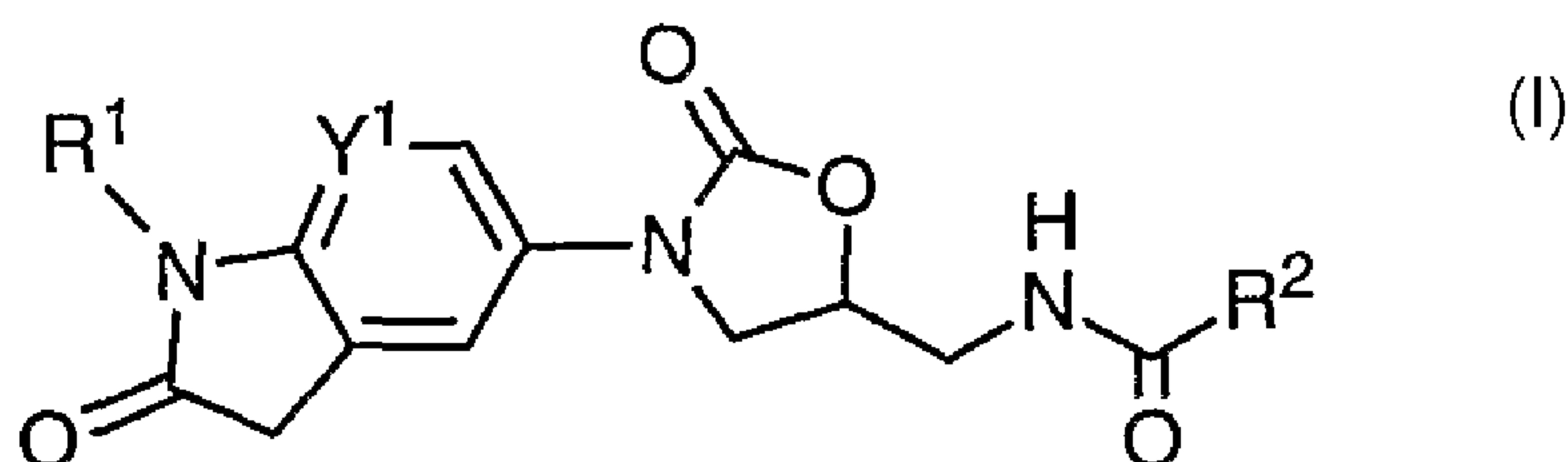




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(54) Title: OXINDOLE OXAZOLIDINONES AS ANTIBACTERIAL AGENTS



(57) **Abrégé/Abstract:**

The present invention relates to novel oxazolidinones derivatives of oxindoles of formula I or a pharmaceutically acceptable salt thereof wherein: Y¹ is CH or CF; R¹ is -C₁₋₄alkyl, optionally substituted with a fluoro atom, or R¹ is -C₃₋₅cycloalkyl; and R² is -C₁₋₂alkyl. These compounds are useful as antibacterial agents.



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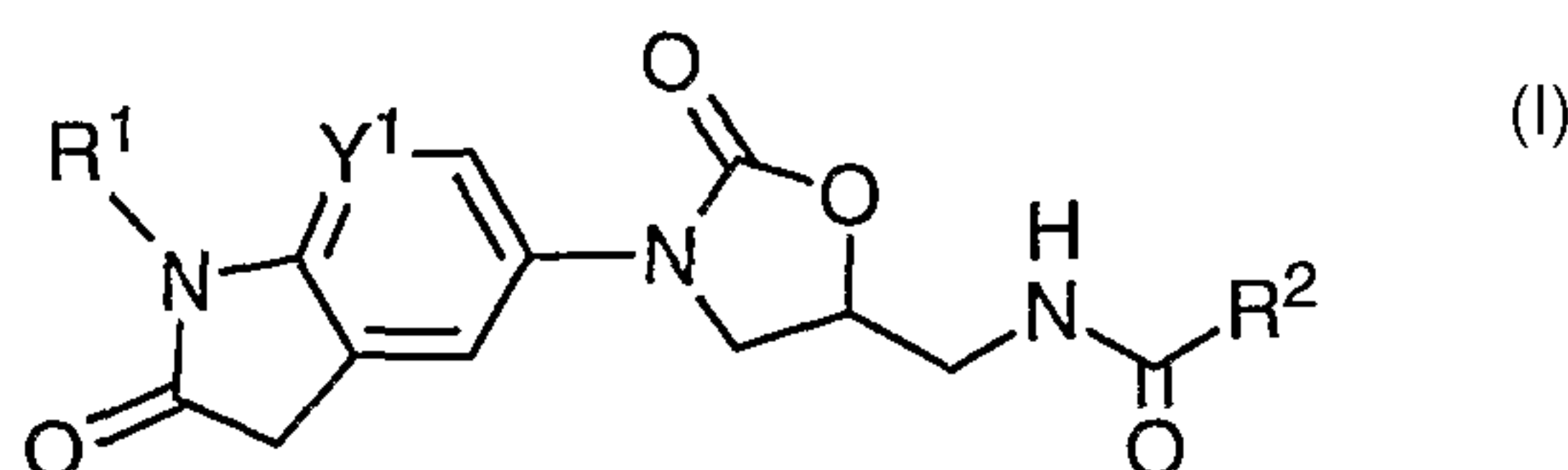
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(54) Title: OXINDOLE OXAZOLIDINONES AS ANTIBACTERIAL AGENTS



(57) Abstract: The present invention relates to novel oxa-
zolidinones derivatives of oxindoles of formula I or a phar-
maceutically acceptable salt thereof wherein: Y¹ is CH or
CF; R¹ is -C₁₋₄alkyl, optionally substituted with a fluoro
atom, or R¹ is -C₃₋₅cycloalkyl; and R² is -C₁₋₂alkyl. These
compounds are useful as antibacterial agents.

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OXINDOLE OXAZOLIDINONES AS ANTIBACTERIAL AGENTS

FIELD OF INVENTION

The present invention relates to novel oxazolidinones derivatives of oxindoles,
5 pharmaceutical compositions thereof, methods for their use, and methods for
preparing these compounds. These compounds have potent activities against against
gram-positive and/or gram-negative bacteria.

BACKGROUND OF THE INVENTION

10 Due to ever-increasing antibiotic resistance, structurally novel antibacterials
with a new mode of action have become increasingly important in the treatment of
bacterial infections. Effective antibacterials exhibit potent activity against a number
of human and veterinary pathogens, including gram-positive aerobic bacteria such as
multiple resistant staphylococci and streptococci, anaerobic organisms such as
15 bacteroides and clostridia species, and acid-fast organisms such as *Mycobacterium*
tuberculosis and *Mycobacterium avium*.

Among newer antibacterial agents, oxazolidinone compounds are the most
recent synthetic class of antimicrobials active against a number of pathogenic
microorganisms. This invention provides novel oxindole derivatives of
20 oxazolidinones, and their preparation.

INFORMATION DISCLOSURE

WO 200281470 discloses oxazolidinone compounds useful for treating
bacterial infection.

25 WO 200032599 discloses oxazolidinone derivatives useful for treatment of
microbial infections.

WO 200029396 discloses 3-phenyl-5-aminomethyl-oxazolidinone derivatives
.useful as antibacterial agents.

WO 9937630 discloses oxazolidinone derivatives including combinatorial
30 libraries.

WO 9737981 discloses oxazolidinones

DE 19604223 discloses new substituted oxazolidinone compounds useful as
antibacterial agents against.

DE 19649095 discloses 5-(acyl-aminomethyl)-3-hetero-aryl-oxazolidinone compounds useful as antibacterial agents.

EP 694543 discloses hetero-aryl subst. oxazolidinone derivatives useful as antibacterial agents.

5 EP 693491 discloses 3-hetero-aryl-2-oxazolidinone derivatives useful as antibacterial agents.

EP 609905 discloses indaxolyl, benzimidazolyl, and benzofrizzolyl oxazolidinone derivatives useful as antibacterial agents.

10 US 5164510 discloses 5-Indolinyloxazolidin-2-one(s) useful as antibacterial agents.

US2002016323 discloses oxazolidinone antibacterial agents.

US 2002032348 discloses process to prepare oxazolidinones.

US2002143009 discloses bicyclic oxazolidinone derivatives useful as antimicrobial agents.

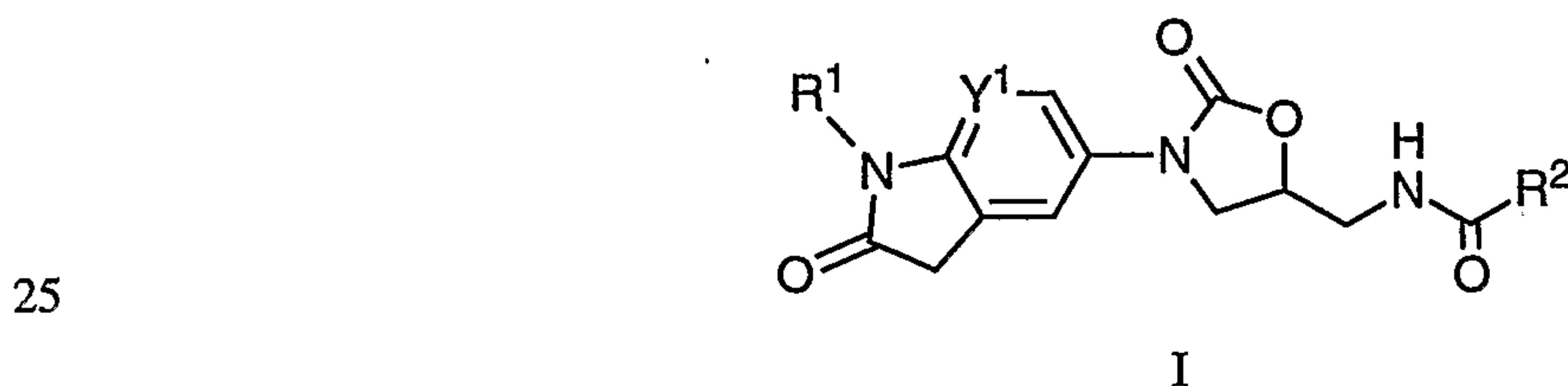
15 US 2003/216330 discloses parenteral, intravenous, and oral administration of oxazolidinones for treating diabetic foot infections.

US 2004/176610 discloses antibacterial indolone oxazolidinone as antibacterial agents.

20 US2004147760 discloses N-aryl-2-oxazolidinone-5-carboxamides having antibacterial activity useful for treating microbial infections.

SUMMARY OF THE INVENTION

The present invention provides a compound of formula I



or a pharmaceutically acceptable salt thereof wherein:

Y¹ is CH or CF;

R¹ is -C₁₋₄alkyl, optionally substituted with a fluoro atom, or R¹ is

30 -C₃₋₅cycloalkyl; and

R² is -C₁₋₂alkyl.

In another aspect, the present invention also provides:

a pharmaceutical composition which comprises a pharmaceutically acceptable carrier and an effective amount of a compound of formula I,

a method for treating gram-positive or gram-negative microbial infections in a mammal by administering to the subject in need a therapeutically effective amount of
5 a compound of formula I or a pharmaceutically acceptable salt thereof, and

a use of a compound of formula I or a pharmaceutically acceptable salt thereof to prepare a medicament for treating gram-positive or gram-negative microbial infections.

The invention may also provide novel intermediates and novel processes that
10 are useful for preparing compounds of formula I.

DETAILED DESCRIPTION OF THE INVENTION

Unless otherwise stated, the following terms used in the specification and claims have the meanings given below:

15 The carbon atom content of various hydrocarbon-containing moieties is indicated by a prefix designating the minimum and maximum number of carbon atoms in the moiety, i.e., the prefix C_{i-j} indicates a moiety of the integer "i" to the integer "j" carbon atoms, inclusive. Thus, for example, C₁₋₆ alkyl refers to alkyl of one to seven carbon atoms, inclusive.

20 The term alkyl refers to both straight and branched groups, but reference to an individual radical such as "propyl" embraces only the straight chain radical, a branched chain isomer such as "isopropyl" being specifically referred to.

The term "C₃₋₅cycloalkyl" refers to a cyclic saturated monovalent hydrocarbon group of three to five carbon atoms, e.g., cyclopropyl, and the like.

25 The term "halo" refers to fluoro (F), chloro (Cl), bromo (Br), or iodo (I). The term "a pharmaceutically acceptable salt" of a compound means a salt that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound.

The term "pharmaceutically acceptable carrier" means a carrier that is useful in
30 preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable, and includes a carrier that is acceptable for veterinary use as well as human pharmaceutical use. "A pharmaceutically acceptable

carrier" as used in the specification and claims includes both one and more than one such carrier.

The term "mammal" refers to human or warm-blooded animals including livestock and companion animals.

5 The term "optional" or "optionally" means that the subsequently described event or circumstance may, but need not, occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not.

Compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or the arrangement of their atoms in space are
10 termed "isomers". Isomers that differ in the arrangement of their atoms in space are termed "stereoisomers".

It will be appreciated by those skilled in the art that compounds of the invention having a chiral center may exist in and be isolated in optically active and racemic forms. Some compounds may exhibit polymorphism. It is to be understood
15 that the present invention encompasses any racemic, optically-active, polymorphic, tautomeric, or stereoisomeric form, or mixture thereof, of a compound of the invention, which possesses the useful properties described herein, it being well known in the art how to prepare optically active forms (for example, by resolution of the racemic form by recrystallization techniques, by synthesis from optically-active
20 starting materials, by chiral synthesis, or by chromatographic separation using a chiral stationary phase) and how to determine antiviral activity using the standard tests described herein, or using other similar tests which are well known in the art.

The term "treating" or "treatment" of a disease includes: (1) preventing the disease, i.e. causing the clinical symptoms of the disease not to develop in a mammal
25 that may be exposed to or predisposed to the disease but does not yet experience or display symptoms of the disease; (2) inhibiting the disease, i.e., arresting or reducing the development of the disease or its clinical symptoms; or (3) relieving the disease, i.e., causing regression of the disease or its clinical symptoms.

The term "therapeutically effective amount" means the amount of a compound
30 that, when administered to a mammal for treating a disease, is sufficient to effect such treatment for the disease. The "therapeutically effective amount" will vary depending on the compound, the disease and its severity and the age, weight, etc., of the mammal to be treated.

The term "leaving group" has the meaning conventionally associated with it in synthetic organic chemistry i.e., an atom or group capable of being displaced by a nucleophile and includes halogen, alkylsulfonyloxy, ester, or amino such as chloro, bromo, iodo, mesyloxy, tosyloxy, trifluorosulfonyloxy, methoxy, N,O-
5 dimethylhydroxyl-amino, and the like.

The compounds of the present invention are generally named according to the IUPAC or CAS nomenclature system.

Abbreviations which are well known to one of ordinary skill in the art may be used (e.g. "Ph" for phenyl, "Me" for methyl, "Et" for ethyl, "h" for an hour or hours
10 and "rt" for room temperature).

Specific and preferred values listed below for radicals, substituents, and ranges, are for illustration only; they do not exclude other defined values or other values within defined ranges for the radicals and substituents.

Specifically, alkyl denotes both straight and branched groups; but reference to
15 an individual radical such as "propyl" embraces only the straight chain radical, a branched chain isomer such as "isopropyl" being specifically referred to.

Specifically, alkyl is methyl, ethyl, propyl, isopropyl, butyl, iso-butyl, sec-butyl, and their isomeric forms thereof.

Specifically, cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, and their
20 isomeric forms thereof.

Specifically, halo is fluoro (F), or chloro (Cl).

Specifically, Y¹ is CH.

Specifically, R¹ is C₁₋₃alkyl.

Specifically, R¹ is methyl, or isopropyl.

25 Specifically, R² is metyl.

Examples of the present invention are:

- (1) (S)-N-[3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- (2) (S)-N-[3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
30
- (3) N-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

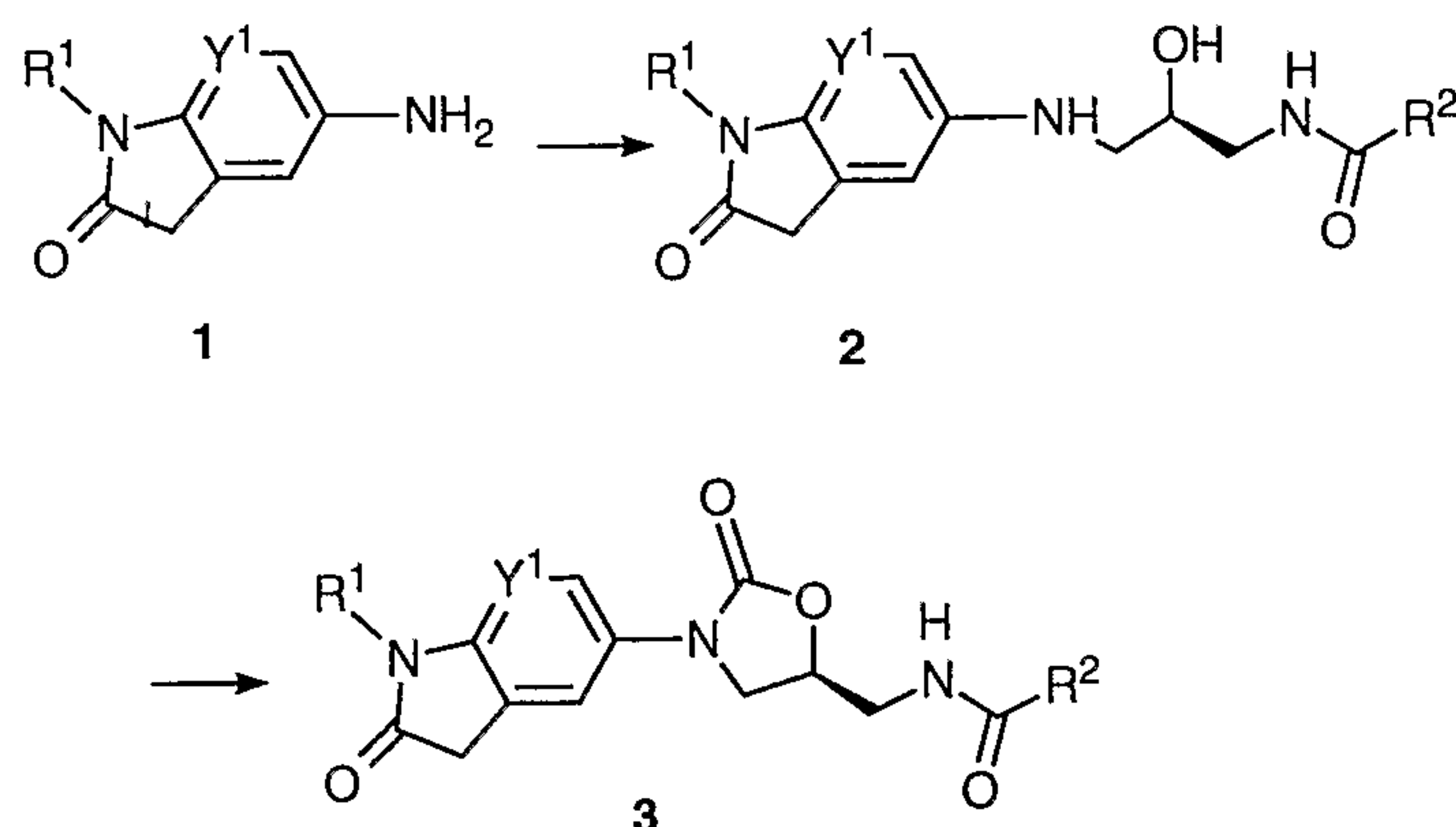
- (4) (S)-N-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (5) (S)-N-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 5 (6) (S)-N-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (7) (S)-N-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- (8) (S)-N-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- 10 (9) (S)-N-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide,
- (10) (S)-N-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-propionamide,
- 15 (11) (S)-N-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide,
- (12) (S)-N-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-propionamide,
- (13) (S)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide
- 20 (14) (S)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (15) (S)-N-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 25 (16) (S)-N-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (17) (S)-N-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-acetamide,
- (18) (S)-N-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-propionamide,
- 30 (19) (S)-N-[3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

- (20) (S)-N-[3-(7-Fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (21) (S)-N-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 5 (22) (S)-N-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (23) (S)-N-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- (24) (S)-N-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 10 (25) (S)-N-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (26) (S)-N-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 15 (27) (S)-N-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (28) (S)-N-{3-[1-(2-fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide, or
- (29) (S)-N-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide.
- 20

Compounds of this invention can be prepared in accordance with one or more of the Schemes discussed below. All of the starting materials may be prepared by the following descriptions, by procedures that would be well known to one of ordinary skill in organic chemistry, or are commercially available. Unless otherwise defined

25 below, variables used in the Schemes are as defined in the specification or in the claims.

SCHEME I



As shown in Scheme I, the substituted 5-amino-1,3-dihydroindol-2-one **1** is

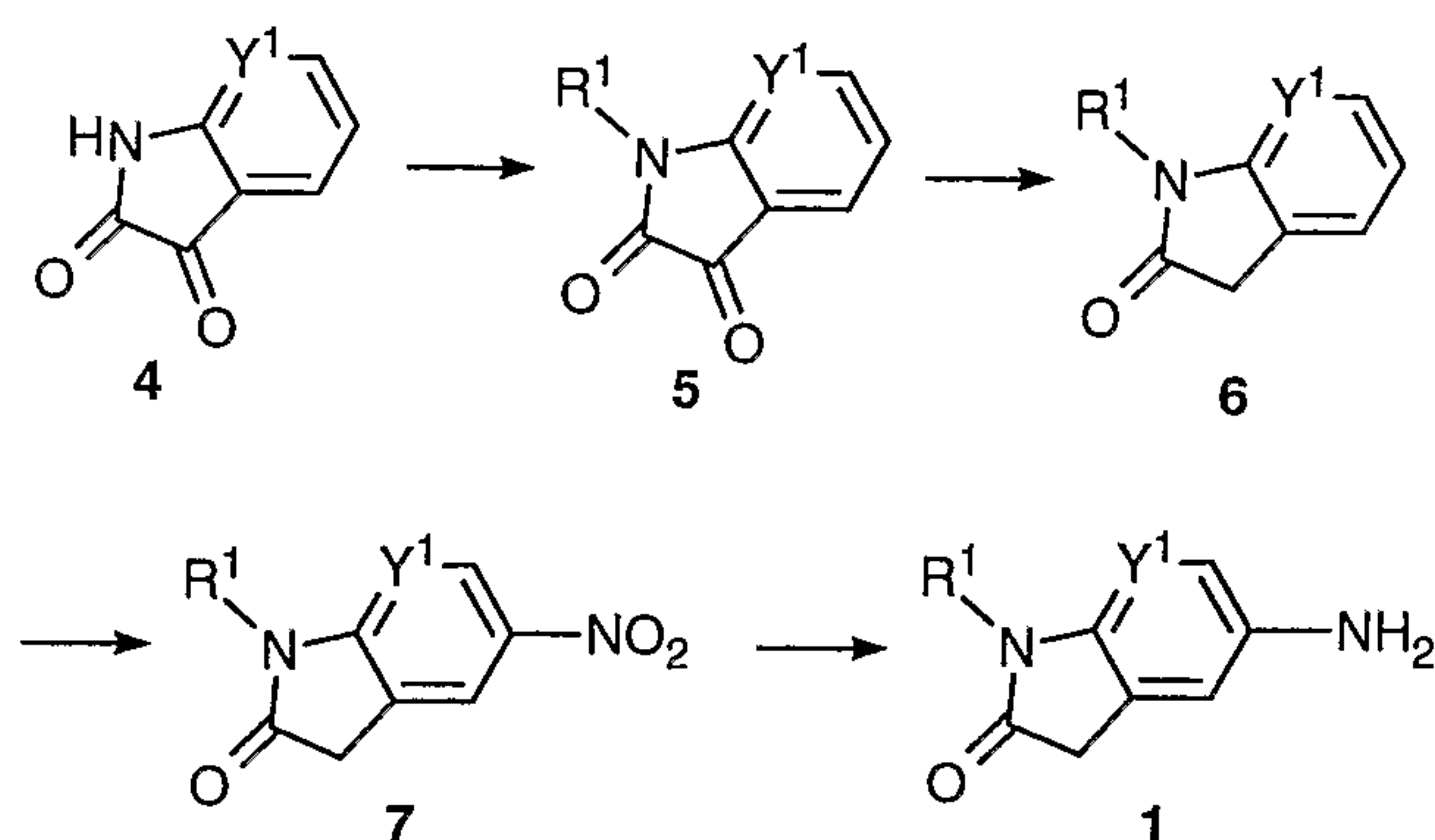
5 reacted with an appropriately protected (*S*)-glycidylamine and a Lewis acid such as lithium triflate in a suitable solvent such as acetonitrile at a suitable temperature, typically in the range from 20 °C to 110 °C depending on the solvent. Acetyl or Boc protected (*S*)-glycidylamines are conveniently prepared following methods described in International Patent Publication No. WO 02/32857. The amino alcohol **2** can then

10 be ring closed to give the aryl oxazolidinones **3** using methods known to one skilled in the art. For instance, treatment of structures **2** with 1,1'-carbonyldiimidazole in a solvent such as acetonitrile or tetrahydrofuran at an appropriate temperature, typically in a range of 20 °C to 60 °C, or with phosgene in a solvent such as toluene or methylene chloride, or mixtures thereof, in the presence of a base such as

15 triethylamine at an appropriate temperature, typically in a range from -10 °C to 25 °C, affords the oxazolidinone **3**. If R² is a *tert*-butyl, the substrate may be further deprotected to the corresponding amine by treatment with an acid such as hydrochloric acid or trifluoroacetic acid in a suitable solvent such as methylene

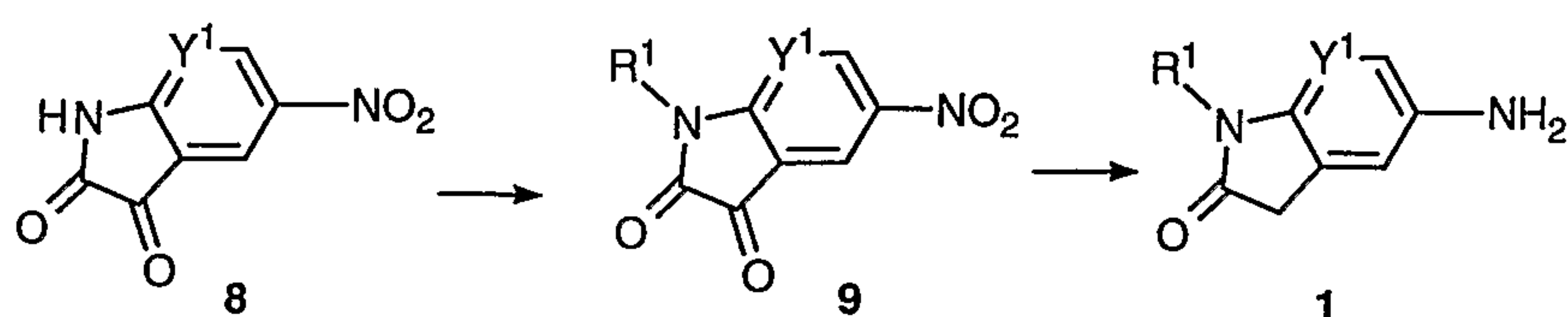
20 alkyl) **3** by treatment with an appropriate isocyanate or acylating reagent such as an acid chloride or anhydride in the presence of a suitable base such as triethylamine or pyridine.

SCHEME II



- Oxindole intermediates may be prepared according to the method of Scheme
- 5 II. Isatin **4**, obtained commercially or conveniently prepared according to the methods of Gassman described in *J. Org. Chem.* **1977**, 42, 1344 and US Patent Nos. 4,188,325 and 4,252,723, is treated with an alkylating agent, e.g., iodomethane, iodoethane, or iodopropane, in the presence of a suitable base (e.g. an amine base such as triethylamine or di-iso-propylethylamine or lithium, sodium, potassium or cesium
- 10 carbonate) in a suitable organic solvent (e.g. DMF, THF, DMSO, dioxane or acetonitrile) at a temperature between 0 °C and 65 °C to afford *N*-alkylated isatin **5**. Isatins **5** may be reduced to 1,3-dihydroindol-2-ones **6** by using red phosphorous and iodic acid, by use of hydrogen sulfide in pyridine/co-solvent mixture, or by the Wolf-Kishner reaction. The most convenient procedure involves heating isatin **5** in neat
- 15 hydrazine hydrate at reflux in the absence of any additional base. 1,3-Dihydroindol-2-one **6** is nitrated regioselectively using methods known to one skilled in the art (e.g., nitric acid in concentrated sulfuric acid or acetic acid, or sodium nitrate in trifluoroacetic acid at temperatures between -20 °C and 25 °C). 5-Nitrooxindole **7** is then reduced by dissolving metal reduction (e.g., iron and ammonium chloride in
- 20 ethanol/water) or catalytic hydrogenation to provide the 5-aminoxindole **1**.

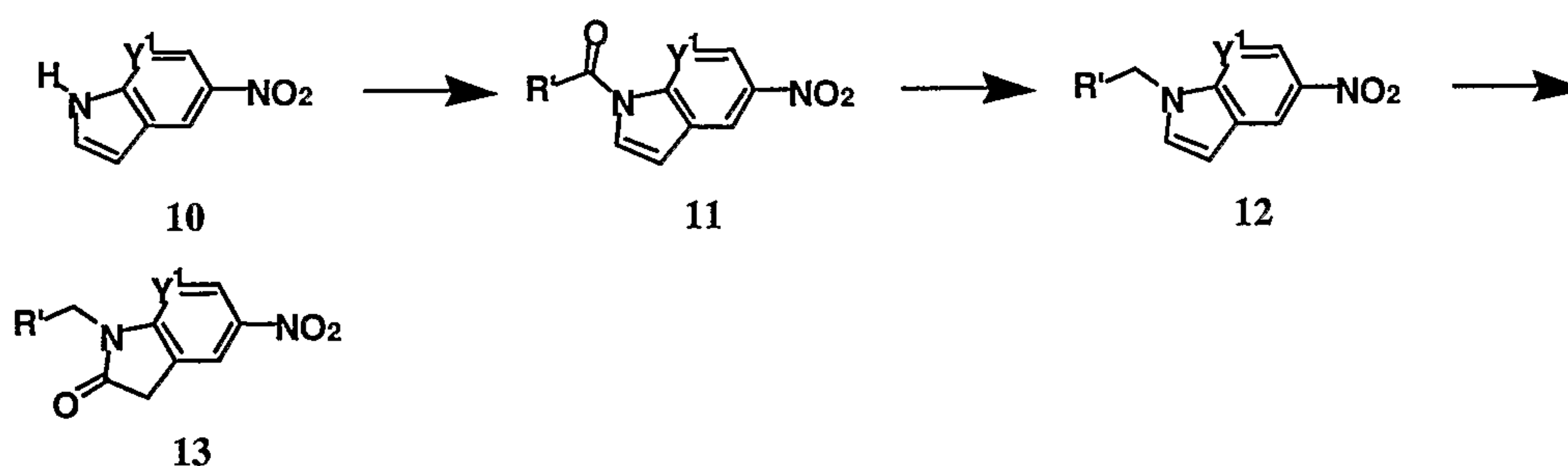
SCHEME III



Alternatively, commercially available 5-nitroisatin **8** is treated with an appropriate alkylating agent, e.g., iodomethane, iodoethane, or iodopropane, in the presence of a suitable base (e.g. an amine base such as triethylamine or di-isopropylethylamine or lithium, sodium, potassium or cesium carbonate) in a suitable organic solvent (e.g. DMF, THF, DMSO, dioxane or acetonitrile) at a temperature between 0 °C and 65 °C to afford *N*-alkylated isatin **9**. Isatin **9** may be reduced in one step to the requisite 5-aminoxindole **1** by heating in neat hydrazine hydrate at reflux temperatures or by catalytic hydrogenation.

10

SCHEME IV

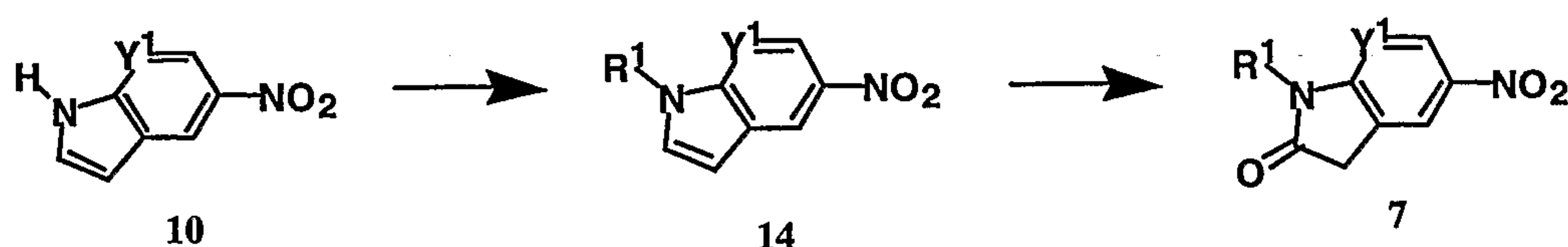


Scheme IV exemplifies another route to prepare 5-nitrooxindole.

Commercially available 5-nitrooxindole **10** is acylated with an appropriate acid chloride or anhydride in the presence of a suitable base such as triethylamine or pyridine and in a suitable solvent such as methylene chloride at temperatures between 0 °C and 25 °C. The resulting *N*-acylated oxindole **11** can be reduced to *N*-alkylindole **12** in high yields by $\text{BH}_3 \cdot \text{THF}$. *N*-Alkylindole **12** is further oxidized to the requisite 5-nitrooxindole **13** by a variety of known methods (e.g. DMSO/HCl, NBS).

20

SCHEME V

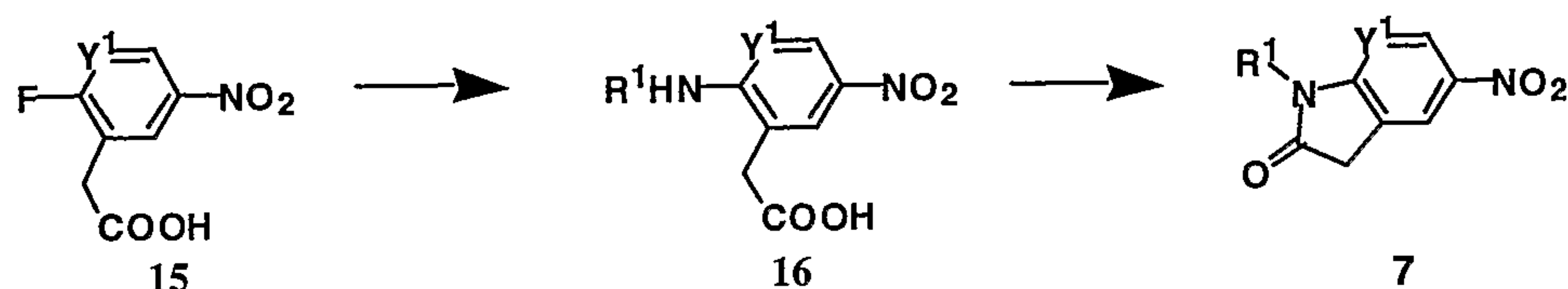


25

Alternatively, commercially available 5-nitrooxindole is treated with an appropriate alkylating agent, e.g., iodomethane, iodoethane, or iodopropane, in the presence of a suitable base (e.g., sodium hydride or lithium hexamethyldisilazane) in a suitable organic solvent (e.g. DMF, THF, or DMSO) at a temperature between 0 °C

and 65 °C to afford *N*-alkylated indole **14**. Indole **14** is oxidized to the requisite oxindole as discussed in Scheme IV.

SCHEME VI



In another route exemplified by Scheme VI, an appropriately substituted 2-halo-5-nitrophenylacetic acid **15** (e.g., preferably 2-fluoro-5-nitrophenylacetic acid) is treated with ammonia or an optionally substituted amine (RNH_2) in a suitable solvent such as DMSO or acetonitrile at temperatures between 35 °C and 85 °C to afford aniline **16** ($R = H$ or optionally substituted alkyl). Aniline **16** is treated with a strong acid such as HCl, H_2SO_4 , or TFA to effect cyclization to the requisite 5-nitrooxindole **7**.

Medical and Veterinary Uses

It is known that as a chemical compound class, oxazolidinones generically inhibit monoamine oxidase (MAO), the enzyme responsible for preventing acute blood pressure elevation by the endogenous and dietary amine, tyramine.

Accordingly, there is a demand to discover oxazolidinone antibiotics, which possess minimum MAO inhibitory activity to lower risk of potential drug-drug interactions. It has been discovered that, compounds of the present invention has unexceptedly weak MAO inhibitory activity, which indicates it possess the capacity to minimize or eliminate potential drug-drug interactions since strong inhibition of monoamine oxidase can result in altered clearance rates for other compounds normally metabolized by it, including several pharmaceuticals.

The compounds of the present invention may be used for the treatment of infectious, Gram-positive bacterial infections caused by a variety of bacterial organisms, including those that require long-term therapy (>28 days).

Examples of the bacterial organisms include gram-positive bacteria such as multiple resistant staphylococci, for example *S. aureus* and *S. epidermidis*; multiple resistant streptococci, for example *S. pneumoniae* and *S. pyogenes*; and multiple

resistant Enterococci, for example *E. faecalis*; gram negative aerobic bacteria such as Haemophilus, for example *H. influenzae* and Moraxella, for example *M. catarrhalis*; as well as anaerobic organisms such as bacteroides and clostridia species, and acid-fast organisms such as Mycobacteria, for example *M. tuberculosis*; and/or

5 *Mycobacterium avium*. Other examples include Escherichia, for example *E. coli*. intercellular microbes, for example Chlamydia and Rickettsiae.

Examples of infections that may be treated with the compounds of the present invention include central nervous system infections, external ear infections, infections of the middle ear, such as acute otitis media, infections of the cranial sinuses, eye

10 infections, infections of the oral cavity, such as infections of the teeth, gums and mucosa, upper respiratory tract infections, lower respiratory tract infections, genitourinary infections, gastrointestinal infections, gynecological infections, septicemia, bone and joint infections, skin and skin structure infections, bacterial endocarditis, burns, antibacterial prophylaxis of surgery, and antibacterial prophylaxis

15 in immunosuppressed patients, such as patients receiving cancer chemotherapy, or organ transplant patients. Specifically, infectious diseases that may be treated with the compounds of the present invention are gram-positive infections such as osteomyelitis, endocarditis and diabetic foot.

Antibacterial activity

20 The *in vitro* antibacterial activity of the compounds of the present invention may be assessed by following procedures recommended in (1) National Committee for Clinical Laboratory Standards (Jan. 2003), *Methods for dilution antimicrobial tests for bacteria that grow aerobically*, Approved Standard (6th ed), M7-A6, NCCLS, Wayne, PA; (2) National Committee for Clinical Laboratory Standards (Mar. 2001),

25 *Methods for antimicrobial susceptibility testing of anaerobic bacteria*, Approved Standard (5th ed), M11-A4, NCCLS, Wayne, PA; (3) National Committee for Clinical Laboratory Standards (Jan.2003), *MIC testing supplemental tables*, M100-S13 (for use with M7-A6), NCCLS, Wayne, PA; and (4) Murray PR, Baron EJ, Jorgensen JH, et al. *Manual of Clinical Microbiology* (8th ed) Washington, DC: American Society

30 for Microbiology Press, 2003. The MIC value is the lowest concentration of drug which prevented macroscopically visible growth under the conditions of the test. Table 1 shows the in vitro testing results.

Table 1

Results of *in vitro* antibacterial activity MIC₉₀ (μg/mL)

Example No.	<i>S. aureus</i> UC-76 SA-1	<i>S. pneumoniae</i> SV1 SP-3	<i>E. faecalis</i> MGH-2 EF 1-1
1	8	1	2
2	8	1	2
3	4	2	4
4	8	2	4
5	8	2	8
6	4	2	2
7	2	2	2
8	4	4	2
9	8	2	2
10	8	2	2
11	4	1	2
12	8	4	4
13	4	2	4
14	8	4	8
15	4	2	2
16	8	4	4
17	4	2	4
18	8	4	8
10	4	2	2
20	8	4	8
21	8	2	4
22	8	4	4
23	8	4	4
24	8	4	4
25	8	8	8
26	8	4	4
27	8	4	8
28	8	2	4
29	2	2	2

Pharmaceutical Salts

The compound of formula I may be used in its native form or as a salt. In cases where forming a stable nontoxic acid or base salt is desired, administration of the compound as a pharmaceutically acceptable salt may be appropriate. Examples of pharmaceutically acceptable salts of the present invention include inorganic salts such as hydrochloride, hydrobromide, sulfate, nitrate, bicarbonate, carbonate salts, and organic salts such as tosylate, methanesulfonate, acetate, citrate, malonate, tartarate, succinate, benzoate, ascorbate, etoglutarate, and glycerophosphate. .

Pharmaceutically acceptable salts may be obtained using standard procedures well known in the art, for example, reacting a sufficiently basic compound such as an amine with a suitable acid affording a physiologically acceptable anion. Alkali metal

(for example, sodium, potassium or lithium) or alkaline earth metal (for example calcium) salts of carboxylic acids can also be made.

Routes of Administration

The oxazolidinone antibacterial prodrugs of this invention have useful activity
5 against a variety of organisms including, but not limiting to, *Staphylococcus aureus*,
Staphylococcus epidermidis, *Enterococcus faecium*, *Streptococcus pneumoniae*,
Streptococcus pyogenes, *Enterococcus faecalis*, *Moraxella catarrhalis* and *H.*
influenzae. In therapeutic use for treating, or combating, bacterial infections in a
mammal (i.e. human and animals) an oxazolidinone prodrug of the present invention
10 or its pharmaceutical compositions can be administered orally, parenterally, topically,
rectally, transmucosally, or intestinally.

Parenteral administrations include indirect injections to generate a systemic
effect or direct injections to the afflicted area. Examples of parenteral administrations
are subcutaneous, intravenous, intramuscular, intradermal, intrathecal, intraocular,
15 intranasal, intraventricular injections or infusions techniques.

Topical administrations include the treatment of infectious areas or organs
readily accessibly by local application, such as, for example, eyes, ears including
external and middle ear infections, vaginal, open wound, skins including the surface
skin and the underneath dermal structures, or other lower intestinal tract. It also
20 includes transdermal delivery to generate a systemic effect.

The rectal administration includes the form of suppositories.

The transmucosal administration includes nasal aerosol or inhalation
applications.

The preferred routes of administration are oral and parenteral.

25 Composition/Formulation

Pharmaceutical compositions of the present invention may be manufactured by
processes well known in the art, e.g., by means of conventional mixing, dissolving,
granulation, dragee-making, levigating, emulsifying, encapsulating, entrapping,
lyophilizing processes or spray drying.

30 Pharmaceutical compositions for use in accordance with the present invention
may be formulated in conventional manner using one or more physiologically
acceptable carriers comprising excipients and auxiliaries which facilitate processing of

the active compounds into preparations which can be used pharmaceutically. Proper formulation is dependent upon the route of administration chosen.

For oral administration, the compounds can be formulated by combining the active compounds with pharmaceutically acceptable carriers well known in the art.

- 5 Such carriers enable the compounds of the invention to be formulated as tablets, pills, lozenges, dragees, capsules, liquids, solutions, emulsions, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient. A carrier can be at least one substance which may also function as a diluent, flavoring agent, solubilizer, lubricant, suspending agent, binder, tablet disintegrating agent, and encapsulating agent.
- 10 Examples of such carriers or excipients include, but are not limited to, magnesium carbonate, magnesium stearate, talc, sugar, lactose, sucrose, pectin, dextrin, mannitol, sorbitol, starches, gelatin, cellulosic materials, low melting wax, cocoa butter or powder, polymers such as polyethylene glycols and other pharmaceutical acceptable materials.

- 15 Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to
- 20 characterize different combinations of active compound doses.

- Pharmaceutical compositions which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with a filler such as lactose, a binder such as starch, and/or a
- 25 lubricant such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, liquid polyethylene glycols, cremophor, capmul, medium or long chain mono-, di- or triglycerides. Stabilizers may be added in these formulations, also.

- 30 Liquid form compositions include solutions, suspensions and emulsions. For example, there may be provided solutions of the compounds of this invention dissolved in water and water-propylene glycol and water-polyethylene glycol systems,

optionally containing suitable conventional coloring agents, flavoring agents, stabilizers and thickening agents.

The compounds may also be formulated for parenteral administration, *e.g.*, by injections, bolus injection or continuous infusion. Formulations for parenteral administration may be presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulating materials such as suspending, stabilizing and/or dispersing agents.

For injection, the compounds of the invention may be formulated in aqueous solution, preferably in physiologically compatible buffers or physiological saline buffer. Suitable buffering agents include trisodium orthophosphate, sodium bicarbonate, sodium citrate, N-methylglucamine, L(+)-lysine and L(+)-arginine.

Parenteral administrations also include aqueous solutions of a water soluble form, such as, without limitation, a salt, of the active compound. Additionally, suspensions of the active compounds may be prepared in a lipophilic vehicle. Suitable lipophilic vehicles include fatty oils such as sesame oil, synthetic fatty acid esters such as ethyl oleate and triglycerides, or materials such as liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers and/or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile, pyrogen-free water, before use.

For suppository administration, the compounds may also be formulated by mixing the agent with a suitable non-irritating excipient which is solid at room temperature but liquid at rectal temperature and therefore will melt in the rectum to release the drug. Such materials include cocoa butter, beeswax and other glycerides.

For administration by inhalation, compounds of the present invention can be conveniently delivered through an aerosol spray in the form of solution, dry powder, or suspensions. The aerosol may use a pressurized pack or a nebulizer and a suitable propellant. In the case of a pressurized aerosol, the dosage unit may be controlled by providing a valve to deliver a metered amount. Capsules and cartridges of, for

example, gelatin for use in an inhaler may be formulated containing a power base such as lactose or starch.

For topical applications, the pharmaceutical composition may be formulated in a suitable ointment containing the active component suspended or dissolved in one or more carriers. Carriers for topical administration of the compounds of this invention include, but are not limited to, mineral oil, liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene, polyoxypropylene compound, emulsifying wax and water. Alternatively, the pharmaceutical compositions can be formulated in a suitable lotion such as suspensions, emulsion, or cream containing the active components suspended or dissolved in one or more pharmaceutically acceptable carriers. Suitable carriers include, but are not limited to, mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, ceteary alcohol, 2-octyldodecanol, benzyl alcohol and water.

For ophthalmic and otitis uses, the pharmaceutical compositions may be formulated as micronized suspensions in isotonic, pH adjusted sterile saline, or preferably, as solutions in isotonic, pH adjusted sterile saline, either with or without a preservative such as a benzylalkonium chloride. Alternatively, for ophthalmic uses, the pharmaceutical compositions may be formulated in an ointment such as petrolatum.

In addition to the formulations described previously, the compounds may also be formulated as depot preparations. Such long acting formulations may be in the form of implants. A compound of this invention may be formulated for this route of administration with suitable polymers, hydrophobic materials, or as a sparingly soluble derivative such as, without limitation, a sparingly soluble salt.

Additionally, the compounds may be delivered using a sustained-release system. Various sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for 24 hours or for up to several days.

Dosage

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an amount sufficient to achieve the intended purpose, *i.e.*, the treatment or prevent of infectious diseases. More specifically, a therapeutically effective amount means an amount of compound

effective to prevent, alleviate or ameliorate symptoms of disease or prolong the survival of the subject being treated.

The quantity of active component, that is the compound of this invention, in the pharmaceutical composition and unit dosage form thereof may be varied or
5 adjusted widely depending upon the manner of administration, the potency of the particular compound and the desired concentration. Determination of a therapeutically effective amount is well within the capability of those skilled in the art. Generally, the quantity of active component will range between 0.5% to 90% by weight of the composition.

10 Generally, a therapeutically effective amount of dosage of active component will be in the range of about 0.1 to about 400 mg/kg of body weight/day, more preferably about 1.0 to about 50 mg/kg of body weight/day. It is to be understood that the dosages may vary depending upon the requirements of each subject and the severity of the bacterial infection being treated. In average, the effective amount of
15 active component is about 200 mg to 800 mg and preferable 600 mg per day.

The desired dose may conveniently be presented in a single dose or as divided doses administered at appropriate intervals, for example, as two, three, four or more sub-doses per day. The sub-dose itself may be further divided, e.g., into a number of discrete loosely spaced administrations; such as multiple inhalations from an
20 insufflator or by application of a plurality of drops into the eye.

Also, it is to be understood that the initial dosage administered may be increased beyond the above upper level in order to rapidly achieve the desired plasma concentration. On the other hand, the initial dosage may be smaller than the optimum and the daily dosage may be progressively increased during the course of treatment
25 depending on the particular situation. If desired, the daily dose may also be divided into multiple doses for administration, e.g., two to four times per day.

In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration and other procedures known in the art may be used to determine the desired dosage amount.

30 Oral Efficacy

EXAMPLES

In the discussion above and in the examples below, the following abbreviations have the following meanings. If an abbreviation is not defined, it has its generally accepted meaning.

5	bm	=	broad multiplet
	BOC	=	<i>tert</i> -butoxycarbonyl
	bd	=	broad doublet
	bs	=	broad singlet
	CDI	=	1,1 <i>O</i> -carbodiimidazole
10	d	=	doublet
	dd	=	doublet of doublets
	dq	=	doublet of quartets
	dt	=	doublet of triplets
	DMF	=	dimethylformamide
15	DMAP	=	dimethylaminopyridine
	DMSO	=	dimethyl sulfoxide
	eq.	=	equivalents
	g	=	grams
	h	=	hours
20	HPLC	=	high pressure liquid chromatography
	HATU	=	N-[(dimethylamino)-1H-1,2,3-triazolo-[4,5-b]pyridin-1-yl-methylene]-N-methylmethanaminium hexafluorophosphate N-oxide
	LG	=	leaving group
25	m	=	multiplet
	M	=	molar
	M%	=	mole percent
	max	=	maximum
	meq	=	milliequivalent
30	mg	=	milligram
	mL	=	milliliter
	mm	=	millimeter
	mmol	=	millimol
	q	=	quartet
35	s	=	singlet
	t or tr	=	triplet
	TBS	=	tributylsilyl
	TFA	=	trifluoroacetic acid
	THF	=	tetrahydrofuran
40	TLC	=	thin layer chromatography
	p-TLC	=	preparative thin layer chromatography
	μL	=	microliter
	N	=	normality
	MeOH	=	methanol
45	DCM	=	dichloromethane
	HCl	=	hydrochloric acid
	ACN	=	acetonitrile
	MS	=	mass spectrometry

	rt	=	room temperature
	EtOAc	=	ethyl acetate
	EtO	=	ethoxy
	Ac	=	acetate
5	NMP	=	1-methyl-2-pyrrolidinone
	μL	=	microliter
	J	=	coupling constant
	NMR	=	Nuclear magnetic resonance
	MHz	=	megahertz
10	Hz	=	hertz
	m/z	=	mass to charge ratio
	min	=	minutes
	Boc	=	<i>tert</i> -butoxycarbonyl
	CBZ	=	benzyloxycarbonyl
15	DCC	=	1,3-dicyclohexylcarbodiimide
	PyBop	=	benzotriazole-1-yl-oxy-trispyrrolidinophosphonium hexafluorophosphate

Preparation 1 Preparation of 5-Amino-1-methyl-1,3-dihydro-indol-2-one

20 Step 1: 1-Methyl-1,3-dihydro-indol-2-one

1-Methyl-1*H*-indole-2,3-dione (5.00 g, 31.0 mmol) is heated with neat hydrazine hydrate (30 ml) at 130 °C for 1.5 hours. The reaction mixture is cooled, diluted with ice water, and extracted with ethyl acetate. The extract is washed with brine, dried over sodium sulfate, and evaporated to give product as a yellowish brown solid (4.38g, 96%); HPLC r.t. 3.69 min; MS for C₉H₉NO m/z 148.1(M+H)⁺.

Step 2: 1-Methyl-5-nitro-1,3-dihydro-indol-2-one

1-Methyl-1,3-dihydro-indol-2-one (Step 1, 2.10 g, 14.3 mmol) is added in portions to 70% nitric acid (10 ml) at -10 °C. After the addition is complete, the reaction is allowed to warm to room temperature and then stirred for 5 hours. The mixture is diluted with ice water and the resulting precipitate filtered, washed with water, and dried under vacuum to give product as a brown solid (1.88g, 70%); HPLC r.t. 3.97 min; MS for C₉H₈N₂O₃ m/z 193.9(M+H)⁺.

Step 3: 5-Amino-1-methyl-1,3-dihydro-indol-2-one

Iron powder (2.09 g, 37.46 mmol) is added in small portion to a mixture of 1-methyl-5-nitro-1, 3-dihydro-indol-2-one (Step 2, 1.8 g, 9.36 mmol) and ammonium chloride (4.96 g, 93.6 mmol) in ethanol (100 ml) and water (50 ml) at 90°C. The reaction mixture is stirred vigorously and heated for 30min, cooled to room temperature, and diluted with dichloromethane (200 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried

over sodium sulfate, and evaporated to give product as a dark brown solid (1.44g, 94.7%); HPLC r.t. 1.06 min; MS for $C_9H_{10}N_2O$ m/z 163.2(M+H)⁺.

Preparation 2 Preparation of 7-fluoro-1-methyl-5-nitro-1,3-dihydro-indol-2-one

5 Step 1: 7-Fluoro-1-methyl-1*H*-indole-2,3-dione

7-Fluoro-1*H*-indole-2,3-dione (prepared according to the method of Gassman as described in US Patent 4,188,325, 1.0 g, 6.05 mmol), iodomethane (1.13 ml, 18.2 mmol) and potassium carbonate (1.65 g, 12.1 mmol) in DMF (15 ml) are stirred at room temperature for 24 hours. The reaction mixture is diluted with ethyl acetate,
10 washed with water and brine, dried (Na_2SO_4), and evaporated to give product as an orange solid (1.05 g, 97%); HPLC r.t. 3.79 min; MS for $C_9H_6FNO_2$ m/z 180.0(M+H)⁺.

Step 2: 7-Fluoro-1-methyl-1,3-dihydro-indol-2-one

7-Fluoro-1-methyl-1*H*-indole-2, 3-dione (Step 1, 1.05 g, 5.86 mmol) is heated
15 with neat hydrazine hydrate (10 ml) at 130 °C for 1 hour. The mixture is cooled, diluted with ice water and extracted with ethyl acetate. The extract is washed with brine, dried (Na_2SO_4), and evaporated to give product as a light yellow solid (0.895g, 92%); HPLC r.t. 4.07 min; MS for C_9H_8FNO m/z 165.16 (M+H)⁺.

Step 3: 7-Fluoro-1-methyl-5-nitro-1,3-dihydro-indol-2-one

20 7-Fluoro-1-methyl-1,3-dihydro-indol-2-one (Step 2, 0.89 g, 5.38 mmol) is added portionwise to 70% nitric acid (5 ml) at -10 °C. After the addition is complete, the reaction is allowed to warm to room temperature and then stirred for 7 hours. The mixture is diluted with ice water and the resulting precipitate filtered, washed with water, and dried under vacuum to give product as a light brown solid (0.84g, 74%);
25 HPLC r.t. 4.32 min.

Preparation 3 Preparation of 5-amino-1-ethyl-1,3-dihydro-indol-2-one

Step 1: 1-Ethyl-1*H*-indole-2,3-dione

1*H*-Indole-2,3-dione (5.00 g, 0.034 mol), iodoethane (5.44 ml, 0.068 mol) and
30 potassium carbonate (9.28 g, 0.068 mol) in DMF (50 ml) are stirred at room temperature for 72 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na_2SO_4) and evaporated to give product as an orange solid (5.95 g, 100%); HPLC r.t. 3.96 min; MS for $C_{10}H_9NO_2$ m/z 176.1 (M+H)⁺.

Step 2: 1-Ethyl-1,3-dihydro-indol-2-one

1-Ethyl-1*H*-indole-2,3-dione (Step 1, 5.60 g, 31.9 mmol) is heated with neat hydrazine hydrate (20 ml) at 130 °C for 1 hour. The reaction mixture is cooled, diluted with ice water, and extracted with ethyl acetate. The organic layer is washed
5 with brine, dried (Na₂SO₄) and evaporated to give product as a yellowish orange solid (4.85 g, 94%); HPLC r.t. 4.12 min; MS for C₁₀H₁₁NO m/z 162.1 (M+H)⁺.

Step 3: 1-Ethyl-5-nitro-1,3-dihydro-indol-2-one

1-Ethyl-1,3-dihydro-indol-2-one (Step 2, 4.00 g, 24.8 mmol) is added to a stirred solution of sodium nitrate (2.10 g, 24.8 mmol) in trifluoroacetic acid (100 ml).
10 The reaction mixture is stirred at room temperature for 30 minutes and then poured on ice. The resulting precipitate was filtered, washed with water, and dried under vacuum to give product as a brown solid (3.7 g, 72%); HPLC r.t. 4.29 min; MS for C₁₀H₁₀N₂O₃ m/z 207.2 (M+H)⁺.

Step 4: 5-Amino-1-ethyl-1,3-dihydro-indol-2-one

15 Iron powder (3.89 g, 69.8 mmol) is added portionwise to a mixture of 1-ethyl-5-nitro-1, 3-dihydro-indol-2-one (Step 3, 3.60 g, 17.5 mmol) and ammonium chloride (9.24 g, 175 mmol) in ethanol (150 ml) and water (75 ml) at 90 °C. The reaction mixture is stirred vigorously and heated for 30 minutes, cooled to room temperature and diluted with dichloromethane (300 ml). The mixture is filtered through celite, the
20 organic layer separated and washed with water and brine, dried over sodium sulfate and evaporated to give product as a dark brown solid (2.74 g, 89%); HPLC r.t. 1.86 min; MS for C₁₀H₁₂N₂O m/z 177.1 (M+H)⁺.

Preparation 4 Preparation of 5-Amino-1-isopropyl-1,3-dihydro-indol-2-one25 Step 1: 1-Isopropyl-1*H*-indole-2,3-dione

1*H*-Indole-2, 3-dione (5.0 g, 0.034 mol), iodopropane (6.83 ml, 0.068 mol) and potassium carbonate (9.28 g, 0.068 mol) in DMF (30 ml) are stirred at room temperature for 72 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated to give product as an orange
30 solid (6.08 g, 94.5%); HPLC r.t. 4.38 min; MS for C₁₁H₁₁NO₂ m/z 190.1 (M+H)⁺.

Step 2: 1-Isopropyl-1,3-dihydro-indol-2-one

1-Isopropyl-1*H*-indole-2,3-dione (Step 1, 3.00 g, 15.9 mmol) was heated with neat hydrazine hydrate (10 ml) at 130 °C for 1.5 hours. The reaction was cooled,

diluted with ice water, and extracted with ethyl acetate. The organic layer is washed with brine, dried (Na_2SO_4), and evaporated to give product as a light brown solid (2.64 g, 95%); HPLC r.t. 4.54 min; MS for $\text{C}_{11}\text{H}_{13}\text{NO}$ m/z 176.1($\text{M}+\text{H}$)⁺.

Step 3: 1-Isopropyl-5-nitro-1,3-dihydro-indol-2-one

5 1-Isopropyl-1,3-dihydro-indol-2-one (Step 2, 2.50 g, 14.3 mmol) is added to a stirred solution of sodium nitrate (1.20g, 14.26mmol) in trifluoroacetic acid (50ml) and stirred at room temperature for 5h. The reaction was diluted with ice water and resulting precipitate filtered, washed with water, and dried under vacuum to give product as a brown solid (2.7g, 86%); HPLC r.t. 4.71 min; MS for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_3$ m/z 219.0($\text{M}-\text{H}$)⁻.

Step 4: 5-Amino-1-isopropyl-1,3-dihydro-indol-2-one

15 Iron powder (2.63 g, 47.2 mmol) is added in small portion to a mixture of 1-isopropyl-5-nitro-1,3-dihydro-indol-2-one (Step 3, 2.60 g, 11.8 mmol) and ammonium chloride (6.27 g, 118 mmol) in ethanol (80 ml) and water (40 ml) at 90 °C. The reaction mixture is stirred vigorously and heated for 45min, then cooled to room temperature and diluted with dichloromethane (250ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried (Na_2SO_4) and evaporated to give product as a dark brown gummy solid (2.2g, 98.2%); HPLC r.t. 2.51 min; MS for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$ m/z 191.1($\text{M}+\text{H}$)⁺.

20

Preparation 5 Preparation of 5-Amino-1-propyl-1,3-dihydro-indol-2-one

Step 1: 5-Nitro-1-propyl-1,3-dihydro-indol-2-one

25 (2-Fluoro-5-nitrophenyl)acetic acid (Step 1, 5.00 g, 0.0251 mol) and *n*-propylamine (5 eq., 10.4 ml, 0.126 mol) are mixed in DMSO (25 ml) and stirred at 45 °C overnight. Excess *n*-propylamine is removed under vacuum and 2N hydrochloric acid (80 ml) added in one portion. The mixture is stirred for 20 minutes at room temperature and the resulting light yellow precipitate filtered, washed with water and dried under vacuum (5.9 g, 96%); HPLC r.t. 4.68 min MS for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_3$ m/z 220.9 ($\text{M}+\text{H}$)⁺.

30 Step 2: 5-Amino-1-propyl-1,3-dihydro-indol-2-one

Iron powder (3.30 g, 59 mmol) is added portionwise to 5-Nitro-1-propyl-1,3-dihydro-indol-2-one (Step 1, 3.25 g, 14.8 mmol) and ammonium chloride (7.8 g, 148 mmol) in ethanol (100 ml) and water (50 ml) at 90 °C. The reaction is stirred

vigorously and heated for 60 min, cooled to room temperature and diluted with dichloromethane (500 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried (Na_2SO_4) and evaporated to give product as a dark brown solid (2.8 g, 99%); HPLC r.t. 2.62 min; MS for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$ m/z 191.1 ($\text{M}+\text{H}$)⁺.

Preparation 6 Preparation of (*R*)-3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propionic acid methyl ester

Step 1: 7-Fluoro-5-nitro-1-propyl-1,3-dihydro-indol-2-one

Crude (2,3-difluoro-5-nitrophenyl)acetic acid (Example 33, Step 1, 2.00 g, 9.2 mmol) and *n*-propylamine (6 eq., 4.54 ml, 0.0553 mol) are mixed in DMSO (10 ml) and stirred at 50 °C for 2 hours. 2N Hydrochloric acid (40 ml) is added in one portion and the mixture stirred at room temperature for 2 hours. The resulting light yellow precipitate is filtered, washed with water and dried under vacuum. The residue is purified by flash column chromatography (20% Ethylacetate/hexane) to give product as a yellow solid (0.93 g, 42% isolated yield, 85% assuming that starting material is 50% desired 5- NO_2 isomer); HPLC r.t. 5.40 min; MS for $\text{C}_{11}\text{H}_{11}\text{FN}_2\text{O}_3$ m/z 239.1 ($\text{M}+\text{H}$)⁺.

Step 2: 5-Amino-7-fluoro-1-propyl-1,3-dihydro-indol-2-one

Iron powder (0.855 g, 15.3 mmol) is added in small portions to 7-Fluoro-5-nitro-1-propyl-1,3-dihydro-indol-2-one (Step 1, 0.910 g, 3.82 mmol) and ammonium chloride (2.02 g, 38.2 mmol) in ethanol (60 ml) and water (30 ml) at 90 °C. The reaction mixture is stirred vigorously and heated for 60 min, cooled to room temperature, and diluted with dichloromethane (300 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried over sodium sulfate and evaporated to give product as a dark brown solid (0.820 g, 99%); HPLC r.t. 3.03 min; MS for $\text{C}_{11}\text{H}_{13}\text{FN}_2\text{O}$ m/z 209.0 ($\text{M}+\text{H}$)⁺.

Step 3: (*R*)-3-(7-Fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propionic acid methyl ester

5-Amino-7-fluoro-1-propyl-1,3-dihydro-indol-2-one (Step 2, 0.300 g, 1.44 mmol), methyl (2*R*)-glycidate (0.147 g, 1.44 mmol) and lithium trifluoromethanesulfonate (0.220 g, 1.44 mmol) in acetonitrile (5 ml) are heated at 90 °C for 8 hours. The reaction is diluted with ethyl acetate, washed with water and

brine, dried (Na_2SO_4) and evaporated. The residue is purified by PTLC (5% methanol/dichloromethane) to give pure product as a yellow solid (0.250 g, 56%); HPLC r.t. 4.03 min; MS for $\text{C}_{15}\text{H}_{19}\text{FN}_2\text{O}_4$ m/z 311.2 ($\text{M}+\text{H}$)⁺.

5 **Preparation 7** Preparation of 5-Amino-1-cyclopropyl-1,3-dihydro-indol-2-one

Step 1: (2-Fluoro-5-nitrophenyl)acetic acid

(2-Fluorophenyl)acetic acid (5 g, 0.0324 mol) is dissolved in concentrated sulfuric acid (20 ml) and the resulting solution cooled to $-10\text{ }^\circ\text{C}$ with vigorous stirring. A solution of nitric acid (2.08 ml, 69.3%, 0.0324 mol) and sulfuric acid (2
10 ml) is added dropwise at a rate such that the temperature remains below $-5\text{ }^\circ\text{C}$. The thickened slurry is stirred for 15 minutes and then poured on ice. The resulting white precipitate is filtered and dried under vacuum (6.5 g, 99%); ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.35 (1H, dd), 8.26-8.18 (1H, m), 7.48 (1H, t), 3.80 (2H, d).

Step 2: 1-Cyclopropyl-5-nitro-1,3-dihydro-indol-2-one

15 (2-Fluoro-5-nitrophenyl)acetic acid (Step 1, 1.00 g, 0.00502 mol) and cyclopropylamine (6 eq., 2.08 ml, 0.0301 mol) are mixed in DMSO (5 ml) and stirred at $45\text{ }^\circ\text{C}$ overnight. Excess cyclopropylamine is removed under vacuum and 2N hydrochloric acid (20 ml) added in one portion. The mixture is stirred for 20 minutes at room temperature and the resulting light yellow precipitate filtered, washed with
20 water and dried under vacuum (0.95 g, 87%).

Step 3: 5-Amino-1-cyclopropyl-1,3-dihydro-indol-2-one

Iron powder (1.26 g, 22.9 mmol) is added portionwise to 1-cyclopropyl-5-nitro-1,3-dihydro-indol-2-one (Step 2, 1.25 g, 5.72 mmol) and ammonium chloride (3.01 g, 57.2 mmol) in ethanol (50 ml) and water (25 ml) at $90\text{ }^\circ\text{C}$. The reaction is
25 stirred vigorously and heated for 30 min, cooled to room temperature and diluted with dichloromethane (150 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried (Na_2SO_4) and evaporated to give product as a dark brown solid (0.98 g, 91%); HPLC r.t. 2.21 min; MS for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}$ m/z 189.1 ($\text{M}+\text{H}$)⁺.

30

Preparation 8 Preparation of 5-amino-1-sec-butyl-1,3-dihydro-indol-2-one

Step 1: 1-sec-Butyl-5-nitro-1,3-dihydro-indol-2-one

(2-Fluoro-5-nitrophenyl)acetic acid (Example 45, Step 1, 2.00 g, 10.0 mmol) and *sec*-butylamine (6 eq., 6.08 ml, 60.2 mmol) are mixed in dimethyl sulfoxide (10 ml) and stirred at 45 °C overnight. Excess *sec*-butylamine is removed under vacuum and 2N hydrochloric acid (40 ml) added in one portion. The mixture is stirred for 1.5
5 hours at 45 °C and then extracted with dichloromethane. The extract is washed with brine, dried (Na₂SO₄) and evaporated. The residue is purified by flash column chromatography to give product as a yellow solid (1.68 g, 71%); HPLC r.t. 5.05 min; MS for C₁₂H₁₄N₂O₃ m/z 235.3 (M+H)⁺.

Step 2: 5-Amino-1-*sec*-butyl-1,3-dihydro-indol-2-one

10 Iron powder (1.55 g, 28.0 mmol) is added portionwise to 1-*sec*-Butyl-5-nitro-1,3-dihydro-indol-2-one (Step 1, 1.64 g, 7.00 mmol) and ammonium chloride (3.70 g, 70 mmol) in ethanol (70 ml) and water (35 ml) at 90 °C. The reaction is stirred vigorously and heated for 45 min, cooled to room temperature and diluted with dichloromethane (200 ml). The mixture is filtered through celite, the organic layer
15 separated and washed with water and brine, dried (Na₂SO₄) and evaporated to give product as a dark brown solid (1.41 g, 99%); HPLC r.t. 2.80 min; MS for C₁₂H₁₆N₂O m/z 205.1 (M+H)⁺.

Preparation 9 Preparation of 5-amino-1-cyclopropylmethyl-1,3-dihydro-indol-2-one

20 Step 1: 1-Cyclopropylmethyl-5-nitro-1,3-dihydro-indol-2-one

(2-Fluoro-5-nitrophenyl)acetic acid (Example 45, Step 1, 1.15 g, 5.75 mmol) and (aminomethyl)cyclopropane (6 eq., 3.00 ml, 34.5 mmol) are mixed in dimethyl sulfoxide (6 ml) and stirred at 45 °C overnight. Excess (aminomethyl)cyclopropane is removed under vacuum and 2N hydrochloric acid (25 ml) added in one portion. The
25 mixture is stirred for 1 hour at room temperature and the resulting precipitate filtered, washed with water, and dried to give product as a yellowish-brown solid (1.25 g, 94%); HPLC r.t. 4.87 min; MS for C₁₂H₁₂N₂O₃ m/z 233.1 (M+H)⁺.

Step 2: 5-Amino-1-cyclopropylmethyl-1,3-dihydro-indol-2-one

Iron powder (1.15 g, 20.7 mmol) is added portionwise to 1-
30 Cyclopropylmethyl-5-nitro-1,3-dihydro-indol-2-one (Step 1, 1.2 g, 5.16 mmol) and ammonium chloride (2.75 g, 51.6 mmol) in ethanol (50 ml) and water (25 ml) at 90 °C. The reaction is stirred vigorously and heated for 30 min, cooled to room temperature and diluted with dichloromethane (250 ml). The mixture is filtered

through celite, the organic layer separated and washed with water and brine, dried (Na_2SO_4) and evaporated to give product as a dark brown solid (1.09 g, 96%); HPLC r.t. 2.68 min; MS for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}$ m/z 203.4 ($\text{M}+\text{H}$)⁺.

5 **Preparation 10** Preparation of 10 5-Amino-1-(2-fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one

Step 1: Toluene-4-sulfonic acid 2-fluoro-1-methyl-ethyl ester

p-Toluenesulfonic anhydride (16.3 g, 49.9 mmol) is added portionwise to 1-fluoro-2-propanol (3.00 g, 38.4 mmol), triethylamine (16.1 ml, 115 mmol) and 4-(dimethylamino)pyridine (1.41 g, 11.5 mmol) in dichloromethane (30 ml) at 0 °C, allowed to warm to room temperature, and then stirred for 2 hours. The mixture is diluted with dichloromethane, washed with citric acid and brine, dried (Na_2SO_4) and evaporated to give product as an oil (7.15 g, 80%).

Step 2: 1-(2-Fluoro-1-methyl-ethyl)-1*H*-indole-2,3-dione

15 Isatin (2.70 g, 18.4 mmol), Toluene-4-sulfonic acid 2-fluoro-1-methyl-ethyl ester (Step 1, 6.40 g, 27.6 mmol) and potassium carbonate (7.61 g, 55.1 mmol) in dimethylformamide (20 ml) are stirred at 50 °C for 24 hours. The reaction is diluted with water and extracted with ethyl acetate. The extract is washed with brine, dried (Na_2SO_4) and evaporated. The residue is purified by flash column chromatography (30% ethyl acetate/hexane) to give product as an orange solid (2.40 g, 63%); HPLC r.t. 4.38 min; MS for $\text{C}_{11}\text{H}_{10}\text{FNO}_2$ m/z 207.9 ($\text{M}+\text{H}$)⁺.

Step 3: 1-(2-Fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one

1-(2-Fluoro-1-methyl-ethyl)-1*H*-indole-2,3-dione (Step 2, 2.30 g, 11.1 mmol) is heated with neat hydrazine hydrate (20 ml) at 130 °C for 30 minutes. The reaction mixture is cooled, diluted with ice water, and extracted with ethyl acetate. The extract is washed with brine, dried over sodium sulfate, and evaporated to give product as a yellowish brown solid (1.78g, 83%); HPLC r.t. 4.50 min.

Step 4: 1-(2-Fluoro-1-methyl-ethyl)-5-nitro-1,3-dihydro-indol-2-one

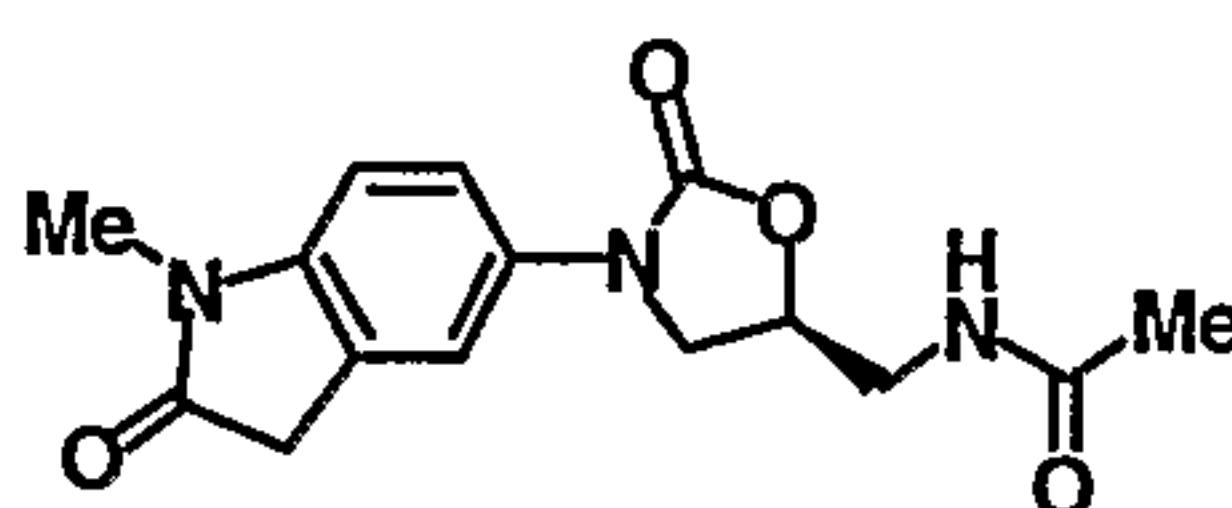
1-(2-Fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one (Step 3, 1.68 g, 8.69 mmol) is added in portions to sodium nitrate (0.737 g, 8.69 mmol) in trifluoroacetic acid (15 ml). After the addition is complete, the reaction is stirred at room temperature for 8 hours. The mixture is diluted with ice water and the resulting precipitate filtered, washed with water, and dried under vacuum. Final purification by

flash column chromatography (30% ethyl acetate/hexane) gives product as a light yellow solid (0.760g, 37%); HPLC r.t. 4.75 min; MS for C₁₁H₁₁FN₂O₃ m/z 239.1(M+H)⁺.

Step 5: 5-Amino-1-(2-fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one

5 Iron powder (0.714 g, 12.8 mmol) is added in small portion to a mixture of 1-methyl-5-nitro-1,3-dihydro-indol-2-one (Step 4, 0.760 g, 3.19 mmol) and ammonium chloride (1.68 g, 31.9 mmol) in ethanol (50 ml) and water (25 ml) at 90°C. The reaction mixture is stirred vigorously and heated for 45 min, cooled to room temperature, and diluted with dichloromethane (250 ml). The mixture is filtered
10 through celite, the organic layer separated and washed with water and brine, dried over sodium sulfate, and evaporated to give product as a dark brown solid (0.665 g, 99%); HPLC r.t. 2.50 min; MS for C₁₁H₁₃FN₂O m/z 209.0 (M+H)⁺.

Example 1 Preparation of (S)-N-[3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide
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Step 1: Preparation of (R)-[2-hydroxy-3-(1-Methyl-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-propyl]-carbamic acid *tert*-butyl ester

20 5-Amino-1-methyl-1,3-dihydro-indol-2-one (Preparation 1, 1.20 g, 7.40 mmol), (S)-oxiranylmethyl-carbamic acid *tert*-butyl ester (1.28 g, 7.40 mmol) and lithium trifluoromethanesulfonate (1.14 g, 7.398 mmol) in acetonitrile (10 ml) are heated at 70 °C for 1 hour. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by flash
25 column chromatography (70% EtOAc/Hexane) to give the title compound as a light brown solid. HPLC r.t. 3.20 min; MS for C₁₇H₂₅N₃O₄ m/z 336.4(M+H)⁺.

Step 2: Preparation of (S)-[3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

30 (R)-[2-Hydroxy-3 -(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-propyl]-carbamic acid *tert*.butyl ester (Step 1, 0.10 g, 0.298 mmol) and 1,1-carbonyldiimidazole (0.053 g, 0.327 mmol) in acetonitrile (3 ml) is stirred and heated

at 60 °C for 2 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue was purified by PTLC (10% MeOH/DCM) to give the title compound as a light brown solid. HPLC r.t. 4.24 min; MS for C₁₈H₂₃N₃O₅ m/z 362.3(M+H)⁺.

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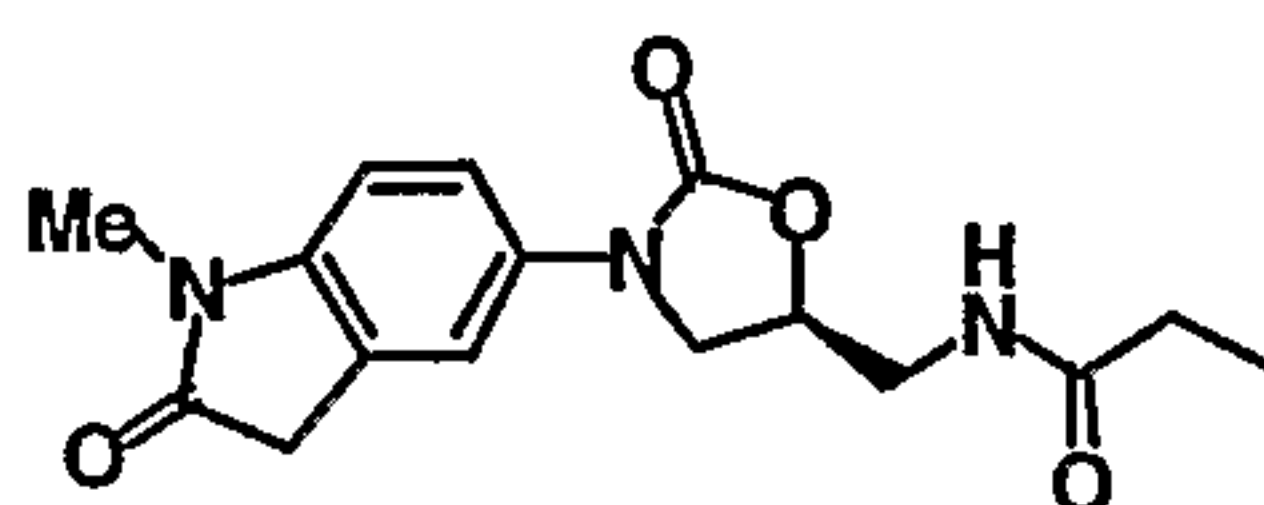
Step 3: Preparation of (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-methyl-1,3-dihydro-indole-2-one

(*S*)-[3-(1-Methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 2, 0.20 g, 0.553 mmol) is treated with 10 50% TFA/DCM (3 ml) for 30 minutes at room temperature. The reaction is evaporated to give the title compound as the TFA salt. HPLC r.t. 2.46 min; MS for C₁₃H₁₅N₃O₃ m/z 262.2(M+H)⁺.

Step 4: Preparation of (*S*)-*N*-[3-(1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.016 ml, 0.166 mmol) is added to (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-methyl-1,3-dihydro-indole-2-one (Step 3, 0.041 g, 0.11 mmol) and diisopropyl ethylamine (0.057 ml, 0.33 mmol) in dichloromethane (3 ml)) at 0 °C. The reaction is stirred at 0°C for 30 minutes and then allowed to warm at 20 room temperature. The mixture is diluted with dichloromethane, washed with water, citric acid and brine, dried (Na₂SO₄), and evaporated under vacuum to give the title compound as an off white solid. HPLC r.t. 3.013 min; ¹H NMR (300 MHz, CDCl₃) 7.58 (s, 1H), 7.27 (dd, *J* = 2.1, 9.3 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.01 (m, 1H), 4.73-4.82 (m, 1H), 4.05 (t, *J* = 9 Hz, 1H), 3.79 (dd, *J* = 6.9, 9.3 Hz, 1H), 3.57-3.76 (m, 25 2H), 3.54 (s, 2H), 3.21 (s, 3H), 2.03 (s, 3H); MS for C₁₅H₁₇N₃O₄ m/z 304 (M+H)⁺.

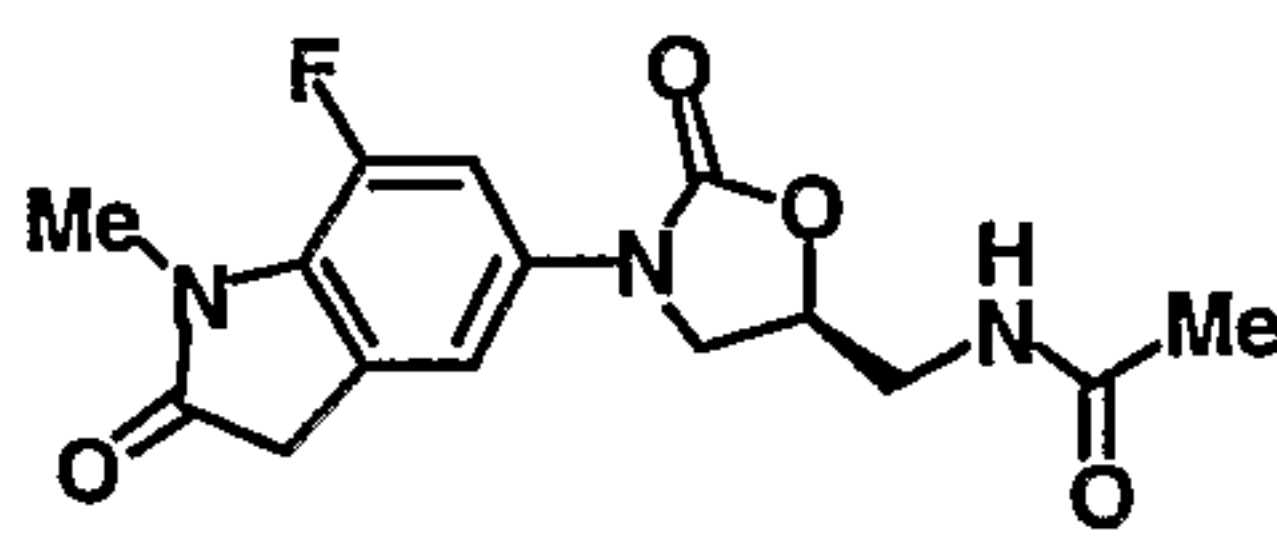
Example 2 Preparation of (*S*)-*N*-[3-(1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide.



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Propionic anhydride (0.024 ml, 0.186 mmol) is added to (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-methyl-1,3-dihydro-indole-2-one (Example 1, 0.035 g, 0.093 mmol) and diisopropylethylamine (0.097 ml, 0.559 mmol) in dichloromethane (3 ml) at 0 °C. The reaction is allowed to warm to room temperature and stirred for 1 hour. The mixture is diluted with dichloromethane, washed with water, citric acid and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.200 min; ¹H NMR (300 MHz, CDCl₃) 7.57 (s, 1H), 7.27 (dd, *J* = 2.1, 8.4 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 1H), 6.07 (m, 1H), 4.73-4.81 (m, 1H), 4.04 (t, *J* = 9 Hz, 1H), 3.81 (dd, *J* = 6.3, 9 Hz, 1H), 3.64-3.71 (m, 2H), 3.53 (s, 2H), 3.20 (s, 3H), 2.25 (q, *J* = 7.5 Hz, 2H), 1.13 (t, *J* = 7.5 Hz, 3H); MS for C₁₆H₁₉N₃O₄ *m/z* 318 (M+H)⁺.

Example 3 Preparation of *N*-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of (*R*)-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

5-Amino-7-fluoro-1-methyl-1,3-dihydro-indol-2-one (Preparation 2, 1.72 g, 9.54 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (1.66 g, 9.54 mmol) and lithium trifluoromethanesulfonate (1.46 g, 9.54 mmol) in acetonitrile (15 ml) are heated at 90 °C for 2 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% Ethyl acetate/hexane) gives the title compound as a yellow foamy solid. HPLC R.T. 3.75 min; MS for C₁₇H₂₄FN₃O₄ *m/z* 354 (M+H)⁺.

Step 2: Preparation of (*S*)-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 2.70 ml, 0.0276 mol) is added to (*R*)-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 5, 1.30 g, 0.00368 mol) and triethylamine (2.55 ml, 0.0184 mol) in dichloromethane (15 ml) at 0 °C and stirred for 30 minutes. The

mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated. The residue is purified by flash column chromatography (65 to 75% Ethyl acetate/hexane) to give the title compound as a light yellow solid. HPLC r.t. 4.68 min; MS for $\text{C}_{18}\text{H}_{22}\text{FN}_3\text{O}_5$ m/z 380 ($\text{M}+\text{H}$)⁺.

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Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-methyl-1,3-dihydro-indol-2-one

(*S*)-[3-(7-Fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 6, 0.320 g, 0.843 mmol) is treated with 50% TFA/DCM (4 ml) for 15 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 2.84 min; MS for $\text{C}_{13}\text{H}_{14}\text{FN}_3\text{O}_3$ m/z 280 ($\text{M}+\text{H}$)⁺.

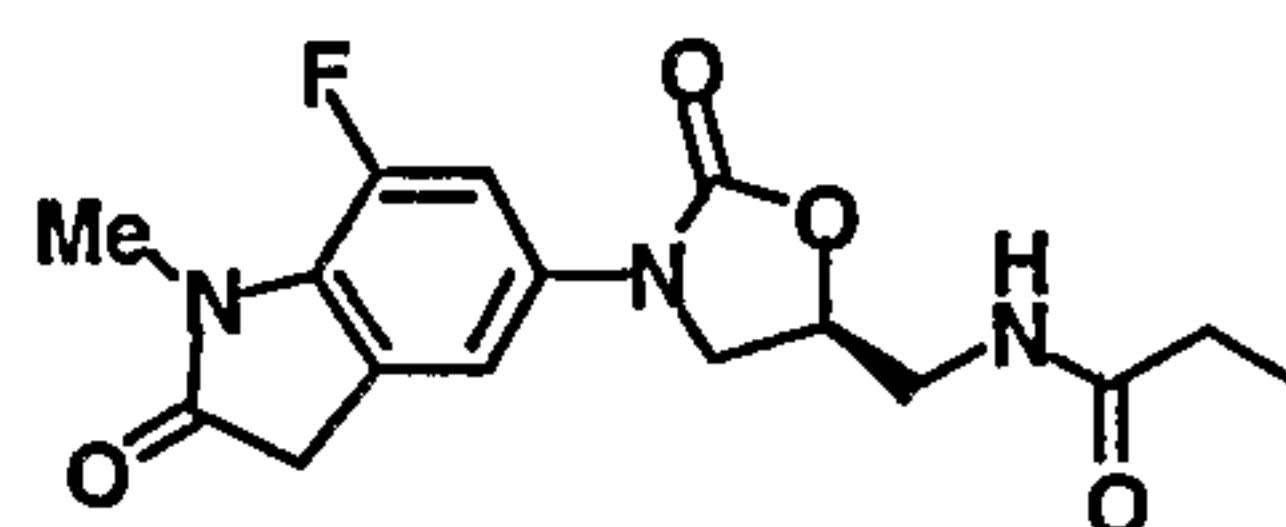
Step 4: Preparation of (*S*)-*N*-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.115 ml, 1.22 mmol) is added to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-methyl-1,3-dihydro-indol-2-one (Step 7, 0.320 g, 0.813 mmol) and *N,N*-diisopropylethylamine (0.567 ml, 3.25 mmol) in dichloromethane (6 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.39 min; ¹H NMR (300 MHz, CDCl_3) 7.27 (m, 1H), 7.23 (m, 1H), 5.96 (t, 1H), 5.98 (m, 1H), 4.74-4.80 (m, 1H), 4.02 (t, $J = 9$ Hz, 1H), 3.76 (d, $J = 6.6$, 9 Hz, 1H), 3.57-3.71 (m, 2H), 3.56 (s, 2H), 3.40 (d, $J = 2.7$ Hz, 3H), 2.03 (s, 3H); MS for $\text{C}_{15}\text{H}_{16}\text{FN}_3\text{O}_4$ m/z 322.0 ($\text{M}+\text{H}$)⁺.

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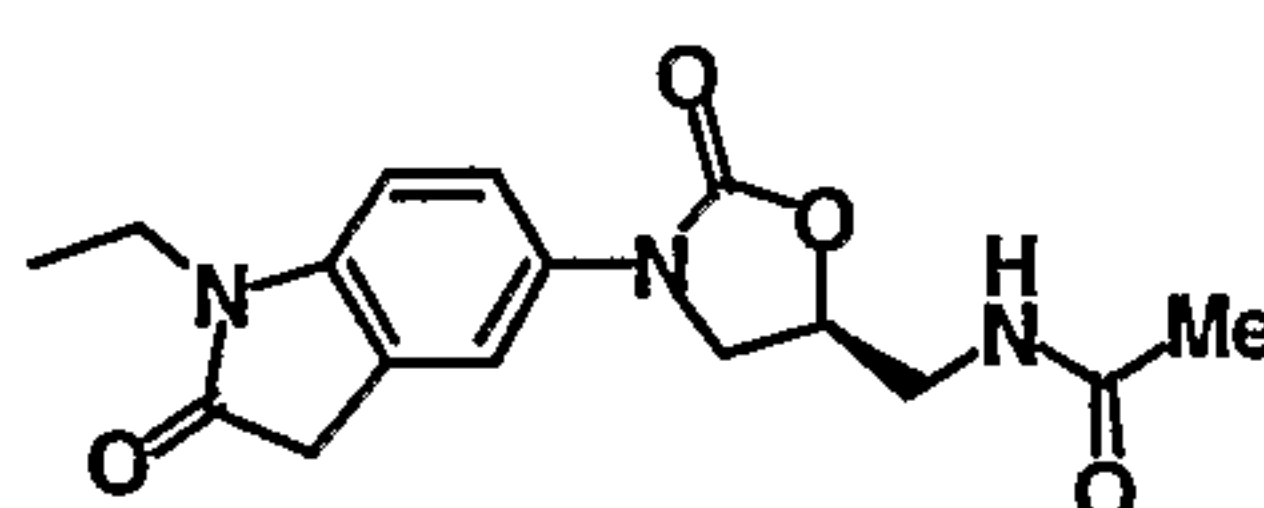
Example 4 Preparation of (*S*)-*N*-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide

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Propionic anhydride (0.202 ml, 1.57 mmol) is added dropwise to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-methyl-1,3-dihydro-indol-2-one (Example 3, 0.310 g, 0.788 mmol) and *N,N*-diisopropylethylamine (0.548 ml, 3.15 mmol) in dichloromethane (5 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% methanol/dichloromethane) to give the title compound as a light yellow solid. HPLC r.t. 3.59 min; ¹H NMR (300 MHz, CDCl₃) 7.27 (m, 1H), 7.23 (m, 1H), 5.94 (t, 1H), 4.74-4.82 (m, 1H), 4.02 (t, *J* = 8.7 Hz, 1H), 3.78 (dd, *J* = 6.6, 9 Hz, 1H), 3.61-3.74 (m, 2H), 3.55 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 3H), 2.24 (q, *J* = 7.5 Hz, 2H), 1.13 (t, *J* = 7.5 Hz, 3H); MS for C₁₆H₁₈FN₃O₄ *m/z* 336.0 (M+H)⁺.

Example 5 Preparation of (*S*)-*N*-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of (*R*)-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

5-Amino-1-ethyl-1,3-dihydro-indol-2-one (Preparation 3 0.91 g, 5.16 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.893 g, 5.16 mmol) and lithium trifluoromethanesulfonate (0.798 g, 5.16 mmol) in acetonitrile (10 ml) are heated at 70 °C for 2 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (30% Acetone / DCM) gives the title compound as a light brown foamy solid. HPLC R.T. 3.39 min; MS for C₁₈H₂₇N₃O₄ *m/z* 350.4 (M+H)⁺.

Step 2: Preparation of (*S*)-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.140 ml, 1.43 mmol) is added to (*R*)-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 1, 0.05 g, 0.143 mmol) and diisopropylethylamine (0.245 ml, 1.43 mmol) in dichloromethane (2 ml) at 0 °C. The reaction is allowed to warm to

room temperature and stirred for 2 hours. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated. The residue is purified by PTLC (5% MeOH / DCM) to give the title compound as a light brown solid (0.04g, 75%); HPLC r.t. 4.48 min; MS for $\text{C}_{19}\text{H}_{25}\text{N}_3\text{O}_5$ m/z 376.3($\text{M}+\text{H}$)⁺.

5

Step 3: Preparation of (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-ethyl-1,3-dihydro-indole-2-one

(*S*)-[3-(1-Ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 2, 0.25 g, 0.665 mmol) is treated with 50% TFA/DCM (4 ml) for 30 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt (0.257 g, 99%); HPLC r.t. 2.68 min; MS for $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_3$ m/z 276.2($\text{M}+\text{H}$)⁺.

10

Step 4: Preparation of (*S*)-*N*-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

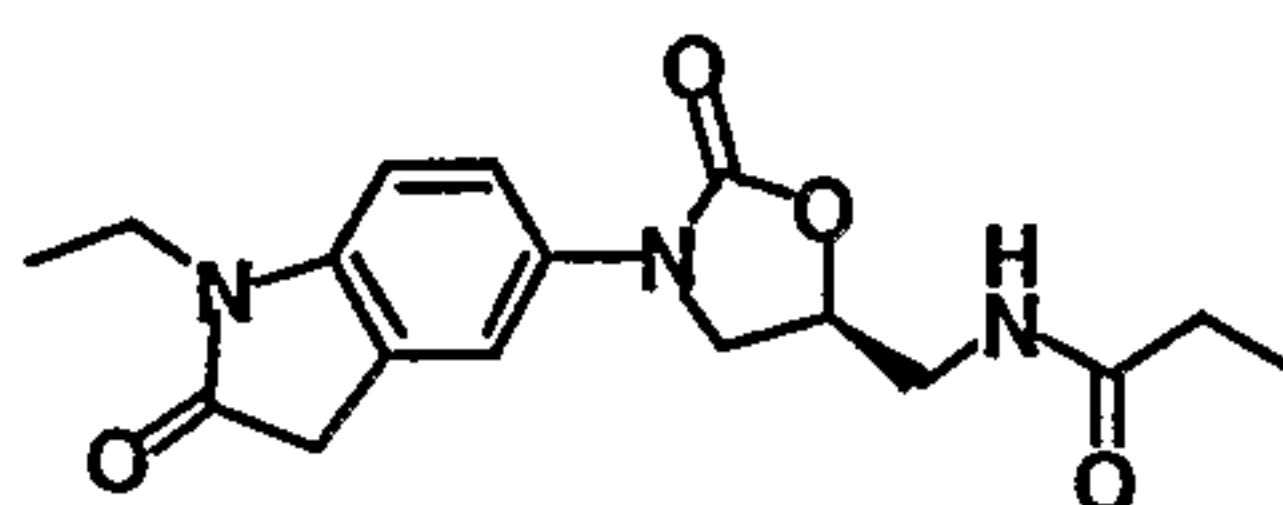
15

Acetic anhydride (0.039 ml, 0.41 mmol) is added to (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-ethyl-1,3-dihydro-indole-2-one (Step 3, 0.080 g, 0.205 mmol) and pyridine (0.165 ml, 2.05 mmol) in dichloromethane (3 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water, citric acid and brine, dried (Na_2SO_4) and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.247 min; ¹H NMR (300 MHz, CDCl_3) 7.57 (s, 1H), 7.28 (dd, $J = 2.4, 8.7$ Hz, 1H), 6.81 (d, $J = 8.4$ Hz, 1H), 5.98 (m, 1H), 4.73-4.82 (m, 1H), 4.05 (t, $J = 8.7$ Hz, 1H), 3.76 (q, $J = 7.5$ Hz, 2H), 3.57-3.82 (m, 3H), 3.53 (s, 2H), 2.03 (s, 3H), 1.26 (t, $J = 7.5$ Hz, 3H); MS for $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4$ m/z 318 ($\text{M}+\text{H}$)⁺.

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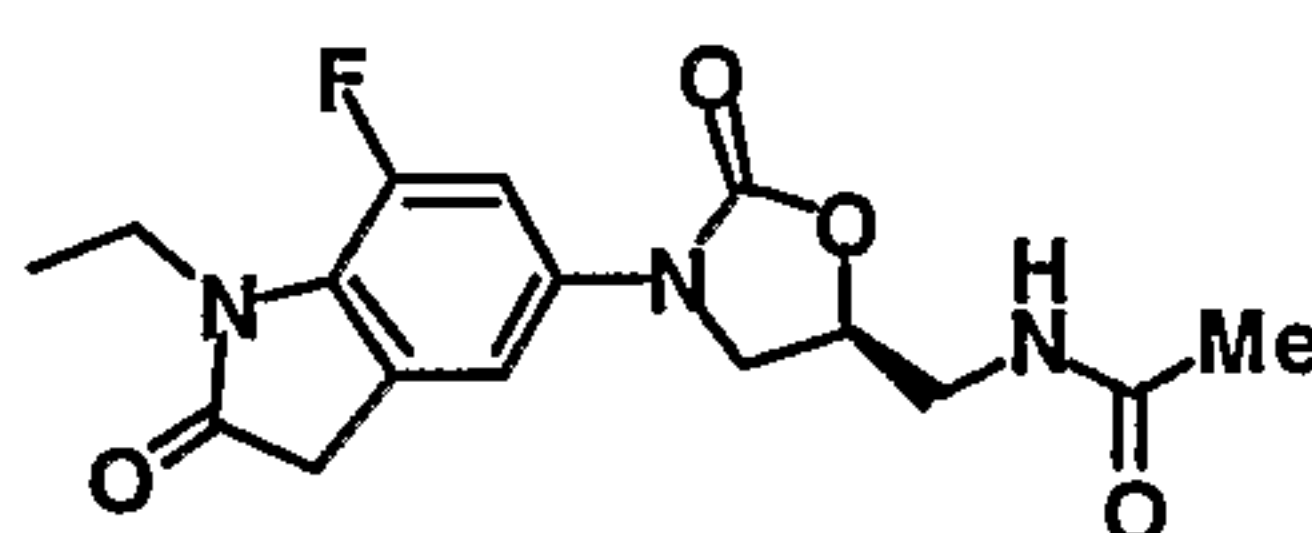
Example 6 Preparation of (*S*)-*N*-[3-(1-ethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



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Propionic anhydride (0.042 ml, 0.334 mmol) is added dropwise to (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-ethyl-1,3-dihydro-indole-2-one (Preparation 3, 0.065 g, 0.167 mmol) and diisopropylethylamine (0.114 ml, 0.668 mmol) in dichloromethane (3 ml) at 0°C. The reaction is stirred at room temperature for 1
 5 hour, then diluted with dichloromethane, washed with water, citric acid and brine, dried (Na₂SO₄), and evaporated to give the title compound as an off white solid. HPLC r.t. 3.432 min; ¹H NMR (300 MHz, CDCl₃) 7.56 (s, 1H), 7.26 (dd, *J* = 2.1, 8.4 Hz, 1H), 6.81 (d, *J* = 8.1 Hz, 1H), 5.91 (m, 1H), 4.77 (m, 1H), 4.04 (t, *J* = 9 Hz, 1H), 3.80 (dd, *J* = 6, 9.3 Hz, 1H), 3.76 (q, *J* = 7.2 Hz, 2H), 3.61-3.70 (m, 2H), 3.53 (s, 2H),
 10 2.25 (q, *J* = 7.5 Hz, 2H), 1.26 (t, *J* = 7.5 Hz, 3H), 1.14 (t, *J* = 7.5 Hz, 3H); MS for C₁₇H₂₁N₃O₄ m/z 332 (M+H)⁺.

Example 7 Preparation of (*S*)-*N*-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



15

Step 1: Preparation of 1-ethyl-7-fluoro-1*H*-indole-2,3-dione

7-Fluoro-1*H*-indole-2,3-dione (prepared according to the method of Gassman as described in US Patent 4,188,325 (4.00 g, 24.2 mmol), iodoethane (3.87 ml, 48.5
 20 mmol) and potassium carbonate (6.61 g, 48.5 mmol) in DMF (20 ml) are stirred at room temperature for 20 hours. The reaction mixture is diluted with cold water and the resulting precipitate filtered and dried to give the title compound as an orange solid. HPLC r.t. 4.48 min; MS for C₁₀H₈FNO₂ m/z 193.9 (M+H)⁺.

25 Step 2: Preparation of 1-ethyl-7-fluoro-1,3-dihydro-indol-2-one

1-Ethyl-7-fluoro-1*H*-indole-2,3-dione (3.60 g, 18.6 mmol) is heated with neat hydrazine hydrate (15 ml) at 130 °C for 60 minutes. The mixture is cooled, diluted with ice water and extracted with ethyl acetate. The extract is washed with brine, dried (Na₂SO₄), and evaporated to give the title compound as an orange solid. HPLC
 30 r.t. 4.60 min; MS for C₁₀H₁₀FNO m/z 198.1 (M+H)⁺.

Step 3: Preparation of 1-ethyl-7-fluoro-5-nitro-1,3-dihydro-indol-2-one

Preparation of 1-Ethyl-7-fluoro-1,3-dihydro-indol-2-one (3.45 g, 19.3 mmol) is added portionwise to a mixture of sodium nitrate (1.64 g, 19.3 mmol) and trifluoroacetic acid (60 ml) and stirred at room temperature for 5 hours. The reaction is diluted with ice water and the resulting precipitate filtered, washed with water, and
5 dried under vacuum to give the title compound as a brownish-yellow solid (3.87 g, 90%); HPLC r.t. 4.88 min; MS for C₁₀H₉FN₂O₃ m/z 223.0 (M-H)⁻.

Step 4: Preparation of 5-amino-1-ethyl-7-fluoro-1,3-dihydro-indol-2-one

Iron powder (3.84 g, 68.7 mmol) is added in small portions to 1-Ethyl-7-fluoro-5-nitro-1,3-dihydro-indol-2-one (Step 3, 3.85 g, 17.2 mmol) and ammonium
10 chloride (8.94 g, 171 mmol) in ethanol (150 ml) and water (75 ml) at 90 °C. The reaction mixture is stirred vigorously and heated for 30 min, cooled to room temperature, and diluted with dichloromethane (600 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried
15 over sodium sulfate and evaporated to give the title compound as a yellow solid. HPLC r.t. 2.60 min; MS for C₁₀H₁₁FN₂O m/z 195.0 (M+H)⁺.

Step 5: Preparation of (R)-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

5-Amino-1-ethyl-7-fluoro-1,3-dihydro-indol-2-one (Step 4, 2.25 g, 11.6
20 mmol), (S)-oxiranylmethyl-carbamic acid *tert*-butyl ester (2.00 g, 11.6 mmol) and lithium trifluoromethanesulfonate (1.80 g, 11.6 mmol) in acetonitrile (12 ml) are heated at 90 °C for 20 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by
25 flash chromatography (70% Ethyl acetate/hexane) gives the title compound as a yellow-brown foamy solid. HPLC r.t. 3.95 min; MS for C₁₈H₂₆FN₃O₄ m/z 368.3 (M+H)⁺.

Step 6: Preparation of (S)-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 3.58 ml, 36.7 mmol) is added to (R)-[3-(1-Ethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 5, 1.80 g, 4.89 mmol) and triethylamine (3.38 ml, 24.5

mmol) in dichloromethane (20 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated to give the title compound as light brown solid. HPLC r.t. 4.92 min; MS for C₁₉H₂₄FN₃O₅ m/z 394.1 (M+H)⁺.

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Step 7: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-ethyl-7-fluoro-1,3-dihydro-indol-2-one

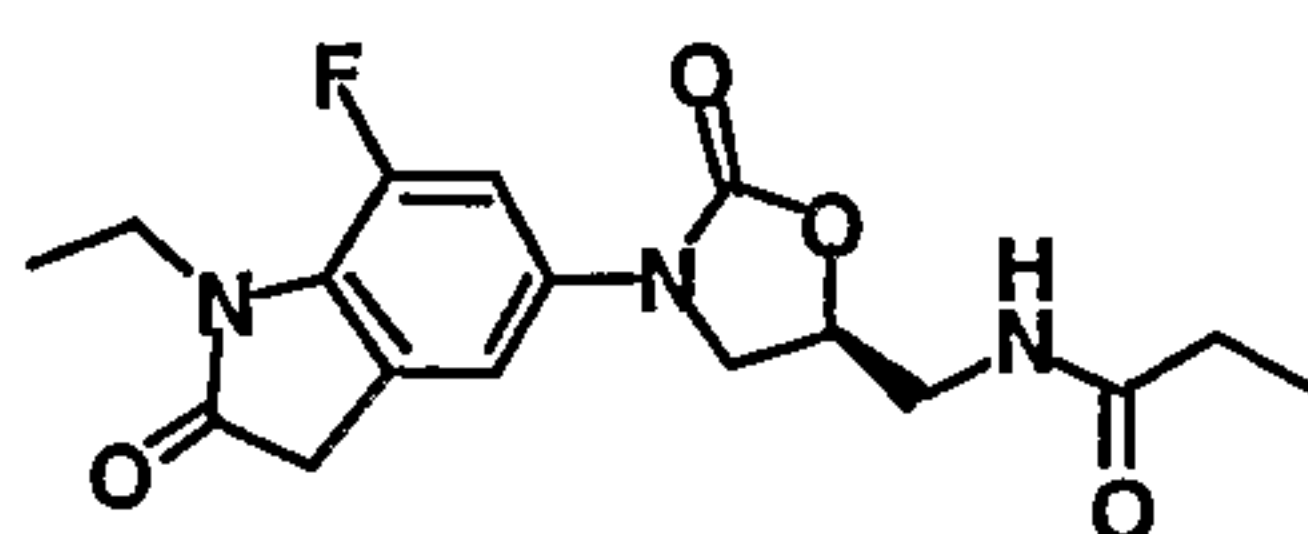
(*S*)-[3-(1-Ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 6, 0.325 g, 0.826 mmol) is treated with 50% TFA/DCM (4 ml) for 15 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.13 min; MS for C₁₄H₁₆FN₃O₃ m/z 294.0 (M+H)⁺.

Step 8: Preparation of (*S*)-*N*-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.116 ml, 1.23 mmol) is added to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-ethyl-7-fluoro-1,3-dihydro-indol-2-one (Step 7, 0.335 g, 0.822 mmol) and *N,N*-diisopropylethylamine (0.572 ml, 3.28 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.67 min; ¹H NMR (400 MHz, CDCl₃) 7.27 (m, 1H), 7.23 (dd, *J* = 2, 13.2 Hz, 1H), 6.04 (t, 1H), 4.76-4.82 (m, 1H), 4.02 (t, *J* = 9.2 Hz, 1H), 3.89 (q, *J* = 7.2 Hz, 2H), 3.77 (dd, *J* = 6.8, 9.2 Hz, 1H), 3.59-3.74 (m, 2H), 3.56 (s, 2H), 2.03 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); MS for C₁₆H₁₈FN₃O₄ m/z 336.0 (M+H)⁺.

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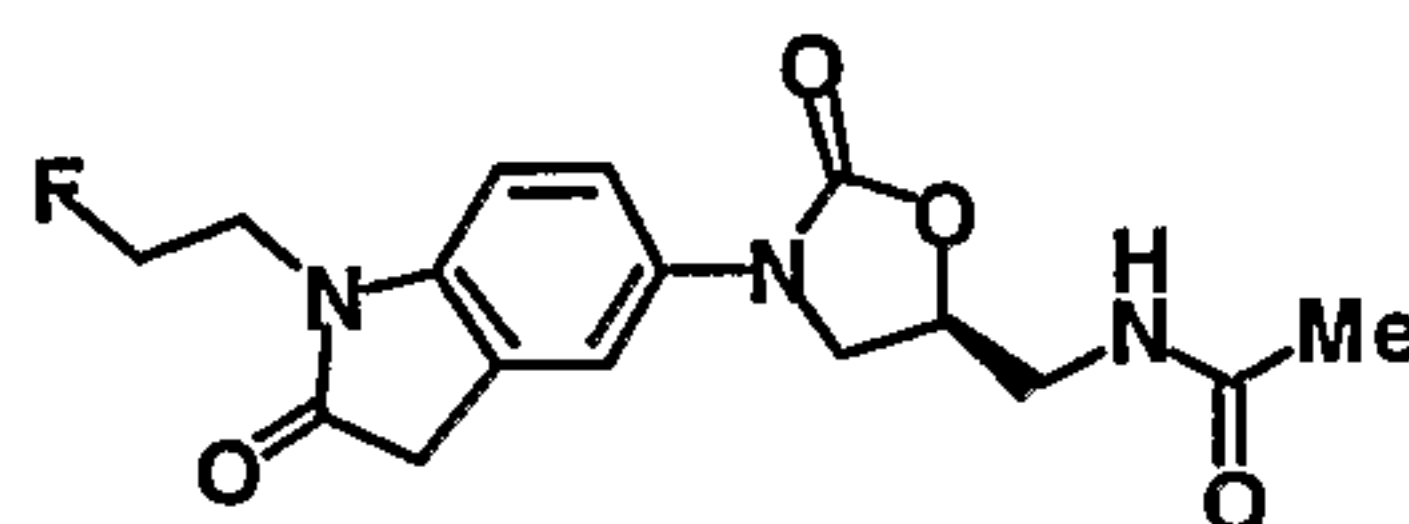
Example 8 Preparation of (*S*)-*N*-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



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Propionic anhydride (0.193 ml, 1.52 mmol) is added dropwise to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-ethyl-7-fluoro-1,3-dihydro-indol-2-one (Example 7, 0.310 g, 0.762 mmol) and diisopropylethylamine (0.532 ml, 3.05 mmol) in dichloromethane (5 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as a yellow solid. HPLC r.t. 3.88 min; ¹H NMR (400 MHz, CDCl₃) 7.27 (m, 1H), 7.23 (dd, *J* = 2.1, 13.2 Hz, 1H), 5.96 (t, *J* = 6 Hz, 1H), 4.75-4.81 (m, 1H), 4.02 (t, *J* = 8.8 Hz, 1H), 3.89 (q, *J* = 6.8 Hz, 2H), 3.79 (dd, *J* = 6.8, 9.2 Hz, 1H), 3.61-3.74 (m, 2H), 3.55 (s, 2H), 2.25 (q, *J* = 8 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.6 Hz, 3H); MS for C₁₇H₂₀FN₃O₄ m/z 350.0 (M+H)⁺.

Example 9 Preparation of (*S*)-*N*-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide



Step 1: Preparation of (*R*)-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino]-2-hydroxy-propyl}-carbamic acid *tert*-butyl ester

5-Amino-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (Example 18, Step 4, 1.00 g, 5.15 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.894 g, 5.15 mmol) and lithium trifluoromethanesulfonate (0.793 g, 5.15 mmol) in acetonitrile (10 ml) are heated at 90 °C for 1 hour. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% ethyl acetate/hexane) gives pure product as a light yellow-brown solid. HPLC r.t. 3.28 min; MS for C₁₈H₂₆FN₃O₄ m/z 368.3 (M+H)⁺.

Step 2: Preparation of (*S*)-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.532 ml, 5.44 mmol) is added to (*R*)-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino]-2-hydroxy-propyl}-carbamic acid *tert*-butyl ester (0.20 g, 0.544 mmol) and triethylamine (0.378 ml, 2.72

mmol) in dichloromethane (5 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated to give the title compound as a light brown solid. HPLC r.t. 4.37 min; MS for C₁₉H₂₄FN₃O₅ m/z 394.1 (M+H)⁺.

5

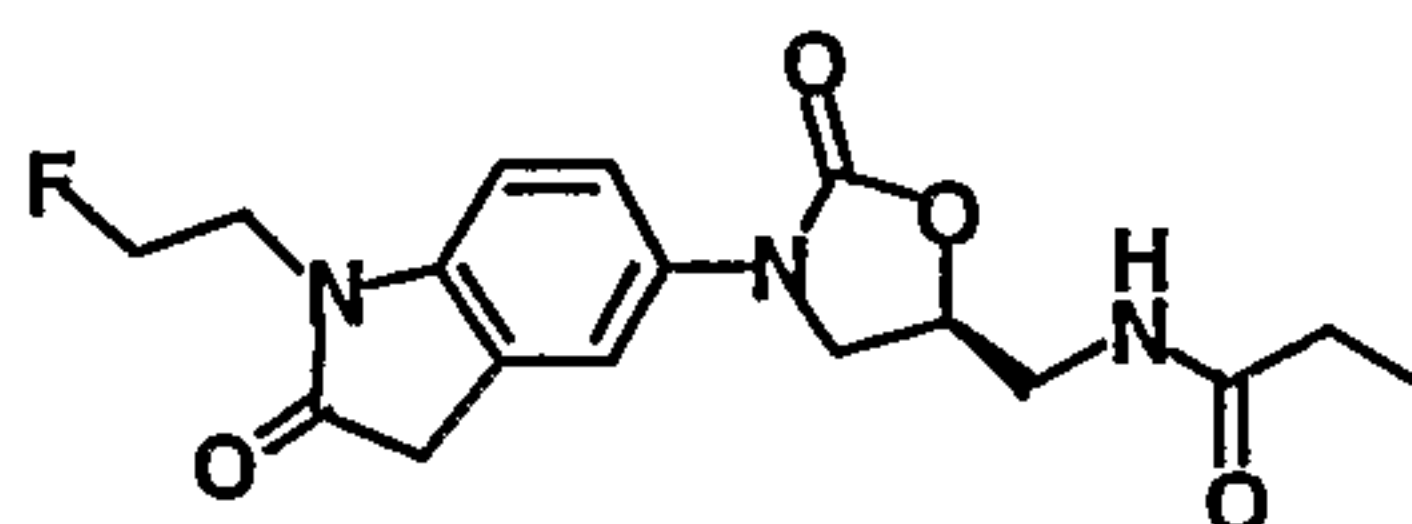
Step 3: Preparation of (R)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one

(S)-{3-[1-(2-Fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-carbamic acid *tert*-butyl ester (0.110 g, 0.280 mmol) is treated with 50% TFA/DCM (3 ml) for 15 minutes at room temperature. The reaction is evaporated and the product isolated as the TFA salt. HPLC r.t. 2.61 min; MS for C₁₄H₁₆FN₃O₃ m/z 294.0 (M+H)⁺.

Step 4: Preparation of (S)-*N*-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

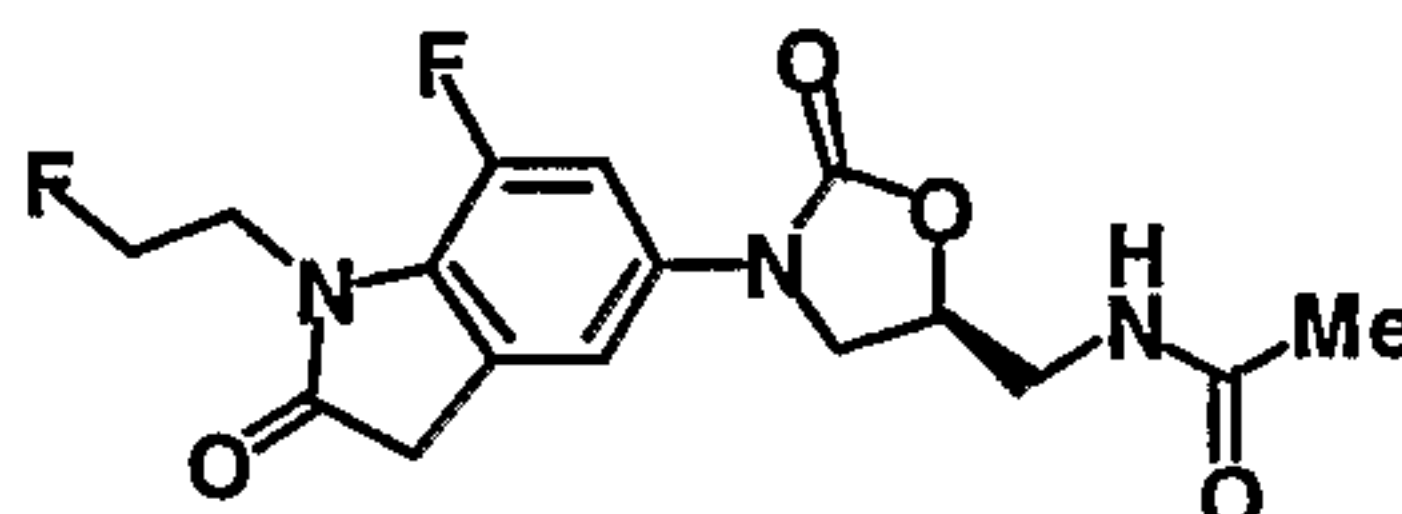
Acetic anhydride (0.041 ml, 0.419 mmol) is added to (R)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (Step 3, 0.114 g, 0.280 mmol) and *N,N*-diisopropylethylamine (0.194 ml, 1.12 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give pure product as an off white solid. HPLC r.t. 3.15 min; ¹H NMR (300 MHz, CDCl₃) 7.61 (m, 1H), 7.23 (m, 1H), 6.91 (m, 1H), 5.96 (t, 1H), 4.75 (m, 1H), 4.74 (t, *J* = 4.8 Hz, 1H), 4.59 (t, *J* = 4.5 Hz, 1H), 4.06 (t, *J* = 4.8 Hz, 1H), 4.04 (t, *J* = 9 Hz, 1H), 3.97 (t, *J* = 4.8 Hz, 1H), 3.78 (dd, *J* = 6.9, 9 Hz, 1H), 3.61-3.75 (m, 2H), 3.58 (s, 2H), 2.03 (s, 3H); MS for C₁₆H₁₈FN₃O₄ m/z 336.0 (M+H)⁺.

Example 10 Preparation of (S)-*N*-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-propionamide



Propionic anhydride (0.072 ml, 0.559 mmol) is added dropwise to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (Example 9, 0.114 g, 0.279 mmol) and diisopropylethylamine (0.194 ml, 1.12 mmol) in dichloromethane (4 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as a yellow solid. HPLC r.t. 3.31 min; ¹H NMR (300 MHz, CDCl₃) 7.61 (m, 1H), 7.22-7.26 (m, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 5.93 (t, 1H), 4.78 (m, 1H), 4.74 (t, *J* = 4.8 Hz, 1H), 4.59 (t, *J* = 4.5 Hz, 1H), 4.06 (t, *J* = 4.8 Hz, 1H), 4.04 (t, *J* = 9 Hz, 1H), 3.97 (t, *J* = 5.1 Hz, 1H), 3.80 (dd, *J* = 6.6, 9 Hz, 1H), 3.61-3.76 (m, 2H), 3.58 (s, 2H), 2.25 (q, *J* = 7.5 Hz, 2H), 1.14 (t, *J* = 7.5 Hz, 3H); MS for C₁₇H₂₀FN₃O₄ *m/z* 350.0 (M+H)⁺.

Example 11 Preparation of (*S*)-*N*-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide



Step 1: Preparation of 7-fluoro-1-(2-fluoro-ethyl)-1*H*-indole-2,3-dione

7-Fluoro-1*H*-indole-2,3-dione (prepared according to the method of Gassman as described in US Patent 4,188,325 (2.00 g, 12.1 mmol), 1-iodo-2-fluoroethane (4.21 g, 24.2 mmol) and potassium carbonate (3.30 g, 24.2 mmol) in DMF (20 ml) are stirred at room temperature for 20 hours. The reaction mixture is diluted with cold water and the resulting precipitate filtered and dried to give the title compound as an orange solid. HPLC r.t. 4.18 min; MS for C₁₀H₇F₂NO₂ *m/z* 212.1 (M+H)⁺.

25

Step 2: Preparation of 7-fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one

7-Fluoro-1-(2-fluoro-ethyl)-1*H*-indole-2,3-dione (1.04 g, 4.92 mmol) is heated with neat hydrazine hydrate (10 ml) at 130 °C for 20 minutes. The mixture is cooled, diluted with ice water and extracted with ethyl acetate. The extract is washed with brine, dried (Na₂SO₄), and evaporated to give the title compound as a brown solid. HPLC r.t. 4.36 min; MS for C₁₀H₉F₂NO *m/z* 198.1 (M+H)⁺.

30

Step 3: Preparation of 7-fluoro-1-(2-fluoro-ethyl)-5-nitro-1,3-dihydro-indol-2-one

7-Fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (0.880 g, 0.0119 mol) is added portionwise to 70% nitric acid (8 ml) at -10 °C. After the addition is complete, the reaction is allowed to warm to room temperature and then stirred for 24 hours.

5 The mixture is diluted with ice water and the resulting precipitate filtered, washed with water, and dried under vacuum to give the title compound as a light brown solid. HPLC r.t. 4.65 min; MS for C₁₀H₈F₂N₂O₃ m/z 243.3 (M+H)⁺.

Step 4: Preparation of 5-Amino-7-fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one

10 Iron powder (0.416 g, 7.43 mmol) is added in small portions to 7-Fluoro-1-(2-fluoro-ethyl)-5-nitro-1,3-dihydro-indol-2-one (0.45 g, 1.86 mmol) and ammonium chloride (0.987 g, 18.6 mmol) in ethanol (40 ml) and water (20 ml) at 90 °C. The reaction mixture is stirred vigorously and heated for 30 min, cooled to room temperature, and diluted with dichloromethane (100 ml). The mixture is filtered
15 through celite, the organic layer separated and washed with water and brine, dried over sodium sulfate and evaporated to give the title compound as a dark brown solid. HPLC r.t. 2.34 min; MS for C₁₀H₁₀F₂N₂O m/z 213.2 (M+H)⁺.

Step 5: Preparation of (R)-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1H-indol-5-ylamino]-2-hydroxy-propyl}-carbamic acid *tert*-butyl ester

20 5-Amino-7-fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (0.39 g, 1.84 mmol), (S)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.319 g, 1.84 mmol) and lithium trifluoromethanesulfonate (0.283 g, 1.84 mmol) in acetonitrile (4 ml) are heated at 90 °C for 6 hours. The reaction mixture is diluted with ethyl acetate, washed
25 with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% Ethyl acetate/hexane) gives the title compound as a yellow-brown foamy solid. HPLC r.t. 3.92 min; MS for C₁₈H₂₅F₂N₃O₄ m/z 386.1 (M+H)⁺.

Step 6: Preparation of (S)-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1H-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-carbamic acid *tert*-butyl ester

30 Phosgene (20% solution in toluene, 0.414 ml, 4.24 mmol) is added to (R)-{3-[7-Fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1H-indol-5-ylamino]-2-hydroxy-propyl}-carbamic acid *tert*-butyl ester (Step 5, 0.150 g, 0.424 mmol) and

triethylamine (0.295 ml, 2.12 mmol) in dichloromethane (3 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated to give the title compound as a light brown solid. HPLC r.t. 4.70 min; MS for C₁₉H₂₃F₂N₃O₅ m/z 380.3 (M+H)⁺.

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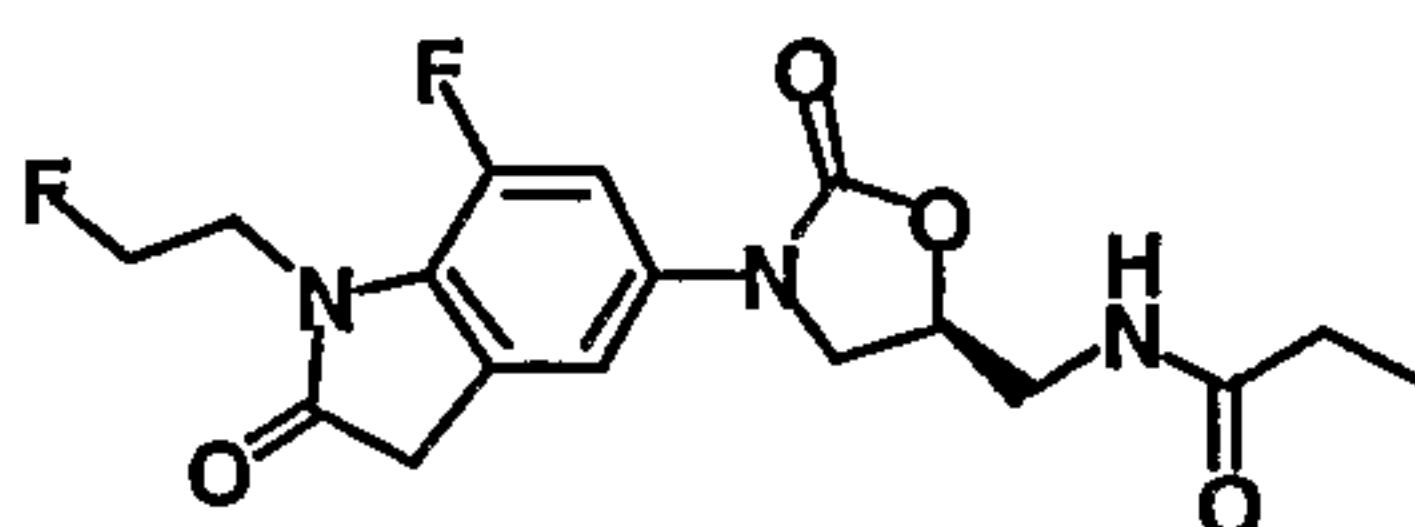
Step 7: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one

(*S*)-{3-[7-Fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-carbamic acid *tert*-butyl ester (Step 6, 0.15 g, 0.395 mmol) is treated with 50% TFA/DCM (3 ml) for 15 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 2.86 min; MS for C₁₄H₁₅F₂N₃O₃ m/z 280.0 (M+H)⁺.

Step 8: Preparation of (*S*)-*N*-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide

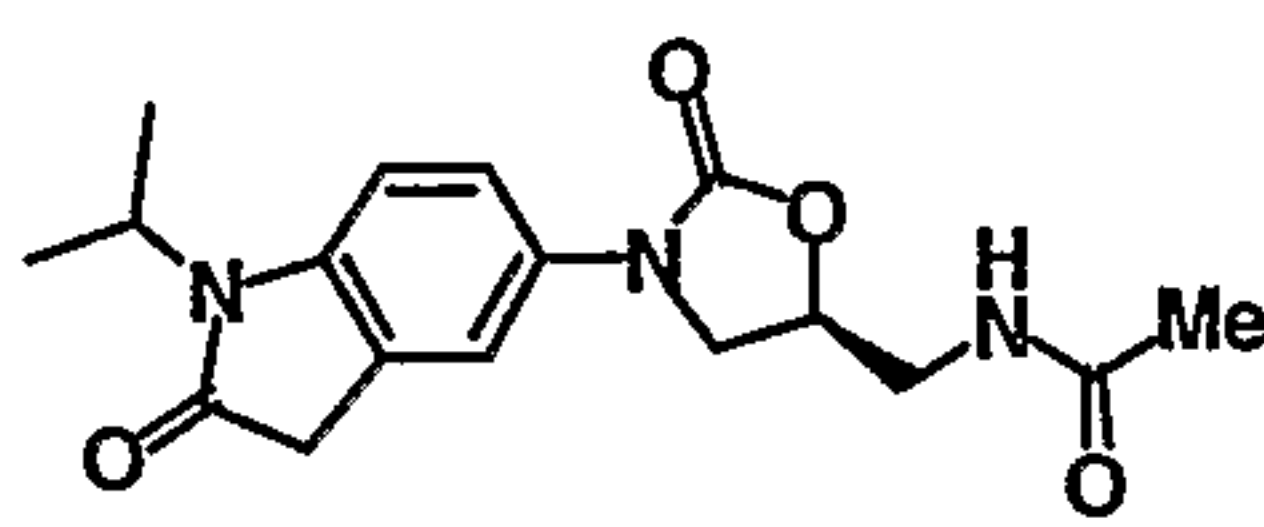
Acetic anhydride (0.083 ml, 0.856 mmol) is added to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (Step 7, 0.243 g, 0.571 mmol) and *N,N*-diisopropylethylamine (0.395 ml, 2.28 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.50 min; ¹H NMR (300 MHz, CDCl₃) 7.30 (m, 1H), 7.25 (m, 1H), 6.02 (t, 1H), 4.78 (m, 1H), 4.73 (t, *J* = 4.5 Hz, 1H), 4.57 (t, *J* = 4.8 Hz, 1H), 4.22 (t, *J* = 4.8 Hz, 1H), 4.14 (t, *J* = 4.8 Hz, 1H), 4.02 (t, *J* = 9.3 Hz, 1H), 3.77 (dd, *J* = 6.6, 9 Hz, 1H), 3.63-3.72 (m, 2H), 3.61 (s, 2H), 2.01 (s, 3H); MS for C₁₆H₁₇F₂N₃O₄ m/z 354.2 (M+H)⁺.

Example 12 Preparation of (*S*)-*N*-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-propionamide



Propionic anhydride (0.056 ml, 0.437 mmol) is added dropwise to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-(2-fluoro-ethyl)-1,3-dihydro-indol-2-one (Example 23, Step 7, 0.093 g, 0.218 mmol) and diisopropylethylamine (0.151 ml, 0.874 mmol) in dichloromethane (2 ml) at 0°C. The reaction is stirred at room
 5 temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated to give the title compound as an off white solid. HPLC r.t. 3.72 min; ¹H NMR (300 MHz, CDCl₃) 7.30 (m, 1H), 7.25 (dd, 1H), 5.94 (t, 1H), 4.79 (m, 1H), 4.73 (t, *J* = 4.5 Hz, 1H), 4.57 (t, *J* = 5.1 Hz, 1H), 4.22 (t, *J* = 3.9 Hz, 1H), 4.14 (t, *J* = 4.2 Hz, 1H), 4.02 (t, *J* = 9 Hz, 1H), 3.79 (dd, *J* = 6.3, 9 Hz, 1H),
 10 3.65-3.74 (m, 2H), 3.61 (s, 2H), 2.24 (q, *J* = 7.5 Hz, 2H), 1.14 (t, *J* = 7.5 Hz, 3H); MS for C₁₇H₁₉F₂N₃O₄ m/z 368.3 (M+H)⁺.

Example 13 Preparation of (*S*)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



15

Step 1: Preparation of (*R*)-[2-hydroxy-3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-propyl]-carbamic acid *tert*-butyl ester

5-Amino-1-isopropyl-1,3-dihydro-indol-2-one (Preparation 4, 0.76 g, 3.99
 20 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.69 g, 3.99 mmol) and lithium trifluoromethanesulfonate (0.617 g, 3.99 mmol) in acetonitrile (10 ml) is heated at 70 °C for 2 hours. The reaction is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (20% Acetone / DCM) gives the title compound as a light brown
 25 foamy solid. HPLC r.t. 3.61 min; MS for C₁₉H₂₉N₃O₄ m/z 364.0(M+H)⁺.

Step 2: Preparation of (*S*)-[3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.602 ml, 6.18 mmol) is added to (*S*)-[2-hydroxy-3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-propyl]-carbamic acid *tert*-butyl ester (0.15 g, 0.412 mmol) and triethylamine (0.28 ml, 2.06 mmol) in dichloromethane (5 ml) at 0°C. The reaction is allowed to warm to room temperature

and stirred for 2h. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated. Final purification by PTLC (5%MeOH / DCM) gives the title compound as a light brown solid. HPLC r.t. 4.78 min; MS for $\text{C}_{20}\text{H}_{27}\text{N}_3\text{O}_5$ m/z 390.3(M+H)⁺.

5

Step 3: Preparation of (R)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-isopropyl-1,3-dihydro-indole-2-one

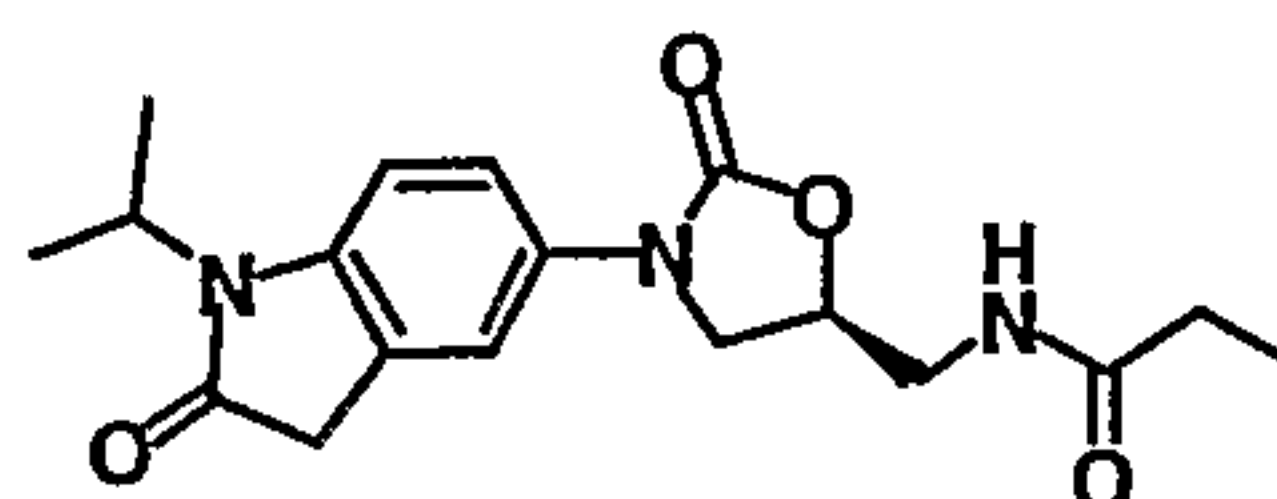
(5R)-[3-(1-Isopropyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (0.25 g, 0.642 mmol) is treated with 50% TFA/DCM (4 ml) for 30 minutes at room temperature. The reaction is evaporated to give the title compound as a TFA salt. HPLC r.t. 3.06 min; MS for $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}_3$ m/z 290.2(M+H)⁺.

Step 4: Preparation of (S)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.93 ml, 0.96 mmol) is added to (R)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-isopropyl-1,3-dihydro-indole-2-one (0.258 g, 0.639 mmol) and diisopropylethylamine (0.44 ml, 2.55 mmol) in dichloromethane (6 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm to room temperature. The mixture is diluted with dichloromethane, washed with water, citric acid and brine, dried (Na_2SO_4) and evaporated to give the title compound as a light brown solid. HPLC r.t. 3.597 min; ¹H NMR (300 MHz, CDCl_3) 7.54 (s, 1H), 7.24 (dd, *J* = 2.4, 8.7 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.12 (t, *J* = 6 Hz, 1H), 4.73-4.82 (m, 1H), 4.61-4.71 (m, 1H), 4.04 (t, *J* = 8.7 Hz, 1H), 3.74 (dd, *J* = 6.6, 9 Hz, 1H), 3.57-3.75 (m, 2H), 3.51 (s, 2H), 2.03 (s, 3H), 1.46 (d, *J* = 7.5 Hz, 6H); MS for $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_4$ m/z 332 (M+H)⁺.

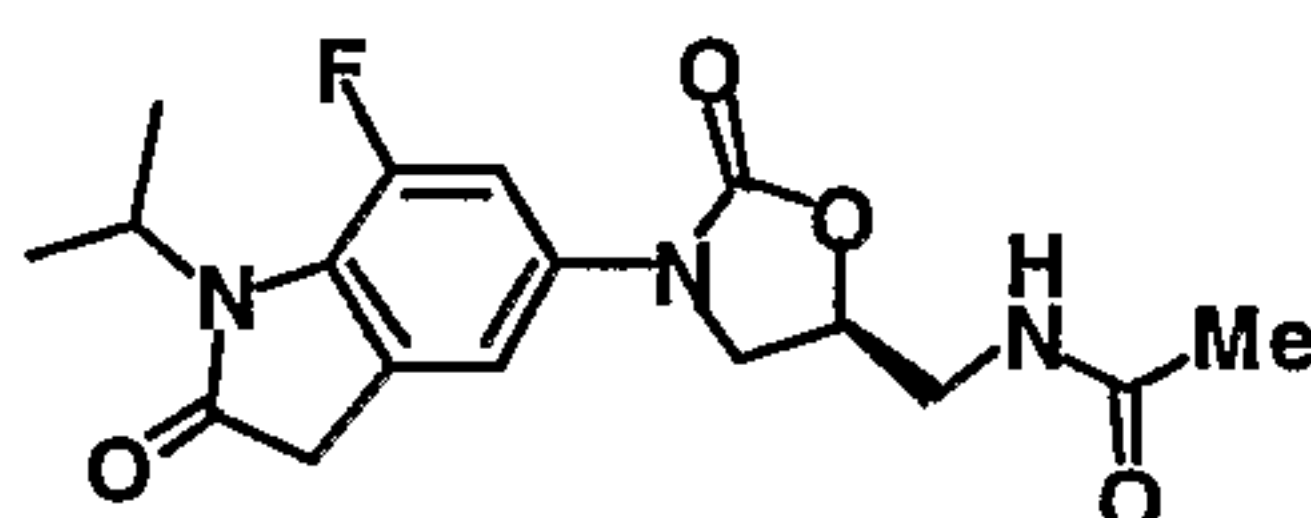
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Example 14 Preparation of (S)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



Propionic anhydride (0.047 ml, 0.371 mmol) is added dropwise to (*R*)-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-isopropyl-1,3-dihydro-indole-2-one (preparation 4, 0.075 g, 0.185 mmol) and diisopropylethylamine (0.126 ml, 0.74 mmol) in dichloromethane (3 ml) at 0 °C. The reaction is allowed to warm to room temperature and stirred for 1 hour. The mixture is diluted with dichloromethane, washed with water, citric acid and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as a light brown solid. HPLC r.t. 3.767 min; ¹H NMR (300 MHz, CDCl₃) 7.54 (s, 1H), 7.24 (dd, *J* = 2.4, 8.7 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 5.94 (m, 1H), 4.73-4.80 (m, 1H), 4.61-4.70 (m, 1H), 4.03 (t, *J* = 8.7 Hz, 1H), 3.80 (dd, *J* = 6.6, 9 Hz, 1H), 3.58-3.72 (m, 2H), 3.50 (s, 2H), 2.24 (q, *J* = 7.5 Hz, 2H), 1.45 (d, *J* = 6.9 Hz, 6H), 1.14 (t, *J* = 7.5 Hz, 3H); MS for C₁₈H₂₃N₃O₄ m/z 346 (M+H)⁺.

Example 15 Preparation of (*S*)-*N*-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of (2,3-difluoro-5-nitrophenyl) acetic acid.

(2,3-Difluoro-phenyl)-acetic acid (5 g, 0.0290 mol) is dissolved in concentrated sulfuric acid (20 ml) and the resulting solution cooled to -10 °C with vigorous stirring. A solution of nitric acid (1.88 ml, 69.3%, 0.0290 mol) and sulfuric acid (2 ml) is added dropwise at a rate such that the temperature remains below -5 °C. The thickened slurry is stirred for 15 minutes and then poured on ice. The resulting white precipitate is filtered and dried under vacuum and consists of a 50/50 mixture of 5 and 6-NO₂ regioisomers suitable for use directly in the next step.

Step 2: Preparation of 7-fluoro-1-isopropyl-5-nitro-1,3-dihydro-indol-2-one

Crude (2,3-difluoro-5-nitrophenyl)acetic acid (1.00 g, 0.00461 mol) and isopropylamine (6 eq., 2.35 ml, 0.0276 mol) are mixed in DMSO (5 ml) and stirred at 45 °C for 1 hour. 2N Hydrochloric acid (20 ml) is added in one portion and the mixture stirred at room temperature for 1 hour. The resulting light yellow precipitate

is filtered, washed with water and ether, and dried under vacuum to give the title compound. HPLC r.t. 5.31 min.

Step 3: Preparation of 5-amino-7-fluoro-1-isopropyl-1,3-dihydro-indol-2-one

5 Iron powder (0.854 g, 15.3 mmol) is added portionwise to a mixture of 7-fluoro-1-isopropyl-5-nitro-1,3-dihydro-indol-2-one (0.91 g, 3.82 mmol) and ammonium chloride (2.04 g, 38.2 mmol) in ethanol (50 ml) and water (25 ml) at 90 °C. The reaction is stirred vigorously and heated for 30min, cooled to room temperature and diluted with dichloromethane (150ml). The mixture is filtered
10 through celite, the organic layer separated and washed with water and brine, dried over sodium sulfate and evaporated to give the title compound as a dark brown gummy solid. HPLC r.t. 2.97 min; MS for $C_{11}H_{13}FN_2O$ m/z 209.1(M+H)⁺.

Step 4: Preparation of (R)-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester
15

5-Amino-7-fluoro-1-isopropyl-1,3-dihydro-indol-2-one (2.33 g, 11.2 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (1.94 g, 11.2 mmol) and lithium trifluoromethanesulfonate (1.73 g, 11.2 mmol) in acetonitrile (20 ml) are heated at 70 °C for 2 hours. The reaction mixture is diluted with ethyl acetate, washed with water
20 and brine, dried (Na_2SO_4) and evaporated. Final purification by flash chromatography (70% ethyl acetate/hexane) gives the title compound as a light brown foamy solid. HPLC r.t. 4.32 min; MS for $C_{19}H_{28}FN_3O_4$ m/z 382.3 (M+H)⁺.

Step 5: Preparation of (*S*)-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester
25

Phosgene (20% solution in toluene, 3.53 ml, 36.2 mmol) is added to (R)-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 4, 1.84 g, 4.82 mmol) and triethylamine (3.33 ml, 24.1 mmol) in dichloromethane (20 ml) at 0 °C. The reaction is allowed to warm to
30 room temperature and stirred for 1 hours. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated to give the title compound suitable for use directly in the next step (1.95 g, 99%); HPLC r.t. 5.28 min; MS for $C_{20}H_{26}FN_3O_5$ m/z 408 (M+H)⁺.

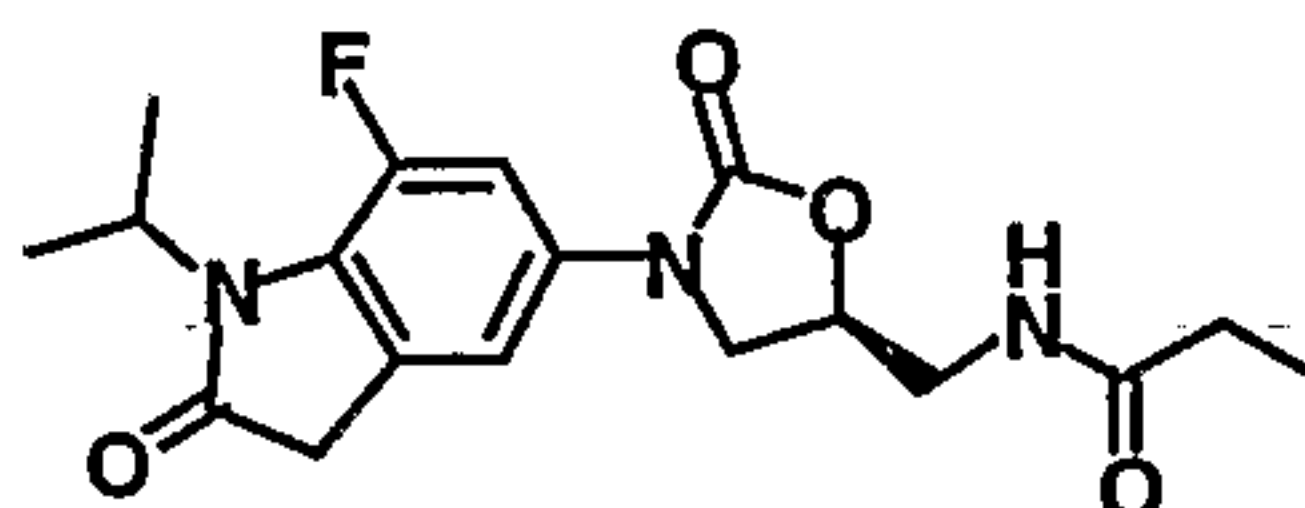
Step 6: Preparation of (*R*)-5-(*R*-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-isopropyl-1,3-dihydro-indol-2-one

(*S*)-[3-(7-Fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 5, 0.345 g, 0.665 mmol) is treated with 50% TFA/DCM (4 ml) for 30 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.43 min; MS for C₁₅H₁₈FN₃O₃ m/z 308 (M+H)⁺.

Step 7: Preparation of (*S*)-*N*-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.671 ml, 7.12 mmol) is added to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-isopropyl-1,3-dihydro-indol-2-one (2.00 g, 4.74 mmol) and *N,N*-diisopropylethylamine (3.30 ml, 19.0 mmol) in dichloromethane (20 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (2% MeOH/DCM) to give the title compound as an off white solid (1.15 g, 70%); HPLC r.t. 4.07 min; ¹H NMR (300 MHz, CDCl₃) 7.31 (m, 1H), 7.23 (m, 1H), 5.97 (t, 1H), 4.86 (m, 1H), 4.78 (m, 1H), 4.02 (t, *J* = 9 Hz, 1H), 3.77 (dd, *J* = 6.6, 9 Hz, 1H), 3.58-3.73 (m, 2H), 3.55 (s, 2H), 2.03 (s, 3H), 1.42 (dd, *J* = 1.5, 7.2 Hz, 6H); MS for C₁₇H₂₀FN₃O₄ m/z 350.0 (M+H)⁺.

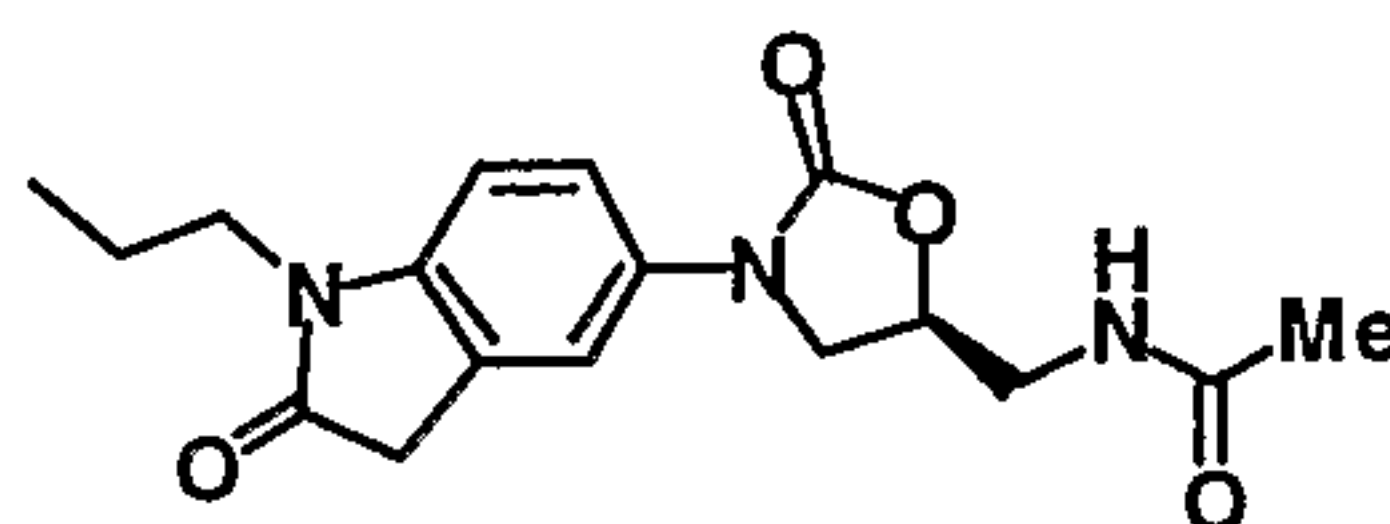
Example 16 Preparation of (*S*)-*N*-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



Propionic anhydride (0.088 ml, 0.688 mmol) is added dropwise to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-isopropyl-1,3-dihydro-indol-2-one (Example 16, 0.145 g, 0.344 mmol) and *N,N*-diisopropylethylamine (0.239 ml, 1.37 mmol) in dichloromethane (5 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried

(Na₂SO₄), and evaporated. The residue is purified by PTLC (10% methanol/dichloromethane) to give the title compound as a light yellow solid. HPLC r.t. 4.18 min; ¹H NMR (300 MHz, CDCl₃) 7.29 (m, 1H), 7.22 (dd, *J* = 1.8, 15.9 Hz, 1H), 5.93 (t, 1H), 4.86 (m, 1H), 4.78 (m, 1H), 4.02 (t, *J* = 9 Hz, 1H), 3.78 (dd, *J* = 6.6, 9 Hz, 1H), 3.60-3.75 (m, 2H), 3.55 (s, 2H), 1.42 (dd, *J* = 1.5, 6.9 Hz, 6H), 1.14 (t, *J* = 7.5 Hz, 3H); MS for C₁₉H₂₂FN₃O₄ *m/z* 364.0 (M+H)⁺.

Example 17 Preparation of (*S*)-*N*-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of (*R*)-[2-hydroxy-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-ylamino)-propyl]-carbamic acid *tert*-butyl ester

5-Amino-1-propyl-1,3-dihydro-indol-2-one (Preparation 5, 0.530 g, 2.78 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.483 g, 2.78 mmol) and lithium trifluoromethanesulfonate (0.428 g, 2.78 mmol) in acetonitrile (7 ml) are heated at 90 °C for 1 hour. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% ethyl acetate/hexane) gives the title compound as a light brown solid. HPLC r.t. 3.66 min; MS for C₁₉H₂₉N₃O₄ *m/z* 364 (M+H)⁺.

Step 2: Preparation of (*S*)-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.978 ml, 10.0 mmol) is added to (*R*)-[2-hydroxy-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-ylamino)-propyl]-carbamic acid *tert*-butyl ester (Step 1, 0.520 g, 1.43 mmol) and triethylamine (0.998 ml, 7.15 mmol) in dichloromethane (10 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated to give the title compound as a light brown solid. HPLC r.t. 4.88 min; MS for C₂₀H₂₇N₃O₅ *m/z* 390 (M+H)⁺.

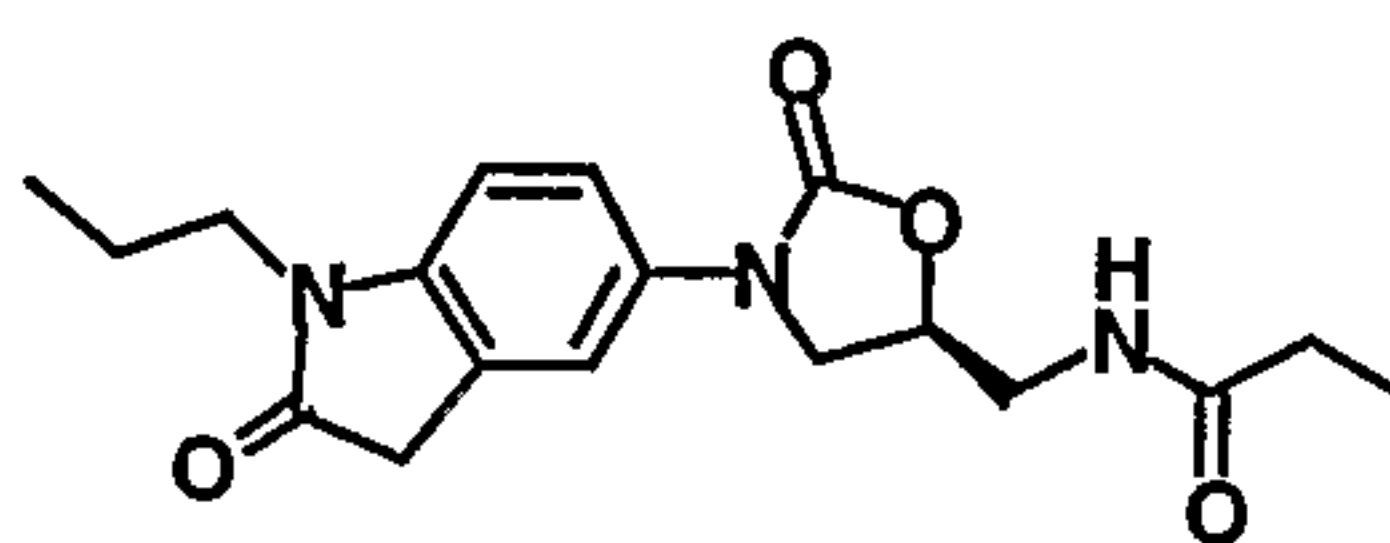
Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-propyl-1,3-dihydro-indol-2-one

(*S*)-[2-Oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 2, 0.220 g, 0.564 mmol) is treated with 50% TFA/DCM (4 ml) for 15 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.05 min; MS for C₁₅H₁₉N₃O₃ m/z 290.2 (M+H)⁺.

Step 4: Preparation of (*S*)-*N*-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.082 ml, 0.848 mmol) is added to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-propyl-1,3-dihydro-indol-2-one (Step 3, 0.228 g, 0.565 mmol) and *N,N*-diisopropylethylamine (0.391 ml, 2.26 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is stirred at 0 °C for 60 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.65 min; ¹H NMR (300 MHz, CDCl₃) 7.56 (m, 1H), 7.24-7.28 (m, 1H), 6.80 (d, *J* = 8.7 Hz, 1H), 6.01 (t, 1H), 4.74-4.82 (m, 1H), 4.05 (t, *J* = 9 Hz, 1H), 3.80 (dd, *J* = 6.6, 9 Hz, 2H), 3.57-3.76 (m, 4H), 3.54 (s, 2H), 2.03 (s, 3H), 1.64-1.74 (m, 2H), 0.97 (t, *J* = 7.5 Hz, 3H); MS for C₁₇H₂₁N₃O₄ m/z 332.1 (M+H)⁺.

Example 18 Preparation of (*S*)-*N*-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-propionamide

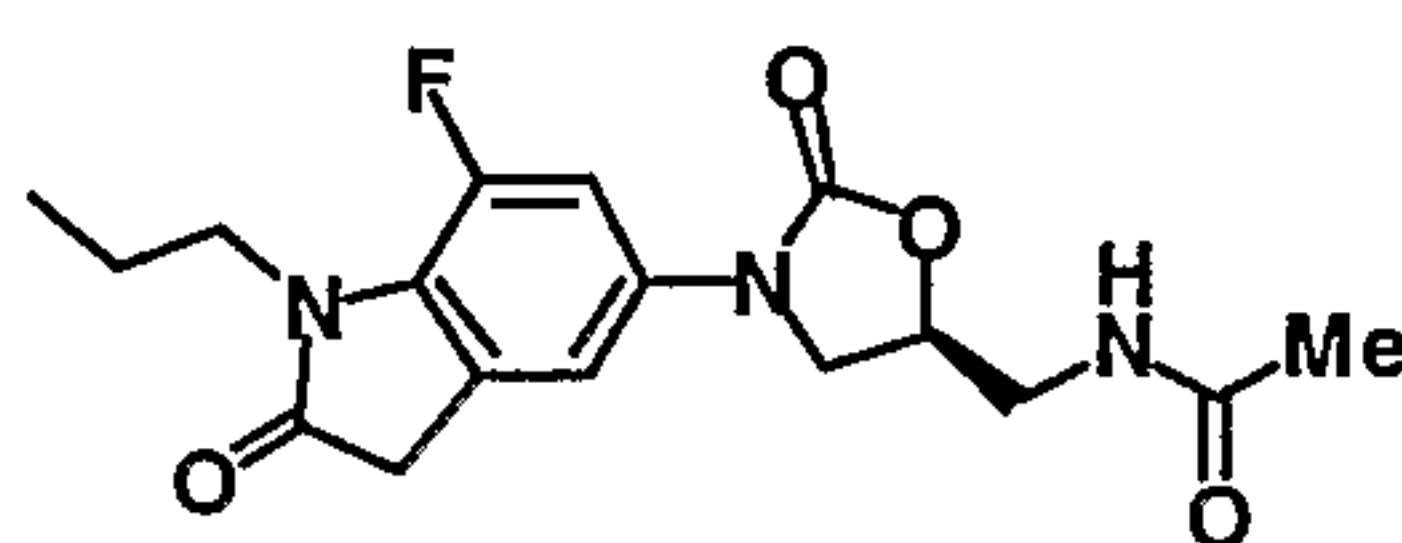


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Propionic anhydride (0.089 ml, 0.694 mmol) is added dropwise to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-propyl-1,3-dihydro-indol-2-one (Example 17, 0.140 g, 0.347 mmol) and diisopropylethylamine (0.340 ml, 1.39 mmol) in dichloromethane (3 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give

the title compound as a yellow solid (0.050 g, 67%); HPLC r.t. 3.79 min; ^1H NMR (300 MHz, CDCl_3) δ 7.56 (m, 1H), 7.23-7.27 (m, 1H), 6.80 (d, $J = 8.4$ Hz, 1H), 5.92 (t, 1H), 4.77 (m, 1H), 4.04 (t, $J = 8.7$ Hz, 1H), 3.80 (dd, $J = 6.6, 9$ Hz, 2H), 3.59-3.75 (m, 4H), 3.54 (s, 2H), 2.25 (q, $J = 7.8$ Hz, 2H), 1.69 (m, 3H), 1.14 (t, $J = 7.5$ Hz, 3H), 0.96 (t, $J = 7.5$ Hz, 3H); MS for $\text{C}_{18}\text{H}_{23}\text{N}_3\text{O}_4$ m/z 346.2 ($\text{M}+\text{H}$) $^+$.

Example 19 Preparation of (*S*)-*N*-[3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



10

Step 1: Preparation of (*R*)-[3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

5-Amino-7-fluoro-1-propyl-1,3-dihydro-indol-2-one (Preparation 6, 0.500 g, 2.40 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.417 g, 2.40 mmol) and lithium trifluoromethanesulfonate (0.368 g, 2.40 mmol) in acetonitrile (8 ml) are heated at 90 °C for 8 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na_2SO_4) and evaporated. Final purification by flash chromatography (70% Ethyl acetate/hexane) gives pure the title compound as a yellow solid. HPLC r.t. 4.30 min; MS for $\text{C}_{19}\text{H}_{28}\text{FN}_3\text{O}_4$ m/z 382.3 ($\text{M}+\text{H}$) $^+$.

20

Step 2: Preparation of (*S*)-[3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.770 ml, 7.86 mmol) is added to (*R*)-[3-(7-Fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 1, 0.400 g, 1.05 mmol) and triethylamine (0.726 ml, 5.24 mmol) in dichloromethane (5 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated to give the title compound as a dark yellow solid. HPLC r.t. 5.28 min; MS for $\text{C}_{20}\text{H}_{26}\text{FN}_3\text{O}_5$ m/z 408.1 ($\text{M}+\text{H}$) $^+$.

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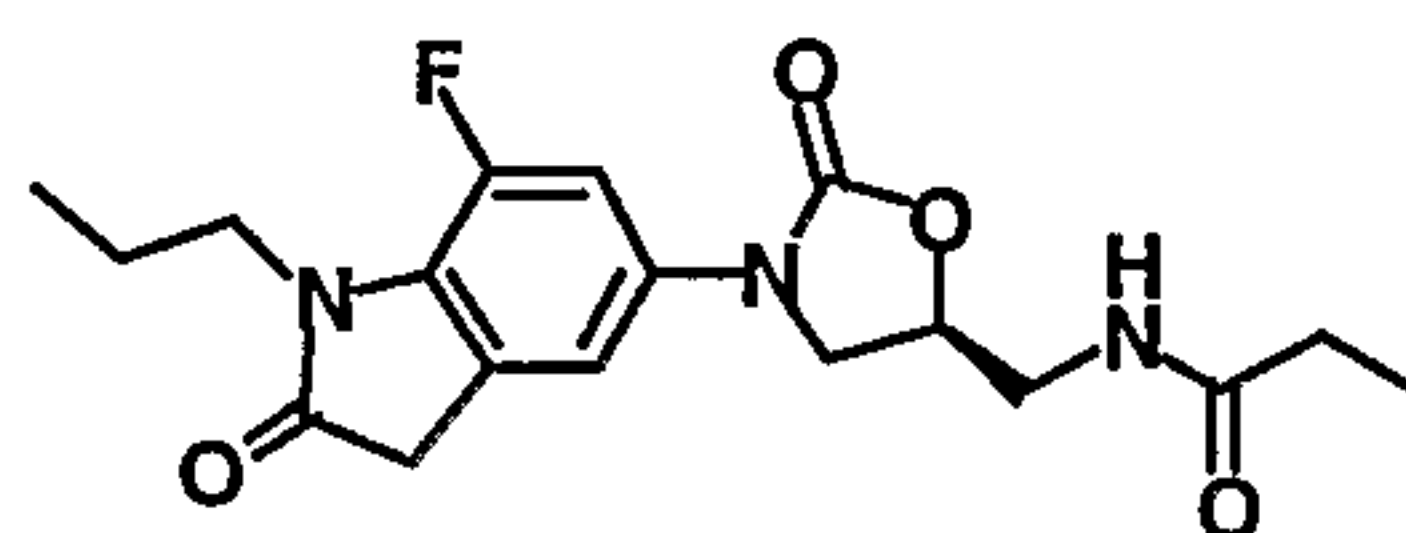
Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-propyl-1,3-dihydro-indol-2-one

(*S*)-[3-(7-Fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (0.20 g, 0.491 mmol) is treated with 50% TFA/DCM (4 ml) for 15 minutes at room temperature. The reaction is evaporated and the product isolated as the TFA salt. HPLC r.t. 3.43 min; MS for
 5 C₁₅H₁₈FN₃O₃ Mol. Wt.: 307.32 m/z 308.0 (M+H)⁺.

Step 4: Preparation of (*S*)-*N*-[3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.069 ml, 0.733 mmol) is added to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-propyl-1,3-dihydro-indol-2-one (0.206 g, 0.489 mmol) and *N,N*-diisopropylethylamine (0.358 ml, 1.96 mmol) in dichloromethane (4 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (5%
 15 MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 4.01 min; ¹H NMR (300 MHz, CDCl₃) 7.24 (m, 1H), 7.19 (m, 1H), 6.04 (t, 1H), 4.78 (m, 1H), 4.02 (t, *J* = 9 Hz, 1H), 3.72-3.81 (m, 3H), 3.59-3.72 (m, 2H), 3.56 (s, 2H), 2.03 (s, 3H), 1.69 (m, 2H), 0.95 (t, *J* = 7.5 Hz, 3H); MS for C₁₇H₂₀FN₃O₄ m/z 350.0 (M+H)⁺.

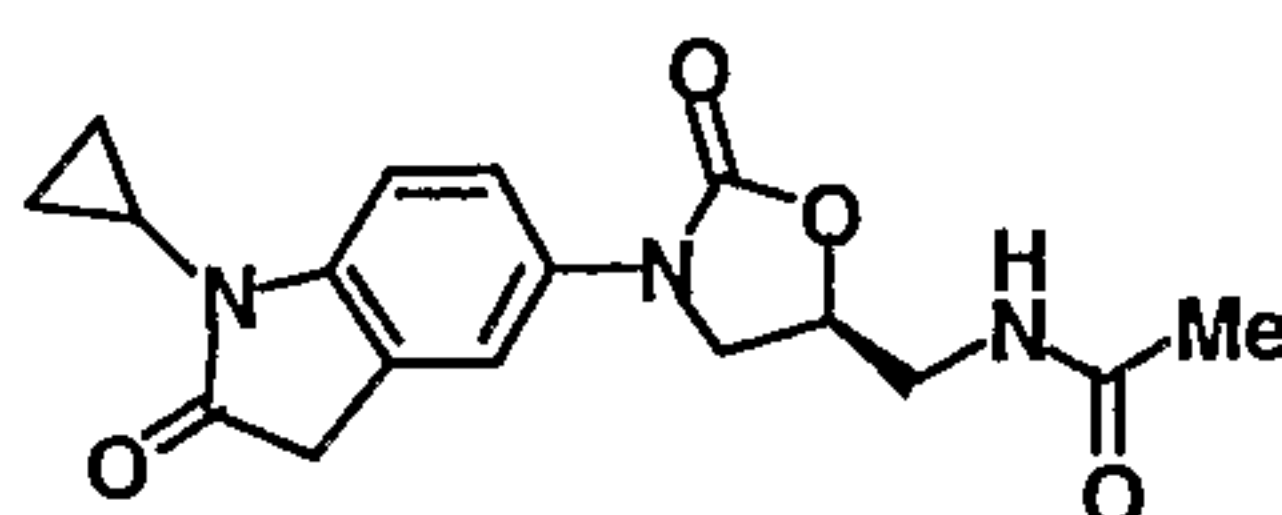
20 **Example 20** Preparation of (*S*)-*N*-[3-(7-Fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



25 Propionic anhydride (0.066 ml, 0.515 mmol) is added dropwise to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-7-fluoro-1-propyl-1,3-dihydro-indol-2-one (Example 19, 0.108 g, 0.257 mmol) and diisopropylethylamine (0.176 ml, 1.03 mmol) in dichloromethane (3 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried
 30 (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as a yellow solid. HPLC r.t. 4.23 min; ¹H NMR (300 MHz, CDCl₃) 7.30 (m, 1H), 7.24 (m, 1H), 7.19 (m, 1H), 5.94 (t, 1H), 4.78 (m, 1H), 4.01 (t, *J*

= 9 Hz, 1H), 3.78 (m, 3H), 3.59-3.78 (m, 2H), 3.56 (s, 2H), 2.24 (q, $J = 7.5$ Hz, 2H), 1.69 (m, 2H), 1.14 (t, $J = 7.5$ Hz, 3H), 0.95 (t, $J = 7.5$ Hz, 3H); MS for $C_{18}H_{22}FN_3O_4$ m/z 364.0 (M+H)⁺.

- 5 **Example 21** Preparation of (*S*)-*N*-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of (*R*)-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

- 10 5-Amino-1-cyclopropyl-1,3-dihydro-indol-2-one (Preparation 7, 1.30 g, 6.90 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (1.20 g, 6.90 mmol) and lithium trifluoromethanesulfonate (1.06 g, 6.90 mmol) in acetonitrile (10 ml) are heated at 90 °C for 3 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na_2SO_4) and evaporated. Final purification by flash
15 chromatography (70% ethyl acetate/hexane) gives pure the title compound as a light brown solid. HPLC r.t. 3.48 min; MS for $C_{19}H_{27}N_3O_4$ m/z 362.3 (M+H)⁺.

Step 2: Preparation of (*S*)-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

- 20 Phosgene (20% solution in toluene, 1.95 ml, 19.9 mmol) is added to (*R*)-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 1, 0.720 g, 1.99 mmol) and triethylamine (1.38 ml, 9.96 mmol) in dichloromethane (10 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and
25 evaporated. The residue is purified by flash column chromatography (70% ethyl acetate/hexane) to give the title compound as an off-white solid (0.58 g, 75%); HPLC r.t. 4.63 min; MS for $C_{20}H_{25}N_3O_5$ m/z 388.2 (M+H)⁺.

- Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropyl-1,3-dihydro-indol-2-one
30

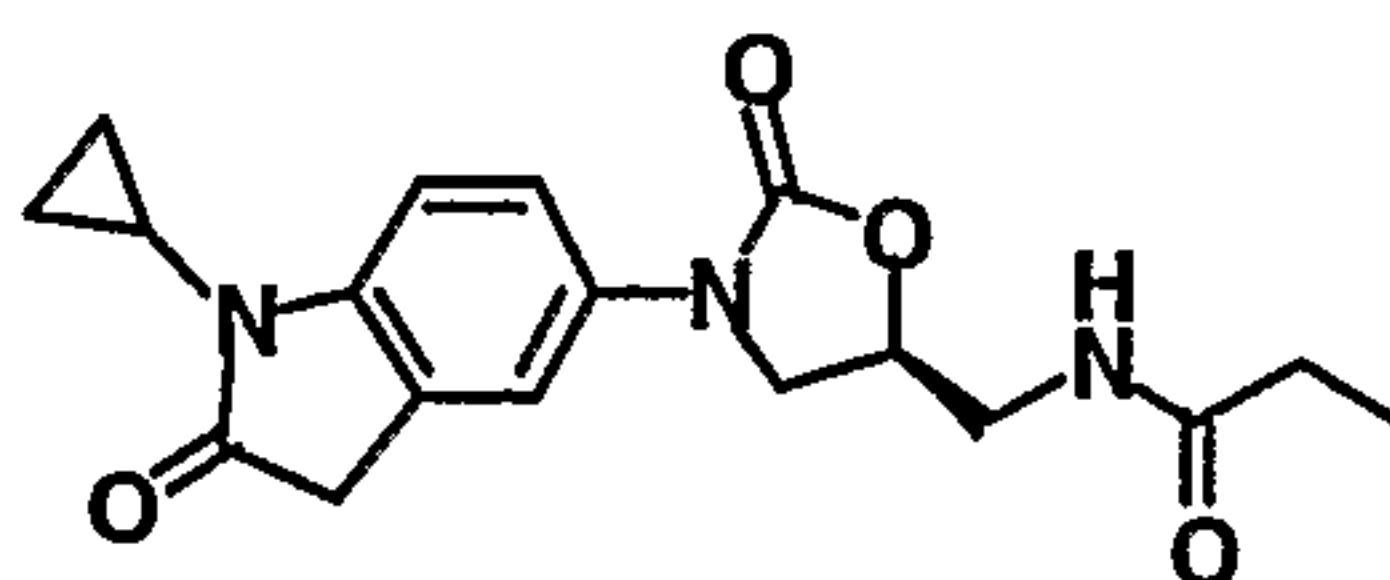
(*S*)-[3-(1-Cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (Step 2, 0.240 g, 0.619 mmol) is treated with

50% TFA/DCM (4 ml) for 15 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 2.81 min; MS for C₁₅H₁₇N₃O₃ m/z 288.1 (M+H)⁺.

5 Step 4: Preparation of (S)-N-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.092 ml, 0.971 mmol) is added to 5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropyl-1,3-dihydro-indol-2-one (Step 3, 0.260 g, 0.647 mmol) and *N,N*-diisopropylethylamine (0.473 ml, 2.58 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is stirred at 0 °C for 60 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.36 min; ¹H NMR (300 MHz, CDCl₃) 7.52 (m, 1H), 7.24-7.27 (m, 1H), 7.05 (dd, *J* = 2.4, 8.7 Hz, 1H), 6.11 (t, 1H), 4.76 (m, 1H), 4.04 (t, *J* = 9 Hz, 1H), 3.79 (dd, *J* = 6.3, 9 Hz, 1H), 3.57-3.74 (m, 2H), 3.49 (s, 2H), 2.63 (m, 1H), 2.03 (s, 3H), 1.07 (m, 2H), 0.89 (m, 2H); MS for C₁₇H₁₉N₃O₄ m/z 330.1 (M+H)⁺.

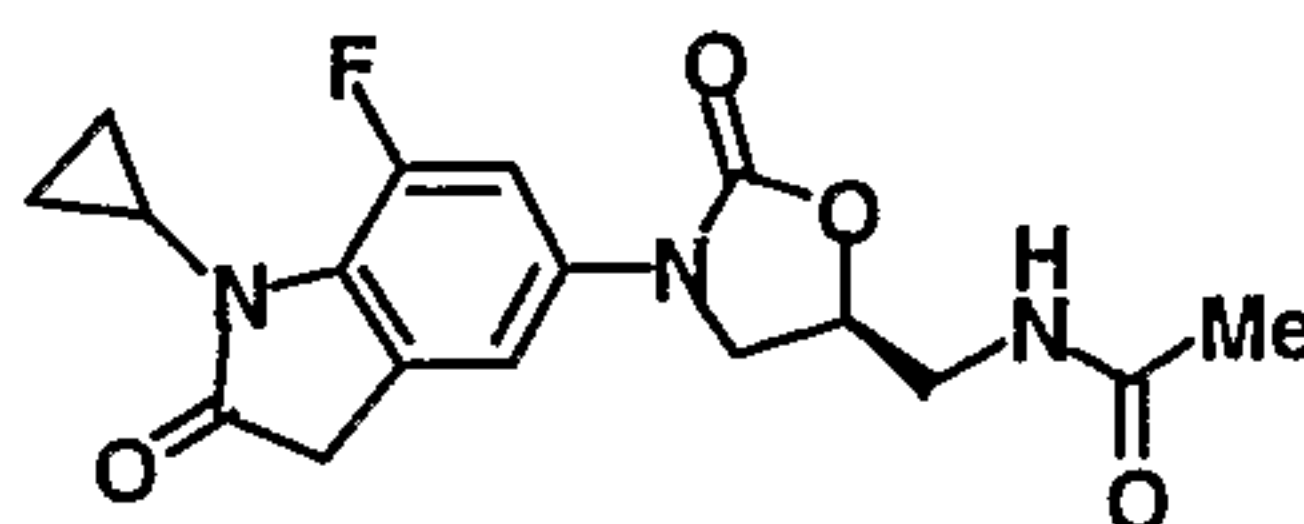
20 **Example 22** Preparation of (S)-N-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



Propionic anhydride (0.099 ml, 0.774 mmol) is added dropwise to (R)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropyl-1,3-dihydro-indol-2-one (Example 21, 0.155 g, 0.387 mmol) and diisopropylethylamine (0.265 ml, 1.55 mmol) in dichloromethane (4 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as a yellow solid. HPLC r.t. 3.55 min; ¹H NMR (300 MHz, CDCl₃) 7.53 (m, 1H), 7.25 (m, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 6.00 (t, *J* = 6 Hz, 1H), 4.77 (m, 1H), 4.04 (t, *J* = 8.7 Hz, 1H), 3.80 (dd, *J* = 6.6, 9.3 Hz, 1H), 3.59-3.77 (m,

2H), 3.49 (s, 2H), 2.63 (m, 1H), 2.25 (q, $J = 7.5$ Hz, 2H), 1.14 (t, $J = 7.5$ Hz, 3H), 1.07 (m, 2H), 0.89 (m, 2H); MS for $C_{18}H_{21}N_3O_4$ m/z 344.1 ($M+H$)⁺.

Example 23 Preparation of (*S*)-*N*-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of 1-cyclopropyl-7-fluoro-5-nitro-1,3-dihydro-indol-2-one

Crude (2,3-difluoro-5-nitrophenyl)acetic acid (Example 15, 2.50 g, 11.5 mmol) and cyclopropylamine (6 eq., 4.78 ml, 0.0691 mol) are mixed in DMSO (10 ml) and stirred at 50 °C for 20 hours. 2N Hydrochloric acid (40 ml) is added in one portion and the mixture stirred at room temperature for 2 hours. The resulting light yellow precipitate is filtered, washed with water and dried under vacuum. The residue is purified by flash column chromatography (20% Ethyl acetate/hexane) to give the title compound as a yellow solid. HPLC r.t. 4.90 min; MS for $C_{11}H_9FN_2O_3$ m/z 235.0 ($M-H$)⁻.

Step 2: Preparation of 5-amino-1-cyclopropyl-7-fluoro-1,3-dihydro-indol-2-one

Iron powder (0.994 g, 17.8 mmol) is added in small portions to 1-cyclopropyl-7-fluoro-5-nitro-1,3-dihydro-indol-2-one (1.05 g, 4.44 mmol) and ammonium chloride (2.32 g, 44.5 mmol) in ethanol (50 ml) and water (25 ml) at 90 °C. The reaction mixture is stirred vigorously and heated for 60 min, cooled to room temperature, and diluted with dichloromethane (250 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried over sodium sulfate and evaporated to give the title compound as a yellowish-brown solid. HPLC r.t. 2.62 min; MS for $C_{11}H_{11}FN_2O$ m/z 207.2 ($M+H$)⁺.

Step 3: Preparation of (*R*)-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

5-Amino-1-cyclopropyl-7-fluoro-1,3-dihydro-indol-2-one (0.560 g, 2.72 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.472 g, 2.72 mmol) and lithium trifluoromethanesulfonate (0.415 g, 2.72 mmol) in acetonitrile (5 ml) are

heated at 85 °C for 4.5 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% Ethyl acetate/hexane) gives the title compound as a yellow solid. HPLC r.t. 3.98 min; MS for C₁₉H₂₆FN₃O₄ m/z 380.1 (M+H)⁺.

5

Step 4: Preparation of (S)-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.754 ml, 7.71 mmol) is added to (R)-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (Step 3, 0.390 g, 1.03 mmol) and triethylamine (0.711 ml, 5.13 mmol) in dichloromethane (5 ml) at 0 °C and stirred for 30 minutes. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated to give the title compound as a yellow solid. HPLC r.t. 4.96 min; MS for C₂₀H₂₄FN₃O₅ m/z 406 (M+H)⁺.

15

Step 5: Preparation of (R)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropyl-7-fluoro-1,3-dihydro-indol-2-one

(S)-[3-(1-Cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (0.20 g, 0.493 mmol) is treated with 50% TFA/DCM (4 ml) for 15 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.17 min; MS for C₁₅H₁₆FN₃O₃ m/z 306.3 (M+H)⁺.

20

Step 6: Preparation of (S)-N-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

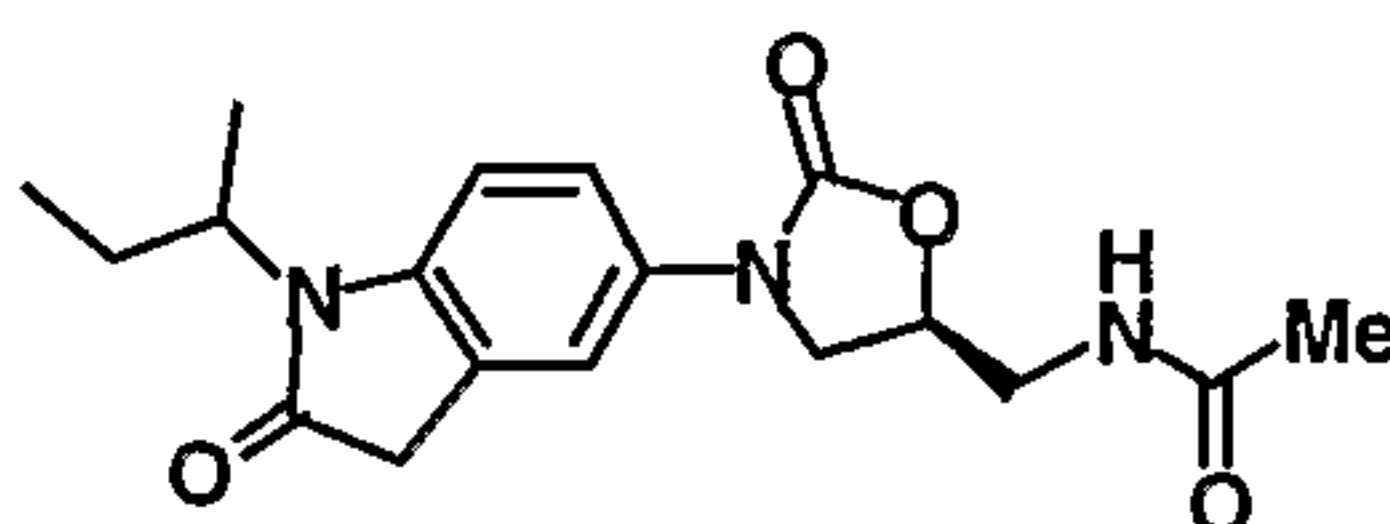
25

Acetic anhydride (0.070 ml, 0.740 mmol) is added to (R)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropyl-7-fluoro-1,3-dihydro-indol-2-one (0.207 g, 0.493 mmol) and *N,N*-diisopropylethylamine (0.344 ml, 1.97 mmol) in dichloromethane (4 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as an off white solid (0.125 g, 73%); HPLC r.t. 3.70 min; ¹H NMR (300 MHz, CDCl₃) 7.24 (m, 1H), 7.19 (m, 1H), 6.04 (t, 1H),

30

4.78 (m, 1H), 4.02 (t, $J = 8.7$ Hz, 1H), 3.76 (dd, $J = 6.6, 9$ Hz, 1H), 3.58-3.70 (m, 2H), 3.51 (s, 2H), 2.84 (m, 1H), 2.03 (s, 3H), 1.05 (m, 2H), 0.96 (m, 2H); MS for $C_{17}H_{18}FN_3O_4$ m/z 348 ($M+H$)⁺.

- 5 **Example 24** Preparation of (*S*)-*N*-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



- Step 1: Preparation of (*R*)-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

10 5-Amino-1-*sec*-butyl-1,3-dihydro-indol-2-one (Preparation 8, 0.480 g, 2.35 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.409 g, 2.35 mmol) and lithium trifluoromethanesulfonate (0.361 g, 2.35 mmol) in acetonitrile (5 ml) are heated at 90 °C for 5 hours. The reaction mixture is diluted with ethyl acetate, washed
15 with water and brine, dried (Na_2SO_4) and evaporated. Final purification by flash chromatography (70% ethyl acetate/hexane) gives the title compound as a light brown foamy solid. HPLC r.t. 3.85 min; MS for $C_{20}H_{31}N_3O_4$ m/z 378.4 ($M+H$)⁺.

- Step 2: Preparation of (*S*)-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.854 ml, 8.74 mmol) is added to (*R*)-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester (0.330 g, 0.874 mmol) and triethylamine (0.610 ml, 4.37 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is allowed to warm to room temperature
25 and stirred for 1 hours. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated to give the title compound suitable for use directly in the next step. HPLC r.t. 5.15 min; MS for $C_{21}H_{29}N_3O_5$ m/z 404 ($M+H$)⁺.

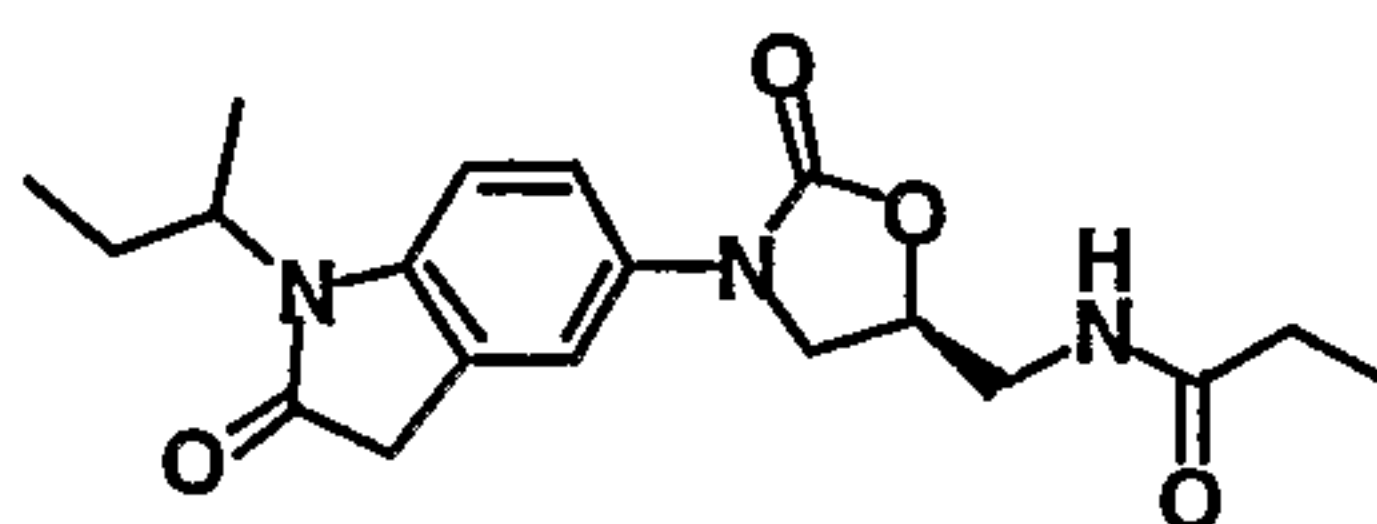
- 30 Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-*sec*-butyl-1,3-dihydro-indol-2-one

[3-(1-*sec*-Butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (0.345 g, 0.665 mmol) is treated with 50% TFA/DCM (4 ml) for 30 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.32 min; MS for
 5 C₁₆H₂₁N₃O₃ m/z 304.2 (M+H)⁺.

Step 4: Preparation of (*S*)-*N*-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.070 ml, 0.718 mmol) is added to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-*sec*-butyl-1,3-dihydro-indol-2-one (Step 3, 0.200 g, 0.479
 10 mmol) and *N,N*-diisopropylethylamine (0.332 ml, 1.91 mmol) in dichloromethane (4 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (5%
 15 MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.87 min; ¹H NMR (300 MHz, CDCl₃) 7.54 (m, 1H), 7.23 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 5.98 (t, 1H), 4.77 (m, 1H), 4.39 (m, 1H), 4.04 (t, *J* = 9 Hz, 1H), 3.78 (dd, *J* = 6.9, 9.6 Hz, 1H), 3.56-3.75 (m, 3H), 3.53 (s, 2H), 2.03 (s, 3H), 1.91-2.01 (m, 1H), 1.77 (m, 1H), 1.44 (d, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); MS for C₁₈H₂₃N₃O₄
 20 m/z 346.2 (M+H)⁺.

Example 25 Preparation of (*S*)-*N*-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide

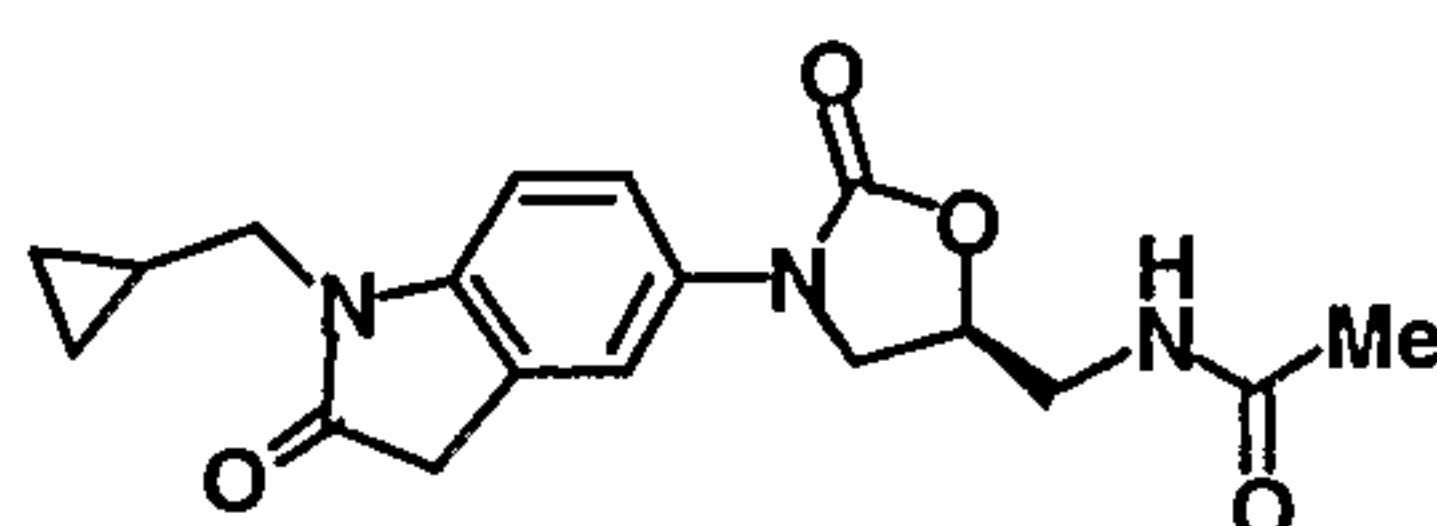


25

Propionic anhydride (0.104 ml, 0.814 mmol) is added dropwise to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-*sec*-butyl-1,3-dihydro-indol-2-one (Example 24, 0.170 g, 0.407 mmol) and diisopropylethylamine (0.279 ml, 1.63 mmol) in dichloromethane (4 ml) at 0°C. The reaction is stirred at room temperature for 1
 30 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as a yellow solid. HPLC r.t. 4.07 min; ¹H NMR (300 MHz,

CDCl₃) 7.54 (m, 1H), 7.22 (dd, $J = 2.7, 8.7$ Hz, 1H), 6.95 (d, $J = 9$ Hz, 1H), 5.93 (t, 1H), 4.77 (m, 1H), 4.39 (m, 1H), 4.03 (t, $J = 8.7$ Hz, 1H), 3.79 (dd, $J = 6.6, 9$ Hz, 1H), 3.58-3.75 (m, 3H), 3.53 (s, 2H), 2.25 (q, $J = 7.5$ Hz, 2H), 1.91-2.01 (m, 1H), 1.77 (m, 1H), 1.44 (d, $J = 6.9$ Hz, 3H), 1.15 (t, $J = 7.5$ Hz, 3H), 0.87 (t, $J = 7.5$ Hz, 3H); MS
 5 for C₁₉H₂₅N₃O₄ m/z 360.2 (M+H)⁺.

Example 26 Preparation of (S)-N-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



10

Step 1: Preparation of (R)-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid *tert*-butyl ester

5-Amino-1-cyclopropylmethyl-1,3-dihydro-indol-2-one (Preparation 7, 0.400 g, 1.98 mmol), (S)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.344 g, 1.98 mmol) and lithium trifluoromethanesulfonate (0.304 g, 1.98 mmol) in acetonitrile (5 ml) are
 15 heated at 90 °C for 4 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% ethyl acetate/hexane) gives the title compound as a light brown foamy solid. HPLC r.t. 3.76 min; MS for C₂₀H₂₉N₃O₄ m/z 376.3 (M+H)⁺.

20

Step 2: Preparation of (S)-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.728 ml, 7.45 mmol) is added to (R)-[3-(1-Cyclopropylmethyl-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-
 25 carbamic acid *tert*-butyl ester (0.280 g, 0.745 mmol) and triethylamine (0.520 ml, 3.73 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is allowed to warm to room temperature and stirred for 1 hours. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated to give the title compound suitable for use directly in the next step. HPLC r.t. 5.01 min; MS for
 30 C₂₁H₂₇N₃O₅ m/z 402 (M+H)⁺.

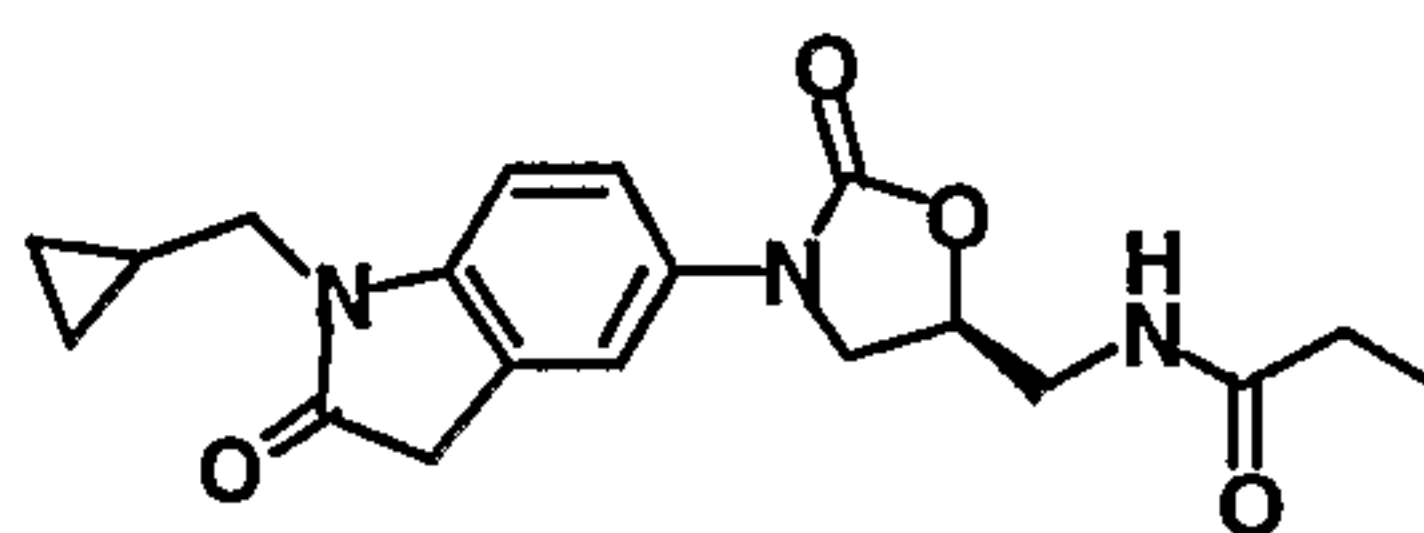
Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropylmethyl-1,3-dihydro-indol-2-one

(*S*)-[3-(1-Cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid *tert*-butyl ester (0.210 g, 0.523 mmol) is treated with 50% TFA/DCM (4 ml) for 30 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.21 min; MS for C₁₆H₁₉N₃O₃ m/z 302.1 (M+H)⁺.

Step 4: Preparation of (*S*)-*N*-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

Acetic anhydride (0.076 ml, 0.784 mmol) is added to (*R*)-5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropylmethyl-1,3-dihydro-indol-2-one (0.217 g, 0.523 mmol) and *N,N*-diisopropylethylamine (0.362 ml, 2.09 mmol) in dichloromethane (4 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 3.75 min; ¹H NMR (300 MHz, CDCl₃) 7.56 (s, 1H), 7.26 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.04 (t, *J* = 6 Hz, 1H), 4.74-4.82 (m, 1H), 4.05 (t, *J* = 8.7 Hz, 1H), 3.79 (dd, *J* = 6.6, 9 Hz, 1H), 3.59-3.75 (m, 2H), 3.59 (d, *J* = 6.9 Hz, 2H), 3.55 (s, 2H), 2.03 (s, 3H), 1.15 (m, 1H), 0.52 (m, 2H), 0.38 (m, 2H); MS for C₁₈H₂₁N₃O₄ m/z 344.1 (M+H)⁺.

Example 27 Preparation of (*S*)-*N*-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide



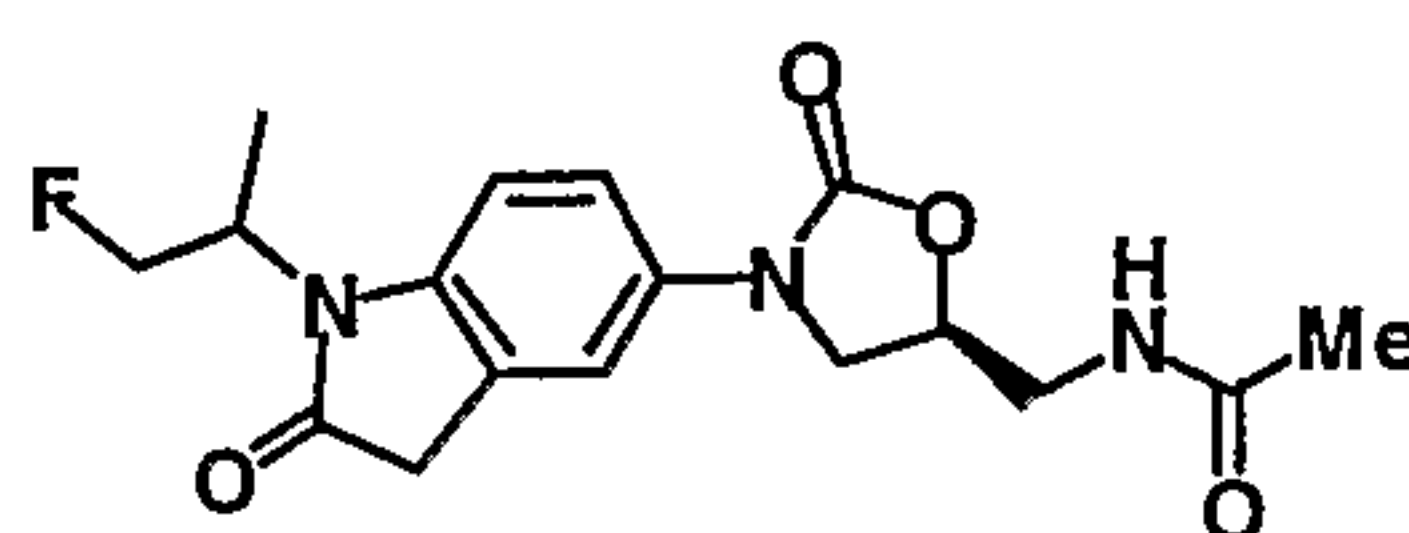
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Propionic anhydride (0.095 ml, 0.746 mmol) is added dropwise to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropylmethyl-1,3-dihydro-indol-2-one (Example 26, 0.155 g, 0.373 mmol) and diisopropylethylamine (0.273 ml, 1.49 mmol) in dichloromethane (3 ml) at 0°C. The reaction is stirred at room temperature for 1 hour, then diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄), and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give

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the title compound as an off-white solid. HPLC r.t. 3.93 min; ^1H NMR (300 MHz, CDCl_3) 7.56 (s, 1H), 7.27 (m, 1H), 6.88 (d, $J = 8.4$ Hz, 1H), 5.95 (t, 1H), 4.73-4.82 (m, 1H), 4.04 (t, $J = 8.7$ Hz, 1H), 3.80 (dd, $J = 6.6, 9$ Hz, 1H), 3.59-3.77 (m, 2H), 3.59 (d, $J = 6.9$ Hz, 2H), 3.55 (s, 2H), 2.25 (q, $J = 7.5$ Hz, 2H), 1.14 (m, 1H), 0.53 (m, 2H), 0.38 (m, 2H); MS for $\text{C}_{19}\text{H}_{25}\text{N}_3\text{O}_4$ m/z 358.1 ($\text{M}+\text{H}$) $^+$.

Example 28 Preparation of (*S*)-*N*-{3-[1-(2-fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide



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Step 1: Preparation of (*R*)-{3-[1-(2-fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino]-2-hydroxy-propyl}-carbamic acid *tert*-butyl ester

5-Amino-1-(2-fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one (Preparation 10, 0.370 g, 1.77 mmol), (*S*)-oxiranylmethyl-carbamic acid *tert*-butyl ester (0.308 g, 1.77 mmol) and lithium trifluoromethanesulfonate (0.271 g, 1.77 mmol) in acetonitrile (5 ml) are heated at 90 °C for 3 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na_2SO_4) and evaporated. Final purification by PTLC (5% methanol/dichloromethane) gives the title compound as an off-white solid. HPLC r.t. 3.59 min; MS for $\text{C}_{19}\text{H}_{28}\text{FN}_3\text{O}_4$ m/z 382.3 ($\text{M}+\text{H}$) $^+$.

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Step 2: Preparation of (*S*)-{3-[1-(2-fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-carbamic acid *tert*-butyl ester

Phosgene (20% solution in toluene, 0.635 ml, 6.48 mmol) is added to (*R*)-{3-[1-(2-Fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-ylamino]-2-hydroxy-propyl}-carbamic acid *tert*-butyl ester (0.330 g, 0.865 mmol) and triethylamine (0.600 ml, 4.32 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is allowed to warm to room temperature and stirred for 1 hours. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na_2SO_4) and evaporated to give the title compound suitable for use directly in the next step. HPLC r.t. 4.78 min; MS for $\text{C}_{20}\text{H}_{26}\text{FN}_3\text{O}_5$ m/z 408.1 ($\text{M}+\text{H}$) $^+$.

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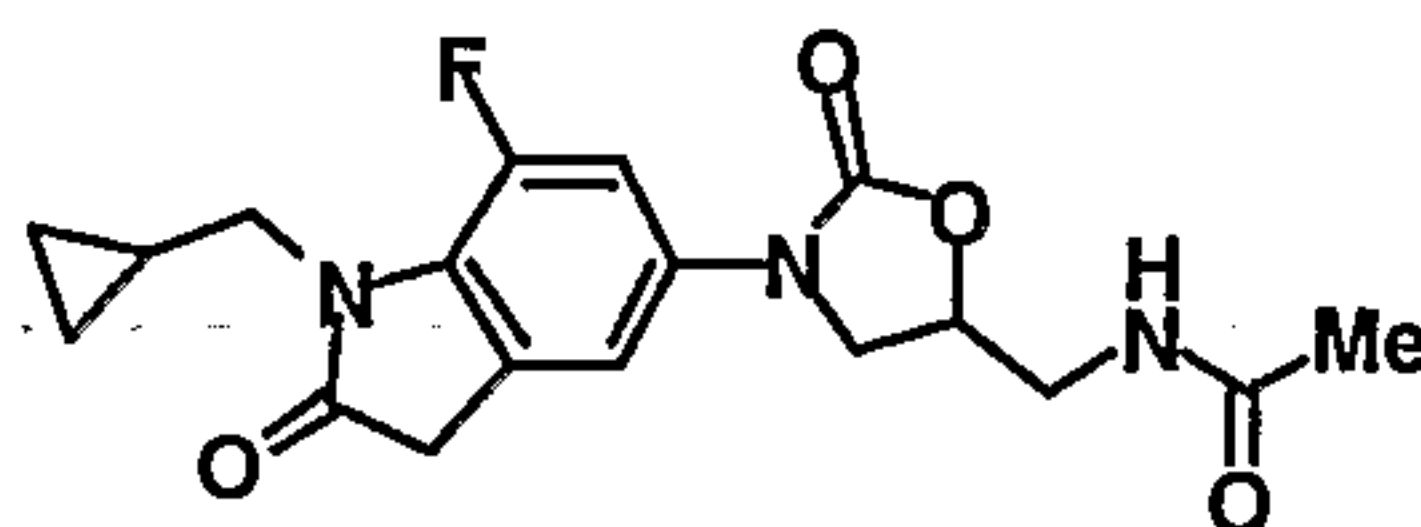
Step 3: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-(2-fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one

(*S*)-{3-[1-(2-Fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-carbamic acid *tert*-butyl ester (0.250 g, 0.614 mmol) is treated with 50% TFA/DCM (4 ml) for 30 minutes at room temperature. The reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 2.95 min; MS for C₁₅H₁₈FN₃O₃ m/z 308.0 (M+H)⁺.

Step 4: Preparation of (*S*)-*N*-{3-[1-(2-fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide

Acetic anhydride (0.084 ml, 0.889 mmol) is added to 5-(5-Aminomethyl-2-oxo-oxazolidin-3-yl)-1-(2-fluoro-1-methyl-ethyl)-1,3-dihydro-indol-2-one (0.250 g, 0.593 mmol) and *N,N*-diisopropylethylamine (0.435 ml, 2.37 mmol) in dichloromethane (5 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and brine, dried (Na₂SO₄) and evaporated. The residue is purified by PTLC (5% MeOH/DCM) to give the title compound as a light brown solid. HPLC r.t. 3.53 min; ¹H NMR (300 MHz, CDCl₃) 7.57 (m, 1H), 7.23 (m, 1H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.04 (t, 1H), 4.93 (m, 1H), 4.52-4.78 (m, 3H), 4.04 (t, *J* = 9 Hz, 1H), 3.78 (dd, *J* = 6.6, 9 Hz, 1H), 3.57-3.75 (m, 2H), 3.55 (s, 2H), 2.03 (s, 3H), 1.50 (dd, *J* = 1.5, 7.2 Hz, 3H); MS for C₁₇H₂₀FN₃O₄ m/z 350.0 (M+H)⁺.

Example 29 Preparation of (*S*)-*N*-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide



Step 1: Preparation of 1-cyclopropylmethyl-7-fluoro-5-nitro-1,3-dihydro-indol-2-one

Crude (2,3-difluoro-5-nitrophenyl) acetic acid (Example 15, 2.50 g, 11.5 mmol) and (aminomethyl)cyclopropane (6 eq., 5.98 ml, 0.0691 mol) are mixed in DMSO (10 ml) and stirred at 45 °C for 20 hours. 2N Hydrochloric acid (40 ml) is added in one portion and the mixture stirred at room temperature for 2 hours. The

resulting light yellow precipitate is filtered, washed with water and ether, and dried under vacuum to give the title compound as a yellow solid. HPLC r.t. 4.91 min; MS for C₁₂H₁₁FN₂O₃ m/z 251.2 (M+H)⁺.

5 Step 2: Preparation of 5-amino-1-cyclopropylmethyl-7-fluoro-1,3-dihydro-indol-2-one

Iron powder (0.995 g, 18.1 mmol) is added in small portion to a mixture of 1-methyl-5-nitro-1, 3-dihydro-indol-2-one (1.00 g, 4.52 mmol) and ammonium chloride (2.40 g, 45.2 mmol) in ethanol (20 ml) and water (10 ml) at 90°C. The reaction
10 mixture is stirred vigorously and heated for 60 minutes, cooled to room temperature, and diluted with dichloromethane (100 ml). The mixture is filtered through celite, the organic layer separated and washed with water and brine, dried over sodium sulfate, and evaporated to give the title compound as a dark brown solid. HPLC r.t. 3.13 min; MS for C₁₆H₁₈FN₃O₃ m/z 221.0 (M+H)⁺.

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Step 3: Preparation of (*R*)-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid tert-butyl ester

5-Amino-1-cyclopropylmethyl-7-fluoro-1,3-dihydro-indol-2-one (Step 2, 1.00
20 g, 4.55 mmol), (*S*)-oxiranylmethyl-carbamic acid tert-butyl ester (0.79 g, 4.55 mmol) and lithium trifluoromethanesulfonate (0.618 g, 4.55 mmol) in acetonitrile (20 ml) are heated at 90 °C for 16 hours. The reaction mixture is diluted with ethyl acetate, washed with water and brine, dried (Na₂SO₄) and evaporated. Final purification by flash chromatography (70% ethyl acetate/hexane) gives the title compound as a white
25 solid. HPLC r.t. 4.35 min; MS for C₂₀H₂₈FN₃O₄ m/z 394.1 (M+H)⁺.

Step 4: Preparation of (*S*)-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid tert-butyl ester

Phosgene (20% solution in toluene, 1.50 ml, 14.1 mmol) is added to (*R*)-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-ylamino)-2-hydroxy-propyl]-carbamic acid tert-butyl ester (0.74 g, 1.88 mmol) and triethylamine (0.95 ml, 9.41 mmol) in dichloromethane (15 ml) at 0 °C and then stirred at 0 °C for 20
30 minutes. The mixture is diluted with dichloromethane, washed with water and brine,

dried (Na_2SO_4) and evaporated. The residue is purified by flash column chromatography (70% ethyl acetate/hexane) to give the title compound as a white solid. HPLC r.t. 5.39 min; MS for $\text{C}_{21}\text{H}_{26}\text{FN}_3\text{O}_5$ m/z 420.1 ($\text{M}+\text{H}$)⁺.

- 5 Step 5: Preparation of (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropylmethyl-7-fluoro-1,3-dihydro-indol-2-one

(*S*)-[3-(1-Cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-carbamic acid tert-butyl ester (0.48 g, 1.14 mmol) is treated with 50% TFA/DCM (10 ml) for 60 minutes at room temperature. The
10 reaction is evaporated and the title compound isolated as the TFA salt. HPLC r.t. 3.61 min; MS for $\text{C}_{16}\text{H}_{18}\text{FN}_3\text{O}_3$ m/z 320.3 ($\text{M}+\text{H}$)⁺.

Step 6: Preparation of (*S*)-N-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide

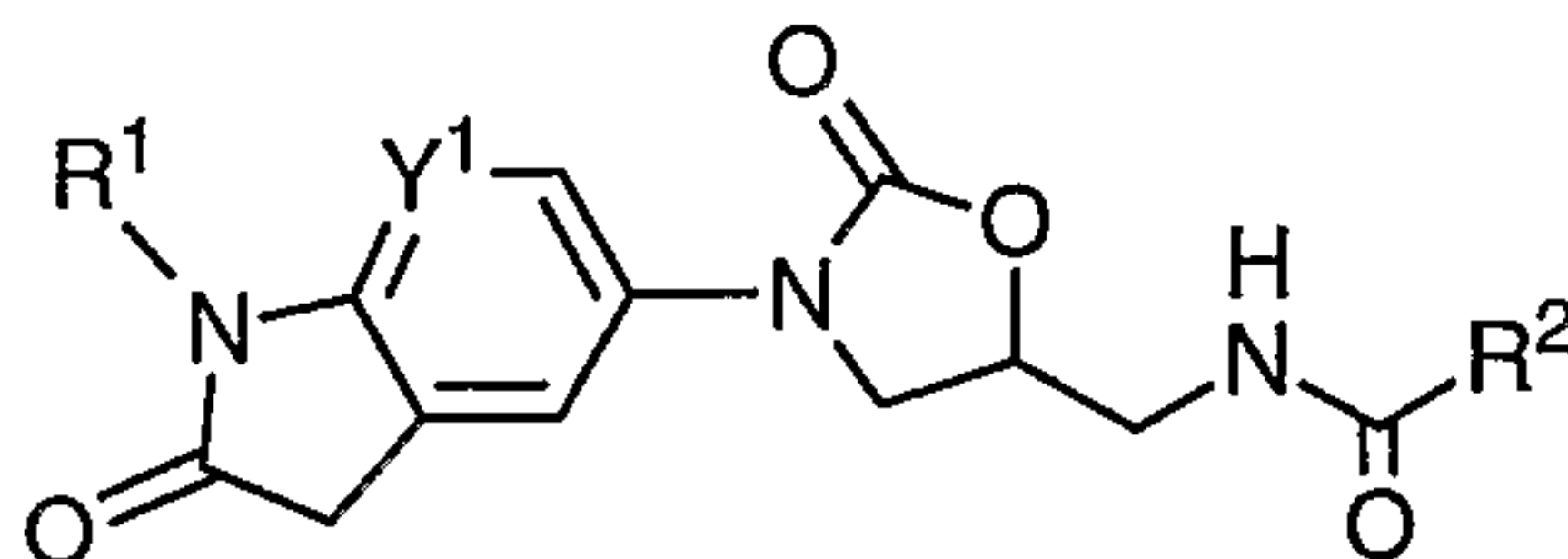
15 Acetic anhydride (0.040 ml, 0.374 mmol) is added to (*R*)-5-(5-aminomethyl-2-oxo-oxazolidin-3-yl)-1-cyclopropylmethyl-7-fluoro-1,3-dihydro-indol-2-one (0.100 g, 0.312 mmol) and pyridine (0.080 ml, 0.938 mmol) in dichloromethane (15 ml) at 0 °C. The reaction is stirred at 0 °C for 30 minutes and then allowed to warm at room temperature. The mixture is diluted with dichloromethane, washed with water and
20 brine, dried (Na_2SO_4) and evaporated. The residue is purified by PTLC (10% MeOH/DCM) to give the title compound as an off white solid. HPLC r.t. 4.17 min; ¹H NMR (300 MHz, CDCl_3) 8.28 (t, 1H), 7.40 (s, 1H), 7.35 (s, 1H), 4.758-4.67 (m, 1H), 4.09 (t, $J = 9.0$ Hz, 1H), 3.74 (dd, $J = 9, 6$ Hz, 1H), 3.69 (s, 2H), 3.60 (d, $J = 7.2$ Hz, 2H), 3.39 (t, $J = 5.4$ Hz, 2H), 1.82 (s, 3H), 1.21-1.12 (m, 1H), 0.47-0.42 (m, 2H),
25 0.32-0.27 (m, 2H); MS for $\text{C}_{18}\text{H}_{20}\text{FN}_3\text{O}_4$ m/z 362.1 ($\text{M}+\text{H}$)⁺.

CLAIMS

We Claim:

1. A compound of formula I

5



I

or a pharmaceutically acceptable salt thereof wherein:

Y¹ is CH or CF;

- 10 R¹ is -C₁₋₄alkyl, optionally substituted with a fluoro atom, or R¹ is -C₃₋₅cycloalkyl; and
R² is -C₁₋₂alkyl.

2. A compound of claim 1 wherein R² is CH₃.

- 15 3. A compound of claim 1 wherein R¹ is methyl, ethyl, propyl, or isopropyl.

4. A compound of claim 1 which is

(1) (S)-N-[3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

20 (2) (S)-N-[3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,

(3) N-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

25 (4) (S)-N-[3-(7-fluoro-1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,

(5) (S)-N-[3-(1-ethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

(6) (S)-N-[3-(1-ethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,

30 (7) (S)-N-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

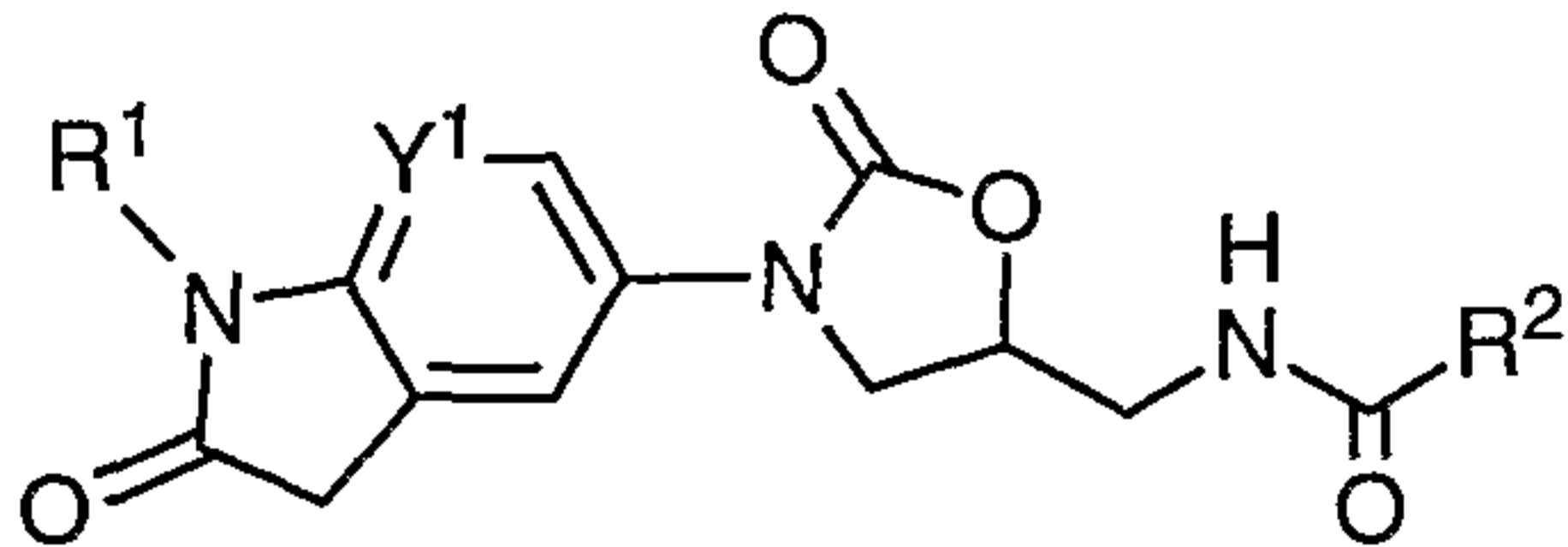
(8) (S)-N-[3-(1-ethyl-7-fluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,

- (9) (S)-N-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide,
- (10) (S)-N-{3-[1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-propionamide,
- 5 (11) (S)-N-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide,
- (12) (S)-N-{3-[7-fluoro-1-(2-fluoro-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-propionamide,
- (13) (S)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide
- 10 (14) (S)-N-[3-(1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (15) (S)-N-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 15 (16) (S)-N-[3-(7-fluoro-1-isopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (17) (S)-N-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-acetamide,
- (18) (S)-N-[2-oxo-3-(2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-oxazolidin-5-ylmethyl]-propionamide,
- 20 (19) (S)-N-[3-(7-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- (20) (S)-N-[3-(7-Fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- 25 (21) (S)-N-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- (22) (S)-N-[3-(1-cyclopropyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (23) (S)-N-[3-(1-cyclopropyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 30 (24) (S)-N-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,

- (25) (S)-N-[3-(1-*sec*-butyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (26) (S)-N-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide,
- 5 (27) (S)-N-[3-(1-cyclopropylmethyl-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-propionamide,
- (28) (S)-N-{3-[1-(2-fluoro-1-methyl-ethyl)-2-oxo-2,3-dihydro-1*H*-indol-5-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide, or
- (29) (S)-N-[3-(1-cyclopropylmethyl-7-fluoro-2-oxo-2,3-dihydro-1*H*-indol-5-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide.
- 10

5. A pharmaceutical composition comprising a compound of formula I or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
- 15 6. A method for treating bacteria infections comprising administering to a mammal being treated a pharmaceutically effective amount of the compound of claim 1.
7. The method of claim 6 wherein the compound of claim 1 is administered orally.
- 20 8. The method of claim 6 wherein the compound of claim 1 is administered parenterally, topically, rectally, or intranasally.
- 25 9. The method of claim 6 wherein said compound is administered in an amount of from about 0.1 to about 100 mg/kg of body weight/day.
10. The method of claim 6 wherein said compound is administered in an amount of from about 1 to about 50 mg/kg of body weight/day.
- 30 11. The bacteria infection of claim 6 which is ear infections, eye infections, respiratory tract infections, skin and skin structure infections, bacterial endocarditis, osteomyelitis, endocarditis or diabetic foot.

12. The bacteria infection of claim 6 which is caused by gram-positive bacteria, gram negative bacteria, anaerobic organisms, and acid-fast organisms.
13. The bacteria infection of claim 6 which is caused by bacteria comprising
5 staphylococci, streptococci, Enterococci, Haemophilus, Moraxella, bacteroides, clostridia, Mycobacteria, or Chlamydia.
14. The bacteria of claim 13 wherein staphylococci is *S. aureus* and *S. epidermidis*; wherein streptococci is *S. pneumoniae* or *S. pyogenes*; wherein
10 Enterococci is *E. faecalis*; wherein Haemophilus is *H. influenzae*; wherein Moraxella is *M. catarrhalis*; and wherein Mycobacteria is *M. tuberculosis*; or *Mycobacterium avium*.
15. The bacteria infections of claim 6, which are infections caused by multi-drug
15 resistant *S. aureus*.



(I)