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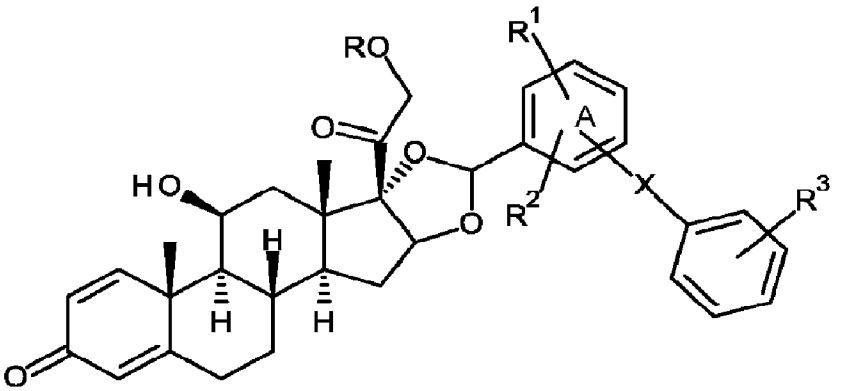
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(54) **Titre : AGONISTES DU RECEPTEUR DES GLUCOCORTICOIDES**
(54) **Title: GLUCOCORTICOID RECEPTOR AGONISTS**



Formula I

(57) **Abrégé/Abstract:**
The present invention provides a compound of Formula I: wherein R is H or R1 is H, halogen, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF3, R2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C4 alkenyl; R3 is NH2, or CH2NH2; and X is O, OCH2, OCH2CH2, OCH(CH3), CH2O, SCH2, CH2S, CH2, NHCH2, CH2NH, N(CH3)CH2, CH2CH2, C?C, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof, wherein the compound of Formula I, or pharmaceutically acceptable salt thereof is useful for treating autoimmune and inflammatory diseases, such as atopic dermatitis and rheumatoid arthritis.

Date Submitted: 2023/08/21

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Abstract:

The present invention provides a compound of Formula I: wherein R is H or R1 is H, halogen, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF3, R2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C4 alkenyl; R3 is NH2, or CH2NH2; and X is O, OCH2, OCH2CH2, OCH(CH3), CH2O, SCH2, CH2S, CH2, NHCH2, CH2NH, N(CH3)CH2, CH2CH2, CC, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof, wherein the compound of Formula I, or pharmaceutically acceptable salt thereof is useful for treating autoimmune and inflammatory diseases, such as atopic dermatitis and rheumatoid arthritis.

GLUCOCORTICOID RECEPTOR AGONISTS

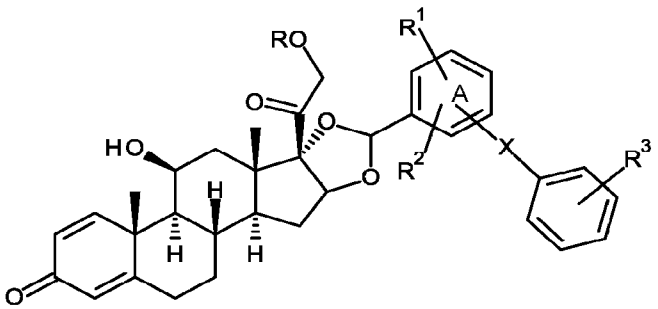
The present disclosure provides compounds that are glucocorticoid receptor agonists and are useful for the treatment of autoimmune and inflammatory diseases, such as atopic dermatitis, inflammatory bowel disease, systemic lupus erythematosus, lupus nephritis, and rheumatoid arthritis, processes for preparing these compounds, pharmaceutical compositions comprising these compounds, and methods of using these compounds and compositions are also provided.

Atopic dermatitis is a chronic, pruritic relapsing and remitting inflammatory skin disease that occurs frequently in children, but also affects many adults. Current treatments of atopic dermatitis include light therapy, topical creams containing corticosteroids or calcineurin inhibitors, or a subcutaneous injectable biologic known as dupilumab. In spite of progress made in treating atopic dermatitis, there remains a significant need for new compounds to treat atopic dermatitis and other inflammatory and autoimmune diseases.

WO2017/210471 discloses certain glucocorticoid receptor agonists and immunoconjugates thereof useful for treating autoimmune or inflammatory diseases. WO2018/089373 discloses novel steroids, protein conjugates thereof, and methods for treating diseases, disorders, and conditions comprising administering the steroids and conjugates.

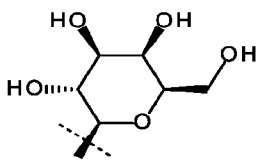
The present invention provides certain novel compounds which are glucocorticoid receptor agonists. The present invention further provides certain novel compounds which are prodrugs of glucocorticoid receptor agonists. In addition, the present invention provides certain novel compounds which are glucocorticoid receptor agonists useful in the treatment of autoimmune and inflammatory diseases such as atopic dermatitis, inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, and lupus nephritis.

Accordingly, in one embodiment, the invention provides a compound of Formula I:



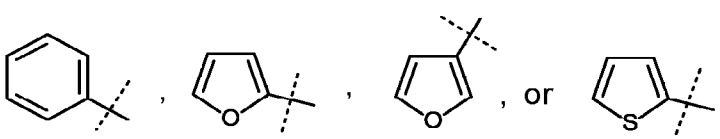
Formula I

wherein R is H or



;

R^1 is H, halogen, CN, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF_3,



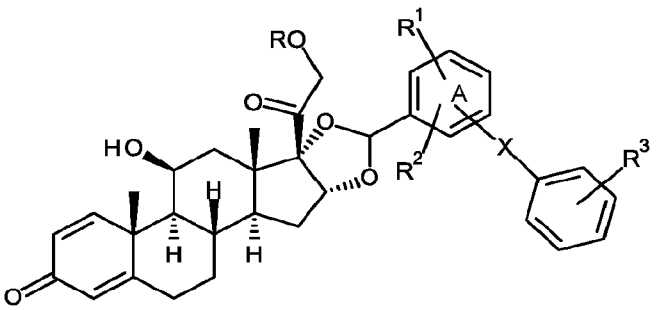
;

R^2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C3 alkenyl;

R^3 is NH_2, or CH_2NH_2; and

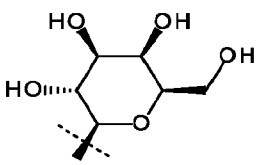
X is O, OCH_2, OCH_2CH_2, CH_2O, SCH_2, CH_2S, CH_2, $NHCH_2$, CH_2NH, $N(CH_3)CH_2$, CH_2CH_2, C≡C, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof.

In one embodiment, the invention provides a compound of Formula Ia:



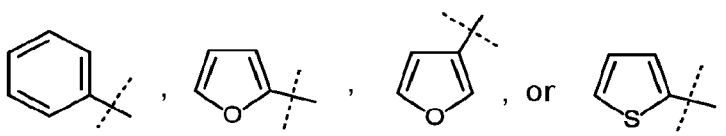
Formula Ia

wherein R is H or



;

R^1 is H, halogen, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF_3,



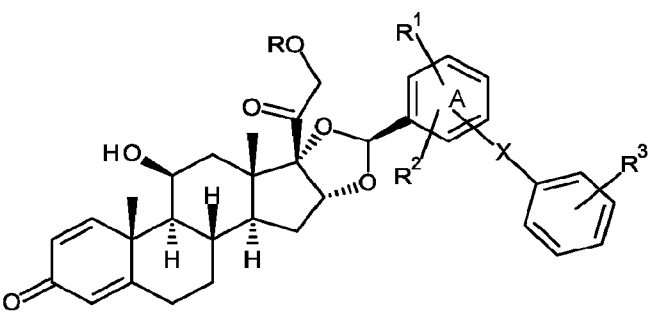
;

R^2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C4 alkenyl;

R^3 is NH_2, or CH_2NH_2; and

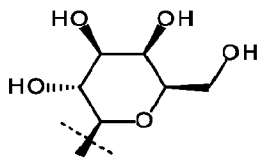
X is O, OCH_2, OCH_2CH_2, $OCH_2C{\equiv}C$, $OCH(CH_3)$, CH_2O, SCH_2, CH_2S, CH_2, $NHCH_2$, CH_2NH, $N(CH_3)CH_2$, CH_2CH_2, $C{\equiv}C$, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof.

In one embodiment, the invention provides a compound of Formula Ib:



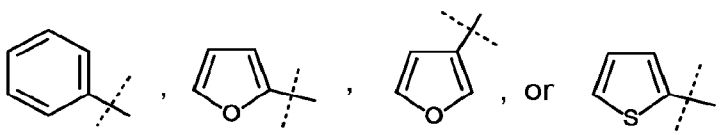
Formula Ib

wherein R is H or



;

R^1 is H, halogen, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF_3,



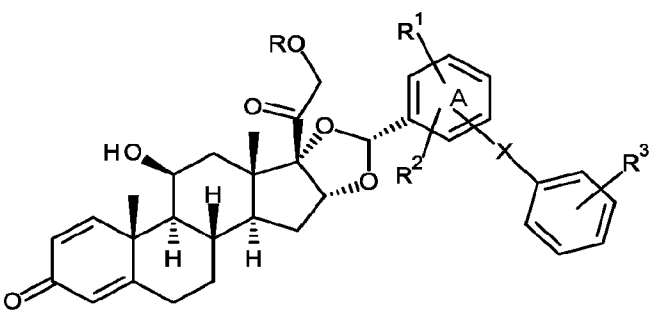
;

R^2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C4 alkenyl;

R^3 is NH_2, or CH_2NH_2; and

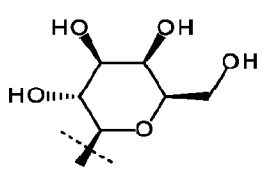
X is O, OCH_2, OCH_2CH_2, $OCH(CH_3)$, CH_2O, SCH_2, CH_2S, CH_2, $NHCH_2$, CH_2NH, $N(CH_3)CH_2$, CH_2CH_2, C=C, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof.

In one embodiment, the invention provides a compound of Formula Ic:



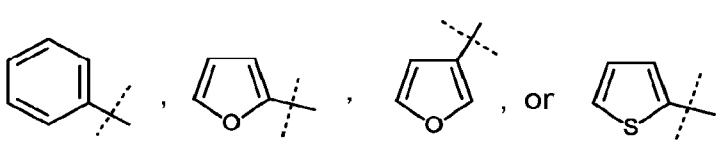
Formula Ic

wherein R is H or



;

R^1 is H, halogen, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF_3,



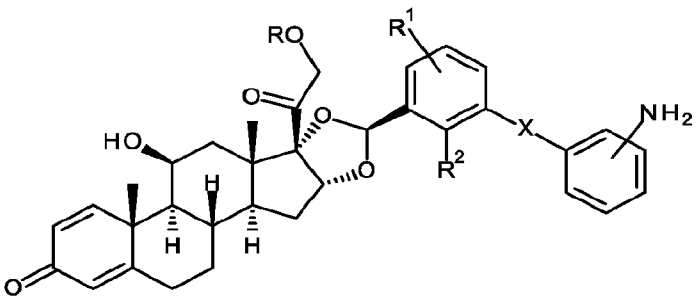
;

R^2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C4 alkenyl;

R^3 is NH_2, or CH_2NH_2; and

X is O, OCH_2, OCH_2CH_2, $OCH(CH_3)$, CH_2O, SCH_2, CH_2S, CH_2, $NHCH_2$, CH_2NH, $N(CH_3)CH_2$, CH_2CH_2, C≡C, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof.

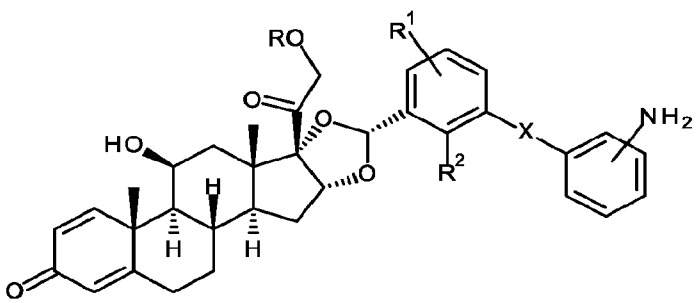
In an embodiment, the invention provides a compound of Formula Ib(i):



Formula Ib(i)

or a pharmaceutically acceptable salt thereof.

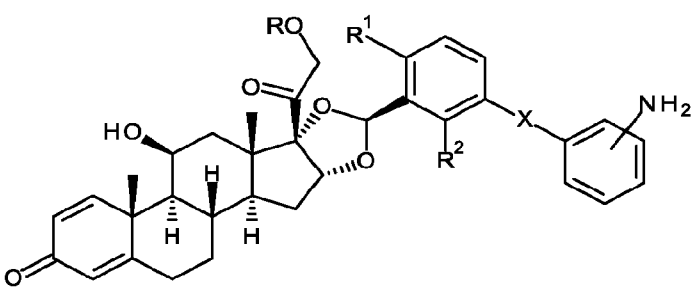
In an embodiment, the invention provides a compound of Formula Ic(i):



Formula Ic(i)

or a pharmaceutically acceptable salt thereof.

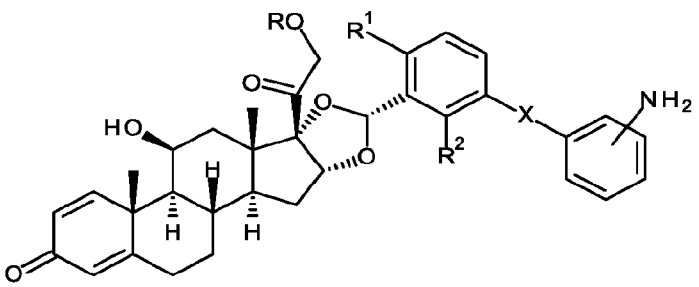
In an embodiment, the invention provides a compound of Formula Ib(ii):



Formula Ib(ii)

or a pharmaceutically acceptable salt thereof.

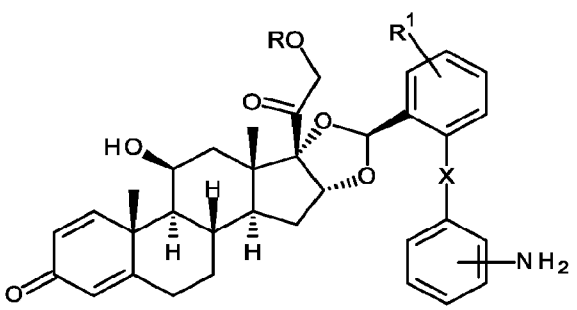
In an embodiment, the invention provides a compound of Formula Ic(ii):



Formula Ic(ii)

or a pharmaceutically acceptable salt thereof.

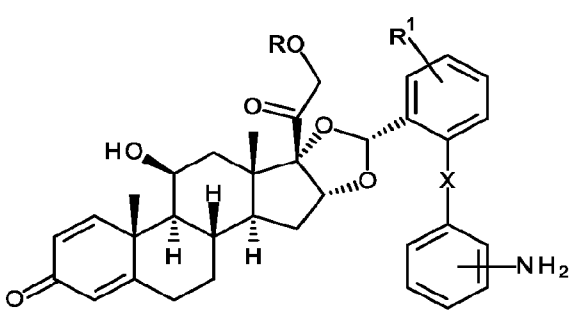
In an embodiment, the invention provides a compound of Formula Ib(iii):



Formula Ib(iii)

or a pharmaceutically acceptable salt thereof.

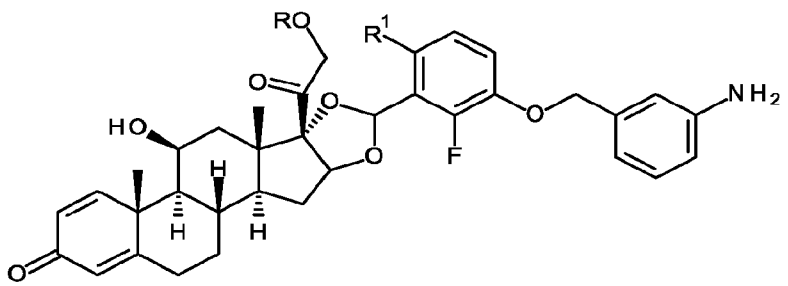
In an embodiment, the invention provides a compound of Formula Ic(iii):



Formula Ic(iii)

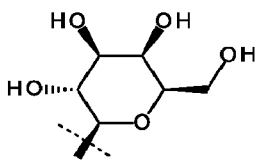
or a pharmaceutically acceptable salt thereof.

In one embodiment, the invention provides a compound of Formula II:



Formula II

wherein R is H or

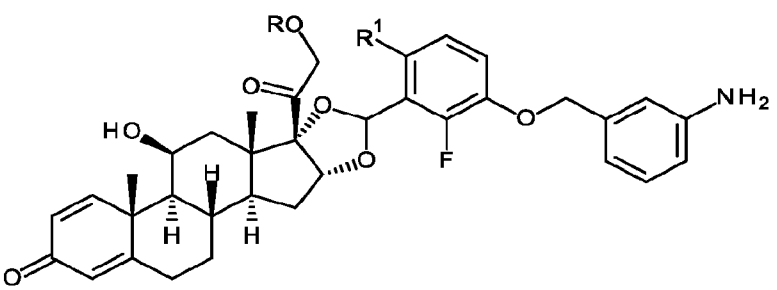


; and

R^1 is $-CH_3$ or $-OCH_3$,

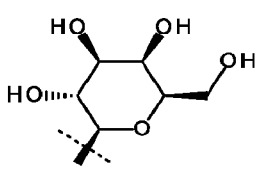
or a pharmaceutically acceptable salt thereof.

In a particular embodiment, the invention provides a compound of Formula IIa:



Formula IIa

wherein R is H or

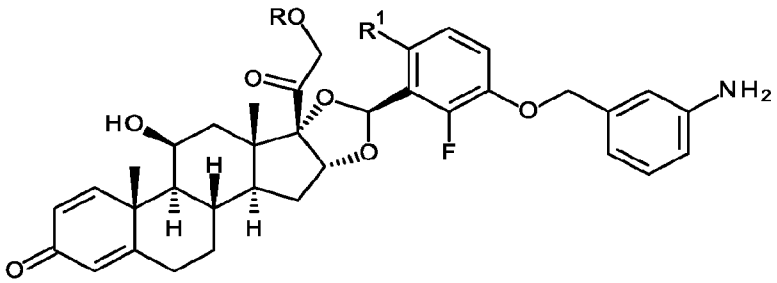


; and

R^1 is $-CH_3$ or $-OCH_3$,

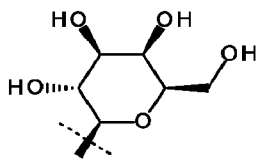
or a pharmaceutically acceptable salt thereof.

In a particular embodiment, the invention provides a compound of Formula IIb:



Formula IIb

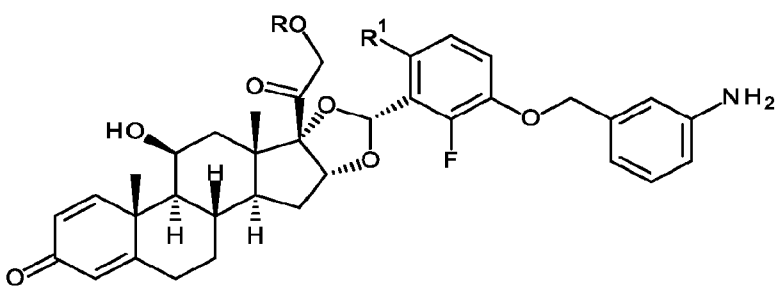
wherein R is H or



; and

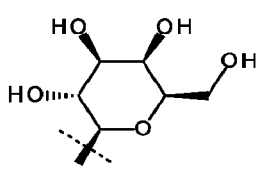
R^1 is $-CH_3$ or $-OCH_3$, or a pharmaceutically acceptable salt thereof.

In a particular embodiment, the invention provides a compound of Formula IIc:



Formula IIc

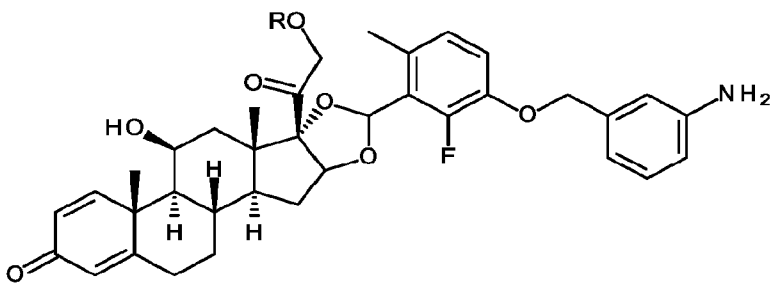
wherein R is H or



; and

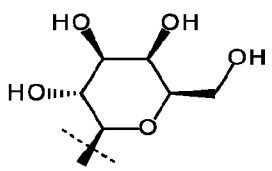
R^1 is $-CH_3$ or $-OCH_3$, or a pharmaceutically acceptable salt thereof.

In an embodiment, the invention provides a compound of Formula III:



Formula III

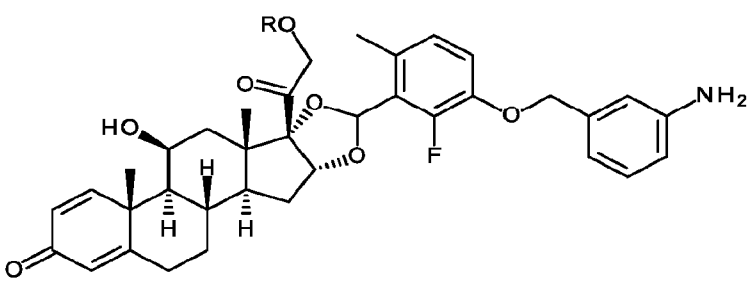
wherein R is H or



,

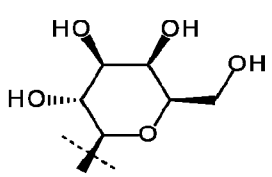
or a pharmaceutically acceptable salt thereof.

In a particular embodiment, the invention provides a compound of Formula IIIa:



Formula IIIa

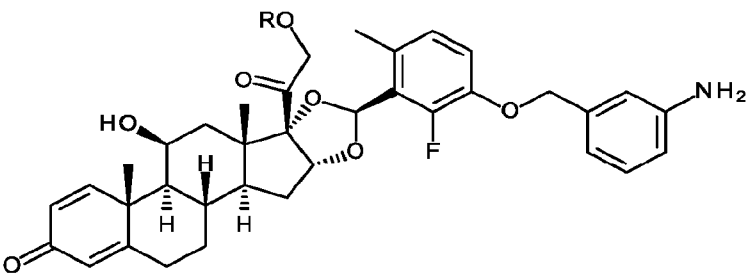
wherein R is H or



,

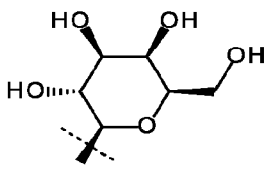
or a pharmaceutically acceptable salt thereof.

In a particular embodiment, the invention provides a compound of Formula IIIb:



Formula IIIb

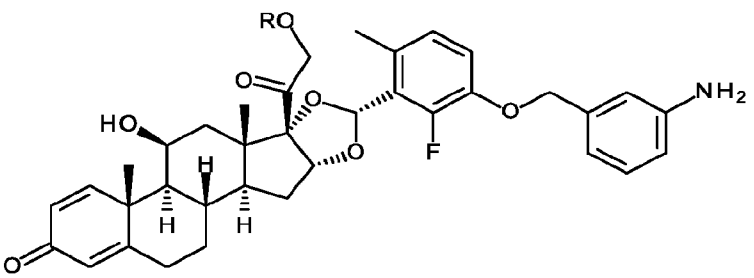
wherein R is H or



,

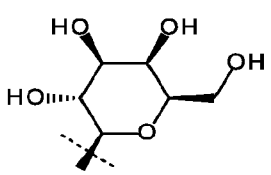
or a pharmaceutically acceptable salt thereof.

In a particular embodiment, the invention provides a compound of Formula IIIc:



Formula IIIc

wherein R is H or

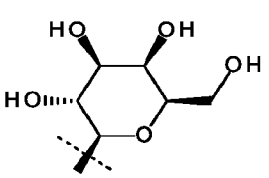


,

or a pharmaceutically acceptable salt thereof.

In an embodiment, R is H.

In an embodiment, R is



.

In an embodiment, R^1 is CH_3.

In an embodiment, R^1 is H.

In an embodiment, R^1 is OCH_3.

In an embodiment, R^1 is F.

In an embodiment, R^2 is H.

In an embodiment, R^2 is CH_3.

In an embodiment, R^2 is F.

In an embodiment, R^2 is OCH_3.

In an embodiment, X is O.

In an embodiment, X is OCH_2.

In an embodiment, X is SCH_2.

In an embodiment, X is CH_2.

In an embodiment, X is a bond.

In an embodiment, R is H, R^1 is CH_3, R^2 is F, and X is OCH_2.

In an embodiment, R is H, R^1 is OCH_3, R^2 is F, and X is OCH_2.

In an embodiment, X is connected to phenyl ring A at the meta position.

In an embodiment, X is connected to phenyl ring A at the ortho position.

In an embodiment, the present invention also provides a method of treating an inflammatory disease in a patient in need of such treatment, comprising administering to the patient an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof. In an embodiment, the present invention also provides a method of treating atopic dermatitis in a patient in need of such treatment, comprising administering to the patient an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof. In an embodiment, the present invention further provides a method of treating inflammatory bowel disease in a patient in need of such treatment, comprising administering to the patient an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof. In an embodiment, the present invention further provides a method of treating rheumatoid arthritis in a patient in need of such treatment, comprising administering to the patient an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof. In an embodiment, the present invention also provides a method of treating systemic lupus erythematosus in a patient in need of such treatment, comprising administering to the

patient an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof. In an embodiment, the present invention also provides a method of treating lupus nephritis in a patient in need of such treatment, comprising administering to the patient an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

In an embodiment, the present invention further provides a compound of Formula I, or a pharmaceutically acceptable salt thereof for use in therapy. In an embodiment, the present invention provides a compound of Formula I, or a pharmaceutically acceptable salt thereof for use in treating an inflammatory disease. In an embodiment, the present invention provides a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in treating atopic dermatitis. In an embodiment, the present invention provides a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in treating rheumatoid arthritis. In an embodiment, the present invention provides a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in treating inflammatory bowel disease. In an embodiment, the present invention provides a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in treating lupus nephritis. In an embodiment, the present invention provides a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in treating systemic lupus erythematosus.

In an embodiment, the present invention also provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating an inflammatory disease. In an embodiment, the present invention provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating atopic dermatitis. In an embodiment, the present invention provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating rheumatoid arthritis. In an embodiment, the present invention further provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating inflammatory bowel disease. In an embodiment, the present invention further provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating lupus nephritis. In an embodiment, the present invention also provides the use of

a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating systemic lupus erythematosus.

In an embodiment, the present invention further provides a pharmaceutical composition, comprising a compound of Formula I, or a pharmaceutically acceptable salt thereof, with one or more pharmaceutically acceptable carriers, diluents, or excipients. In an embodiment, the present invention further provides a process for preparing a pharmaceutical composition, comprising admixing a compound of Formula I, or a pharmaceutically acceptable salt thereof, with one or more pharmaceutically acceptable carriers, diluents, or excipients. In an embodiment, the present invention also encompasses novel intermediates and processes for the synthesis of compounds of Formula I.

As used herein, the terms "treating", "treatment'', or "to treat" includes restraining, slowing, stopping, or reversing the progression or severity of an existing symptom or disorder.

As used herein, the term "patient" refers to a mammal, in particular a human.

As used herein, the term "effective amount" refers to the amount or dose of compound of the invention, or a pharmaceutically acceptable salt thereof which, upon single or multiple dose administration to the patient, provides the desired effect in the patient under diagnosis or treatment.

An effective amount can be determined by one skilled in the art by the use of known techniques and by observing results obtained under analogous circumstances. In determining the effective amount for a patient, a number of factors are considered by the attending diagnostician, including, but not limited to: the species of patient; its size, age, and general health; the specific disease or disorder involved; the degree of or involvement or the severity of the disease or disorder; the response of the individual patient; the particular compound administered; the mode of administration; the bioavailability characteristics of the preparation administered; the dose regimen selected; the use of concomitant medication; and other relevant circumstances.

As used herein, it is understood that Formula I encompasses Formulas Ia, Ib, Ic, Ib(i), Ic(i), Ib(ii), Ic(ii), Ib(iii), Ic(iii), II, IIa, IIb, IIc, III, IIIa, IIIb, and IIIc, and all references to Formula I herein should be read as including Formulas Ia, Ib, Ic, Ib(i), Ic(i), Ib(ii), Ic(ii), Ib(iii), Ic(iii), II, IIa, IIb, IIc, III, IIIa, IIIb, and IIIc.

As used herein, it is understood that Formula II encompasses Formulas IIa, IIb, and IIc, and all references to Formula II herein should be read as including Formulas IIa, IIb, and IIc.

As used herein, it is understood that Formula III encompasses Formulas IIIa, IIIb, and IIIc, and all references to Formula III herein should be read as including Formulas IIIa, IIIb, and IIIc.

As used herein "halogen" refers to F, Cl, Br, and I.

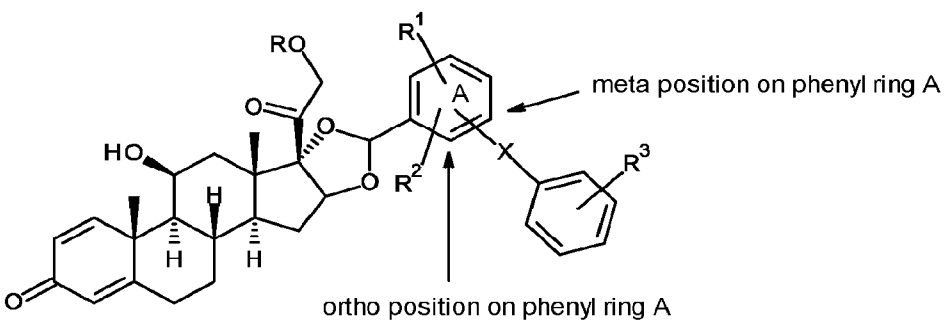
As used herein "C1-C3 alkyl" refers to CH_3, CH_2CH_3, $CH_2CH_2CH_3$, and $CH(CH_3)_2$.

As used herein "C3-C6 cycloalkyl" refers to cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

As used herein "C1-C3 alkoxy" refers to OCH_3, OCH_2CH_3, $OCH_2CH_2CH_3$, and $OCH(CH_3)_2$.

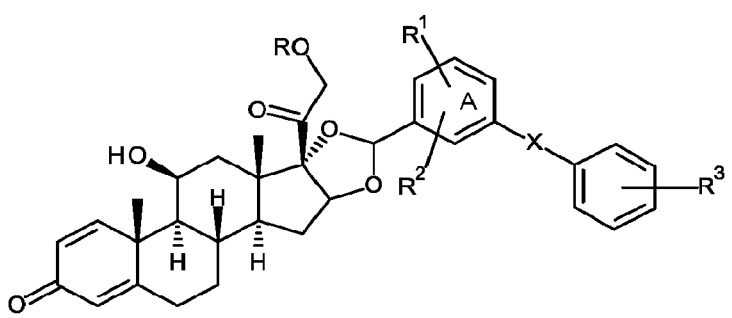
As used herein "C2-C3 alkenyl" refers to $HC=CH_2$, and $C(CH_3)=CH_2$.

As used herein, the ortho and meta positions on phenyl ring A are shown in Formula I below:



Formula I

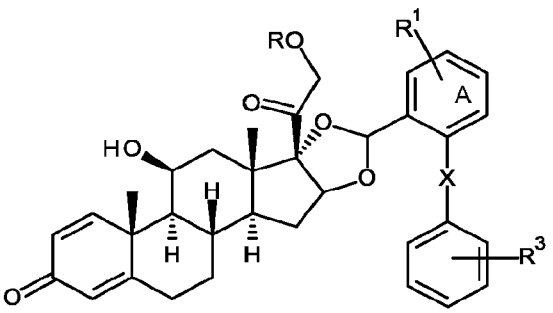
For example, the compound of Formula I' illustrates X connected to phenyl ring A at the meta position:



Formula I'

;

and the compound of Formula I" illustrates X connected to phenyl ring A at the ortho position:



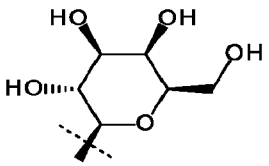
Formula I"

It is appreciated by one of ordinary skill in the art that when X is connected to phenyl ring A at the ortho position as shown in Formula I", then R^2 is H.

In addition, a compound of the present invention can be conjugated with an antibody to form an antibody drug conjugate (ADC) by methods understood by one of skill in the art. One example of such conjugation would include connection of a compound of the present invention to an antibody via a linker compound. Linker compounds known to those of skill in the art include, for example, cleavable linkers and noncleavable linkers. Such an ADC can deliver the compound of the present invention to specific target tissues or cells. Accordingly, provided herein are also ADCs comprising a compound of Formula I. In some embodiments, the compound of Formula I is conjugated to an antibody via a linker, e.g., a cleavable linker or a noncleavable linker.

The compounds or conjugates of the present invention can be formulated as pharmaceutical compositions administered by any route which makes the compound or conjugate bioavailable including, for example, oral, topical, or subcutaneous administration. Such pharmaceutical compositions, including ADCs, can be prepared using techniques and methods known in the art. Such pharmaceutical compositions, including ADCs can be prepared using techniques and methods known in the art (See, e.g., Remington: The Science and Practice of Pharmacy, A. Adejare, Editor, 23rd Edition, published 2020, Elsevier Science; WO 2017/062271, and WO 2017/210471).

Furthermore, compounds of the present invention that have the hydroxy group at C21 capped wherein R is:



behave as prodrugs and are metabolized *in vitro* or *in vivo* to provide the active glucocorticoid receptor agonist wherein R is H.

Included within the scope of the present invention is a pharmaceutically acceptable salt of Formula I. A pharmaceutically acceptable salt of a compound of the invention, such as a compound of Formula I can be formed, for example, by reaction of an appropriate free base of a compound of the invention with an appropriate pharmaceutically acceptable acid in a suitable solvent such as diethyl ether under standard conditions well known in the art. See, for example, Berge, S.M., *et al.*, "Pharmaceutical Salts," *Journal of Pharmaceutical Sciences*, **66**: 1-19, (1977).

Certain compounds described in the following preparations may contain a suitable nitrogen protecting group referred to herein as "Pg". It is understood that protecting groups may be varied as appreciated by one of skill in the art depending on the particular reaction conditions and the particular transformations to be performed. The protection and deprotection conditions are well known to the skilled artisan and are described in the literature (See for example "*Greene's Protective Groups in Organic Synthesis*", Fourth Edition, by Peter G.M. Wuts and Theodora W. Greene, John Wiley and Sons, Inc. 2007).

Table 1: Abbreviations and definitions

Term	Definition
ACN	acetonitrile
aq	aqueous
Å	angstrom(s)
BOC / Boc	tert-butyloxycarbonyl
C18	octadecylsilane
DCM	dichloromethane
DEA	diethylamine
DIBAL-H	diisobutylaluminum hydride
DMEA	dimethylethylamine

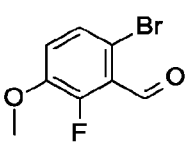
Term	Definition
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
dppf	1,1′-bis(diphenylphosphino)ferrocene
equiv	equivalent(s)
ES/MS	electrospray mass spectrometry
EtOAc	ethyl acetate
EtOH	ethanol
FA	formic acid
g	gram(s)
h	hour(s)
HPLC	high performance liquid chromatography
IPA	isopropanol
IPAm	isopropylamine
L	liter(s)
LC	liquid chromatography
LCMS	liquid chromatography mass spectrometry
LDA	lithium diisopropylamide
M	molar
mbar	millibar(s)
MeOH	methanol
min	minute(s)
mL	milliliter(s)
mM	millimolar
mmol	millimole(s)
mol	mole(s)
MS	mass spectrometry
MTBE	methyl tert-butyl ether
MW	molecular weight
m/z	mass-to-charge ratio
nm	nanometer(s)

Term	Definition
NMR	nuclear magnetic resonance
Pet ether	petroleum ether
ppm	parts per million
ROE	rotating-frame Overhauser enhancement
RP-HPLC	reverse-phase HPLC
rt	room temperature
satd	saturated
SFC	supercritical fluid chromatography
SM	starting material
THF	tetrahydrofuran
wt	weight

The compounds of the present invention, or salts thereof, may be readily prepared by a variety of procedures known to one of ordinary skill in the art, some of which are illustrated in the preparations and examples below. One of ordinary skill in the art recognizes that the specific synthetic steps for each of the routes described may be combined in different ways, or in conjunction with steps from different schemes, to prepare compounds of the invention, or salts thereof. The product of each step can be recovered by conventional methods well known in the art, including extraction, evaporation, precipitation, chromatography, filtration, trituration, and crystallization. All substituents unless otherwise indicated, are as previously defined. The reagents and starting materials are readily available to one of ordinary skill in the art. The following preparations, examples, and assays further illustrate the invention, but should not be construed to limit the scope of the invention in any way.

Preparation 1

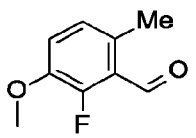
6-Bromo-2-fluoro-3-methoxybenzaldehyde



Two reactions were carried out in parallel. To a solution of 4-bromo-2-fluoro-1-methoxybenzene (250 g, 1.2 mol) in THF (1500 mL) was added LDA (2 M, 730 mL) slowly at -78 °C, over 30 min. After an additional 30 min, DMF (140 mL, 1.8 mol) was added at -78 °C slowly over 30 min. After 1 h, the two reactions were combined and the mixture was diluted with aq citric acid (2000 mL) and extracted with EtOAc (1500 mL x 2). The combined organic layers were washed with saturated brine (1000 mL) and concentrated under reduced pressure to give a residue. The residue was triturated with petroleum ether (1000 mL) at rt over 12 h to give the title compound (382 g, 67% yield). ES/MS m/z 233.9 (M+H).

Preparation 2

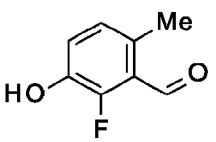
2-Fluoro-3-methoxy-6-methylbenzaldehyde



Three reactions were carried out in parallel. 6-Bromo-2-fluoro-3-methoxybenzaldehyde (120 g, 5.3 mol), methylboronic acid (47 g, 7.9 mol), $Pd(dppf)Cl_2$ (12 g, 0.02 mol), and Cs_2CO_3 (340 g, 1.1 mol) were added to a mixture of dioxane (600 mL) and water (120 mL). The mixture was stirred at 120 °C. After 12 h, the three reactions were combined and the mixture was diluted with satd aq NH_4Cl (1000 mL) and extracted with MTBE (1500 mL x 2). The combined organic layers were washed with satd aq NaCl (1000 mL) and concentrated under reduced pressure to give a residue. The residue was purified by normal phase chromatography, eluting with 40:1 Pet ether: EtOAc to give the title compound (180 g, 59% yield). ES/MS m/z 169.3 (M+H).

Preparation 3

2-Fluoro-3-hydroxy-6-methylbenzaldehyde

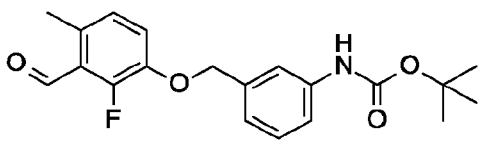


2-Fluoro-3-methoxy-6-methylbenzaldehyde (175 g, 1.0 mol) was added into DCM (1050 mL). BBr_3 (200 mL, 2.1 mol) was added slowly into the solution at 0 °C. The

reaction was stirred at rt. After 1 h, the mixture was diluted with satd aq sodium bicarbonate (1000 mL) until pH=7-8 and was extracted with MTBE (1500 mL x 2). The combined organic layers were washed with satd aq NaCl (1000 mL) and concentrated under reduced pressure to give the title compound (110 g, 68% yield). ES/MS m/z 154.9 (M+H).

Preparation 4

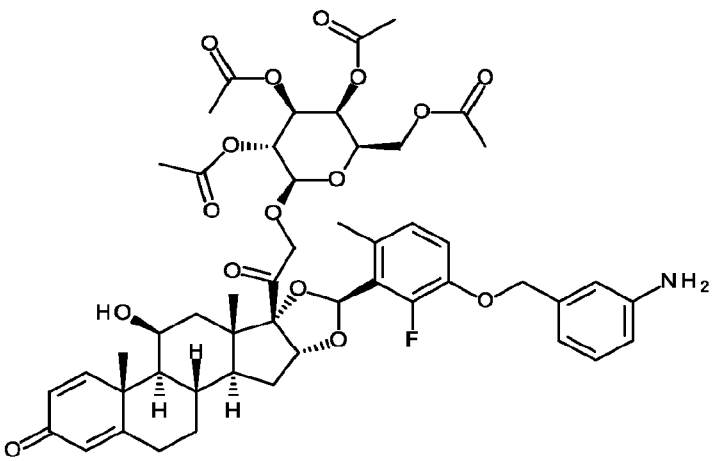
tert-Butyl N-[3-[(2-fluoro-3-formyl-4-methyl-phenoxy)methyl]phenyl]carbamate



2-Fluoro-3-hydroxy-6-methylbenzaldehyde (130 g, 0.84 mol), tert-butyl (3-(bromomethyl)phenyl)carbamate (200 g, 0.70 mol), and potassium carbonate (350 g, 2.5 mol) were added in acetonitrile (780 mL) at rt and then heated to 50 °C. After 5 h, the reaction was diluted with water (600 mL) and extracted with EtOAc (800 mL x 2). The combined organic layers were washed with brine (800 mL) and concentrated under reduced pressure to give a residue. The residue was purified by normal phase chromatography, eluting with 50:1 Pet ether: EtOAc to give crude product. The crude product was triturated with MTBE (500 mL) at rt for 30 min to give the title compound (103 g, 32% yield). ES/MS m/z 382.1 (M+Na).

Preparation 5

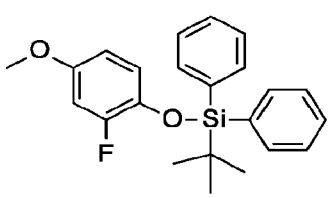
(2R,3S,4S,5R,6R)-2-(Acetoxymethyl)-6-(2-((6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-6a,8a-dimethyl-4-oxo-1,2,4,6a,6b,7,8,8a,11a,12,12a,12b-dodecahydro-8bH-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-8b-yl)-2-oxoethoxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate



3Å Molecular sieves (5 g) were added to (6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one (150 mg, 0.24 mmol, Example 2 below), 2,3,4,6-tetra-O-acetyl-alpha-D-galactopyranosyl bromide (155 mg, 0.37 mmol), and DCM (5 mL) at rt. After 1 h, the reaction was cooled to 0 °C. Silver(I) oxide (115 mg, 0.49 mmol) and trimethylsilyl trifluoromethanesulfonate (45 μL, 0.24 mmol) were added. After 30 min, the reaction was quenched with satd aq sodium bicarbonate, filtered over diatomaceous earth, and rinsed with DCM (10 mL) and methanol (10 mL). The combined organic layers were concentrated under reduced pressure to give a residue. The residue was purified by reverse phase chromatography, eluting with 1:5 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile to give the title compound (43 mg, 19% yield). ES/MS m/z 948.0 (M+1).

Preparation 6

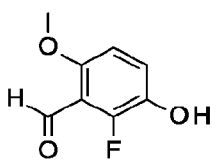
tert-Butyl (2-fluoro-4-methoxyphenoxy)diphenylsilane



To a solution of 2-fluoro-4-methoxyphenol (25 g, 180 mmol) in DMF (350 mL 0.5 M) was added imidazole (18 g, 260 mmol) and tert-butylchlorodiphenylsilane (55 mL, 200 mmol). The reaction was stirred for 18 h at rt. The mixture was diluted with ethyl acetate. The organic solution was washed with water and brine, dried over Na_2SO_4, filtered, and concentrated to a crude residue. The residue was purified by normal phase purification, eluting with 5:1 hexanes:ethyl acetate to give the title compound (67 g, 93% yield). ^{1}H NMR (399.8 MHz, d_6-DMSO) δ 7.67-7.65 (m, 4H), 7.51-7.44 (m, 6H), 6.82 (dd, J= 2.9, 12.7 Hz, 1H), 6.59 (t, J= 9.4 Hz, 1H), 6.47 (ddd, J= 9.0, 3.0, 1.4 Hz, 1H), 3.64 (s, 3H), 1.06 (s, 9H).

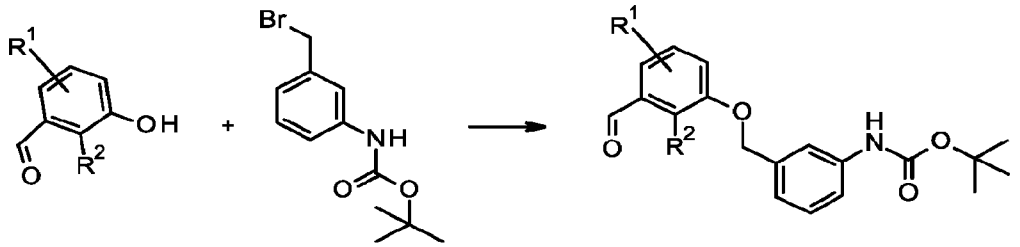
Preparation 7

2-Fluoro-3-hydroxy-6-methoxybenzaldehyde



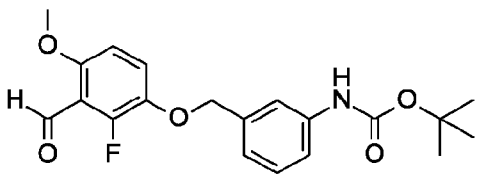
tert-Butyl (2-fluoro-4-methoxyphenoxy)diphenylsilane (56 g, 150 mmol, Preparation 6) was dissolved in 50 mL toluene and concentrated under vacuum for 18 h. The dried solid was dissolved in THF (500 mL) and cooled to -80 °C. n-Butyllithium (1.7 M, 100 mL, 170 mmol) was added rapidly to the cooled solution with a large bore cannula. After 1.5 h, DMF (25 mL, 320 mmol) was added to the solution and the ice bath was removed. After 30 min, 5N aqueous HCl (35 mL) was added to the reaction, then tetrabutylammonium fluoride (1 M in THF, 185 mL, 185 mmol) was added. After 2.5 h, the organic layer was evaporated, acidified with 5N aqueous HCl, and partitioned between ethyl acetate and water (500 mL). The combined organic extracts were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated to a crude residue. The residue was purified by normal phase purification, eluting with 1:1 hexanes:ethyl acetate to give the title compound (22 g, 88% yield). MS m/z 170.8 (M+H).

Scheme 1



Preparation 8

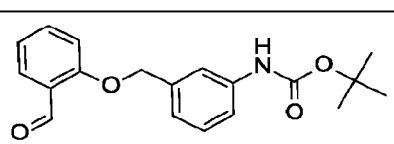
tert-Butyl (3-((2-fluoro-3-formyl-4-methoxyphenoxy)methyl)phenyl)carbamate

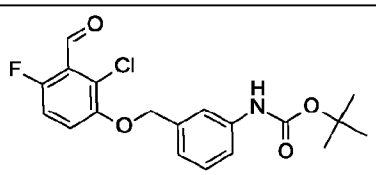
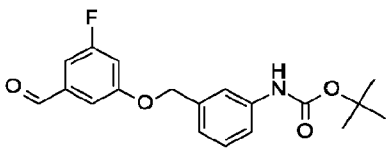
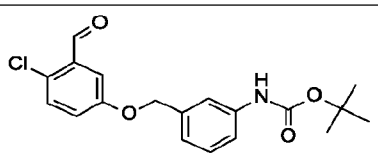
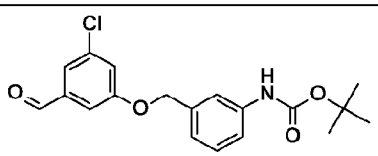
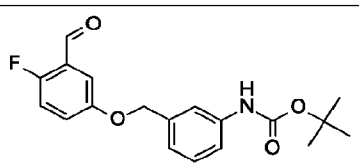
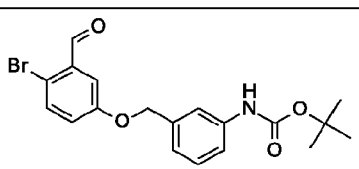
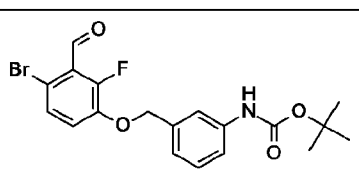
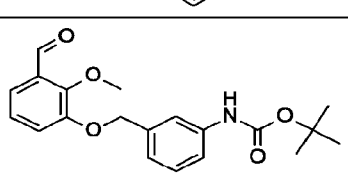
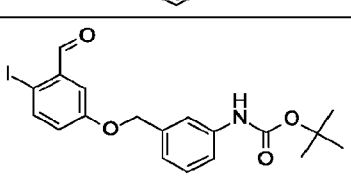


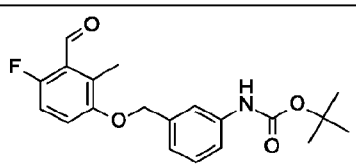
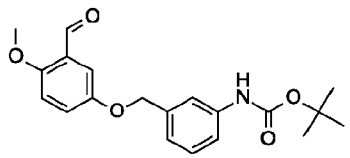
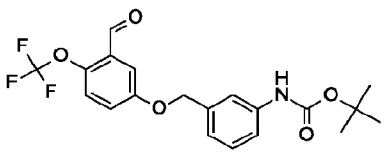
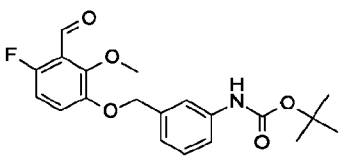
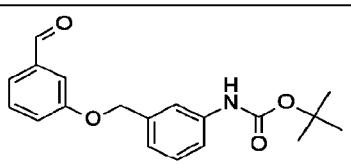
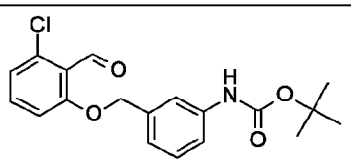
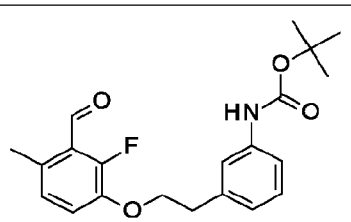
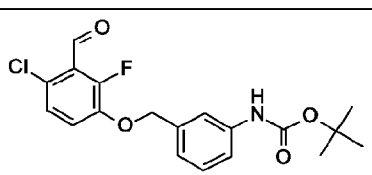
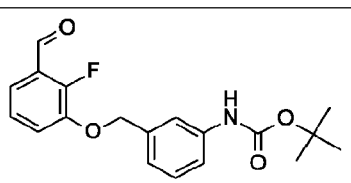
2-Fluoro-3-hydroxy-6-methoxybenzaldehyde (2.5 g, 15 mmol) and tert-butyl N-[3-(bromomethyl)phenyl]carbamate (5.1 g, 18 mmol) were dissolved in acetonitrile (50 mL). Potassium carbonate (2.9 g, 29 mmol) was added to the slurry and the reaction was stirred at rt. After 1 h, the reaction was warmed to 40 °C. After 3 h, the reaction was cooled, filtered, and the solvent was evaporated. The crude residue was purified by normal phase purification, eluting with 7:3 hexanes:EtOAc to give the title compound (3.1 g, 57% yield). MS m/z 374.4 (M-H).

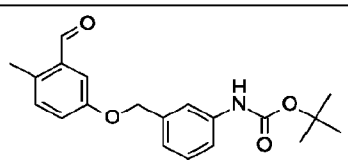
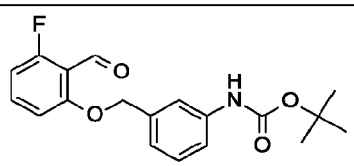
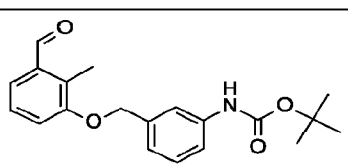
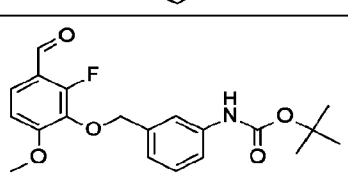
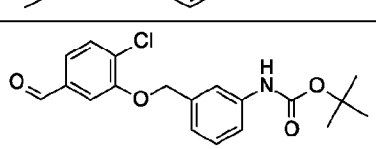
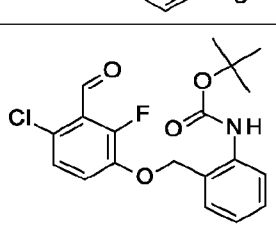
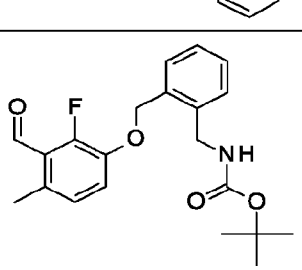
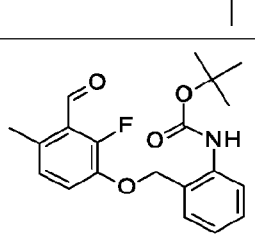
The following compounds in Table 2 were prepared in a manner essentially analogous to the procedure described in Preparation 8.

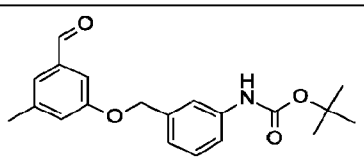
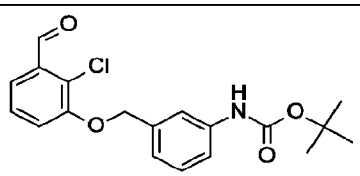
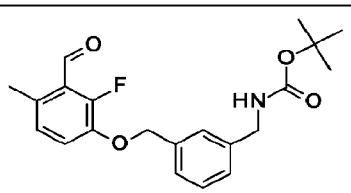
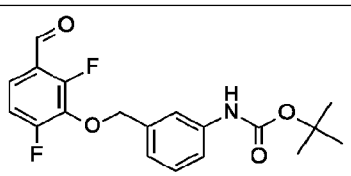
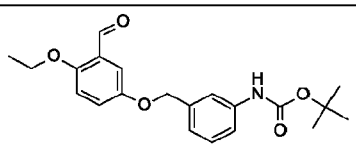
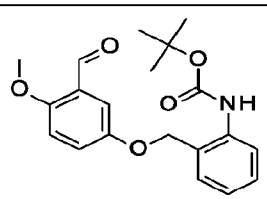
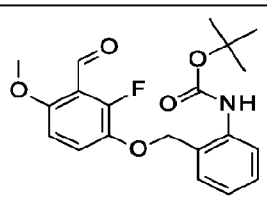
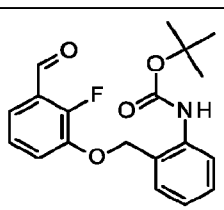
Table 2: Preparations 9-50

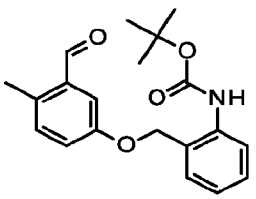
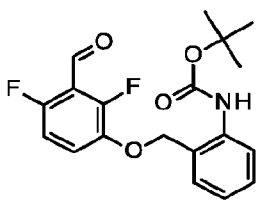
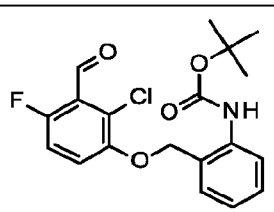
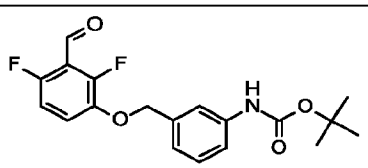
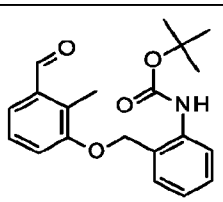
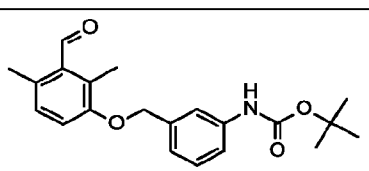
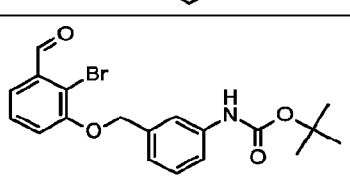
Prep. No.	Structure	ES/MS (m/z) (M+H)	Starting phenol
9		326.0	2-hydroxybenzaldehyde

10		379.0	2-chloro-6-fluoro-3-hydroxybenzaldehyde
11		344.0	3-fluoro-5-hydroxybenzaldehyde
12		360.0	2-chloro-5-hydroxybenzaldehyde
13		360.0	3-chloro-5-hydroxybenzaldehyde
14		344.0	2-fluoro-5-hydroxybenzaldehyde
15		404.0	2-bromo-5-hydroxybenzaldehyde
16		422.0 (M-H)	6-bromo-2-fluoro-3-hydroxybenzaldehyde
17		356.4 (M-H)	3-hydroxy-2-methoxybenzaldehyde
18		451.4 (M-H)	5-hydroxy-2-iodobenzaldehyde

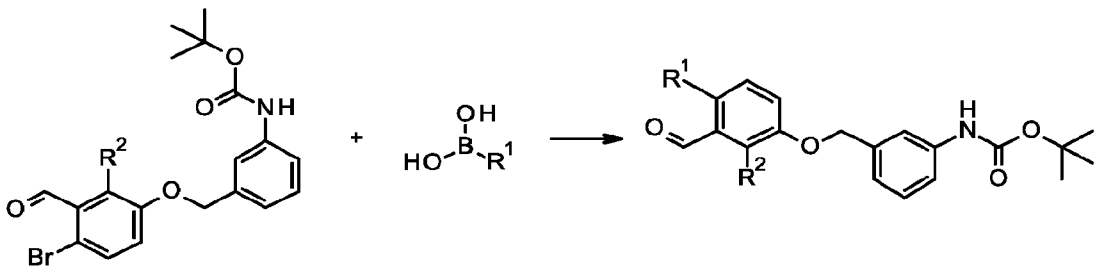
19		359.2	6-fluoro-3-hydroxy-2-methylbenzaldehyde
20		356.0 (M-H)	5-hydroxy-2-methoxybenzaldehyde
21		410.6 (M-H)	5-hydroxy-2-(trifluoromethoxy)benzaldehyde
22		374.5 (M-H)	6-fluoro-3-hydroxy-2-methoxybenzaldehyde
23		363.2	3-hydroxybenzaldehyde
24		360.0 (M-H)	2-chloro-6-hydroxybenzaldehyde
25		372.0 (M-H)	2-fluoro-3-hydroxy-6-methylbenzaldehyde
26		378.0 (M-H)	6-chloro-2-fluoro-3-hydroxybenzaldehyde
27		246.0 (M+H-Boc)	2-fluoro-3-hydroxybenzaldehyde

28		340.0 (M-H)	5-hydroxy-2-methylbenzaldehyde
29		344.0 (M-H)	2-fluoro-6-hydroxybenzaldehyde
30		340.2 (M-H)	3-hydroxy-2-methylbenzaldehyde
31		374.2 (M-H)	2-fluoro-3-hydroxy-4-methoxybenzaldehyde
32		360.0 (M-H)	4-chloro-3-hydroxybenzaldehyde
33		402.2 (M+Na)	6-chloro-2-fluoro-3-hydroxybenzaldehyde
34		396.2 (M+Na)	2-fluoro-3-hydroxy-6-methylbenzaldehyde
35		382.2 (M+Na)	2-fluoro-3-hydroxy-6-methylbenzaldehyde

36		382.2 (M+Na)	3-hydroxy-5-methylbenzaldehyde
37		379.2 ($M+NH_4$)	2-chloro-3-hydroxybenzaldehyde
38		396.2 (M+Na)	2-fluoro-3-hydroxy-6-methylbenzaldehyde
39		396.2 (M+Na)	2,4-difluoro-3-hydroxybenzaldehyde
40		370.4 (M-H)	2-ethoxy-5-hydroxybenzaldehyde
41		356.4 (M-H)	5-hydroxy-2-methoxybenzaldehyde
42		374.4 (M-H)	2-fluoro-3-hydroxy-6-methoxybenzaldehyde
43		344.2 (M-H)	2-fluoro-3-hydroxybenzaldehyde

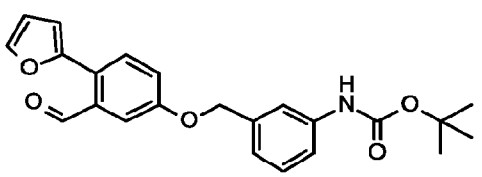
44		340.2 (M-H)	5-hydroxy-2-methylbenzaldehyde
45		362.0 ($M+NH_4$)	2,6-difluoro-3-hydroxybenzaldehyde
46		378.0 (M-H)	2-chloro-6-fluoro-3-hydroxybenzaldehyde
47		362.2 (M-H)	2,6-difluoro-3-hydroxybenzaldehyde
48		340.3 (M-H)	3-hydroxy-2-methylbenzaldehyde
49		372.8 ($M+NH_4$)	3-hydroxy-2,6-dimethylbenzaldehyde
50		406.6	2-bromo-3-hydroxybenzaldehyde

Scheme 2



Preparation 51

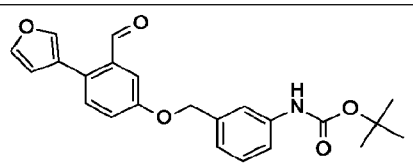
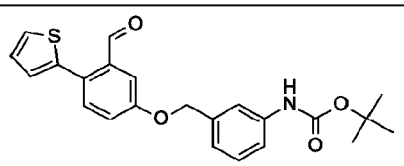
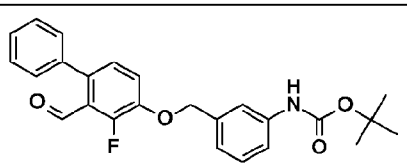
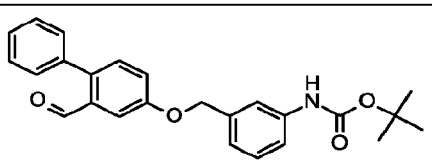
tert-Butyl (3-((3-formyl-4-(furan-2-yl)phenoxy)methyl)phenyl)carbamate



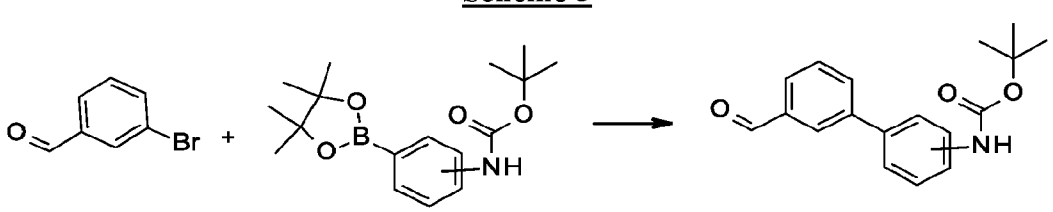
In a microwave tube, tert-butyl (3-((4-bromo-3-formylphenoxy)methyl)phenyl)carbamate (0.73 g, 1.8 mmol), 2-furylboronic acid (0.30 g, 2.7 mmol), tetrakis(triphenylphosphine)palladium(0) (0.10 g, 0.09 mmol,), and N,N-diisopropylethylamine (1.6 mL, 1.2 mmol) were dissolved in DMF (2 mL, 26 mmol). The tube was flushed with N_2 and capped. The reaction was microwaved at 140 °C for 45 min. The reaction was cooled, poured onto iced water, extracted with EtOAc, and washed with brine. The organic layer was dried over Na_2SO_4, filtered, and evaporated to give the title compound (0.70 g, 98% yield). MS m/z 392.2 (M-H).

The following compounds in Table 3 were prepared in a manner essentially analogous to the procedure described in Preparation 51.

Table 3: Preparations 52-55

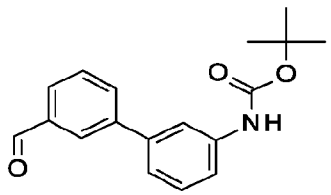
Prep. No.	Structure	ES/MS (m/z) (M+H)	Boronic acid
52		392.2	furan-3-ylboronic acid
53		408.4 (M-H)	thiophen-2-ylboronic acid
54		420.6 (M-H)	phenylboronic acid
55		402.2 (M-H)	phenylboronic acid

Scheme 3



Preparation 56

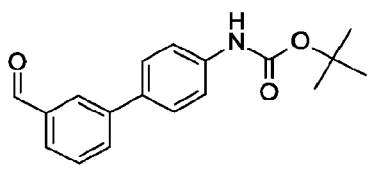
tert-Butyl (3'-formyl-[1,1'-biphenyl]-3-yl)carbamate



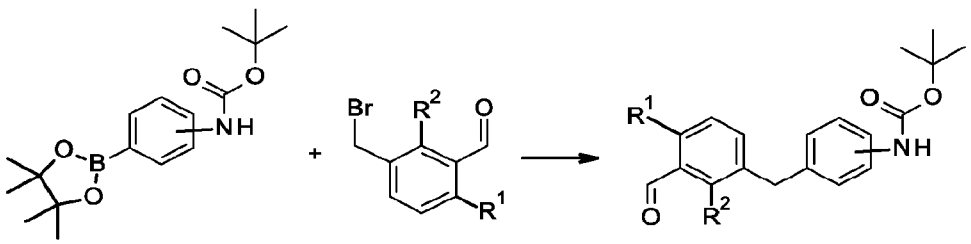
3-Bromobenzaldehyde (1.5 g, 8.1 mmol), tert-butyl (3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate (2.1 g, 6.4 mmol), and potassium carbonate (3.3 g, 24 mmol) were dissolved in 1,4 dioxane (11 mL) and water (3 mL) in a 40-mL reaction vial. The resulting homogenous mixture was stirred and degassed three times. 1,1' Bis(di-tert-butylphosphino)ferrocene dichloropalladium(II) dichloromethane complex (530 mg, 0.81 mmol) was added and the mixture was degassed, capped, and heated to 90 °C for 2.25 h. The reaction was cooled, filtered over diatomaceous earth, and the solvent was evaporated. The crude residue was purified by normal phase chromatography, eluting with 7:3 hexanes:EtOAc to give the title compound (1.5 g, 63% yield). MS m/z 315.4 (M+18).

The following compound in Table 4 was prepared in a manner essentially analogous to the procedure described in Preparation 56.

Table 4: Preparation 57

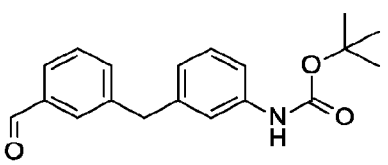
Prep. No.	Structure	ES/MS (m/z) (M+H)	Boronic acid
57		296.2 (M-H)	tert-butyl (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate

Scheme 4



Preparation 58

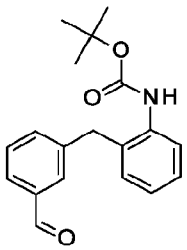
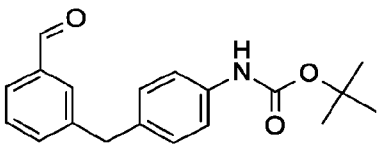
tert-Butyl (3-(3-formylbenzyl)phenyl)carbamate



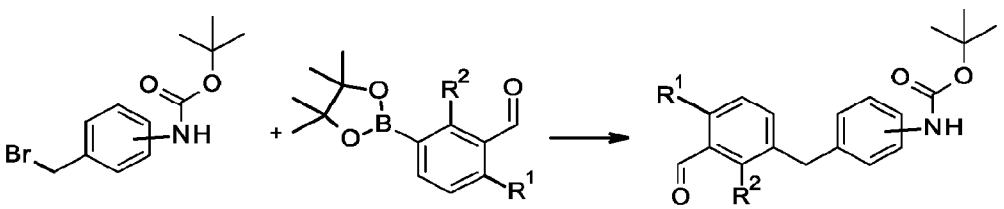
3-(Bromomethyl)benzaldehyde (320 mg, 1.5 mmol), tert-butyl (3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate (300 mg, 0.94 mmol), and potassium carbonate (410 mg, 3.0 mmol) were dissolved in toluene (9 mL) and water (1 mL) in a vial. The reaction was purged with argon. 1,1' Bis(di-tert-butylphosphino)ferrocene dichloropalladium(II) dichloromethane complex (80 mg, 0.10 mmol) was added, the vial was capped and heated to 100 °C for 1.5 h. The reaction was cooled, filtered over diatomaceous earth, and the solvent was evaporated. The crude residue was purified by normal phase chromatography, eluting with 7:3 heptane:EtOAc to give the title compound (300 mg, 54% yield). MS m/z 329.4 (M+18).

The following compounds in Table 5 were prepared in a manner essentially analogous to the procedure described in Preparation 58.

Table 5: Preparations 59-60

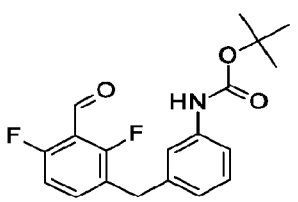
Prep. No.	Structure	ES/MS (m/z) (M+H)	Boronic acid/ester
59		329.4 ($M+NH_4$)	tert-butyl (2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate
60		329.4 ($M+NH_4$)	tert-butyl (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate

Scheme 5



Preparation 61

2,6-Difluoro-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde

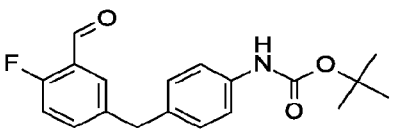
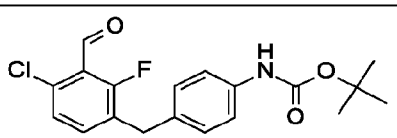
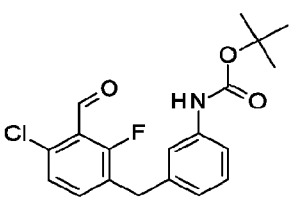
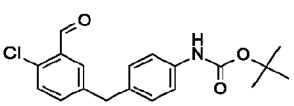


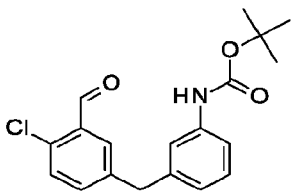
tert-Butyl 3-(bromomethyl)phenylcarbamate (1.5 g, 5.0 mmol), 2,6-difluoro-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (1.5 g, 5.6 mmol), and potassium carbonate (2.1 g, 3.0 mmol) were placed in a reaction vial with water (1 mL)

and toluene (9 mL). The reaction mixture was bubbled with N_2, 1,1'-bis(di-tert-butylphosphino)ferrocene dichloropalladium(II) dichloromethane complex (310 mg, 0.37 mmol) was added, and the vial was capped and heated at 100 °C for 10 min. The reaction was cooled, filtered, and the filtrate was evaporated. The crude residue was purified by normal phase chromatography, eluting with 1:1 heptane:EtOAc to give the title compound (1.38 g, 3.85 mmol, 77% yield). MS m/z 365.2 ($M+NH_4$).

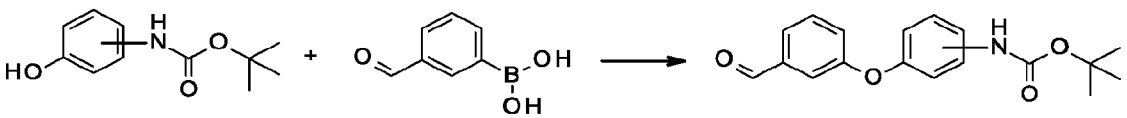
The following compounds in Table 6 were prepared in a manner essentially analogous to the procedure described in Preparation 61.

Table 6: Preparations 62-66

Prep. No.	Structure	ES/MS (m/z) (M+H)	Boronic acid/ester
62		No ion	2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde
63		381.0 ($M+NH_4$)	(4-chloro-2-fluoro-3-formylphenyl)boronic acid
64		381.2 ($M+NH_4$)	(4-chloro-2-fluoro-3-formylphenyl)boronic acid
65		363.2 ($M+NH_4$)	(4-chloro-3-formylphenyl)boronic acid

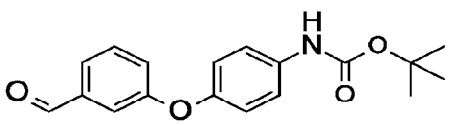
66		363.2 (M+H)	(4-chloro-3-formylphenyl)boronic acid

Scheme 6



Preparation 67

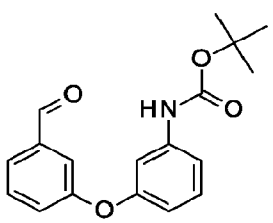
tert-Butyl (4-(3-formylphenoxy)phenyl)carbamate



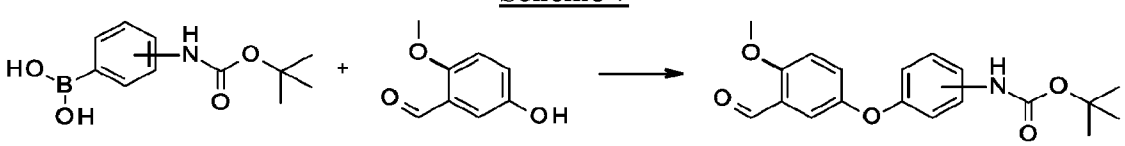
(3-Formylphenyl)boronic acid (610 mg, 4.1 mmol), tert-butyl (4-hydroxyphenyl)carbamate (420 mg, 2.0 mmol), copper(II) acetate (370 mg, 2.0 mmol), triethylamine (1.4 mL, 10 mmol), and 4 Å molecular sieves (500 mg) were added in DCM (15 mL) in a vial. The reaction was incubated at rt for 10 h. The reaction was filtered over diatomaceous earth and the solvent was evaporated. The crude residue was purified by normal phase chromatography, eluting with 7:3 hexanes:EtOAc to give the title compound (180 mg, 29% yield). MS m/z 312.2 (M-H).

The following compounds in Table 7 were prepared in a manner essentially analogous to the procedure described in Preparation 67.

Table 7: Preparation 68

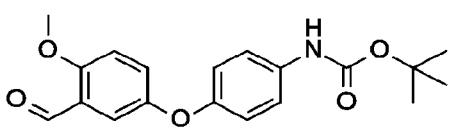
Prep. No.	Structure	ES/MS (m/z) (M+H)	Phenol
68		312.2 (M-H)	tert-butyl (3-hydroxyphenyl)carbamate

Scheme 7



Preparation 69

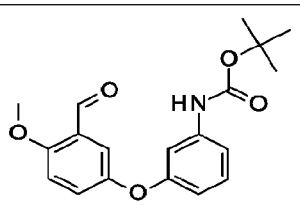
tert-Butyl (4-(3-formylphenoxy)phenyl)carbamate



5-Hydroxy-2-methoxybenzaldehyde (1.00 g, 6.57 mmol), [4-(tert-butoxycarbonylamino)phenyl]boronic acid (3.12 g, 13.2 mmol), copper(II) acetate (1.19 g, 6.57 mmol), and 4 Å molecular sieves (1.0 g) were added to a flask. DCM (60 mL) and triethylamine (4.6 mL, 33 mmol) were then added. The reaction mixture was stirred at rt overnight. More [4-(tert-butoxycarbonylamino)phenyl]boronic acid (1.1 g, 4.6 mmol) and copper(II) acetate (400 mg, 2.2 mmol) were added and the reaction mixture was stirred at rt for three days. The reaction was filtered and the solvent was evaporated. The crude residue was purified by normal phase chromatography, eluting with heptane:EtOAc to give the title compound (400 mg, 18% yield). MS m/z 361.0 ($M+NH_4$).

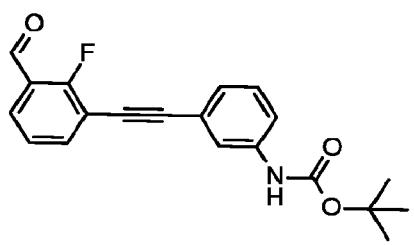
The following compounds in Table 8 were prepared in a manner essentially analogous to the procedure described in Preparation 69.

Table 8: Preparation 70

Prep. No.	Structure	ES/MS (m/z) (M+H)	Boronic acid
70		361.0 ($M+NH_4$)	[3-(tert-butoxycarbonylamino)phenyl]boronic acid

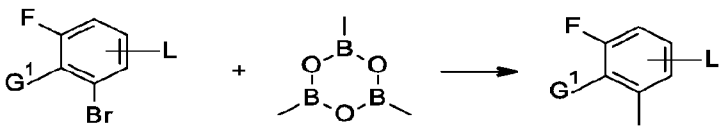
Preparation 71

tert-Butyl (3-((2-fluoro-3-formylphenyl)ethynyl)phenyl)carbamate

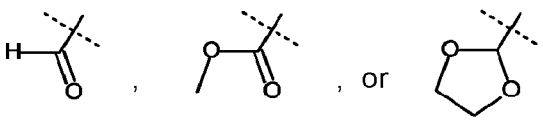


3-Ethynyl-2-fluorobenzaldehyde (0.25 g, 1.7 mmol) was mixed with tert-butyl N-(3-iodophenyl)carbamate (0.55 g, 1.7 mmol), bis(triphenylphosphine)palladium(II) dichloride (0.025 g, 0.036 mmol), and copper(I) iodide (0.01 g., 0.05 mmol) in triethylamine (10 mL, 72 mmol) under N_2. The reaction mixture was stirred at rt overnight. The reaction mixture was diluted with EtOAc and filtered through diatomaceous earth. The filtrate was washed with 1 M aq HCl, brine, dried over Na_2SO_4, and filtered. The solvent was evaporated to give the title compound (0.57 g, 100% yield). MS m/z 338.2 (M-H).

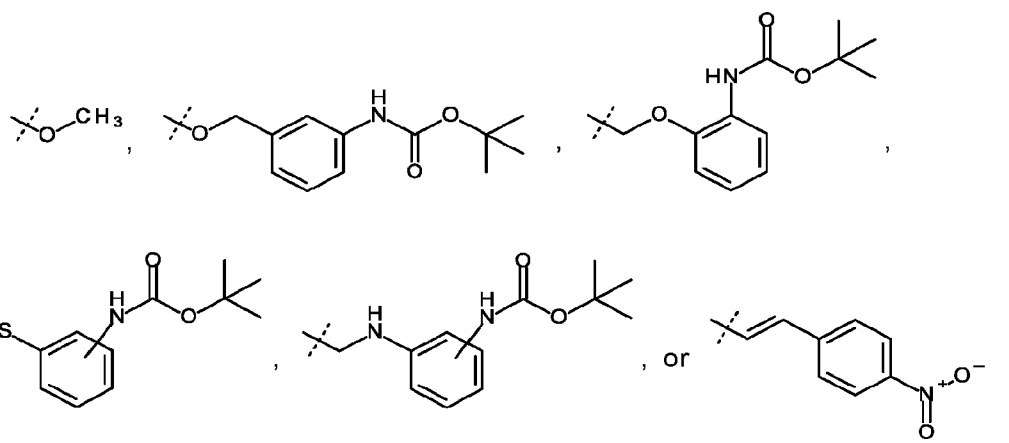
Scheme 8



Wherein G^1 is

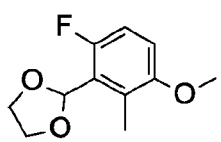


Wherein L is



Preparation 72

2-(6-Fluoro-3-methoxy-2-methylphenyl)-1,3-dioxolane

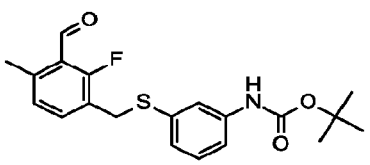
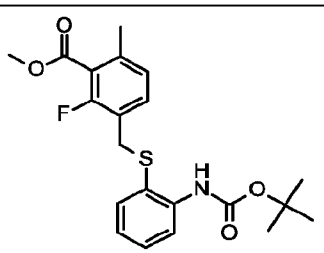
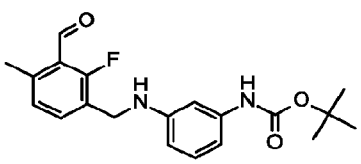
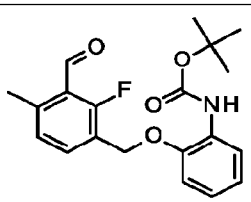
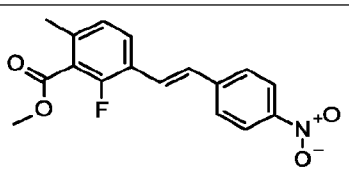


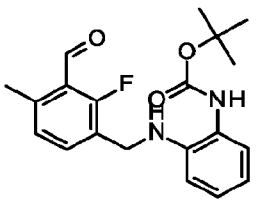
To a microwave vial, added 2-(2-bromo-6-fluoro-3-methoxyphenyl)-1,3-dioxolane (970 mg, 3.5 mmol), trimethylboroxine (50 mass%) in THF (600 µL, 4.3 mmol), and cesium carbonate (2.3 g, 7.1 mmol) in 1,4-dioxane (12 mL, 140 mmol) and water (2 mL, 110 mmol). Degassed the solution with N_2 for 2 min. [1,1'-Bis(diphenylphosphino)ferrocene]dichloro palladium(II) (130 mg, 0.17 mmol) was added and degassed the solution with N_2 for 2 min. The vial was capped and microwaved at 110 °C for 1 h. The reaction mixture was diluted with water (10 mL) and extracted with EtOAc (10 mL). The organic layer was dried with Na_2SO_4, filtered through paper, and

rotary evaporated to a crude oil. The crude oil was purified by normal phase chromatography, eluting with 7:3 hexanes:MTBE to give the title compound (0.61 g, 82% yield). MS m/z 212.8 (M+H).

The following compounds in Table 9 were prepared in a manner essentially analogous to the procedure described in Preparation 72.

Table 9: Preparations 73-78

Prep. No.	Structure	ES/MS (m/z) (M+H)	Bromide
73		No ion*	tert-butyl (3-((4-bromo-2-fluoro-3-formylbenzyl)thio)phenyl)carbamate
74		305.9 (M-Boc+H)	methyl 6-bromo-3-(((2-((tert-butoxycarbonyl)amino)phenyl)thio)methyl)-2-fluorobenzoate
75		359.0	tert-butyl (3-((4-bromo-2-fluoro-3-formylbenzyl)amino)phenyl)carbamate
76		No ion**	tert-butyl (2-((4-bromo-2-fluoro-3-formylbenzyl)oxy)phenyl)carbamate
77		315.9	methyl (E)-6-bromo-2-fluoro-3-(4-nitrostyryl)benzoate

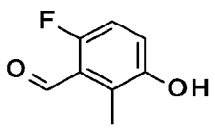
78		359.0	tert-butyl (2-((4-bromo-2-fluoro-3-formylbenzyl)amino)phenyl)carbamate

*^{1}H NMR (400.14 MHz, DMSO): δ 10.40 (s, 1H), 9.39 (s, 1H), 7.55-7.50 (m, 2H), 7.26 (d, J= 8.3 Hz, 1H), 7.19 (t, J= 7.9 Hz, 1H), 7.08 (d, J= 7.9 Hz, 1H), 6.96 (d, J= 7.8 Hz, 1H), 4.22 (s, 2H), 1.46 (s, 10H)

**^{1}H NMR (400.21 MHz, DMSO): δ 10.45 (s, 1H), 7.97 (s, 1H), 7.78 (t, J= 7.8 Hz, 1H), 7.65-7.61 (m, 1H), 7.22-7.20 (m, 1H), 7.14-7.12 (m, 1H), 7.07-7.02 (m, 1H), 6.95-6.91 (m, 1H), 5.21 (s, 2H), 2.57 (s, 3H), 1.43 (s, 9H)

Preparation 79

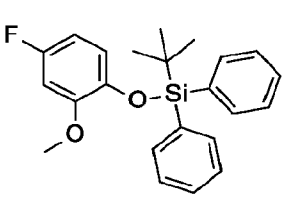
6-Fluoro-3-hydroxy-2-methylbenzaldehyde



Boron tribromide in DCM (14 mL, 14 mmol, 1 mol/L) was added over a period of 2 min to a solution of 2-(6-fluoro-3-methoxy-2-methylphenyl)-1,3-dioxolane (600 mg, 2.8 mmol) in DCM (14 mL, 220 mmol) cooled to 0 °C. The bath was removed after the addition. After 30 min, the reaction was quenched with satd aq NH_4Cl. The reaction was diluted with DCM, washed with 2 M aq NaOH, and then washed with 5 M aq HCl. The organic layer was dried with Na_2SO_4, filtered through paper, and rotary evaporated to a crude residue. The crude residue was purified by normal phase chromatography, eluting with 7:3 hexanes:EtOAc to give the title compound (130 mg, 30% yield). MS m/z 153.0 (M-H).

Preparation 80

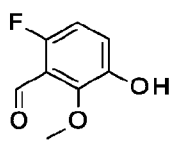
tert-Butyl (4-fluoro-2-methoxyphenoxy)diphenylsilane



To a solution of 4-fluoro-2-methoxy-phenol (2.3 g, 16 mmol) in DCM (35 mL) was added imidazole (2.8 g, 41 mmol) and tert-butylchlorodiphenylsilane (6 mL, 23 mmol). After 1.75 h, the solvent was evaporated, and the residue was partitioned between 200 mL of 10% EtOAc in hexanes and 100 mL water. The organics were washed once with brine, dried over $MgSO_4$, filtered, and evaporated. The crude residue was purified by normal phase chromatography, eluting with 9:1 hexanes:EtOAc to give the title compound (6.7 g, quantitative yield). ^1H NMR (399.8 MHz, d_6-DMSO) δ7.64 (dd, J= 1.5, 7.9 Hz, 4H), 7.48-7.43 (m, 6H), 6.82 (dd, J= 2.9, 10.5 Hz, 1H), 6.60 (dd, J= 5.9, 8.8 Hz, 1H), 6.48 (td, J= 8.5, 3.0 Hz, 1H), 3.56 (s, 3H), 1.05 (s, 9H)

Preparation 81

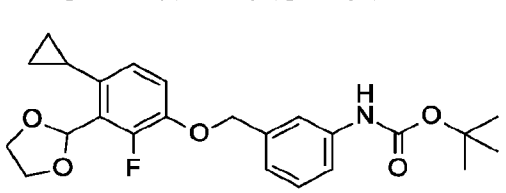
6-Fluoro-3-hydroxy-2-methoxybenzaldehyde



tert-Butyl (4-fluoro-2-methoxyphenoxy)diphenylsilane (3.2 g, 8.5 mmol) was dissolved in tetrahydrofuran (30 mL) and cooled to -78 °C. n-Butyllithium (7 mL, 11 mmol, 1.6 M) was added over 3 minutes. After 1.5 h, DMF (2 mL) was added at -78 °C. After 1 h, added about 4 mL of 10% aq NH_4Cl and warmed to rt over 1.5 h. Evaporated the solvent to a crude residue, then made acidic with 1 M aq HCl, and partitioned between water and 300 mL EtOAc. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered, and evaporated. The crude residue was purified by normal phase chromatography, eluting with 3:2 hexanes:EtOAc to give the title compound (0.79 g, 55% yield). MS m/z 171.0 (M+H).

Preparation 82

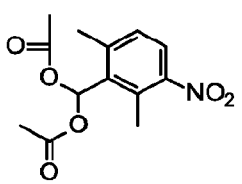
tert-Butyl (3-((4-cyclopropyl-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate



tert-Butyl (3-((4-bromo-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate (200 mg, 0.43 mmol), cyclopropyl boronic acid (0.21 g, 2.4 mmol), and potassium phosphate tribasic (0.28 g, 1.3 mmol) were placed in a 25 mL vial purged with N_2. Toluene (3 mL) and water (0.75 mL) were added. The reaction mixture was degassed with N_2 for 5 min and then tetrakis(triphenylphosphine)palladium(0) (0.10 g, 0.09 mmol) was added in one portion. The reaction was heated to 100 °C overnight. Upon cooling to rt, EtOAc and water were added; the phases were separated, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to a crude residue. The crude residue was purified by normal phase chromatography, eluting with 1:1 hexanes:EtOAc to give the title compound (170 mg, 94% yield). MS m/z 428.4 (M-H).

Preparation 83

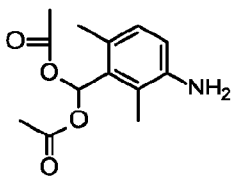
(2,6-Dimethyl-3-nitrophenyl)methylene diacetate



2,6-Dimethyl-3-nitrobenzaldehyde (1.9 g, 10 mmol) was dissolved in DCM (23 mL), then acetic anhydride (1.3 mL, 14 mmol) and copper(II) trifluoromethanesulfonate (41 mg, 0.11 mmol) were added. The solution was stirred at rt for 3.5 h. The reaction was quenched with satd aq $NaHCO_3$. The organic layer was separated, washed with water, brine, dried over Na_2SO_4, filtered, and concentrated to a crude residue. The crude residue was purified by normal phase chromatography, eluting with 3:2 hexanes:EtOAc to give the title compound (2.4 g, 81% yield). ^{1}H NMR (400.13 MHz, DMSO-d6): 7.96 (s, 1H), 7.80 (d, J= 8.3 Hz, 1H), 7.35 (d, J= 8.4 Hz, 1H), 2.58 (s, 3H), 2.53 (s, 2H), 2.12 (s, 6H).

Preparation 84

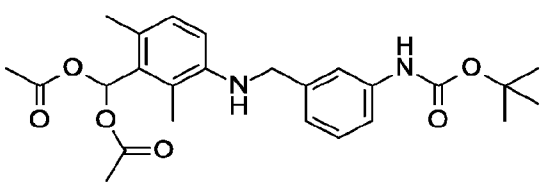
(3-Amino-2,6-dimethylphenyl)methylene diacetate



Sulfided 5wt% platinum on carbon (1.0 g, 5.2 mmol) was added to a 500-mL Parr shaker bottle and degassed with N_2. Added 25 mL EtOAc, then added (2,6-dimethyl-3-nitrophenyl)methylene diacetate (2.7 g, 9.6 mmol) in 25 mL EtOAc to the bottle. The bottle was sealed, purged with N_2, purged with H_2, and pressurized to 60 psi H_2 for 1.5 h at rt. The reaction mixture was filtered and concentrated to give the title compound (2.1 g, quant yield). MS m/z 251.8 (M+H).

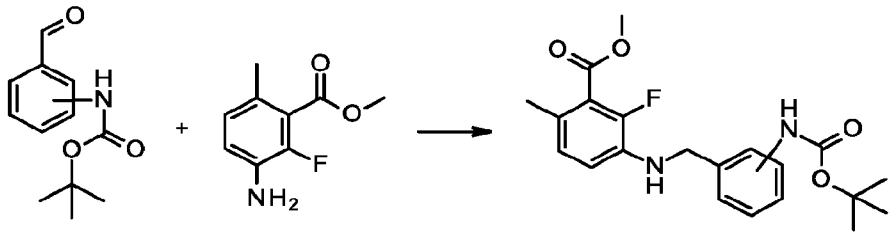
Preparation 85

(3-((3-((tert-Butoxycarbonyl)amino)benzyl)amino)-2,6-dimethylphenyl)methylene diacetate



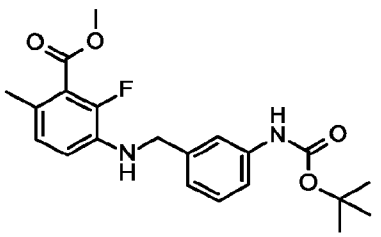
A mixture of (3-amino-2,6-dimethylphenyl)methylene diacetate (276 mg, 1.10 mmol) and potassium carbonate (435 mg, 3.15 mmol) in DMF (3 mL) was stirred at rt for 1 h. tert-Butyl N-[3-(bromomethyl)phenyl]carbamate (300 mg, 1.05 mmol) was added to the slurry and the reaction was stirred at 50 °C for 1 h. After cooling, the reaction mixture was partitioned between ethyl acetate and water. The phases were separated. The organic phase was transferred to a round-bottom flask, and the solvent evaporated in vacuo. Residual DMF was evaporated (azeotroped) with xylenes giving residue as a clear paste. The crude residue was purified by normal phase purification, eluting with 1:1 EtOAc:hexanes to give the title compound (363 mg, 76% yield). MS m/z 457.2 (M+H).

Scheme 9



Preparation 86

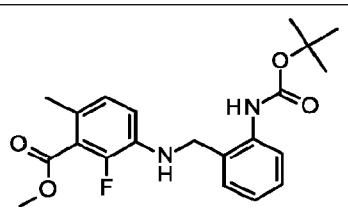
Methyl 3-((3-((tert-butoxycarbonyl)amino)benzyl)amino)-2-fluoro-6-methylbenzoate



tert-Butyl (3-formylphenyl)carbamate (1.2 g, 5.2 mmol), methyl 3-amino-2-fluoro-6-methylbenzoate (950 mg, 4.8 mmol), and acetic acid (0.55 mL, 9.6 mmol) was dissolved in methanol (5 mL) and cooled to 0 °C. Sodium cyanoborohydride (0.61 g, 9.5 mmol) was carefully added into the solution. The ice bath was removed, and the reaction mixture stirred at rt overnight under N_2. The reaction was quenched by addition of water (10 mL). The reaction mixture was partitioned between EtOAc and water. The combined organic extracts were washed with brine, dried with Na_2SO_4, filtered, and concentrated to a crude residue. The crude residue was purified by normal phase chromatography, eluting with 3:2 Pet ether:EtOAc to give the title compound (1.9 g, 75% yield). MS m/z 389.0 (M+H).

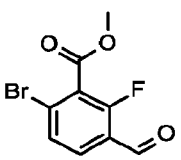
The following compound in Table 10 was prepared in a manner essentially analogous to the procedure described in Preparation 86.

Table 10: Preparation 87

Prep. No.	Structure	ES/MS (m/z) (M+H)	Formyl starting material
87		389.0	tert-butyl (2-formylphenyl)carbamate

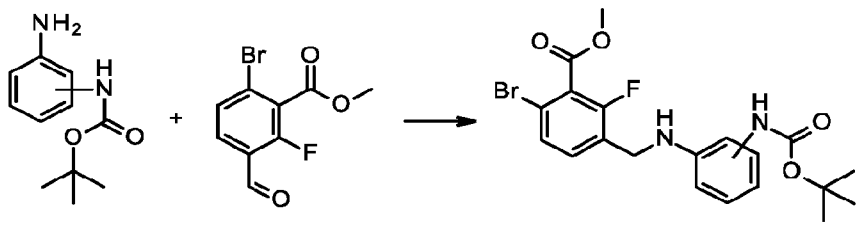
Preparation 88

Methyl 6-bromo-2-fluoro-3-formylbenzoate



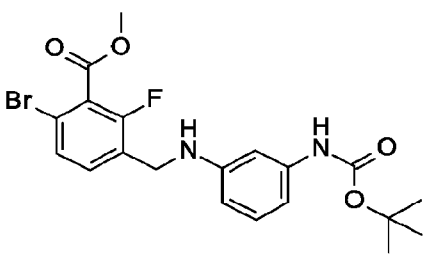
N-Bromosuccinimide (5.8 g, 31 mmol) was added to a solution of methyl 6-bromo-2-fluoro-3-methylbenzoate (3.9 g, 14 mmol) in carbon tetrachloride (36 mL), followed by 2,2'-azobis(2-methylpropionitrile (0.24 g, 1.4 mmol), and the reaction mixture was stirred at 85 °C overnight. The mixture was diluted with DCM, washed with brine, dried over Na_2SO_4, and concentrated to a crude residue. The residue was dissolved in ACN and purified by preparative C18 HPLC (35%-60% water [0.225% FA]-ACN). The eluent was concentrated to give methyl 6-bromo-3-(dibromomethyl)-2-fluorobenzoate (1.9 g, 4.6 mmol). The material was dissolved in ethanol (15 mL). A mixture of silver nitrate (2.0 g, 12 mmol) in water (10 mL) was added and the reaction mixture was heated at 75 °C for 6 h under N_2. The reaction mass was filtered and washed with EtOAc. The filtrate was concentrated to giver a crude residue. The crude residue was purified by normal phase chromatography, eluting with 8% EtOAc:Pet ether to give the title compound (1.1 g, 91% yield).

Scheme 10



Preparation 89

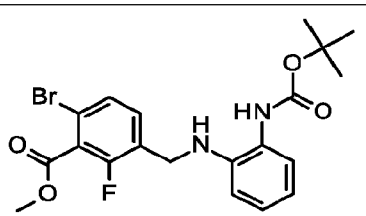
Methyl 6-bromo-3-(((3-((tert-Butoxycarbonyl)amino)phenyl)amino)methyl)-2-fluorobenzoate



Methyl 6-bromo-2-fluoro-3-formylbenzoate (1.0 g, 3.7 mmol), tert-butyl N-(3-aminophenyl)carbamate (870 mg, 4.1 mmol), and acetic acid (0.43 mL, 7.5 mmol) were dissolved in methanol (9 mL) and cooled to 0 °C. Sodium cyanoborohydride (480 mg, 7.5 mmol) was carefully added into the solution. The ice bath was removed, and the reaction mixture stirred at rt overnight under N_2. The reaction was quenched by addition of water (30 mL). The reaction mixture was partitioned between EtOAc and water. The combined organic extracts were washed with brine, dried with Na_2SO_4, filtered, and concentrated to a crude residue. The crude residue was purified by normal phase chromatography, eluting with 7:3 Pet ether:EtOAc to give the title compound (1.7 g, 89% yield). MS m/z 454.9 (M+H).

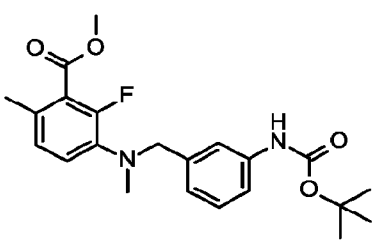
The following compound in Table 11 was prepared in a manner essentially analogous to the procedure described in Preparation 89.

Table 11: Preparation 90

Prep. No.	Structure	ES/MS (m/z) (M+H)	Formyl starting material
90		454.9	methyl 6-bromo-2-fluoro-3-formylbenzoate

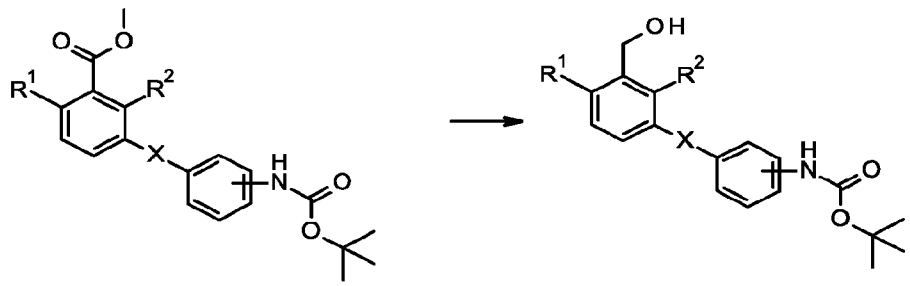
Preparation 91

Methyl 3-((3-((tert-butoxycarbonyl)amino)benzyl)(methyl)amino)-2-fluoro-6-methylbenzoate



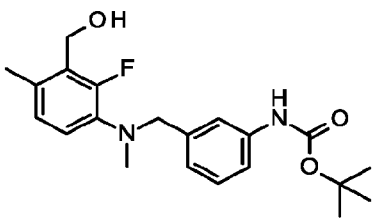
To a solution of methyl 3-((3-((tert-butoxycarbonyl)amino)benzyl)amino)-2-fluoro-6-methylbenzoate (1.7 g, 3.3 mmol) in methanol (5 mL) was added sodium cyanoborohydride (420 mg, 6.5 mmol) and acetic acid (0.5 mL, 9 mmol). Formaldehyde in water (730 µL, 9.8 mmol, 37 mass%) was then added at 25 °C. The mixture was stirred at rt overnight under N_2. The crude mixture was purified by normal phase chromatography, eluting with 4:1 Pet ether:EtOAc to give the title compound (1.3 g, 92% yield). MS m/z 403.0 (M+H).

Scheme 11



Preparation 92

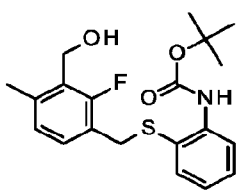
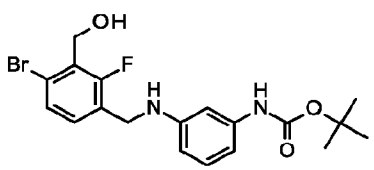
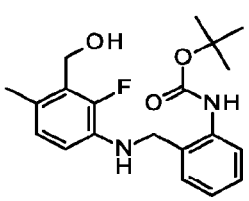
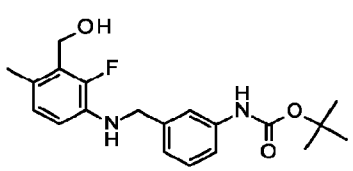
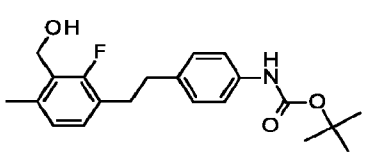
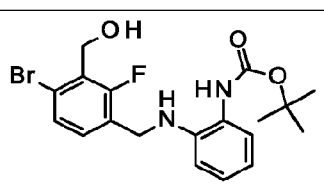
tert-Butyl (3-(((2-fluoro-3-(hydroxymethyl)-4-methylphenyl)(methyl)amino)methyl)phenyl)carbamate



To a solution methyl 3-((3-((tert-butoxycarbonyl)amino)benzyl)(methyl)amino)-2-fluoro-6-methylbenzoate (1.2 g, 2.8 mmol) in DCM (10 mL) was added DIBAL-H in toluene (7 mL, 7.0 mmol, 1.0 mol/L) at 0 °C. The reaction mixture was warmed to rt for 3 h. The solution was cooled back to 0 °C and satd aq Rochelle salt and DCM were added, followed by extraction with DCM. The organic layer was washed with brine, dried over Na_2SO_4, passed through a silica gel plug, and concentrated to a crude residue. The residue was purified by normal phase chromatography, eluting with 1:1 Pet ether:EtOAc to give the title compound (640 mg, 57% yield). MS m/z 375.0 (M+H).

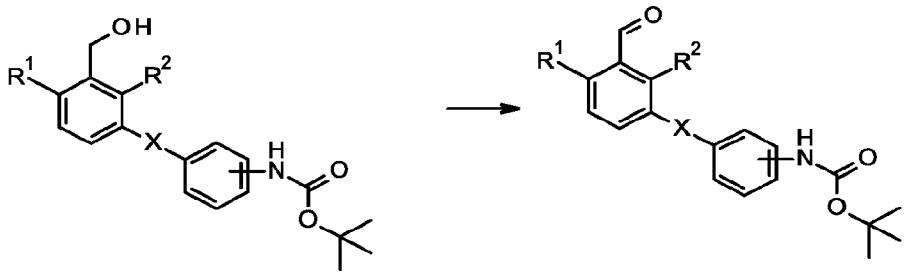
The following compounds in Table 12 were prepared in a manner essentially analogous to the procedure described in Preparation 92.

Table 12: Preparations 93-98

Prep. No.	Structure	ES/MS (m/z) (M+H)	Ester SM
93		278.0 (M-Boc+H)	methyl 3-(((2-((tert-butoxycarbonyl)amino)phenyl)thio)methyl)-2-fluoro-6-methylbenzoate
94		426.9	methyl 6-bromo-3-(((3-((tert-butoxycarbonyl)amino)phenyl)amino)methyl)-2-fluorobenzoate
95		361.0	methyl 3-((2-((tert-butoxycarbonyl)amino)benzyl)amino)-2-fluoro-6-methylbenzoate
96		361.2	methyl 3-((3-((tert-butoxycarbonyl)amino)benzyl)amino)-2-fluoro-6-methylbenzoate
97		No ion*	methyl 3-(4-((tert-butoxycarbonyl)amino)phenethyl)-2-fluoro-6-methylbenzoate
98		426.9	methyl 6-bromo-3-(((2-((tert-butoxycarbonyl)amino)phenyl)amino)methyl)-2-fluorobenzoate

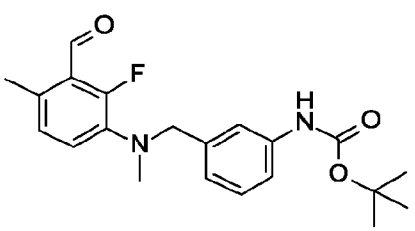
*^{1}H NMR (400.14 MHz, DMSO): δ 9.23 (s, 1H), 7.35-7.31 (m, 2H), 7.09-7.02 (m, 3H), 6.89 (d, J= 7.8 Hz, 1H), 4.92 (t, J= 5.3 Hz, 1H), 4.49-4.48 (m, 2H), 4.03 (q, J= 7.1 Hz, 1H), 2.79-2.72 (m, 4H), 2.33 (s, 3H), 1.46 (s, 9H).

Scheme 12



Preparation 99

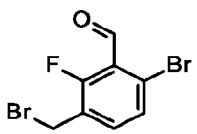
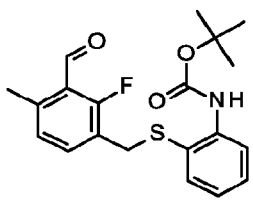
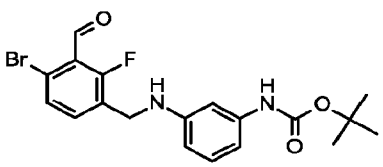
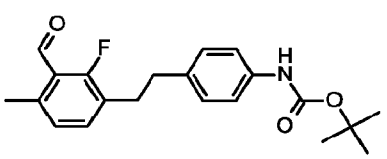
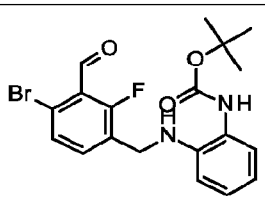
tert-Butyl (3-(((2-fluoro-3-formyl-4-methylphenyl)(methyl)amino)methyl)phenyl)carbamate



To a solution of tert-butyl (3-(((2-fluoro-3-(hydroxymethyl)-4-methylphenyl)(methyl)amino)methyl)phenyl)carbamate (590 mg, 1.5 mmol) in EtOAc (5 mL) was added 2-iodoxybenzoic acid (630 mg, 2.2 mmol). The reaction mixture was stirred at 80 °C for 6 h. The solids were filtered out and the filtrate was concentrated to a crude residue. The residue was purified by normal phase chromatography, eluting with 7:3 Pet ether:EtOAc to give the title compound (580 mg, 94% yield). MS m/z 373.0 (M+H).

The following compounds in Table 13 were prepared in a manner essentially analogous to the procedure described in Preparation 99.

Table 13: Preparations 100-104

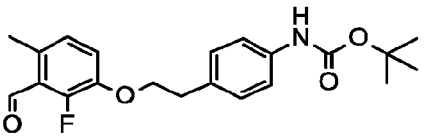
Prep. No.	Structure	ES/MS (m/z) (M+H)	Alcohol starting material
100		No ion*	(6-bromo-3-(bromomethyl)-2-fluorophenyl)methanol
101		275.9 (M-Boc+H)	tert-butyl (2-((2-fluoro-3-(hydroxymethyl)-4-methylbenzyl)thio)phenyl)carbamate
102		424.9	tert-butyl (3-((4-bromo-2-fluoro-3-(hydroxymethyl)benzyl)amino)phenyl)carbamate
103		No ion**	tert-butyl (4-(2-fluoro-3-(hydroxymethyl)-4-methylphenethyl)phenyl)carbamate
104		425.0	tert-butyl (2-((4-bromo-2-fluoro-3-(hydroxymethyl)benzyl)amino)phenyl)carbamate

*^{1}H NMR (400.15 MHz, DMSO): δ 10.31 (d, J= 0.8 Hz, 1H), 7.90-7.86 (m, 1H), 7.78 (dd, J= 0.8, 8.4 Hz, 1H), 4.84 (d, J= 1.0 Hz, 2H)

**^{1}H NMR (400.15 MHz, DMSO): δ 10.42 (s, 1H), 9.23 (s, 1H), 7.44-7.40 (m, 1H), 7.36-7.33 (m, 2H), 7.09-7.05 (m, 3H), 2.92-2.81 (m, 4H), 2.50 (s, 3H), 1.47 (s, 9H).

Preparation 105

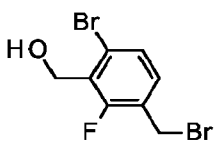
tert-Butyl (4-(2-(2-fluoro-3-formyl-4-methylphenoxy)ethyl)phenyl)carbamate



To a solution of 2-fluoro-3-hydroxy-6-methylbenzaldehyde (250 mg, 1.5 mmol) and 4-((tert-butoxycarbonyl)amino)phenethyl 4-methylbenzenesulfonate (760 mg, 1.9 mmol) in acetonitrile (10 mL) was added potassium carbonate (670 mg, 4.9 mmol). The suspension was stirred at 80 °C for 16 h. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water (40 mL), extracted with EtOAc (20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by normal phase chromatography, eluting with 17:3 Pet ether:EtOAc to give the title compound (510 mg, 85% yield). ^{1}H NMR (400.15 MHz, $CDCl_3$): δ 10.47 (s, 1H), 7.24 (d, J= 8.4 Hz, 2H), 7.15 (d, J= 8.5 Hz, 2H), 6.96 (t, J= 8.4 Hz, 1H), 6.82 (d, J= 8.4 Hz, 1H), 6.37-6.35 (m, 1H), 4.12 (t, J= 7.0 Hz, 2H), 3.01 (t, J= 6.9 Hz, 2H), 2.45 (s, 3H), 1.45 (s, 8H).

Preparation 106

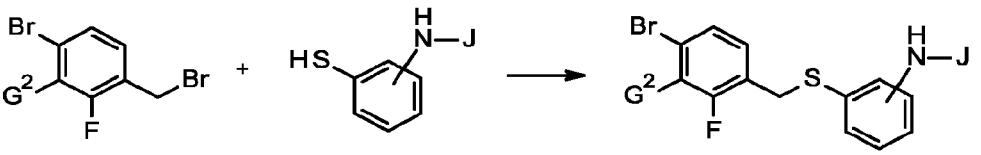
(6-Bromo-3-(bromomethyl)-2-fluorophenyl)methanol



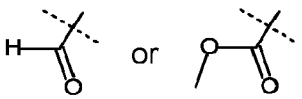
To a solution of 6-bromo-3-(bromomethyl)-2-fluorobenzoic acid (4.9 g, 11 mmol) in THF (100 mL) under a nitrogen atmosphere and cooled in an ice bath, borane-THF complex in THF (35 mL, 35 mmol, 1 mol/L) was added dropwise. The reaction mixture was allowed to warm to rt for overnight. The reaction was quenched by addition of MeOH (100 mL) and concentrated in vacuo. The resulting residue was partitioned between EtOAc (100 mL) and 1 M HCl (30 mL) and the aqueous layer was extracted once with EtOAc (100 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated to give a crude residue. The residue was purified by normal phase chromatography, eluting with 7:3 Pet ether:EtOAc to give the title compound (2.9

g, 62% yield). ^{1}H NMR (400.15 MHz, DMSO): δ7.50-7.42 (m, 2H), 5.38-5.23 (m, 1H), 4.70 (d, J= 0.5 Hz, 2H), 4.59 (d, J= 1.5 Hz, 2H).

Scheme 13



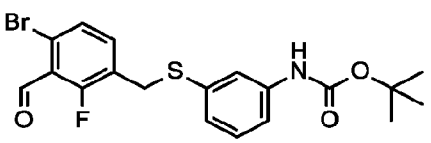
Wherein G^2 is



Wherein J is hydrogen or Boc.

Preparation 107

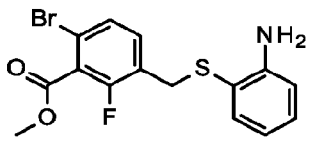
tert-Butyl (3-((4-bromo-2-fluoro-3-formylbenzyl)thio)phenyl)carbamate



To a mixture of 6-bromo-3-(bromomethyl)-2-fluorobenzaldehyde (620 mg, 1.9 mmol) and tert-butyl N-(3-sulfanylphenyl)carbamate (500 mg, 2.0 mmol) in DCM (10 mL) was added triethylamine (530 µL, 3.8 mmol) under N_2. The mixture was stirred at rt for 2 h. The reaction mixture was partitioned between DCM (30 mL) and water (30 mL). The combined organic extracts were concentrated under vacuum to give the crude residue. The residue was purified by normal phase chromatography, eluting with 3:1 Pet ether:EtOAc to give the title compound (780 mg, 89% yield). ^{1}H NMR (400.15 MHz, DMSO): δ 10.19 (s, 1H), 9.39 (s, 1H), 7.57-7.51 (m, 2H), 7.47 (s, 1H), 7.27 (d, J= 8.6 Hz, 1H), 7.19 (t, J= 7.9 Hz, 1H), 6.96 (d, J= 7.8 Hz, 1H), 4.21 (s, 2H), 1.46 (s, 9H).

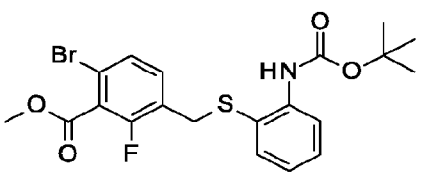
The following compound in Table 14 was prepared in a manner essentially analogous to the procedure described in Preparation 107.

Table 14: Preparation 108

Prep. No.	Structure	ES/MS (m/z) (M+H)	Thiol starting material
108		371.8	2-aminobenzenethiol

Preparation 109

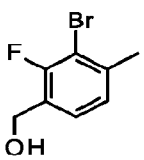
Methyl 6-bromo-3-(((2-((tert-butoxycarbonyl)amino)phenyl)thio)methyl)-2-fluorobenzoate



To a solution of methyl 3-(((2-aminophenyl)thio)methyl)-6-bromo-2-fluorobenzoate (1.3 g, 3.4 mmol) in tert-butanol (13 mL, 140 mmol) was added di-tert-butyl dicarbonate (3.5 mL, 15 mmol). The mixture was stirred at 50 °C overnight under N_2. The reaction was concentrated under vacuum to give the crude residue. The residue was purified by normal phase chromatography, eluting with 10:1 Pet ether:EtOAc to give the title compound (1.6 g, quantitative yield). MS m/z 371.8 (M-Boc+H).

Preparation 110

(3-Bromo-2-fluoro-4-methylphenyl)methanol

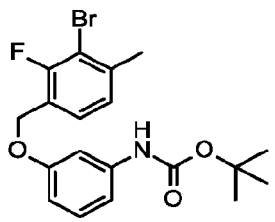


To a solution of 3-bromo-2-fluoro-4-methylbenzaldehyde (2 g, 6.6 mmol) in MeOH was added sodium borohydride (620 mg, 16 mmol) at 0 °C. The mixture was stirred for 1 h. The mixture was slowly quenched with 1 M aq HCl (30 mL) under N_2,

adjusting to pH 6. The reaction mixture was concentrated under vacuum to give crude residue. The residue was purified by normal phase chromatography, eluting with 1:2 Pet ether:EtOAc to give the title compound (820 mg, 51% yield).

Preparation 111

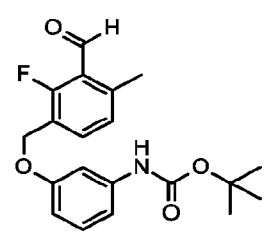
tert-Butyl (3-((3-bromo-2-fluoro-4-methylbenzyl)oxy)phenyl)carbamate



To a solution of (3-bromo-2-fluoro-4-methylphenyl)methanol (650 mg, 2.7 mmol), tert-butyl (3-hydroxyphenyl)carbamate (870 mg, 4.0 mmol), and tetrabutylphosphine (1.1 g, 5.4 mmol) in THF (10 mL, 120 mmol) was added N,N,N′,N′-tetramethylazodicarboxamide (940 mg, 5.4 mmol). The reaction mixture was stirred at rt for 2 h under anhydrous N_2. The reaction mixture was partitioned between EtOAc (100 mL) and water (100 mL). The combined organic extracts were washed with brine (200 mL), dried with Na_2SO_4, filtered, and concentrated under vacuum to give crude residue. The residue was purified by normal phase chromatography, eluting with 9:1 Pet ether:EtOAc to give the title compound (1.2 g, 96% yield). MS m/z 355.8 (M-tBu+H).

Preparation 112

tert-Butyl (3-((2-fluoro-3-formyl-4-methylbenzyl)oxy)phenyl)carbamate

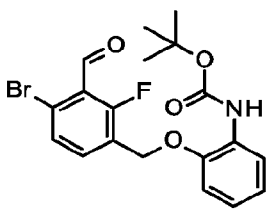


To a solution of tert-butyl (3-((3-bromo-2-fluoro-4-methylbenzyl)oxy)phenyl)carbamate (0.82 g, 1.8 mmol) in THF (5 mL, 62 mmol) was added isopropylmagnesium chloride lithium chloride complex solution in THF (3.1 mL, 4.0 mmol, 1.3 mol/L) at 0 °C and stirred for 30 min. DMF (450 µL, 5.7 mmol) was

added to the mixture at 0 °C. The mixture was warmed to rt for 1.5 h and then quenched by addition of satd aq NH_4Cl (5 mL). The reaction mixture was partitioned between EtOAc (30 mL) and water (30 mL). The combined organic extracts were concentrated under vacuum to give the crude product. The residue was purified by normal phase chromatography, eluting with 95:5 Pet ether:EtOAc to give the title compound (220 mg, 25% yield). MS m/z 259.9 (M-Boc+H).

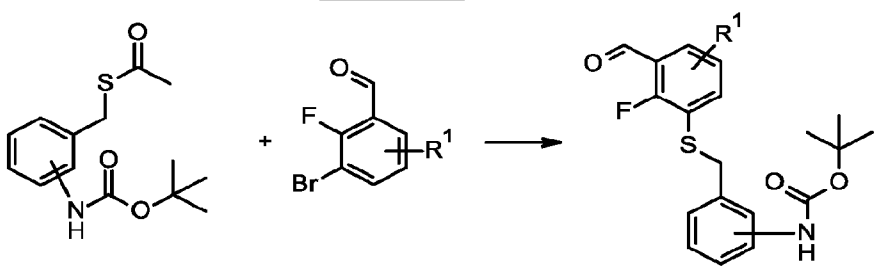
Preparation 113

tert-Butyl (2-((4-bromo-2-fluoro-3-formylbenzyl)oxy)phenyl)carbamate



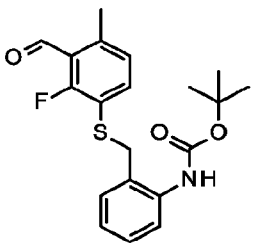
Cesium carbonate (230 mg, 0.71 mmol) was added to a solution of tert-butyl (2-hydroxyphenyl)carbamate (100 mg, 0.47 mmol) and 6-bromo-3-(bromomethyl)-2-fluoro-benzaldehyde (160 mg, 0.51 mmol) in DMF (3 mL). The reaction mixture was stirred at rt for 1 h under N_2 and then quenched with the addition of water. The reaction mixture was partitioned between EtOAc (20 mL) and water (20 mL). The combined organic extracts were concentrated under vacuum to give the crude product. The residue was purified by normal phase chromatography, eluting with 4:1 Pet ether:EtOAc to give the title compound (210 mg, quantitative yield). ^{1}H NMR (400.21 MHz, DMSO): δ 10.24 (s, 1H), 8.08 (s, 1H), 7.82 (t, J= 7.9 Hz, 1H), 7.69 (d, J= 8.3 Hz, 1H), 7.63 (d, J= 7.6 Hz, 1H), 7.10 (dd, J= 1.0, 8.1 Hz, 1H), 7.06-7.02 (m, 1H), 6.95-6.91 (m, 1H), 5.21 (s, 2H), 1.44 (s, 9H).

Scheme 14



Preparation 114

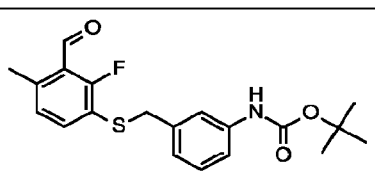
tert-Butyl (2-(((2-fluoro-3-formyl-4-methylphenyl)thio)methyl)phenyl)carbamate

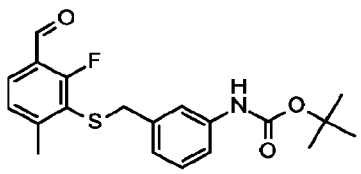


To a solution of S-(2-((tert-butoxycarbonyl)amino)benzyl) ethanethioate (670 mg, 2.2 mmol) in 1,4-dioxane (10 mL) and water (2 mL) was added 3-bromo-2-fluoro-6-methyl-benzaldehyde (550 mg, 1.8 mmol), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (220 mg, 0.44 mmol), potassium carbonate (610 mg, 4.4 mmol), and tris(dibenzylideneacetone)dipalladium(0) (210 mg, 0.22 mmol). The mixture was heated to 100 °C overnight. Upon completion, the reaction mixture was concentrated under reduced pressure. The residue was diluted with water (20 mL) and extracted with EtOAc (20 mL x 2). The combined organic layers were washed with brine (40 mL), dried over Na_2SO_4, and concentrated in vacuo to give a residue. The residue was purified by normal phase chromatography, eluting with 95:5 Pet ether:EtOAc to give the title compound (670 mg, 54% yield). MS m/z 275.9 (M-Boc+H).

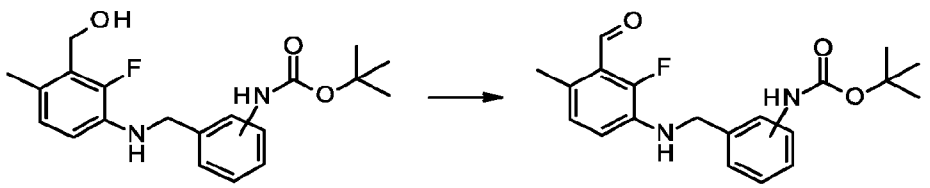
The following compounds in Table 15 were prepared in a manner essentially analogous to the procedure described in Preparation 114.

Table 15: Preparations 115-116

Prep. No.	Structure	ES/MS (m/z) (M+H)	Thioate SM
115		398.2 (M+Na)	S-(3-((tert-butoxycarbonyl)amino)benzyl) ethanethioate

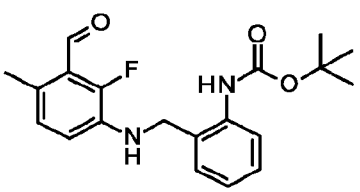
116		275.9 (M-Boc+H)	S-(3-((tert-butoxycarbonyl)amino)benzyl) ethanethioate

Scheme 15



Preparation 117

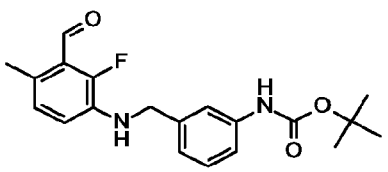
tert-Butyl (2-(((2-fluoro-3-formyl-4-methylphenyl)amino)methyl)phenyl)carbamate



To a solution tert-butyl (2-(((2-fluoro-3-(hydroxymethyl)-4-methylphenyl)amino)methyl)phenyl)carbamate (950 mg, 2.4 mmol) in THF (20 mL) was added manganese dioxide (2.2 g, 25 mmol) at rt. The resulting mixture was stirred at 70 °C overnight. Additional manganese dioxide (2.2 g, 25 mmol) was added to the incomplete reaction and continued stirring at 70 °C for 4 h. Upon completion, the reaction mixture was filtered and washed with MeOH:DCM (1:1) through a pad of diatomaceous earth and the filtrate was concentrated under reduced pressure to afford the crude product. The residue was purified by normal phase chromatography, eluting with 9:1 Pet ether:EtOAc to give the title compound (220 mg, 20% yield). MS m/z 359.0 (M+H).

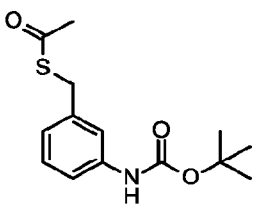
The following compound in Table 16 was prepared in a manner essentially analogous to the procedure described in Preparation 117.

Table 16: Preparation 118

Prep. No.	Structure	ES/MS (m/z) (M+H)	Alcohol SM
118		303.0 (M-tBu+H)	tert-butyl (3-(((2-fluoro-3-(hydroxymethyl)-4-methylphenyl)amino)methyl)phenyl)carbamate

Preparation 119

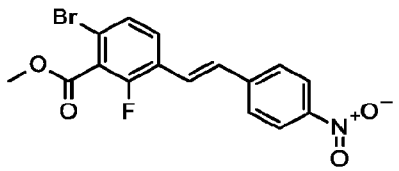
S-(3-((tert-Butoxycarbonyl)amino)benzyl) ethanethioate



Dissolved tert-butyl (3-(bromomethyl)phenyl)carbamate (2.0 g, 6.7 mmol) and potassium thioacetate (1.6 g, 14 mmol) in DMF (9 mL, 120 mmol) and stirred at rt under N_2 for 2 h. The reaction was quenched by addition of a satd aq NH_4Cl (20 mL) and extracted with EtOAc (3 x 30 mL). The combined organic extracts were washed with brine (20 mL), dried with Na_2SO_4, filtered, and concentrated under vacuum to give the crude product. The residue was purified by normal phase chromatography, eluting with 17:3 Pet ether:EtOAc to give the title compound (1.8 g, 89% yield). MS m/z 225.9 (M-tBu+H).

Preparation 120

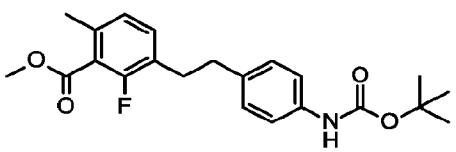
Methyl (E)-6-bromo-2-fluoro-3-(4-nitrostyryl)benzoate



To a solution of diethyl (4-nitrobenzyl)phosphonate (1.7 g, 6.1 mmol) and 15-crown-5 (1.3 g, 5.7 mmol) in DMF (30 mL) was added sodium hydride in oil (340 mg, 8.5 mmol, 60 mass%). After stirring at 0 °C for 30 min, methyl 6-bromo-2-fluoro-3-formylbenzoate (1.5 g, 5.7 mmol) was added under N_2. After 1.5 h, the reaction was quenched by addition of satd aq NH_4Cl (40 mL) to precipitate a yellow solid. The solid was collected by suction filtration, washed with water, and dried under vaccum to give the title compound (2.2 g, 89% yield). MS m/z 379.9, 381.9 (M+H).

Preparation 121

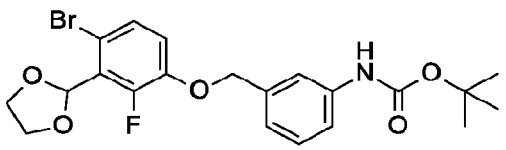
Methyl 3-(4-((tert-butoxycarbonyl)amino)phenethyl)-2-fluoro-6-methylbenzoate



To a solution of methyl (E)-2-fluoro-6-methyl-3-(4-nitrostyryl)benzoate (710 mg, 2.2 mmol) in MeOH (15 mL) was added palladium (650 mg, 0.31 mmol) and di-tert-butyl dicarbonate (0.57 mL, 2.5 mmol). The mixture was stirred at rt for 2 h under H_2 (15 psi). The reaction mixture was filtered through a pad of diatomaceous earth and the filtrate was concentrated under reduced pressure to afford the crude product. The residue was purified by normal phase chromatography, eluting with 3:2 Pet ether:EtOAc to give the title compound (620 mg, 69% yield). ^{1}H NMR (400.21 MHz, DMSO): δ 9.24 (s, 1H), 7.34 (d, J= 8.3 Hz, 2H), 7.26 (t, J= 7.9 Hz, 1H), 7.05 (dd, J= 8.2, 14.8 Hz, 3H), 3.87 (s, 3H), 2.86-2.68 (m, 4H), 2.26 (s, 3H), 1.47 (s, 10H).

Preparation 122

tert-Butyl (3-((4-bromo-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate



With a Dean-Stark trap attached, a solution of tert-butyl (3-((4-bromo-2-fluoro-3-formylphenoxy)methyl)phenyl)carbamate (1.0 g, 2.5 mmol), ethylene glycol (0.55 mL, 9.8 mmol), and p-toluenesulfonic acid monohydrate (47 mg, 0.25 mmol) in toluene (16 mL, 150 mmol) was refluxed at 135 °C for 1 h. The reaction solution was cooled to rt and diluted with water (15 mL) and EtOAc (25 mL). The phases were separated, and the aqueous was extracted with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered, and evaporated to give a crude residue. The residue was purified by normal phase chromatography, eluting with 24:1 DCM:MeOH to give the title compound (1.2 g, 44% yield). MS m/z 486.8 ($M+NH_4$).

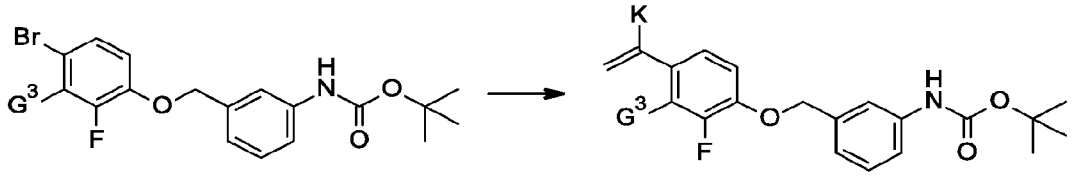
Alternative Preparation 122

tert-Butyl (3-((4-bromo-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate

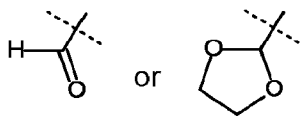
With a Dean-Stark trap attached, a solution of 6-bromo-2-fluoro-3-hydroxybenzaldehyde (1.04 g, 4.75 mmol), ethylene glycol (1.1 mL, 20 mmol), and p-toluenesulfonic acid monohydrate (88 mg, 0.46 mmol) in toluene (32 mL) was refluxed at 135 °C for 1 h. The reaction solution was cooled to rt and washed with water (15 mL). The phases were separated. The organic layer was dried with Na_2SO_4, filtered, and evaporated to give a crude residue. The residue was purified by normal phase chromatography, eluting with 20:1 DCM:MeOH to give 4-bromo-3-(1,3-dioxolan-2-yl)-2-fluoro-phenol (1.06 g, 4.03 mmol). This material was dissolved in DMF (8.0 mL) and potassium carbonate (1.40 g, 10.1 mmol) was added. This mixture was stirred at rt for 5 min. tert-Butyl 3-(bromomethyl)phenylcarbamate (1.21 g, 4.23 mmol) was then added and the mixture stirred for 75 min. The mixture was then diluted with water (40 mL) and extracted with EtOAc (40 mL). The phases were separated. The organic layer was dried with Na_2SO_4, filtered, and evaporated to give a crude residue. The residue was purified by normal phase chromatography, eluting with 3:1 EtOAc:hexanes to give tert-butyl (3-

((4-bromo-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate (1.72 g, 3.66 mmol, 77% yield). MS m/z 485.0, 487.2 ($M+NH_4$).

Scheme 16



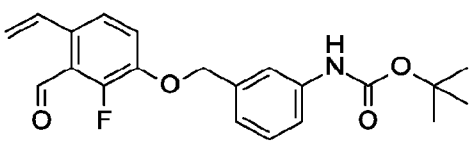
Wherein G^3 is



Wherein K is hydrogen or methyl.

Preparation 123

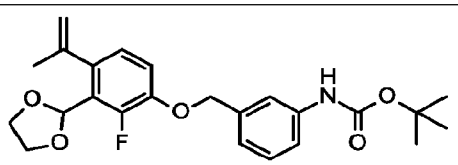
tert-Butyl (3-((2-fluoro-3-formyl-4-vinylphenoxy)methyl)phenyl)carbamate



tert-Butyl (3-((4-bromo-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate (400 mg, 0.85 mmol), potassium vinyltrifluoroborate (0.14 g, 1.0 mmol), and cesium carbonate (0.84 g, 2.6 mmol) were placed in a 25-mL microwave vial that was purged with N_2. THF (9 mL) and water (1 mL, 56 mmol) were added. The mixture was degassed by bubbling sub-surface N_2 for 5 minutes, palladium(II) acetate (10 mg, 0.04 mmol) was added, and the reaction was heated to 100 °C overnight. The reaction was cooled to rt for 3 days. EtOAc and water were added, the phases were separated, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to a crude residue. The residue was purified by normal phase chromatography, eluting with 3:2 hexanes:EtOAc to give the title compound (320 mg, 16% yield). MS m/z 369.6 (M-H).

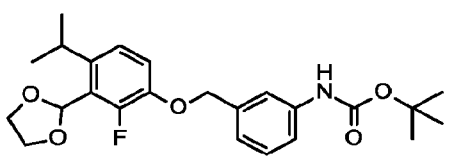
The following compound in Table 17 was prepared in a manner essentially analogous to the procedure described in Preparation 123.

Table 17: Preparation 124

Prep. No.	Structure	ES/MS (m/z) (M+H)	Borate SM
124		428.2 (M-H)	trifluoro(prop-1-en-2-yl)borate potassium(I)

Preparation 125

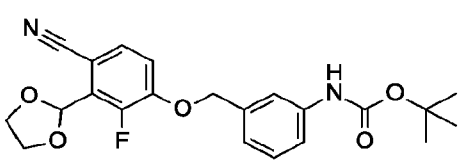
tert-Butyl N-[3-[[3-(1,3-dioxolan-2-yl)-2-fluoro-4-isopropyl-phenoxy]methyl]phenyl]carbamate



Sulfided 5wt% platinum on carbon (0.057 g, 0.29 mmol) was added to a 70-mL Parr shaker bottle and degassed with N_2. Added 5 mL EtOAc, then added tert-butyl (3-((3-(1,3-dioxolan-2-yl)-2-fluoro-4-(prop-1-en-2-yl)phenoxy)methyl)phenyl)carbamate (0.231 g, 0.538 mmol) in 6 mL EtOAc to the bottle. The bottle was sealed, purged with N_2, purged with H_2, and pressurized to 60 psi H_2 for 5 h at rt. The reaction mixture was filtered and concentrated to give the title compound (255 mg, quant yield). MS m/z 430.4 (M-H).

Preparation 126

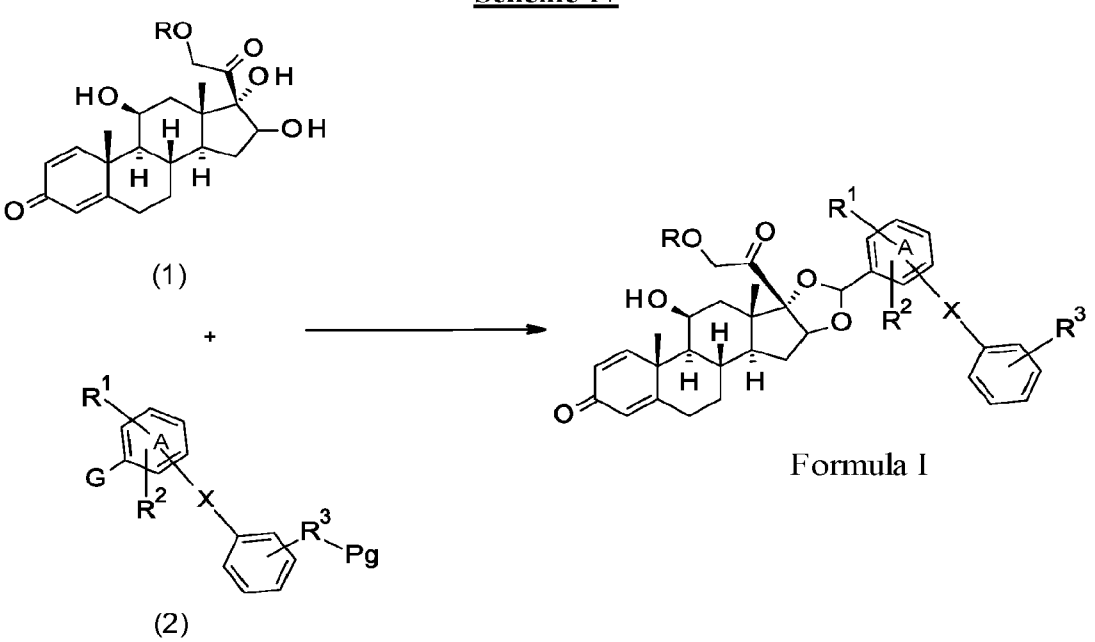
tert-Butyl (3-((4-cyano-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate



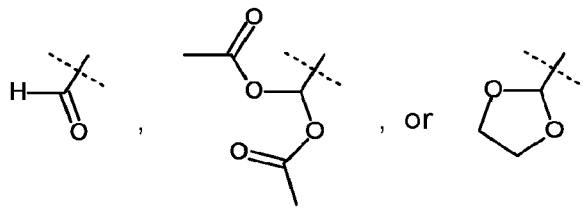
In a microwave vial, a mixture of tert-butyl (3-((4-bromo-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate (240 mg, 0.50 mmol), zinc cyanide (130 mg,

1.1 mmol), and zinc chloride in THF (1.0 mL, 0.50 mmol, 0.500 mol/L) in DMF (2.5 mL, 32 mmol) was bubbled with N_2. Tetrakis(triphenylphosphine)palladium(0) (31 mg, 0.03 mmol) was added. The reaction mixture was bubbled with N_2, capped, and microwaved at 110 °C for 1 h. Additional zinc cyanide (120 mg, 1.0 mmol) and tetrakis(triphenylphosphine)palladium(0) (27 mg, 0.02 mmol) were added. The reaction mixture was bubbled with N_2, capped, and microwaved at 120 °C for 30 min. The reaction solution was washed with water (15 mL). The organic layer was dried with Na_2SO_4, filtered through paper, and rotary evaporated to give crude residue. The residue was purified by normal phase chromatography, eluting with 7:3 hexanes:EtOAc to give the title compound (90 mg, 43% yield). MS m/z 412.6 (M-H).

Scheme 17



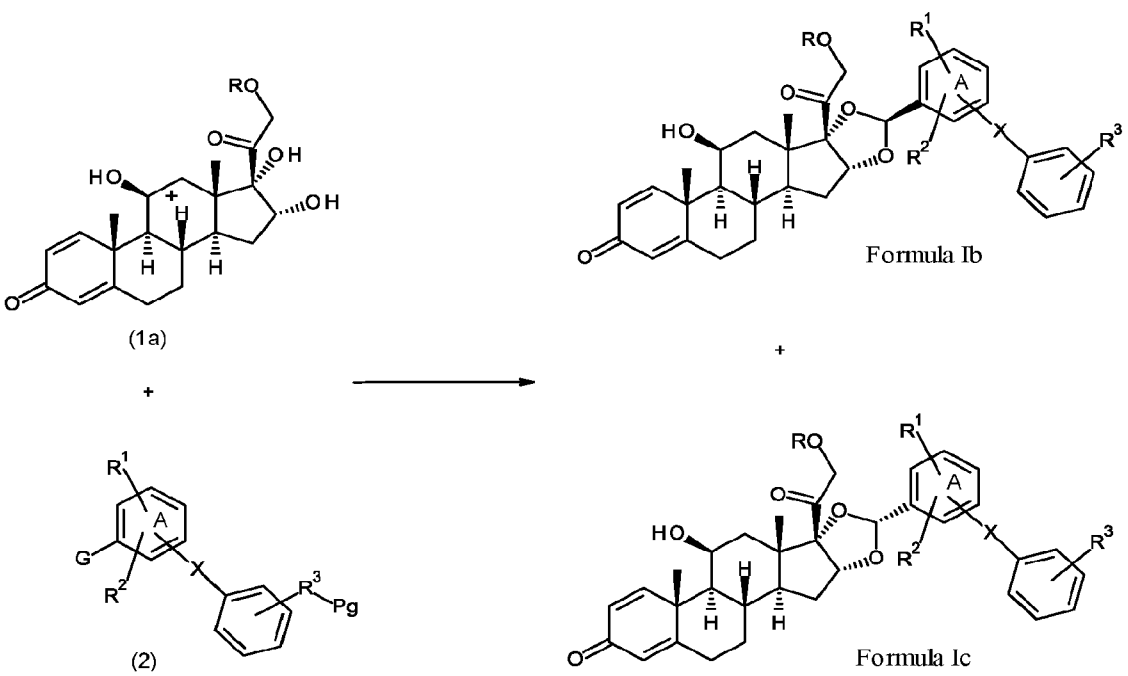
In Scheme 17, the compound of structure 1, wherein R is H, is reacted with a compound of structure 2, wherein Pg is a suitable nitrogen protecting group, such as a tert-butyloxy carbonyl, and wherein G is:



under conditions well known to one of ordinary skill in the art to provide the compound of Formula I wherein R is hydrogen.

More specifically, as shown in Scheme 17A below, the compound of structure 1a, wherein R is H, is reacted with the compound of structure 2, wherein Pg and G are defined as above, under conditions well known to one of ordinary skill in the art to provide the compounds of Formula Ib and Formula Ic.

Scheme 17A

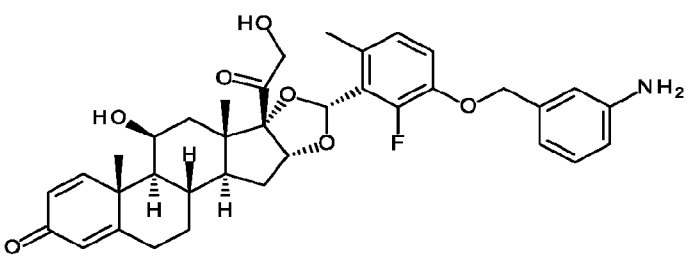


For example, about 1 equivalent of the compound of structure 1a, wherein R is H, and about 1 equivalent of a compound of structure 2, wherein Pg and G are as defined in Scheme 17, are suspended in a suitable organic solvent, such as acetonitrile. The suspension is cooled to about -10 °C to about -25 °C and then treated with about 5 equivalents of a suitable acid, such as perchloric acid (70% in water) or trifluoroacetic

acid. The reaction mixture is then warmed to room temperature and allowed to stir for about 1 to 8 hours. Additional organic solvents may be added, such as acetonitrile and dimethylformamide, and the mixture is allowed to stir for about 2 additional hours. The reaction is then quenched using standard conditions, such as with saturated aqueous sodium bicarbonate and the products are isolated using standard techniques well known in the art, such as extraction with suitable organic solvents, such as methylene chloride:isopranol, drying the organic extracts over magnesium sulfate, filtering, and concentration under vacuum to provide the crude product mixture. This crude mixture can be purified and the products of Formula Ib and Formula Ic separated using techniquest well know in the art, such as chromatography, including for example normal phase chromatography with a suitable eluent, such as MeOH in DCM, and reverse phase chromatography with a suitable eluent, such as 2:1 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile.

Example 1

(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-Aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

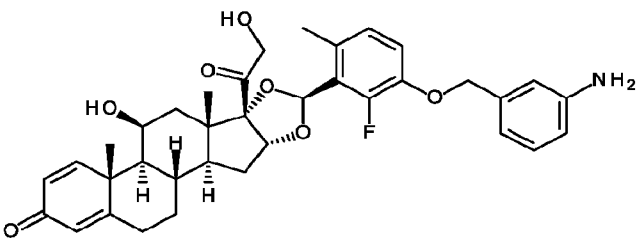


Perchloric acid (70% in water, 4.8 mL) was added to a suspension of (8S,9S,10R,11S,13S,14S,16R,17S)-11,16,17-trihydroxy-17-(2-hydroxyacetyl)-10,13-dimethyl-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-3-one (4.4 g, 12 mmol, also referred to as "16alpha-hydroxyprednisolone") and tert-butyl N-[3-[(2-fluoro-3-formyl-4-methyl-phenoxy)methyl]phenyl]carbamate (4.0 g, 11 mmol, preparation 4) in acetonitrile (110 mL) at -10 °C and was warmed to rt. After 1 h, DMF (10 mL) was added to the suspension at rt. After 18 h, the reaction was quenched with saturated

aqueous sodium bicarbonate and extracted with 9:1 methylene chloride:isopropanol. The organic layers were combined; dried over magnesium sulfate; filtered, and concentrated under reduced pressure to give a residue. The residue was purified by reverse phase chromatography, eluting with 1:1 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile to give the title compound, peak 1 (1.72 g, 25% yield). ES/MS m/z 618.6 (M+H). ^{1}H NMR (400.13 MHz, d_6-DMSO) δ 0.93-0.87 (m, 6H), 1.40 (s, 3H), 1.71-1.60 (m, 1H), 1.89-1.76 (m, 4H), 2.18-2.12 (m, 2H), 2.29 (s, 4H), 4.23-4.17 (m, 1H), 4.32-4.30 (m, 1H), 4.50-4.43 (m, 1H), 4.81 (d, J= 3.2 Hz, 1H), 4.98-4.95 (m, 3H), 5.16-5.10 (m, 3H), 5.61 (s, 1H), 5.95 (s, 1H), 6.18-6.15 (m, 1H), 6.53-6.48 (m, 2H), 6.58 (s, 1H), 6.90-6.86 (m, 1H), 6.99 (t, J= 7.7 Hz, 1H), 7.12 (t, J= 8.5 Hz, 1H), 7.33-7.30 (m, 1H).

Example 2

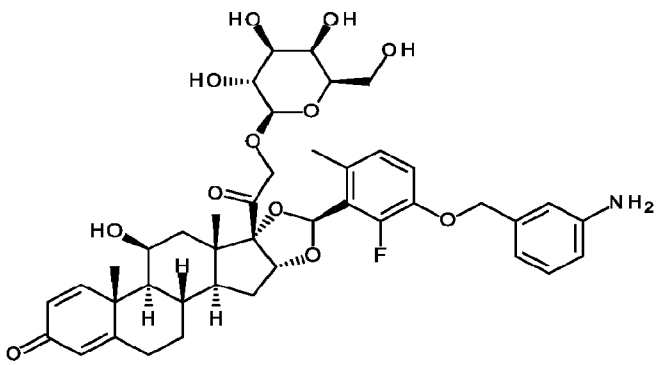
(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-Aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one



From Example 1, the residue was purified by reverse phase chromatography, eluting with 1:1 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile to give the title compound peak 2 (1.24 g, 18% yield). ES/MS m/z 618.6 (M+H). ^{1}H NMR (400.13 MHz, d_6-DMSO) δ ^{1}H NMR (400.13 MHz, DMSO): 0.88 (s, 3H), 1.24-1.12 (m, 2H), 1.40 (s, 3H), 1.69-1.56 (m, 1H), 1.91-1.76 (m, 4H), 2.08-2.01 (m, 2H), 2.22 (s, 3H), 2.39-2.29 (m, 1H), 3.18 (d, J= 5.2 Hz, 1H), 4.12-4.00 (m, 1H), 4.37-4.30 (m, 2H), 4.79 (d, J= 3.1 Hz, 1H), 5.00-4.93 (m, 2H), 5.10-5.06 (m, 3H), 5.31 (d, J= 6.7 Hz, 1H), 5.95 (s, 1H), 6.18 (dd, J= 1.8, 10.1 Hz, 1H), 6.34 (s, 1H), 6.53-6.48 (m, 2H), 6.58 (s, 1H), 6.87 (d, J= 8.5 Hz, 1H), 6.99 (t, J= 7.7 Hz, 1H), 7.09 (t, J= 8.5 Hz, 1H), 7.33 (d, J= 10.1 Hz, 1H).

Example 3

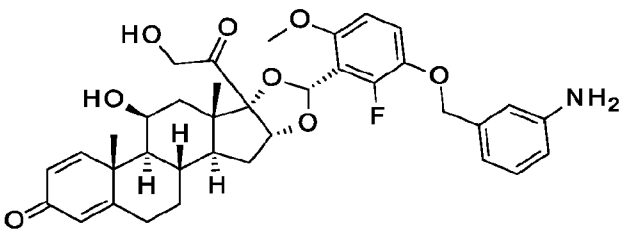
(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-Aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-6a,8a-dimethyl-8b-(2-(((2R,3R,4S,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)acetyl)-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one



(2R,3S,4S,5R,6R)-2-(Acetoxymethyl)-6-(2-((6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-6a,8a-dimethyl-4-oxo-1,2,4,6a,6b,7,8,8a,11a,12,12a,12b-dodecahydro-8bH-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-8b-yl)-2-oxoethoxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate (40 mg, 0.04 mmol, Preparation 5) was added to methanol (2 mL) and potassium carbonate (20 mg, 0.20 mmol). After 1 h, the mixture was loaded onto a diatomaceous earth and was purified by reverse phase chromatography, eluting with 1:2 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile to give the title compound (19 mg, 57% yield). ES/MS m/z 780.4 (M+H). ^{1}H NMR (500.11 MHz, d_6-DMSO) δ 0.90 (s, 3H), 1.28-1.27 (m, 2H), 1.41 (s, 3H), 1.72-1.69 (m, 1H), 1.92-1.88 (m, 4H), 2.11-2.10 (m, 2H), 2.22 (s, 3H), 2.40-2.35 (m, 1H), 3.50-3.46 (m, 1H), 3.57-3.53 (m, 1H), 3.64-3.61 (m, 1H), 4.17-4.15 (m, 1H), 4.34-4.32 (m, 1H), 4.43-4.39 (m, 2H), 4.57-4.52 (m, 1H), 4.64-4.62 (m, 1H), 4.75-4.72 (m, 2H), 5.00-4.93 (m, 3H), 5.12-5.08 (m, 2H), 5.31-5.29 (m, 1H), 5.95 (d, J= 0.4 Hz, 1H), 6.20-6.17 (m, 1H), 6.34 (s, 1H), 6.54-6.49 (m, 2H), 6.59 (s, 1H), 6.88 (d, J= 8.5 Hz, 1H), 7.00 (t, J= 7.7 Hz, 1H), 7.12-7.08 (m, 1H), 7.35-7.33 (m, 1H).

Example 4

(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-Aminobenzyl)oxy)-2-fluoro-6-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

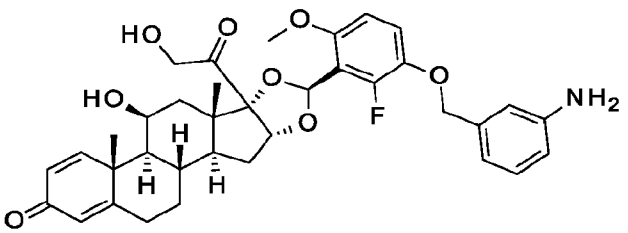


To a suspension of tert-butyl (3-((2-fluoro-3-formyl-4-methoxyphenoxy)methyl)phenyl)carbamate (2.6 g, 6.9 mmol, preparation 8) and 16alpha-hydroxyprednisolone (2.5 g, 6.6 mmol) in acetonitrile (100 mL) at -20 °C was added perchloric acid (70% in water, 3.3 mL, 5 equiv) dropwise. The mixture was stirred at -20 °C for 7 h. The solution was transferred to a separatory funnel. The solution was added dropwise to an aqueous solution of sodium hydroxide (7.5 mL 5N aq NaOH in 1 L water). After the addition was completed, the pH was measured at 5 and the pH was adjusted to 8 with 5N aq NaOH. The suspension was stirred for 10 minutes. The solid was collected by vacuum filtration and the solid was washed with water. The solid was dried on the filter overnight. The solid was purified by reverse phase chromatography, eluting with 1:1 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile to give the title compound, peak 1 (804 mg, 18% yield). MS m/z 634.2 (M+H).

^{1}H NMR (399.8 MHz, d_6-DMSO) δ 7.33 (d, J= 10.1 Hz, 1H), 7.17 (t, J= 9.2 Hz, 1H), 6.98 (t, J= 7.8 Hz, 1H), 6.76 (dd, J= 1.0, 9.2 Hz, 1H), 6.56 (d, J= 1.6 Hz, 1H), 6.52-6.48 (m, 2H), 6.17 (dd, J= 1.9, 10.1 Hz, 1H), 5.96 (s, 1H), 5.71 (s, 1H), 5.17 (t, J= 6.0 Hz, 1H), 5.10 (s, 2H), 4.94-4.90 (m, 3H), 4.79 (d, J= 3.1 Hz, 1H), 4.44-4.38 (m, 1H), 4.33-4.31 (m, 1H), 4.22-4.15 (m, 1H), 3.70 (s, 3H), 2.37-2.33 (m, 1H), 2.14-2.04 (m, 2H), 1.96-1.88 (m, 1H), 1.82-1.70 (m, 3H), 1.64-1.56 (m, 1H), 1.41 (s, 3H), 0.86 (s, 5H).

Example 5

(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-Aminobenzyl)oxy)-2-fluoro-6-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one



From Example 4, the residue was purified by reverse phase chromatography, eluting with 1:1 10 mM ammonium bicarbonate water + 5% methanol:acetonitrile to give the title compound peak 2 (1.19 g, 27% yield). MS m/z 634.2 (M+H).

^{1}H NMR (399.8 MHz, d_6-DMSO) δ 7.32 (d, J= 10.0 Hz, 1H), 7.17-7.12 (m, 1H), 6.99 (t, J= 7.7 Hz, 1H), 6.72 (d, J= 8.8 Hz, 1H), 6.58 (s, 1H), 6.53-6.46 (m, 3H), 6.18 (dd, J= 1.7, 10.1 Hz, 1H), 5.95 (s, 1H), 5.25 (d, J= 6.5 Hz, 1H), 5.10 (s, 2H), 5.00-4.90 (m, 3H), 4.78 (d, J= 3.1 Hz, 1H), 4.37-4.31 (m, 2H), 4.02-3.96 (m, 1H), 3.63 (s, 3H), 2.34-2.31 (m, 1H), 2.11-2.02 (m, 2H), 1.88-1.76 (m, 4H), 1.60-1.54 (m, 1H), 1.40 (s, 3H), 1.23-1.18 (m, 2H), 0.87 (s, 3H).

Alternative Preparation of Example 5

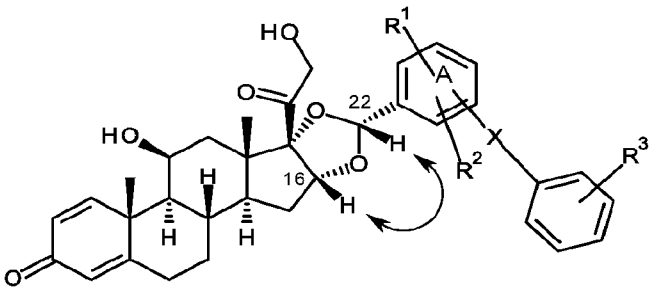
All solid handling steps were handled in a disposable glove bag including charging the flask with 16alpha-hydroxyprednisolone, solid filtration steps and solid transfer steps.

To a suspension of tert-butyl (3-((2-fluoro-3-formyl-4-methoxyphenoxy)methyl)phenyl)carbamate (25 g, 67 mmol, preparation 8) and 16alpha-hydroxyprednisolone (25 g, 65 mmol) in ACN (1000 mL) at -25 °C in a 2-L round bottom flask was added perchloric acid in water (31 mL, 330 mmol, 10.6 mol/L) dropwise. The mixture was stirred at -20 °C while monitoring the reaction by LCMS. Internal temperature monitoring indicated a small exotherm upon addition of perchloric acid. The internal temperature was kept below -19 °C with dry ice addition. The mixture was kept below -19 °C for 2 h and then was allowed to warm to -10 °C. The mixture split in

two and added dropwise to two separate beakers (Beaker 1 and Beaker 2) containing 76 mL of 5 M aq NaOH in 2 L of water, each. A solid formed upon addition and complete quench of perchloric acid was tested (pH 10). The sticky solid from each addition was transferred and combined to a third beaker (Beaker 3) containing 10% MeOH in DCM. The mixture was stirred until the sticky solid completely dissolved. The remaining solutions (Beaker 1 and Beaker 2) were then filtered through paper to collect residual solids. The isolated solids were rinsed with water and transferred to Beaker 3. Beaker 3 was stirred until all solids were dissolved. The solution was dried for 2 h with Na_2SO_4, filtered and evaporated to give a tan foam. The filtrates from the solid collection were extracted with three portions 10% IPA in DCM. The combined organic extracts were dried over Na_2SO_4 with stirring overnight, then filtered and evaporated to give additional crude residue. The crude products were dissovled in 150 mL 1% MeOH in DCM and purified by normal phase chromatography using 0-5% MeOH in DCM to give a solid. It was diluted with 600 mL EtOH and spun on the rotary evaporator at 45 °C for 5 minutes. The heat bath was turned up to 60 °C. When the heat bath reached 60 °C it was turned off and the flask spun until the bath reached rt. The flask was taken off the rotary evaporator, capped and allowed to stand overnight at room temperature.

The solid was collected by vacuum filtration in a glove bag. The solids were rinsed with EtOH and dried on the filter for 5 h. The solid redissolved in 20% EtOH in DCM (1.5 L). Additional DCM was added to achieve a near clear solution (some haze persisted). Solvent exchange was achieved by rotary evaporation at 450 mbar and 45 °C to remove DCM. Once distillation had stopped, the pressure was decreased to 100 mbar to bring off EtOH to approximately 600 mL. The mixture was removed from the rotary evaporator and allowed to stand for 5 h at rt. The solid was collected by vacuum filtration and the solids washed twice with additional EtOH. The filter cake was dried in a vacuum oven at rt for 48 h to give the title compound (42 g, 38% yield). MS m/z 634.6 (M+H).

Structural assignment by NMR



Two dimensional through-space ROE NMR analysis of acetal isomers consistently gave a cross peak for H22 (acetal) and H16 in the *R* configuration. Alternatively, H22 in the *S* configuration consistently gave about 1 ppm larger shift. All other compounds were assigned essentially by the same method.

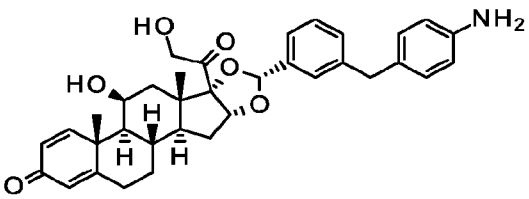
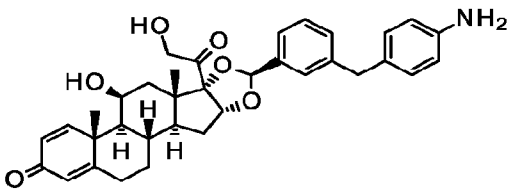
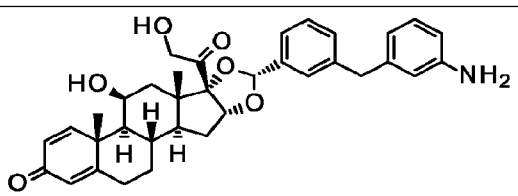
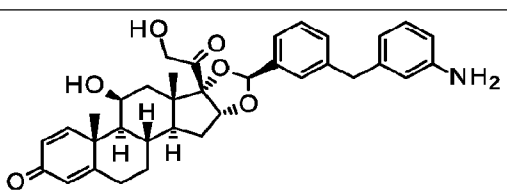
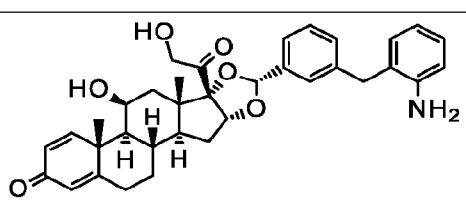
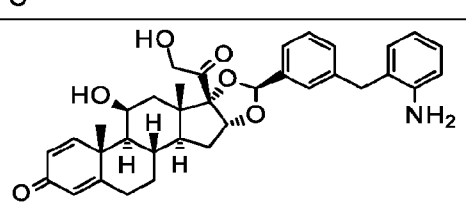
The following compounds in Table 18a were prepared in a manner essentially analogous to the procedures described in Examples 1 to 4 utilizing the corresponding starting material of structure 1a and starting material of structure 2 as prepared in the corresponding preparations and tables 2-17 described above or prepared using standard procedures well known to one of ordinary skill in the art. Purification of final products was performed essentially by the following methods:

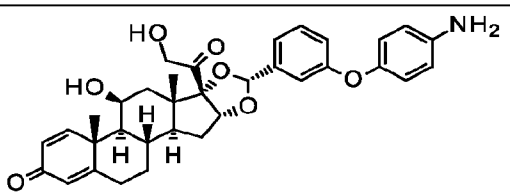
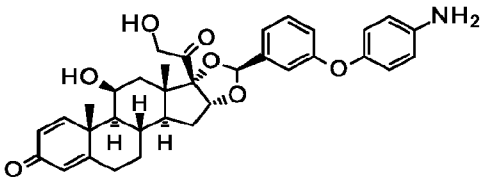
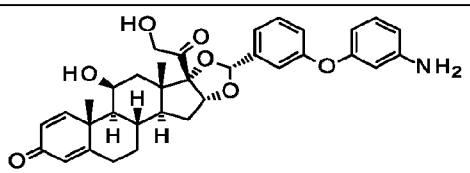
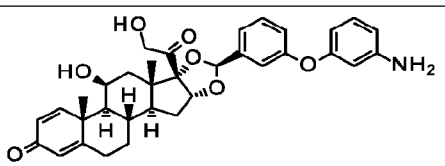
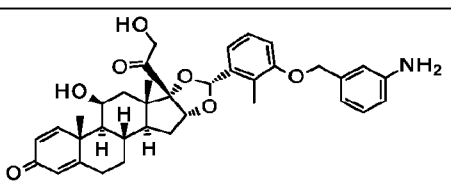
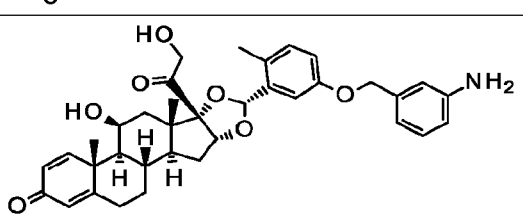
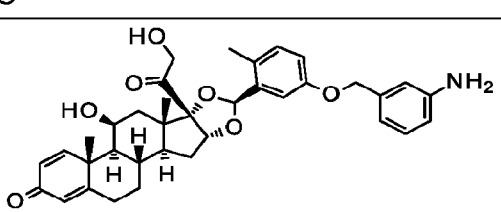
A. C18 column using eluent 10mM NH_4HCO_3 in water + 5% MeOH:ACN
B. C18 column using eluent 0.1% FA in water:ACN
C. SFC Chiralpak AY using eluent EtOH + 0.05% DEA:CO_2
D. Chiralpak IC using eluent MeOH + 0.2% IPAm
E. SFC Lux Amylose-2 using eluent IPA + 0.5% DMEA:CO_2
F. SFC Chiralpak AD-H using eluent IPA + 0.5% DMEA:CO_2
G. Chiralpak IC using eluent EtOH + 0.1% NH_3H_2O:heptane
H. SFC Chiralpack AD using eluent IPA + 0.1% NH_3H_2O:CO_2
I. Chiralcel IH using eluent EtOH+ACN (0.1% DEA):heptane
J. SFC Chiralpak AD using eluent EtOH + 0.5% DEA:CO_2
K. Chiralpak IE using eluent EtOH + 0.1% NH_3H_2O:ACN
L. Chiralpak AD-H using eluent EtOH:ACN + 0.2% IPAm
M. Chiralpak AD-H using eluent EtOH:ACN

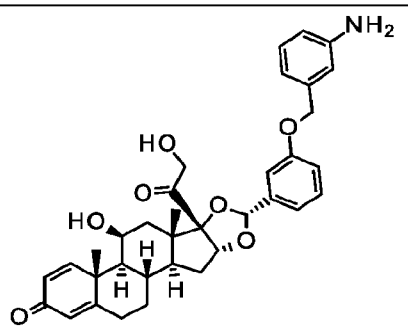
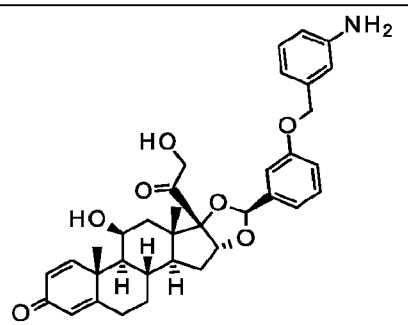
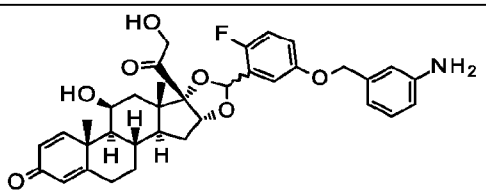
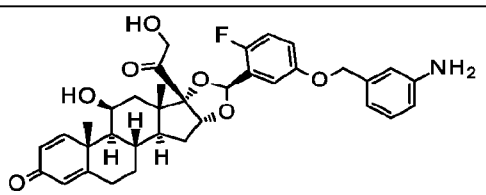
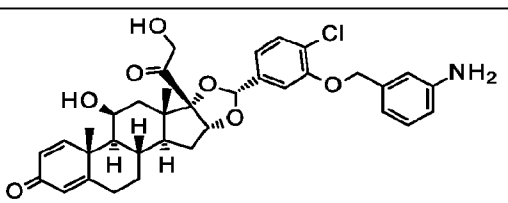
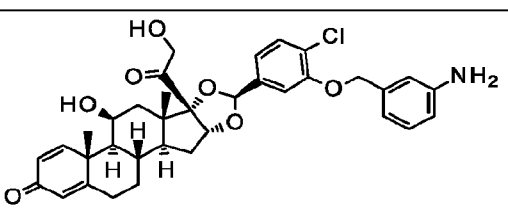
N. SFC Chiralpak IC using eluent EtOH + 0.05% DMEA:CO_2

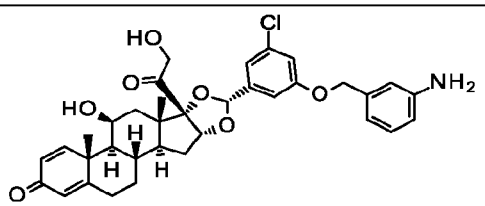
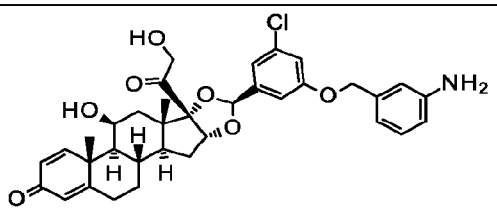
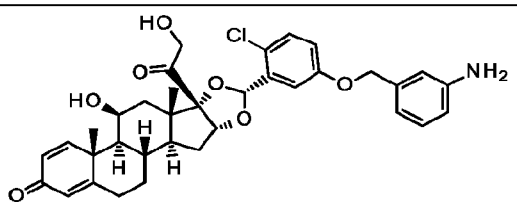
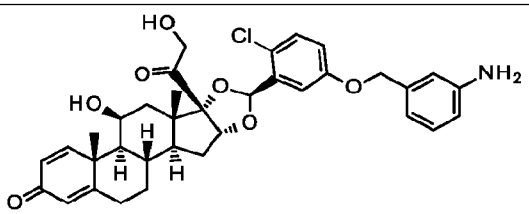
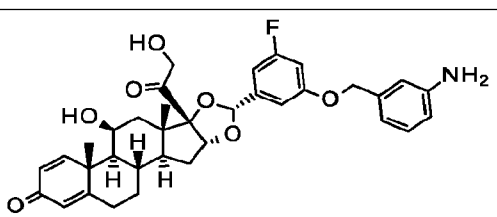
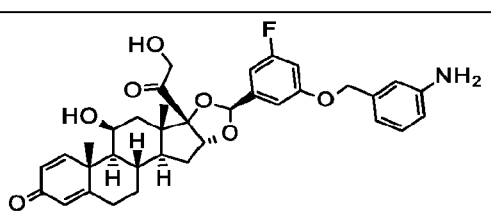
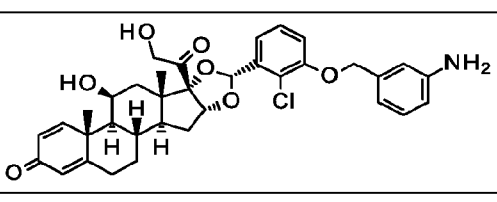
O. SFC Chiralcel OJ-H using eluent MeOH + 0.5% DMEA:CO_2

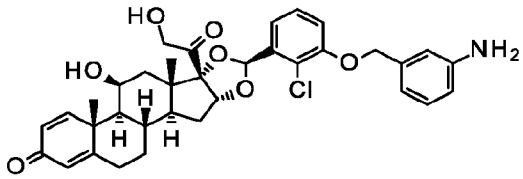
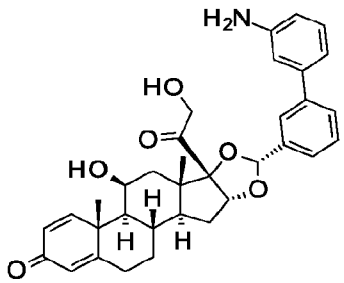
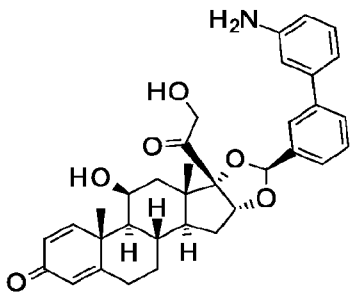
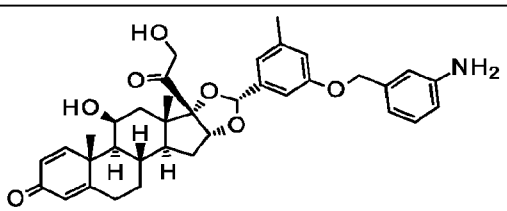
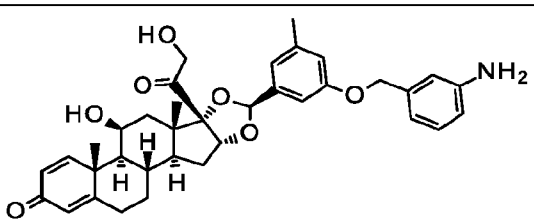
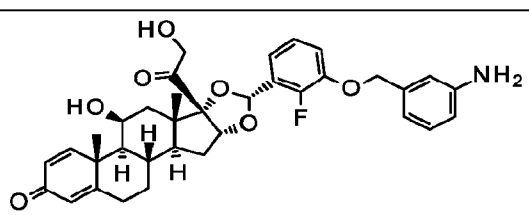
Table 18a: Examples 6-158 (structures)

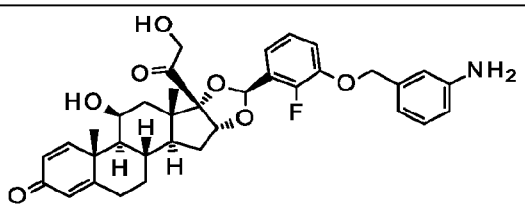
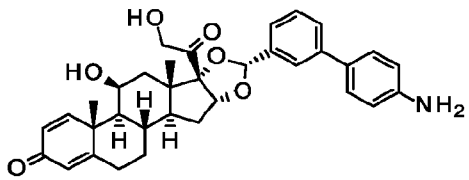
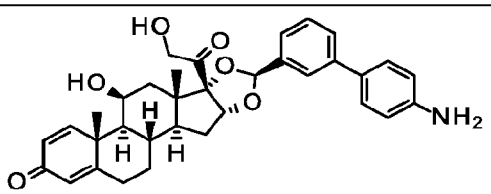
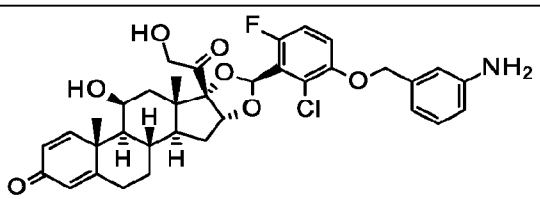
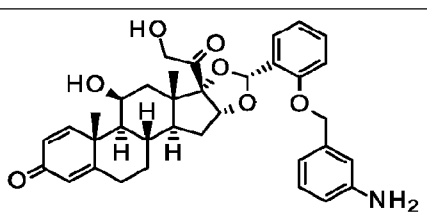
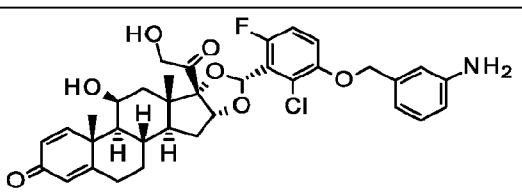
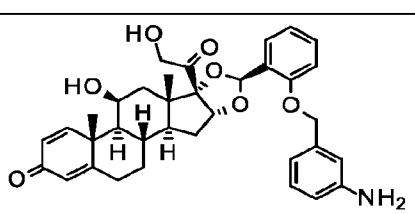
Ex No.	Structure	ES/MS (m/z) (M+H)	Purification method*
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7		570.4	A
8		570.4	A
9		570.4	A
10		571.4	B
11		570.4	B

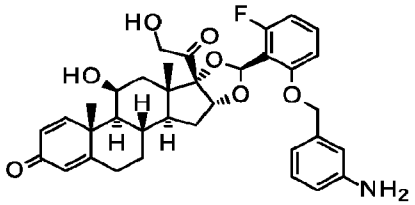
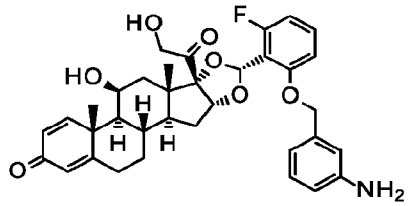
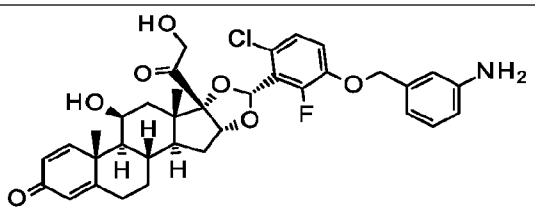
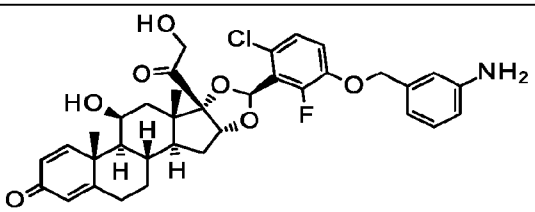
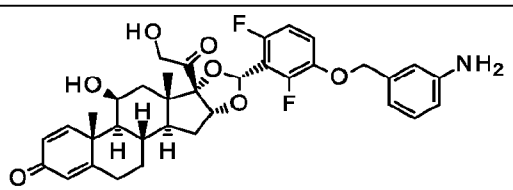
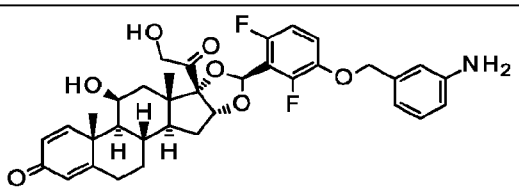
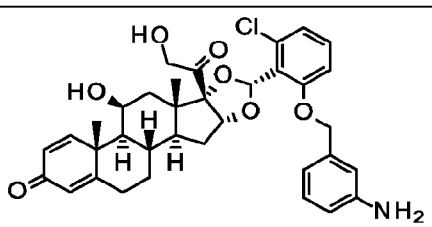
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13		572.2	A
14		572.2	A
15		572.2	A
16		600.2	A
17		600.2	A
18		600.2	A

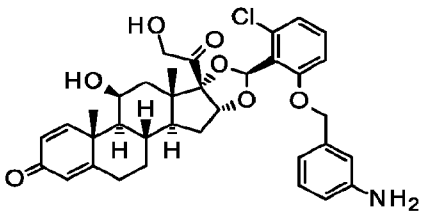
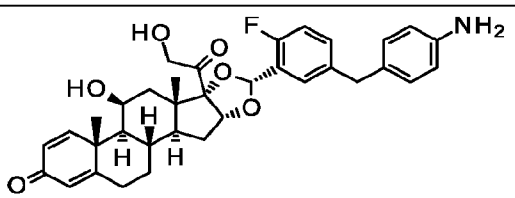
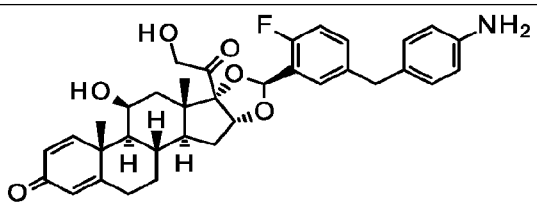
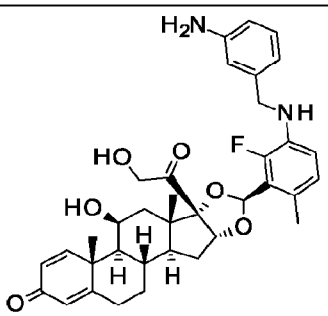
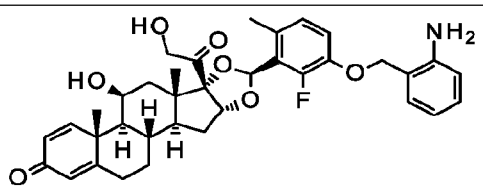
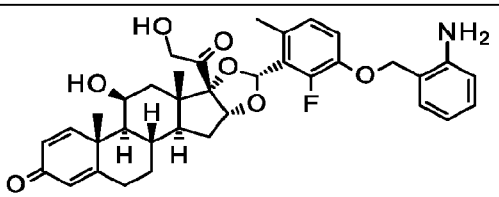
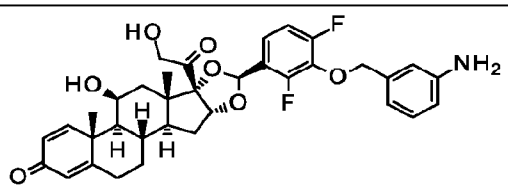
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20		586.2	A
21		604.2	A
22		604.2	A, O
23		620.2	A
24		620.2	A

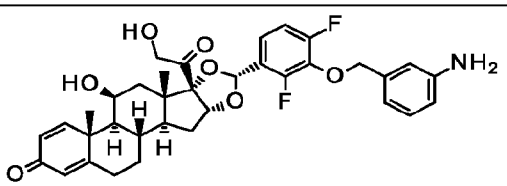
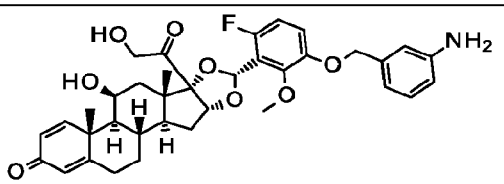
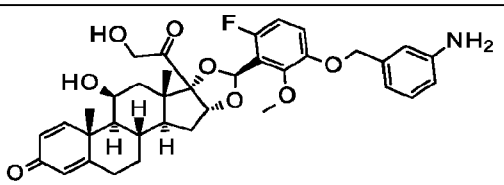
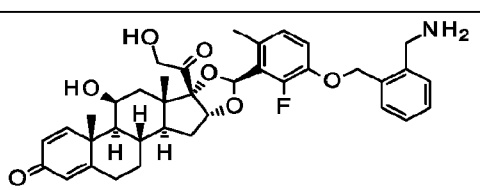
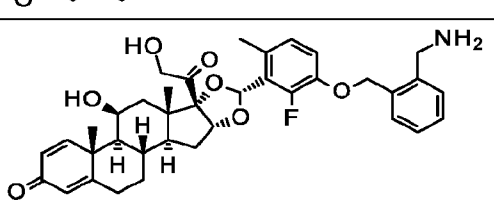
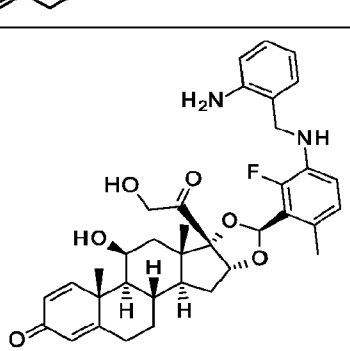
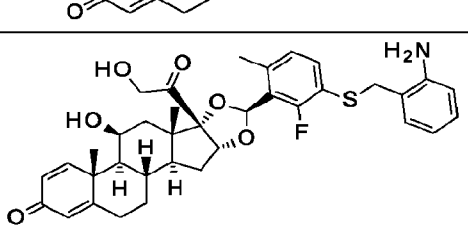
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27		620.2	A
28		620.2	A
29		604.2	A
30		604.2	A
31		620.4	M

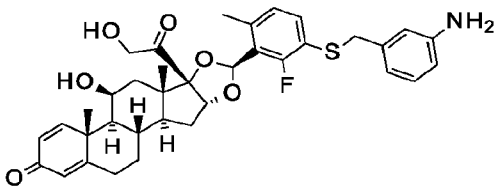
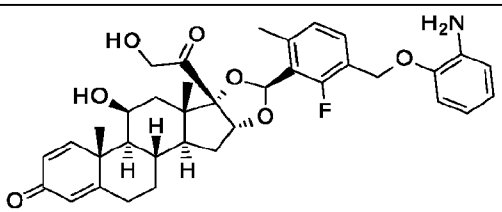
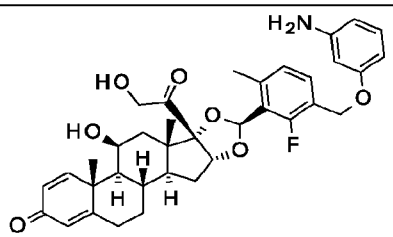
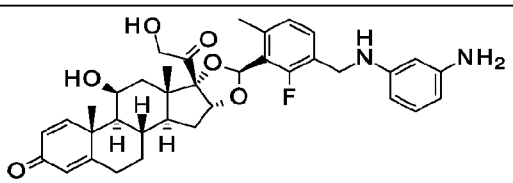
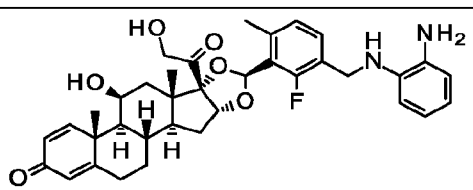
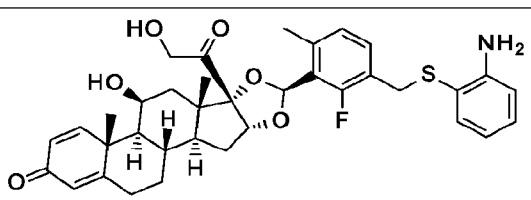
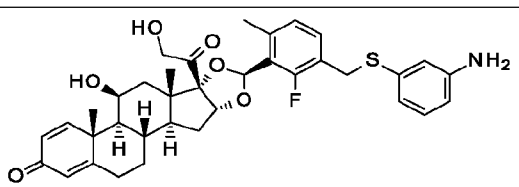
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33		556.2	A
34		556.2	A
35		600.2	A
36		600.2	A
37		604.2	A

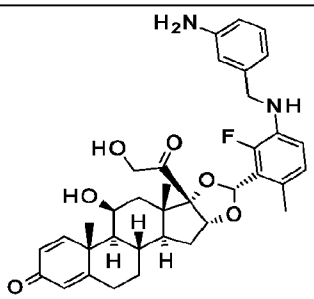
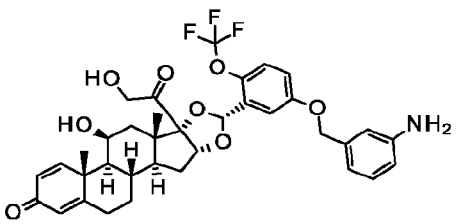
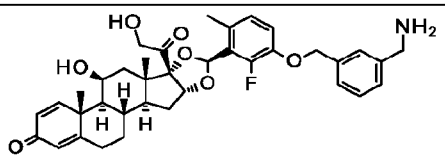
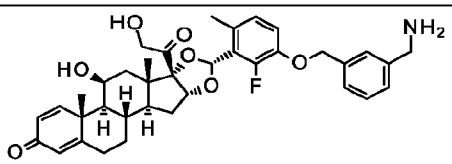
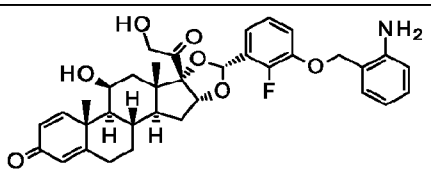
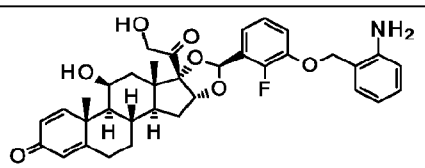
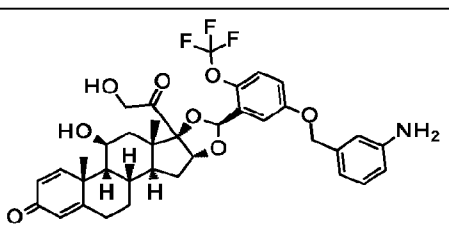
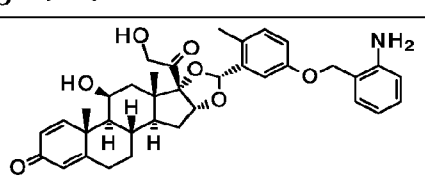
38		604.2	A
39		556.2	A
40		556.2	A
41		638.4	A, L
42		586.4	A, L
43		638.4	A, L
44		586.4	A, L

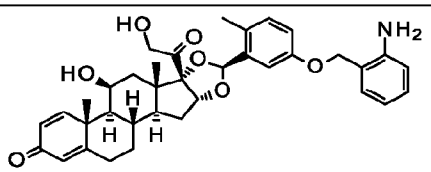
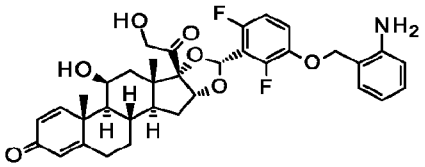
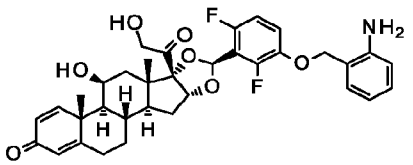
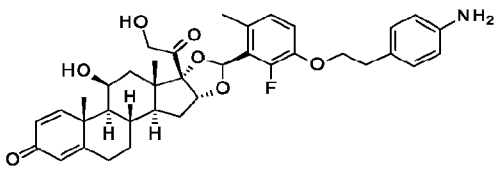
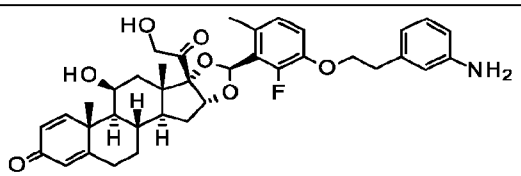
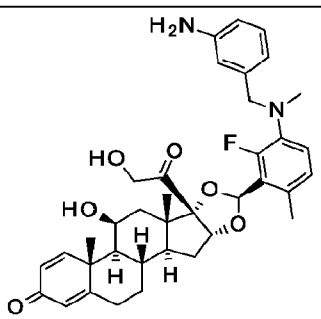
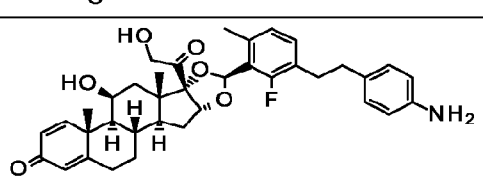
45		604.4	A, O
46		604.4	A, O
47		638.2	A
48		638.2	A
49		622.3	A
50		622.3	A
51		620.5	A, O

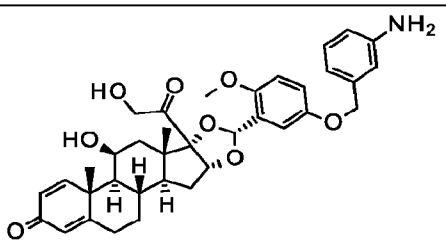
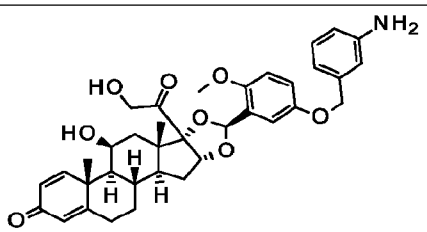
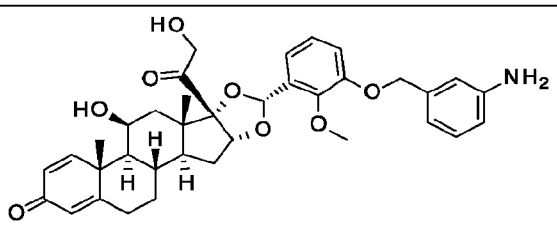
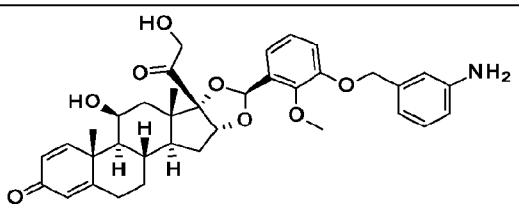
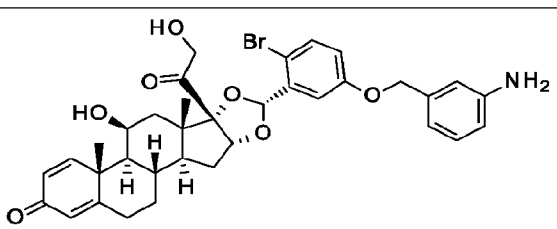
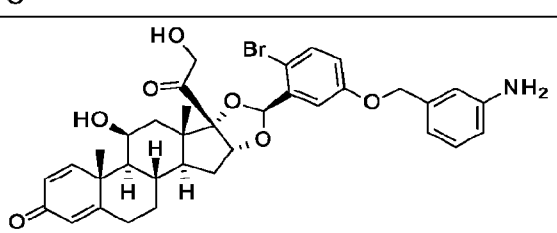
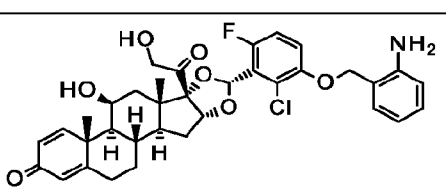
52		620.5	A, O
53		588.2	A
54		588.2	A
55		617.5	B, C
56		618.4	A
57		618.4	A
58		622.0	A

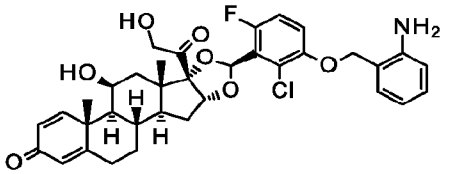
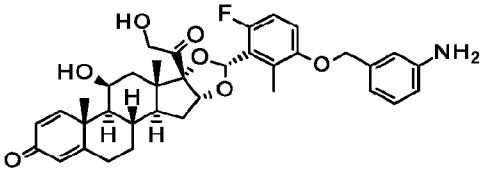
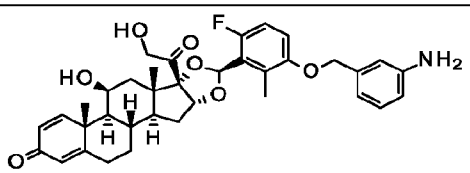
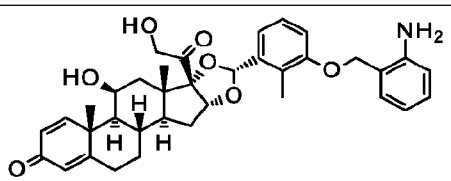
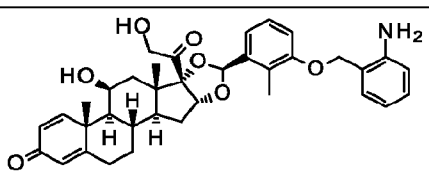
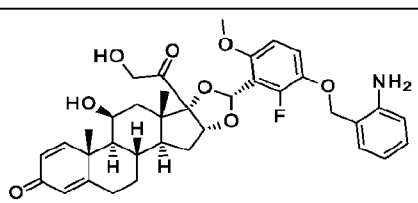
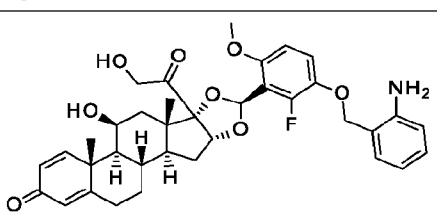
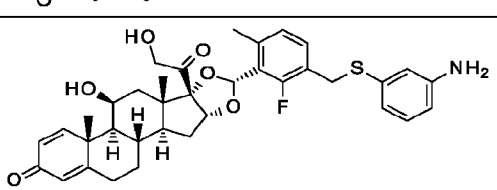
59		622.4	A
60		634.3	A
61		634.3	A
62		632.4	A
63		632.4	A
64		617.6	B, J
65		634.5	B

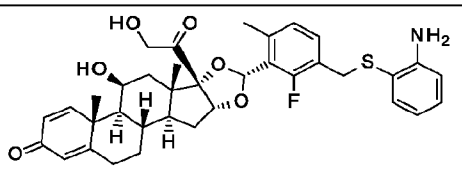
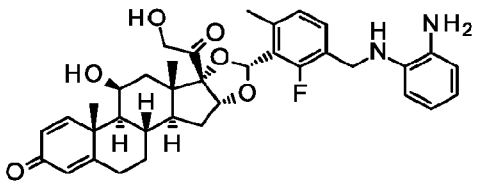
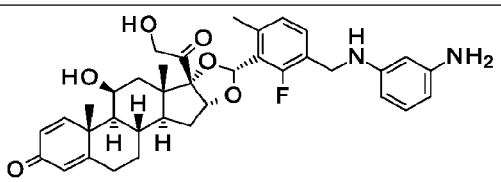
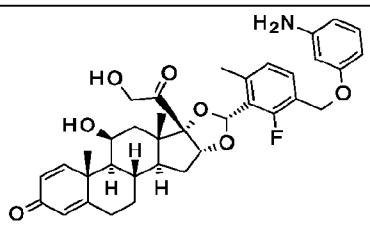
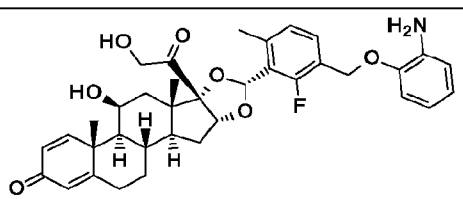
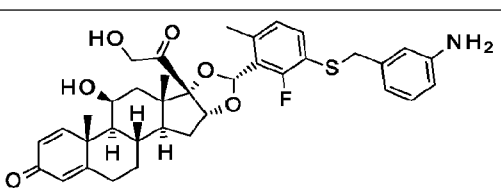
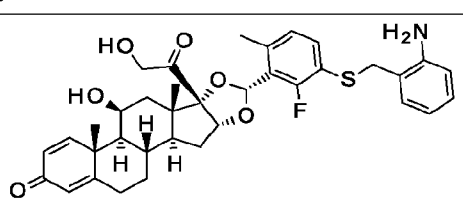
66		634.5	B
67		618.5	B, I
68		618.5	B
69		617.5	B
70		617.0	B, K
71		634.5	A, G
72		634.1	B, H

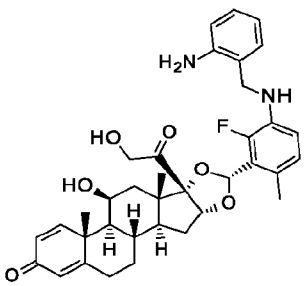
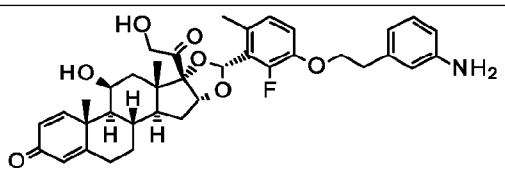
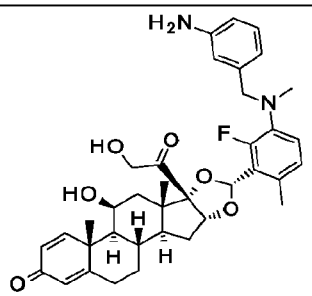
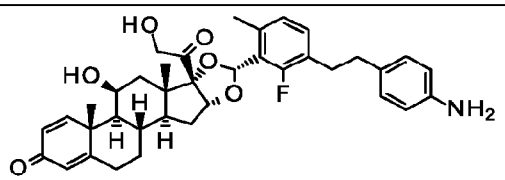
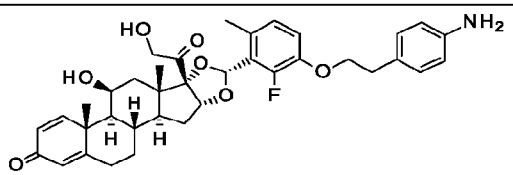
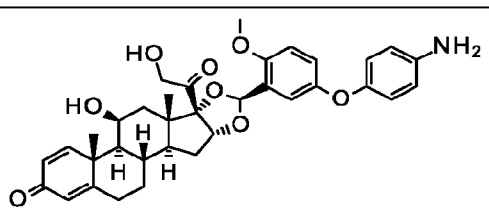
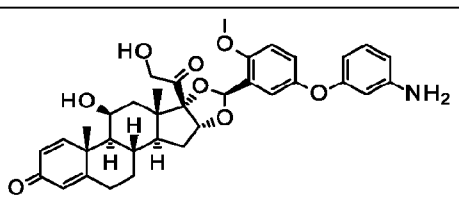
73		617.5	B, C
74		670.4	A
75		632.2	A
76		632.2	A
77		604.4	A
78		604.3	A
79		670.4	A
80		600.6	A

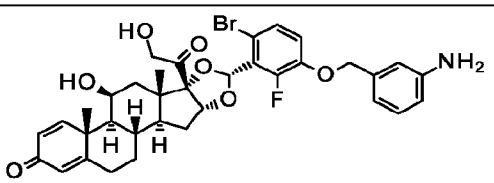
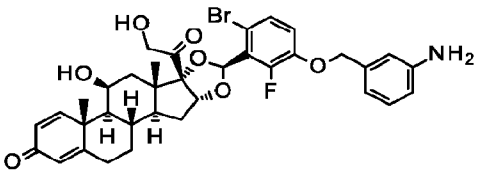
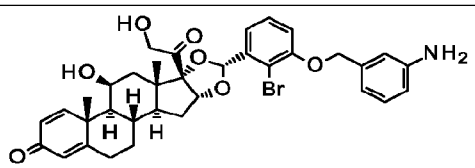
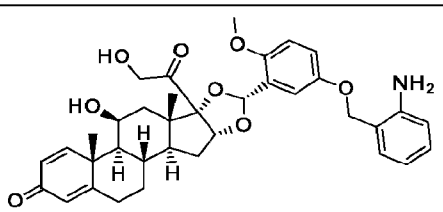
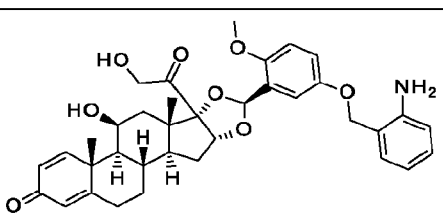
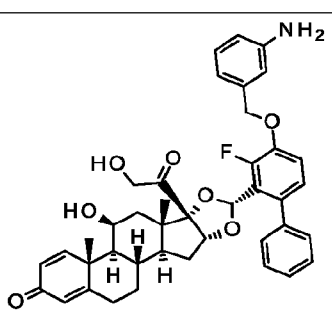
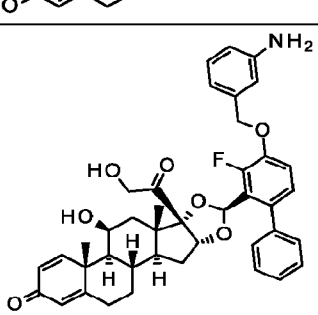
81		600.6	A
82		622.4	A
83		622.3	A
84		632.4	B, H
85		632.4	A
86		631.5	B,G
87		616.5	B

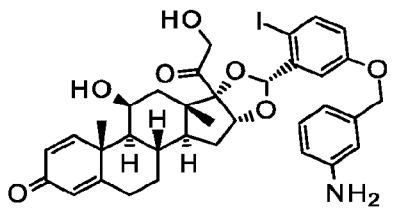
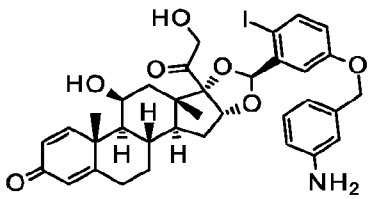
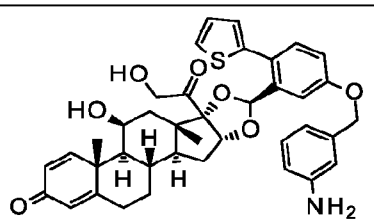
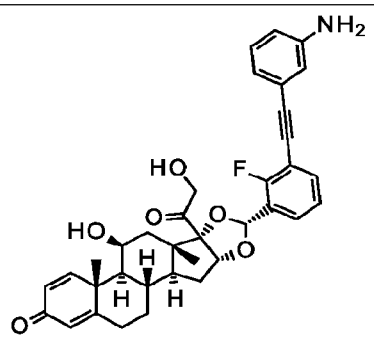
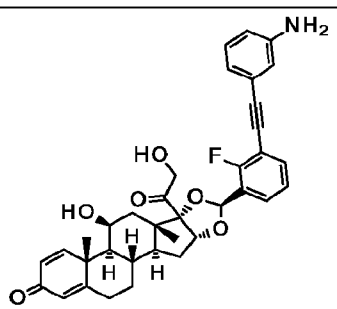
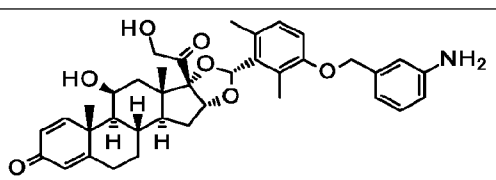
88		616.4	A
89		616.4	A
90		616.4	A
91		616.6	A
92		664.4	A
93		664.4	A
94		638.4	D

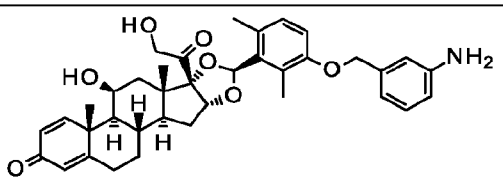
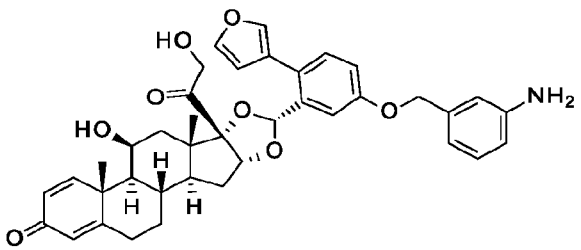
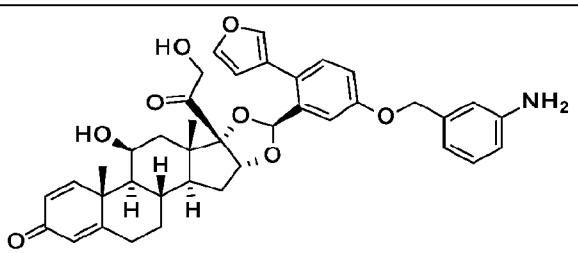
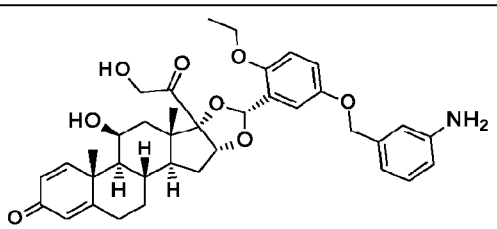
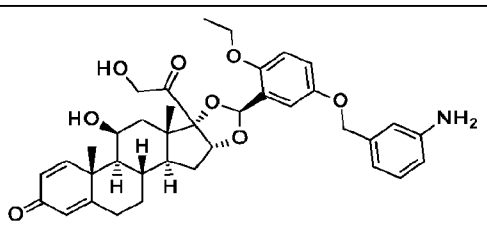
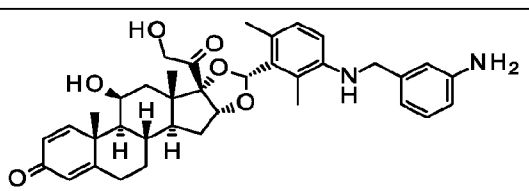
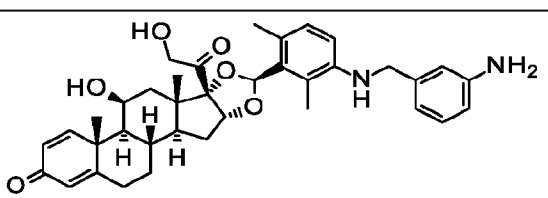
95		638.4	D
96		618.6	N
97		618.6	N
98		600.2	B
99		600.2	B
100		634.4	A
101		634.4	A
102		634.5	B, H

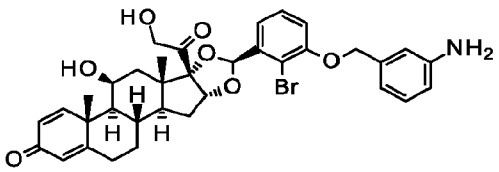
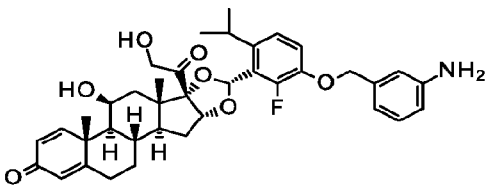
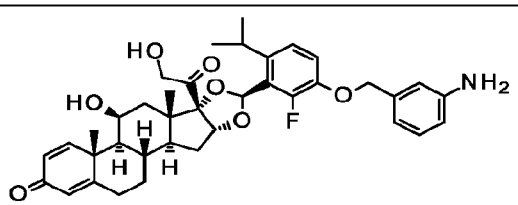
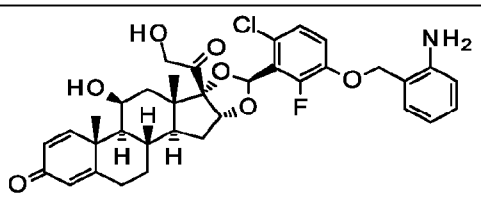
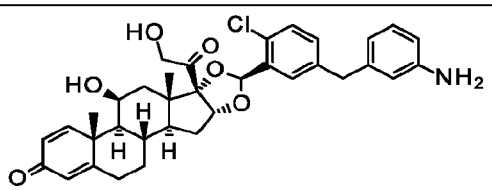
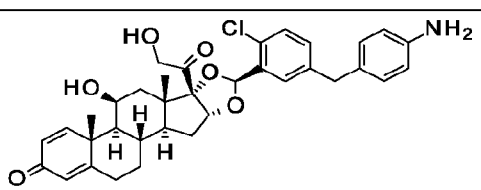
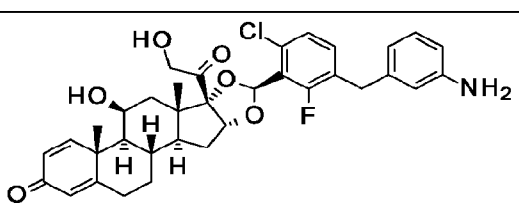
103		634.5	B, G
104		617.1	B, K
105		617.5	B
106		618.5	B
107		618.5	B, I
108		634.5	B
109		634.5	B

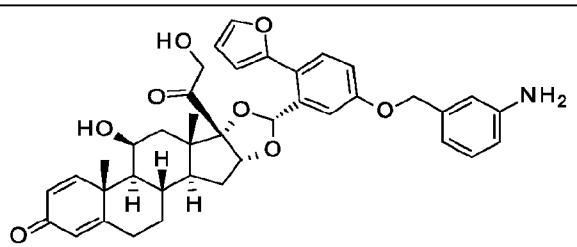
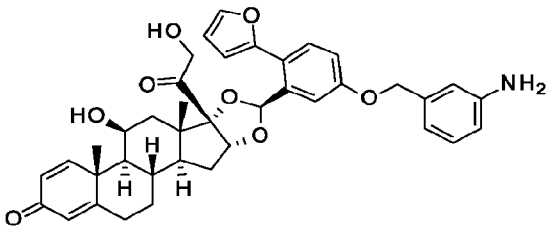
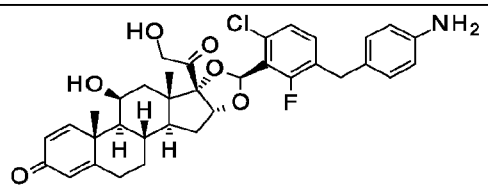
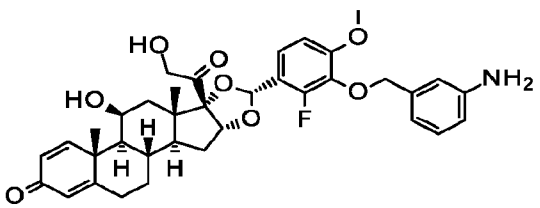
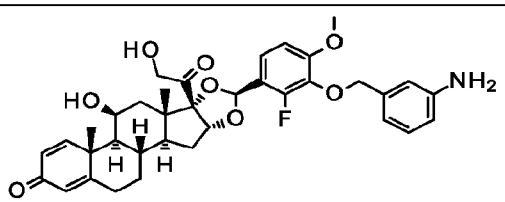
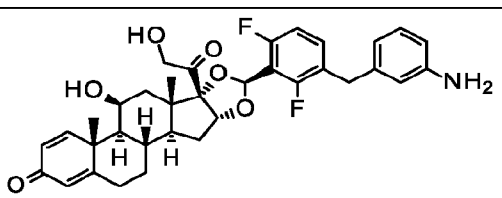
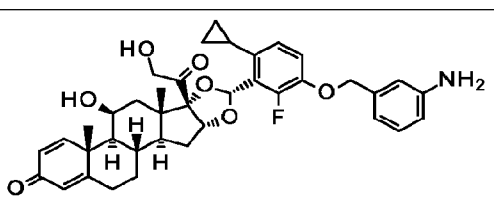
110		617.6	B, J
111		632.2	A
112		631.4	B, G
113		616.5	B
114		632.4	B, H
115		602.2	A
116		602.2	A

117		682.2	A
118		682.2	A
119		666.4	F
120		616.4	A
121		616.4	A
122		680.6	B
123		679.8	B

124		711.6	A
125		712.0	A
126		667.8	B
127		597.8	A
128		597.8	A
129		614.6	F

130		614.6	F
131		651.8	B
132		651.8	B
133		630.4	A
134		630.4	A
135		613.6	E
136		613.6	E

137		666.4	F
138		646.4	A
139		646.4	A
140		638.1	A
141		604.4	A
142		604.4	A
143		622.2	A

144		651.8	B
145		651.8	B
146		622.0	A
147		634.2	A
148		634.4	A
149		606.4	A
150		644.4	A

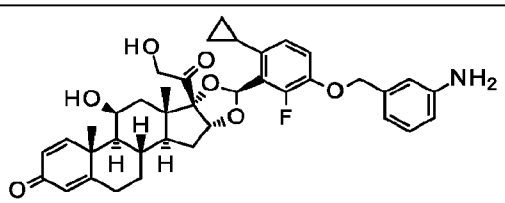
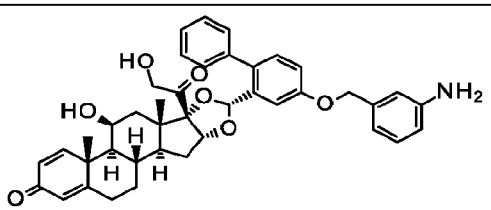
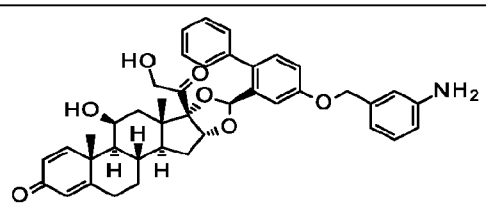
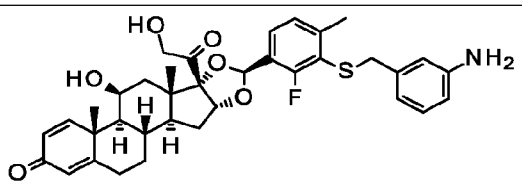
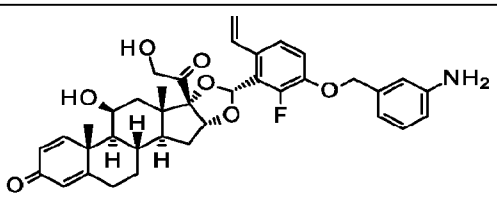
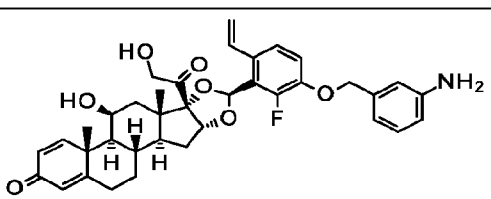
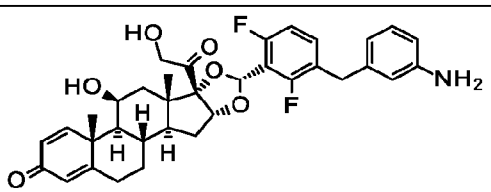
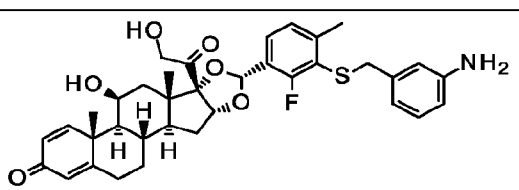
151		644.4	A
152		662.4	A
153		662.4	A
154		634.5	B
155		630.4	A
156		630.4	A
157		606.4	A
158		634.5	B

Table 18b: Examples 6-158 (chemical names)

Ex No.	Chemical Name
6	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(4-aminobenzyl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
7	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(4-aminobenzyl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
8	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(3-aminobenzyl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
9	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(3-aminobenzyl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
10	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(2-aminobenzyl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
11	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(2-aminobenzyl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
12	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(4-aminophenoxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

13	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(4-aminophenoxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
14	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(3-aminophenoxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
15	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(3-aminophenoxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
16	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
17	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
18	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
19	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
20	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

21	(6aR,6bS,7S,8aS,8bS,10RS,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
22	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
23	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-4-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
24	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-4-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
25	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-5-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
26	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-5-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
27	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
28	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-

	1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
29	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-5-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
30	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-5-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
31	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
32	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
33	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3'-amino-[1,1'-biphenyl]-3-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
34	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3'-amino-[1,1'-biphenyl]-3-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
35	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-5-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
36	

	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-5-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
37	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
38	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
39	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(4'-amino-[1,1'-biphenyl]-3-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
40	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(4'-amino-[1,1'-biphenyl]-3-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
41	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-chloro-6-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
42	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(2-((3-aminobenzyl)oxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
43	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-chloro-6-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

44	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(2-((3-aminobenzyl)oxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
45	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(2-((3-aminobenzyl)oxy)-6-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
46	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(2-((3-aminobenzyl)oxy)-6-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
47	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-chloro-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
48	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-chloro-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
49	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2,6-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
50	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2,6-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
51	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(2-((3-aminobenzyl)oxy)-6-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

52	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(2-((3-aminobenzyl)oxy)-6-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
53	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-(4-aminobenzyl)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
54	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-(4-aminobenzyl)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
55	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)amino)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
56	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
57	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
58	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2,4-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
59	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2,4-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-

	1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
60	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-fluoro-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
61	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-fluoro-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
62	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-(aminomethyl)benzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
63	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-(aminomethyl)benzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
64	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)amino)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
65	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)thio)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
66	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)thio)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
67	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminophenoxy)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-

	hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
68	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminophenoxy)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
69	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(((3-aminophenyl)amino)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
70	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(((2-aminophenyl)amino)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
71	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(((2-aminophenyl)thio)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
72	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(((3-aminophenyl)thio)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
73	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)amino)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
74	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(trifluoromethoxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
75	

	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-(aminomethyl)benzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
76	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-(aminomethyl)benzyl)oxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
77	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
78	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodccahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
79	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(trifluoromethoxy)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
80	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((2-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
81	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((2-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
82	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2,6-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

83	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2,6-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
84	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(4-aminophenethoxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
85	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(3-aminophenethoxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
86	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)(methyl)amino)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
87	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(4-aminophenethyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
88	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
89	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
90	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

91	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
92	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-bromophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
93	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-bromophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
94	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-chloro-6-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
95	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-chloro-6-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
96	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-fluoro-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
97	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-fluoro-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
98	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-

	1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
99	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
100	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-fluoro-6-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
101	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-2-fluoro-6-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
102	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(((3-aminophenyl)thio)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
103	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(((2-aminophenyl)thio)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
104	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(((2-aminophenyl)amino)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
105	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(((3-aminophenyl)amino)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
106	

	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminophenoxy)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
107	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminophenoxy)methyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
108	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)thio)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
109	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)thio)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
110	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)amino)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
111	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(3-aminophenethoxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
112	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)(methyl)amino)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
113	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(4-aminophenethyl)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

114	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(4-aminophenethoxy)-2-fluoro-6-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
115	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-(4-aminophenoxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
116	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-(3-aminophenoxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
117	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-bromo-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
118	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-bromo-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
119	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-bromophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
120	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((2-aminobenzyl)oxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
121	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((2-aminobenzyl)oxy)-2-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

122	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(4-((3-aminobenzyl)oxy)-3-fluoro-[1,1'-biphenyl]-2-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
123	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(4-((3-aminobenzyl)oxy)-3-fluoro-[1,1'-biphenyl]-2-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
124	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-iodophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
125	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-iodophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
126	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(thiophen-2-yl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
127	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminophenyl)ethynyl)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
128	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminophenyl)ethynyl)-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
129	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2,6-dimethylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-

	1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
130	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2,6-dimethylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
131	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(furan-3-yl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
132	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(furan-3-yl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
133	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-ethoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
134	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-ethoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
135	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)amino)-2,6-dimethylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
136	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)amino)-2,6-dimethylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
137	

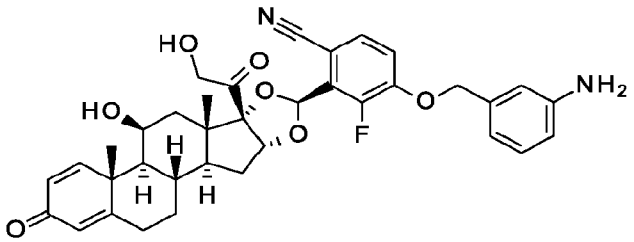
	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-bromophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
138	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-isopropylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
139	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-isopropylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
140	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((2-aminobenzyl)oxy)-6-chloro-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
141	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-(3-aminobenzyl)-2-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
142	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-(4-aminobenzyl)-2-chlorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
143	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(3-aminobenzyl)-6-chloro-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
144	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(furan-2-yl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

145	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(5-((3-aminobenzyl)oxy)-2-(furan-2-yl)phenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
146	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(4-aminobenzyl)-6-chloro-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
147	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-4-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
148	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-4-methoxyphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
149	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-(3-aminobenzyl)-2,6-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
150	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-cyclopropyl-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
151	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-6-cyclopropyl-2-fluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
152	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(4-((3-aminobenzyl)oxy)-[1,1'-biphenyl]-2-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

153	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(4-((3-aminobenzyl)oxy)-[1,1'-biphenyl]-2-yl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
154	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)thio)-2-fluoro-4-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
155	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-vinylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
156	(6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)oxy)-2-fluoro-6-vinylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
157	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-(3-aminobenzyl)-2,6-difluorophenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one
158	(6aR,6bS,7S,8aS,8bS,10R,11aR,12aS,12bS)-10-(3-((3-aminobenzyl)thio)-2-fluoro-4-methylphenyl)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-1,2,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-4H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-4-one

Example 159

4-((3-Aminobenzyl)oxy)-3-fluoro-2-((6aR,6bS,7S,8aS,8bS,10S,11aR,12aS,12bS)-7-hydroxy-8b-(2-hydroxyacetyl)-6a,8a-dimethyl-4-oxo-2,4,6a,6b,7,8,8a,8b,11a,12,12a,12b-dodecahydro-1H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-10-yl)benzonitrile



Trifluoromethanesulfonic acid (920 μL, 10 mmol) was added dropwise to a suspension of 16alpha-hydroxyprednisolone (140 mg, 0.36 mmol) and tert-butyl (3-((4-cyano-3-(1,3-dioxolan-2-yl)-2-fluorophenoxy)methyl)phenyl)carbamate (140 mg, 0.34 mmol) in ACN (5 mL, 95 mmol) at 0 °C. The reaction was quenched with satd aq $NaHCO_3$ and extracted with 10% IPA in DCM. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated to a crude residue. The crude residue was purified by reverse phase purification, eluting with 1:1 10mM NH_4HCO_3 in water + 5% MeOH:ACN to give the title compound (12 mg, 6% yield). MS m/z 630.0 (M+H). ^1H NMR (400.13 MHz, d_6-DMSO) δ 7.70-7.67 (m, 1H), 7.45-7.41 (m, 1H), 7.33 (d, J= 10.1 Hz, 1H), 7.04-7.00 (m, 1H), 6.61-6.51 (m, 3H), 6.45 (s, 1H), 6.20-6.17 (m, 1H), 5.95 (s, 1H), 5.37-5.35 (m, 1H), 5.15 (s, 4H), 4.86-4.84 (m, 1H), 4.32-4.31 (m, 2H), 4.07-4.01 (m, 1H), 2.14-2.12 (m, 2H), 1.92-1.88 (m, 4H), 1.67-1.66 (m, 1H), 1.40-1.39 (m, 3H), 1.25-1.20 (m, 2H), 0.89-0.88 (m, 3H).

hGR CoActivator Recruitment Assay

The activity of glucocorticoid compounds was measured using the LanthaScreen TR-Fret GR Coactivator Assay from Life Technologies (A15899). The compounds were acoustically transferred to an assay plate in a 3-fold 10-point serial dilution with a top concentration of 200 nM. Ten microliters of a 2x solution of GR-LBD was added to the compound plate and incubated for 10 min. Then ten microliters of a 2x solution of Fluoresein-SRC1-4 and Tb labelled anti-GST antibody were added to the plate. The plate was incubated in the dark for two hours and then read on an Envision plate reader, with excitation at 340 nm and emission at 520 nm (Fluorescein) and 490 nm (Terbium). The emission ratio of 520/490 was analyzed in Genedata. To obtain percent activity, the data was compared to a negative control of DMSO and positive control of 4uM dexamethasone. The following exemplified compounds were tested following the procedure as essentially described above and exhibited the following activity as listed in Table 19.

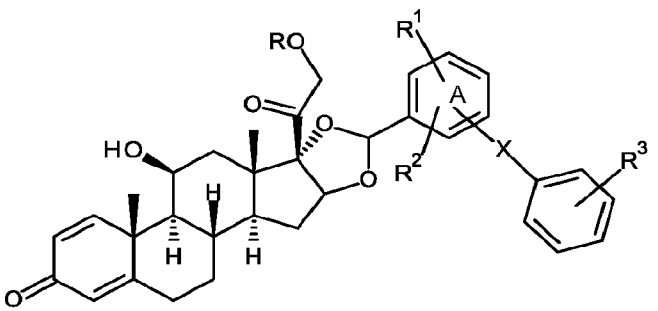
Table 19: *In vitro* potency of compounds of Examples 1, 2, 4, and 5 in the hGR CoActivator Recruitment Assay

Example No.	**IC_{50} (nM)**
1	2.12
2	1.44
4	2.47
5	1.40

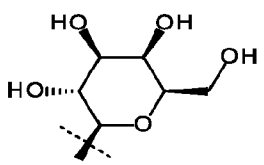
The compounds of Examples 6-44, 46-51, 53-79, and 81-158 provided a relative IC_{50} of less than 200 nM. The compounds of Examples 45, 52, and 80 provided a relative IC_{50} of greater than 200 nM.

WHAT IS CLAIMED IS:

1. A compound of the formula:

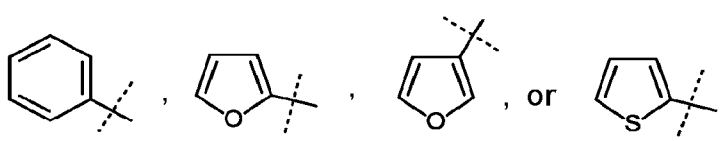


wherein R is H or



;

R^1 is H, halogen, CN, C1-C3 alkyl, C3-C6 cycloalkyl, C1-C3 alkoxy, C2-C3 alkenyl, OCF_3,



;

R^2 is H, halogen, C1-C3 alkyl, C1-C3 alkoxy, or C2-C3 alkenyl;

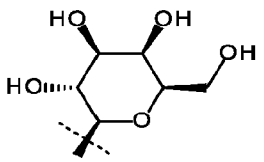
R^3 is NH_2, or CH_2NH_2; and

X is O, OCH_2, OCH_2CH_2, CH_2O, SCH_2, CH_2S, CH_2, $NHCH_2$, CH_2NH, $N(CH_3)CH_2$, CH_2CH_2, C≡C, or a bond, wherein X is connected to phenyl ring A at the ortho or the meta position, or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1 wherein R^3 is NH_2, or a pharmaceutically acceptable salt thereof.

3. The compound according to either claim 1 or claim 2 wherein R is H, or a pharmaceutically acceptable salt thereof.

4. The compound according to either claim 1 or claim 2 wherein R is



,

or a pharmaceutically acceptable salt thereof.

5. The compound according to any one of claims 1-4 wherein R^1 is C1-C3 alkyl, or a pharmaceutically acceptable salt thereof.

6. The compound according to any one of claims 1-4 wherein R^1 is CH_3, or a pharmaceutically acceptable salt thereof.

7. The compound according to any one of claims 1-4 wherein R^1 is C1-C3 alkoxy, or a pharmaceutically acceptable salt thereof.

8. The compound according to any one of claims 1-4 wherein R^1 is OCH_3, or a pharmaceutically acceptable salt thereof.

9. The compound according to any one of claims 1-4 wherein R^1 is F, or a pharmaceutically acceptable salt thereof.

10. The compound according to any one of claims 1-9 wherein R^2 is F, or a pharmaceutically acceptable salt thereof.

11. The compound according to any one of claims 1-10 wherein X is OCH_2, or a pharmaceutically acceptable salt thereof.

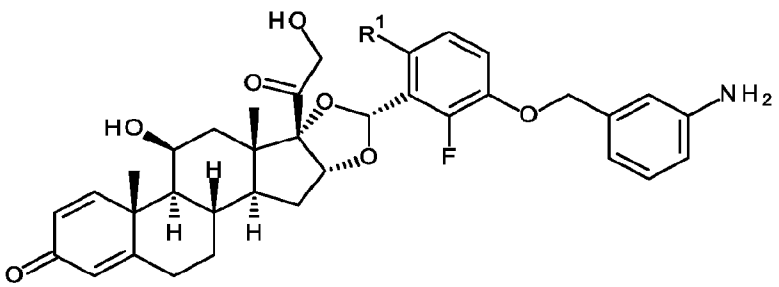
12. The compound according to any one of claims 1-10 wherein X is O, or a pharmaceutically acceptable salt thereof.

13. The compound according to any one of claims 1-10 wherein X is CH_2, or a pharmaceutically acceptable salt thereof.

14. The compound according to any one of claims 1-10 wherein X is SCH_2, or a pharmaceutically acceptable salt thereof.

15. The compound according to any one of claims 1-10 wherein X is a bond, or a pharmaceutically acceptable salt thereof.

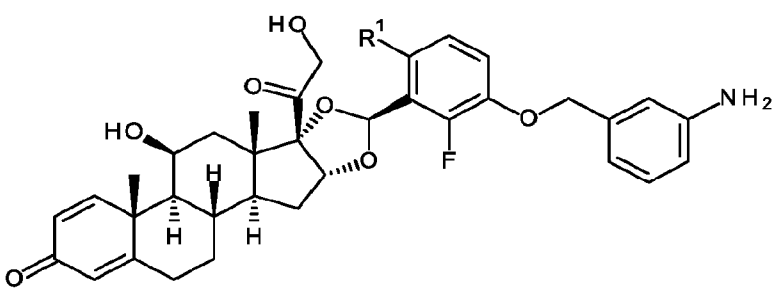
16. The compound according to claims 1 wherein the compound is of the formula:



,

or a pharmaceuticall acceptable salt thereof.

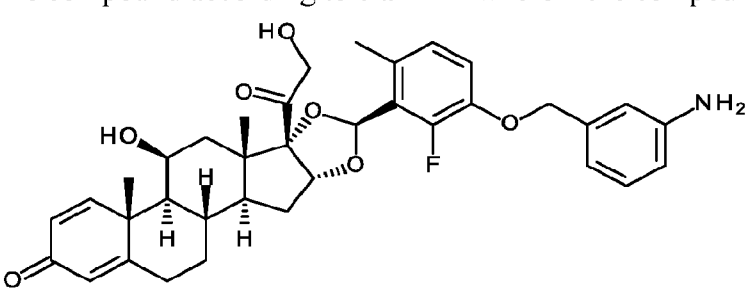
17. The compound according to claim 1 wherein the compound is of the formula:



,

or a pharmaceuticall acceptable salt thereof.

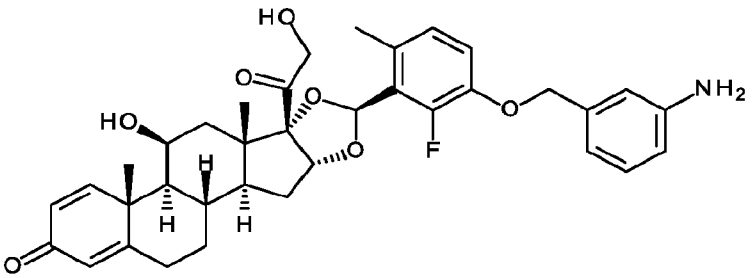
18. The compound according to claim 17 wherein the compound is:



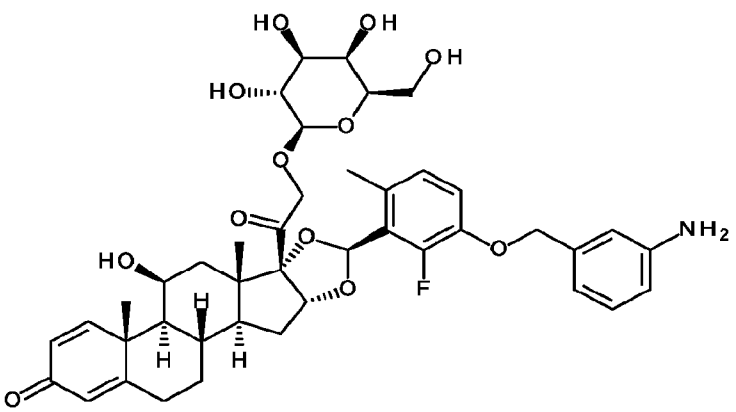
,

or a pharmaceutically acceptable salt thereof.

19. The compound according to claim 18 which is:

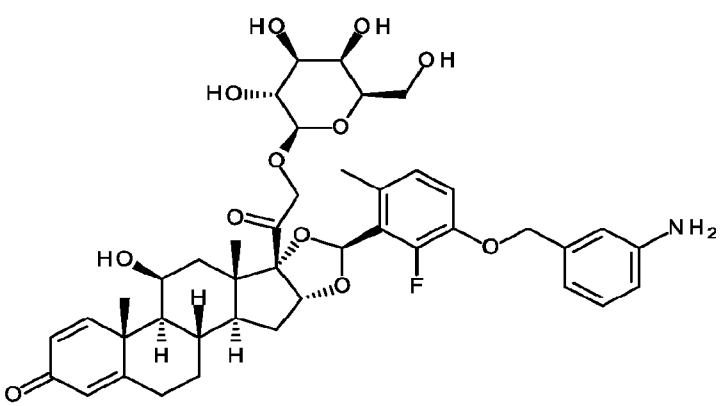


20. The compound according to claim 1 wherein the compound is:

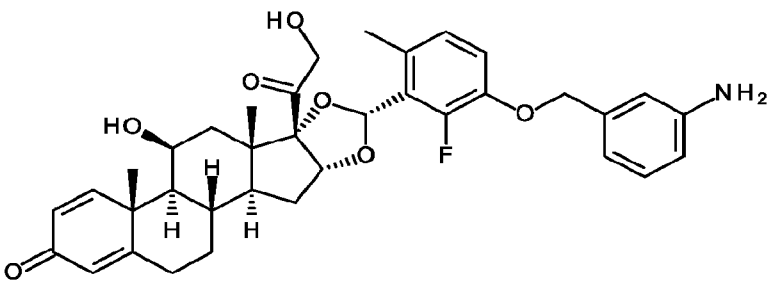


or a pharmaceutically acceptable salt thereof.

21. The compound according to claim 20, which is:



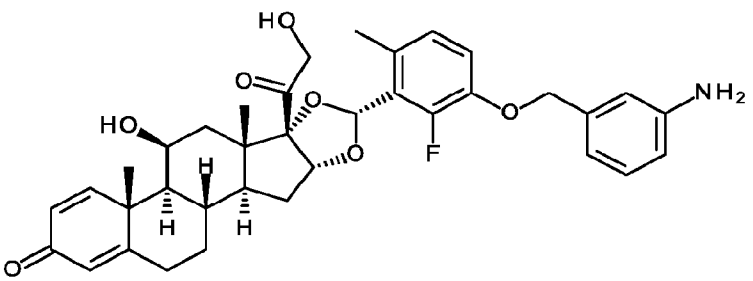
22. The compound according to claim 16 wherein the compound is:



,

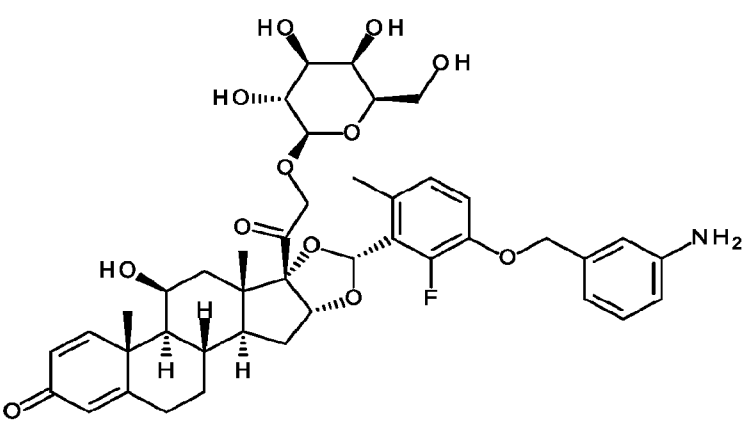
or a pharmaceutically acceptable salt thereof.

23. The compound according to claim 22 which is:



.

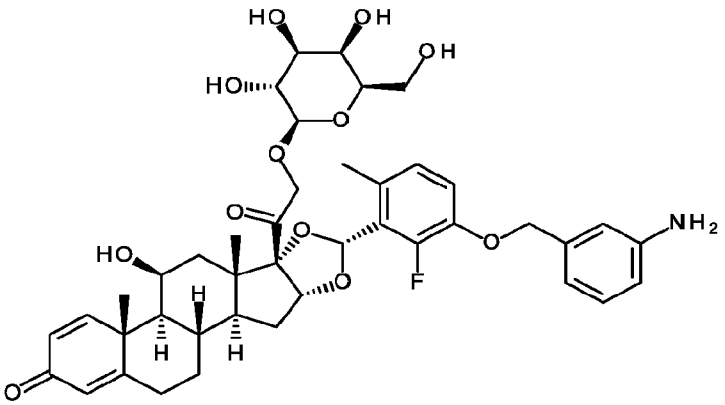
24. The compound according to claim 1 wherein the compound is:



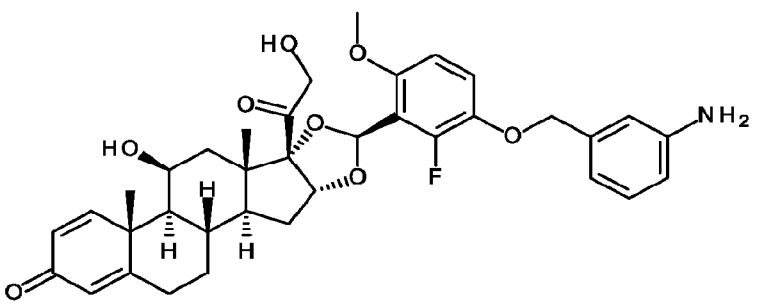
,

or a pharmaceutically acceptable salt thereof.

25. The compound according to claim 24 which is:

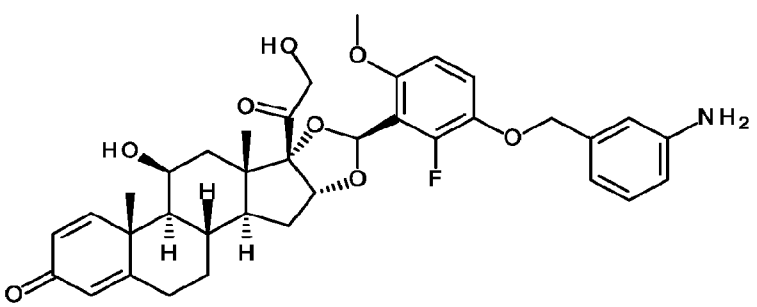


26. The compound according to claim 1 wherein the compound is:

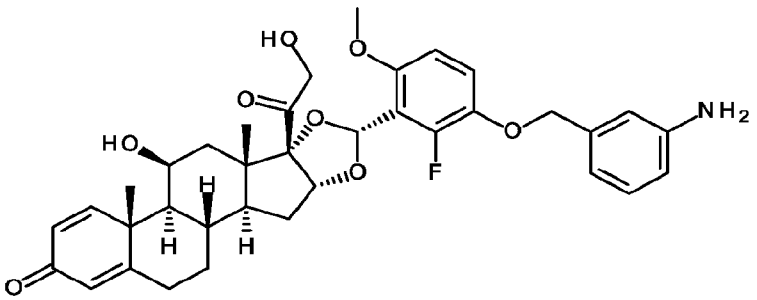


or a pharmaceutically acceptable salt thereof.

27. The compound according to claim 26 which is:



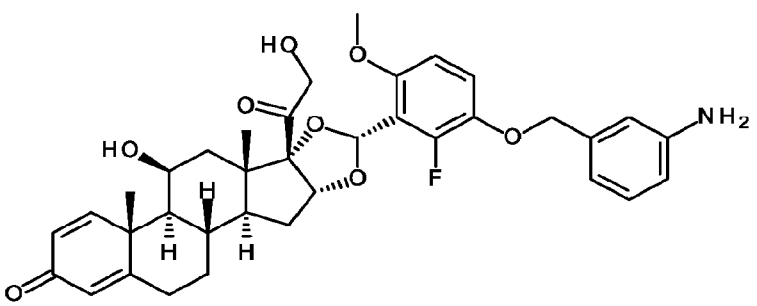
28. The compound according to claim 1 wherein the compound is:



,

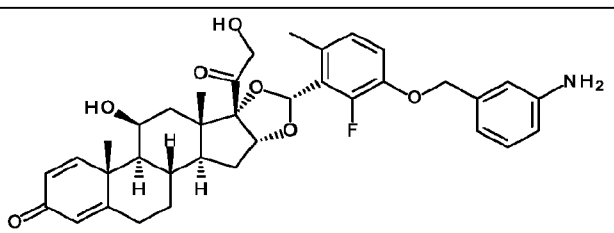
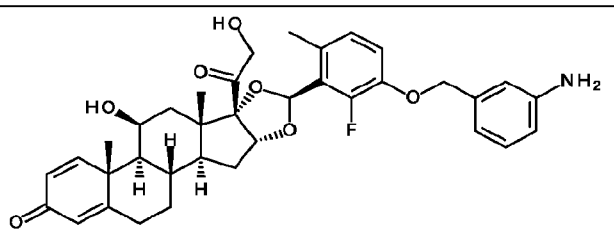
or a pharmaceutically acceptable salt thereof.

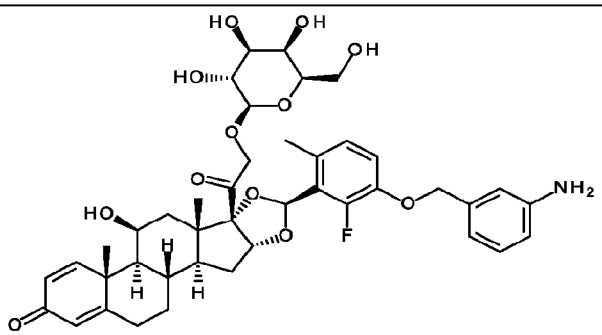
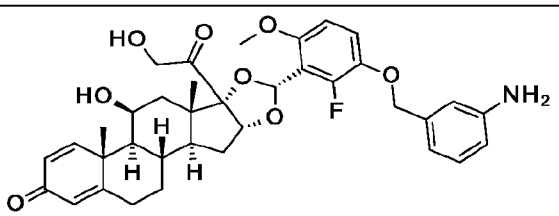
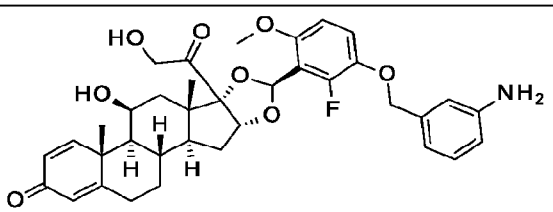
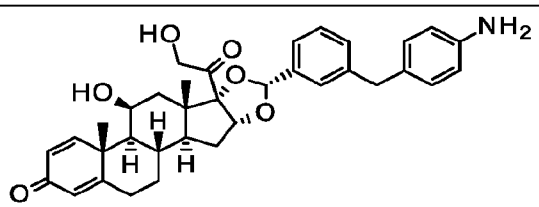
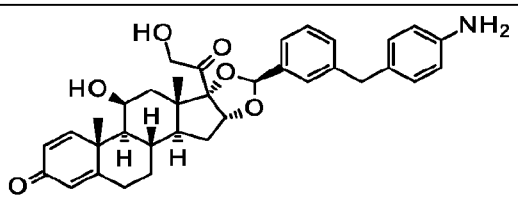
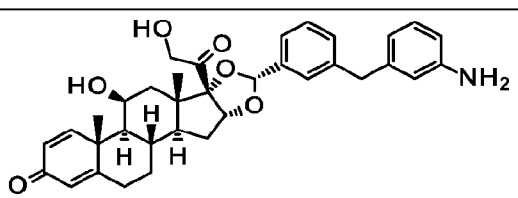
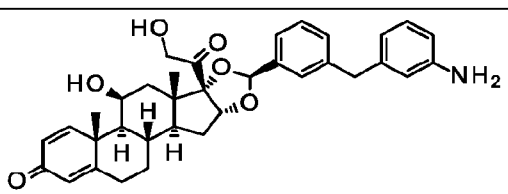
29. The compound according to claim 28 which is:

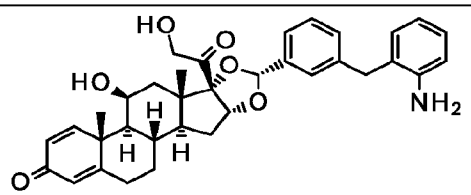
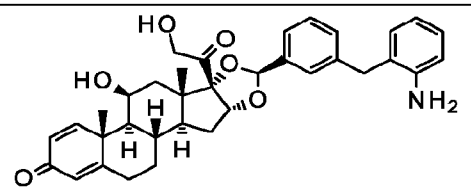
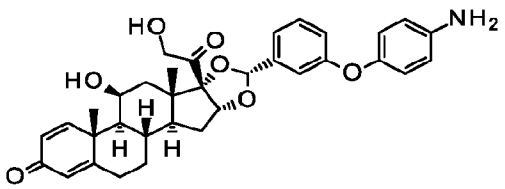
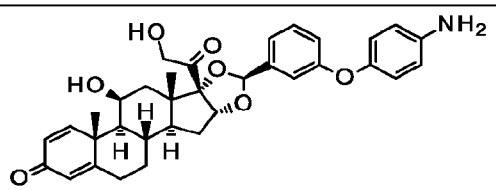
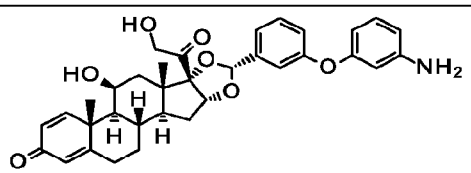
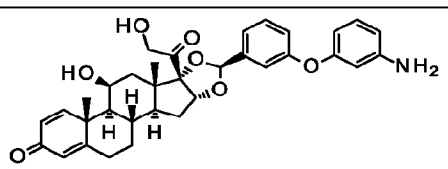
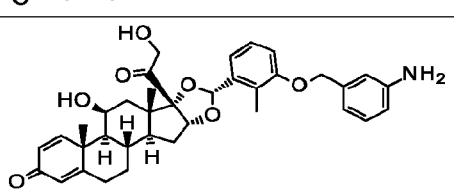
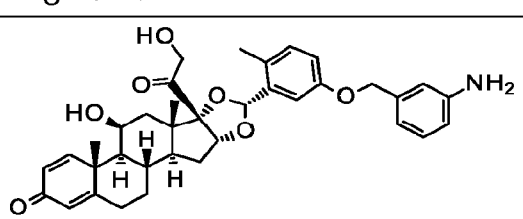


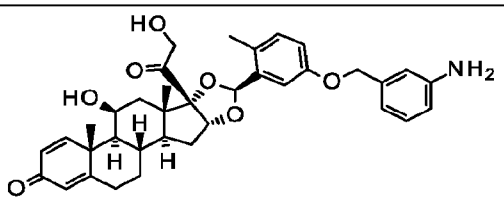
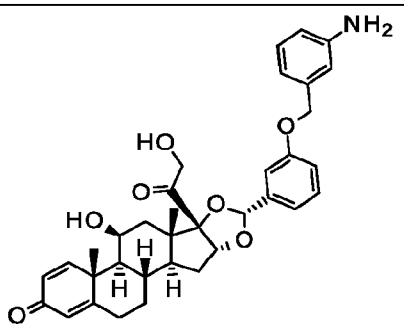
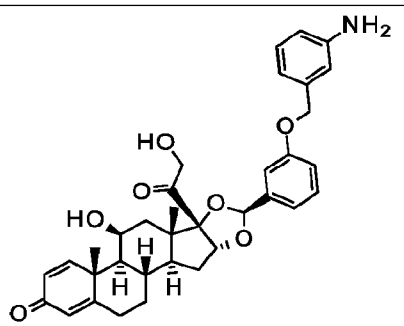
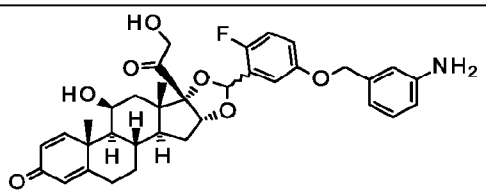
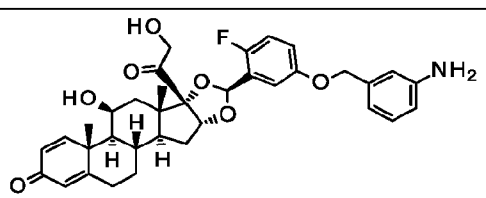
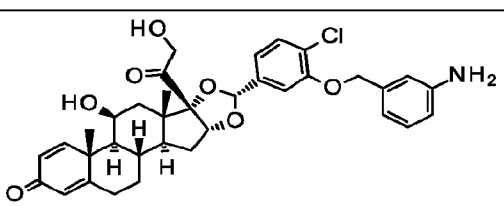
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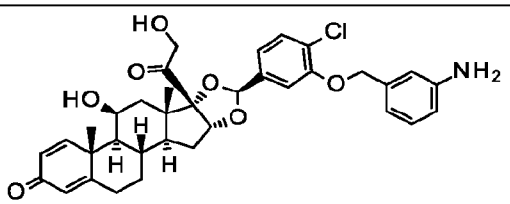
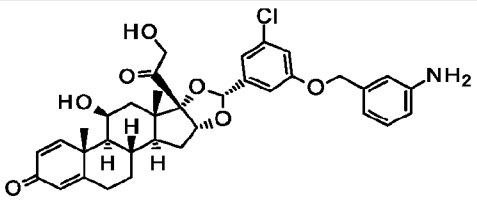
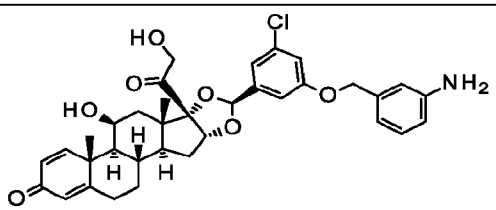
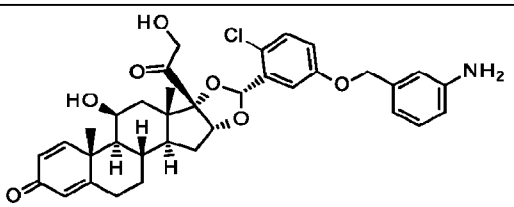
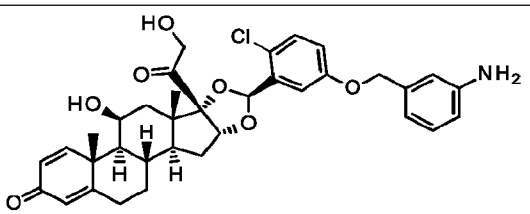
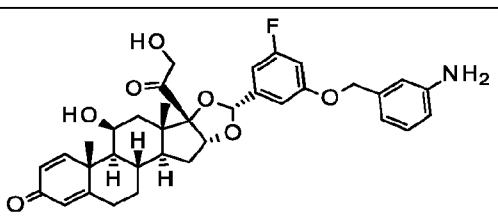
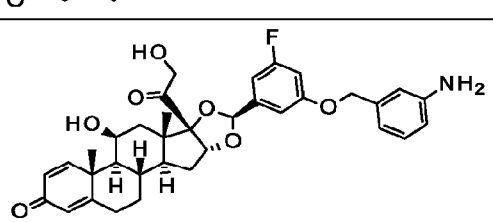
30. The compound according to claim 1 selected from the group consisting of:

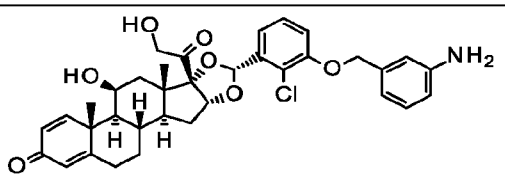
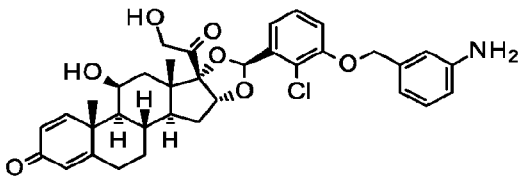
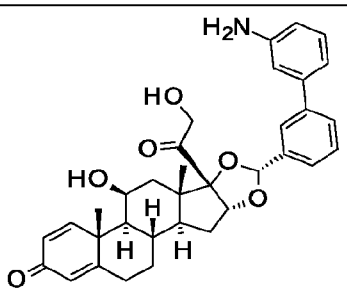
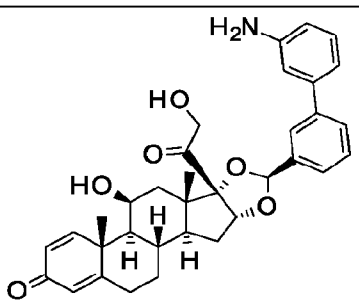
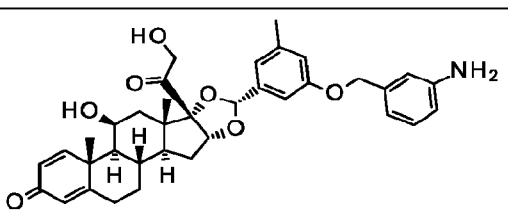
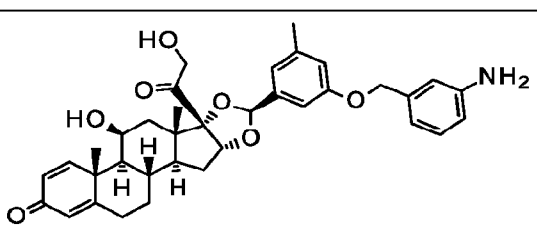
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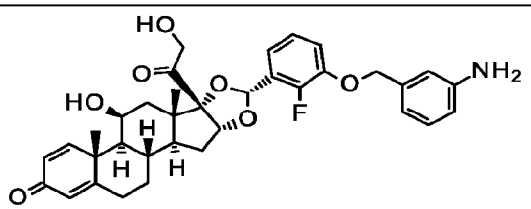
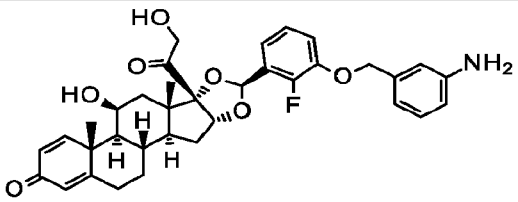
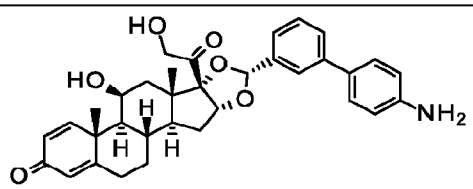
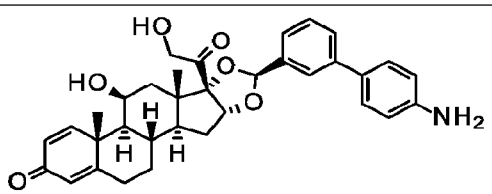
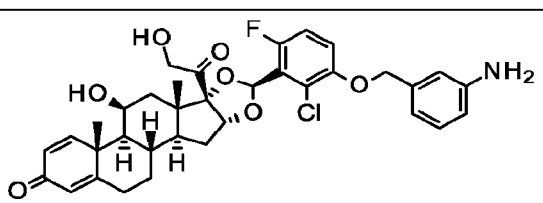
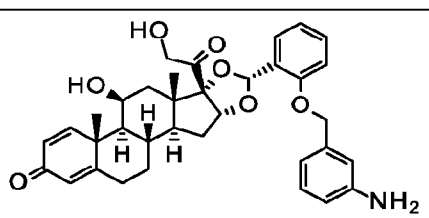
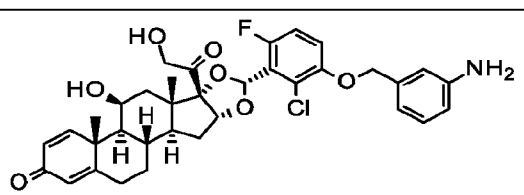
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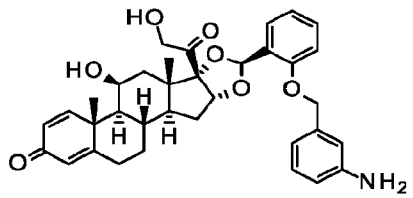
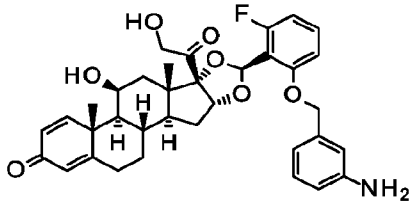
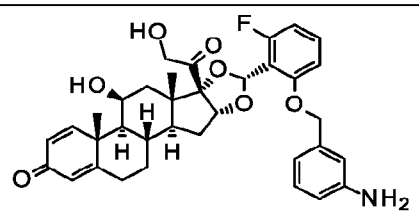
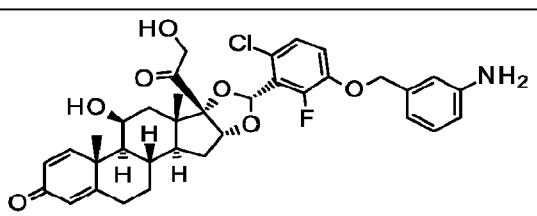
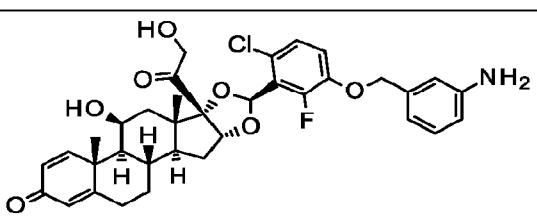
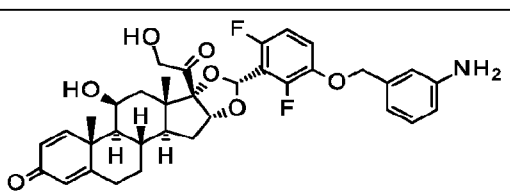
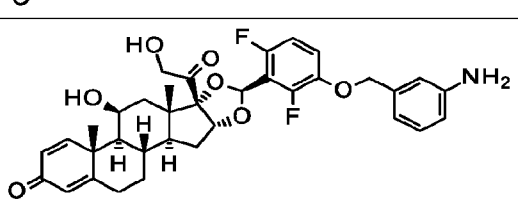
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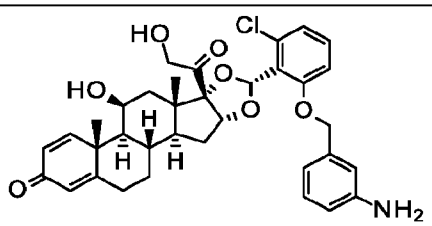
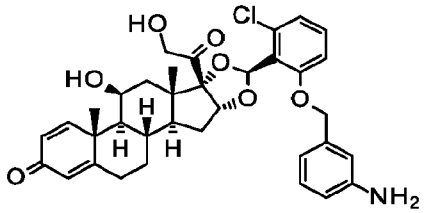
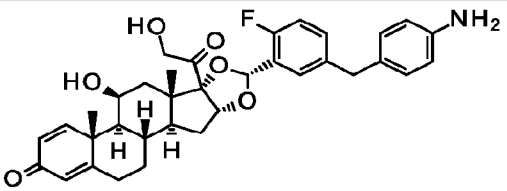
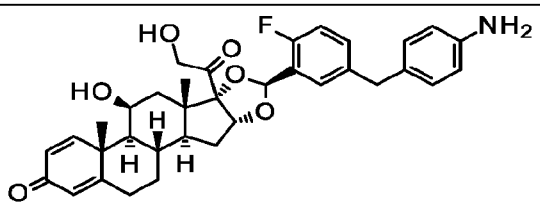
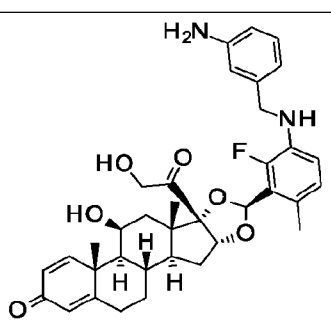
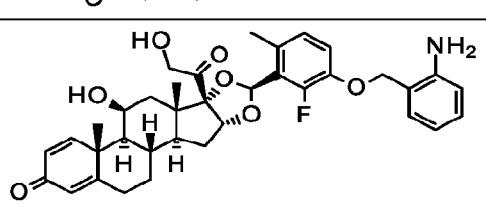
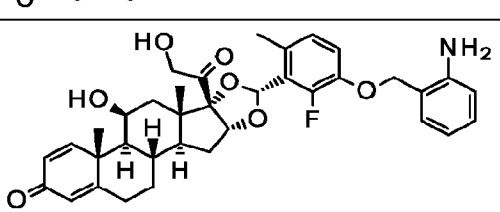
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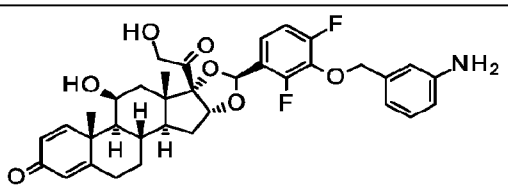
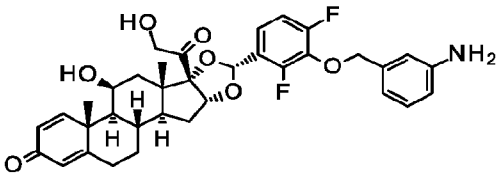
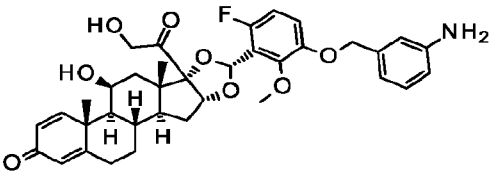
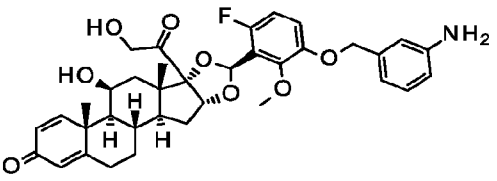
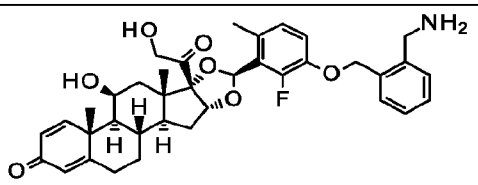
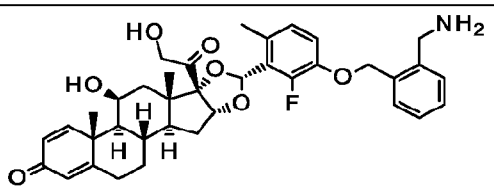
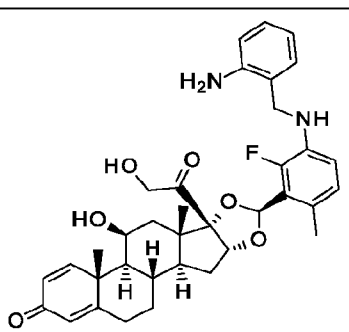
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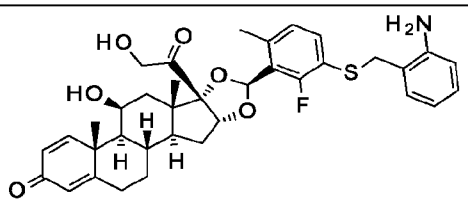
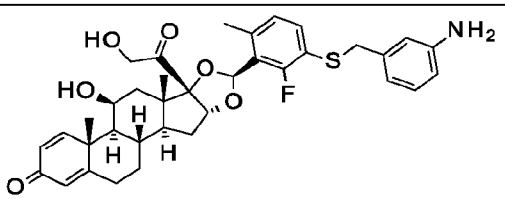
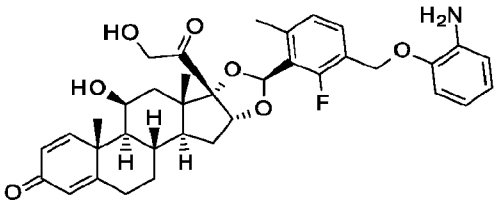
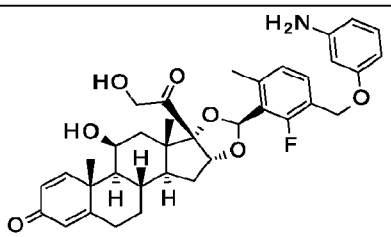
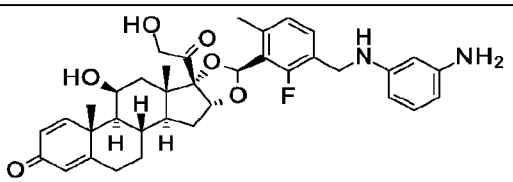
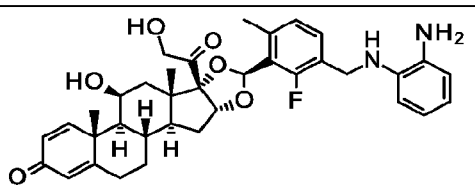
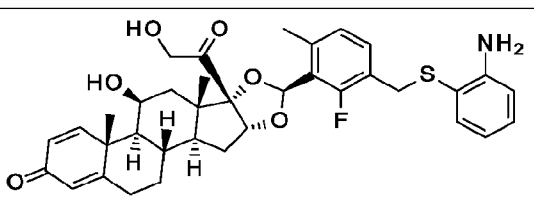
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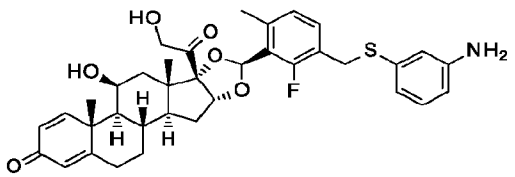
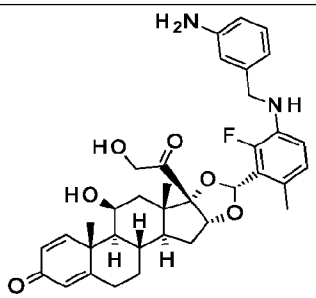
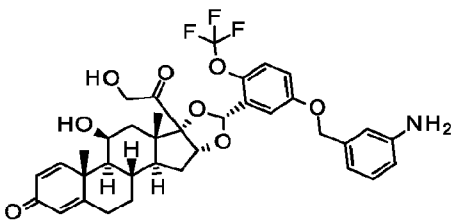
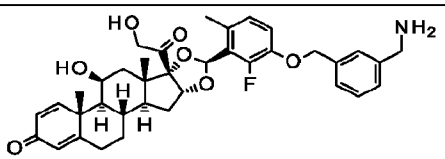
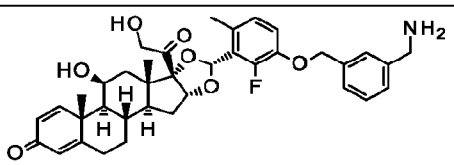
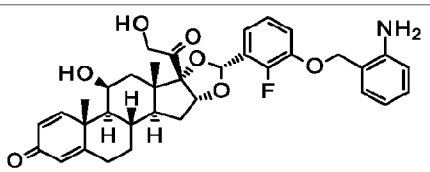
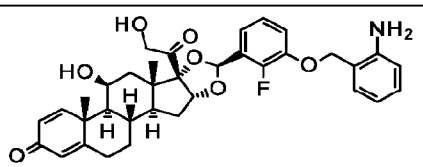
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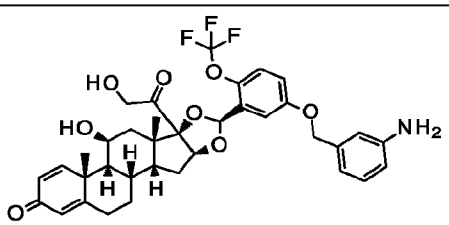
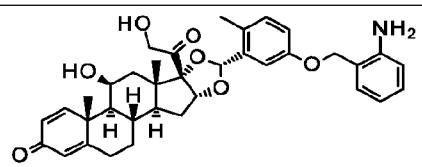
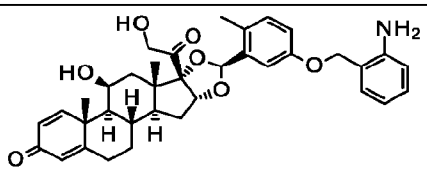
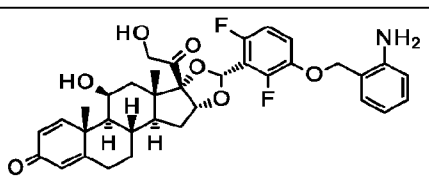
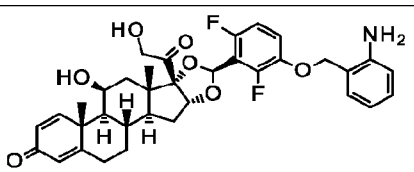
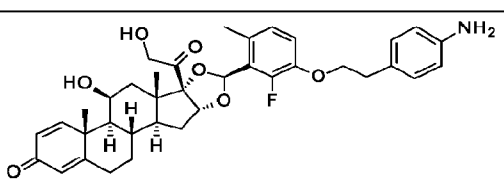
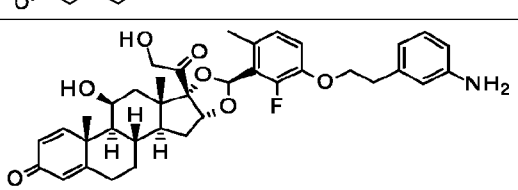
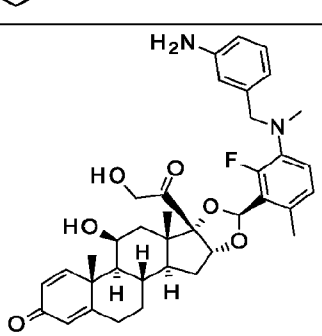
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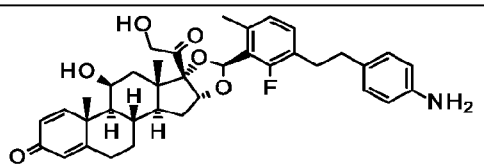
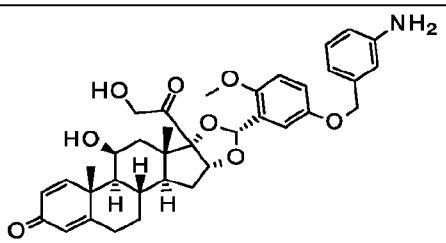
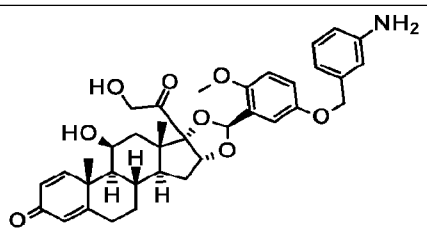
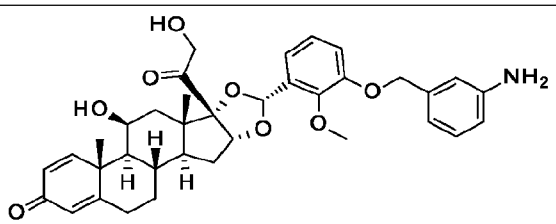
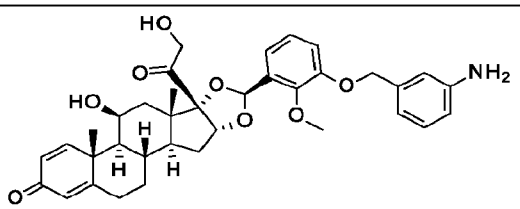
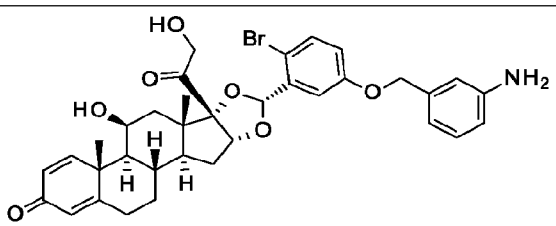
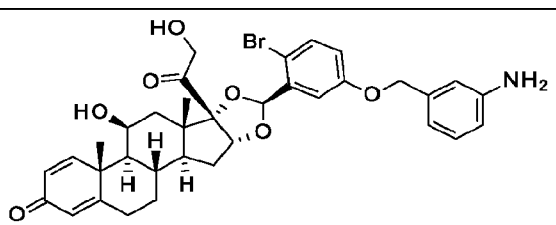
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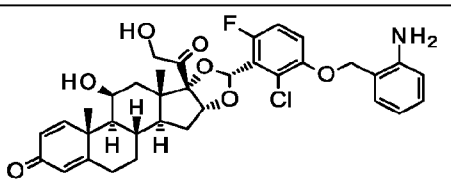
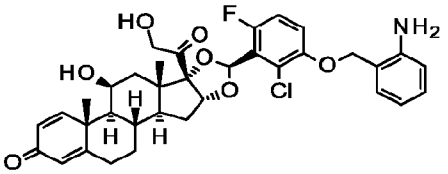
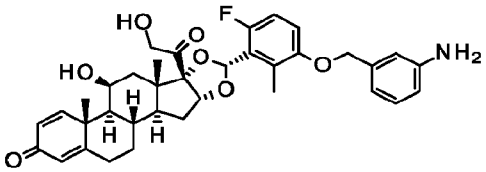
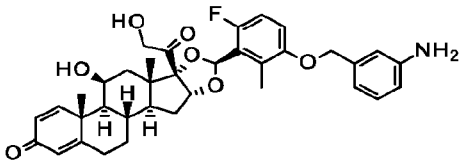
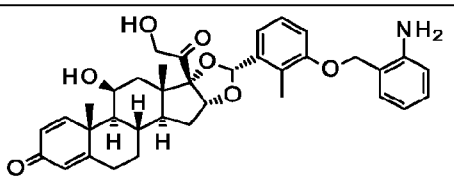
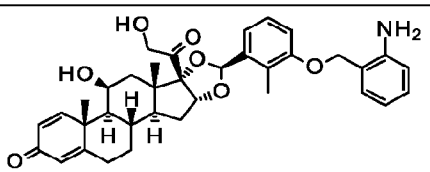
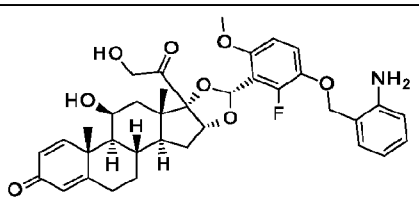
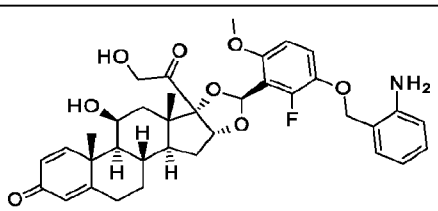
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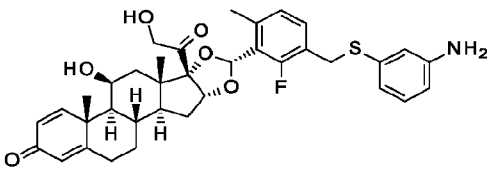
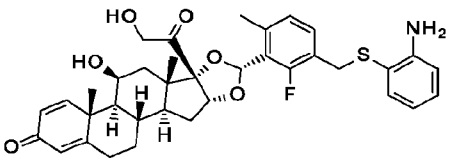
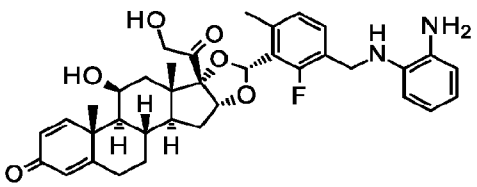
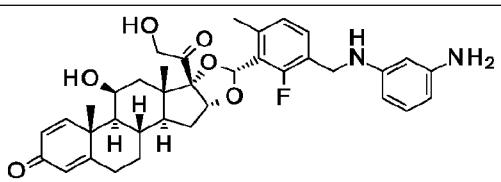
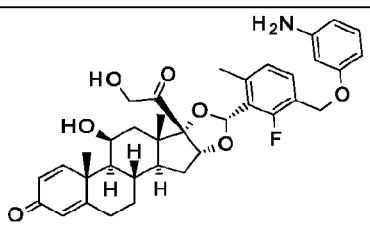
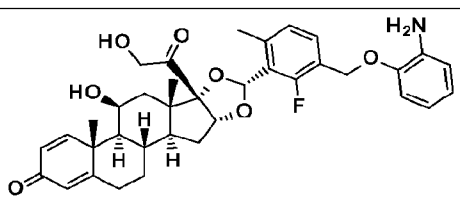
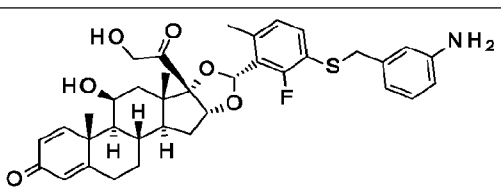
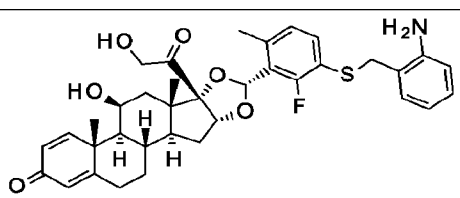
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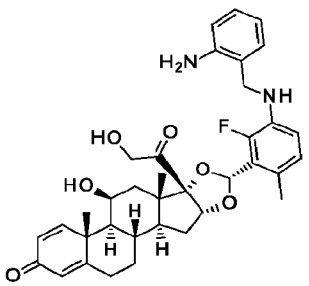
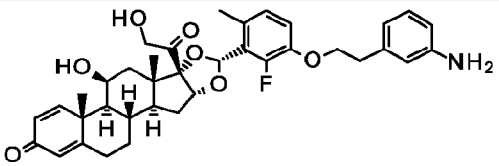
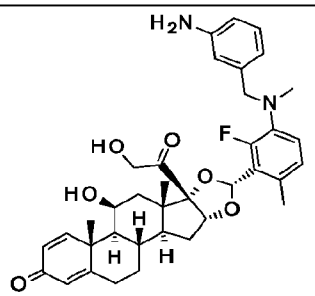
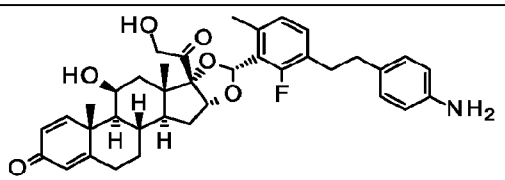
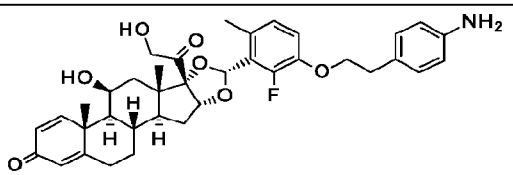
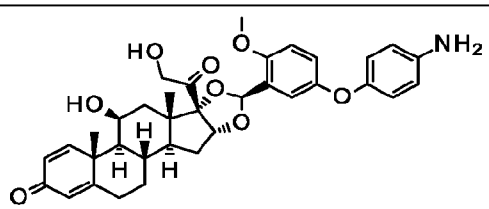
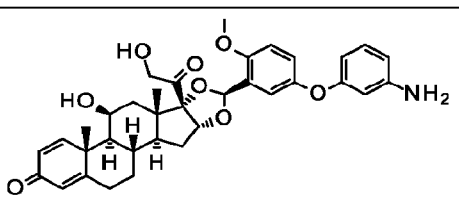
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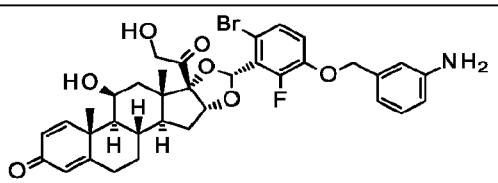
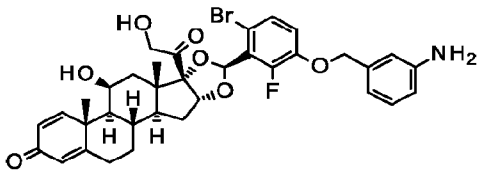
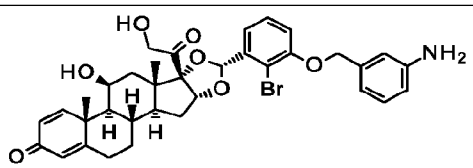
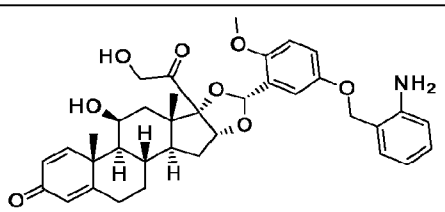
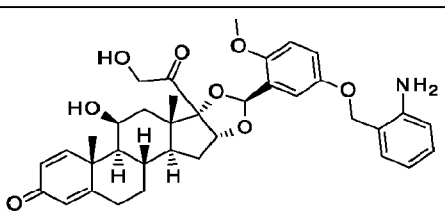
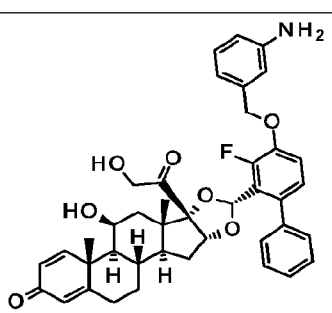
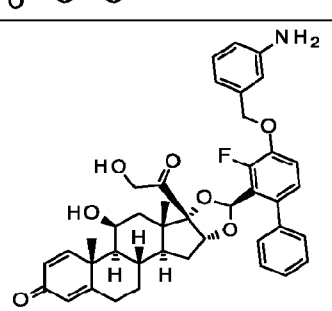
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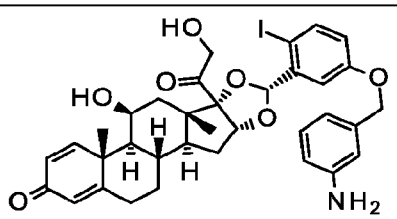
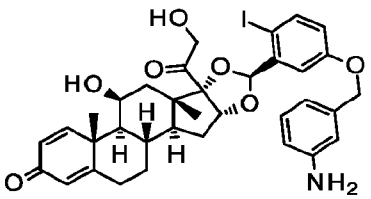
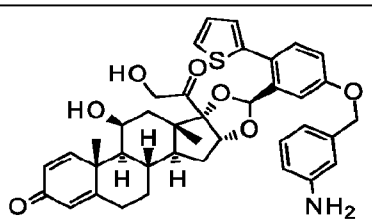
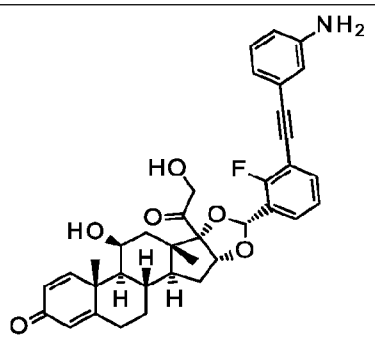
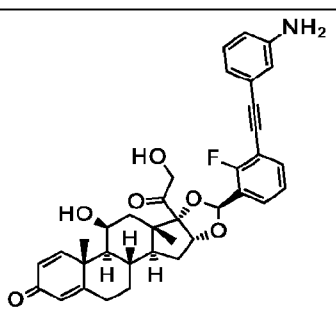
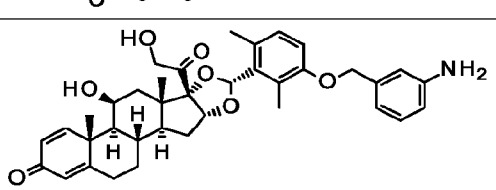
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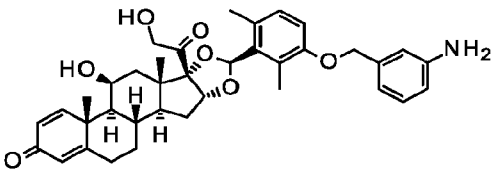
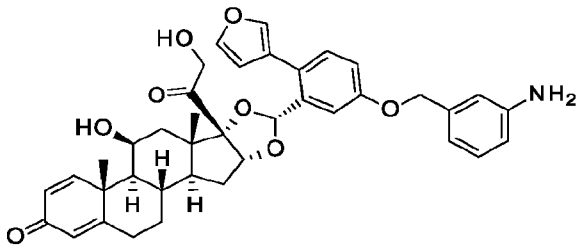
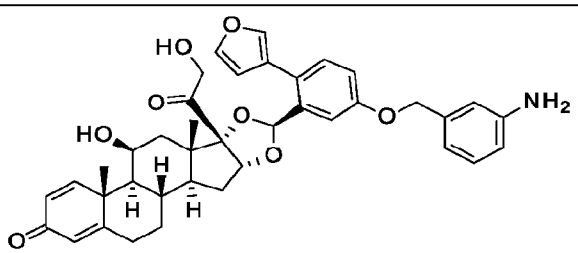
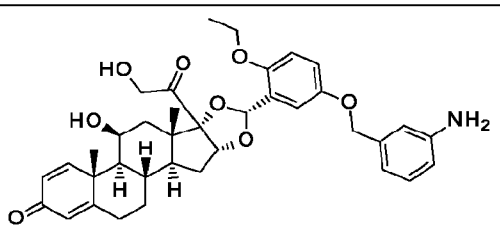
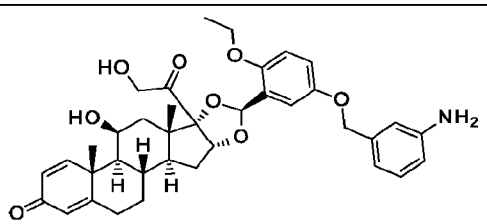
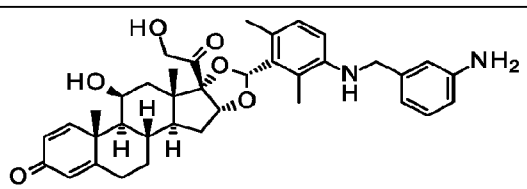
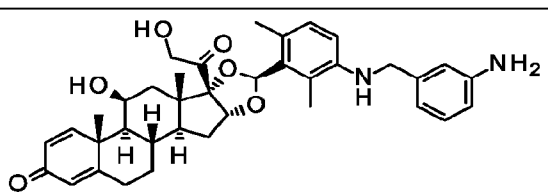
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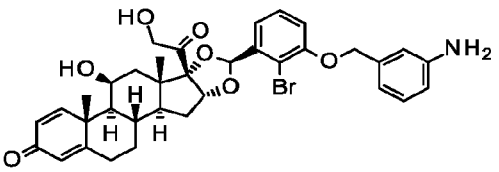
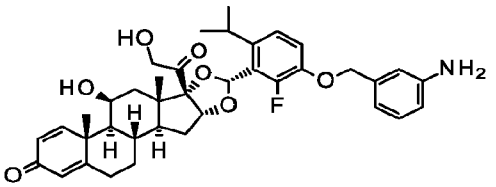
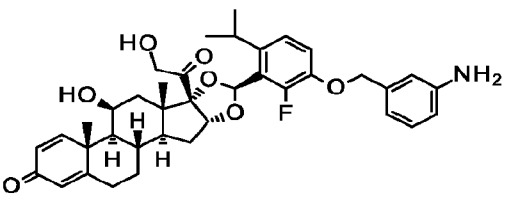
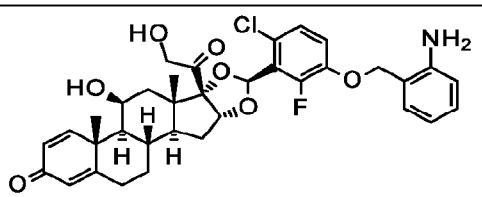
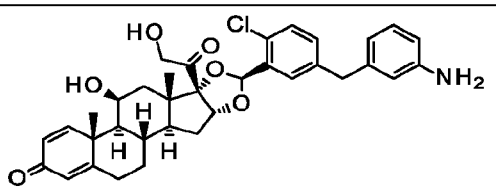
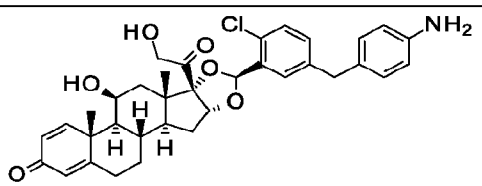
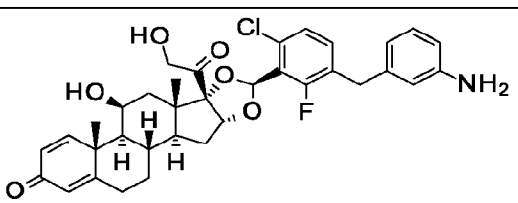
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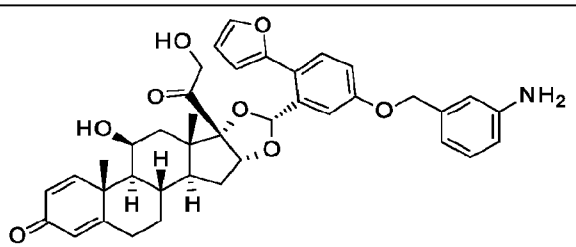
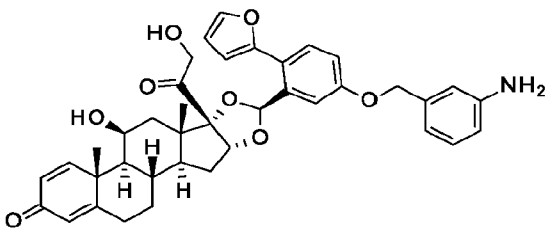
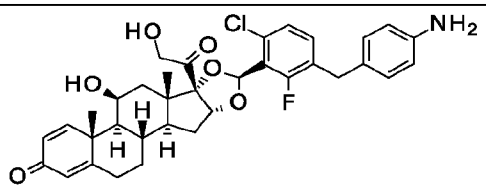
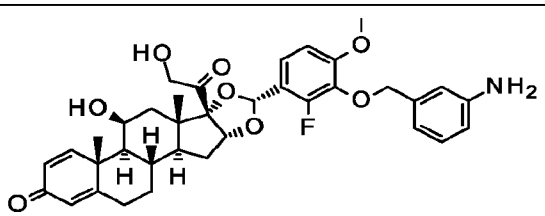
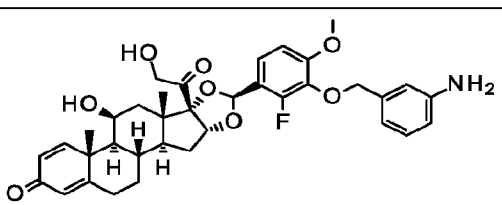
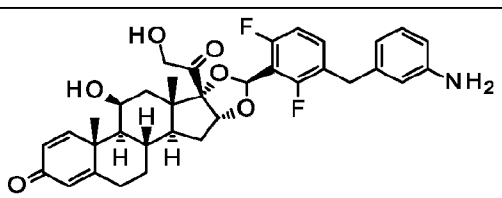
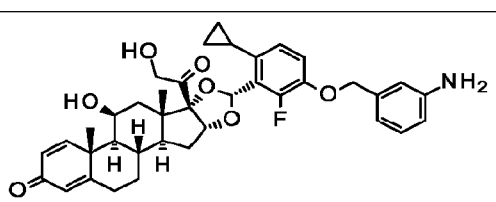
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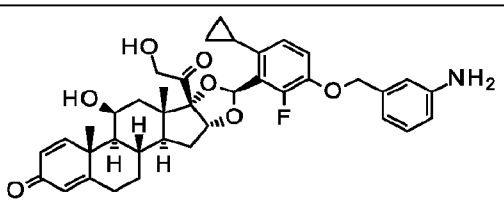
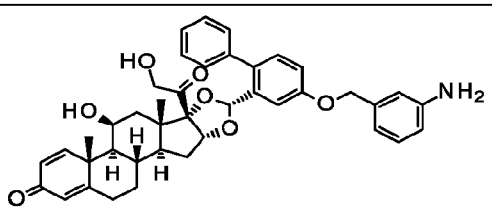
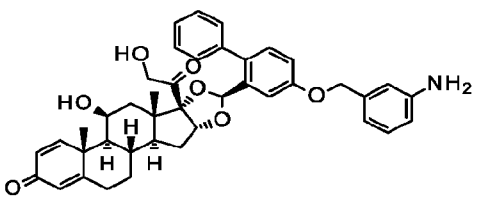
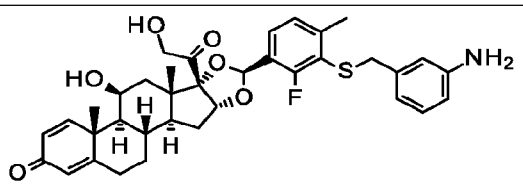
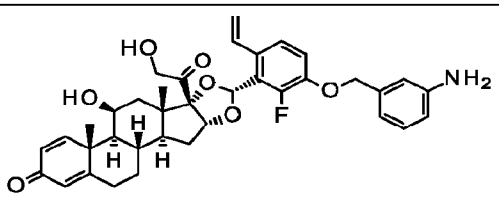
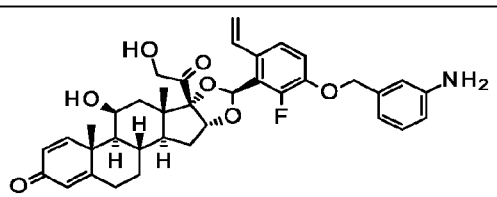
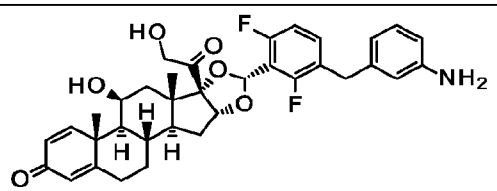
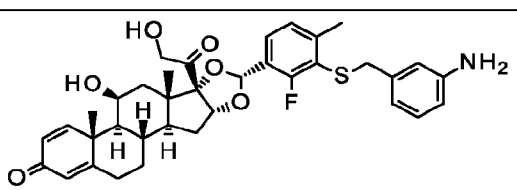
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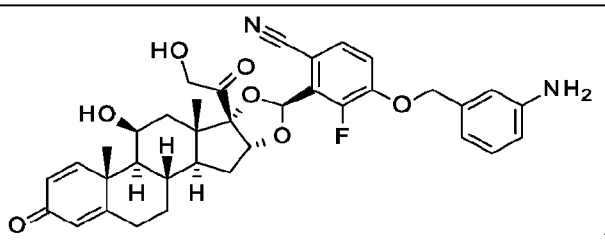
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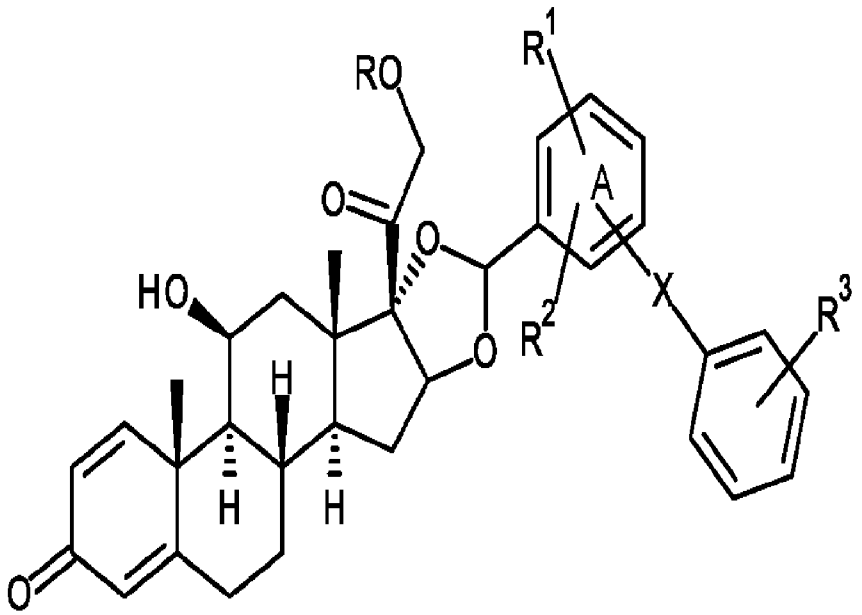
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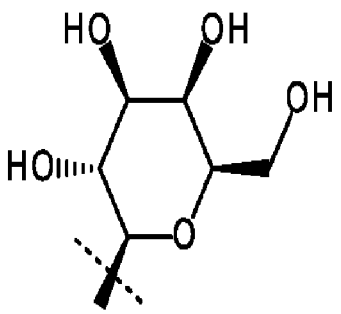
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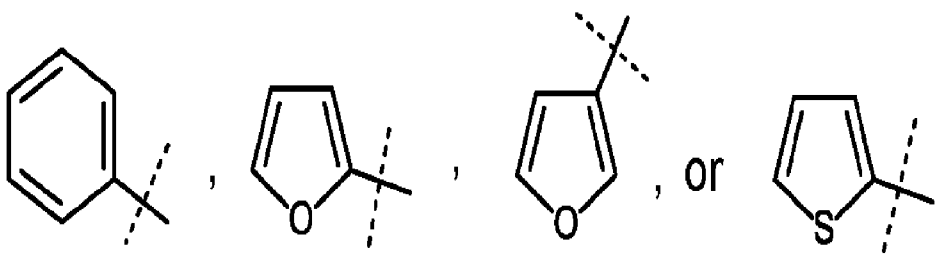
and pharmaceutically acceptable salts thereof.

31. A method of treating atopic dermatitis in a patient, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof.
32. A method of treating rheumatoid arthritis in a patient, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof.
33. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 30 for use in therapy.
34. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 30 for use in treating atopic dermatitis.
35. A compound or pharmaceutically acceptable salt thereof, according to any one of claims 1 to 30 for use in treating rheumatoid arthritis.
36. The use of a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 30 for the manufacture of a medicament for treating atopic dermatitis.
37. The use of a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 30 for the manufacture of a medicament for treating rheumatoid arthritis.
38. A pharmaceutical composition, comprising a compound or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 30 with one or more pharmaceutically acceptable carriers, diluents, or excipients.
39. A process for preparing a pharmaceutical composition, comprising admixing a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 30 with one or more pharmaceutically acceptable carriers, diluents, or excipients.



Formula I





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