)-3-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (30)

**[0114]** 8-(4-(difluoromethyl)-3-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (31)

**[0115]** 8-(2-(fluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (32)

**[0116]** 8-(2-(difluoromethoxy)-3-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (33)

**[0117]** 8-(3-chloro-2-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (34)

**[0118]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1, (35)

**[0119]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2, (36)

**[0120]** 8-(2-(difluoromethyl)-4-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (37)

**[0121]** 8-(3-fluoro-2-(fluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (38)

**[0122]** 8-(2-ethyl-3-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (39)

**[0123]** 8-(3-fluoro-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (40)

**[0124]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(3-methoxy-2-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (41)

**[0125]** 8-(3-chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-ol, (42)

**[0126]** 8-(2-(difluoromethyl)-4-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (43)

**[0127]** 8-(4-(difluoromethyl)-2-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (44)

**[0128]** 8-(2-(difluoromethyl)-5-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (45)

**[0129]** 8-(3-chloro-2-ethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (46)

**[0130]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(5-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (47)

**[0131]** 8-(2-cyclopropyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (48)

**[0132]** 8-(3-chloro-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (49)

**[0133]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(3-methoxy-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (50)

**[0134]** 8-(4-(difluoromethyl)-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (51)

**[0135]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(3-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (52)

**[0136]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(3-methyl-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (53)

**[0137]** 8-(4-(difluoromethyl)-2-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (54)

**[0138]** 8-(4-(difluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (55)

**[0139]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(trans-4-methylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (56)

**[0140]** 8-(2-(difluoromethyl)-5-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (57)

**[0141]** 8-(2-(difluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (58)

**[0142]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(2-methoxy-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (59)

**[0143]** 8-(2-(difluoromethyl)-3-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (60)

**[0144]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(cis-4-methylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (61)

**[0145]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(4-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (62)

**[0146]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)phenyl)-8-(2-methoxy-3-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (63)

**[0147]** 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (64)

**[0148]** 8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (65)

**[0149]** 9-(5-((1-(3,3-difluoropropyl)azetidin-3-ylidene) methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (66)

**[0150]** 8-(chroman-8-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (67)

**[0151]** 8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (68)

**[0152]** 8-(2,4-dichlorophenyl)-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1, (69)

**[0153]** 8-(2,4-dichlorophenyl)-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2, (70)

**[0154]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4,6-bis(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (71)

**[0155]** 8-(2,4-dimethyl-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (72)

**[0156]** 8-(3-fluoro-2-methyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (73)

**[0157]** 8-(2,6-diethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (74)

**[0158]** 8-(3-fluoro-2,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (75)

**[0159]** 8-(2-fluoro-4,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (76)

**[0160]** 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-6-(trifluoromethoxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (77)

**[0161]** 8-(2,5-dimethyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (78)

**[0162]** 8-(2,3-bis(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (79)

**[0163]** 8-(2,6-diethyl-4-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (80)

**[0164]** 8-(2,3-dimethoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (81)

**[0165]** 8-(3,4-dimethoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (82)

**[0166]** 8-(4-chloro-2-methoxy-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (83)

**[0167]** 8-(2,6-dimethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (84).

**[0168]** Another embodiment is a compound selected from the above list, or a pharmaceutically acceptable salt thereof, for use in therapy, especially as an inhibitor and degrader of estrogen receptors.

**[0169]** Another embodiment is a compound selected from the above list, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer, especially breast cancer.

**[0170]** Another embodiment is a method of inhibiting and degrading estrogen receptors, comprising administering to a subject in need thereof, in particular a human, a therapeutically effective amount of a compound selected from the above list, or a pharmaceutically acceptable salt thereof.

**[0171]** Another embodiment is a method of treating ovulatory dysfunction, cancer, endometriosis, osteoporosis, benign prostatic hypertrophy or inflammation, comprising administering to a subject in need thereof, in particular a human, a therapeutically effective amount of a compound selected from the above list, or a pharmaceutically acceptable salt thereof.

**[0172]** Another embodiment is a method of treating cancer, comprising administering to a subject in need thereof, in particular a human, a therapeutically effective amount of a compound selected from the above list, or a pharmaceutically acceptable salt thereof.

**[0173]** Another embodiment is a pharmaceutical composition comprising as active principle an effective dose of a compound selected from the above list, or a pharmaceutically acceptable salt thereof, and also at least one pharmaceutically acceptable excipient.

**[0174]** The compounds of the formula (I) can be prepared by the following processes.

**[0175]** The compounds of the formula (I) and other related compounds having different substituents are synthesized using techniques and materials described below or otherwise known by the skilled person in the art. In addition, solvents, temperatures and other reaction conditions presented below may vary as deemed appropriate to the skilled person in the art.

**[0176]** General below methods for the preparation of compounds of formula (I) optionally modified by the use of appropriate reagents and conditions for the introduction of the various moieties found in the formula (I) as described below.

**[0177]** The following abbreviations and empirical formulae are used:

| | |
|---|---|
| MeCN | Acetonitrile |
| $NH_4Cl$ | Ammonium chloride |
| BuLi | Butyl lithium |
| CO | Carbon monoxide |
| $Cs_2CO_3$ | Cesium carbonate |
| DBU | 1,8-Diazabicyclo[5.4.0]undec-7-ene |
| DCM | Dichloromethane |
| $Et_2O$ | Diethyl ether |
| DIEA | Diisopropylethylamine |
| DMF | N,N-dimethylformamide |
| DMSO | Dimethyl sulfoxide |
| Dppf | 1,1'-Bis(diphenylphosphino)ferrocene |
| EtOH | Ethanol |
| EtOAc | Ethyl acetate |
| h | hour |
| $H_2$ | Hydrogen |
| HCl | Hydrochloric acid |
| HPLC | High performance liquid chromatography |
| LiOH | Lithium hydroxide |
| LiHMDS | Lithium hexamethyldisilazane |
| MeOH | Methanol |
| $MgSO_4$ | Magnesium sulfate |
| MTBE | Methyl tert-butyl ether |
| MeTHF | 2-Methyltetrahydrofuran |
| min | minute |
| n-BuLi | n-Butyllithium |
| $P_2O_5$ | Phosphorus pentoxide |
| Pd/C | Palladium on carbon |
| KOAc | Potassium acetate |

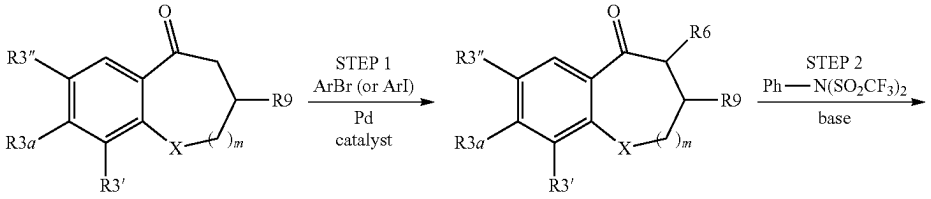
-continued

| | |
|---|---|
| $K_2CO_3$ | Potassium carbonate |
| KHMDS | Potassium hexamethyldisilazane |
| KOH | Potassium hydroxide |
| $NaBH_4$ | Sodium borohydride |
| $NaHCO_3$ | Sodium bicarbonate |
| NaH | Sodium hydride |
| NaOH | Sodium hydroxide |
| $Na_2SO_4$ | Sodium sulfate |
| $NaHSO_3$ | Sodium bisulfate |
| SCX | Strong cation exchange |
| $Pd(dppf)Cl_2$ | [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) |

-continued

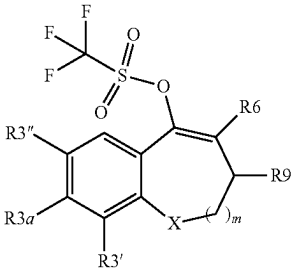
| | |
|---|---|
| $Pd(PPh_3)_2Cl_2$ | bis (triphenylphosphine) palladium(II) dichloride |
| $Pd(PPh_3)_4$ | tetrakis(triphenylphosphine)palladium(0) |
| $Pd_2(dba)_3$ | tris(dibenzylideneacetone)dipalladium(0) |
| PhOK | Potassium phenolate |
| SFC | Supercritical Fluid Chromatography |
| TEA | Triethylamine |
| TFA | Trifluoroacetic acid |
| THF | Tetrahydrofuran |
| $PPh_3$ | Triphenylphosphine |
| RT | Room temperature |
| Ar | Argon |
| DABCO | 1, 4-diazabicyclo[2.2.2]octane |

SCHEME 1a - Part-1:
Preparation of compounds of the formula (I) - General process

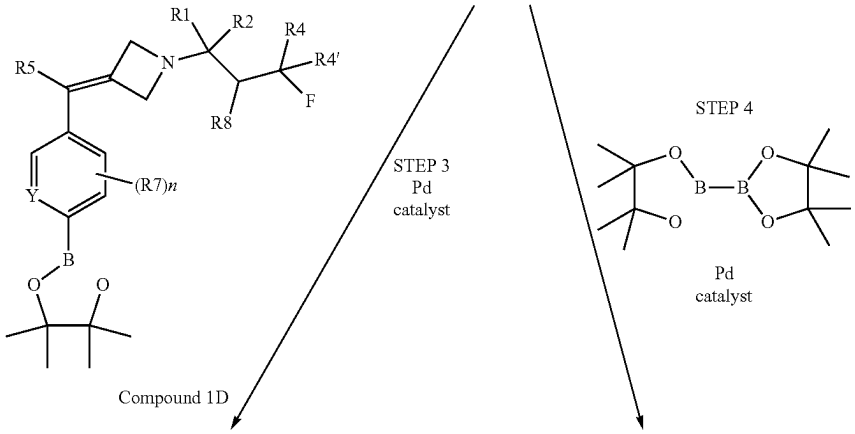



Compound 1A

Compound 1B

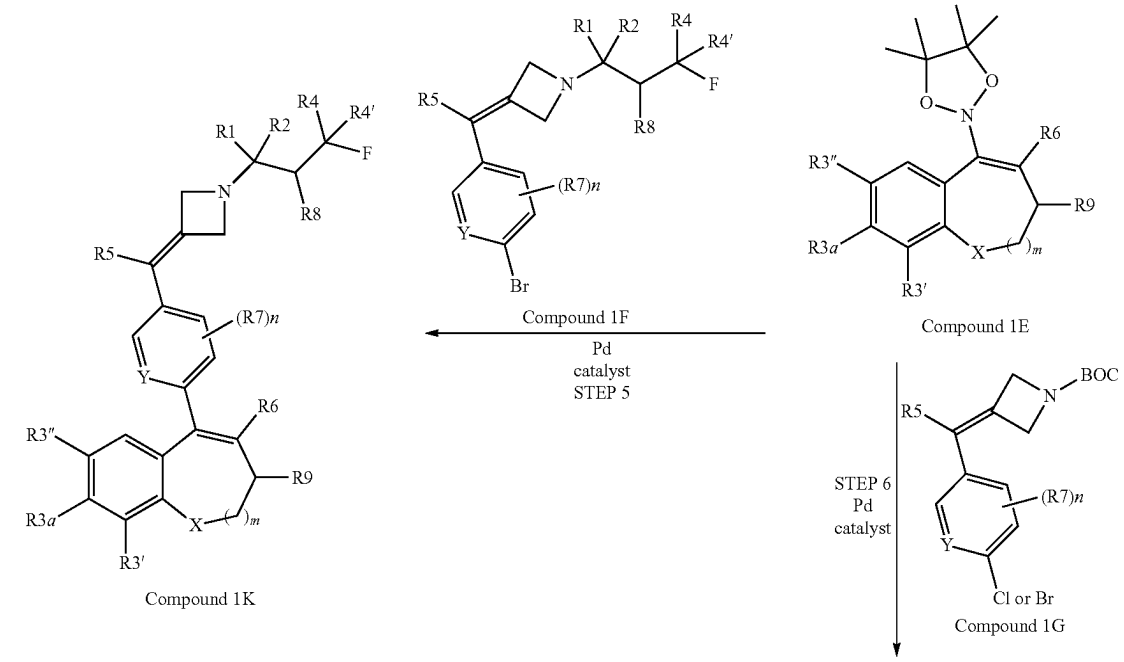


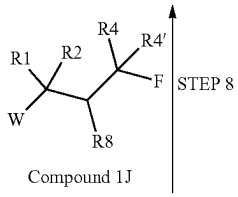

Compound 1C

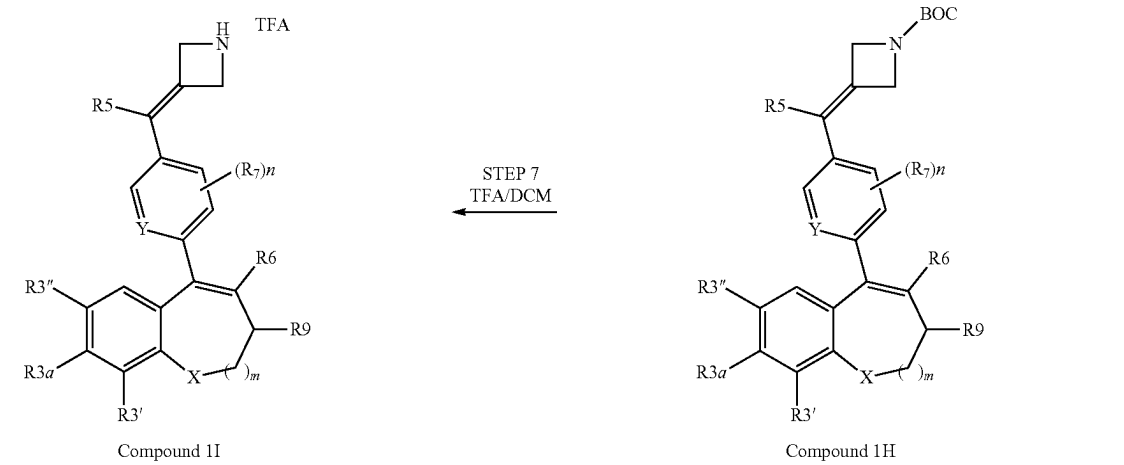



Compound 1D

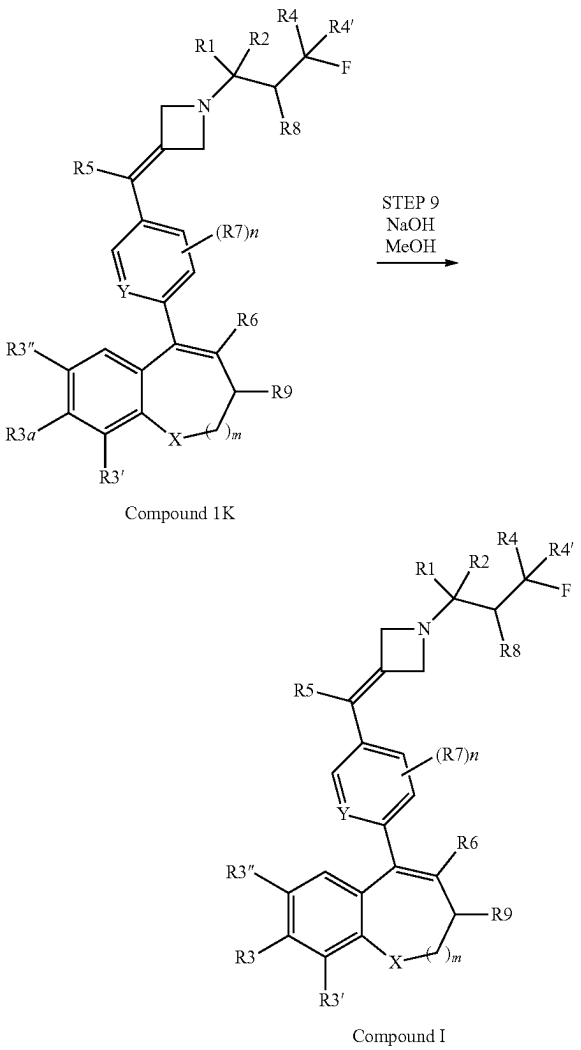
-continued


Compound 1K
Compound 1F
Pd
catalyst
STEP 5
Compound 1E
STEP 6
Pd
catalyst
Compound 1G


STEP 8
Compound 1J


TFA
STEP 7
TFA/DCM
Compound 1I
Compound 1H

SCHEME 1a - Part-2




**[0178]** According to SCHEME 1a—Part-1 and Part-2, in which R3a is H or a carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, and R9 is a hydrogen atom, R1, R2, R3, R3', R3", R4, R4', R5, R6, R7, R8, X, m, n and Y are as defined above, compound 1A can be converted in STEP 1 to compound 1B by treatment with aryl or heteroaryl bromide or iodide in the presence of a palladium catalyst, for example tris(dibenzylideneacetone) dipalladium(0) $Pd_2(dba)_3$, and a phosphine such as (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane) (XANTPHOS) in solution in toluene by heating up to reflux of solvent, in presence of a base such as $K_2CO_3$ or $Cs_2CO_3$. Alternative way to prepare compound 1B, wherein R6 can be any of the groups defined above for R6 in formula (I), is described in SCHEME 1e below.

**[0179]** Compound 1B can be converted in STEP 2 to compound 1C by treatment with N,N-bis(trifluoromethylsulfonyl)aniline in the presence of base such as DBU or NaH, or KHMDS at −50° C., in a solvent such as MeTHF.

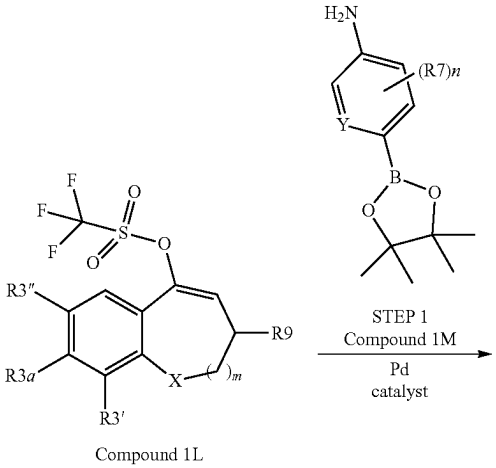
**[0180]** Compound 1C, can be converted in STEP 4 to compound 1E by treatment for example with bis(pinacolato) diboron, and with a palladium catalyst, for example bis (triphenylphosphine) palladium(II) dichloride $Pd(PPh_3)_2Cl_2$, and a phosphine, such as triphenylphosphine, in solution in toluene by heating up to reflux of solvent, in presence of a base such as KOPh.

**[0181]** Compound 1K can be prepared in a Suzuki coupling reaction either between compounds 1C and 1D in STEP 3 or between compounds 1E and 1F in STEP 5 using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) ($Pd(dppf)Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent.

**[0182]** Alternatively, compound 1E can be converted in STEP 6 to compound 1H in a Suzuki coupling reaction with compound 1G using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) ($Pd(dppf)Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent. Compound 1H can be converted in STEP 7 to compound 11 by treatment with TFA in solution in DCM or HCl in solution in dioxane. Compound 1I can be converted in STEP 8 to compound 1K by treatment with compound 1J, wherein W is Br, I or $OSO_2R$ with R=$CH_3$, PhMe, $CF_3$ or $CF_2CF_2CF_2CF_3$, in presence of a base such as potassium carbonate in DMF at 70° C. or in presence of sodium hydroxide or potassium hydroxide in THF at room temperature or in presence of aqueous sodium hydroxide in DCM at room temperature.

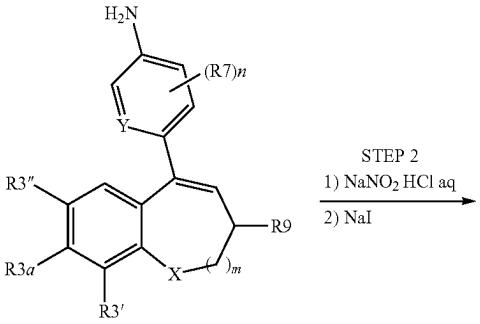
**[0183]** When R3a is COOMe, COOEt, or a protected OH such as O-pivaloyl, compound 1K can be deprotected into compound I in STEP 9 by treating with an aqueous solution of sodium hydroxide (NaOH) or lithium hydroxide (LiOH), in MeOH. When R3 is COOH, extraction of compound can give the sodium salt of compound I. The acidification with an aqueous solution of HCl 2N to pH 6-7 can give the neutral form. The acidification with an aqueous solution of HCl 2N to pH 1-2 can give the hydrochloride salt. The purification using HPLC can give the formate or trifluoroacetate salt.

SCHEME 1b - Part 1:
Preparation of compounds of the formula (I) - General process



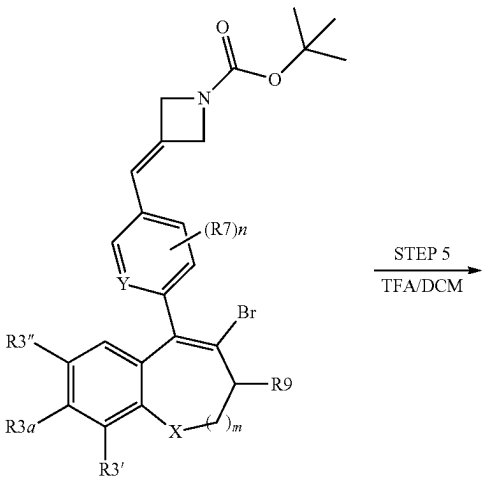

Compound 1L

-continued

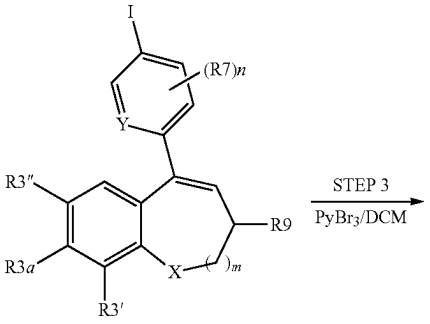



Compound 1N

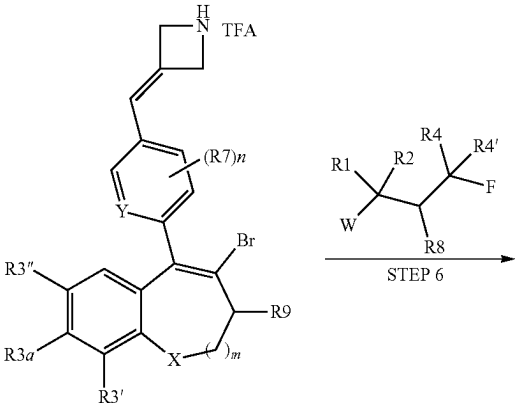
-continued



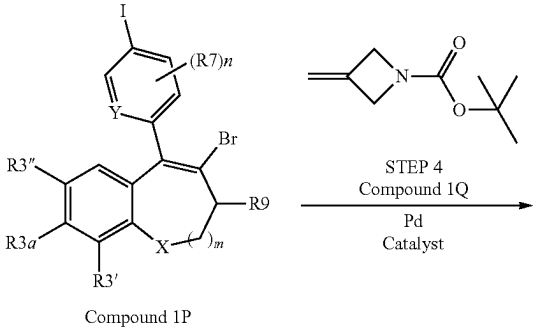

Compound 1R



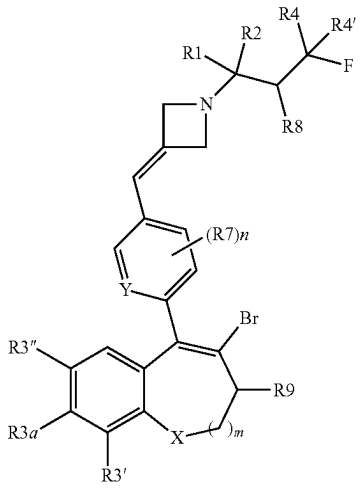

Compound 1O




Compound 1S

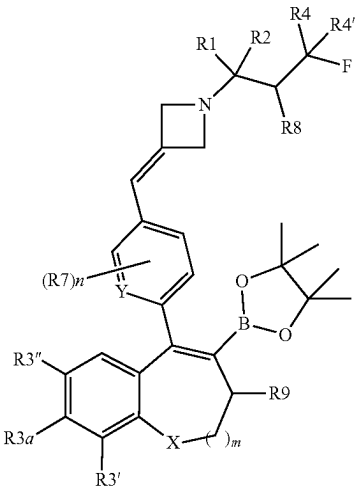



Compound 1P

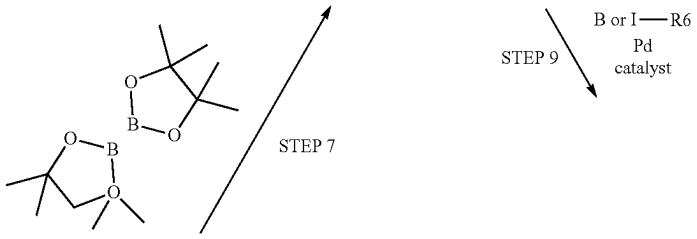


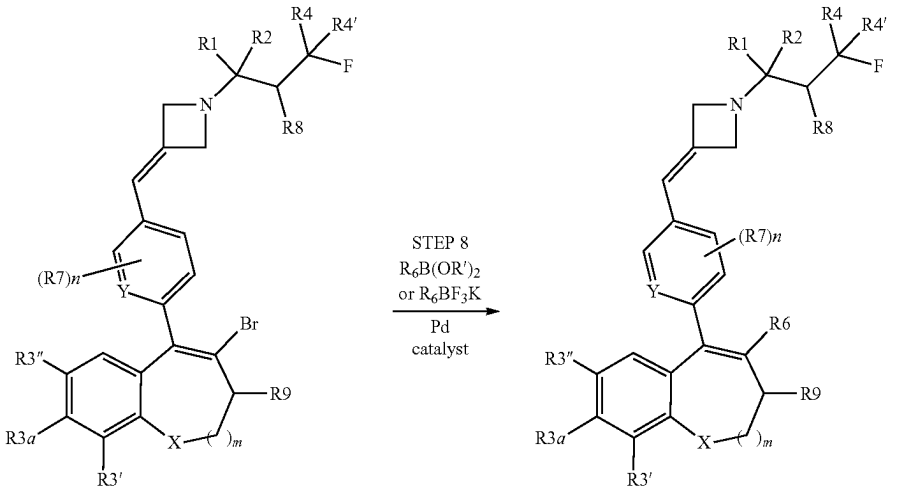

Compound 1T

SCHEME 1b - Part 2



Compound 1U

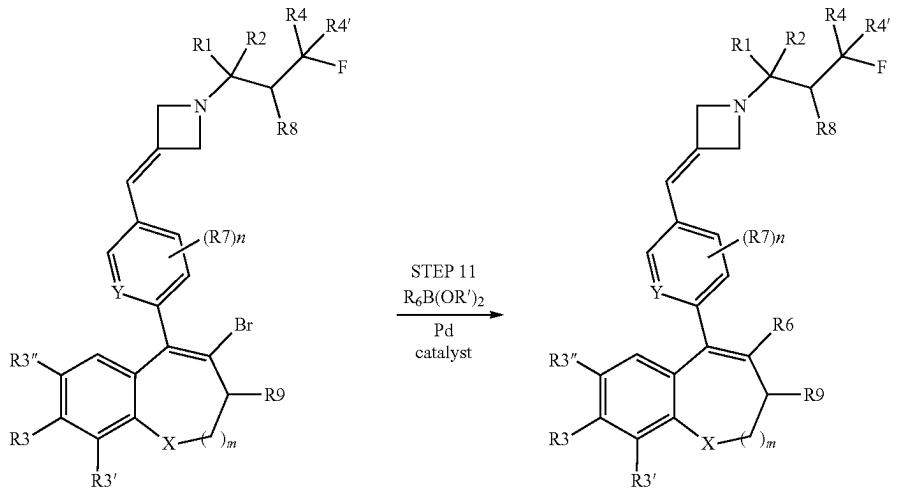



Compound 1T

Compound 1K

-continued




Compound 1Ta

Compound I

**[0184]** According to SCHEME 1b—Part-1 and Part-2, in which R3a is H, a carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, R1, R2, R3, R3', R3", R4, R4', R6, R7, R8, R9, X, n, m and Y are as defined above, compound 1L can be converted in STEP 1 to compound 1N in a Suzuki coupling reaction with compound 1M using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) (Pd(dppf)$Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent.

**[0185]** Compound 1N can be converted in STEP 2 to compound 1O by treatment with sodium nitrite followed by a treatment with sodium iodide in solvents such as a mixture of water and acetonitrile.

**[0186]** Compound 1O can be converted in STEP 3 to compound 1P by treatment for example with pyridinium tribromide in DCM or THF at room temperature. Compound 1P can be converted in STEP 4 to compound 1R in a Heck coupling reaction with compound 1Q using for example palladium (II) acetate as catalyst in a solvent such as DMF.

**[0187]** Compound 1R can be converted in STEP 5 to compound 1S by treatment with TFA in solution in DCM or HCl in solution in dioxane.

**[0188]** Compound 1S can be converted in STEP 6 to compound 1T by treatment with compound 1J, wherein W is Cl, Br or I or $OSO_2R$ with R═$CH_3$, PhMe, $CF_3$ or $CF_2CF_2CF_2CF_3$, in presence of a base such as potassium carbonate in DMF at 70° C. or in presence of sodium hydroxide or potassium hydroxide in THF at room temperature or in presence of aqueous sodium hydroxide in DCM at room temperature.

**[0189]** Compound 1T can be converted in STEP 7 to compound 1U by treatment for example with bis(pinacolato) diboron, and with a palladium catalyst, for example bis (triphenylphosphine) palladium(II) dichloride Pd($PPh_3$)$_2Cl_2$, and a phosphine such as triphenylphosphine in solution in toluene by heating up to reflux of solvent in presence of a base such as KOPh.

**[0190]** Compound 1K can be prepared in a Suzuki coupling reaction either between compounds 1T and R6B(OR')$_2$ or R6$BF_3$K in STEP 8 or between compounds 1U and R6Br or R6I in STEP 9 using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) (Pd(dppf)$Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent.

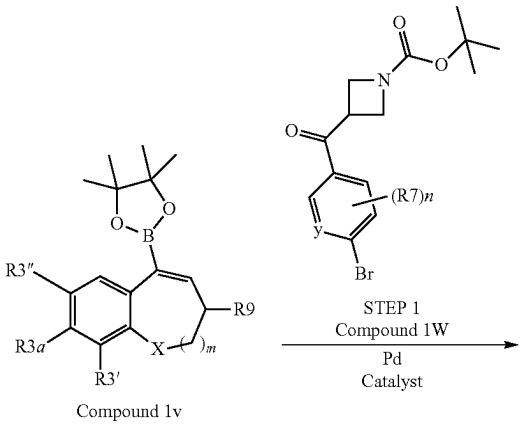
**[0191]** Compound 1K can be converted in STEP 12 to compound of formula (I) in presence of a source of hydroxide ions such as NaOH in solution in methanol (MeOH).

**[0192]** Intermediate 1T can be converted in STEP 10 to compound 1Ta in the presence of a source of hydroxide ions such as NaOH in solution in methanol (MeOH).

**[0193]** This compound 1Ta can be converted in STEP 11 to compound I through Suzuki conditions using a suitable boronic reagent R6B(OR')$_2$ or R6$BF_3$K, wherein —B(OR')$_2$ is a boronic acid or a pinacolate ester and R6 is as above defined, using for example Pd(dppf)$Cl_2$, complex with DCM, as catalyst, in a mixture of dioxane and water as solvent and in the presence of a base, for example $Cs_2CO_3$, at room temperature or by heating up to reflux of solvents.

**[0194]** When R3a is COOMe, COOEt, or a protected OH such as O-pivaloyl, compound 1K can be deprotected into compound I in STEPS 12 by treating with an aqueous solution of sodium hydroxide (NaOH) or lithium hydroxide (LiOH), in MeOH. When R3 is COOH, extraction of compound can give the sodium salt of compound I. The acidification with an aqueous solution of HCl 2N to pH 6-7 can give the neutral form. The acidification with an aqueous solution of HCl2N to pH 1-2 can give the hydrochloride salt. The purification using HPLC can give the formate or trifluoroacetate salt.

SCHEME 1c Part-1:
Alternative processes to prepare Intermediate 1T




Compound 1v

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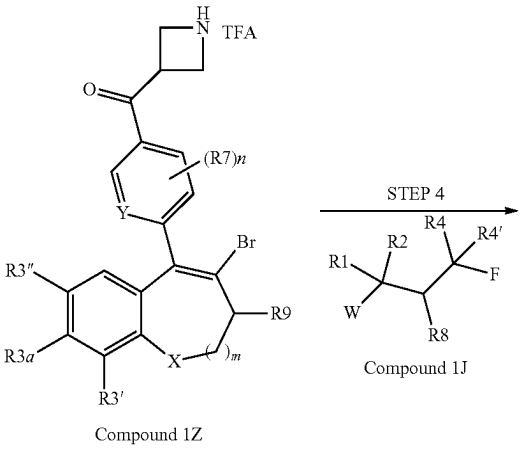
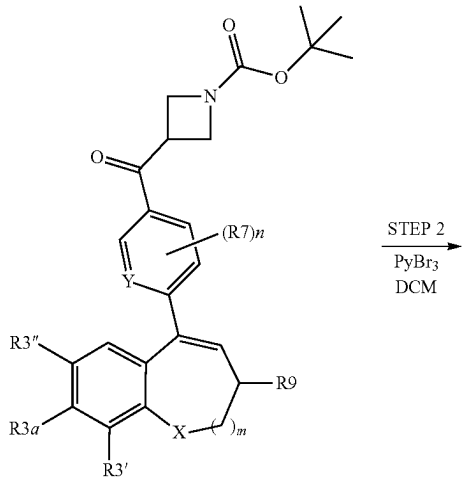
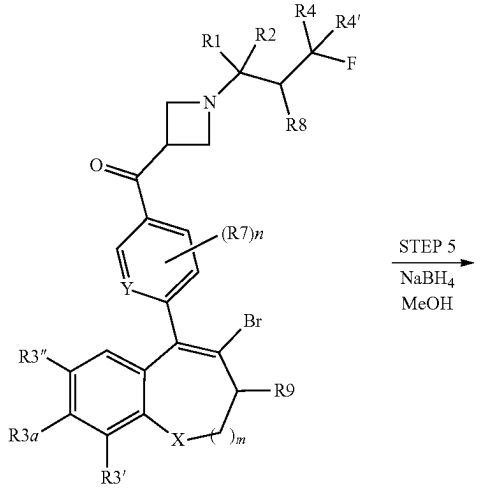



Compound 1Z

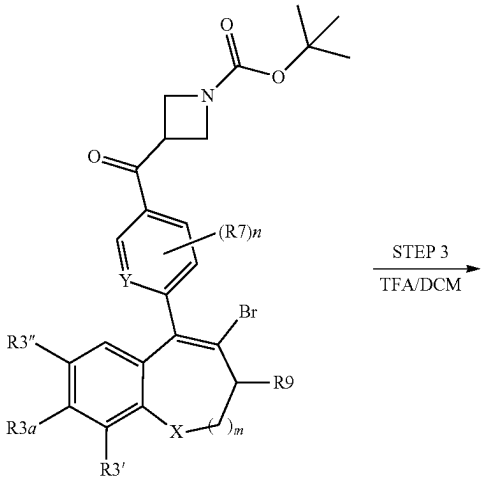
Compound 1J



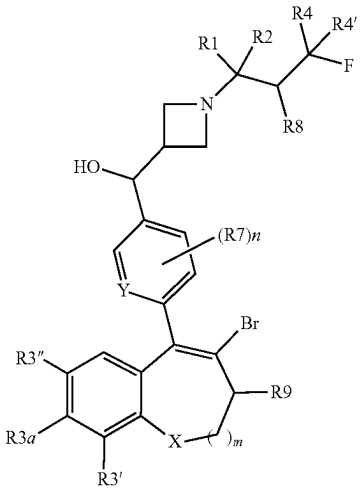

Compound 1X




Compound 1AA

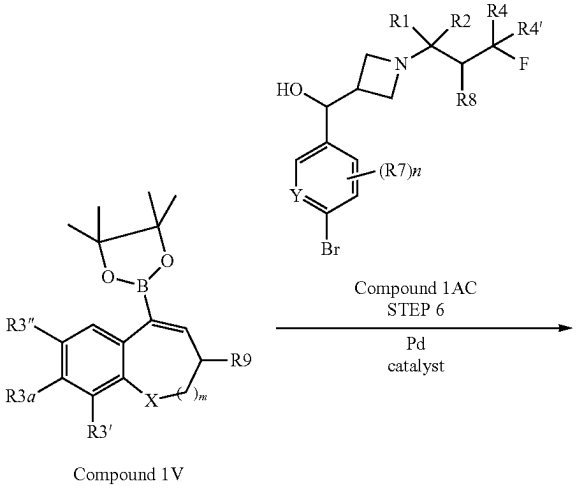



Compound 1Y



Compound 1AB

SCHEME 1c - Part-2




Compound 1V

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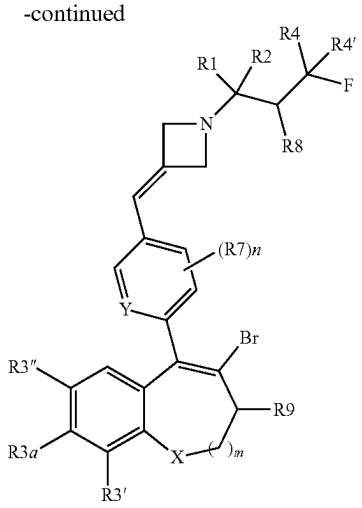
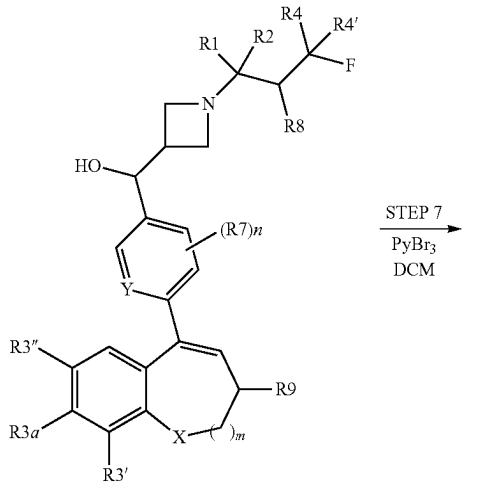
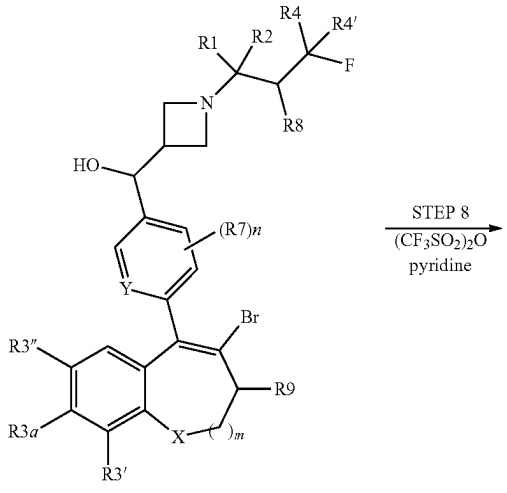



Compound 1T




Compound 1AD




Compound 1AB

**[0195]** According to SCHEME 1c—Part-1 and Part-2, in which R3a is H, carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, R1, R2, R3, R3', R3", R4, R7, R8, R9, X, n, m and Y are as defined above, compound 1V can be converted in STEP 1 to compound 1X in a Suzuki coupling reaction with compound 1W using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) (Pd(dppf)$Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent.

**[0196]** Compound 1X can be converted in STEP 2 to compound 1Y by treatment for example with pyridinium tribromide in DCM or THF at room temperature.

**[0197]** Compound 1Y can be converted in STEP 3 to compound 1Z by treatment with with TFA in solution in DCM or HCl in solution in dioxane.

**[0198]** Compound 1Z can be converted in STEP 4 to compound 1AA by treatment with compound 1J, wherein W is Cl, Br or I or $OSO_2R$ with R═$CH_3$, PhMe, $CF_3$ or $CF_2CF_2CF_2CF_3$, in presence of a base such as potassium carbonate in DMF at 70° C. or in presence of sodium hydroxide of potassium hydroxide in THF at room temperature.

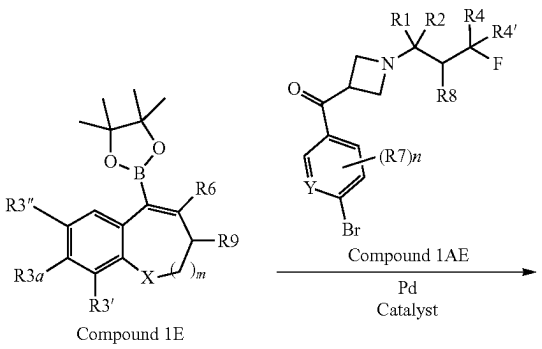
**[0199]** Compound 1AA can be converted in STEP 5 to compound 1AB by treatment with sodium borohydride in solution in MeOH.

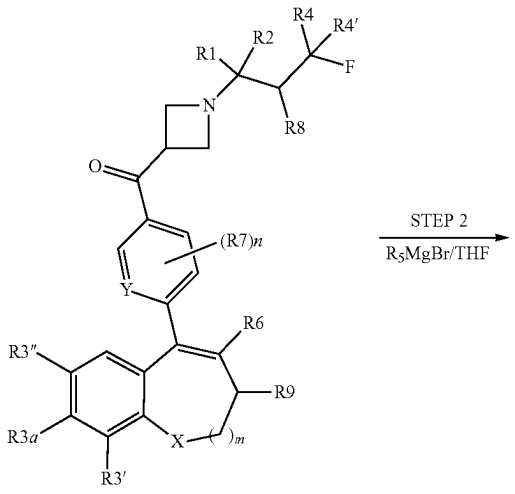
**[0200]** Compound 1AB can also be prepared from compound 1V using Suzuki coupling reaction with compounds 1AC in STEP 6 using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) (Pd(dppf)$Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent followed by bromination of the resulting compound 1AD in STEP 7 by treatment for example with pyridinium tribromide in DCM or THF at room temperature.

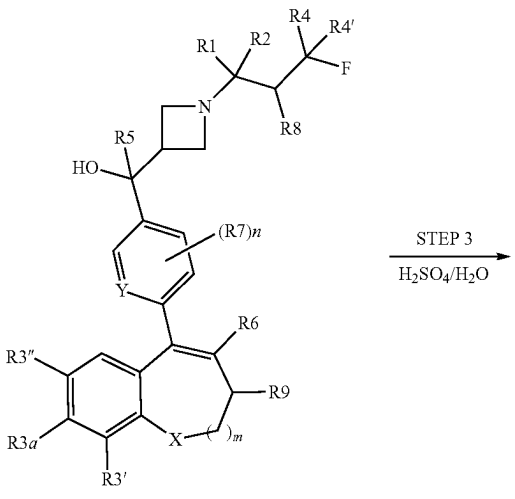
**[0201]** Compound 1AB can be converted in STEP 8 to compound 1T by treatment with trifluoromethanesulfonic anhydride and pyridine in DCM.

SCHEME 1d:

Preparation of compounds of the formula (I) - General process

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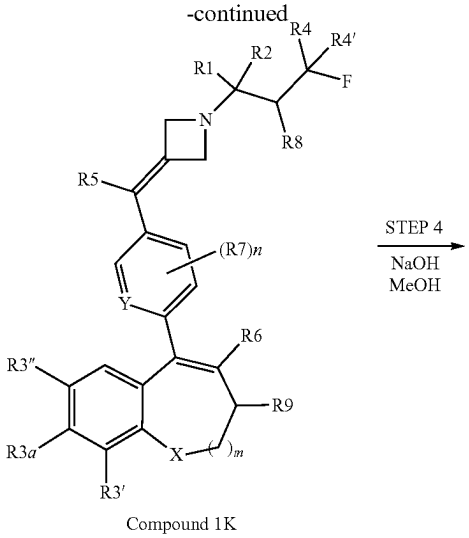
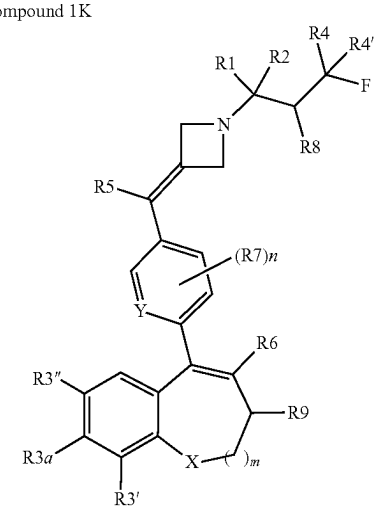



**[0202]** According to SCHEME 1d, in which R3a is H, carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, and R9 is a hydrogen atom R1, R2, R3, R3', R3", R4, R4', R5, R6, R7, R8, X, n, m and Y are as defined above, compound 1E can be converted in STEP 1 to compound 1AF in a Suzuki coupling reaction by treatment with compound 1AE using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) (Pd(dppf) $Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent.

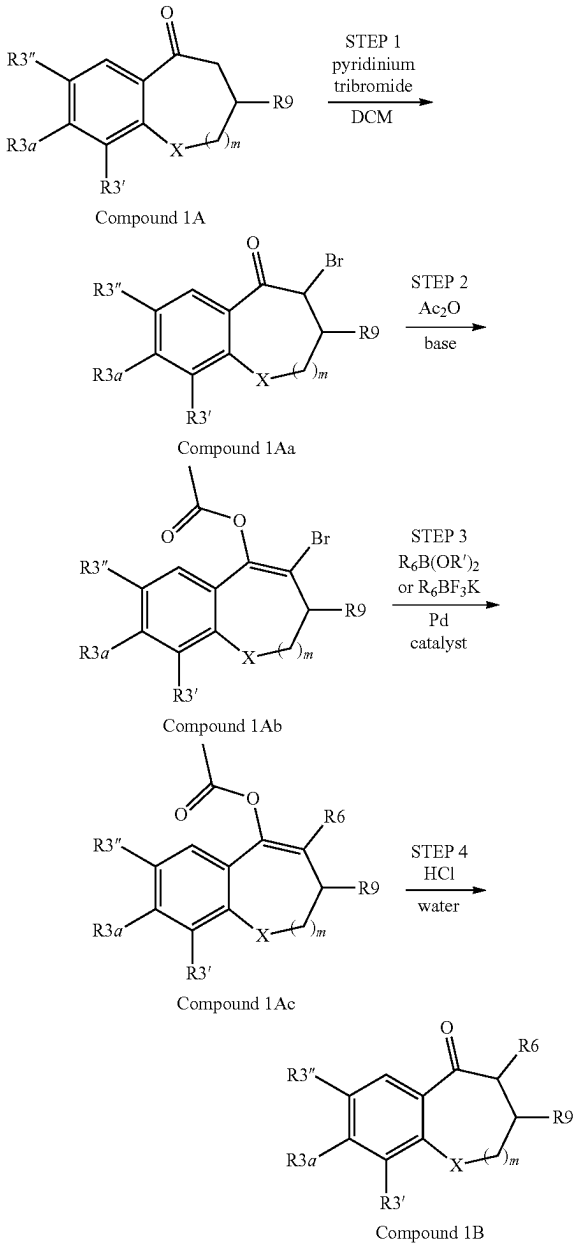
**[0203]** Compound 1AF can be converted in STEP 2 to compound 1AG by treatment with alkyl magnesium bromide in a solvent such as THF.

**[0204]** Compound 1AG can be converted in STEP 3 to compound 1K by treatment with sulfuric acid in water.

**[0205]** When R3a is COOMe, COOEt, or a protected OH such as O-pivaloyl, compound 1K can be deprotected into compound I in STEP 4 by treating with an aqueous solution of sodium hydroxide (NaOH) or lithium hydroxide (LiOH), in MeOH. When R3 is COOH, extraction of compound can give the sodium salt of compound I. The acidification with

an aqueous solution of HCl 2N to pH 6-7 can give the neutral form. The acidification with an aqueous solution of HCl 2N to pH 1-2 can give the hydrochloride salt. The purification using HPLC can give the formate or trifluoroacetate salt.

SCHEME 1e: Alternative preparation of compounds of the formula (1B) - General process



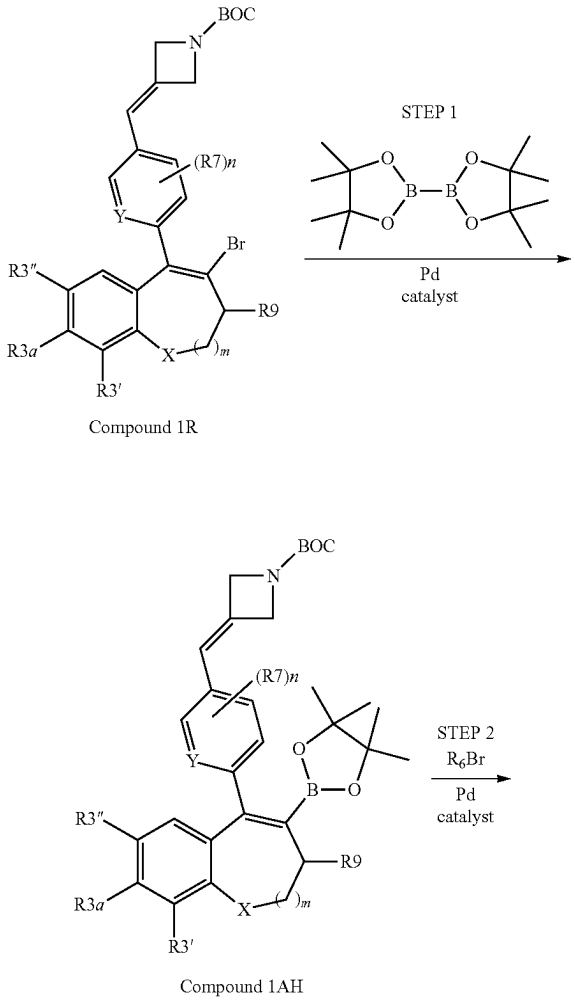

**[0206]** According to SCHEME 1e, in which R3a is H, a carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, R3', R3", R9, X and m are as defined above, compound 1B can alternatively be prepared as follows: compound 1A can be converted in STEP 1 to compound 1Aa by treatment with pyridinium tribromide in DCM or THF at room temperature for example.

**[0207]** Compound 1Aa can be converted in STEP 2 to compound 1Ab by deprotonation with a base such as LiHMDS in THF followed by treatment with acetic anhydride.

**[0208]** Compound 1Ac can be prepared in STEP 3 in a Suzuki coupling reaction between compounds 1Ab and $R6B(OR')_2$ or $R6BF_3K$ using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) (Pd(dppf)$Cl_2$), complex with DCM, as catalyst, in a mixture of toluene and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent. When R6 is a substituted cycloalkene, heterocycloalkene or aliphatic ethylene, it may be reduced by hydrogenation with a catalyst such as Pd/C under hydrogen pressure ($H_2$) around 5 bars for example at temperature up to 70° C. to give the corresponding saturated compound 1Ac.

**[0209]** Compound 1Ac can be converted in STEP 4 to compound 1B by hydrolysis with aqueous HCl solution by heating in methanol and DCM for example.

SCHEME 1f:
Alternative process to prepare Intermediate 1H wherein R5 = H



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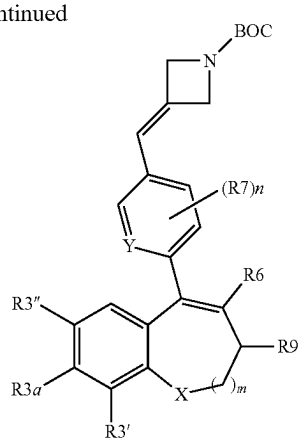
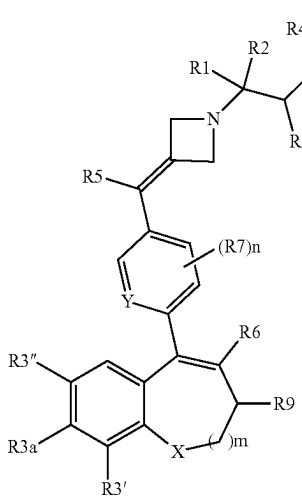


Compound 1H with R5 = H

**[0210]** According to SCHEME If, in which R3a is H or a carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, and R9 is a hydrogen atom, R3', R3", R6, R7, R8, X, m, n and Y are as defined above, compound 1R can be converted in STEP 1 to compound 1AH by treatment for example with bis(pinacolato)diboron, and with a palladium catalyst, for example bis(triphenylphosphine) palladium(II) dichloride $Pd(PPh_3)_2Cl_2$, and a phosphine, such as triphenylphosphine, in solution in toluene by heating up to reflux of solvent, in presence of a base such as KOPh.

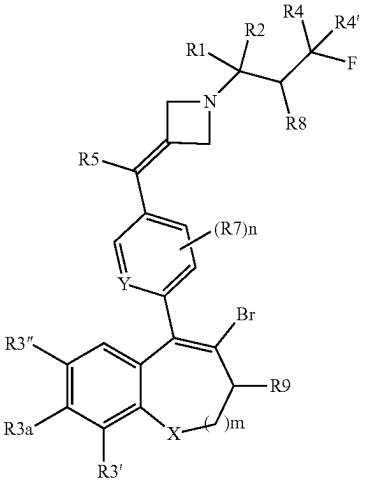
**[0211]** Compound 1AH can be converted in STEP 2 to compound 1H wherein R5=H in a Suzuki coupling reaction with an aryl or heteroaryl bromide or iodide using for example [1,1'-bis(diphenylphosphino) ferrocene]dichloropalladium(II) ($Pd(dppf)Cl_2$), complex with DCM, as catalyst, in a mixture of dioxane and water and in the presence of a base, for example cesium carbonate ($Cs_2CO_3$), by heating up to reflux of solvent.

**[0212]** Herein is also provided a process for preparing a compound of formula (I) as defined above, wherein a compound of formula 1K



1K

**[0213]** wherein R1, R2, R3', R3", R4, R4', R5, R6, R7, R8, R9, m, n, X and Y are as defined above and R3a is carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, is converted to compound of formula (I), in presence of a source of hydroxide ions, such as NaOH in solution in methanol, said step being optionally preceded by a step for obtaining compound 1K, wherein a compound of formula 1T

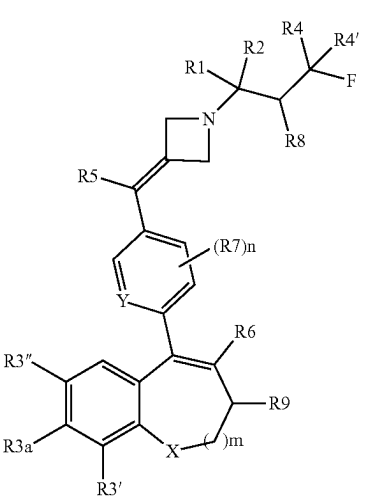


1T

**[0214]** wherein, R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is as defined above,

**[0215]** is subjected to a Suzuki coupling with a boronic reagent $R6B(OR')_2$ or $R6BF_3K$, wherein —$B(OR')_2$ is a boronic acid or a pinacolate ester and R6 is as defined above.

**[0216]** Herein is also provided a process for preparing a compound of formula (I) as defined above, wherein a compound of formula 1K

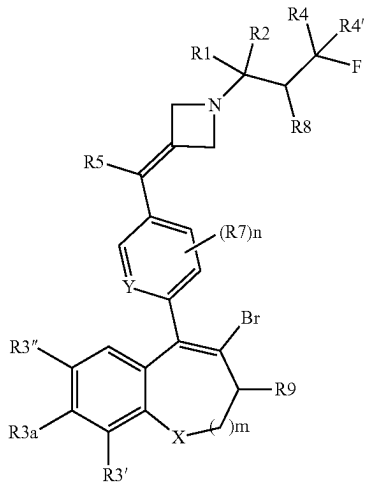


1K

**[0217]** wherein R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl, and R6 represents a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group,

**[0218]** is converted to compound of formula (I), in presence of a source of hydroxide ions, such as NaOH in solution in methanol, said step being optionally preceded by a step for obtaining compound 1K, wherein a compound of formula 1T

1T

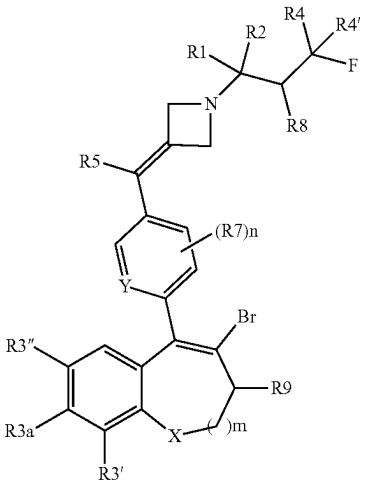



**[0219]** wherein, R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is as defined above,

**[0220]** is subjected to a Suzuki coupling with a boronic reagent R6B(OR')$_2$ or R6B$F_3$K, wherein —B(OR')$_2$ is a boronic acid or a pinacolate ester and R6 is as defined above.

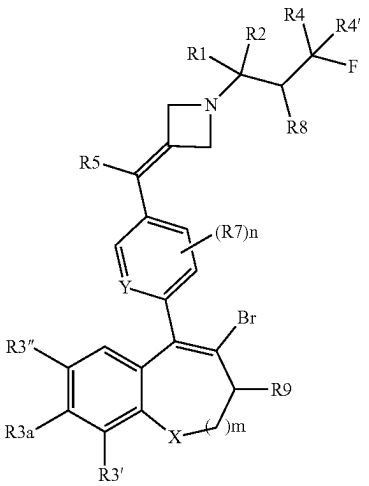
**[0221]** Herein is also provided a process for preparing a compound of formula (I) as defined above, wherein a compound of formula 1Ta

1Ta




**[0222]** wherein R1, R2, R3a, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above, is submitted to a Suzuki coupling with a boronic reagent R6B(OR')$_2$ or R6B$F_3$K, wherein —B(OR')$_2$ is a boronic acid or a pinacolate ester and R6 is defined above, said step being optionally preceded by a step for obtaining compound 1Ta, wherein a compound of formula 1T

1T

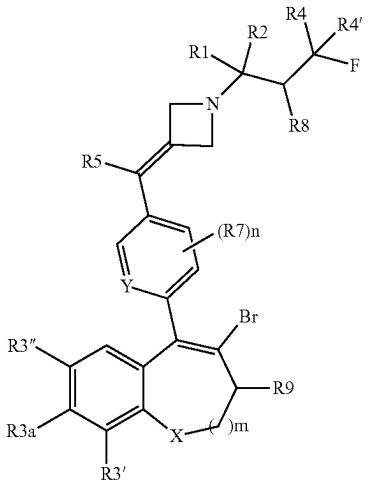



**[0223]** wherein R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is as defined above,

**[0224]** is converted to a compound 1Ta in the presence of a source of hydroxide ions, such as NaOH in solution in methanol.

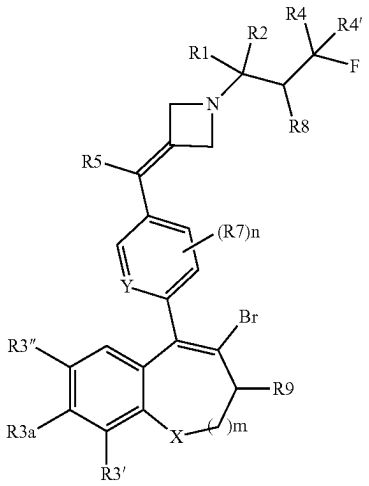
**[0225]** Herein is also provided a process for preparing a compound of formula (I) as defined above, wherein a compound of formula 1Ta

1Ta



**[0226]** wherein R1, R2, R3a, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above, is submitted to a Suzuki coupling with a boronic reagent $R6B(OR')_2$ or $R6BF_3K$, wherein $—B(OR')_2$ is a boronic acid or a pinacolate ester and R6 represents a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group, said step being optionally preceded by a step for obtaining compound 1Ta, wherein a compound of formula 1T

1T

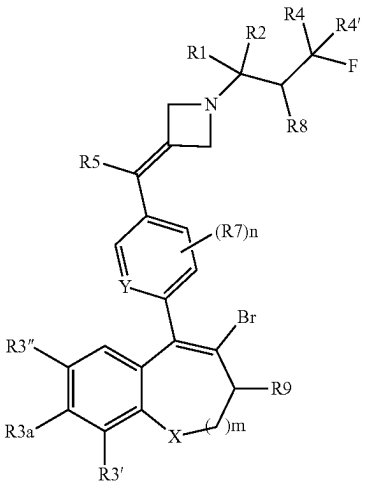


**[0227]** wherein R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is as defined above,

**[0228]** is converted to a compound 1Ta in the presence of a source of hydroxide ions, such as NaOH in solution in methanol.

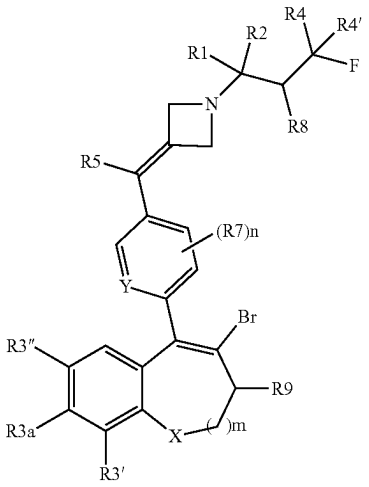
**[0229]** Herein are also described the intermediate compounds selected from compounds of formula 1T and 1Ta, or any of their pharmaceutically acceptable salt,

1T



**[0230]** and

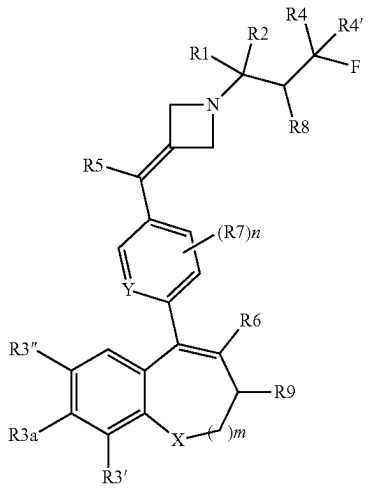
1Ta



**[0231]** wherein R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl.

[0232] Herein is also described the intermediate compound 1K or any of its pharmaceutically acceptable salt,

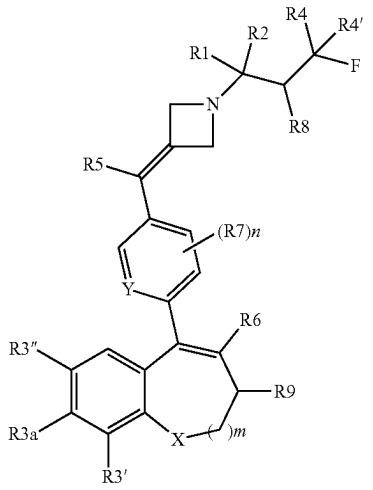
1K



[0233] wherein R1, R2, R3, R3', R3", R4, R4' R5, R6, R7, R8, R9, m, n, X and Y are as defined above and R3a is carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl.

[0234] Herein is also provided the intermediate compound 1K or any of its pharmaceutically acceptable salt,

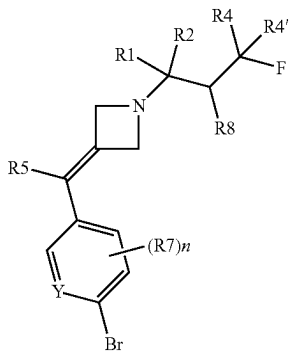
1K



[0235] wherein R1, R2, R3, R3', R3", R4, R4' R5, R7, R8, R9, m, n, X and Y are as defined above and R3a is carboxylic ester such as COOMe, COOEt, or protected OH such as O-pivaloyl and R6 represents a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group.

[0236] Herein is further described the intermediate compound of formula 1F, or any of its pharmaceutically acceptable salt

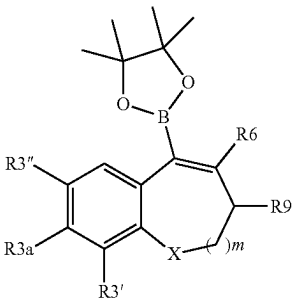
1F



[0237] wherein R1, R2, R4, R4', R5, R7, R8, Y and n are as defined above.

[0238] The present application also describes the intermediate compound of formula 1E, or any of its pharmaceutically acceptable salt

1E



[0239] wherein R3a, R3', R3", X, m, R6 and R9 are as defined above.

[0240] In another aspect, herein is also provided a process for the preparation of a compound of formula (I), wherein R3 is a —COOH group, comprising a deprotection step of a compound of formula 1K as defined above.

[0241] The $^1$H NMR Spectra at 400 and 500 MHz were performed on a Bruker Avance DRX-400 and Bruker Avance DPX-500 spectrometer, respectively, with the chemical shifts (δ in ppm) in the solvent dimethyl sulfoxide-d6 (d6-DMSO) referenced at 2.5 ppm at a temperature of 303 K. Coupling constants (J) are given in Hertz.

[0242] The liquid chromatography/mass spectra (LC/MS) were obtained on a UPLC Acquity Waters instrument, light scattering detector Sedere and SQD Waters mass spectrometer using UV detection DAD 210-400 nm and flash Acquity UPLC CSH C18 1.7 μm, dimension 2.1×30 mm, mobile phase $H_2O$+0.1% $HCO_2H$/$CH_3CN$+0.1% $HCO_2H$.

[0243] The following tables 1a and 1b comprise respectively specific compounds of formula (I) (name and structure) in accordance with the present disclosure as well their characterization ($^1$H NMR and liquid chromatography/mass).

TABLE 1a

(the first column "Ex" corresponds to the compound and example number)

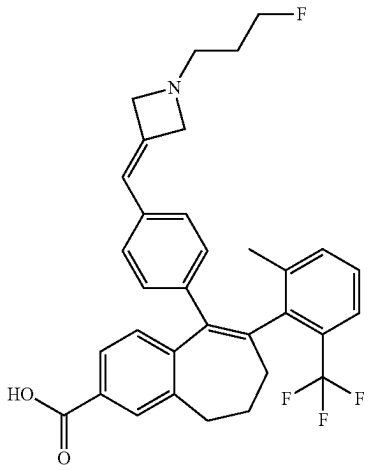
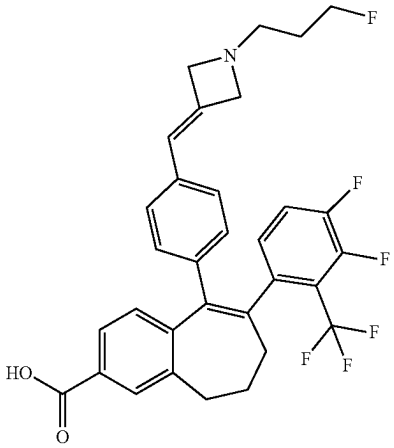
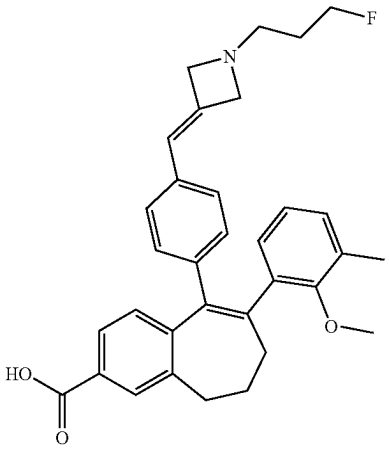
| Ex | Structure | Name |
|---|---|---|
| 1 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-6-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 2 |  | 8-(3,4-difluoro-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 3 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

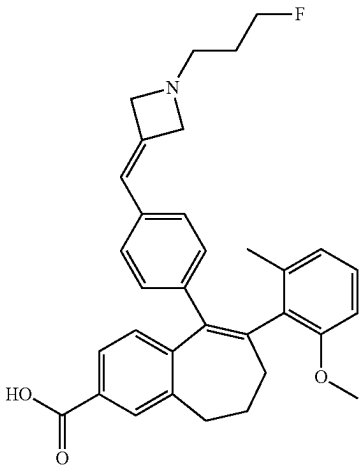
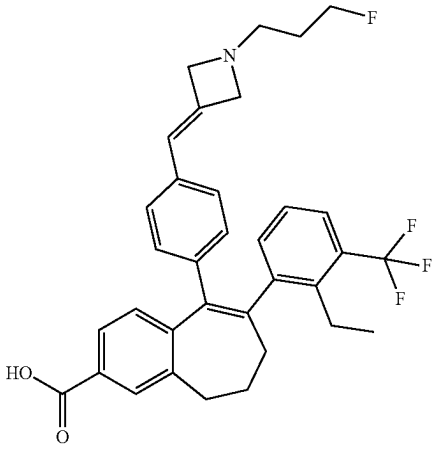
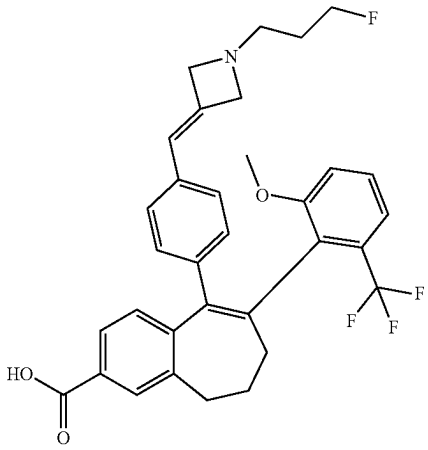
| Ex | Structure | Name |
|---|---|---|
| 4 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-6-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 5 |  | 8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 6 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-6-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

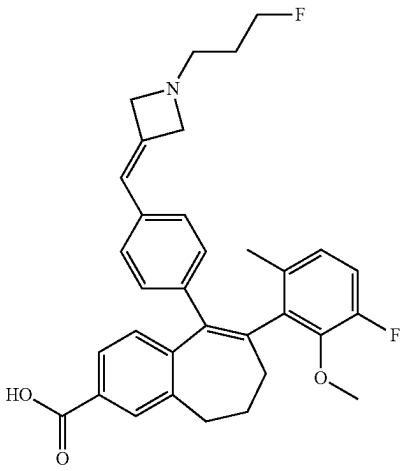
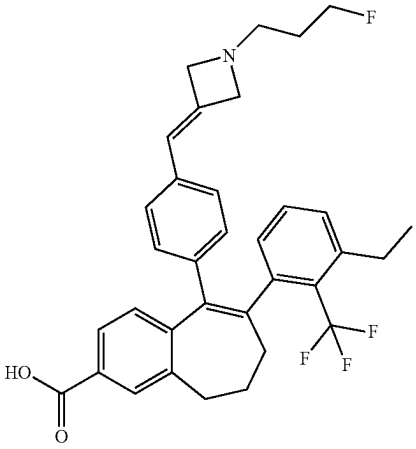
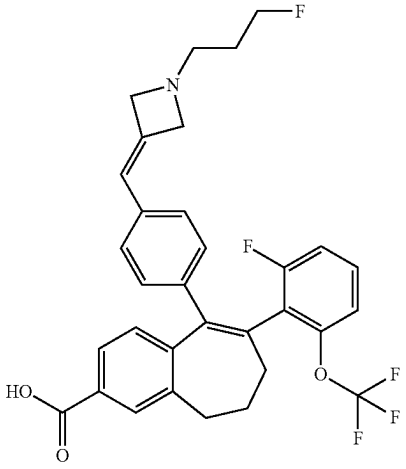
| Ex | Structure | Name |
|---|---|---|
| 7 |  | 8-(3-fluoro-2-methoxy-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 8 |  | 8-(3-ethyl-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 9 |  | 8-(2-fluoro-6-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

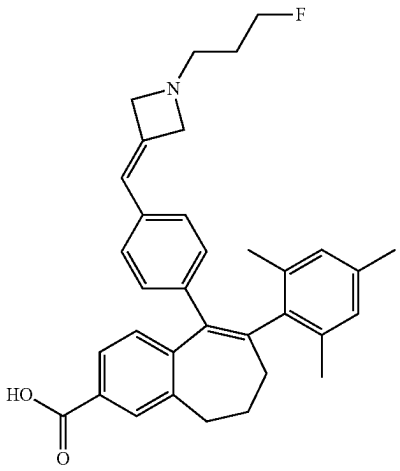
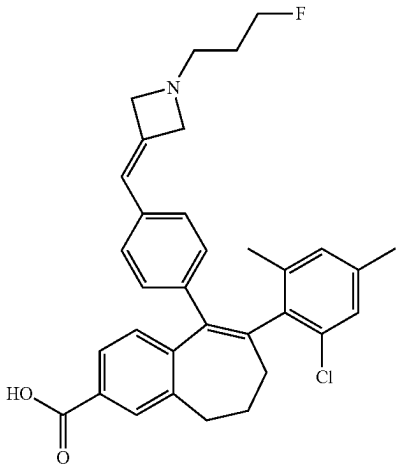
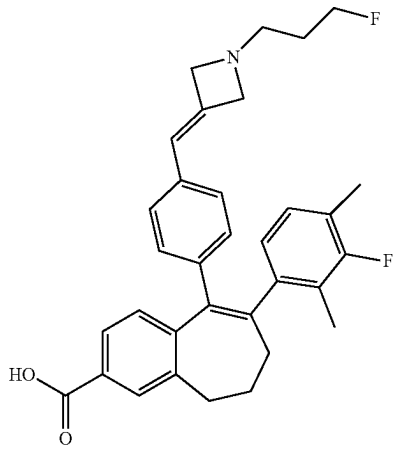
| Ex | Structure | Name |
|---|---|---|
| 10 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-mesityl-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 11 |  | 8-(2-chloro-4,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 12 |  | 8-(3-fluoro-2,4-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

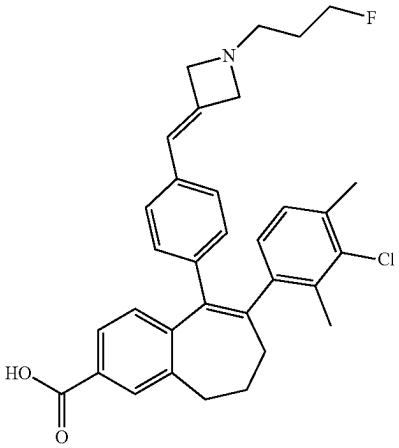
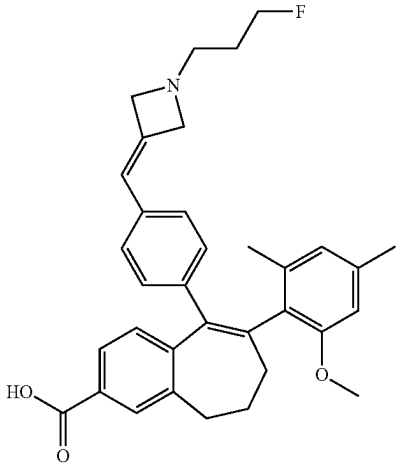
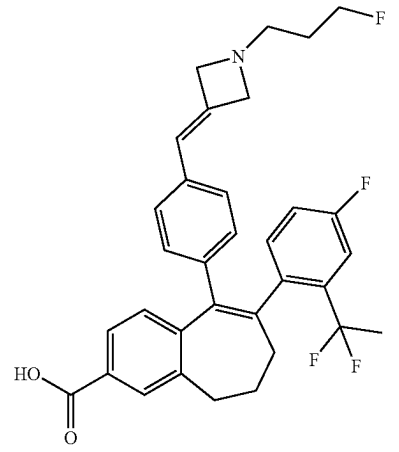
| Ex | Structure | Name |
|---|---|---|
| 13 |  | 8-(3-chloro-2,4-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 14 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4,6-dimethylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 15 |  | 8-(2-(1,1-difluoroethyl)-4-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

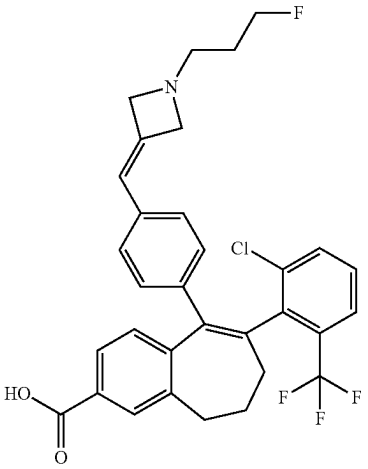
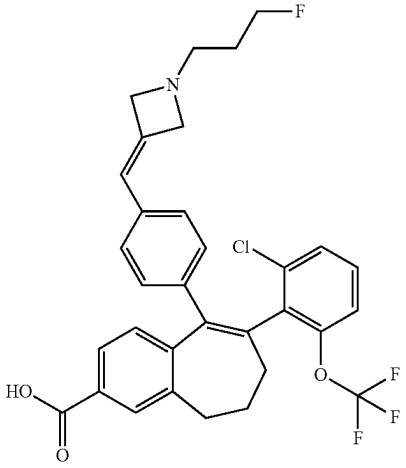
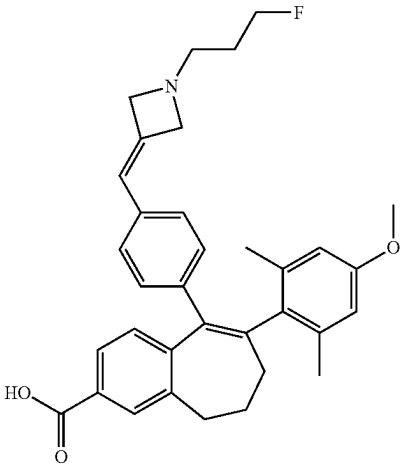
| Ex | Structure | Name |
|---|---|---|
| 16 |  | 8-(2-chloro-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 17 |  | 8-(2-chloro-6-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 18 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4-methoxy-2,6-dimethylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

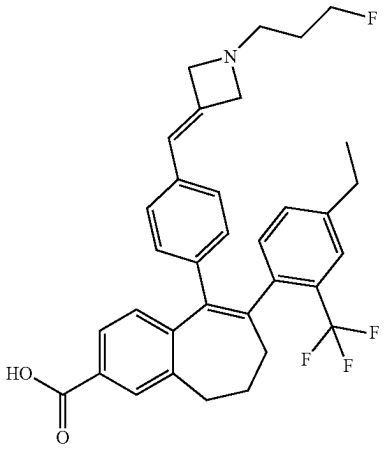
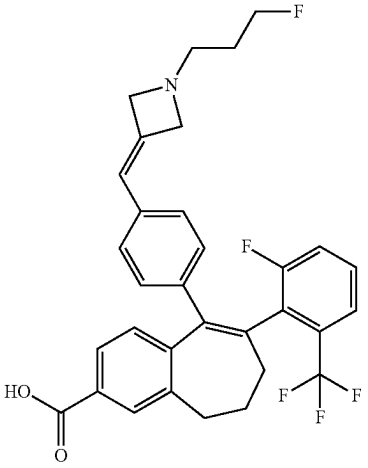
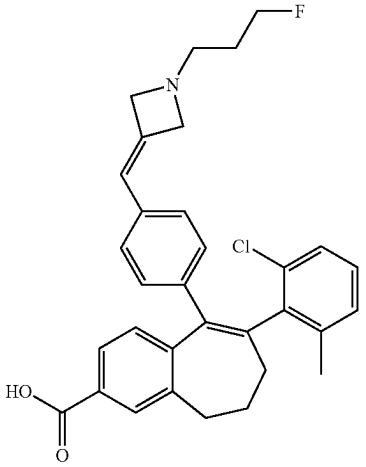
| Ex | Structure | Name |
|---|---|---|
| 19 |  | 8-(4-ethyl-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 20 |  | 8-(2-fluoro-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 21 |  | 8-(2-chloro-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

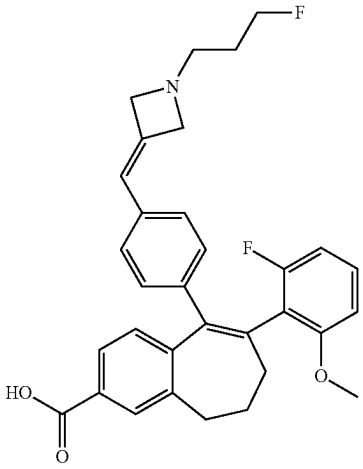
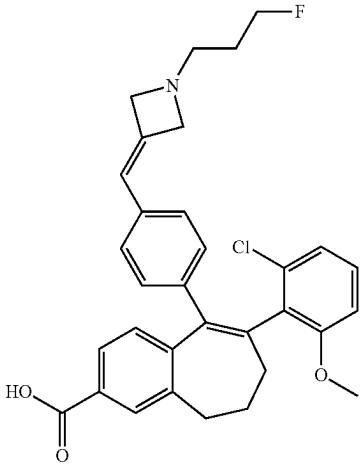
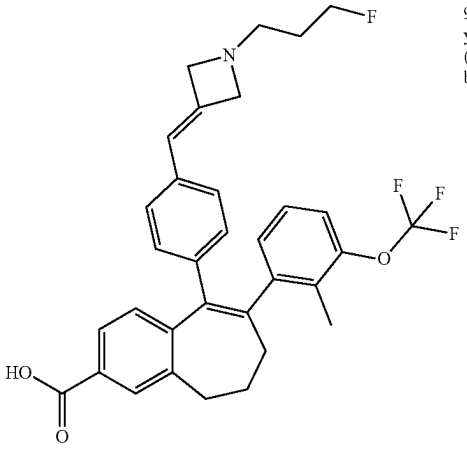
| Ex | Structure | Name |
|---|---|---|
| 22 |  | 8-(2-fluoro-6-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 23 |  | 8-(2-chloro-6-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 24 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-3-(trifluoromethoxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

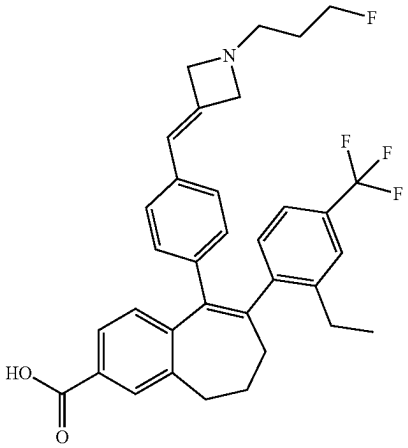
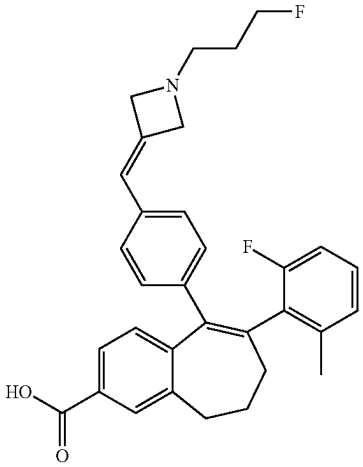
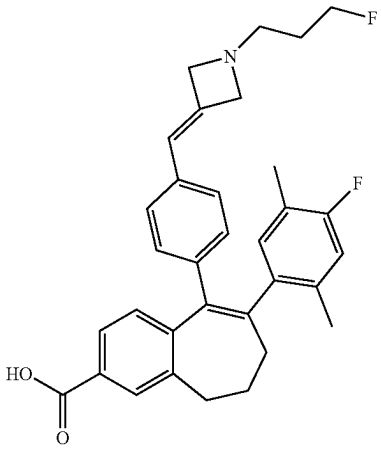
| Ex | Structure | Name |
|---|---|---|
| 25 |  | 8-(2-ethyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 26 |  | 8-(2-fluoro-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 27 |  | 8-(4-fluoro-2,5-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

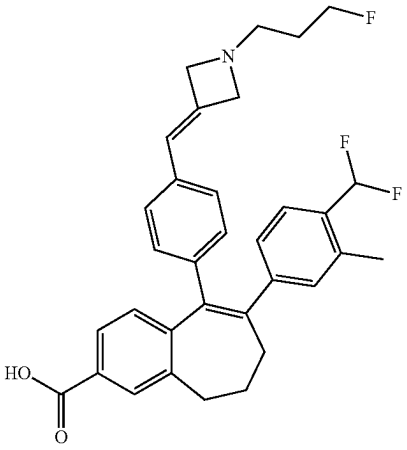
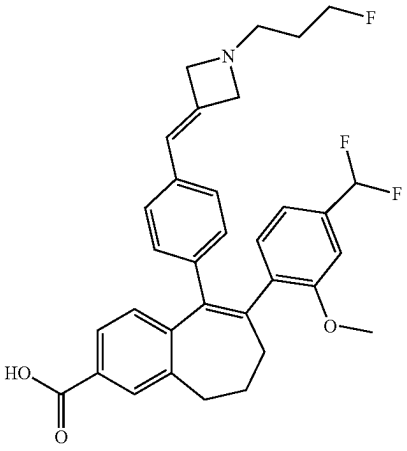
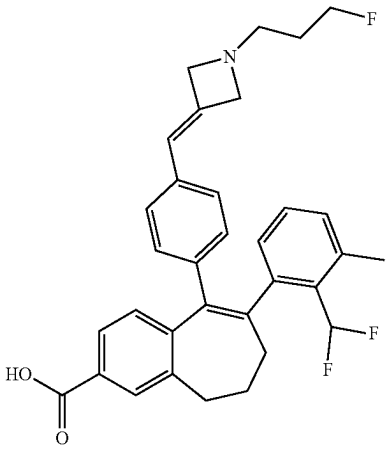
| Ex | Structure | Name |
|---|---|---|
| 28 |  | 8-(4-(difluoromethyl)-3-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 29 |  | 8-(4-(difluoromethyl)-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 30 |  | 8-(2-(difluoromethyl)-3-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

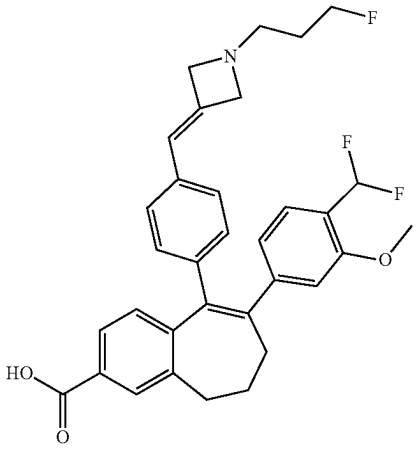
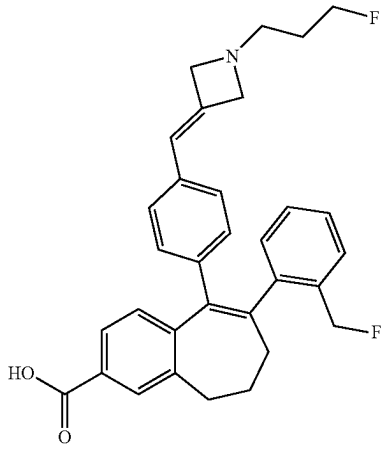
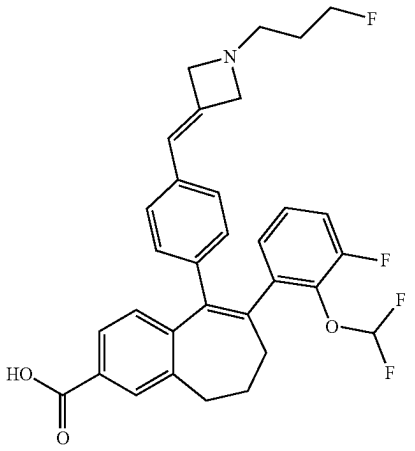
| Ex | Structure | Name |
|---|---|---|
| 31 |  | 8-(4-(difluoromethyl)-3-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 32 |  | 8-(2-(fluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 33 |  | 8-(2-(difluoromethoxy)-3-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

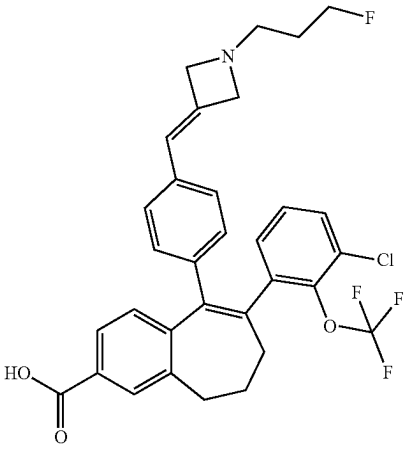
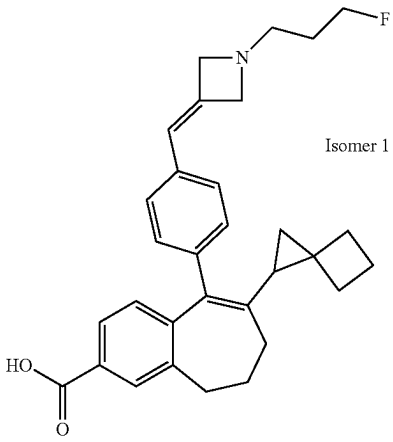
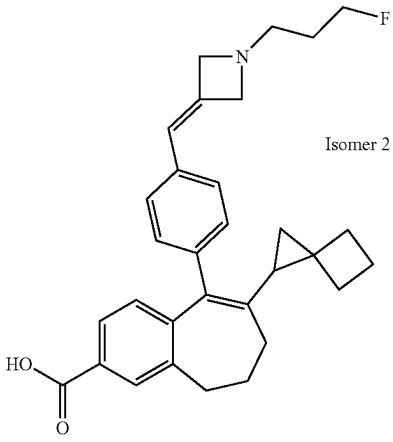
| Ex | Structure | Name |
|---|---|---|
| 34 |  | 8-(3-chloro-2-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 35 |  Isomer 1 | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1 |
| 36 |  Isomer 2 | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2 |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

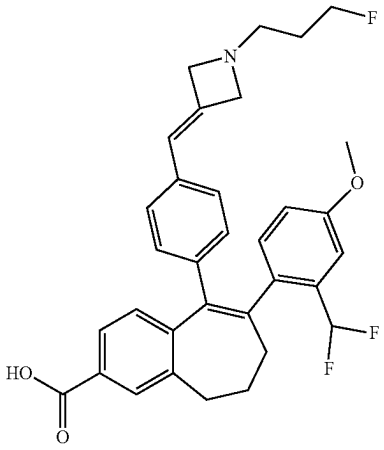
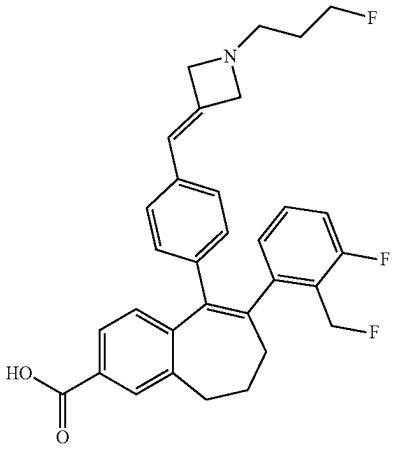
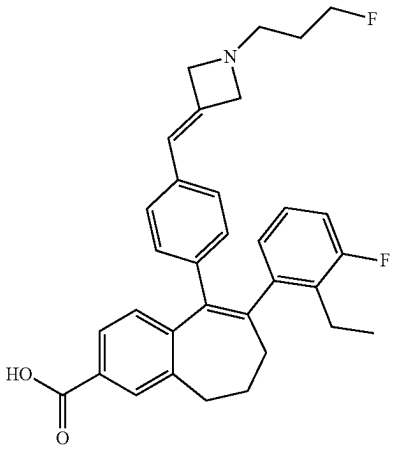
| Ex | Structure | Name |
|---|---|---|
| 37 |  | 8-(2-(difluoromethyl)-4-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 38 |  | 8-(3-fluoro-2-(fluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 39 |  | 8-(2-ethyl-3-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

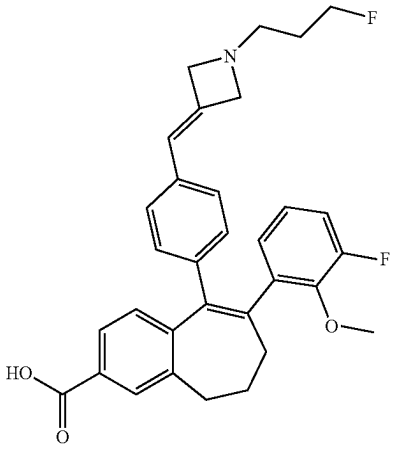
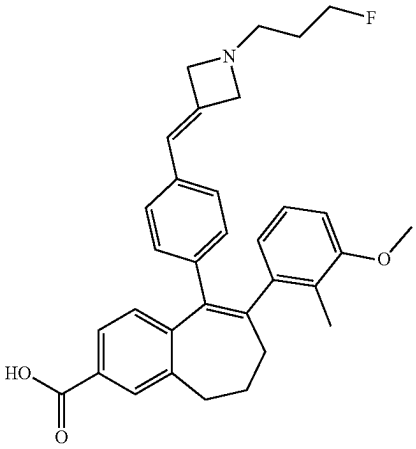
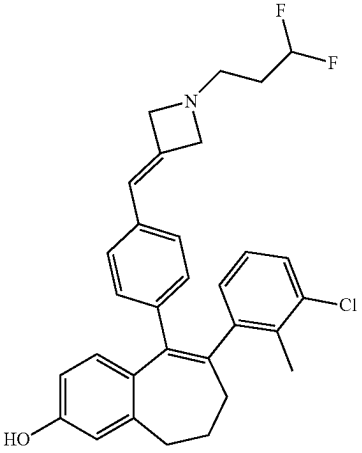
| Ex | Structure | Name |
|---|---|---|
| 40 |  | 8-(3-fluoro-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 41 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methoxy-2-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 42 |  | 8-(3-chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-ol |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

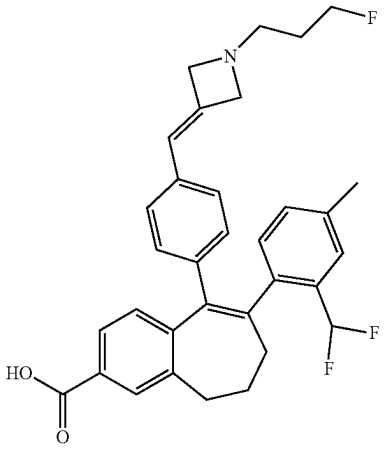
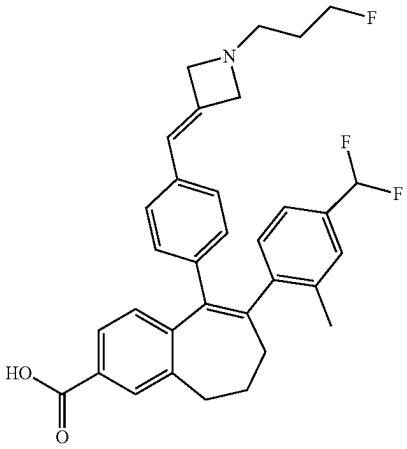
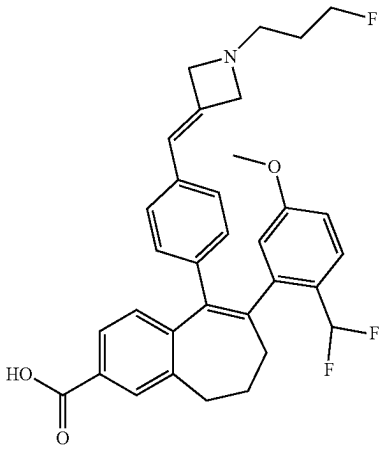
| Ex | Structure | Name |
|---|---|---|
| 43 |  | 8-(2-(difluoromethyl)-4-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 44 |  | 8-(4-(difluoromethyl)-2-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 45 |  | 8-(2-(difluoromethyl)-5-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

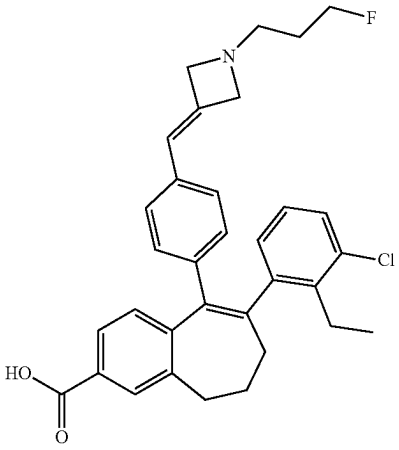
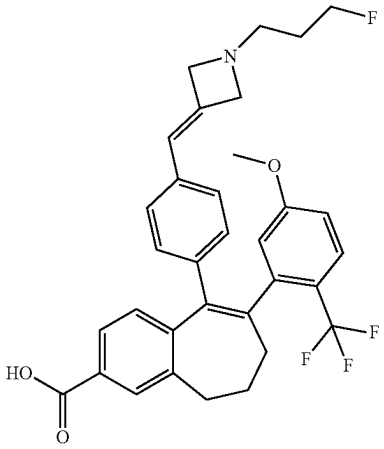
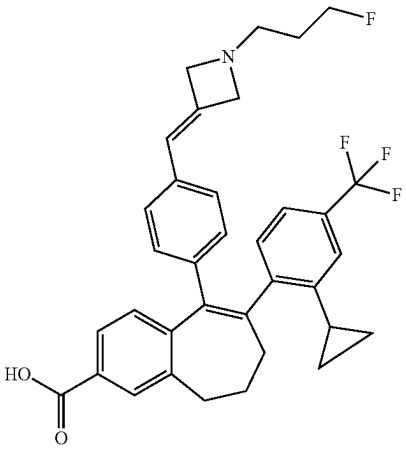
| Ex | Structure | Name |
|---|---|---|
| 46 |  | 8-(3-chloro-2-ethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 47 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(5-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 48 |  | 8-(2-cyclopropyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

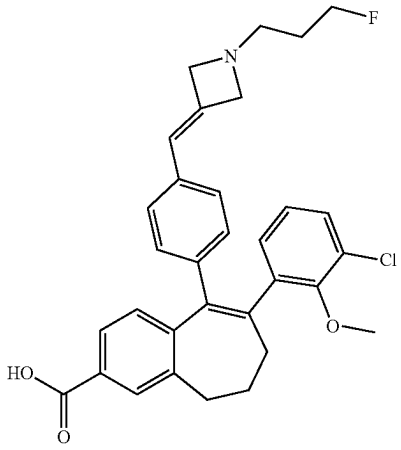
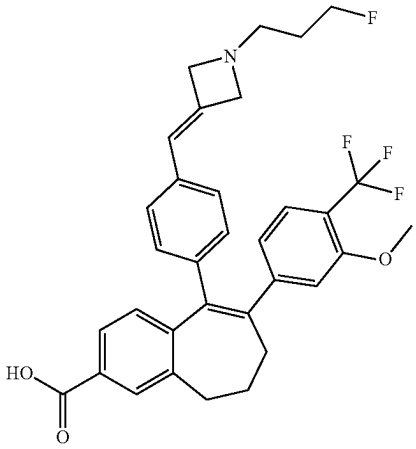
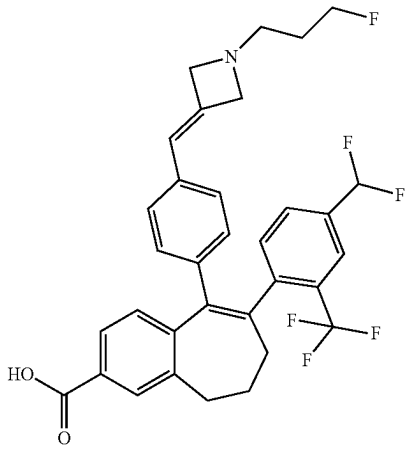
| Ex | Structure | Name |
|---|---|---|
| 49 |  | 8-(3-chloro-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 50 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methoxy-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 51 |  | 8-(4-(difluoromethyl)-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

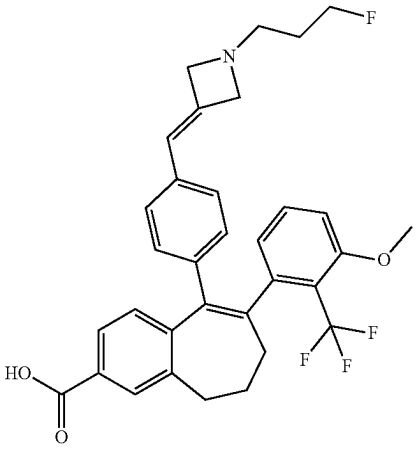
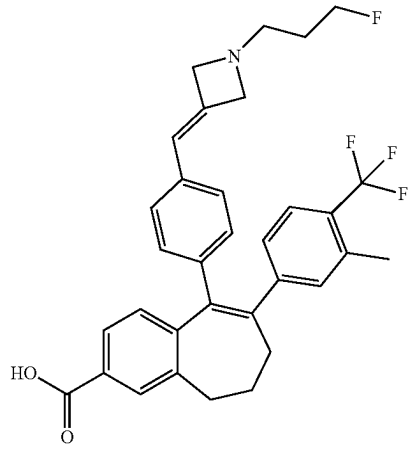
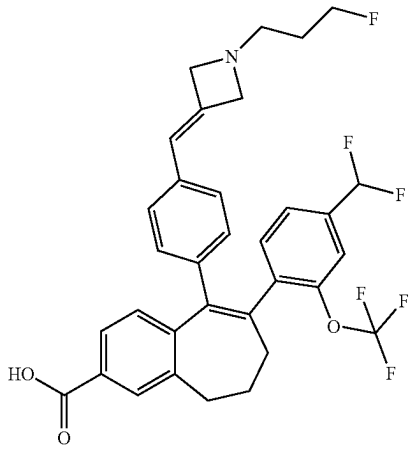
| Ex | Structure | Name |
|---|---|---|
| 52 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 53 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methyl-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 54 |  | 8-(4-(difluoromethyl)-2-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

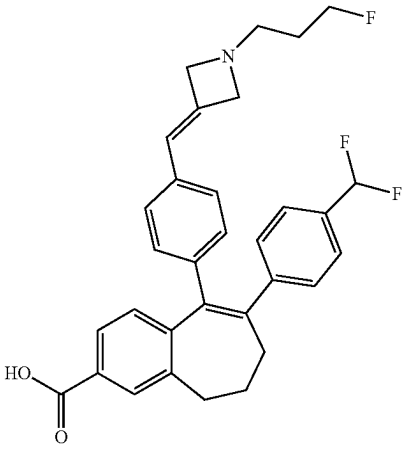
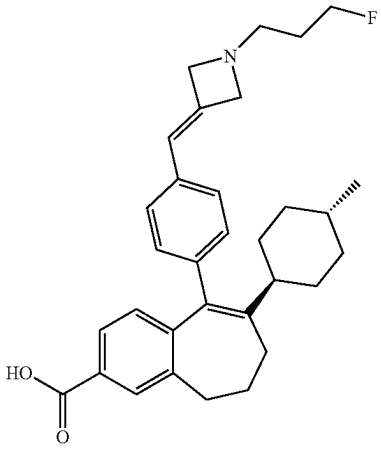
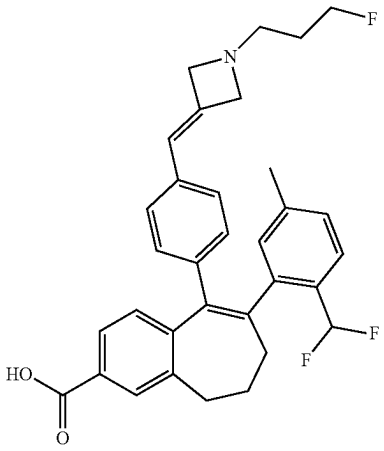
| Ex | Structure | Name |
|---|---|---|
| 55 |  | 8-(4-(difluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 56 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(trans-4-methylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 57 |  | 8-(2-(difluoromethyl)-5-methylpheny1)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

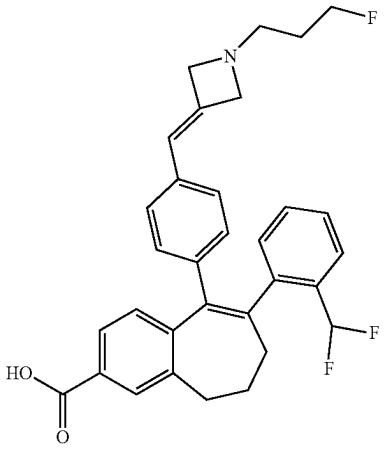
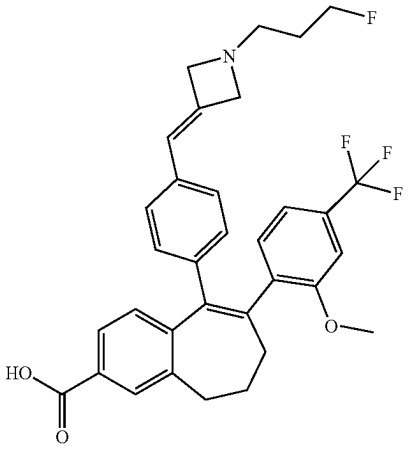
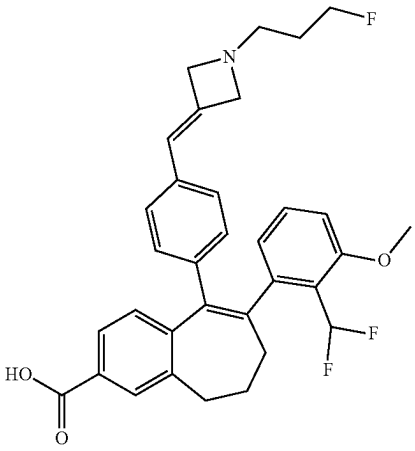
| Ex | Structure | Name |
|---|---|---|
| 58 |  | 8-(2-(difluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 59 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 60 |  | 8-(2-(difluoromethyl)-3-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

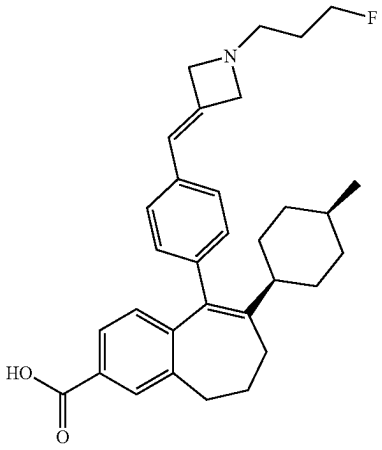
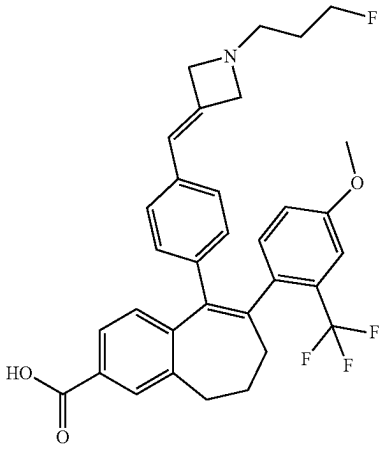
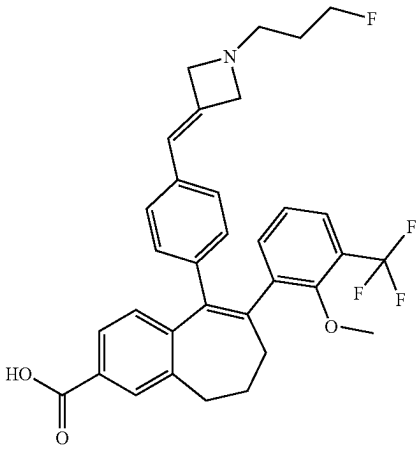
| Ex | Structure | Name |
|---|---|---|
| 61 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(cis-4-methylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 62 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 63 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

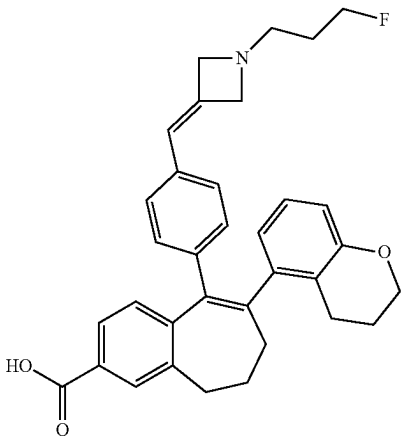
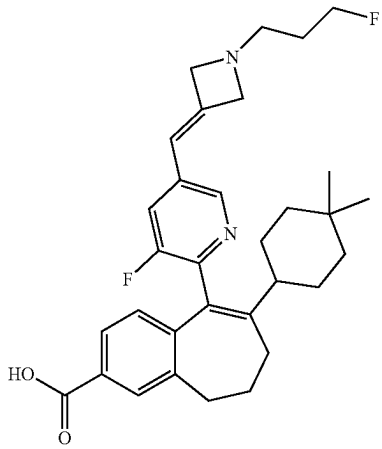
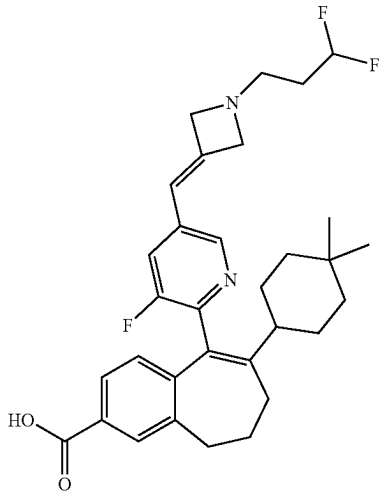
| Ex | Structure | Name |
|---|---|---|
| 64 |  | 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 65 |  | 8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 66 |  | 9-(5-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

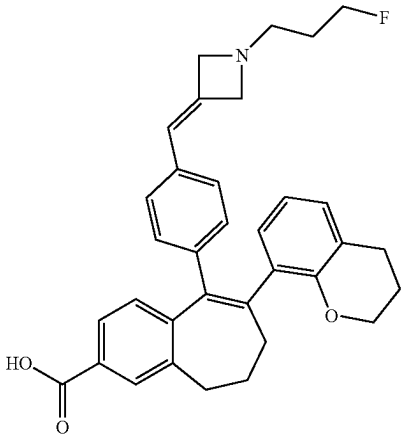
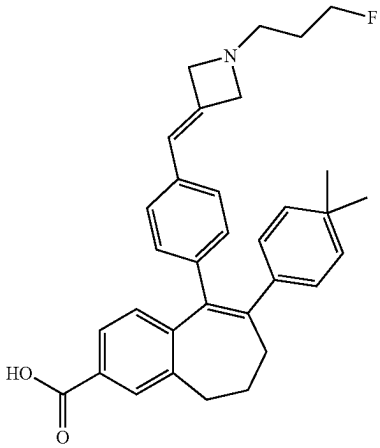
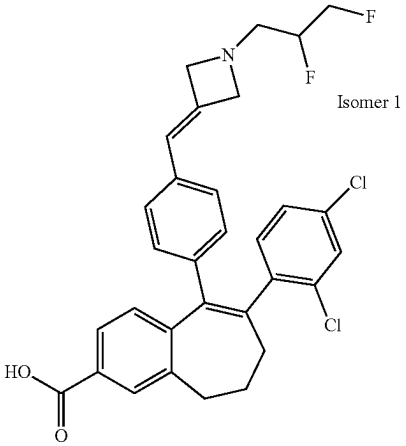
| Ex | Structure | Name |
|---|---|---|
| 67 |  | 8-(chroman-8-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 68 |  | 8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 69 |  | 8-(2,4-dichlorophenyl)-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1 |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

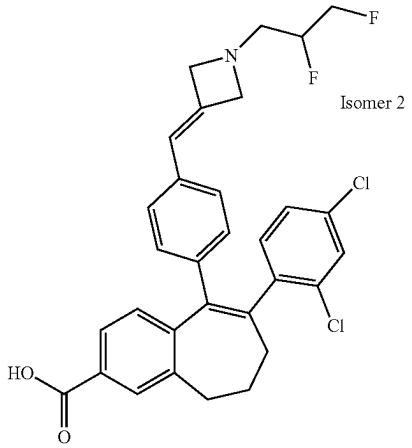
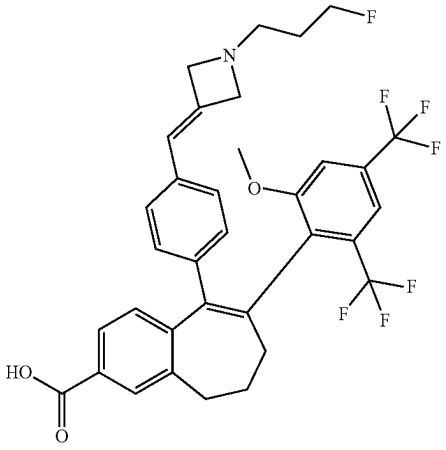
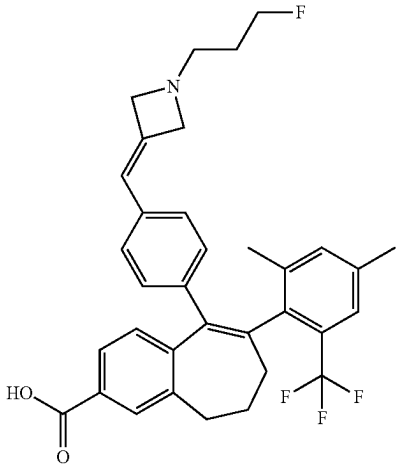
| Ex | Structure | Name |
|---|---|---|
| 70 |  Isomer 2 | 8-(2,4-dichlorophenyl)-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2 |
| 71 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4,6-bis(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 72 |  | 8-(2,4-dimethyl-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

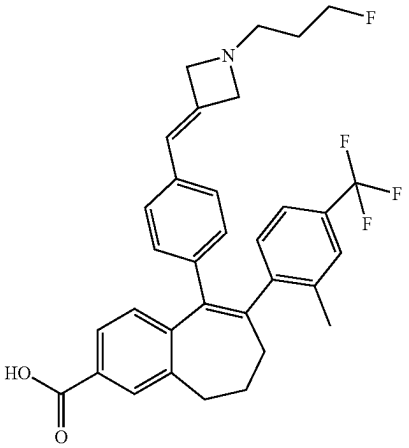
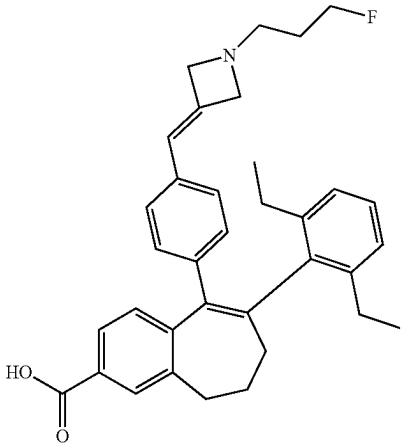
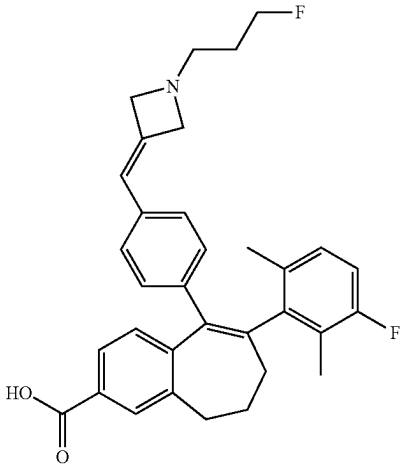
| Ex | Structure | Name |
|---|---|---|
| 73 |  | 8-(3-fluoro-2-methyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 74 |  | 8-(2,6-diethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 75 |  | 8-(3-fluoro-2,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

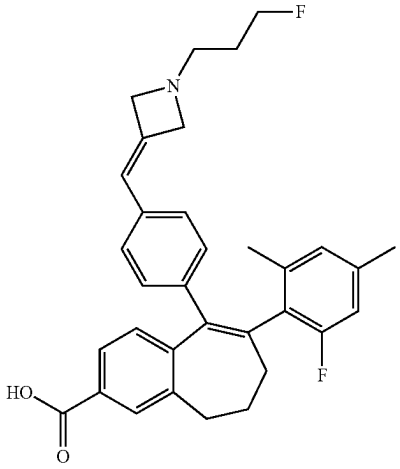
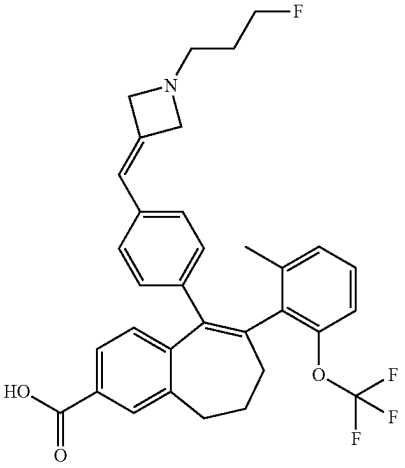
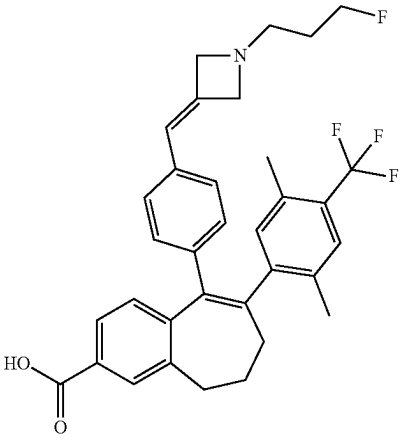
| Ex | Structure | Name |
|---|---|---|
| 76 |  | 8-(2-fluoro-4,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 77 |  | 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-6-(trifluoromethoxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 78 |  | 8-(2,5-dimethyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

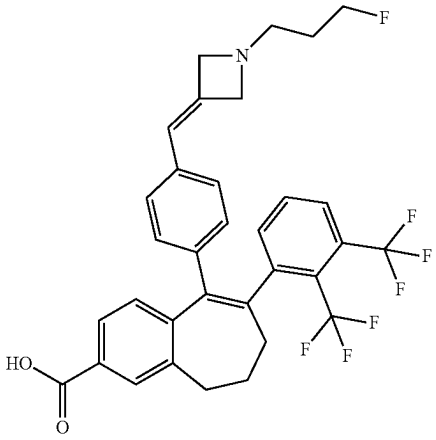
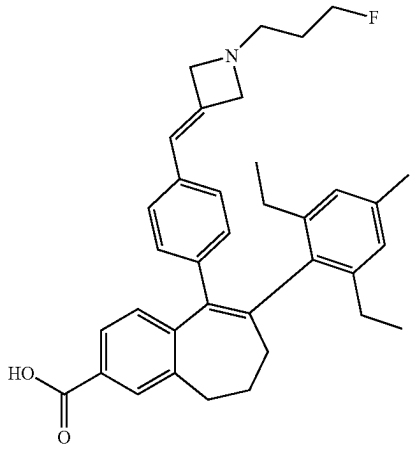
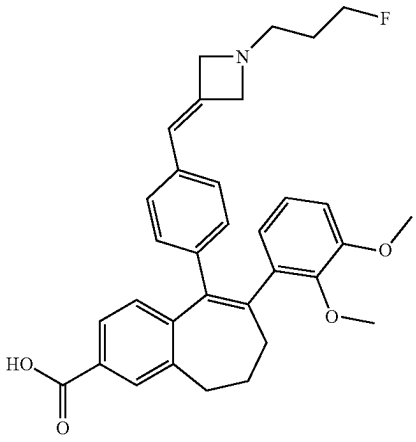
| Ex | Structure | Name |
|---|---|---|
| 79 |  | 8-(2,3-bis(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 80 |  | 8-(2,6-diethyl-4-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 81 |  | 8-(2,3-dimethoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |

TABLE 1a-continued

(the first column "Ex" corresponds to the compound and example number)

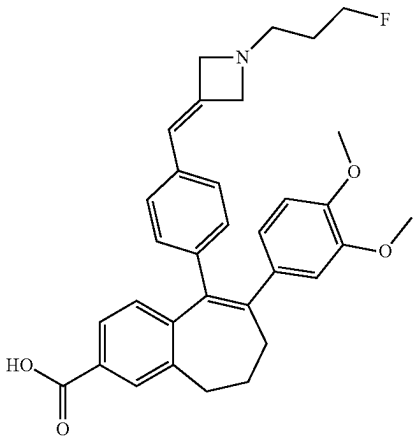
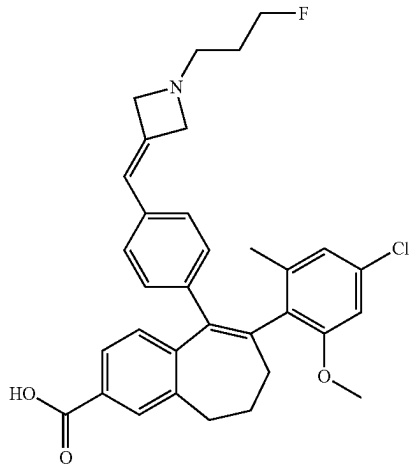
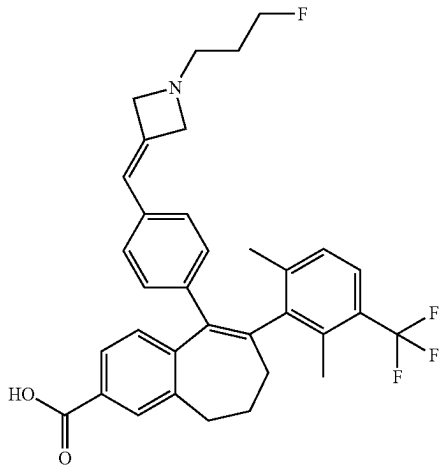
| Ex | Structure | Name |
|---|---|---|
| 82 |  | 8-(3,4-dimethoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 83 |  | 8-(4-chloro-2-methoxy-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid |
| 84 |  | 8-(2,6-dimethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5 H-benzo[7]annulene-3-carboxylic acid |

TABLE 1b

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| 1 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.10-2.23 (m, 4 H), 2.22 (s, 3 H), 2.60 (t, J = 7 Hz, 2 H), 2.92-2.98 (m, 2 H), 3.89 (br s, 2 H), 4.04 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.69 (d, J = 7 Hz, 2 H), 6.78-6.86 (m, 3 H), 7.36 (t, J = 8 Hz, 1 H), 7.45 (d, J = 8 Hz, 1 H), 7.56 (d, J = 8 Hz, 1 H), 7.74 (dd, J = 8 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 550 |
| 2 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.76 (m, 2 H), 2.06-2.27 (m, 4 H), 2.59 (br t, J = 7 Hz, 2 H), 2.84 (br d, J = 13 Hz, 1 H), 2.96-3.04 (m, 1 H), 3.87 (br s, 2 H), 4.04 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.79 (d, J = 8 Hz, 2 H), 6.86 (d, J = 8 Hz, 1 H), 6.93 (d, J = 8 Hz, 2 H), 7.05 (br dd, J = 9 Hz, 1 H), 7.55-7.63 (m, 1 H), 7.75 (dd, J = 8 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 572 |
| 3 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.62-1.75 (m, 2 H), 2.01-2.20 (m, 4 H), 2.22 (s, 3 H), 2.60 (t, J = 7 Hz, 2 H), 2.84-2.92 (m, 2 H), 3.75 (s, 3 H), 3.89 (br s, 2 H), 4.05 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.74-6.89 (m, 7 H), 7.02 (m, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 512 |
| 4 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 1.99-2.18 (m, 4 H), 2.07 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.88-3.01 (m, 2 H), 3.70 (s, 3 H), 3.80-3.92 (m, 2 H), 3.95-4.07 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.65 (d, J = 8 Hz, 1 H), 6.73-6.86 (m, 6 H), 7.07 (t, J = 7 Hz, 1 H), 7.72 (dd, J = 8 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 512 |
| 5 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.17 (t, J = 7 Hz, 3 H), 1.67 (dquin, J = 26, 6 Hz, 2 H), 2.15-2.31 (m, 4 H), 2.55-2.66 (m, 3 H), 2.79-3.09 (m, 3 H), 3.81-3.93 (m, 2 H), 3.94-4.08 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (quin, J = 2 Hz, 1 H), 6.71 (d, J = 8 Hz, 2 H), 6.83 (d, J = 9 Hz, 2 H), 6.89 (d, J = 8 Hz, 1 H), 7.30 (t, J = 8 Hz, 1 H), 7.38 (d, J = 7 Hz, 1 H), 7.55 (dd, J = 8, 1 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H), 11.20-13.93 (m, 1 H) | 564 |
| 6 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.74 (m, 2 H), 2.08-2.19 (m, 4 H), 2.57 (t, J = 6 Hz, 2 H), 2.87 (m, 1 H), 3.05 (m, 1 H), 3.70 (s, 3 H), 3.79-3.91 (m, 2 H), 3.92-4.07 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.03 (t, J = 2 Hz, 1 H), 6.74-6.86 (m, 5 H), 7.22 (d, J = 8 Hz, 2 H), 7.39 (t, J = 8 Hz, 1 H), 7.72 (dd, J = 8, 2 Hz, 1 H), 7.89 (d, J = 2 Hz, 1 H), 11.49-13.82 (m, 1 H) | 566 |
| 7 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.67 (dquin, J = 25, 7 Hz, 2 H), 2.03-2.22 (m, 4 H), 2.10 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.84-3.02 (m, 2 H), 3.68 (d, J = 2 Hz, 3 H), 3.84-3.89 (m, 2 H), 3.99-4.04 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (quin, J = 2 Hz, 1 H), 6.77 (d, J = 8 Hz, 2 H), 6.79-6.88 (m, 4 H), 7.00 (dd, J = 12, 8 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | 530 |
| 8 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.20 (t, J = 8 Hz, 3 H), 1.67 (dquin, J = 24, 7 Hz, 2 H), 2.03-2.27 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.72-2.87 (m, 3 H), 2.99 (m, 1 H), 3.79-3.92 (m, 2 H), 3.97-4.05 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (quin, J = 2 Hz, 1 H), 6.77-6.88 (m, 5 H), 6.96 (t, J = 5 Hz, 1 H), 7.28-7.34 (m, 2 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.89 (d, J = 2 Hz, 1 H) | 564 |
| 9 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.62-1.75 (m, 2 H), 2.12-2.25 (m, 4 H), 2.60 (t, J = 7 Hz, 2 H), 2.88-2.94 (m, 2 H), 3.83-3.92 (m, 2 H), 3.96-4.10 (m, 2 H), 4.47 (dt, J = 47, 6 Hz, 2 H), 6.08 (quin, J = 2 Hz, 1 H), 6.77 (d, J = 8 Hz, 2 H), 6.84-6.93 (m, 3 H), 7.12 (dd, J = 9, 1 Hz, 1 H), 7.20 (t, J = 8 Hz, 1 H), 7.41 (td, J = 9, 7 Hz, 1 H), 7.76 (dd, J = 8, 2 Hz, 1 H), 7.94 (d, J = 2 Hz, 1 H) | 570 |
| 10 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.76 (m, 2 H), 2.02-2.23 (m, 4 H), 2.12 (s, 6 H), 2.18 (s, | 510 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| | | 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.95 (t, J = 7 Hz, 2 H), 3.79-3.94 (m, 2 H), 3.95-4.08 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.71 (d, J = 9 Hz, 2 H), 6.78 (s, 2 H), 6.83 (d, J = 8 Hz, 3 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 11.21-14.25 (m, 1 H) | |
| 11 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H), 2.07-2.20 (m, 4 H), 2.14 (s, 3 H), 2.21 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.89-3.07 (m, 2 H), 3.87 (br s, 2 H), 4.02 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.77-6.84 (m, 3 H), 6.87 (d, J = 8 Hz, 2 H), 6.91 (br s, 1 H), 7.10 (br s, 1 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | 530 |
| 12 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.70-1.94 (m, 2 H), 2.07 (d, J = 3 Hz, 3 H), 2.12-2.20 (m, 7 H), 2.80-3.06 (m, 4 H), 4.31-4.40 (m, 2 H), 4.50 (dt, J = 47, 6 Hz, 2 H), 4.52-4.63 (m, 2 H), 6.18-6.25 (m, 1 H), 6.75-6.82 (m, 3 H), 6.85 (d, J = 8 Hz, 1 H), 6.90 (d, J = 8 Hz, 2 H), 6.95 (t, J = 8 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 10.06-13.96 (m, 2 H) | 514 |
| 13 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.73-1.88 (m, 2 H), 2.08-2.23 (m, 4 H), 2.26 (s, 3 H), 2.27 (s, 3 H), 2.79-3.03 (m, 4 H), 4.29-4.38 (m, 2 H), 4.50 (dt, J = 47, 6 Hz, 2 H), 4.47-4.53 (m, 2 H), 6.20 (br s, 1 H), 6.78 (d, J = 8 Hz, 2 H), 6.85 (d, J = 8 Hz, 1 H), 6.87-6.93 (m, 3 H), 7.03 (d, J = 8 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 9.72-11.24 (m, 1 H), 11.89-13.59 (m, 1 H) | 530 |
| 14 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.67 (dquin, J = 25, 6 Hz, 2 H), 1.96-2.15 (m, 4 H), 2.02 (s, 3 H), 2.21 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.89-2.97 (m, 2 H), 3.69 (s, 3 H), 3.84-3.89 (m, 2 H), 4.02 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (quin, J = 2 Hz, 1 H), 6.47 (s, 1 H), 6.62 (s, 1 H), 6.76 (d, J = 8 Hz, 2 H), 6.78-6.84 (m, 3 H), 7.71 (dd, J = 8, 2 Hz, 1 H), 7.89 (d, J = 2 Hz, 1 H) | 526 |
| 15 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.68 (dquin, J = 25, 6 Hz, 2 H), 1.99 (t, J = 19 Hz, 3 H), 2.09-2.22 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.78-2.91 (m, 1 H), 2.91-3.03 (m, 1 H), 3.84-3.88 (m, 2 H), 4.00-4.04 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (quin, J = 2 Hz, 1 H), 6.76-6.90 (m, 5 H), 7.04-7.18 (m, 2 H), 7.43 (dd, J = 10, 3 Hz, 1 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.89 (d, J = 2 Hz, 1 H) | 550 |
| 16 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.74 (m, 2 H), 2.09-2.30 (m, 4 H), 2.58 (t, J = 8 Hz, 2 H), 2.93 (m, 1 H), 3.09 (m, 1 H), 3.83-3.89 (m, 2 H), 3.97-4.05 (m, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.77 (d, J = 9 Hz, 2 H), 6.80 (d, J = 8 Hz, 1 H), 6.86 (d, J = 8 Hz, 2 H), 7.49 (td, J = 8, 1 Hz, 1 H), 7.66-7.79 (m, 3 H), 7.92 (d, J = 2 Hz, 1 H) | 570 |
| 17 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.15-2.23 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.93-3.00 (m, 2 H), 3.87-3.87 (m, 2 H), 3.94-4.09 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.77 (d, J = 8 Hz, 2 H), 6.84-6.90 (m, 3 H), 7.22 (d, J = 8 Hz, 1 H), 7.38 (t, J = 8 Hz, 1 H), 7.48 (d, J = 8 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 586 |
| 18 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.67 (dquin, J = 25, 7 Hz, 2 H), 2.08 (s, 4 H), 2.13 (s, 6 H), 2.59 (t, J = 7 Hz, 2 H), 2.94 (br t, J = 7 Hz, 2 H), 3.68 (s, 3 H), 3.87 (br s, 2 H), 3.94-4.12 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (quin, J = 2 Hz, 1 H), 6.55 (s, 2 H), 6.71 (d, J = 7 Hz, 2 H), 6.83 (dd, J = 8, 5 Hz, 3 H), 7.72 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 526 |
| 19 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.16 (t, J = 8 Hz, 3 H), 1.67 (dquin, J = 26, 7 Hz, 2 H), 2.07-2.24 (m, 4 H), 2.54-2.66 (m, 4 H), 2.85 (m, 1 H), 2.93-3.03 (m, 1 H), 3.80-3.91 (m, 2 H), 3.96-4.05 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.04 (quin, J = 2 Hz, 1 H), 6.78 (d, J = 9 Hz, 2 H), 6.81-6.88 (m, 3 H), 7.11 | 564 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| | | (d, J = 8 Hz, 1 H), 7.29 (d, J = 8 Hz, 1 H), 7.53 (d, J = 2 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | |
| 20 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.76 (m, 2 H), 2.10-2.26 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.81-3.05 (m, 2 H), 3.83-3.90 (m, 2 H), 4.01 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.79 (d, J = 9 Hz, 2 H), 6.84-6.92 (m, 3 H), 7.42 (m, 1 H), 7.50 (m, 1 H), 7.58 (dd, J = 8, 1 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 11.99-14.17 (m, 1 H) | 554 |
| 21 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.74 (m, 2 H), 2.08-2.28 (m, 4 H), 2.19 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.92-3.08 (m, 2 H), 3.86 (m, 2 H), 4.02 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.76-6.89 (m, 5 H), 7.03-7.18 (m, 2 H), 7.26 (dd, J = 8, 1 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H), 11.14-14.71 (m, 1 H) | 516 |
| 22 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H), 2.03-2.19 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.86-2.94 (m, 2 H), 3.74 (s, 3 H), 3.86 (br q, J = 3 Hz, 2 H), 3.94-4.09 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.63 (t, J = 8 Hz, 1 H), 6.78 (d, J = 8 Hz, 2 H), 6.81 (d, J = 8 Hz, 1 H), 6.82-6.88 (m, 3 H), 7.19 (td, J = 8, 7 Hz, 1 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H), 11.14-14.22 (m, 1 H) | 516 |
| 23 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H), 2.05-2.19 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.93-3.08 (m, 2 H), 3.70 (s, 3 H), 3.81-3.92 (m, 2 H), 4.01-4.02 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.77-6.88 (m, 5 H), 6.88-6.94 (m, 2 H), 7.18 (t, J = 8 Hz, 1 H), 7.72 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H), 11.22-13.99 (m, 1 H) | 532 |
| 24 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.57-1.82 (m, 2 H), 2.11 (s, 3 H), 2.13-2.27 (m, 4 H), 2.61-2.69 (m, 2 H), 2.82-3.00 (m, 2 H), 3.96-3.96 (m, 2 H), 4.05-4.15 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.09 (quin, J = 2 Hz, 1 H), 6.72 (d, J = 9 Hz, 2 H), 6.81-6.92 (m, 3 H), 7.08-7.22 (m, 3 H), 7.76 (d, J = 8 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 566 |
| 25 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.15 (t, J = 8 Hz, 3 H), 1.59-1.75 (m, 2 H), 2.10-2.27 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.64-2.77 (m, 2 H), 2.84-3.02 (m, 2 H), 3.86 (br s, 2 H), 4.01 (br s, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.74 (d, J = 8 Hz, 2 H), 6.82-6.90 (m, 3 H), 7.26 (d, J = 8 Hz, 1 H), 7.40 (dd, J = 8, 2 Hz, 1 H), 7.52 (d, J = 2 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 11.39-14.07 (m, 1 H) | 564 |
| 26 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.73 (dquin, J = 25, 7 Hz, 2 H), 2.14-2.29 (m, 4 H), 2.25 (s, 3 H), 2.64 (t, J = 7 Hz, 2 H), 2.93-3.05 (m, 2 H), 3.92 (br s, 2 H), 4.07 (br s, 2 H), 4.52 (dt, J = 47, 6 Hz, 2 H), 6.12 (quin, J = 2 Hz, 1 H), 6.83 (d, J = 9 Hz, 2 H), 6.92 (d, J = 8 Hz, 3 H), 6.95-7.04 (m, 2 H), 7.20 (td, J = 8, 6 Hz, 1 H), 7.80 (dd, J = 8, 2 Hz, 1 H), 7.99 (d, J = 2 Hz, 1 H), 10.78-14.18 (m, 1 H) | 500 |
| 27 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.77 (m, 2 H), 2.08 (s, 3 H), 2.10 (s, 3 H), 2.12-2.21 (m, 4 H), 2.61 (t, J = 7 Hz, 2 H), 2.83-2.99 (m, 2 H), 3.89 (br s, 2 H), 4.05 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.74 (d, J = 8 Hz, 2 H), 6.82-6.91 (m, 4 H), 6.99 (d, J = 8 Hz, 1 H), 7.74 (d, J = 8 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 11.04-13.76 (m, 1 H) | 514 |
| 28 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.58-1.77 (m, 2 H), 2.04-2.19 (m, 2 H), 2.24-2.31 (m, 5 H), 2.59 (t, J = 7 Hz, 2 H), 2.85 (br t, J = 7 Hz, 2 H), 3.88 (br s, 2 H), 4.04 (br s, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.09 (t, J = 2 Hz, 1 H), 6.73-7.21 (m, 8 H), 7.30 (d, J = 8 Hz, 1 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.89 (d, J = 2 Hz, 1 H) | 532 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| 29 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.51-1.83 (m, 2 H), 2.05-2.19 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.82-2.94 (m, 2 H), 3.78 (s, 3 H), 3.83-3.92 (m, 2 H), 3.99-4.06 (m, 2 H), 4.46 (dt, J = 46, 7 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.74-6.81 (m, 2 H), 6.85 (m, 3 H), 6.90-6.98 (m, 2 H), 7.06 (d, J = 8 Hz, 1 H), 7.14 (d, J = 2 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H), 11.65-13.69 (m, 1 H) | 548 |
| 30 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.01-2.20 (m, 3 H), 2.27 (m, 1 H), 2.44 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.85 (m, 1 H), 2.96 (m, 1 H), 3.87 (m, 2 H), 3.98-4.07 (m, 2 H), 4.46 (dt, J = 47, 5 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.70-7.33 (m, 9 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 11.84-13.61 (m, 1 H) | 532 |
| 31 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.57-1.79 (m, 2 H), 2.07-2.24 (m, 2 H), 2.27-2.36 (m, 2 H), 2.60 (t, J = 7 Hz, 2 H), 2.87 (br t, J = 7 Hz, 2 H), 3.63 (s, 3 H), 3.89 (br s, 2 H), 4.03 (br s, 2 H), 4.47 (dt, J = 48, 6 Hz, 2 H), 6.11 (t, J = 2 Hz, 1 H), 6.71-7.17 (m, 8 H), 7.30 (d, J = 8 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 11.32-14.17 (m, 1 H) | 548 |
| 32 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.19 (m, 4 H), 2.58 (br t, J = 7 Hz, 2 H), 2.83-2.98 (m, 2 H), 3.82-3.90 (m, 2 H), 3.93-4.08 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 4.98-5.55 (m, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.72-6.79 (m, 2 H), 6.79-6.87 (m, 3 H), 7.17-7.39 (m, 4 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 11.42-14.05 (m, 1 H) | 500 |
| 33 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.63-1.83 (m, 2 H), 2.08-2.28 (m, 4 H), 2.70-2.78 (m, 2 H), 2.90 (t, J = 7 Hz, 2 H), 4.07 (br s, 2 H), 4.24 (br s, 2 H), 4.48 (dt, J = 47, 6 Hz, 2 H), 6.14 (br s, 1 H), 6.81 (d, J = 8 Hz, 2 H), 6.84 (d, J = 8 Hz, 1 H), 6.90 (d, J = 8 Hz, 2 H), 6.94-7.33 (m, 4 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 12.66 (s, 1 H) | 552 |
| 34 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.64-1.84 (m, 2 H), 2.12-2.30 (m, 4 H), 2.78 (br s, 2 H), 2.92-3.00 (m, 2 H), 4.10 (br s, 2 H), 4.26 (br s, 2 H), 4.48 (dt, J = 47, 6 Hz, 2 H), 6.14 (br s, 1 H), 6.80 (d, J = 8 Hz, 2 H), 6.84-6.94 (m, 3 H), 7.24 (m, 1 H), 7.31 (t, J = 8 Hz, 1 H), 7.41 (m, 1 H), 7.76 (m, 1 H), 7.94 (d, J = 2 Hz, 1 H), 12.63 (br s, 1 H) | 586 |
| 35 | C | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.78-0.89 (m, 2 H), 1.32-1.57 (m, 3 H), 1.64-1.79 (m, 2 H), 1.93-2.18 (m, 8 H), 2.60-2.73 (m, 4 H), 3.87-3.98 (m, 2 H), 4.07-4.18 (m, 2 H), 4.49 (dt, J = 47, 6 Hz, 2 H), 6.20 (t, J = 2 Hz, 1 H), 6.78 (d, J = 8 Hz, 1 H), 7.14 (s, 4 H), 7.68 (dd, J = 8, 2 Hz, 1 H), 7.82 (d, J = 2 Hz, 1 H), 11.93-13.45 (m, 1 H) | 472 |
| 36 | C | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.76-0.91 (m, 2 H), 1.33-1.59 (m, 3 H), 1.61-1.80 (m, 2 H), 1.88-2.21 (m, 8 H), 2.63 (t, J = 7 Hz, 2 H), 2.94-3.23 (m hidden, 2 H), 3.93 (br s, 2 H), 4.12 (br s, 2 H), 4.48 (dt, J = 47, 6 Hz, 2 H), 6.20 (t, J = 2 Hz, 1 H), 6.78 (d, J = 8 Hz, 1 H), 7.13 (s, 4 H), 7.67 (dd, J = 8, 2 Hz, 1 H), 7.82 (d, J = 2 Hz, 1 H) | 472 |
| 37 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.12-2.26 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.82-2.97 (m, 2 H), 3.77 (s, 3 H), 3.87 (m, 2 H), 4.03 (m, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.71-7.18 (m, 9 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H), 12.30-13.35 (m, 1 H) | 548 |
| 38 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.63-1.87 (m, 2 H), 2.14-2.30 (m, 4 H), 2.83-2.97 (m, 4 H), 4.18-4.31 (m, 2 H), 4.35-4.47 (m, 2 H), 4.49 (dt, J = 47, 6 Hz, 2 H), 5.39 (ddd, J = 49, 32, 10 Hz, 2 H), 6.17 (br s, 1 H), 6.78-6.84 (m, 2 H), 6.84-6.91 (m, 3 H), 7.00 (d, J = 8 Hz, 1 H), 7.13 (t, J = 9 Hz, 1 H), 7.33 (m, 1 H), 7.76 (dd, J = 8, 2 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 518 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| 39 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.07 (t, J = 8 Hz, 3 H), 1.61-1.85 (m, 2 H), 2.13-2.24 (m, 4 H), 2.48-2.66 (m partially hidden, 2 H), 2.76 (t, J = 7 Hz, 2 H), 2.86 (m, 1 H), 2.95 (m, 1 H), 4.09 (br s, 2 H), 4.26 (br s, 2 H), 4.48 (dt, J = 47, 6 Hz, 2 H), 6.12 (br s, 1 H), 6.76 (d, J = 8 Hz, 2 H), 6.87 (dd, J = 8, 2 Hz, 3 H), 6.90 (dd, J = 8, 1 Hz, 1 H), 6.98 (m, 1 H), 7.10 (td, J = 8, 6 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | 514 |
| 40 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.81 (m, 2 H), 2.08-2.25 (m, 4 H), 2.59-2.72 (m, 2 H), 2.85-2.93 (m, 2 H), 3.77 (d, J = 2 Hz, 3 H), 3.95 (br s, 2 H), 4.11 (br s, 2 H), 4.47 (dt, J = 47, 6 Hz, 2 H), 6.09 (m, 1 H), 6.75-6.94 (m, 7 H), 7.08 (ddd, J = 12, 8, 2 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 516 |
| 41 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.73-1.93 (m, 2 H), 2.04 (s, 3 H), 2.05-2.21 (m, 4 H), 2.83-3.00 (m, 2 H), 3.01-3.07 (m, 2 H), 3.75 (s, 3 H), 4.32-4.48 (m, 2 H), 4.50 (dt, J = 47, 6 Hz, 2 H), 4.59-4.69 (m, 2 H), 6.22 (br s, 1 H), 6.63 (d, J = 7 Hz, 1 H), 6.74-6.90 (m, 6 H), 7.01 (t, J = 8 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 9.40-11.45 (m, 1 H), 11.69-13.47 (m, 1 H) | 512 |
| 42 | G | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.09-1.42 (m, 2 H), 1.76-1.97 (m, 2 H), 2.01-2.27 (m, 4 H), 2.23 (s, 3 H), 2.62-2.88 (m, 2 H), 3.94 (br s, 2 H), 4.10 (br s, 2 H), 6.09 (tt, J = 57, 5 Hz, 1 H), 6.08 (m, 1 H), 6.52-6.61 (m, 2 H), 6.73 (m, 3 H), 6.83 (d, J = 8 Hz, 2 H), 6.95 (m, 1 H), 7.02 (m, 1 H), 7.21 (dd, J = 8, 1 Hz, 1 H), 9.41 (s, 1 H) | 506 |
| 43 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H), 2.11-2.27 (m, 4 H), 2.31 (s, 3 H), 2.58 (t, J = 7 Hz, 2 H), 2.79-3.02 (m, 2 H), 3.80-3.92 (m, 2 H), 3.94-4.09 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.75-6.89 (m, 5 H), 6.93 (t, J = 56 Hz, 1 H), 7.10 (d, J = 8 Hz, 1 H), 7.21 (d, J = 8 Hz, 1 H), 7.33 (s, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 532 |
| 44 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.74 (m, 2 H), 2.11-2.21 (m, 4 H), 2.23 (s, 3 H), 2.59 (br t, J = 7 Hz, 2 H), 2.83-3.02 (m, 2 H), 3.81-3.93 (m, 2 H), 3.94-4.09 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.74 (d, J = 8 Hz, 2 H), 6.92 (t, J = 56 Hz, 1 H), 6.82-6.89 (m, 3 H), 7.18(m, 1 H), 7.24 (m, 1 H), 7.33 (s, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | 532 |
| 45 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.14-2.31 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.84-2.98 (m, 2 H), 3.72 (s, 3 H), 3.87 (br s, 2 H), 4.02 (br s, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.66-7.01 (m, 8 H), 7.44 (d, J = 9 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 548 |
| 46 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.13 (t, J = 7 Hz, 3 H), 1.59-1.77 (m, 2 H), 2.13-2.28 (m, 4 H), 2.53-2.65 (m, 3 H), 2.72-2.82 (m, 1 H), 2.82-3.06 (m, 2 H), 3.84-3.99 (m, 2 H), 4.01-4.13 (m, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.07 (br d, J = 2 Hz, 1 H), 6.70-6.80 (m, 2 H), 6.82-6.92 (m, 3 H), 7.00-7.13 (m, 2 H), 7.26 (dd, J = 8, 2 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 12.77 (br s, 1 H) | 530 |
| 47 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H), 2.13-2.24 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.85 (m, 1 H), 3.01 (m, 1 H), 3.69 (s, 3 H), 3.88 (br s, 2 H), 4.04 (br s, 2 H), 4.46 (dt, J = 49, 7 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.68 (d, J = 3 Hz, 1 H), 6.80-6.91 (m, 5 H), 6.94 (m, 1 H), 7.64 (d, J = 9 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 566 |
| 48 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.71 (m, 1 H), 0.85 (m, 1 H), 0.93-1.07 (m, 2 H), 1.58-1.76 (m, 2 H), 2.00 (m, 1 H), 2.12-2.34 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.88 (m, 1 H), 2.98 (m, 1 H), 3.84-3.89 (m, 2 H), 3.98-4.05 (m, 2 H), 4.46 (dt, J = 48, 6 | 576 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| | | Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.79-6.90 (m, 5 H), 7.03 (d, J = 2 Hz, 1 H), 7.17 (d, J = 8 Hz, 1 H), 7.31 (dd, J = 8, 1 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | |
| 49 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.62-1.76 (m, 2 H), 2.10-2.31 (m, 4 H), 2.63 (br t, J = 7 Hz, 2 H), 2.90 (t, J = 5 Hz, 2 H), 3.81 (s, 3 H), 3.93 (br s, 2 H), 4.09 (br s, 2 H), 4.47 (dt, J = 48, 6 Hz, 2 H), 6.09 (t, J = 2 Hz, 1 H), 6.82-6.96 (m, 6 H), 6.98 (m, 1 H), 7.30 (dd, J = 8, 2 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 532 |
| 50 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.58-1.78 (m, 2 H), 2.08-2.24 (m, 2 H), 2.29-2.38 (m, 2 H), 2.60 (t, J = 7 Hz, 2 H), 2.88 (br t, J = 7 Hz, 2 H), 3.67 (s, 3 H), 3.89 (br s, 2 H), 4.04 (br s, 2 H), 4.46 (dt, J = 48, 6 Hz, 2 H), 6.11 (t, J = 2 Hz, 1 H), 6.81-6.95 (m, 6 H), 7.01 (s, 1 H), 7.41 (d, J = 8 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 12.87 (br s, 1 H) | 566 |
| 51 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.58-1.76 (m, 2 H), 2.09-2.30 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.87 (m, 1 H), 3.01(m, 1 H), 3.86 (br d, J = 3 Hz, 2 H), 4.01 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.79 (d, J = 8 Hz, 2 H), 6.84-6.90 (m, 3 H), 7.09 (t, J = 56 Hz, 1 H), 7.40 (d, J = 8 Hz, 1 H), 7.68 (br d, J = 8 Hz, 1 H), 7.76 (dd, J = 8, 2 Hz, 1 H), 7.89-7.95 (m, 2 H), 12.07-13.71 (m, 1 H) | 586 |
| 52 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.76 (m, 2 H), 1.99-2.23 (m, 4 H), 2.61 (br t, J = 7 Hz, 2 H), 2.83 (m, 1 H), 2.99 (m, 1 H), 3.84-3.96 (m, 2 H), 3.87 (s, 3 H), 4.05-4.08 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.67 (d, J = 8 Hz, 1 H), 6.78-6.92 (m, 5 H), 7.08 (d, J = 9 Hz, 1 H), 7.34 (t, J = 8 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 566 |
| 53 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.62-1.75 (m, 2 H), 2.08-2.20 (m, 2 H), 2.24-2.37 (m, 5 H), 2.61 (t, J = 7 Hz, 2 H), 2.87 (br t, J = 7 Hz, 2 H), 3.84-3.96 (m, 2 H), 3.98-4.13 (m, 2 H), 4.47 (dt, J = 48, 6 Hz, 2 H), 6.11 (t, J = 2 Hz, 1 H), 6.82 (d, J = 8 Hz, 2 H), 6.85 (d, J = 8 Hz, 1 H), 6.91 (d, J = 8 Hz, 2 H), 7.12 (d, J = 8 Hz, 1 H), 7.29 (s, 1 H), 7.45 (d, J = 8 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 550 |
| 54 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H), 2.12-2.29 (m, 4 H), 2.59 (t, J = 8 Hz, 2 H), 2.90 (t, J = 6 Hz, 2 H), 3.84-3.91 (m, 2 H), 3.95-4.09 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.08 (t, J = 2 Hz, 1 H), 6.76 (d, J = 8 Hz, 2 H), 6.87 (dd, J = 12, 8 Hz, 3 H), 7.05 (t, J = 56 Hz, 1 H), 7.41 (s, 1 H), 7.44-7.55 (m, 2 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 602 |
| 55 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.75 (m, 2 H), 2.07-2.20 (m, 2 H), 2.30 (t, J = 6 Hz, 2 H), 2.60 (t, J = 7 Hz, 2 H), 2.87 (br t, J = 7 Hz, 2 H), 3.83-3.94 (m, 2 H), 3.96-4.11 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.09 (t, J = 2 Hz, 1 H), 6.78-7.11 (m, 6 H), 7.31 (m, 2 H), 7.37-7.42 (m, 2 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 11.02-14.07 (m, 1 H) | 518 |
| 56 | D | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.62-0.87 (m, 4 H), 1.17-1.80 (m, 10 H), 1.81-1.95 (m, 2 H), 2.05-2.18 (m, 2 H), 2.27-2.37 (m, 1 H), 2.62 (t, J = 7 Hz, 2 H), 2.70 (br t, J = 7 Hz, 2 H), 3.90-3.95 (m, 2 H), 4.09-4.14 (m, 2 H), 4.48 (dt, J = 48, 6 Hz, 2 H), 6.19 (t, J = 2 Hz, 1 H), 6.71 (d, J = 8 Hz, 1 H), 7.00 (d, J = 8 Hz, 2 H), 7.09 (d, J = 9 Hz, 2 H), 7.63 (dd, J = 8, 2 Hz, 1 H), 7.80 (d, J = 2 Hz, 1 H) | 488 |
| 57 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.58-1.77 (m, 2 H), 2.13-2.22 (m, 4 H), 2.26 (s, 3 H), 2.59 (t, J = 7 Hz, 2 H), 2.85-2.98 (m, 2 H), 3.82-3.93 (m, 2 H), 3.98-4.06 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), | 532 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| | | 6.06 (t, J = 2 Hz, 1 H), 6.88 (t, J = 55 Hz, 1 H), 6.76-6.87 (m, 5 H), 7.06 (s, 1 H), 7.17 (d, J = 8 Hz, 1 H), 7.40 (d, J = 8 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.91 (br d, J = 2 Hz, 1 H) | |
| 58 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.55-1.79 (m, 2 H), 2.13-2.30 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.81-3.01 (m, 2 H), 3.80-3.90 (m, 2 H), 4.00-4.04 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.76-6.89 (m, 5 H), 6.96 (t, J = 55 Hz, 1 H), 7.21 (d, J = 7 Hz, 1 H), 7.33-7.43 (m, 2 H), 7.53 (d, J = 7 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | 518 |
| 59 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.54-1.81 (m, 2 H), 2.06-2.18 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.89 (br t, J = 5 Hz, 2 H), 3.81 (s, 3 H), 3.85-3.91 (m, 2 H), 4.00-4.05 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.75-6.80 (m, 2 H), 6.80-6.88 (m, 3 H), 7.08-7.16 (m, 2 H), 7.23 (d, J = 1 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 566 |
| 60 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.76 (m, 2 H), 2.09-2.27 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.83 (m, 1 H), 2.95 (m, 1 H), 3.82 (s, 3 H), 3.84-3.88 (m, 2 H), 3.94-4.10 (m, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.66 (d, J = 8 Hz, 1 H), 6.79-6.88 (m, 5 H), 7.05 (br t, J = 54 Hz, 1 H), 6.98 (d, J = 9 Hz, 1 H), 7.27 (t, J = 8 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 548 |
| 61 | D | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.98 (d, J = 7 Hz, 3 H), 1.29-1.94 (m, 14 H), 2.06-2.23 (m, 2 H), 2.37 (m, 1 H), 2.62 (t, J = 7 Hz, 2 H), 2.71 (br t, J = 7 Hz, 2 H), 3.90-3.95 (m, 2 H), 4.08-4.16 (m, 2 H), 4.49 (dt, J = 47, 6 Hz, 2 H), 6.19 (t, J = 2 Hz, 1 H), 6.73 (d, J = 8 Hz, 1 H), 7.00 (m, 2H), 7.07-7.12 (m, 2 H), 7.64 (dd, J = 8, 2 Hz, 1 H), 7.81 (d, J = 2 Hz, 1 H) | 488 |
| 62 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.77 (m, 2 H), 2.09-2.22 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.79-2.91 (m, 1 H), 2.98 (m, 1 H), 3.78 (s, 3 H), 3.83-3.91 (m, 2 H), 3.95-4.11 (m, 2 H), 4.46 (dt, J = 46, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.78 (d, J = 8 Hz, 2 H), 6.82-6.90 (m, 3 H), 7.02 (dd, J = 9, 3 Hz, 1 H), 7.11 (d, J = 9 Hz, 1 H), 7.19 (d, J = 3 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H), 12.82 (br s, 1 H) | 566 |
| 63 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.77 (m, 2 H), 2.07-2.23 (m, 4 H), 2.60 (t, J = 7 Hz, 2 H), 2.79-3.01 (m, 2 H), 3.86-3.93 (m, 2 H), 3.91 (s, 3 H), 3.98-4.11 (m, 2 H), 4.46 (dt, J = 46, 6 Hz, 2 H), 6.09 (t, J = 2 Hz, 1 H), 6.85-6.95 (m, 5 H), 7.04 (t, J = 8 Hz, 1 H), 7.22 (dd, J = 8, 2 Hz, 1 H), 7.49 (dd, J = 8, 2 Hz, 1 H), 7.76 (dd, J = 8, 2 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H), 11.97-13.75 (m, 1 H) | 566 |
| 64 | E | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.78 (m, 3 H), 1.90 (m, 1 H), 2.09-2.22 (m, 4 H), 2.54-2.74 (m, 4 H), 2.81-2.97 (m, 2 H), 3.83-4.09 (m, 6 H), 4.46 (dt, J = 46, 7 Hz, 2 H), 6.07 (t, J = 2 Hz, 1 H), 6.53-6.62 (m, 2 H), 6.70-6.78 (m, 2 H), 6.82-6.94 (m, 4 H), 7.74 (d, J = 8 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 11.26-13.91 (m, 1 H) | 524 |
| 65 | F | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.83 (s, 3 H), 0.90 (s, 3 H), 0.94-1.05 (m, 2 H), 1.35 (br d, J = 13 Hz, 2 H), 1.41-1.49 (m, 2 H), 1.50-1.78 (m, 4 H), 1.94-2.05 (m, 3 H), 2.18 (br t, J = 7 Hz, 2 H), 2.61-2.65 (m, 2 H), 2.70-2.78 (m, 2 H), 3.86-4.05 (m, 2 H), 4.17 (m, 2 H), 4.49 (dt, J = 48, 6 Hz, 2 H), 6.29 (br s, 1 H), 6.81 (d, J = 8 Hz, 1 H), 7.36 (dd, J = 11, 2 Hz, 1 H), 7.66 (dd, J = 8, 2 Hz, 1 H), 7.83 (d, J = 2 Hz, 1 H), 8.28 (t, J = 2 Hz, 1 H), 12.81 (br s, 1 H) | 521 |
| 66 | F | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.83 (s, 3 H), 0.90 (s, 3 H), 0.94-1.05 (m, 2 H), 1.35 (br d, J = 13 Hz, 2 H), 1.41-1.61 (m, 4 H), 1.82-2.02 (m, 5 H), 2.10-2.22 (m, 2 H), 2.67 (t, J = 7 Hz, 2 H), 2.74 (t, J = 6 Hz, 2 H), 3.94-4.02 (m, 2 H), 4.15- | 539 |

TABLE 1b-continued

| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| | | 4.25 (m, 2 H), 6.11 (t, J = 57 Hz, 1 H), 6.30 (br s, 1 H), 6.81 (d, J = 8 Hz, 1 H), 7.36 (dd, J = 11, 2 Hz, 1 H), 7.66 (dd, J = 8, 2 Hz, 1 H), 7.83 (d, J = 2 Hz, 1 H), 8.28 (t, J = 2 Hz, 1 H), 9.84-13.69 (m, 1 H) | |
| 67 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.59-1.77 (m, 2 H), 1.80-1.93 (m, 2 H), 2.02-2.21 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.71 (br t, J = 6 Hz, 2 H), 2.86 (t, J = 6 Hz, 2 H), 3.81-3.94 (m, 2 H), 4.00-4.11 (m, 4 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.59 (t, J = 6 Hz, 1 H), 6.71 (dd, J = 7, 2 Hz, 1 H), 6.74-6.89 (m, 6 H), 7.72 (dd, J = 8, 2 Hz, 1 H), 7.88 (d, J = 2 Hz, 1 H), 10.52-13.69 (m, 1 H) | 524 |
| 68 | D | 1H NMR (400 MHz, DMSO-d6) δ ppm 0.83 (s, 3 H), 0.91 (s, 3 H), 0.96-1.09 (m, 2 H), 1.31-1.46 (m, 4 H), 1.53-1.69 (m, 2 H), 1.86-2.03 (m, 4 H), 2.07-2.20 (m, 2 H), 2.22-2.35 (m, 1 H), 2.73 (t, J = 7 Hz, 2 H), 3.29-3.30 (m hidden, 2 H), 4.56 (dt, J = 47, 6 Hz, 2 H), 4.77 (br s, 2 H), 5.02 (br s, 2 H), 6.45 (br s, 1 H), 6.72 (d, J = 8 Hz, 1 H), 7.06 (m, 2 H), 7.12-7.19 (m, 2 H), 7.66 (dd, J = 8, 2 Hz, 1 H), 7.83 (d, J = 2 Hz, 1 H), 10.02-13.97 (m, 1 H) | 502 |
| 69 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 2.10-2.26 (m, 4 H), 2.78-2.90 (m, 2 H), 2.93 (br s, 2 H), 3.98 (br s, 2 H), 4.14 (br s, 2 H), 4.39-4.91 (m, 3 H), 6.07 (br s, 1 H), 6.67-6.97 (m, 5 H), 7.17-7.31 (m, 2 H), 7.58 (d, J = 2 Hz, 1 H), 7.74 (br d, J = 8 Hz, 1 H), 7.91 (br s, 1 H) | 554 |
| 70 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 2.09-2.27 (m, 4 H), 2.77-2.88 (m, 2 H), 2.89-2.98 (m, 2 H), 3.98 (br s, 2 H), 4.14 (br s, 2 H), 4.24-4.87 (m, 3 H), 6.07 (t, J = 2 Hz, 1 H), 6.77-6.92 (m, 5 H), 7.20 (m, 1 H), 7.28 (m, 1 H), 7.58 (d, J = 2 Hz, 1 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 554 |
| 71 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.56-1.79 (m, 2 H), 2.07-2.23 (m, 4 H), 2.58 (t, J = 7 Hz, 2 H), 2.81-2.97 (m, 1 H), 3.01-3.08 (m, 1 H), 3.82 (s, 3 H), 3.86 (br s, 2 H), 4.00 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.77 (d, J = 8 Hz, 2 H), 6.81-6.96 (m, 3 H), 7.53 (br d, J = 6 Hz, 2 H), 7.73 (dd, J = 8 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 634 |
| 72 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.60-1.75 (m, 2 H), 2.04-2.25 (m, 4 H), 2.18 (s, 3 H), 2.31 (s, 3 H), 2.57 (t, J = 7 Hz, 2 H), 2.86-3.02 (m, 2 H), 3.86 (br s, 2 H), 4.01 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.05 (t, J = 2 Hz, 1 H), 6.71 (d, J = 8 Hz, 2 H), 6.77 (d, J = 8 Hz, 1 H), 6.84 (d, J = 8 Hz, 2 H), 7.26 (br s, 1 H), 7.36 (br s, 1 H), 7.72 (dd, J = 8 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 564 |
| 73 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.58-1.76 (m, 2 H), 2.10-2.24 (m, 7 H), 2.59 (t, J = 7 Hz, 2 H), 2.84-3.00 (m, 2 H), 3.87 (br s, 2 H), 4.02 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.08 (t, J = 2 Hz, 1 H), 6.76 (d, J = 8 Hz, 2 H), 6.88 (m, 3 H), 7.10 (d, J = 8 Hz, 1 H), 7.45 (t, J = 8 Hz, 1 H), 7.76 (dd, J = 8 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 568 |
| 74 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.05 (t, J = 8 Hz, 6 H), 1.56-1.78 (m, 2 H), 2.06-2.24 (m, 4 H), 2.39-2.66 (m, 6 H), 2.95 (br t, J = 7 Hz, 2 H), 3.88 (br s, 2 H), 4.02 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.04 (t, J = 2 Hz, 1 H), 6.67 (d, J = 8 Hz, 2 H), 6.80 (d, J = 9 Hz, 2 H), 6.85 (d, J = 8 Hz, 1 H), 7.04 (d, J = 8 Hz, 2 H), 7.11-7.18 (m, 1 H), 7.74 (dd, J = 8 Hz, 1 H), 7.92 (d, J = 2 Hz, 1 H) | 524 |
| 75 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.58-1.77 (m, 2 H), 2.03-2.23 (m, 10 H), 2.58 (t, J = 7 Hz, 2 H), 2.97 (t, J = 7 Hz, 2 H), 3.87 (br s, 2 H), 4.02 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.06 (t, J = 2 Hz, 1 H), 6.71 (d, J = 8 Hz, 2 H), 6.78-6.93 (m, 4 H), 6.98 (m, 1 H), 7.74 (dd, J = 8 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H) | 514 |
| 76 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.53-1.84 (m, 2 H), 2.06-2.25 (m, 4 H), 2.15 (s, 3 H), 2.22 (s, 3 H), 2.61 (t, J = 7Hz, 2 H), 2.85-3.00 (m, 2 H), 3.88 (br s, 2 H), 4.04 (br s, 2 H), 4.47 (dt, J = 47, 6 | 514 |

TABLE 1b-continued

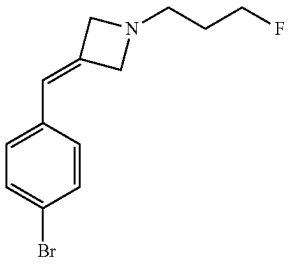
| Ex | Preparation Method | NMR | MASS: LC/MS (m/z, MH+): |
|---|---|---|---|
| | | Hz, 2 H), 6.08 (m, 1 H), 6.75-6.82 (m, 4 H), 6.87 (m, 3 H), 7.75 (dd, J = 8 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H), 12.1-13.4 (m, 1 H) | |
| 77 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.53-1.76 (m, 2 H), 2.08-2.21 (m, 4 H), 2.24 (s, 3 H), 2.59 (t, J = 7 Hz, 2 H), 2.86-3.08 (m, 2 H), 3.87 (br s, 2 H), 4.02 (br s, 2 H), 4.47 (dt, J = 47, 6 Hz, 2 H), 6.07 (br s, 1 H), 6.72 (d, J = 8 Hz, 2 H), 6.81-6.92 (m, 3 H), 7.07 (br d, J = 8 Hz, 1 H), 7.13-7.19 (m, 1 H), 7.22-7.34 (m, 1 H), 7.76 (dd, J = 8, 2 Hz, 1 H), 7.94 (d, J = 2 Hz, 1 H), 12.2-13.6 (m, 1 H) | 566 |
| 78 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.55-1.78 (m, 2 H), 2.05-2.26 (m, 4 H), 2.16 (s, 3 H), 2.32 (s, 3 H), 2.59 (t, J = 7 Hz, 2 H), 2.83-3.04 (m, 2 H), 3.87 (br s, 2 H), 4.02 (br s, 2 H), 4.47 (dt, J = 47, 6 Hz, 2 H), 6.07 (br s, 1 H), 6.76 (d, J = 8 Hz, 2 H), 6.83 (d, J = 8 Hz, 1 H), 6.87 (d, J = 8 Hz, 2 H), 7.18 (s, 1 H), 7.40 (s, 1 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H), 12-14 (m, 1 H) | 564 |
| 79 | B | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.57-1.77 (m, 2 H), 2.06-2.31 (m, 4 H), 2.59 (t, J = 7 Hz, 2 H), 2.87 (m, 1 H), 3.04 (m, 1 H), 3.87 (br s, 2 H), 4.03 (br s, 2 H), 4.47 (dt, J = 47, 6 Hz, 2 H), 6.07 (m, 1 H), 6.81 (d, J = 9 Hz, 2 H), 6.88 (d, J = 8 Hz, 1 H), 6.91 (d, J = 9 Hz, 2 H), 7.54 (d, J = 8 Hz, 1 H), 7.66 (t, J = 8 Hz, 1 H), 7.77 (dd, J = 8, 2 Hz, 1 H), 7.89 (d, J = 8 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H), 12-14 (m, 1 H) | 604 |
| 80 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.05 (t, J = 8 Hz, 6 H), 1.54-1.76 (m, 2 H), 2.00-2.23 (m, 4 H), 2.24 (s, 3 H), 2.36-2.65 (m, 6 H), 2.94 (br t, J = 7 Hz, 2 H), 3.86 (br s, 2 H), 4.01 (br s, 2 H), 4.46 (dt, J = 47, 6 Hz, 2 H), 6.04 (m, 1 H), 6.69 (d, J = 8 Hz, 2 H), 6.78-6.87 (m, 5 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.91 (d, J = 2 Hz, 1 H) | 538 |
| 81 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.56-1.81 (m, 2 H), 2.01-2.23 (m, 4 H), 2.60 (br t, J = 7 Hz, 2 H), 2.83-2.98 (m, 2 H), 3.70 (s, 3 H), 3.78 (s, 3 H), 3.88 (br s, 2 H), 4.04 (br s, 2 H), 4.47 (dt, J = 47, 6 Hz, 2 H), 6.07 (m, 1 H), 6.58 (dd, J = 7, 2 Hz, 1 H), 6.76-7.02 (m, 7 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 528 |
| 82 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.72-1.92 (m, 2 H), 2.07-2.21 (m, 2 H), 2.31 (t, J = 7 Hz, 2 H), 2.85 (t, J = 7 Hz, 2 H), 2.98-3.07 (m, 2 H), 3.49 (s partially hidden, 3 H), 3.71 (s, 3 H), 4.33-4.69 (m, 4 H), 4.52 (dt, J = 47, 6 Hz, 2 H), 6.26 (m, 1 H), 6.70 (d, J = 2 Hz, 1 H), 6.74 (dd, J = 8, 2 Hz, 1 H), 6.78-6.86 (m, 2 H), 6.89 (d, J = 8 Hz, 2 H), 6.95 (d, J = 8 Hz, 2 H), 7.73 (dd, J = 8, 2 Hz, 1 H), 7.90 (d, J = 2 Hz, 1 H) | 528 |
| 83 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.83-2.22 (m, 6 H), 2.08 (s, 3 H), 2.83-3.02 (m, 2 H), 3.14-3.50 (m hidden, 2 H), 3.74 (s, 3 H), 4.54 (dt, J = 47, 6 Hz, 2 H), 4.73-4.87 (m, 2 H), 4.95-5.06 (m, 2 H), 6.34 (m, 1 H), 6.78 (d, J = 2 Hz, 1 H), 6.82 (dd, J = 8, 6 Hz, 3 H), 6.89 (d, J = 2 Hz, 1 H), 6.94 (d, J = 8 Hz, 2 H), 7.74 (dd, J = 8, 2 Hz, 1 H), 7.93 (d, J = 2 Hz, 1 H), 9.69-14.15 (m, 2 H) | 546 |
| 84 | A | 1H NMR (400 MHz, DMSO-d6) δ ppm 1.61-1.74 (m, 2 H) 2.05-2.28 (m, 7 H) 2.33 (s, 3H) 2.58 (br t, J = 7 Hz, 2 H) 2.92-3.02 (m, 2 H) 3.86 (br s, 2 H) 4.01 (br s, 1 H) 4.46 (dt, J = 47, 6 Hz, 1 H) 6.06 (m, 1 H) 6.70 (d, J = 8 Hz, 2 H) 6.79 (d, J = 8 Hz, 1H) 6.85 (d, J = 8 Hz, 2 H) 7.17 (d, J = 8 Hz, 1 H) 7.44 (d, J = 8 Hz, 1 H) 7.72 (dd, J = 8, 2 Hz, 1 H) 7.91 (d, J = 2 Hz, 1 H) 11.2-13.7 (m, 1 H) | 564 |

**[0244]** The examples which follow describe the preparation of some compounds of formula (I) described herein. The numbers of the compounds exemplified below match those given in the Tables 1a and 1b above. All reactions are performed under inert atmosphere, unless otherwise stated.

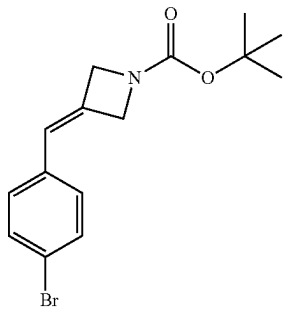
**[0245]** In the following examples, when the source of the starting products is not specified, it should be understood that said products are known compounds.

INTERMEDIATES

Intermediate 1:
3-(4-Bromobenzylidene)-1-(3-fluoropropyl)azetidine




Step 1: Tert-butyl
3-(4-bromobenzylidene)azetidine-1-carboxylate




Method 1

**[0246]** To a solution of (4-bromobenzyl)triphenylphosphonium bromide (79.2 g, 155 mmol) in DMF (400 mL) was added NaH (6.18 g, 155 mmol, 60% purity in weight) at 0° C. The mixture was stirred at 0° C. for 15 min. To this reaction mixture, a solution of tert-butyl 3-oxoazetidine-1-carboxylate (24.1 g, 141 mmol) in DMF (160 mL) was added. The mixture was stirred at 20° C. for 9 hours. The reaction mixture was quenched by addition of saturated aqueous solution of $NH_4Cl$ (100 mL) at 0° C. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure to give 60.0 g (crude) of tert-butyl 3-(4-bromobenzylidene)azetidine-1-carboxylate as a yellow solid.

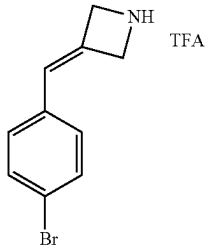
**[0247]** LC/MS (m/z, MH+): 324

Method 2

**[0248]** A mixture of tert-butyl 3-methyleneazetidine-1-carboxylate (12.5 g, 73.9 mmol), 1-bromo-4-iodobenzene (23 g, 81.3 mmol), potassium carbonate (20.4 g, 148 mmol), tetrabutylammonium bromide (23.8 g, 73.9 mmol) and palladium(II) acetate (1.66 g, 7.39 mmol) in DMF (125 mL) was heated to 60° C. for 16 hours. After cooling to room temperature, EtOAc (500 ml) and water (500 mL) were added. After decantation, the organic phase was washed twice with water (500 ml), dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash chromatography, eluting with DCM to give 20.7 g (86%) of tert-butyl 3-(4-bromobenzylidene)azetidine-1-carboxylate as a beige solid.

**[0249]** LC/MS (m/z, MH+): 324

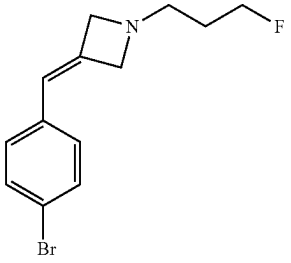
Step 2: 3-(4-Bromobenzylidene)azetidine,
2,2,2-trifluoroacetic acid




**[0250]** A mixture of tert-butyl 3-(4-bromobenzylidene) azetidine-1-carboxylate (60 g, 185 mmol) and TFA (192 mL, 2.59 mol) in DCM (300 mL) was stirred at room temperature for 15 hours. The reaction mixture was concentrated under reduced pressure to give a residue. The crude product was triturated with EtOAc (50 mL) and filtered to give 28 g (45%) of 3-(4-bromobenzylidene)azetidine, 2,2,2-trifluoroacetic acid.

**[0251]** LC/MS (m/z, MH+): 224

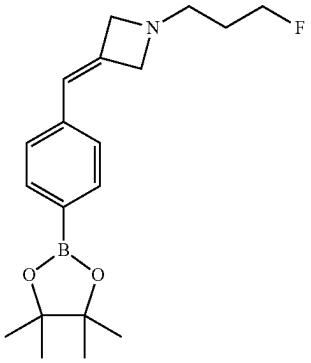
Step 3:
3-(4-Bromobenzylidene)-1-(3-fluoropropyl)azetidine




**[0252]** A mixture of 1-fluoro-3-iodopropane (11.5 g, 61.2 mmol), 3-[(4-bromophenyl)methylene]-azetidine, 2,2,2-trifluoroacetic acid (23.0 g, 68.0 mmol), KOH (5.72 g, 102 mmol) in DMF (100 ml) was stirred at room temperature for 10 hours. The reaction mixture was quenched by addition of water (200 mL), and then extracted with EtOAc (500 mL). After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and the residue obtained was purified by flash chromatography, eluting with a gradient of DCM/MeOH: from 100/00 to 95/05 to give 8.9 g (47% yield) of 3-(4-bromobenzylidene)-1-(3-fluoropropyl)azetidine.

**[0253]** LC/MS (m/z, MH+): 284

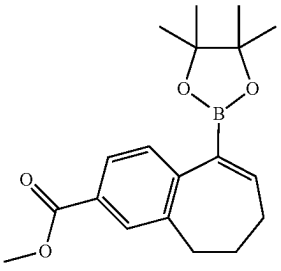
Intermediate 2: 1-(3-Fluoropropyl)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylidene) azetidine



**[0254]** A mixture of 3-(4-bromobenzylidene)-1-(3-fluoropropyl)azetidine (2 g, 7.04 mmol), bis(pinacolato)diboron (2.5 g, 9.85 mmol), KOAc (1.73 g, 17.6 mmol) and Pd(dppf)$Cl_2$ (257 mg, 0.35 mmol) in dioxane (40 mL) was degassed and purged with argon and then the mixture was refluxed for 2.5 hours. After cooling to room temperature, AcOEt (50 mL), $Et_2O$ (20 mL), water (30 mL) and brine (30 mL) were added under stirring. After decantation, the organic phase was washed twice with 30 mL of brine then concentrated under reduced pressure. The residue obtained was purified by flash chromatography eluting with a gradient of cyclohexane/AcOEt from 100/0 to 0/100 then a gradient of DCM/MeOH from 99/01 to 95/05 to give 1.2 g (51% yield) of 1-(3-fluoropropyl)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylidene)azetidine.

**[0255]** LC/MS (m/z, MH+): 332

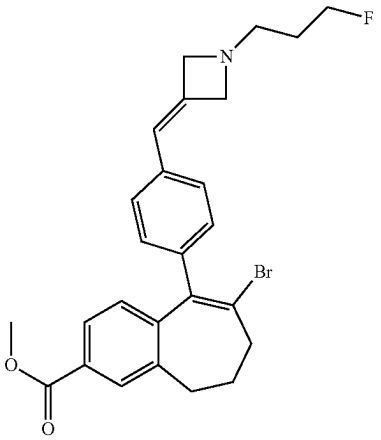
Intermediate 3: Methyl 9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0256]** A mixture of methyl 9-(((trifluoromethyl)sulfonyl) oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (15 g, 42.82 mmol) (prepared according to WO2017140669), in toluene (150 ml), $Pd(PPh_3)_2Cl_2$ (1.53 g, 2.14 mmol), $PPh_3$ (673.87 mg, 2.57 mmol), bis(pinacolato)diboron (144.08 g, 52.67 mmol) and PhOK (8.04 g, 60.80 mmol) was heated to 75° C. for 1.5 h. The yellow suspension becomes orange then brown. After cooling to room temperature, DCM (150 mL) and water (150 mL) were added, and decantation was done by hydrophobic column. The organic phase was concentrated under reduced pressure. The residue obtained was purified by flash chromatography, eluting with a gradient of heptane/DCM: from 85/15 to 20/80 to give 10.1 g (72%) of methyl 9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate as a white solid.

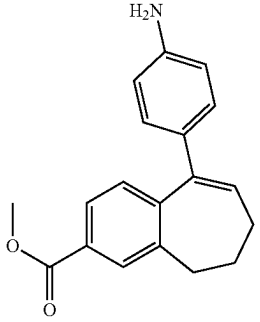
**[0257]** LC/MS (m/z, MH+): 329

Intermediate 4: Methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



Method 1

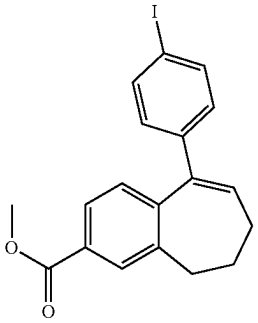
Step 1: Methyl 9-(4-aminophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0258]** A mixture of methyl 9-(((trifluoromethyl)sulfonyl) oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (20 g, 57.09 mmol) (prepared according to WO2017140669), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (13.13 g, 59.95 mmol), $Cs_2CO_3$ (37.21 g, 114.2 mmol), and Pd(dppf)$Cl_2$, complex with DCM (1.25 g, 1.71 mmol) in dioxane (160 mL) and water (40 mL) was heated to 95° C. for 1 hour. Water (200 mL) and EtOAc (500 mL) were added. After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure and the residue obtained was purified by flash chromatography eluting with cyclohexane/EtOAc: 85/15 to give 14.5 g (87%) of methyl 9-(4-aminophenyl)-6,7-dihydro-5H-benzo [7]annulene-3-carboxylate.

**[0259]** LC/MS (m/z, MH+): 294

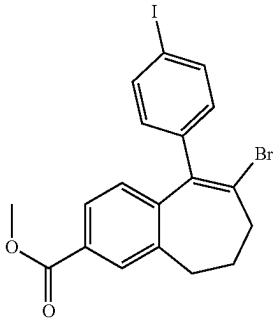
Step 2: Methyl 9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0260]** To a mixture of methyl 9-(4-aminophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (14.5 g, 49.4 mmol) in MeCN (270 mL) and 4N HCl (300 mL, 1200 mmol) cooled at 0° C., was slowly added a solution of sodium nitrite (3.58 g, 51.9 mmol) in water (20 mL). After stirring of the reaction mixture for 1 hour at 0° C., a solution of sodium iodide (14.8 g, 98.9 mmol) in water (40 mL) was added. The cooling bath was removed allowing the temperature to warm up to room temperature. After stirring for 4 hours at room temperature, $Et_2O$ (500 mL) and a 2N solution of $NaHSO_3$ (200 mL) were added. After decantation, the organic phase was washed twice with water (100 mL), then with brine (100 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure and the residue obtained was purified by flash chromatography eluting with cyclohexane/EtOAc: 95/05 to give 14.8 g (74%) of methyl 9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0261]** LC/MS (m/z, MH+): 405

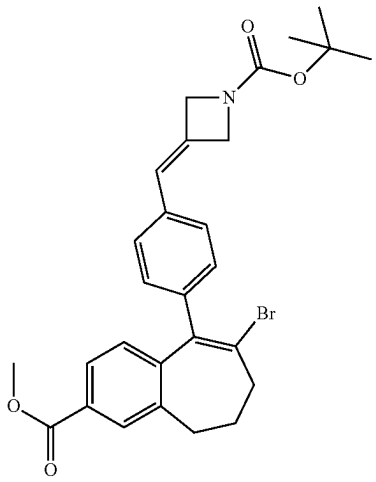
Step 3: Methyl 8-bromo-9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0262]** To a mixture of methyl 9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (14.8 g, 36.6 mmol) in DCM (500 mL) was added pyridinium tribromide (12.9 g, 40.3 mmol). The reaction mixture was stirred for 18 hours at room temperature then diluted with $Et_2O$ (500 mL) and pentane (500 mL) and washed with a 0.2N solution of $NaHSO_3$ (100 mL) and twice with water (200 mL). After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure to give 17.7 g (100%) of methyl 8-bromo-9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0263]** LC/MS (m/z, MH+): 484

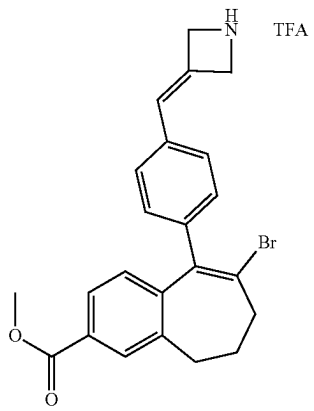
Step 4: Tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate



**[0264]** A solution of tert-butyl 3-methyleneazetidine-1-carboxylate (7.44 g, 44 mmol) and methyl 8-bromo-9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (17.7 g, 36.6 mmol) in DMF (200 mL) was degassed and purged with Ar for 5 min. To this solution under stirring was added $K_2CO_3$ (10.1 g, 73.3 mmol), tetrabutylammonium bromide (11.8 g, 36.6 mmol) and palladium(II) acetate (0.83 g, 3.66 mmol). The mixture was heated to 50° C. for 30 hours then cooled to room temperature. $Et_2O$ (300 mL) and water (300 mL) were added. After decantation, the aqueous phase was extracted with another 300 mL of $Et_2O$ and the combined organic phases were washed twice with water (200 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash chromatography, eluting with a gradient of cyclohexane/EtOAc (95/05 to 80/20) to give 14.7 g (76%) tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl) benzylidene)azetidine-1-carboxylate.

**[0265]** LC/MS (m/z, MH+): 525

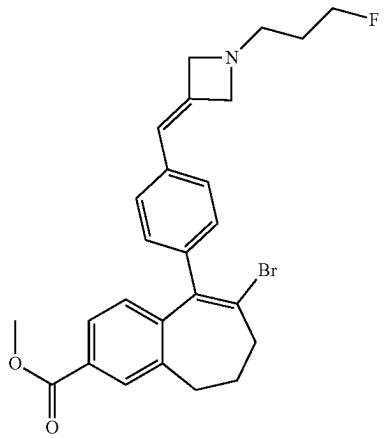
Step 5: Methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid



**[0266]** Step 5 of Intermediate 4 was prepared following a similar procedure to that of Step 2 of Intermediate 1 from tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate to give 9.66 g (94%) of methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid.

**[0267]** LC/MS (m/z, MH+): 425

Step 6: Methyl 8-bromo-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

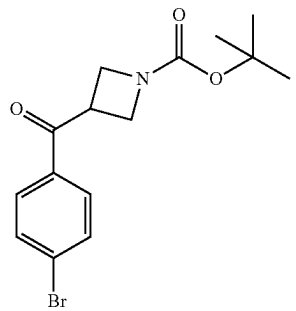


**[0268]** A mixture of 1-fluoro-3-iodopropane (2.88 g, 15.3 mmol) and methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid (8.24 g, 15.3 mmol) in a mixture of NaOH 1N (46 mL, 46 mmol) and DCM (70 mL) was stirred at room temperature for 48 hours. DCM (200 mL) and water (100 mL) were added. After decantation, the organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a residue. The residue obtained was purified by flash chromatography, eluting with a gradient of cyclohexane/EtOAc: from 100/00 to 00/100 to give 4.41 g (59% yield) of methyl 8-bromo-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0269]** LC/MS (m/z, MH+): 485

Method 2

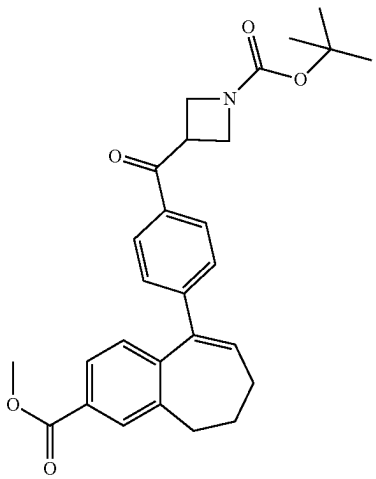
Step 1: Tert-butyl 3-(4-bromobenzoyl)azetidine-1-carboxylate



**[0270]** To a solution of 1,4-dibromobenzene (290 g, 1.23 mol, 157 mL) in THF (1050 mL) was added n-BuLi (2.5 M, 491 mL) at −70° C. The mixture was stirred for 30 minutes before addition of tert-butyl 3-(methoxy(methyl)carbamoyl) azetidine-1-carboxylate (200 g, 819 mmol) in THF (420 mL) at −70° C. The reaction mixture was stirred for 1.5 hours. The solution was warmed up to −25° C. and slowly quenched by aqueous solution of saturated $NH_4Cl$ (2000 mL). The mixture was extracted twice with MTBE (800 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The obtained residue was purified by flash chromatography eluting with a gradient of petroleum ether/EtOAc from 10/1 to 0/1 to give 180 g (65%) of tert-butyl 3-(4-bromobenzoyl)azetidine-1-carboxylate as a white solid.

**[0271]** LC/MS (m/z, MH+): 340

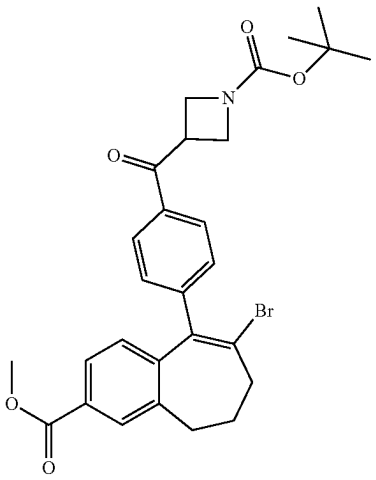
Step 2: Tert-butyl 3-(4-(3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzoyl)azetidine-1-carboxylate



**[0272]** Step 2 of Intermediate 4 (Method 2) was prepared following a similar procedure to that of step 1 of Intermediate 4 (Method 1) from methyl 9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 3) and tert-butyl 3-(4-bromobenzoyl)azetidine-1-carboxylate to give 8.5 g (99%) of tert-butyl 3-(4-(3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzoyl)azetidine-1-carboxylate

LC/MS (m/z, MH+): 462

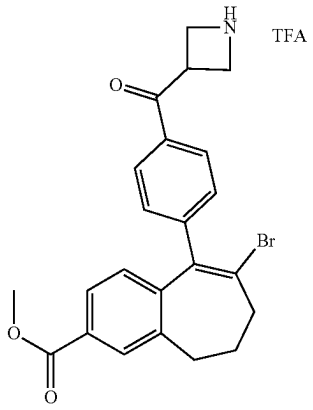
Step 3: Tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzoyl) azetidine-1-carboxylate



**[0273]** Step 3 of Intermediate 4 (Method 2) was prepared following a similar procedure to that of step 3 of Intermediate 4 (Method 1) from tert-butyl 3-(4-(3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzoyl)azetidine-1-carboxylate to give 6.1 g (88%) of tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7] annulen-9-yl)benzoyl)azetidine-1-carboxylate.

**[0274]** LC/MS (m/z, MH+): 540

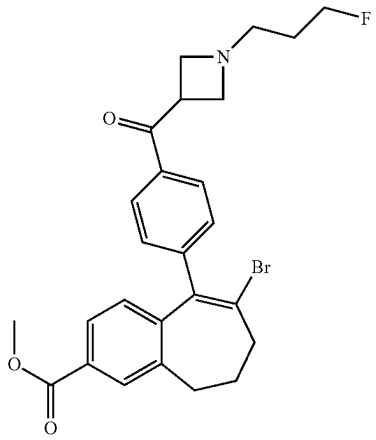
Step 4: Methyl 9-(4-(azetidine-3-carbonyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid



**[0275]** Step 4 of Intermediate 4 (Method 2) was prepared following a similar procedure to that of step 2 of Intermediate 1 from tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzoyl)azetidine-1-carboxylate to give 5 g (100%) of methyl 9-(4-(azetidine-3-carbonyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7] annulene-3-carboxylate, 2,2,2-trifluoroacetic acid.

**[0276]** LC/MS (m/z, MH+): 440

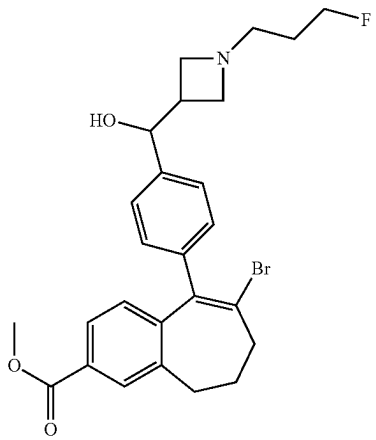
Step 5: Methyl 8-bromo-9-(4-(1-(3-fluoropropyl) azetidine-3-carbonyl)phenyl)-6,7-dihydro-5H-benzo [7]annulene-3-carboxylate



**[0277]** A mixture of 1-fluoro-3-iodopropane (4.27 g, 22.7 mmol), methyl 9-(4-(azetidine-3-carbonyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid (5 g, 9.24 mmol), $K_2CO_3$ (4.71 g, 34 mmol) in MeCN (200 mL) was heated to 70° C. for 1 hour. The reaction mixture was quenched by addition of water (200 mL), and then extracted with EtOAc (500 mL). After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and the residue obtained was purified by flash chromatography, eluting with a gradient of cyclohexane/EtOAc: from 100/00 to 00/100 to give 3 g (53%) of methyl 8-bromo-9-(4-(1-(3-fluoropropyl)azetidine-3-carbonyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0278]** LC/MS (m/z, MH+): 500

Step 6: Methyl 8-bromo-9-(4-((1-(3-fluoropropyl) azetidin-3-yl)(hydroxy)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

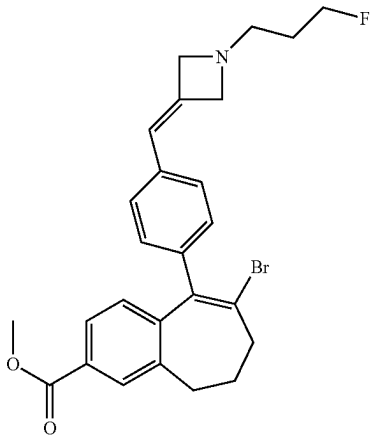


**[0279]** To a mixture of methyl 8-bromo-9-(4-(1-(3-fluoropropyl)azetidine-3-carbonyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (3 g, 6 mmol) in methanol

(5 mL) cooled at 0° C. was added $NaBH_4$ (340 mg, 9 mmol). The reaction mixture was stirred at 0° C. for 30 minutes. 10% citric acid aqueous solution (20 mL) and DCM (250 mL) were added. After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and the residue obtained was purified by flash chromatography, eluting with a gradient of DCM/MeOH: from 100/00 to 05/95 to give 3 g (99%) of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-yl)(hydroxy)methyl) phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0280]** LC/MS (m/z, MH+): 502

Step 7: Methyl 8-bromo-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

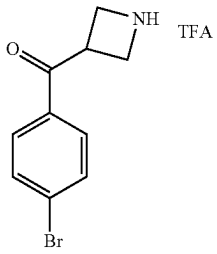



**[0281]** To a mixture of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-yl)(hydroxy)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (3 g, 5.97 mmol) in DCM (200 mL) were added pyridine (945 mg, 11.94 mmol, 0.96 mL) and trifluoromethylsulfonyl trifluoromethanesulfonate (3.37 g, 11.94 mmol, 2 mL). The reaction mixture was stirred at room temperature for 18 hours. DCM (400 mL) and a saturated aqueous solution of hydrogenocarbonate (300 mL) were added. After decantation, the organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure to give a residue. The residue obtained was purified by flash chromatography, eluting with a gradient of DCM/MeOH: from 100/00 to 05/95 to give 1.9 g (66%) of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0282]** LC/MS (m/z, MH+): 484

Alternative Method for Preparation of Step 6 of Intermediate 4 (Method 2)

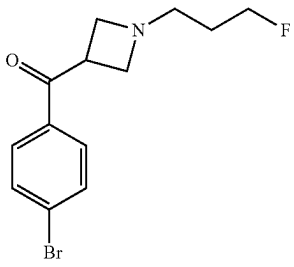
Step 1: 3-Azetidinyl(4-bromophenyl)-methanone, 2,2,2-trifluoroacetic acid




**[0283]** Step 1 was prepared following a similar procedure to that of Step 2 of Intermediate 1 from tert-butyl 3-(4-bromobenzoyl)azetidine-1-carboxylate to give 41.6 g (100%) of 3-azetidinyl(4-bromophenyl)-methanone, 2,2,2-trifluoroacetic acid.

**[0284]** LC/MS (m/z, MH+): 240

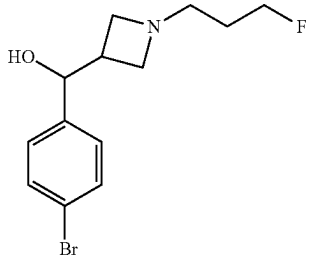
Step 2: (4-Bromophenyl)(3-fluoropropyl)azetidin-3-ylmethanone




**[0285]** Step 2 was prepared following a similar procedure to that of step 3 of intermediate 1 from 3-azetidinyl(4-bromophenyl)-methanone, 2,2,2-trifluoroacetic acid to give 20 g (54%) of (4-bromophenyl)(3-fluoropropyl)azetidin-3-ylmethanone.

**[0286]** LC/MS (m/z, MH+): 300

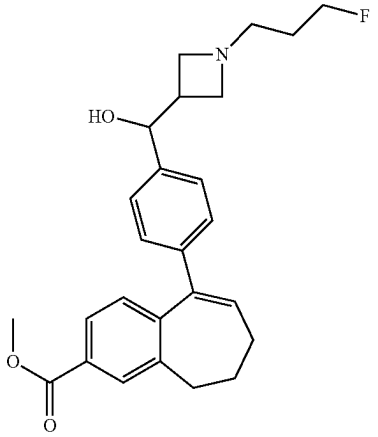
Step 3: (4-Bromophenyl)(1-(3-fluoropropyl)azetidin-3-yl)methanol



**[0287]** To a solution of (4-bromophenyl)(3-fluoropropyl) azetidin-3-ylmethanone (20.0 g, 66.6 mmol) in MeOH (100 mL) was added $NaBH_4$ (5.04 g, 133 mmol) at 0° C. The mixture was stirred at 15° C. for 1 hour. The reaction mixture was slowly quenched by water (100 mL) and concentrated under reduced pressure to remove MeOH. The aqueous phase was extracted three times with EtOAc (80 mL). After decantation, the organic phase was dried over $Na_2SO_4$, filtered, concentrated under reduced pressure, and the residue obtained was purified by flash chromatography eluting with a gradient of DCM: MeOH from 98/02 to 90/10 to give 16 g (77%) of (4-bromophenyl)(1-(3-fluoropropyl) azetidin-3-yl)methanol as a mixture of two isomers.

**[0288]** LC/MS (m/z, MH+): 302

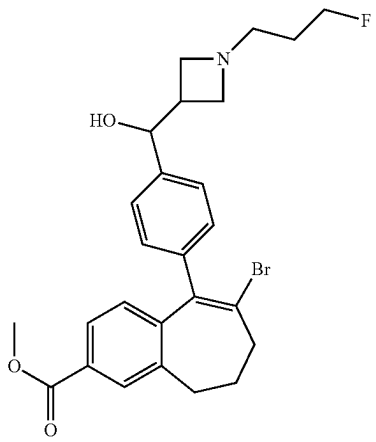
Step 4: Methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-yl)(hydroxy)methyl)phenyl)-6,7-dihydro-5H-benzo [7]annulene-3-carboxylate



**[0289]** Step 4 was prepared following a similar procedure to that of step 1 of Intermediate 4 (Method 1) from methyl 9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 3) and (4-bromophenyl)(1-(3-fluoropropyl)azetidin-3-yl) methanol to give 1.39 g (79%) of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-yl)(hydroxy)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0290]** LC/MS (m/z, MH+): 424

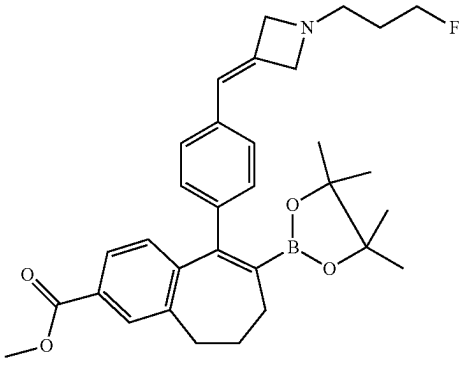
Step 5: Methyl 8-bromo-9-(4-((1-(3-fluoropropyl) azetidin-3-yl)(hydroxy)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0291]** Step 5 was prepared following a similar procedure to that of step 3 of Intermediate 4 (Method 1) from methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-yl)(hydroxy)methyl) phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 1.59 g (100%) of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-yl)(hydroxy)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0292]** LC/MS (m/z, MH+): 502

Intermediate 5: Methyl 9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

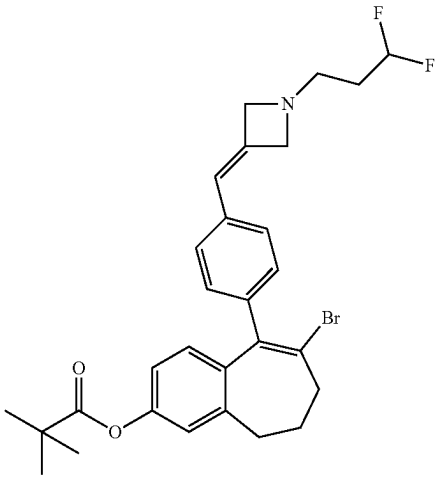


**[0293]** A mixture of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 4) (605 mg, 1.25 mmol) in toluene (30 mL), $Pd(PPh_3)_2Cl_2$ (35 mg, 50 μmol), $PPh_3$ (26 mg, 100 μmol), bis(pinacolato)diboron (793 mg, 3.12 mmol), $K_2CO_3$ (38 mg, 0.27 mmol) and PhOK (413 mg, 3.12 mmol) was degassed and purged with Ar for 5 min. then heated to 75° C. for 6 hours. After cooling to room temperature, $Et_2O$ (100 mL) and a 5% solution of $Na_2CO_3$ (50 mL) were added. After decantation, the organic phase was washed with water (50 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure, and the resi-

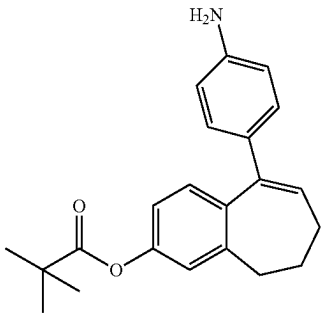
due obtained was purified by flash chromatography, eluting with a gradient of cyclohexane/EtOAc: from 100/00 to 00/100 to give 500 mg (75%) of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0294]** LC/MS (m/z, MH+): 532

Intermediate 6: 8-Bromo-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate



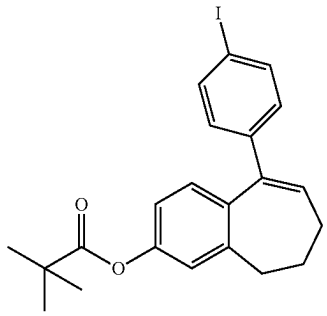

Step 1: 9-(4-Aminophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate




**[0295]** Step 1 of Intermediate 6 was prepared following a similar procedure to that of step 1 of Intermediate 4 (Method 1) from 9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate (prepared according to WO2018091153) and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline to give 376 mg (88%) of 9-(4-aminophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate.

**[0296]** LC/MS (m/z, MH+): 336

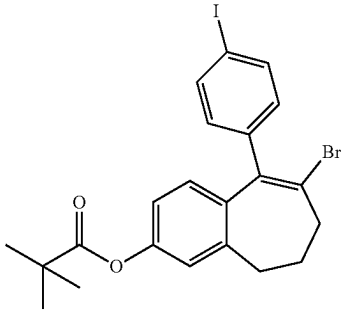
Step 2: 9-(4-Iodophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate




**[0297]** Step 2 of Intermediate 6 was prepared following a similar procedure to that of step 2 of Intermediate 4 (Method 1) from 9-(4-aminophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate to give 285 mg (57%) of 9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate.

**[0298]** LC/MS (m/z, MH+): 447

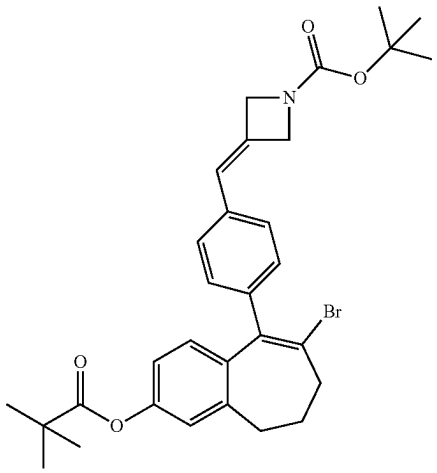
Step 3: 8-Bromo-9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate




**[0299]** Step 3 of Intermediate 6 was prepared following a similar procedure to that of step 3 of Intermediate 4 (Method 1) from 9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate to give 340 mg (100%) of 8-bromo-9-(4-iodophenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate.

**[0300]** LC/MS (m/z, MH+): 524

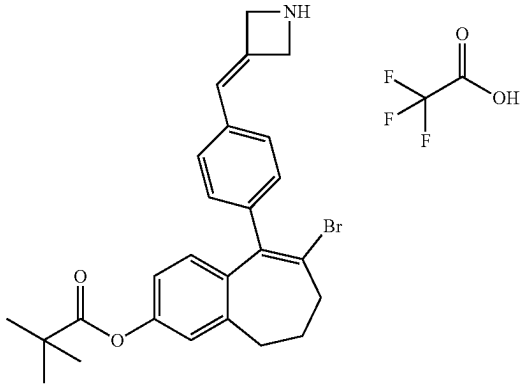
Step 4: Tert-butyl 3-(4-(8-bromo-3-(pivaloyloxy)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene) azetidine-1-carboxylate



**[0301]** Step 4 of Intermediate 6 was prepared following a similar procedure to that of step 4 of Intermediate 4 (Method 1) from 8-bromo-9-(4-iodophenyl)-6,7-dihydro-5H-benzo [7]annulen-3-yl pivalate and tert-butyl 3-methyleneazetidine-1-carboxylate to give 233 mg (64%) of tert-butyl 3-(4-(8-bromo-3-(pivaloyloxy)-6,7-dihydro-5H-benzo[7] annulen-9-yl)benzylidene)azetidine-1-carboxylate.

**[0302]** LC/MS (m/z, MH+): 566

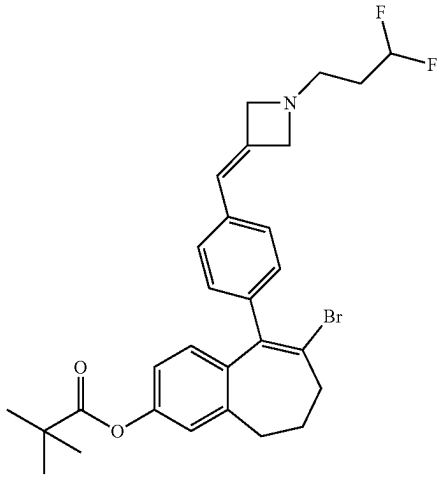
Step 5: 9-(4-(Azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate, 2,2,2-trifluoroacetic acid



**[0303]** Step 5 of Intermediate 6 was prepared following a similar procedure to that of step 2 of Intermediate 1 (Method 1) from tert-butyl 3-(4-(8-bromo-3-(pivaloyloxy)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate to give 250 mg (100%) of 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7] annulen-3-yl pivalate, 2,2,2-trifluoroacetic acid.

**[0304]** LC/MS (m/z, MH+): 466

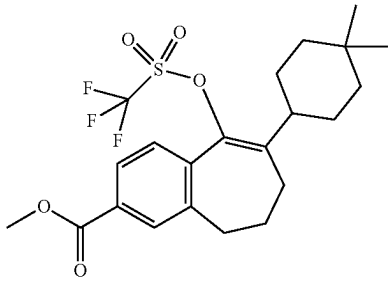
Step 6: 8-Bromo-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo [7]annulen-3-yl pivalate



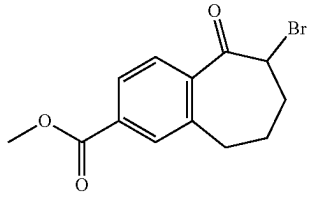
**[0305]** Step 6 of Intermediate 6 was prepared following a similar procedure to that of step 6 of Intermediate 4 (Method 1) from 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate, 2,2,2-trifluoroacetic acid and 3,3-difluoropropyl trifluoromethanesulfonate (Intermediate 11) to give 38 mg (28%) of 8-bromo-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene) methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate.

**[0306]** LC/MS (m/z, MH+): 544

Intermediate 7: Methyl 8-(4,4-dimethylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



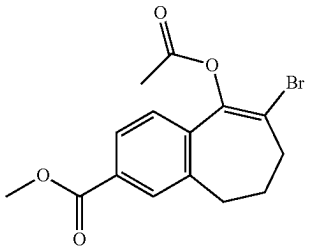
Step 1: Methyl 6-bromo-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate



**[0307]** To a mixture of methyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate (9.42 g, 43.2 mmol) in DCM (400 mL) was portionwise added pyridinium tribromide (16.12 g, 45.4 mmol). The reaction mixture was stirred overnight at room temperature. Water (500 ml) and ethyl ether (1 L) were added. After decantation, the organic phase was washed twice with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure to give 14.4 g (90%) of methyl 6-bromo-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate.

**[0308]** LC/MS (m/z, MH+): 297

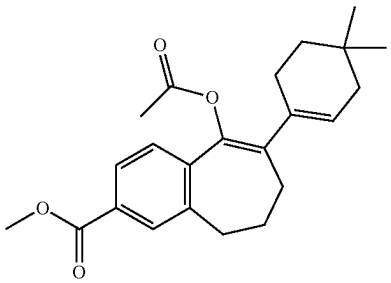
Step 2: Methyl 9-acetoxy-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0309]** To a solution of methyl 6-bromo-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate (7.4 g, 25 mmol) in THF (80 mL) at −78° C. under Ar atmosphere was added LiHMDS (1 M, 27 mL). The mixture was stirred for 2 hours then treated with acetic anhydride (8.8 mL, 75 mmol) allowing the temperature to warmed up to 0° C. After pouring onto diisopropyl ether and water, the aqueous layer was separated and extracted with diisopropyl ether. After decantation, the combined organic layers were washed with water, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography with a 0-50% gradient of EtOAc in cyclohexane to give 6.97 g (83%) of methyl 9-acetoxy-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0310]** LC/MS (m/z, MH+): 339

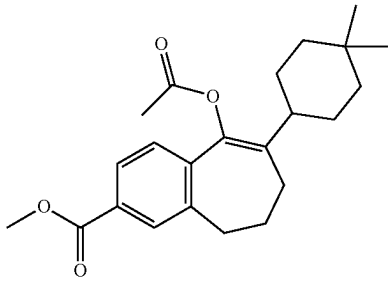
Step 3: Methyl 9-acetoxy-8-(4,4-dimethylcyclohex-1-en-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0311]** Step 3 of Intermediate 7 was prepared following a similar procedure to that of step 1 of Example 3 from methyl 9-acetoxy-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate and 2-(4,4-dimethylcyclohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane to give 1.55 g (65%) of methyl 9-acetoxy-8-(4,4-dimethylcyclohex-1-en-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

**[0312]** LC/MS (m/z, MH+): 369

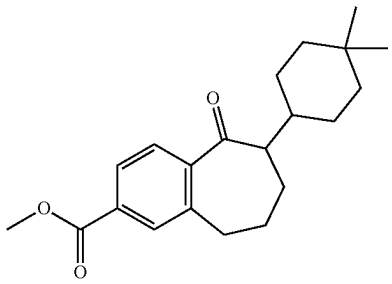
Step 4: Methyl 9-acetoxy-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0313]** A mixture of methyl 9-acetoxy-8-(4,4-dimethylcyclohex-1-en-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (2.08 g, 5.65 mmol) and Pd/C 10% (400 mg) in EtOAc (50 ml) was hydrogenated at room temperature and 2.5 bars of $H_2$ for 5 hours. The reaction mixture was filtered. The filtrate was evaporated under reduced pressure to give 1.96 g (94%) of methyl 9-acetoxy-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

**[0314]** LC/MS (m/z, MH+): 371

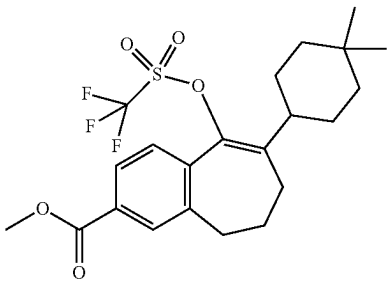
Step 5: Methyl 6-(4,4-dimethylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate



**[0315]** To a solution of methyl 9-acetoxy-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (1.96 g, 5.29 mmol) in MeOH (32 mL) and DCM (16 mL) was added a 12 N solution of HCl (5.29 mL, 63.5 mmol). The resulting reaction mixture was stirred overnight at room temperature. After pouring onto diethyl ether (20 ml), EtOAc (30 ml) and water (50 ml), the organic layer was separated, washed with water (50 ml), a 5% aqueous solution of $Na_2CO_3$ (50 ml) and water (50 ml) then dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue obtained was purified by flash chromatography with a 0-20% gradient of Ethyl acetate in cyclohexane to give 1.59 g (87%) of methyl 6-(4,4-dimethylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate.

**[0316]** LC/MS (m/z, MH+): 329

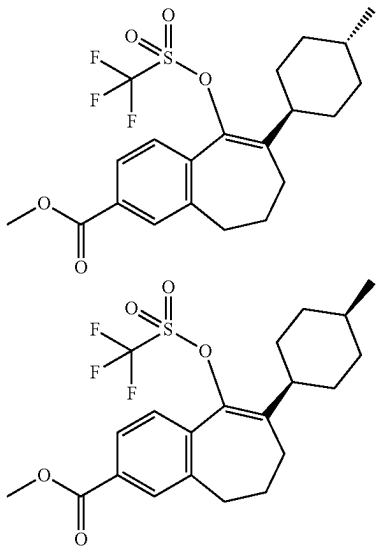
Step 6: Methyl 8-(4,4-dimethylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



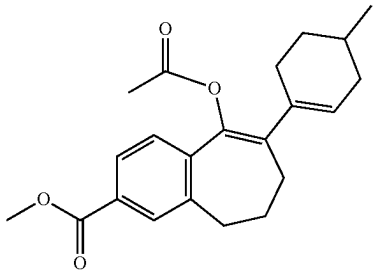
**[0317]** To a solution of methyl 6-(4,4-dimethylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate (1.35 g, 4.11 mmol) in THF (30 mL) at −55° C. under Ar atmosphere was added KHMDS (1 M, 4.93 ml, 4.93 mmol). After stirring at −55° C. for 30 minutes, N,N-bis(trifluoromethylsulfonyl)aniline (1.51 g, 4.23 mmol) was added. The reaction mixture was stirred for 30 minutes. Addition of diethyl ether (50 ml) and a water solution of $Na_2CO_3$ (5%) (30 ml). After decantation, the organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with cyclohexane/EtOAc (95/05) to give 1.75 g (93%) of methyl 8-(4,4-dimethylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0318]** LC/MS (m/z, MH+): 461

Intermediate 8: Methyl 8-(trans-4-methylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate and methyl 8-(cis-4-methylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



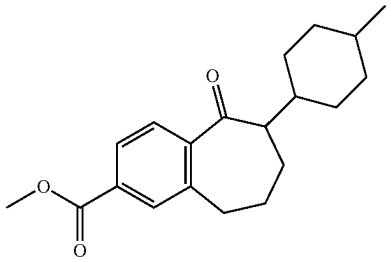
Step 1: Methyl 9-acetoxy-8-(4-methylcyclohex-1-en-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0319]** Step 1 of Intermediate 8 was prepared following a similar procedure to that of step 1 of Example 3 from methyl 9-acetoxy-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate and (4-methylcyclohexen-1-yl)boronic acid to give 4.12 g (95%) of methyl 9-acetoxy-8-(4-methylcyclohex-1-en-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0320]** LC/MS (m/z, MH+): 355

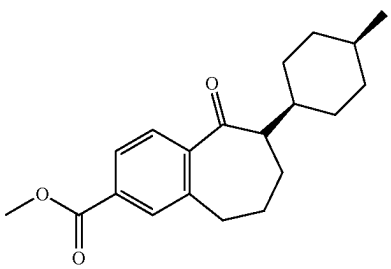
Step 2: Methyl 6-(4-methylcyclohexylidene)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate



**[0321]** Step 2 of Intermediate 8 was prepared following a similar procedure to that of step 5 of Intermediate 7 from methyl 9-acetoxy-8-(4-methylcyclohex-1-en-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 3.8 g (100%) of methyl 6-(4-methylcyclohexylidene)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate.

LC/MS (m/z, MH+): 313

Step 3: Methyl 6-(cis-4-methylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate and methyl 6-(trans-4-methylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate



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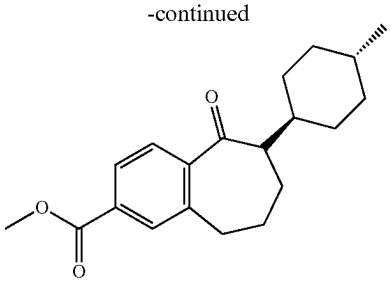
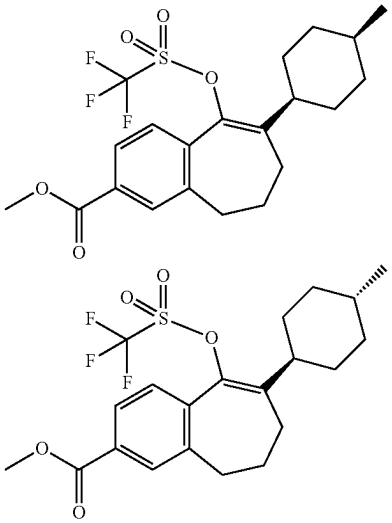


**[0322]** Step 3 of Intermediate 8 was prepared following a similar procedure to that of step 4 of Intermediate 7 from methyl 6-(4-methylcyclohexylidene)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate to give 1.97 g (65%) of a 70/30 mixture of methyl 6-(cis-4-methylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate and methyl 6-(trans-4-methylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate.

**[0323]** LC/MS (m/z, MH+): 315

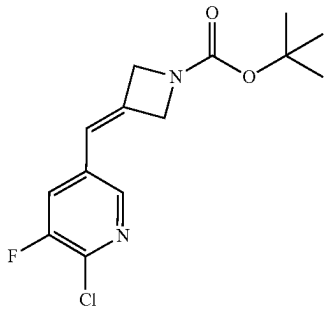
Step 4: Methyl 8-(cis-4-methylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate and methyl 8-(trans-4-methylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0324]** Step 4 of Intermediate 8 was prepared following a similar procedure to that of step 6 of Intermediate 7 from a mixture of methyl 6-(trans-4-methylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate and methyl 6-(cis-4-methylcyclohexyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-carboxylate to give 1.04 g (37%) of a 70/30 mixture of methyl 8-(cis-4-methylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate and methyl 8-(trans-4-methylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0325]** LC/MS (m/z, MH+): 447

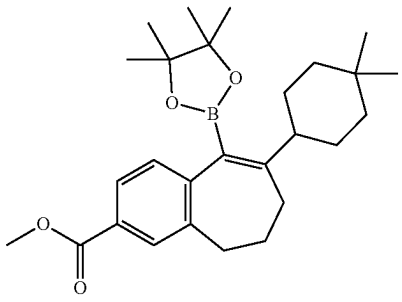
Intermediate 9: Tert-butyl 3-((6-chloro-5-fluoropyridin-3-yl)methylene)azetidine-1-carboxylate



**[0326]** To a mixture of 2-chloro-3-fluoro-5-iodopyridine (4.82 g, 18.7 mmol), tert-butyl 3-methyleneazetidine-1-carboxylate (3.17 g, 18.7 mmol), $K_2CO_3$ (5.18 g, 37.4 mmol) and t-butyl ammonium bromide (6 g, 18.7 mmol) in anhydrous DMF (100 ml) under argon were added palladium(II) acetate (420 mg, 1.87 mmol) and the mixture was heated at 55° C. for 16 h then cooled to RT. After dilution with $Et_2O$ (500 ml), the mixture was washed with water (3×500 ml), dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with a gradient of EtOAc in cyclohexane (100/0 to 0/100, v/v) to give 3.06 g (55%) of tert-butyl 3-((6-chloro-5-fluoropyridin-3-yl)methylene)azetidine-1-carboxylate after trituration in pentane.

**[0327]** LC/MS (m/z, MH+): 299

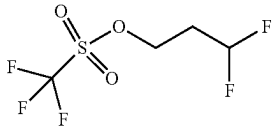
Intermediate 10: Methyl 8-(4,4-dimethylcyclohexyl)-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0328]** Intermediate 10 was prepared following a similar procedure to that of Intermediate 3 from methyl 8-(4,4-dimethylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 7) to give 1.08 g (73%) of methyl 8-(4,4-dimethylcyclohexyl)-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

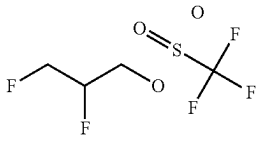
**[0329]** LC/MS (m/z, MH+): 439

Intermediate 11: 3,3-Difluoropropyl trifluoromethanesulfonate



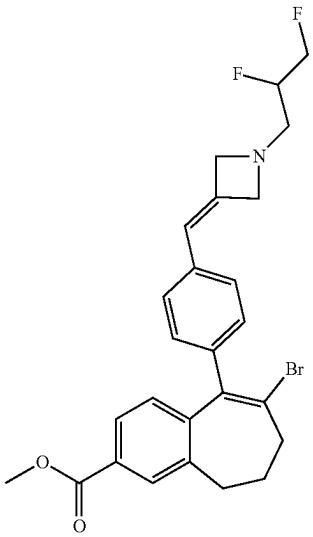
**[0330]** To a solution of 3,3-difluoropropan-1-ol (1 g, 10.41 mmol) and 2,6-lutidine (2.66 mL, 22.9 mmol) in DCM (20 mL) cooled at 0° C. was dropwise added trifluoromethanesulfonic anhydride (1.93 mL, 11.45 mmol). The mixture was stirred at 0° C. for 30 minutes. $Et_2O$ and water were added. The aqueous phase was separated and extracted three times with ether. The combined organic phases were washed twice with a 10% aqueous solution of citric acid then water and dried over $Na_2SO_4$, filtered and concentrated under reduced pressure to give 2.06 g (86%) of 3,3-difluoropropyl trifluoromethanesulfonate which was used in the next step without further purification, which was used in the next step without further purification.

Intermediate 12: 2,3-Difluoropropyl trifluoromethanesulfonate



**[0331]** Intermediate 12 was prepared following a similar procedure to that of Intermediate 11 from 2,3-difluoropropan-1-ol to give 0.96 g (93%) of 2,3-difluoropropyl trifluoromethanesulfonate which was used in the next step without further purification.

Intermediate 13: Methyl 8-bromo-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



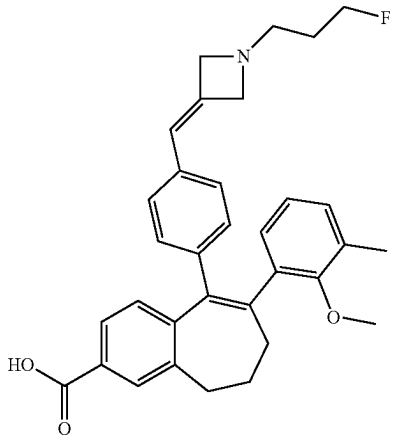
**[0332]** Intermediate 13 was prepared following a similar procedure to that of step 6 of Intermediate 4 (Method 1) from methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-bromo-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid (Intermediate 4, method 1, Step 5) and 2,3-difluoropropyl trifluoromethanesulfonate (Intermediate 12) by decantation of the reaction mixture and direct purification by flash chromatography without concentration of the crude under reduced pressure to give 272 mg (17%) of methyl 8-bromo-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0333]** LC/MS (m/z, MH+): 502

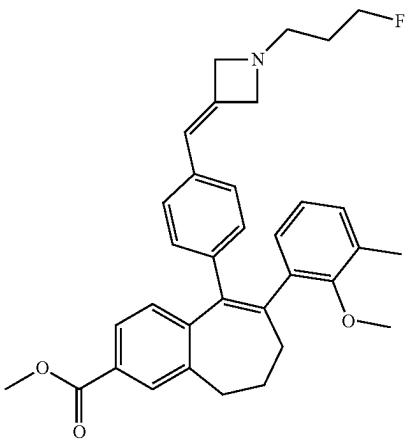
EXAMPLES: COMPOUNDS OF FORMULA (I)

Method A

Example 3: 9-(4-((1-(3-Fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



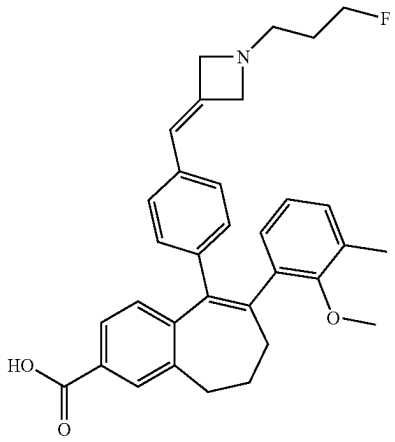
Step 1: methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0334]** A mixture of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 4) (200 mg, 413 μmol), (2-methoxy-3-methyl-phenyl)boronic acid (137 mg, 826 μmol), $Cs_2CO_3$ (283 mg, 867 μmol), and Pd(dppf)$Cl_2$, complex with DCM (30 mg, 41 μmol) in dioxane (8 mL) and water (2 mL) was heated to 90° C. for 30 minutes. After cooling to room temperature, addition of EtOAc (200 mL) and water (50 mL). After decantation, the organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure and the residue obtained was purified by flash chromatography eluting with a gradient of cyclohexane/EtOAc (100/0 to 0/100, v/v) to give 153 mg (70%) of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0335]** LC/MS (m/z, MH+): 526

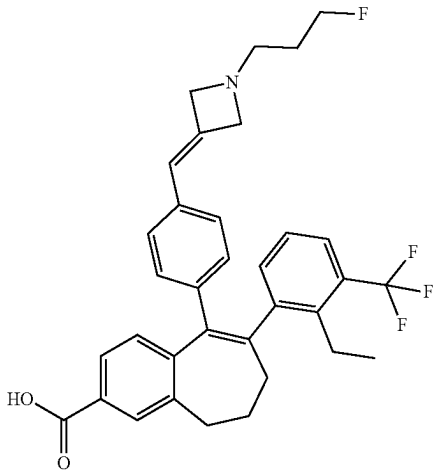
Step 2: 9-(4-((1-(3-Fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



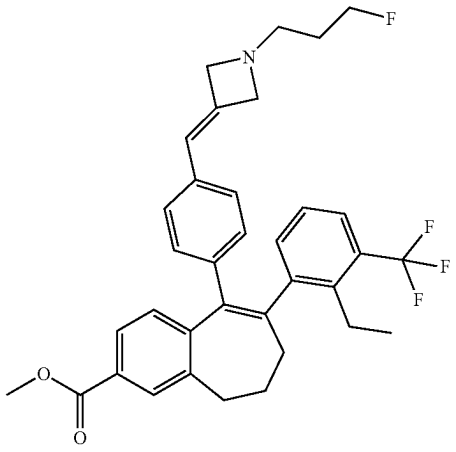

**[0336]** To a solution of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (153 mg, 291.1 μmol) in MeOH (40 mL) and water (8 mL) was added LiOH (28 mg, 1.16 mmol) and the reaction mixture was stirred at RT overnight. Water (50 mL), EtOAc (100 mL) and $Et_2O$ (100 mL) were added and pH was adjusted to 7 with HCl 0.1N. After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure and the residue obtained was purified by flash chromatography eluting with a gradient of MeOH in DCM (100/0 to 80/20, v/v) to give 148 mg (99%) of 8-(2-chloro-4-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid as a white solid.

Method B

Example 5: 8-(2-Ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid




Step 1: Methyl 8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate

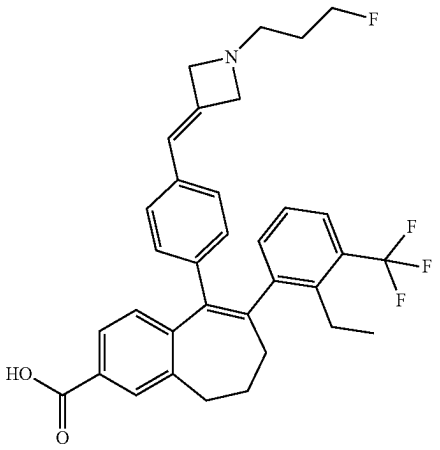



**[0337]** A mixture of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 5) (200 mg, 338 μmol), 1-bromo-2-ethyl-3-(trifluoromethyl)benzene (129 mg, 508 μmol), $Cs_2CO_3$ (232 mg, 711 μmol), and Pd(dppf)$Cl_2$, complex with DCM (25 mg, 34 μmol) in dioxane (8 mL) and water (2 mL) was heated to 90° C. for 1 hour. After cooling to room temperature, addition of EtOAc (200 mL) and water (50 mL). After decantation, the organic phase was dried over $MgSO_4$, filtered concentrated under reduced pressure and the residue obtained was purified by flash chromatography

eluting with a gradient of cyclohexane/EtOAc (100/0 to 0/100, v/v) to give 113 mg (58%) of methyl 8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0338]** LC/MS (m/z, MH+): 578

Step 2: 8-(2-Ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid

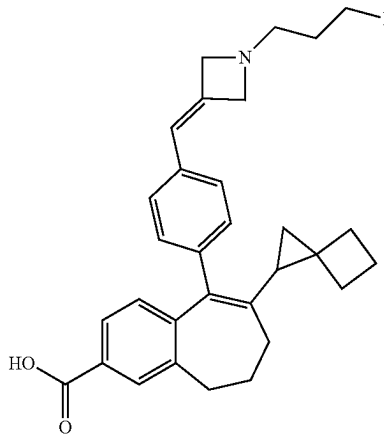


**[0339]** Step 2 of Example 5 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 71 mg (64%) of 8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid.

Method C

Examples 35 and 36: 9-(4-((1-(3-Fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1 and Isomer 2

Isomer 1



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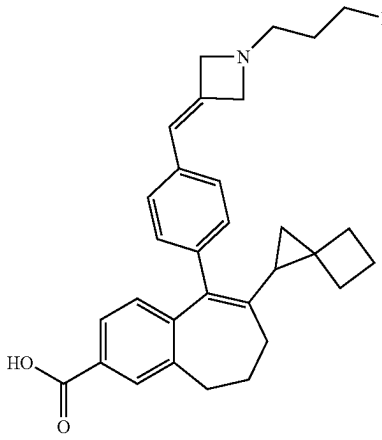
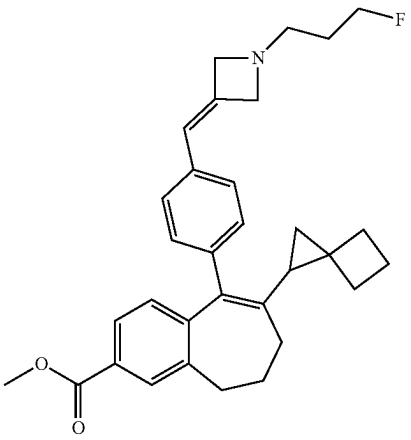
Isomer 2

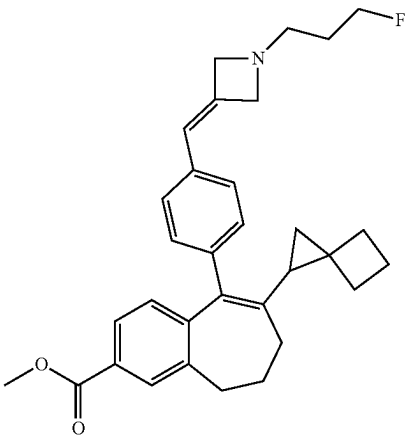


Step 1: Methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, Isomer 1 and Isomer 2

Isomer 1



Isomer 2



**[0340]** A mixture of methyl 8-bromo-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-

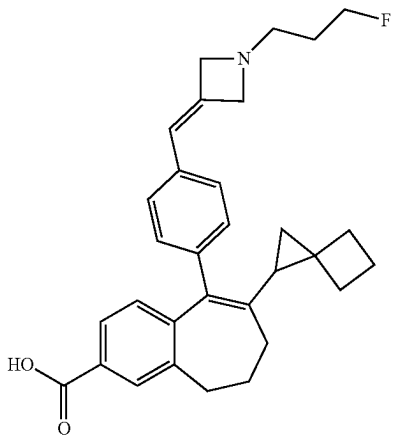
benzo[7]annulene-3-carboxylate (Intermediate 4) (250 mg, 516 μmol), potassium trifluoro(spiro[2.3]hexan-1-yl)borate (194 mg, 1032 μmol), $Cs_2CO_3$ (336 mg, 1032 μmol), and $Pd(dppf)Cl_2$, complex with DCM (37 mg, 52 μmol) in toluene (6 mL) and water (2 mL) was heated to 90° C. for 4 hours in a sealed tube. After cooling to room temperature, addition of EtOAc (200 mL) and water (50 mL). After decantation, the organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure and the residue obtained was purified by flash chromatography eluting with a gradient of cyclohexane/EtOAc (100/0 to 0/100, v/v) and reverse phase preparative HPLC on a RP-18 column with a gradient of ACN in water (30/70 to 100/0, v/v) to give 76 mg (30%) of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate as a racemic mixture of Isomer 1 and Isomer 2.

**[0341]** LC/MS (m/z, MH+): 486

**[0342]** The racemic mixture of methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate was separated by chiral SFC (column CHIRALPAK IJ, supercritical $CO_2$ 80%/MeOH 20%/TEA 0.1%) to give 28 mg of Isomer 1 and 29 mg of Isomer 2.

Step 2 of Example 35: 9-(4-((1-(3-Fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1

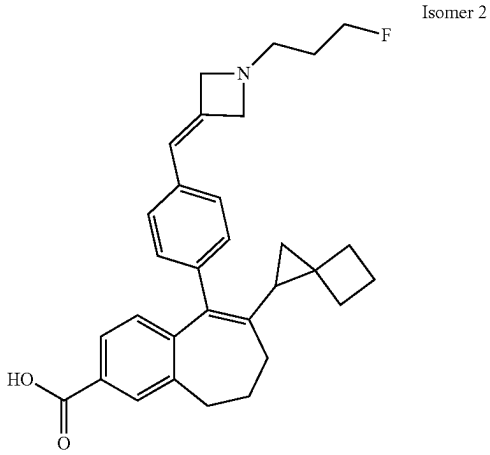
Isomer 1




**[0343]** Step 2 of Example 35 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, Isomer 1 to give 12 mg (44%) of 9-(4-((1-(3-Fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1.

Step 2 of Example 36: 9-(4-((1-(3-Fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2

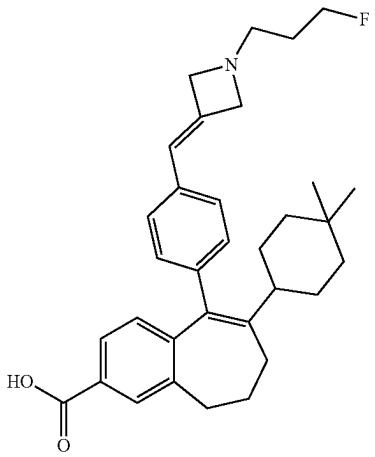
Isomer 2



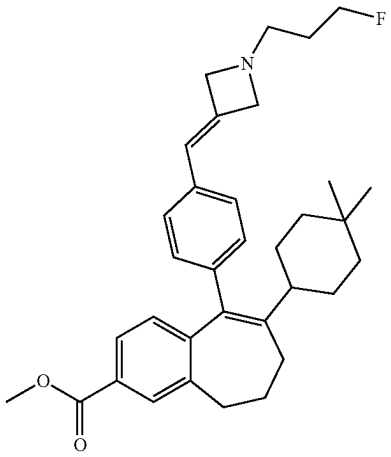

**[0344]** Step 2 of Example 36 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, Isomer 2 to give 16 mg (57%) of 9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acids, Isomer 2.

Method D

Example 68: 8-(4,4-Dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



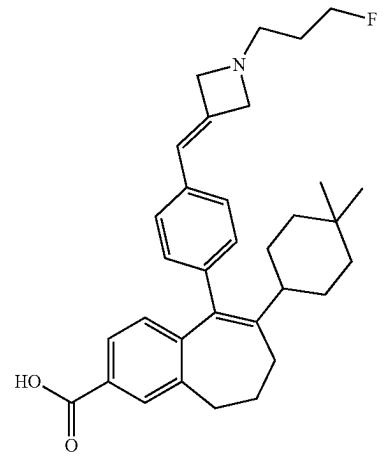
Step 1: Methyl 8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0345]** A mixture of methyl 8-(4,4-dimethylcyclohexyl)-9-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 7) (162 mg, 350 μmol), 1-(3-fluoropropyl)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylidene)azetidine (Intermediate 2) (140 mg, 420 μmol), Pd(dppf)$Cl_2$ complex with DCM (26 mg, 40 μmol), $Cs_2CO_3$ (229 mg, 0.7 mmol) in dioxane (6 ml) and water (1.5 ml) was heated to 95° C. for 1 hour. After cooling to room temperature, water (50 mL), EtOAc (100 mL) and $Et_2O$ (100 mL) were added. After decantation, the organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure. The residue obtained was purified by flash chromatography eluting with a gradient of cyclohexane/EtOAc (100/0 to 0/100, v/v) to give 120 mg (66%) of methyl 8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0346]** LC/MS (m/z, MH+): 516

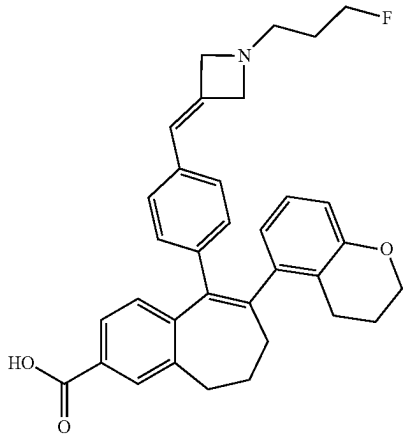
Step 2: 8-(4,4-Dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



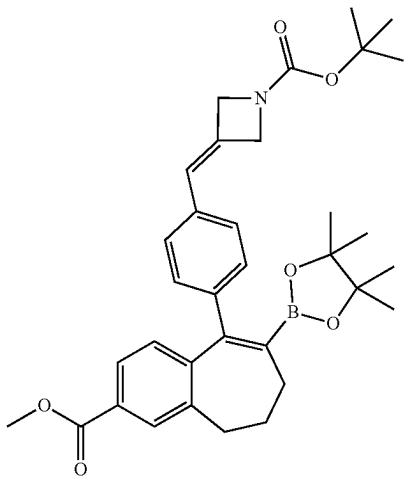
**[0347]** Step 2 of Example 68 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 110 mg (94%) of 8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid.

Method E

Example 64: 8-(Chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



Step 1: Tert-butyl 3-(4-(3-(methoxycarbonyl)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate

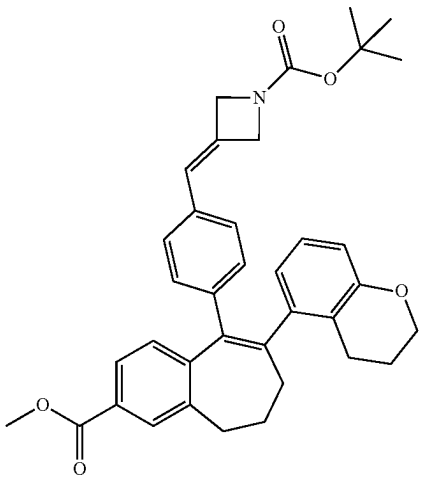


**[0348]** Step 1 of Example 64 was prepared following a similar procedure to that of Intermediate 5 from tert-butyl 3-(4-(8-bromo-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate (Intermediate 4, Method 1, Step 4) to give 1.37 g (63%) of

tert-butyl 3-(4-(3-(methoxycarbonyl)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate.

**[0349]** LC/MS (m/z, MH+): 516

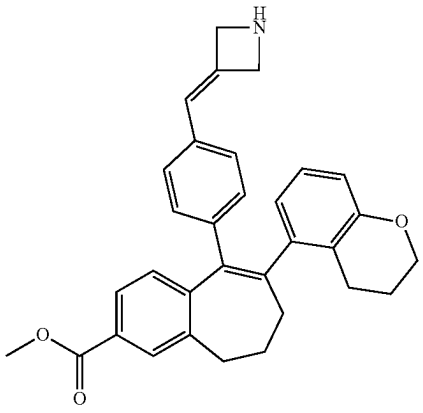
Step 2: Tert-butyl 3-(4-(8-(chroman-5-yl)-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate



**[0350]** Step 2 of Example 64 was prepared following a similar procedure to that of step 1 of Example 5 from tert-butyl 3-(4-(3-(methoxycarbonyl)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate and 5-bromochromane to give 120 mg (59%) of tert-butyl 3-(4-(8-(chroman-5-yl)-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate.

**[0351]** LC/MS (m/z, MH+): 578

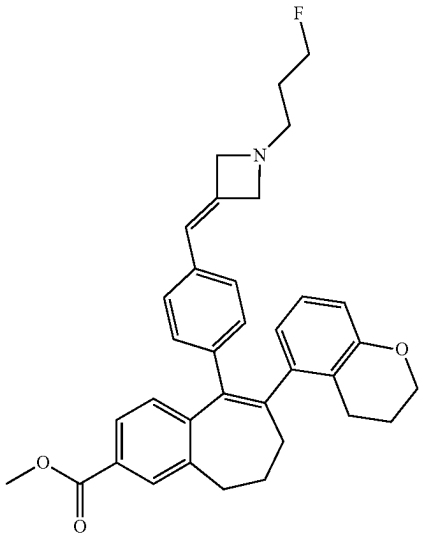
Step 3: Methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-(chroman-5-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0352]** Step 3 of Example 64 was prepared following a similar procedure to that of step 2 of Intermediate 1 from tert-butyl 3-(4-(8-(chroman-5-yl)-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)benzylidene)azetidine-1-carboxylate including additional quenching with saturated aqueous $NaHCO_3$ solution to give 100 mg (100%) of methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-(chroman-5-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0353]** LC/MS (m/z, MH+): 478

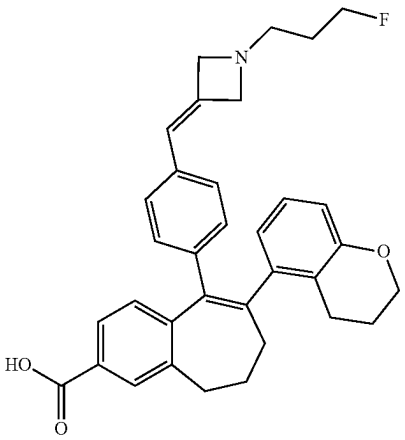
Step 4: Methyl 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0354]** Step 4 of Example 64 was prepared following a similar procedure to that of step 5 of Intermediate 4 (Method 2) from methyl 9-(4-(azetidin-3-ylidenemethyl)phenyl)-8-(chroman-5-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 35 mg (31%) of methyl 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0355]** LC/MS (m/z, MH+): 538

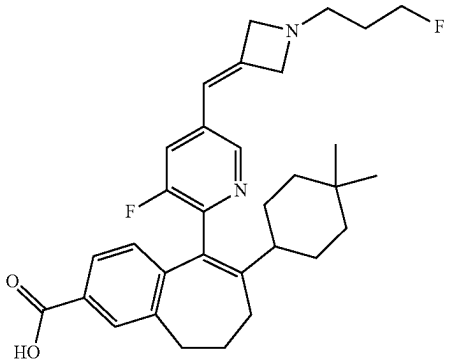
Step 5: 8-(Chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



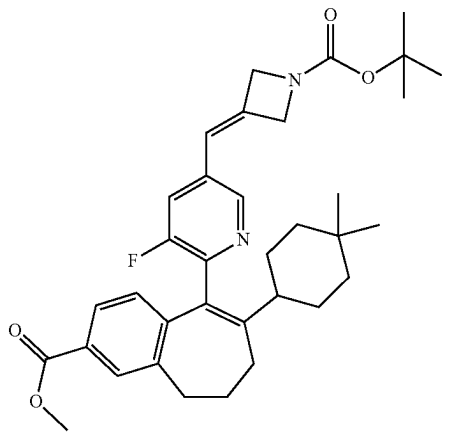
**[0356]** Step 5 of Example 64 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 31 mg (91%) of 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid.

Method F

Example 65: 8-(4,4-Dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene) methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



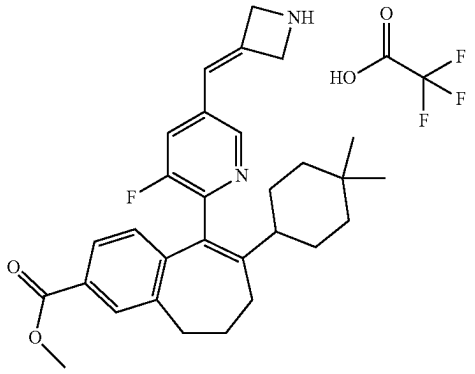
Step 1: Tert-butyl 3-((6-(8-(4,4-dimethylcyclohexyl)-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo [7]annulen-9-yl)-5-fluoropyridin-3-yl)methylene) azetidine-1-carboxylate



**[0357]** A mixture of tert-butyl 3-((6-chloro-5-fluoropyridin-3-yl)methylene)azetidine-1-carboxylate (Intermediate 9) (715 mg, 2.4 mmol), methyl 8-(4,4-dimethylcyclohexyl)-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate (Intermediate 10) (700 mg, 1.6 mmol), $Cs_2CO_3$ (1.56 g, 4.79 mmol) in 40 ml of toluene and 10 ml of water in a sealed tube was degazed with argon for 5 min. CataCXium A Pd G3 ((di(1-adamantyl)-n-butylphosphine)-2-(2'-amino-1,1'-biphenyl) palladium(II) methanesulfonate, CAS number 1651823-59-4) (116 mg, 0.16 mmol) was added. The tube was sealed and the reacting mixture was stirred at 90° C. for 18 h. Water (10 ml) and $Et_2O$ (30 ml) were added and the organic layer was washed with 10 ml of water, dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with a gradient of EtOAc in cyclohexane (100/0 to 50/50, v/v) to give 560 mg (60%) of tert-butyl 3-((6-(8-(4,4-dimethylcyclohexyl)-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7]annulen-9-yl)-5-fluoropyridin-3-yl)methylene)azetidine-1-carboxylate.

**[0358]** LC/MS (m/z, MH+): 575

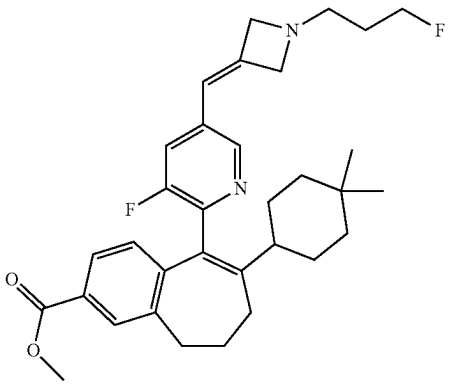
Step 2: Methyl 9-(5-(azetidin-3-ylidenemethyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid



**[0359]** A mixture of tert-butyl 3-((6-(8-(4,4-dimethylcyclohexyl)-3-(methoxycarbonyl)-6,7-dihydro-5H-benzo[7] annulen-9-yl)-5-fluoropyridin-3-yl)methylene)azetidine-1-carboxylate (640 mg, 1.11 mmol) in DCM (4 ml) and trifluoroacetic acid (4 ml) was stirred at RT for 1 h then concentrated under reduced pressure to give 1.3 g of crude methyl 9-(5-(azetidin-3-ylidenemethyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7] annulene-3-carboxylate, 2,2,2-trifluoroacetic acid which was used as such in the next step.

**[0360]** LC/MS (m/z, MH+): 475.

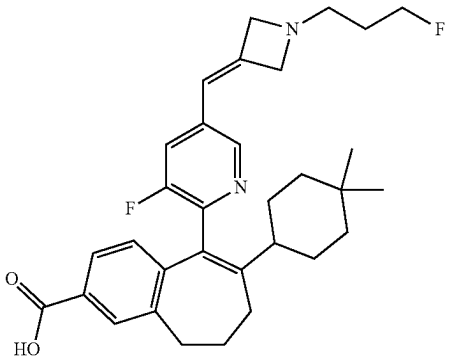
Step 3: Methyl 8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0361]** A mixture of crude methyl 9-(5-(azetidin-3-ylidenemethyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid (370 mg, 0.47 mmole), 1-fluoro-3-iodopropane (97 mg, 0.52 mmole) and DIEA (244 mg, 1.89 mmol) in acetonitrile (10 ml) was stirred at RT for 20 h then half concentrated under reduced pressure and directly purified by flash chromatography eluting with a gradient of a mixture AcOEt/MeOH:80/20 in cyclohexane (100/0 to 0/100, v/v) to give 100 mg (40%) of methyl 8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

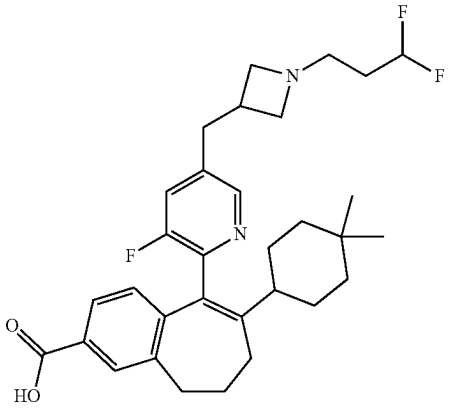
**[0362]** LC/MS (m/z, MH+): 535

Step 4: 8-(4,4-Dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid

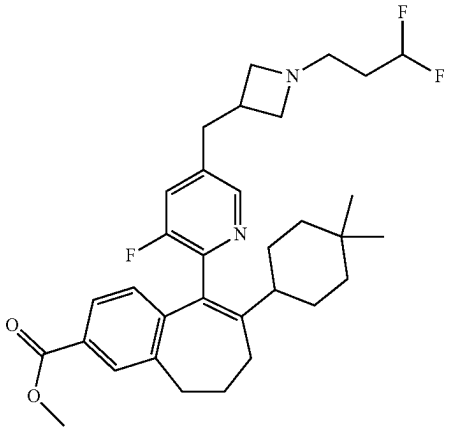


**[0363]** Step 5 of Example 65 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 51 mg (35%) of 8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid.

Example 66: 9-(5-((1-(3,3-Difluoropropyl)azetidin-3-ylidene)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



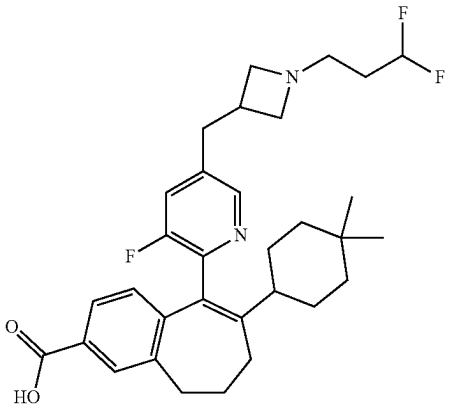
Step 1: Methyl 9-(5-((1-(3,3-difluoropropyl)azetidin-3-yl)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate



**[0364]** Step 1 of Example 66 was prepared following a similar procedure to that of step 3 of Example 65 from methyl 9-(5-(azetidin-3-ylidenemethyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate, 2,2,2-trifluoroacetic acid and 3,3-difluoropropyl trifluoromethanesulfonate (Intermediate 11) to give 174 mg (46%) of methyl 9-(5-((1-(3,3-difluoropropyl)azetidin-3-yl)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate.

**[0365]** LC/MS (m/z, MH+): 555

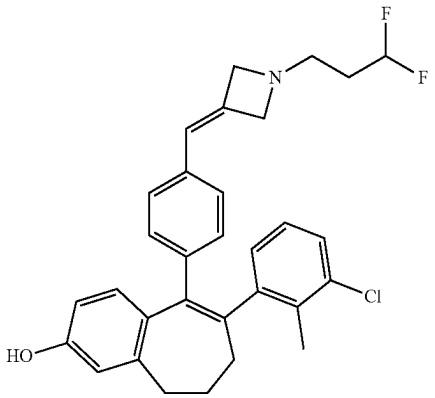
Step 2: 9-(5-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid



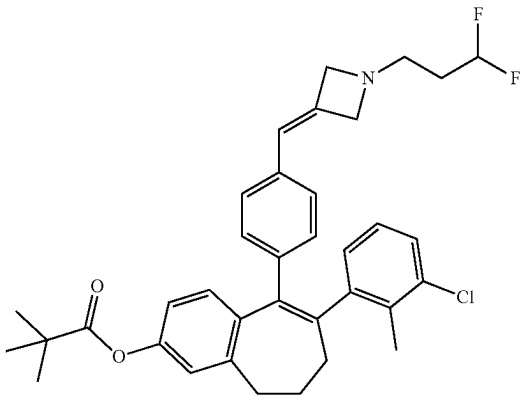
**[0366]** Step 2 of Example 66 was prepared following a similar procedure to that of step 2 of Example 3 from methyl 9-(5-((1-(3,3-difluoropropyl)azetidin-3-yl)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylate to give 32 mg (16%) of 9-(5-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid.

Method G

Example 42: 8-(3-Chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-ol



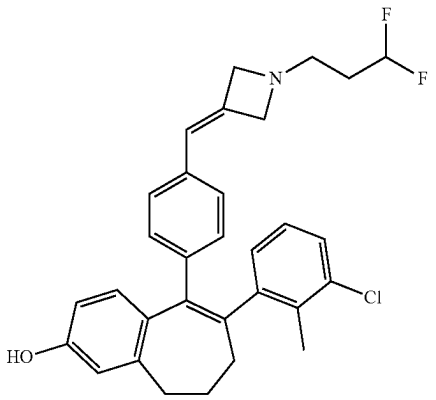
Step 1: 8-(3-Chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate



**[0367]** Step 1 of Example 42 was prepared following a similar procedure to that of step 1 of Example 3 from 8-bromo-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate (Intermediate 6) and (3-chloro-2-methyl-phenyl)boronic acid to give 21 mg (61%) of 8-(3-chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate.

**[0368]** LC/MS (m/z, MH+): 590

Step 2: 8-(3-Chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-ol



**[0369]** Step 2 of Example 42 was prepared following a similar procedure to that of step 2 of Example 3 from 8-(3-chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-yl pivalate to give 12.5 mg (69%) of 8-(3-chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-ol.

**[0370]** The compounds according to Table 1a above were subjected to pharmacological tests for determining their degradation effects on estrogen receptors.

Test: Estrogen Receptor Degradation Activity

**[0371]** Said test involves measuring the in vitro degradation activity of the compounds of the Table 1a.

**[0372]** The measurements of the degradation activities were made using a breast cancer cell ERα in cell western assay as described hereunder.

**[0373]** MCF7 cells (ATCC) were seeded in 384 wells microplate (collagen coated) at a concentration of 10000 cells/30 μL per well in red phenol free MEM alpha medium (invitrogen) containing 5% charcoal dextran striped FBS. The following day, 9 points serial 1:5 dilution of each compound was added to the cells in 2.5 μL at final concentrations ranging from 0.3-0.0000018 μM (in table 2), or 0.1 μM for fulvestrant (using as positive control). At 4 hours post compound addition the cells were fixed by adding 25 μL of formalin (final concentration 5% formalin containing 0.1% triton) for 10 minutes at room temperature and then washed twice with PBS. Then, 50 μL of LI-COR blocking buffer containing 0.1% Triton was added to plate for 30 minutes at room temperature. LI-COR blocking buffer was removed and cells were incubated overnight at cold room with 50 μL anti-ER rabbit monoclonal antibody (Thermo scientific MA1-39540) diluted at 1:1000 in LI-COR blocking buffer containing 0.1% tween-20. Wells which were treated with blocking buffer but no antibody were used as background control. Wells were washed twice with PBS (0.1% tween-20) and incubated at 37° C. for 60 minutes in LI-COR (0.1% tween-20) containing goat anti-rabbit antibody Alexa 488 (1:1000) and Syto-64 a DNA dye (2 μM final concentration). Cells were then washed 3 times in PBS and scanned in ACUMEN explorer (TTP-Labtech). Integrated intensities in the green fluorescence and red fluorescence were measured to determine the levels of ERα and DNA respectively.

**[0374]** The degradation activity with respect to estrogen receptors in this test is given by the concentration which degrades 50% of the estrogen receptor (or $IC_{50}$) in nM.

**[0375]** The % of ERα levels decrease were determined as follows: % inhibition=100*(1−(sample−fulvestrant: DMSO−fulvestrant)).

**[0376]** The Table 2 below indicates the estrogen receptor degradation activity results for the compounds of Table 1a tested at 0.3 μM, and demonstrates that said compounds have a significant degradation activity on estrogen receptors.

TABLE 2

| Compound No. | Degradation $IC_{50}$ (nM) | % Degradation At 0.3 μM |
|---|---|---|
| 1 | 0.3 | 92 |
| 2 | 1 | 90 |
| 3 | 0.7 | 90 |
| 4 | 1.1 | 90 |
| 5 | 0.3 | 93 |
| 6 | 0.3 | 91 |
| 7 | 0.5 | 94 |
| 8 | 0.8 | 93 |
| 9 | 0.6 | 96 |
| 10 | 0.5 | 93 |
| 11 | 0.4 | 92 |
| 12 | 0.7 | 92 |
| 13 | 0.4 | 91 |
| 14 | 0.6 | 91 |
| 15 | 0.4 | 91 |
| 16 | 0.3 | 92 |
| 17 | 0.5 | 91 |

TABLE 2-continued

| Compound No. | Degradation $IC_{50}$ (nM) | % Degradation At 0.3 μM |
|---|---|---|
| 18 | 0.6 | 91 |
| 19 | 0.2 | 92 |
| 20 | 0.6 | 94 |
| 21 | 0.5 | 93 |
| 22 | 0.5 | 94 |
| 23 | 0.4 | 91 |
| 24 | 0.5 | 91 |
| 25 | 0.4 | 91 |
| 26 | 0.2 | 91 |
| 27 | 0.5 | 93 |
| 28 | 0.5 | 94 |
| 29 | 0.6 | 93 |
| 30 | 0.4 | 91 |
| 31 | 37.8 | 95 |
| 32 | 0.3 | 91 |
| 33 | 0.3 | 91 |
| 34 | 0.7 | 94 |
| 35 | 0.3 | 91 |
| 36 | 0.2 | 92 |
| 37 | 0.6 | 91 |
| 38 | 0.4 | 90 |
| 39 | 0.3 | 92 |
| 40 | 0.5 | 91 |
| 41 | 0.7 | 91 |
| 42 | 6.4 | 53 |
| 43 | 0.5 | 91 |
| 44 | 0.5 | 93 |
| 45 | 0.6 | 93 |
| 46 | 0.5 | 91 |
| 47 | 0.5 | 93 |
| 48 | 0.9 | 94 |
| 49 | 0.5 | 93 |
| 50 | 8.5 | 92 |
| 51 | 0.5 | 92 |
| 52 | 0.4 | 94 |
| 53 | 1.2 | 91 |
| 54 | 0.5 | 95 |
| 55 | 0.6 | 94 |
| 56 | 0.7 | 92 |
| 57 | 0.7 | 93 |
| 58 | 0.2 | 93 |
| 59 | 0.9 | 92 |
| 60 | 0.6 | 93 |
| 61 | 0.9 | 91 |
| 62 | 0.5 | 93 |
| 63 | 1.0 | 94 |
| 64 | 3.1 | 96 |
| 65 | 0.8 | 91 |
| 66 | 1.7 | 86 |
| 67 | 1.0 | 90 |
| 68 | 0.7 | 86 |
| 69 | 1.3 | 74 |
| 70 | 1.8 | 81 |
| 71 | 0.5 | 95 |
| 72 | 0.3 | 100 |
| 73 | 0.3 | 85 |
| 74 | 0.8 | 90 |
| 75 | 0.2 | 95 |
| 76 | 0.2 | 95 |
| 77 | 0.7 | 95 |
| 78 | 0.4 | 94 |
| 79 | 0.4 | 100 |
| 80 | 1.2 | 105 |
| 81 | 0.7 | 92 |
| 82 | 1.4 | 95 |
| 83 | 0.4 | 94 |
| 84 | 0.6 | 91 |

**[0377]** It is therefore apparent that the tested compounds have degradation activities for estrogen receptors, with IC50 less than 1 μM and with degradation levels greater than 50%. The compounds of formula (I) can therefore be used for

preparing medicaments, especially medicaments which are degraders of estrogen receptors.

**[0378]** Accordingly, also provided herein are medicaments which comprise a compound of the formula (I), or a pharmaceutically acceptable salt thereof.

**[0379]** Herein are also provided the compounds of formula (I) defined above, or pharmaceutically acceptable salts thereof, for use as medicines.

**[0380]** Herein are also provided the compounds of formula (I) defined above, or pharmaceutically acceptable salt thereof, for use in therapy, especially as inhibitors and degraders of estrogen receptors.

**[0381]** Herein are also provided the compounds of formula (I) defined above, or a pharmaceutically acceptable salts thereof, for use in the treatment of ovulatory dysfunction, cancer, endometriosis, osteoporosis, benign prostatic hypertrophy or inflammation.

**[0382]** A particular aspect is a compound of formula (I) defined above, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer.

**[0383]** In an embodiment, the cancer is a hormone dependent cancer.

**[0384]** In another embodiment, the cancer is an estrogen receptor dependent cancer, particularly the cancer is an estrogen receptor a dependent cancer.

**[0385]** In another embodiment, the cancer is selected from breast, ovarian, endometrial, prostate, uterine, cervical and lung cancer, or a metastasis thereof.

**[0386]** In another embodiment, the metastasis is a cerebral metastasis.

**[0387]** In another embodiment, the cancer is breast cancer. Particularly, the breast cancer is an estrogen receptor positive breast cancer (ERα positive breast cancer).

**[0388]** In another embodiment, the cancer is resistant to anti-hormonal treatment.

**[0389]** In a further embodiment, the compound of formula (I) is as used as single agent or in combination with other agents such as CDK4/6, mTOR or PI3K inhibitors.

**[0390]** According to another aspect, herein is provided a method of treating the pathological conditions indicated above, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof. In an embodiment of this method of treatment, the subject is a human.

**[0391]** Herein is also provided the use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament useful in treating any of the pathological conditions indicated above, more particularly useful in treating cancer.

**[0392]** Herein are also provided the pharmaceutical compositions comprising as active principle a compound of formula (I). These pharmaceutical compositions comprise an effective dose of at least one compound of formula (I), or a pharmaceutically acceptable salt thereof, and also at least one pharmaceutically acceptable excipient.

**[0393]** The said excipients are selected, in accordance with the pharmaceutical form and method of administration desired, from the customary excipients, which are known to a person skilled in the art.

**[0394]** In the pharmaceutical compositions for oral, sublingual, subcutaneous, intramuscular, intravenous, topical, local, intra-tracheal, intranasal, transdermal or rectal administration, the active principle of formula (I) above, or its base, acid, zwitterion or salt thereof, may be administered in a unit administration form, in a mixture with conventional pharmaceutical excipients, to animals and to human beings for the treatment of the above disorders or diseases.

**[0395]** The unit administration forms appropriate include oral forms such as tablets, soft or hard gel capsules, powders, granules and oral solutions or suspensions, sublingual, buccal, intra-tracheal, intra-ocular and intra-nasal administration forms, forms for inhalative, topical, transdermal, subcutaneous, intra-muscular or intravenous administration, rectal administration forms and implants. For topical application it is possible to use the compounds of formula (I) in creams, gels, ointments or lotions.

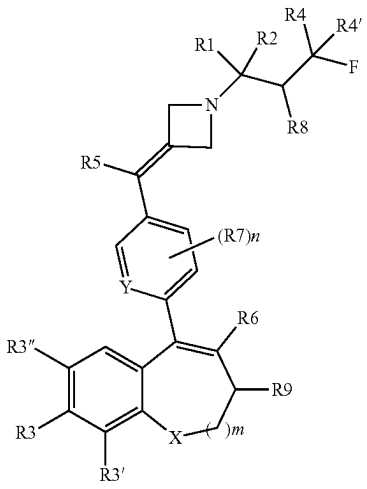
**[0396]** As an example, a unit administration form of a compound of formula (I) in tablet form may comprise the following components:

| | |
|---|---|
| Compound of formula (I) | 50.0 mg |
| Mannitol | 223.75 mg |
| Sodium croscarmellose | 6.0 mg |
| Corn starch | 15.0 mg |
| Hydroxypropylmethylcellulose | 2.25 mg |
| Magnesium stearate | 3.0 mg |

**[0397]** There may be particular cases in which higher or lower dosages are appropriate. According to usual practice, the dosage that is appropriate for each patient is determined by the doctor according to the mode of administration and the weight and response of the said patient.

**1**. A compound of the formula (I) or a pharmaceutically acceptable salt thereof:

(I)




wherein:

R1 and R2 independently represent a hydrogen atom or a deuterium atom;

R3 represents a hydrogen atom, a —COOH group or a —OH group;

R3' and R3" independently represent a hydrogen atom, a methyl group, a methoxy group, a chlorine atom, a fluorine atom or a cyano group;

R4 and R4' independently represent a hydrogen atom or a fluorine atom;

R5 represents a hydrogen atom, a fluorine atom or a ($C_1$-$C_3$)alkyl group;

R6 represents a group selected from:

a phenyl group, said phenyl group being optionally substituted by 1 to 3 substituents independently selected from a halogen atom; a ($C_1$-$C_6$)alkyl group, optionally substituted with a cyano group or a —OH group; a ($C_1$-$C_6$)fluoroalkyl group; a ($C_3$-$C_6$)cycloalkyl group; a ($C_1$-$C_6$)alkoxy group; a ($C_1$-$C_6$)fluoroalkoxy group; a cyano group; a trifluoromethylsulfonyl group; a ($C_1$-$C_4$)alkylthio group; a ($C_1$-$C_4$)fluoroalkylthio group; a ($C_1$-$C_4$)alkylsulfonyl group and a —OH group;

a fused phenyl group, selected from phenyl groups fused with a ($C_3$-$C_6$)cycloalkyl, said ($C_3$-$C_6$)cycloalkyl optionally comprises an unsaturation, and wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group;

a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$)alkoxy group;

a bicyclic group comprising 5 to 12 carbon atoms, optionally comprising 1 to 2 unsaturations; optionally substituted with 1 to 4 substituents independently selected from: a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group and an oxo group;

a heteroaryl group comprising 2 to 9 carbon atoms and comprising from 1 to 3 heteroatoms independently selected from oxygen, nitrogen and sulfur, and at least 5 atoms including carbon atoms and heteroatoms, said heteroaryl group being optionally substituted with 1 to 3 substituents independently selected from a halogen atom, a ($C_1$-$C_6$)alkyl group, a ($C_1$-$C_6$)fluoroalkyl group, a ($C_1$-$C_6$)alkoxy group, a ($C_1$-$C_6$)fluoroalkoxy group, a cyano group, a carbamoyl group and a —OH group;

a cycloalkyl group comprising 3 to 7 carbon atoms, said cycloalkyl group being saturated or partially saturated and being optionally substituted with 1 to 4 substituents independently selected from:

a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group, an oxo group,

a ($C_3$-$C_6$)cycloalkyl group and a phenyl group, said ($C_3$-$C_6$)cycloalkyl or phenyl groups being optionally substituted with one or two halogen atom(s) or ($C_1$-$C_3$)alkyl group(s);

a ($C_3$-$C_6$)cycloalkyl($C_1$-$C_3$)alkyl group, optionally substituted on the cycloalkyl with 1 to 4 substituents independently selected from: a fluorine atom, a —OH group, a ($C_1$-$C_4$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)fluoroalkoxy group and an oxo group;

a 4 to 7 membered-heterocycloalkyl group comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulfur, said heterocycloalkyl group being saturated or partially saturated and being optionally substituted with 1 to 3 substituents independently selected from: a fluorine atom, a ($C_1$-$C_3$) alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$) fluoroalkoxy group, an oxo group, a ($C_1$-$C_3$)alkoxy group, and a —OH group;

a ($C_1$-$C_6$)alkyl group, a methyl group or an ethyl group, said alkyl group being optionally substituted with 1 to 4 substituents independently selected from: a fluorine atom, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$) fluoroalkoxy group and a —OH group; and

a phenyl($C_1$-$C_2$)alkyl group, said phenyl group being optionally substituted with 1 to 3 substituents independently selected from a halogen atom; a ($C_1$-$C_3$) alkyl group; a ($C_1$-$C_3$)fluoroalkyl group; a ($C_1$-$C_3$) alkoxy group; a ($C_1$-$C_3$)fluoroalkoxy group; a cyano group; and a —OH group;

X represents —$CH_2$—, —O— or —S—;

Y represents —CH═, —N═ or —CR"═, wherein R" represents a ($C_1$-$C_3$)alkyl group, a halogen atom, a cyano group, or a ($C_1$-$C_3$)fluoroalkyl group;

R7 independently represents a ($C_1$-$C_3$)alkyl group, a halogen atom, a cyano group, or a ($C_1$-$C_3$)fluoroalkyl group;

R8 represents a hydrogen atom or a fluorine atom;

R9 represents a hydrogen atom, a ($C_1$-$C_3$)alkyl group or a cyclopropyl;

n is 0, 1 or 2; and

m is 0 or 1.

**2**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R1 and R2 are a hydrogen atom.

**3**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R3 is —COOH.

**4**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R3' and R3" represent a hydrogen atom.

**5**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R4 and R4' represent a hydrogen atom.

**6**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that X represents —$CH_2$—.

**7**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R5 represents a hydrogen atom.

**8**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R6 represents a phenyl group, said phenyl group being optionally substituted with 1 to 3 substituents independently selected from a chlorine atom, a fluorine atom, a methyl group, an ethyl group, a trifluoromethyl group, a cyclopropyl group, a methoxy group, a trifluoromethoxy group, a 1,1-difluoroethyl group, a difluoromethyl group, a difluoromethoxy group, a fluoromethyl group and a cyano group.

**9**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R6 represents a fused phenyl group, selected from a bicyclo[4.2.0]octatrienyl group, an indanyl group or a tet-

rahydronaphthalenyl group, optionally substituted with one or two fluorine atom or R6 represents a chromanyl group.

**10**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R6 represents a bicyclic group selected from a bicyclo [4.1.0]heptanyl, a bicyclo[3.1.0]hexanyl, a spiro[2.3]hexanyl and a bicyclo[3.2.1]octan-3-yl, optionally substituted with 1 to 4 substituents independently selected from: a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$) fluoroalkoxy group and an oxo group.

**11**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R6 represents a cycloalkyl chosen from a cyclohexyl or a cyclopropyl group, said cycloalkyl being optionally substituted with 1 to 4 substituents independently selected from:

a fluorine atom, a —OH group, a ($C_1$-$C_3$)alkyl group, a ($C_1$-$C_3$)fluoroalkyl group, a ($C_1$-$C_3$)alkoxy group, a ($C_1$-$C_3$)fluoroalkoxy group, an oxo group,

a ($C_3$-$C_6$)cycloalkyl group and a phenyl group said ($C_3$-$C_6$)cycloalkyl or phenyl group being optionally substituted with one or two halogen atom(s) or ($C_1$-$C_3$)alkyl group(s).

**12**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that R7 independently represents a methyl group, a cyano group, a trifluoromethyl group or a fluorine atom, and n is 0, 1 or 2.

**13**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein Y represents —CH═, —N═ or —CR"═, and R" represents a fluorine atom, a cyano group, or a trifluoromethyl group.

**14**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein m is 1.

**15**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein R6 represents a phenyl group fused with a hetero($C_4$-$C_6$)cycloalkyl, which hetero($C_4$-$C_6$)cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a ($C_1$-$C_3$)alkyl group, a hydroxy group, a halogen atom, a ($C_1$-$C_6$)fluoroalkyl group and a ($C_1$-$C_3$) alkoxy group.

**16**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein R6 represents a phenyl group, said phenyl group being optionally substituted by 1 to 3 substituents independently selected from a halogen atom; a ($C_1$-$C_6$)alkyl group, optionally substituted with a cyano group or a —OH group; a ($C_1$-$C_6$) fluoroalkyl group; a ($C_3$-$C_6$)cycloalkyl group; a ($C_1$-$C_6$) alkoxy group; a ($C_1$-$C_6$)fluoroalkoxy group; a cyano group; a trifluoromethylsulfonyl group; a ($C_1$-$C_4$)alkylthio group; a ($C_1$-$C_4$)fluoroalkylthio group; a ($C_1$-$C_4$)alkylsulfonyl group; and a —OH group; wherein said phenyl is substituted by at least one trifluoromethoxy group, by at least one 1,1-difluoroethyl group, by at least one difluoromethyl group, by at least one difluoromethoxy group or by at least one fluoromethyl group.

**17**. The compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, characterized in that said compound is selected from the following compounds:

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-6-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (1)

8-(3,4-difluoro-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (2)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (3)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-6-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (4)

8-(2-ethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (5)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-6-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (6)

8-(3-fluoro-2-methoxy-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (7)

8-(3-ethyl-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (8)

8-(2-fluoro-6-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (9)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-mesityl-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (10)

8-(2-chloro-4,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (11)

8-(3-fluoro-2,4-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (12)

8-(3-chloro-2,4-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (13)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4,6-dimethylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (14)

8-(2-(1,1-difluoroethyl)-4-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (15)

8-(2-chloro-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (16)

8-(2-chloro-6-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (17)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4-methoxy-2,6-dimethylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (18)

8-(4-ethyl-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (19)

8-(2-fluoro-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (20)

8-(2-chloro-6-methylphenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (21)

8-(2-fluoro-6-methoxyphenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (22)

8-(2-chloro-6-methoxyphenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (23)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-3-(trifluoromethoxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (24)

8-(2-ethyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (25)

8-(2-fluoro-6-methylphenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (26)

8-(4-fluoro-2,5-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (27)

8-(4-(difluoromethyl)-3-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (28)

8-(4-(difluoromethyl)-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (29)

8-(2-(difluoromethyl)-3-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (30)

8-(4-(difluoromethyl)-3-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (31)

8-(2-(fluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (32)

8-(2-(difluoromethoxy)-3-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (33)

8-(3-chloro-2-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (34)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1, (35)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(spiro[2.3]hexan-1-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2, (36)

8-(2-(difluoromethyl)-4-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (37)

8-(3-fluoro-2-(fluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (38)

8-(2-ethyl-3-fluorophenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (39)

8-(3-fluoro-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (40)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methoxy-2-methylphenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (41)

8-(3-chloro-2-methylphenyl)-9-(4-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulen-3-ol, (42)

8-(2-(difluoromethyl)-4-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (43)

8-(4-(difluoromethyl)-2-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (44)

8-(2-(difluoromethyl)-5-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (45)

8-(3-chloro-2-ethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (46)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(5-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (47)

8-(2-cyclopropyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (48)

8-(3-chloro-2-methoxyphenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (49)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methoxy-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (50)

8-(4-(difluoromethyl)-2-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (51)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (52)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(3-methyl-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (53)

8-(4-(difluoromethyl)-2-(trifluoromethoxy)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (54)

8-(4-(difluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (55)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(trans-4-methylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (56)

8-(2-(difluoromethyl)-5-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (57)

8-(2-(difluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl) azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (58)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (59)

8-(2-(difluoromethyl)-3-methoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (60)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(cis-4-methylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (61)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(4-methoxy-2-(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (62)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-3-(trifluoromethyl)phenyl)-6,7-di-

hydro-5H-benzo[7]annulene-3-carboxylic acid, (63) 8-(chroman-5-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (64)

8-(4,4-dimethylcyclohexyl)-9-(3-fluoro-5-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)pyridin-2-yl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (65)

9-(5-((1-(3,3-difluoropropyl)azetidin-3-ylidene)methyl)-3-fluoropyridin-2-yl)-8-(4,4-dimethylcyclohexyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (66) 8-(chroman-8-yl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (67)

8-(4,4-dimethylcyclohexyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (68)

8-(2,4-dichlorophenyl)-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 1, (69)

8-(2,4-dichlorophenyl)-9-(4-((1-(2,3-difluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, Isomer 2, (70)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methoxy-4,6-bis(trifluoromethyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (71)

8-(2,4-dimethyl-6-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (72)

8-(3-fluoro-2-methyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (73)

8-(2,6-diethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (74)

8-(3-fluoro-2,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (75)

8-(2-fluoro-4,6-dimethylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (76)

9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-8-(2-methyl-6-(trifluoromethoxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (77)

8-(2,5-dimethyl-4-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (78)

8-(2,3-bis(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (79)

8-(2,6-diethyl-4-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (80)

8-(2,3-dimethoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (81)

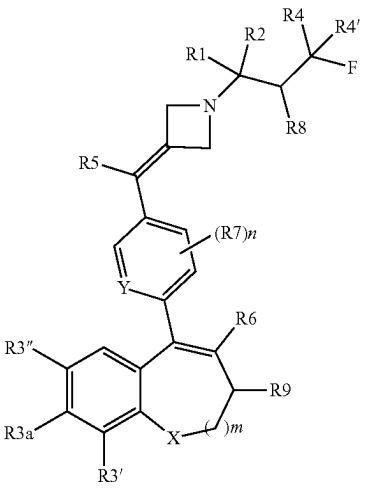
8-(3,4-dimethoxyphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (82)

8-(4-chloro-2-methoxy-6-methylphenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (83) or

8-(2,6-dimethyl-3-(trifluoromethyl)phenyl)-9-(4-((1-(3-fluoropropyl)azetidin-3-ylidene)methyl)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid, (84).

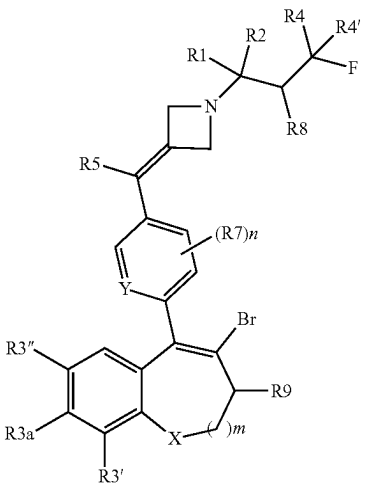
**18**. A process for preparing a compound of formula (I) as defined in claim **1**, wherein a compound of formula 1K;

1K




wherein R1, R2, R3', R3", R4, R4', R5, R6, R7, R8, R9, m, n, X and Y are as defined in claim **1** and R3a is a carboxylic ester or protected OH, is converted to compound of formula (I), in presence of a source of hydroxide ions, said step being optionally preceded by a step for obtaining compound 1K, wherein a compound of formula 1T

1T

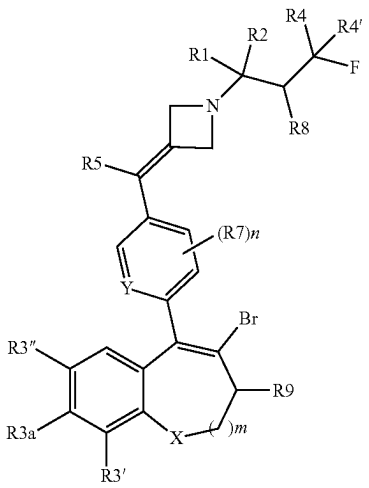



wherein, R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined in claim **1** and R3a is a carboxylic ester or protected OH,

is subjected to a Suzuki coupling with a boronic reagent $R6B(OR')_2$ or $R6BF_3K$, wherein $—B(OR')_2$ is a boronic acid or a pinacolate ester and R6 is as defined in claim **1**.

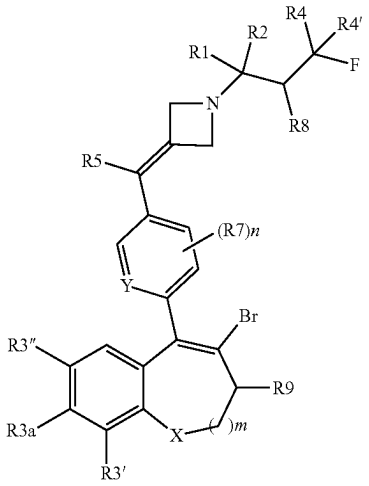
**19**. A process for preparing a compound of formula (I) as defined in claim **1**, wherein a compound of formula 1Ta:

1Ta



wherein R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X, and Y are as defined in claim **1** and R3a is a carboxylic ester or protected OH, is submitted to a Suzuki coupling with a boronic reagent $R6B(OR')_2$ or $R6BF_3K$, wherein $—B(OR')_2$ is a boronic acid or a pinacolate ester and R6 is defined as in claim **1**, said step being optionally preceded by a step for obtaining compound 1Ta, wherein a compound of formula 1T:

1T

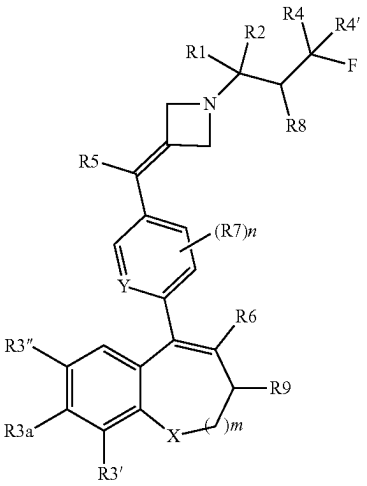


wherein R1, R2, R3', R3", R4, R4', R5, R7, R8, R9, m, n, X and Y are as defined in claim **1** and R3a is a carboxylic ester or protected OH,

is converted to a compound 1Ta in the presence of a source of hydroxide ions.

**20**. A compound of formula 1K or pharmaceutically acceptable salt thereof,

1K



wherein

R1 and R2 independently represent a hydrogen atom or a deuterium atom;

R3 represents a hydrogen atom, a —COOH group or a —OH group;

R3' and R3" independently represent a hydrogen atom, a methyl group, a methoxy group, a chlorine atom, a fluorine atom or a cyano group;

R4 and R4' independently represent a hydrogen atom or a fluorine atom;

R5 represents a hydrogen atom, a fluorine atom or a $(C_1\text{-}C_3)$alkyl group;

R7 independently represents a $(C_1\text{-}C_3)$alkyl group, a halogen atom, a cyano group, or a $(C_1\text{-}C_3)$fluoroalkyl group;

R8 represents a hydrogen atom or a fluorine atom;

R9 represents a hydrogen atom, a $(C_1\text{-}C_3)$alkyl group or a cyclopropyl;

m is 0 or 1;

n is 0, 1 or 2;

X represents $—CH_2—$, —O— or —S—;

Y represents —CH═, —N═ or —CR"═, wherein R" represents a $(C_1\text{-}C_3)$alkyl group, a halogen atom, a cyano group, or a $(C_1\text{-}C_3)$fluoroalkyl group;

R3a is carboxylic ester or protected OH and

R6 represents a phenyl group fused with a hetero$(C_4\text{-}C_6)$cycloalkyl, which hetero$(C_4\text{-}C_6)$cycloalkyl ring optionally comprises an unsaturation and, wherein the fused phenyl group is optionally substituted with 1 to 3 substituents independently selected from a $(C_1\text{-}C_3)$alkyl group, a hydroxy group, a halogen atom, a $(C_1\text{-}C_6)$fluoroalkyl group and a $(C_1\text{-}C_3)$ alkoxy group.

**21**. (canceled)

**22**. A pharmaceutical composition, characterized in that it comprises a compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

**23**. A method for inhibiting and degrading estrogen receptors, which method comprises administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof.

**24**. A method of treating ovulatory dysfunction, cancer, endometriosis, benign prostatic hypertrophy or inflammation, which method comprises administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I) according to claim **1**, or a pharmaceutically acceptable salt thereof.

**25**. The method of claim **24**, which method comprises the treatment of cancer.

* * * * *